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United Arab Emirates University

College of Food and Agriculture

THE EFFECT OF SPICE POWDER ON BLOOD GLUCOSE, LIPID PROFILE AND BODY COMPOSITION IN ADULTS AT RISK OF CARDIOVASCULAR DISEASE: A CONTROLLED, RANDOMIZED, SINGLE-BLIND, PARALLEL-DESIGN STUDY

Dana Hasan Mustafa Alkhatib

This dissertation is submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy

Under the Supervision of Dr. Ayesha Salem Obaid Al Dhaheri

November 2018

Declaration of Original Work

I, Dana Hasan Mustafa Alkhatib, the undersigned, a graduate student at the United Arab Emirates University (UAEU), and the author of this dissertation entitled "*The Effect of Spice Powder on Blood Glucose, Lipid Profile and Body Composition in Adults at Risk of Cardiovascular Disease: A Controlled, Randomized, Single-blind, Parallel-design Study*", hereby, solemnly declare that this dissertation is my own original research work that has been done and prepared by me under the supervision of Dr. Ayesha Salem Obaid Al Dhaheri, in the College of Food and Agriculture at UAEU. This work has not previously been presented or published, or formed the basis for the award of any academic degree, diploma or a similar title at this or any other university. Any materials borrowed from other sources (whether published or unpublished) and relied upon or included in my dissertation have been properly cited and acknowledged in accordance with appropriate academic conventions. I further declare that there is no potential conflict of interest with respect to the research, data collection, authorship, presentation and/or publication of this dissertation.

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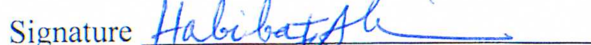
   Signature  Date 20/11/2018

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Abstract

A cluster of risk factors for cardiovascular disease and type 2 diabetes mellitus have become known as the Metabolic Syndrome (MetS). In the United Arab Emirates, 42% of the population was diagnosed with MetS. Previous researchers observed the anti-diabetic, hypolipidemic anti-oxidative, anti-inflammatory and anti-antitumorigenic properties of spices on body composition, blood parameters and blood pressure. The aim of the study was to assess the macronutrient, micronutrient, sugar and caffeine content for seven commonly consumed spices. Moreover, the aim of the study was to measure the effect of ginger *(Zingiber officinale)*, cinnamon *(Cinnamomum)* and black seed *(Nigella sativa)* consumption on blood glucose, lipid profile and body composition in participants at risk of cardiovascular diseases.

Seven spices were analyzed to investigate their proximate content, minerals, vitamins, sugars and caffeine. One hundred and twenty (N=120) participants with risk of cardiovascular diseases were randomly allocated to three treatment arms (ginger, cinnamon and black seed) and a control group (placebo) for a period of 12-weeks. Each participant consumed 3 g/day of powder (spice or placebo). Data related to different parameters were collected from participants at baseline, midpoint and at endpoint of the intervention.

Analysis of the chemical composition of spices showed that the spices had considerable amount of macronutrients (especially oils) and micronutrients. Therefore, spices' active compounds could be used in nutritional supplements and for treatments considering their decent source of valuable nutrients. Furthermore, consumption of spices powder significantly improved waist circumference, body fat mass, weight, body mass index, percent body fat, fasting blood glucose and triglycerides when compared to placebo group ($P \leq 0.05$). Ingestion of 3 grams per day for 12 weeks of spices powder showed significant improvement in body composition, blood glucose and lipid profile. Overall this study demonstrates that the consumption of ginger, cinnamon and black seed powder could help in the management of cardiovascular risk factors.

Keywords: Ginger, cinnamon, black seed, metabolic syndrome, lipid profile, body composition, proximate analysis, blood glucose.

Title and Abstract (in Arabic)

تأثير مطحون التوابل على مستوى سكر الدم ودهون الدم ومكونات الجسم في البالغين المعرضين للإصابة بأمراض القلب والأوعية الدموية: دراسة خاضعة للسيطرة، عشوائية، منفردة وموازية التصميم

الملخص

أصبحت مجموعة عوامل خطر الإصابة بأمراض القلب والأوعية الدموية وداء السكري من النوع الثاني معروفة باسم المتلازمة الأيضية. في دولة الإمارات العربية المتحدة، تم تشخيص نحو 42% من السكان بالمتلازمة الأيضية.

لاحظ باحثون أسبقون خصائص متعددة للتوابل منها خاضية مكافحة السكري و خاصية مضادات الأكسدة وخاصية مضادات اللالتهابات وأيضا خاصية مضادات السرطنة ومدى تأثيرها على تركيبة الجسم ومقاييس الدم وضغطه. تهدف هذه الدراسة البحثية لتحليل سبعة أنواع من التوابل الشائع استخدامها لمعرفة ما تحتويه من مغذيات كبيرة المقدار و زهيدة المقدار ومن سكريات و دهون و فيتامينات. كما تهدف أيضا لقياس مدى تأثير استهلاك الزنجبيل والقرفة وحبة البركة (الحبة السوداء) على مستوى السكر في الدم ومستوى الدهون وتركيبة الجسم لمشاركين معرضين لخطر الإصابة بأمراض القلب والأوعية الدموية.

تم تحليل سبع أنواع من البهارات الشائع استخدامها للتحري عن محتوياتها التقريبية من المعادن والسكريات و الدهون و الفيتامينات. إضافة إلى ذلك، تم تقسيم 120 مشترك معرضين لخطر الإصابة بأمراض القلب والأوعية الدموية بشكل عشوائي على أربع مجموعات علاجية. تم توزيع المشتركين عشوائيا على ثلاث مجموعات علاجية (مجموعة الزنجبيل ومجموعة القرفة ومجموعة حبة البركة) و كانت هناك مجموعة أخرى للعلاج الوهمي (البلاسيبو) لمدة 12 أسبوعا. قام كل مشارك باستهلاك ثلاثة غرامات في اليوم الواحد من مطحون التوابل أو مطحون البلاسيبو.

تم جمع البيانات المتعلقة بمؤشرات مختلفة من المشاركين في في بداية التجربة وفي منتصفها وعند نهايتها. تم جمع البيانات المتعلقة بمؤشرات مختلفة من المشاركين في في بداية التجربة وفي منتصفها وعند نهايتها. و لوحظ أن تناول مطحون التوابل بأنواعها قد حسن من قياس محيط الخصر و كتلة الدهون في الجسم و الوزن و نسبة كتلة الجسم ونسبة الدهون بالدم و تركيز غلوكوز الدم "على الريق" و الدهون الثلاثية بشكل كبير، مقارنة مع مجموعة العلاج الوهمي ($P \leq 0.05$).

أظهرت نتائج تحاليل مكونات التوابل الكيميائي بأنها تحتوي على مغذيات كبيرة المقدار (الزيوت تحديدا) و زهيدة المقدار. لذلك، يمكن استخدام المركبات الفعالة في التوابل المكملات الغذائية وذلك لما تحتويه من مستوى عالٍ من المغديات القيمة. و تبين أن تناول ثلاثة غرامات يوميا من التوابل (الزنجبيل و القرفة و حبة البركة) على مدار 12 أسبوع يساعد وبشكل ملحوظ في تحسين تركيبة الجسم ومستوى السكر بالدم ونسبة الدهون. بشكل عام أثبتت هذه الدراسة أن استهلاك مطحون التوابل (الزنجبيل و القرفة و حبة البركة) ساعد على تنظيم و تقليل مخاطر الإصابة بالأمراض القلبية والأوعية الدموية.

مفاهيم البحث الرئيسية: الزنجبيل، القرفة، حبة البركة، المتلازمة الأيضية، مستوى الدهون، تركيبة الجسم، تحليل تقريبي، مستوى السكر بالدم.

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Dedication

To my beloved parents, husband, kids and family

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List of Abbreviations

ADA	American Diabetes Association
AHA	American Heart Association
AMPK	Adenosine Monophosphate-activated Protein Kinase
AOAC	Association Official Analytical Chemist
ATP III	Adult Treatment Panel lll
BFM	Body Fat Mass
BMI	Body Mass Index
BP	Blood Pressure
CVDs	Cardiovascular Diseases
DXA	Dual Energy X-ray Absorptiometry
EGIR	European Group for the Study of Insulin Resistance
ESHA	Food Processor Nutrition Analysis software
FAME	Fatty Acid Methyl Esters
FBG	Fasting Blood Glucose
GC	Gas Chromatograph
GCC	Gulf Council Countries
GLUT 4	Glucose Transporter Type 4
Hb	Hemoglobin
HbA1c	Glycated Hemoglobin
HDL	High Density Lipoprotein
HEPA	Health Enhancing Physical Activity
HPLC	High Performance Liquid Chromatography
ICD9	International Classification of Diseases, Ninth Revision
IDF	International Diabetes Federation
IPAQ	International Physical Activity Questionnaire

LDL	Low Density Lipoprotein
MetS	Metabolic Syndrome
NCDs	Non-Communicable Diseases
NCEP	National Cholesterol Education Program’s
NS	Nigella Stevia
PBF	Percent Body Fat
SD	Standard Deviation
SMM	Skeletal Muscle Mass
TC	Total Cholesterol
TG	Triglycerides
TNFα	Tumor Necrosis Factor α
TQ	Thymoquinone
T2DM	Type 2 Diabetes Mellitus
UAE	United Arab Emirates
UAEU	United Arab Emirates University
USEPA	United States Environmental Protection Agency
UV	Ultra Violet
VLDL	Very Low Density Lipoprotein
WC	Waist Circumference
WHO	World Health Organization
2-hPG	2-hour Post-prandial Glucose

Chapter 1: Introduction

According to the World Health Organization (WHO), the number of deaths caused by non-communicable diseases (NCDs) is increasing worldwide. In 2015, 70% of deaths globally were caused by NCDs, and most of these resulted from complications of four main NCDs: cardiovascular diseases (CVD), cancers, diabetes, and chronic lung diseases [1].

Of these four, the most frequent cause of death is CVD. Of 40 million NCD deaths annually, 17.7 million (45%) are attributed to CVD [1]. Obesity, type 2 diabetes, hypertension, and high blood lipid levels are the main causes of CVD [2-4].

Metabolic syndrome (MetS) is a combination of medical illnesses that can include high fasting blood glucose (FBG) levels, elevated blood pressure, central obesity, high blood triglyceride (TG) levels, insulin resistance, diabetes, elevated blood low density lipoprotein (LDL) levels, and reduced blood high density lipoprotein (HDL) levels [5]. The characteristics of a MetS diagnosis are controversial, although all definitions agreed on three common characteristics: reduced HDL, elevated blood pressure, and insulin resistance [5-7]. MetS management aims to reduce the risk of clinical factors that could lead to CVD. Changing the lifestyle of a patient with MetS could help to treat symptoms and improve the quality of life for people at risk of CVD [8, 9].

Dietary factors include improving the nutritional components in an individual's diet. For example, reducing the fat content of the diet and managing the carbohydrate content could improve the regulation of insulin sensitivity, blood glucose and blood lipid levels [10, 11]. One method used to manage blood parameters that could affect the risk factors leading to MetS is herbal therapy. Herbal therapy is broadly used in

many countries as a treatment or as a preventive measure to manage MetS risk factors, including blood glucose, blood pressure, and blood lipid levels [12-16].

On the other hand, chemical analysis could assist to comprehend the positive effects of herbs and spices on people at risk for CVD, by breaking down the components of the individual spice to understand the medical and nutritional value of each item. Additionally, spices such as ginger (*Zingiber officinale*), cinnamon (*Cinnamomum*), black seed (*Nigella sativa*), fenugreek (*Trigonella foenum graecum*), cardamom (*Elettaria cardamomum*), cloves (*Eugenia aromaticum*), and saffron (*Crocus sativus*) were tested in previous studies, and a positive effect was noted on blood glucose, body composition, the lipid profile, inflammation markers, tumor necrosis, and the level of oxidation in blood and tissues because of the availability of active compounds and their considerably high content of vitamins and minerals [17-23]. In this study, the above seven spices will be analyzed to explore with the possibility of their use as treatments or supplements.

The primary objectives of the study is to chemically analyze seven commonly used spices: ginger (*Zingiber officinale*), cinnamon (*Cinnamomum*), black seed (*Nigella stevia*), fenugreek (*Trigonella foenum graecum*), cardamom (*Elettaria cardamomum*), cloves (*Eugenia aromaticum*), and saffron (*Crocus sativus*), and to evaluate the effects of ginger (*Zingiber officinale*), cinnamon (*Cinnamomum*), and black seed (*Nigella sativa*) powders on FBG, hemoglobin (Hb) levels, glycated hemoglobin (HbA1c) levels, blood pressure, the blood lipid profile, and waist circumference (WC) among participants at risk for CVD.

Chapter 2: Literature Review

2.1 Introduction to Metabolic Syndrome

2.1.1 History of Metabolic Syndrome

From the early 1920s to the late 1980s, scientists noticed the relationship between the risk factors (upper body obesity, diabetes, hyperlipidemia) and a higher risk of CVD [24, 25]. However, in 1977, the term “metabolic syndrome” was utilized to describe different associations of a cluster of abnormalities. MetS was described by Haller et al. when discussing the association between diabetes mellitus, obesity, hyperlipoproteinemia, hyperuricemia, and hepatic steatosis, when describing the cumulative effects of risk factors on atherosclerosis [26]. Additionally, in 1977, MetS was used to describe the correlation of obesity, gout, diabetes mellitus, and hypertension with hyperlipoproteinemia [27]. One year later, Philip et al. [28] developed a concept suggesting that risk factors of myocardial infarction produce a gathering of abnormalities. These risk factors include: glucose intolerance, hyperinsulinemia, hypercholesterolemia, hypertriglyceridemia, and high blood pressure and are correlated with heart diseases and with aging and obesity [28].

MetS, or ‘Syndrome X’, was first introduced in 1988 as a group of abnormalities, including hyperglycemia, dyslipidemia, and high blood pressure that could lead to CVD. It was suggested that all of these abnormalities were caused by insulin resistance in one way or another [29]. Different names, such as MetS, American syndrome, syndrome X, and insulin resistance syndrome, describe the gathering of abnormalities that could lead to CVD and type 2 diabetes.

2.1.2 Definition of Metabolic Syndrome

The definition of MetS could differ according to its diagnostic characteristics. The characteristics of a MetS diagnosis remain controversial, although all definitions agreed on three common characteristics: reduced HDL levels, elevated blood pressure, and insulin resistance [5-7]. Unfortunately, there was no universal agreement to accurately define this syndrome and its specific characteristics. A universal definition of MetS and suitable treatments for the components of this syndrome are crucial to provide the best health outcomes and to improve the patient's quality of life. Table 2.1 explains five different definitions of MetS:

1- The World Health Organization (WHO) definition [30]

2- The National Cholesterol Education Program's (NCEP) Adult Treatment Panel III (ATP III) [31]

3- American Heart Association (AHA) definition [8]

4- The International Diabetes Federation (IDF) definition [32]

5- The International Classification of Diseases, ninth revision (ICD-9) definition, where MetS's code is (277.7) [33]

Table 2.1 Definitions of Metabolic Syndrome

Diagnostic Characteristics	WHO (1998)	ATP III (2001)	AHA (2005)	IDF (2006)	ICD-9 (volume 2015)
Insulin Resistance	✓	✓	✓	✓	✓
Low HDL	✓	✓	✓	✓	✓
Hypertension	✓	✓	✓	✓	✓
High TGs	✓	✓	✓	X	✓
Central Obesity	✓	✓	✓	X	✓
Glucose intolerance	✓	✓	✓	X	X
Diabetes	✓	X	✓	✓	X
High HDL*	X	X	X	✓	X

WHO: The World Health Organization; ATP III: Adult Treatment Panel III; AHA: American Heart Association; IDF: International Diabetes Federation; ICD-9: International Classification of Diseases, ninth revision.
✓ Diagnostic characteristic included in the definition
X Diagnostic characteristic is not included in the definition

The most commonly used published definitions of MetS are those of the National Cholesterol Education Program’s (NCEP) Adult Treatment Panel III (ATP III) and the World Health Organization (WHO) [5].

2.1.2.1 ATP III Definition

MetS is detected when at least three of the following risk factors are present:

1. High waist circumference:

    a. Men: greater than 94 cm

    b. Women: greater than 80 cm

2. Increased TGs: greater than or equal to 150 mg/dL (1.7 mmol/L)

3. Reduced HDL (“good”) cholesterol:

    a. Men: less than 40 mg/dL (1.03 mmol/L)

    b. Women: less than 50 mg/dL (1.29 mmol/L)

4. High blood pressure: greater than or equal to 130/85 mm Hg or receiving antihypertensive medication

5. Elevated fasting glucose: ≥100 mg/dL (5.6 mmol/L) or receiving a medication of hyperglycemia

2.1.2.2 WHO Definition

According to the WHO definition [30], MetS is present in individuals with FBG >110 mg/dL and at least two of the following characteristics:

1. Abdominal obesity: ≥ waist-to-hip ratio of 0.90
2. Elevated TG levels: greater than or equal to 150 mg/dL (1.7 mmol/L)
3. Elevated blood pressure: ≥140/90 mm Hg or receiving antihypertensive medication

2.2 Metabolic Syndrome Diagnostic Criteria

The definitive importance of MetS is due to its assistance to recognize individuals who are at high risk of type 2 diabetes and CVD [7]. Therefore, numerous studies have tried

to outline the diagnostic criteria for MetS. In 1999, the WHO focused on insulin resistance or diabetes or impaired glucose tolerance as crucial components of MetS, with at least two of the following: hypertriglyceridemia, high blood pressure, low HDL, obesity, and microalbuminuria [34]. In the same year, the European Group for the Study of Insulin Resistance (EGIR) altered the WHO criteria eliminating people with diabetes but still demanding the existence of hyperinsulinemia. Waist circumference was the measure of obesity, however, different cut-off values were considered for the other variables such as central obesity, hypertension, dyslipidemia and impaired fasting glucose. In 2001, The US National Cholesterol Education Program: Adult Treatment Panel III (NCEP ATP III) excluded the obligatory of insulin resistance and considered hyperglycemia to be a diagnostic criterion along with the following: elevated TG, low HDL, central obesity, and elevated blood pressure. On the other hand, the NCEP concluded that to be diagnosed with MetS, any three of the five diagnostic criteria that were listed by NCEP ATP III must present [31]. In 2004, the International Diabetes Federation (IDF) amended the WHO definition by requiring the central obesity criteria for the definition along with four of the following criteria: increased TG, high blood pressure, high FBG, and reduced HDL [32].

Other parties also refined the previous MetS diagnostic criteria: the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) proposed lowering the FBG cutoff point to ≥100 mg/dL instead the ATP III FBG cutoff point (≥110 mg/dL). They also did not use ethnic-specific values for central obesity and did not include central obesity as a diagnostic criterion [35]. These differences in identifying the MetS diagnosis criteria led to confusion among research studies, and therefore, a meeting was held between the International Diabetes Federation (IDF)

Task Force on Epidemiology and Prevention, the National Heart, Lung, and Blood Institute (NHLBI), the American Heart Association (AHA), the World Heart Federation (WHF), and the International Atherosclerosis Society (IAS) to standardize the criteria. At this meeting, it was approved that there should not be a mandatory diagnostic criterion, and that waist circumference (central obesity) should be a main screening tool. The meeting outcomes also concluded that three abnormal risk factors out of five would qualify as a diagnosis of MetS, and these five criteria are as follows: elevated blood pressure, central obesity, elevated TG, elevated FBG, and reduced HDL [36]. Moreover, WC cut-off point determined were based on ethnicity and gender. Unfortunately, until now there are no data for Eastern Mediterranean and Middle East (Arab) population, therefore using European cut-off point was recommended until the availability of more specific data on WC for Arab population.

2.3 Metabolic Syndrome Risk Factors

Diet, physical inactivity, age, sex, genetics, stress, and ethnicity are factors that could contribute to MetS risk factors such as abnormalities in blood glucose, blood pressure, central obesity, lipid levels, and insulin resistance. Many researchers have linked obesity and high WC to CVD [37-39]. According to the WHO, obesity is a medical condition recognized when there is high accumulation of body fat which could lead to serious health issues [40]. This will increase the fat tissue in different parts of the body, which will cause an increase in some inflammatory markers in the blood. The increase in adipocytes (fat tissue) will increase tumor necrosis factor (TNF)α levels, which could affect metabolic pathways and increase the level of cytokines in the blood. Moreover, TNFα, with the help of the TNFα receptors, will stimulate cell signaling, which could lead to increased insulin resistance [41]. Another result of increasing the

adipocyte count is the increase of cytokines that regulate the balance between humoral and cell-based immune responses. This could lead to imbalances in the immune response and inflammation and subsequently, atherosclerosis [42]. Figure 2.1 illustrates the relationship between increased adipocytes and insulin sensitivity, and the relationship between adipocytes and the cytokines.

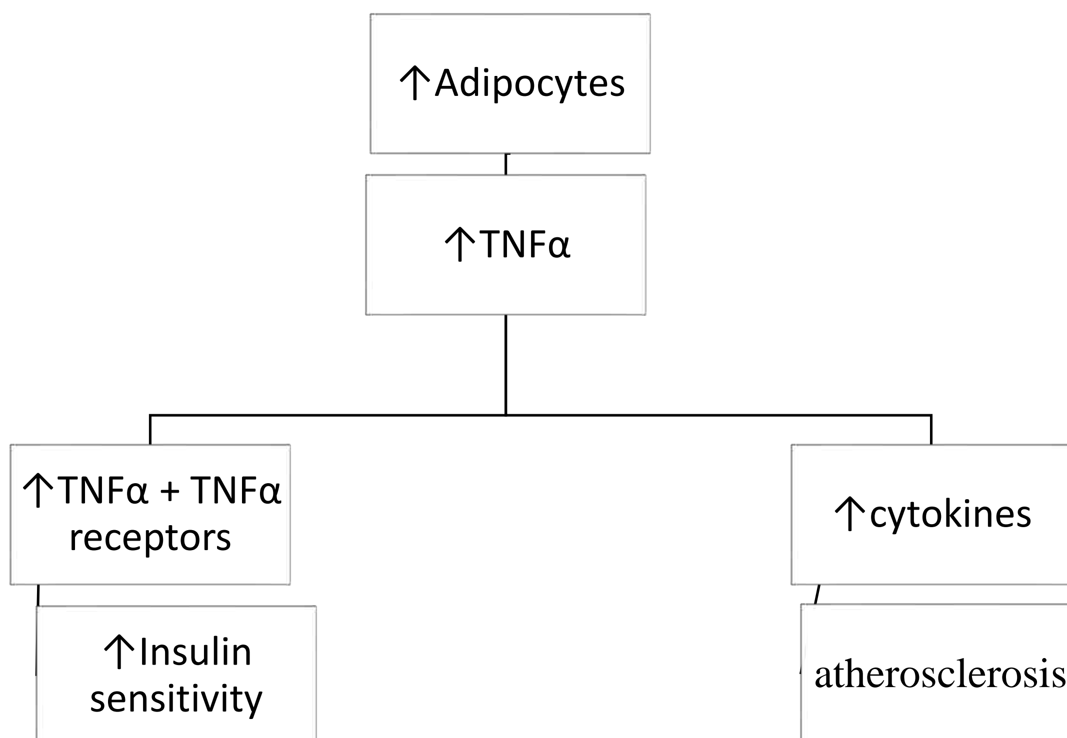

Figure 2.1: Effects of Increasing Adipocytes on Insulin Sensitivity and Atherosclerosis

TNF α: Tumor Necrosis Factor α

Increased blood pressure is considered to be one of the distinguishing causes contributing to CVD [43]. Additionally, increased blood pressure could lead to impediments that would have a substantial impact on health such as stroke. High blood pressure could cause strokes, dementia, CVD, and chronic kidney disease [44-46]. Earlier studies showed that decreasing blood pressure by 5 mmHg can decrease the

possibility of having ischemic heart disease by 21% and stroke by 34%, and reduce the probability of heart failure, dementia, and mortality from CVD [44].

Dyslipidemia was also shown to be one of the main causes of CVD. A meta-analysis showed that elevated TG levels in the blood could lead to CVD and other health complications [47]. Moreover, low HDL and high LDL levels in the blood were shown to be correlated with an increased risk of CVD [48, 49].

Borg et al. reported a strong relationship between glycated hemoglobin (HbA1c) and CVD, where there was a correlation between high blood glucose and an increased risk of CVD in patients with diabetes [50]. Another study of 237, 468 participants showed that prolonged abnormal high levels of glucose in the blood led to 1, 661 strokes and 816 ischemic heart disease (IHD) events [51]. In conclusion, MetS and CVD are strongly related, and to manage CVD, management of MetS risk factors is crucial. MetS is crucial. Many studies have called the effects of MetS risk factors into question and evidenced the direct effects of these risk factors on CVD, quality of life, and morbidity rate [52-54].

Being under stress for a long period of time could play a negative role by disturbing the hormonal system and result in flow, which could result in a serious health problems. Stress could disturb the hypothalamic–pituitary–adrenal axis (HPA-axis) [55], which could lead to an increase in cortisol levels in the blood and further complications such as increased blood pressure [56], blood sugar [57], insulin resistance [58], dyslipidemia [56, 59], and visceral adiposity [60]. All of these factors can significantly increase the risk of CVD, type 2 diabetes, and stroke [53, 61], as displayed in Figure 2.2.

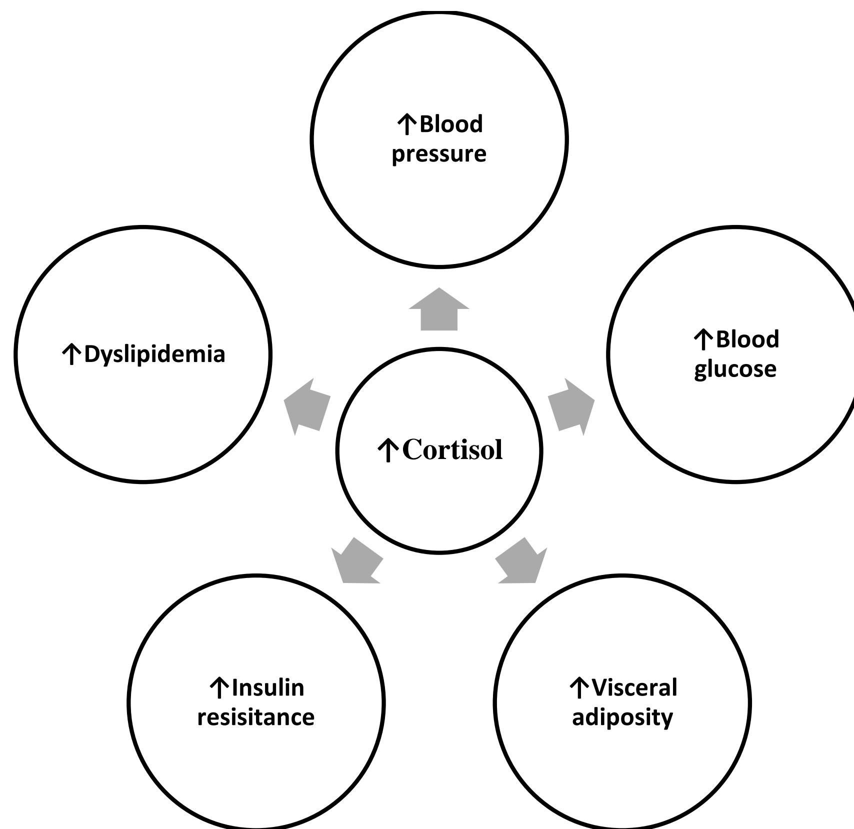

Figure 2.2: Long-term Effects of Increased Cortisol Levels in the Blood

2.4 Prevalence of Metabolic Syndrome

Accurate estimates of the prevalence of MetS are challenging based on the many definitions employed in different studies within the same testing group. Accordingly, the extent of the problem is challenging to quantify [62]. Irrespective of the definition, MetS affects many adults worldwide with an estimated 22.8% of US adult men and 22.6% of adult women affected among all the diverse ethnic groups [63].

Third National Health and Nutrition Examination Survey III (NHANES III) (a survey of 8814 adults) using ATP III diagnostic characteristics reported that 38.6% had abdominal obesity, 30.0% had elevated TG levels, 37.1% had low HDL levels, 34.0% had elevated blood pressure, and 12.6% had hyperglycemia/diabetes. The data indicate a high occurrence of MetS. Prevalence among adults aging 20 years or older was 24%

and among those who were >50 years old, it was 44% [64, 65]. In other studies in the United States, 24% of participants met the ATP III criteria and almost a same percentage met the WHO criteria for MetS in the Framingham Offspring Study [66]. However, pooled data from eight studies in Europe among participants 40–55 years of age show that 7%–36% of men and 5%–22% of women met the WHO diagnostic criteria of MetS [67].

The prevalence of the MetS in the Gulf Cooperation Council Countries (GCC) is considered 10%–15% higher than in most developed countries, with an increased prevalence ratios for women [68]. In the United Arab Emirates (UAE), 42% of the population was diagnosed with MetS, as shown in an earlier study in 2008 [69]. Moreover, a cross-sectional study that included 555 Emirati females between the ages of 18 and 55 years indicated that the prevalence of MetS was 6.8%. MetS prevalence was higher for obese participants (34.5%) compared with non-obese participants (10.1% overweight and 1.7% normal weight) [70]. In 2017, a meta-analysis of cross-sectional studies about the prevalence of MetS performed in the Middle East showed that the prevalence of MetS was 2.2%–44% in Turkish, 16%–41% in Saudi-Arabian, 22%–50% in Emirati, 14%–63% in Pakistani, 26%–33% in Qatari, 9%–36% in Kuwaiti, 6%–42% in Iranian, and up to 23% in Yemeni people [71].

2.5 Management and Treatment of Metabolic Syndrome

Multiple studies have recommended that the management of MetS must be individualized and should start with lifestyle changes [9, 72, 73]. As MetS is characterized by a group of factors that elevate the risk for CVD and type 2 diabetes, therefore, MetS should begin with managing of each factor. This can be achieved by a variety of means, including elevating the level of physical activity, attention to the diet,

and clinical management. Clinical review and management could include the use of medications or surgery to reduce the MetS effect by improving blood pressure and HDL, TG, and glucose to reach normal levels. Factors that helped to enhance the quality of life for patients with MetS include physical activity management, surgical and medical intervention, and dietary adjustments (Figure 2.3) [8, 9].

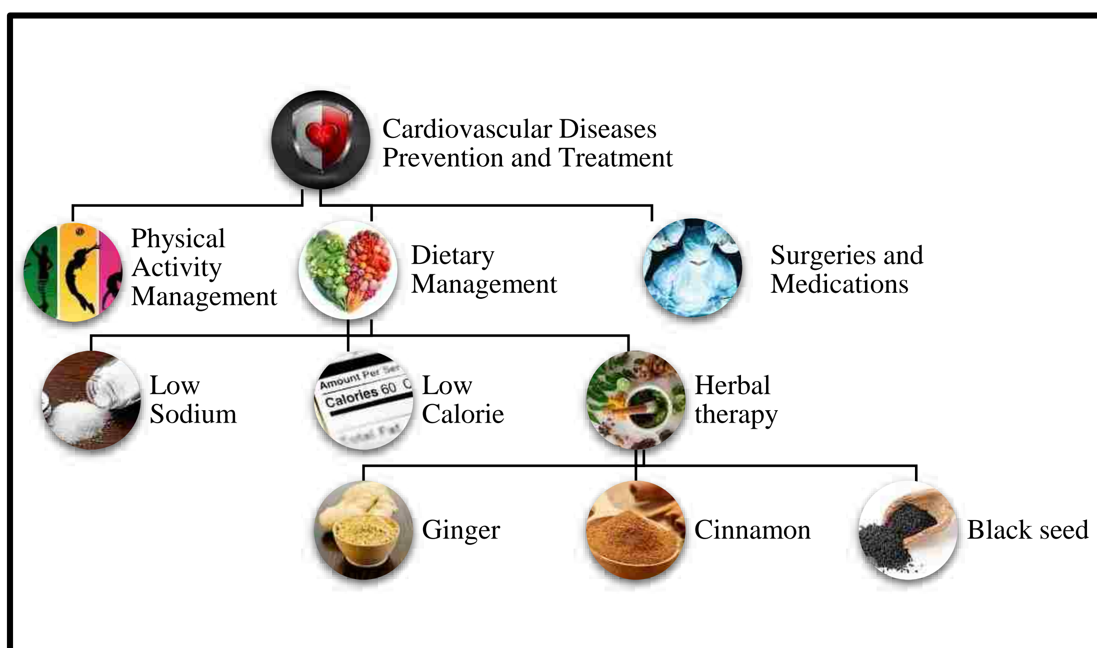

Figure 2.3: CVD Prevention and Treatment

2.5.1 Physical Activity Management

Obesity and a sedentary lifestyle are important contributors to the development of MetS [74-76], therefore, treating these two factors should be prioritized. Previous studies reported the effects of increasing the physical activity level on blood parameters that could positively affect blood pressure and FBG. This could lead to better management of the MetS and therefore to a better quality of life [77-83]. However, other studies reported the ineffectiveness of physical activity in reducing MetS risk factors such as blood pressure [77, 84].

Physical activity was shown to improve body composition by reducing body fat accumulated in the abdominal area [85, 86]. Physical activity also improves the blood parameters that are associated with MetS and CVD risk, including HDL and TGs [85, 87-89]. High C-reactive protein levels have been associated with chronic inflammation and therefore CVD and physical activity lowers the levels of C-reactive protein [79]. This evidence may clarify the positive effects of physical activity in managing MetS risk factors and thereby CVD risk factors.

2.5.2 Dietary Management

The main goal of clinical and dietary attention and management in people with MetS is to decrease the risk of CVD by managing high blood pressure, diabetes, and the lipid profile. For individuals who have diabetes, managing diabetes alone must be a first-line therapy because of their higher risk of CVD [90].

To manage MetS, primary risk factors should be controlled through managing physical activity, obesity, and a controlled atherogenic diet. Lifestyle changes have been shown to reduce all of the CVD factors [8], and dietary management was considered to be one of the most important tools to manage these risk factors [10, 91-93].

Grundy et al. recommended different types of diets to manage MetS risk factors [8, 72]. Many crash diets (short-term diets that are intensive, aimed to meet a weight loss goal rapidly) were not effective for long-term weight reduction maintenance because these diets are based on very low calorie intake or high fat and low carbohydrate intake [94, 95]. However, to treat obesity/abdominal obesity, Stern et al. [96] and Wing et al. [97] recommended reduced-energy diets, reducing 500–1000 kcal per day, aiming for an 8%–10% of the total body weight reduction in 6–12 months. Weight loss on these

diets is better maintained when combined with exercise. These types of diets were shown to have a better long-term weight maintenance results compared with crash diets [96, 97].

General dietary recommendations were made by the ATP III for patients with MetS to manage the CVD risk factors [98-100] and include a diet that is low in total fat (25% to 35% of total calories) where saturated fat is <7% of total calories, low in cholesterol (i.e. <200 mg/dL) and trans fats, and most of the dietary fats must be unsaturated, reducing the consumption of simple sugars and reducing sodium intake to 1500 mg/day. They also advise increasing the dietary fiber intake that requires an increased intake of whole grains, fruits, and vegetables [8, 101, 102]. These types of diets have a positive effect on all blood parameters that are known to be risk factors for MetS [31, 103, 104].

AHA, NHLBI, and the American Diabetes Association (ADA) published an article that discusses the guidelines for the diagnosis and treatment of MetS, the main goal being to prevent CVD and type 2 diabetes mellitus in higher-risk patients as presented in Table 2.2.

Table 2.2: AHA/NHLBI Guidelines (2009) for Metabolic Syndrome Management

Metabolic Risk Factors	**Management Guidelines**
Abdominal Obesity	7%–10% reduction of body weight through the first year of treatment, and continue the weight loss to reach the ideal body weight.
Physical Activity	Minimum of 30 min/day 5 days/week of moderate intensity exercise, and when possible, 60 min/day or more every day is preferable.
Atherogenic Dyslipidemia	Primary goal: lowering LDL Secondary goal: lowering non-HDL Tertiary goal: increasing HDL
Pro-thrombotic State	Reduce fibrinolytic and thrombotic risk factors
Pro-inflammatory State	Lifestyle therapies
Atherogenic Diet	Reduce saturated fat intake (<7% of total calories), trans fat, cholesterol (<200 mg/dL), and total fat (25% to 35% of total calories)
High Blood Pressure	Lower to <140/90 mmHg or to <130/80 mmHg in the case of diabetes
High Glucose	Delay type 2 diabetes mellitus in the case of impaired fasting glucose, and lower HbA1c to <7.0% in the case of diabetes

Another approach is the ABCDE approach. This approach uses alphabetical order to simplify the process of managing MetS, and is summarized in Figure 2.4 [105]

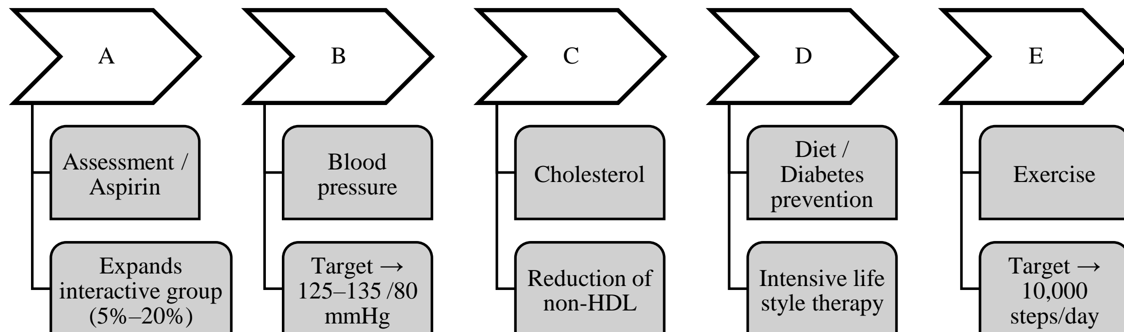

Figure 2.4: Summary of the ABCDE Approach with Recommendations

2.5.3 Surgery and Medications

In some cases of obesity (morbid obesity), a medical intervention other than medications or dietary modifications is needed. Bariatric surgery is considered to be a solution that could help to enhance the quality of life for people who are obese by assisting them to reduce their body weight [106-108]. Bariatric surgery is performed on patients who are morbidly obese, and it requires decreasing the stomach size using a gastric band, removing a portion of the stomach, or re-routing the small intestine to a small stomach pouch.

Previous studies recommended and showed the efficiency of bariatric surgery in treating the complications and risk factors that could lead to CVD and death (e.g. central obesity, diabetes, high blood pressure, lipid profile, and sleep apnea) [106, 108-110]. Table 2.3 clarifies the classification of bariatric surgeries and provides examples of each type of surgery [111, 112].

Table 2.3: Definitions of Bariatric Surgeries

Bariatric surgery	Definitions and examples
Malabsorptive surgeries	Surgery that aims to remove portion of the stomach, which creates a physiological condition of malabsorption. These surgeries include: biliopancreatic diversion, jejunoileal bypass, and endoluminal sleeve.
Restrictive surgeries	Surgery that aims to decrease the oral intake by restricting the stomach capacity and therefore, resulting in early satiety. These types of surgeries include: vertical banded gastroplasty, adjustable gastric band, sleeve gastrectomy, intragastric balloon (gastric balloon), and gastric plication.
Mixed surgeries	Surgery that applies both techniques. Mixture of malabsorption and restrictive surgeries. These types include: gastric bypass surgery, sleeve gastrectomy with duodenal switch and implantable gastric stimulation

Ikramuddin et al. concluded that gastric bypass surgery in addition to lifestyle and medical management in participants with type 2 diabetes was associated with an improved blood glucose and lipid profile [113]. Another study also proved the positive effect of sleeve laparoscopic gastrectomy on weight loss and CVD risk factors [114].

Treatment of the CVD risk factors should be individualized to match each patient's needs. Therefore, some patients will need more invasive medical help using medications, especially if changes in lifestyle factors have not made a significant difference in the parameters that contribute to CVD. Each parameter should be treated

separately when using medications because each medication treats a specific symptom. Table 2.4 explains the medications taken to treat each MetS risk factor.

Table 2.4: Medications Prescribed to Treat Metabolic Syndrome Risk Factors

MetS Risk Factor	**Medications**
High blood pressure	- Thiazide diuretics - Beta blockers - Angiotensin-converting enzyme inhibitors - Angiotensin II receptor blockers - Calcium channel blockers. - Renin inhibitors [115]
Hyperglycemia/diabetes	- Alpha glucosidase - Amylin analogues - Biguanides - Incretin enhancers - Incretin mimetics - Insulin secretagogues: sulfonylureas

Table 2.4: Medications Prescribed to Treat Metabolic Syndrome Risk Factors (continued)

MetS Risk Factor	**Medications**
Hyperglycemia/diabetes	- Insulin secretagogues: nonsulfonylureas - Thiazolidinediones [116]
Hypertriglyceridemia	- Niacin (Vitamin B3) - Fibrates - Omega-3-fatty acids - Lipoprotein lipase gene therapy (alipogene tiparvovec) Additionally, medications that are prescribed to lower LDL cholesterol were shown to lower the TG level in the blood, such as: - Ezetimibe - PCSK9 inhibitors - Lomitapide - Statins - Mipomersen [117]

Table 2.4: Medications Prescribed to Treat Metabolic Syndrome Risk Factors (continued)

MetS Risk Factor	- **Medications**
Lowering HDL	- Fibrates - Niacin (Vitamin B3) - Statins [118]
Abdominal Obesity/Obesity	- Orlistat - Rimonabant - Sibutramine - Lorcaserin - Metformin - Exenatide - Phentermine - Tesofensine [119, 120]

2.5.4 Herbal Therapy

To manage MetS risk factors that could lead to CVD, the use of herbs and spices as remedies for lowering FBG, reducing high blood pressure, weight loss, and improving the lipid profile is common in eastern culture [12, 121]. Herbal therapy or alternative therapy has been mainly prescribed to relieve and treat symptoms of different diseases [121]. Hasani-Rnjbar et al. reported that in 41 animal studies, weight loss or a significant restriction of weight gain was found using herbal therapy [122]. Moreover,

individuals with a higher income and higher education were more likely to be taking herbal product with the goal of health improvement as reported by Philips et al. [123], while Kaye et al. [124] and Cappuccio et al. [125] reported a significant use of herbal therapy among different ethnic groups.

Several herbs and spices were found to be effective in managing obesity/abdominal obesity, improving the lipid profile, and lowering FBG by improving insulin sensitivity [12, 122]. Additionally, in some studies, CVD patients reported an improvement in blood pressure levels when consuming the right herbal therapy [126].

Furthermore, improvements in the waist-to-hip ratio and waist circumference were reported in studies that used one or more herbal/spice extract, including the use of *Zingiber officinale* as Ignjatovic et al. [127] and Boozer et al. [128] demonstrated. On the other hand, Hackman et al. [129] and Abidov et al. [130] studies reported decreased appetite in obese individuals after regular consumption of some herbs. This decreased appetite resulted in reducing the caloric intake and therefore helped with the weight reduction process [130]. As an example of the clinical use some herbs and spices, Table 2.5 contains 13 studies that were conducted on humans to observe the effects of herbs and spices on MetS risk factors.

Table 2.5: Studies and Clinical Trials on the Effects of Herbs and Spices on Metabolic Syndrome Risk Factors

Herbs	**Target/ Groups**	**Dose / Duration**	**Main outcome**	**Study Reference**
Slimax: extract of several plants: Hordeum vulgare, Polygonatum multiflorum, Dimocarpus longan, Ligusticum sinense, Lilium brownie, and Zingiber officinale	Healthy participants	6 weeks	Significant decrease in body weight and body mass index (BMI) Significant reduction in waist and hip circumference	[127]
Herbal supplement: (Ma Huang & Guarana)	Overweight participants - Control group (n=24) / Intervention group (n=24)	72 mg of ephedra and 240 mg of caffeine for 8 weeks	Significant decrease in body weight and total body fat. Significant reduction in hip and waist circumference	[128]

Table 2.5: Studies and Clinical Trials on the Effects of Herbs and Spices on Metabolic Syndrome Risk Factors (continued)

Herbs	**Target/ Groups**	**Dose / Duration**	**Main outcome**	**Study Reference**
A compound of *Aralia mandshurica* (A) and *Engelhardtia chrysolepis* (E) extracts called ARALOX	Obese non-diabetic women, n=32 -Control group: Diet placebo, n=16 -Intervention group: Diet compound, n=16	450 mg of *Aralia mandshurica* (A) and 450 mg of *Engelhardtia chrysolepis* (E) per day for 15 weeks	Decrease in total body weight and fat weight Reduction in plasma TGs	[131]

Table 2.5: Studies and Clinical Trials on the Effects of Herbs and Spices on Metabolic Syndrome Risk Factors (continued)

Herbs	**Target/ Groups**	**Dose / Duration**	**Main outcome**	**Study Reference**
White bean extract *(Phaseolus vulgaris)*	Obese adults -Control group: placebo, n=25 -Intervention group: white bean extract, n=25	3000 mg per day of each for 8 weeks	Weight reduction in the intervention group Decrease in plasma TGs	[132]
Turmeric (*Curcuma longa L*)	Prediabetic adults -Control group: placebo, n=25	750 mg per day of each for 9 months	16.4% of subjects in the placebo group were diagnosed with type 2 diabetes mellitus	[133]

Table 2.5: Studies and Clinical Trials on the Effects of Herbs and Spices on Metabolic Syndrome Risk Factors (continued)

Herbs	**Target/ Groups**	**Dose / Duration**	**Main outcome**	**Study Reference**
Turmeric (*Curcuma longa L*)	-Intervention group: *Curcuma longa*, n=25		None of the participants from the *Curcuma longa*-treated group were diagnosed with type 2 diabetes mellitus	
Korean red ginseng (KRG) (*Panax ginseng*)	Overweight, n=19, well-controlled type 2 diabetes -Control group: placebo, n=9 -Intervention group: KRG, n=10	6 g per day of each for 12 weeks	No change in HbA1c in both groups Intervention group maintained good glycemic control and improved plasma glucose and plasma insulin regulation.	[134]

Table 2.5: Studies and Clinical Trials on the Effects of Herbs and Spices on Metabolic Syndrome Risk Factors (continued)

Herbs	**Target/ Groups**	**Dose / Duration**	**Main outcome**	**Study Reference**
Bitter lemon (*Momordica charantia*)	Newly diagnosed with diabetes adults, -Control group: placebo, n=20 / Intervention group: *Momordica charantia*, n=20	3 g per day of each for 12 weeks	There was no significant effect on mean FBG, total cholesterol, and weight in both groups	[135]
Cinnamon (*Cinnamomum*)	Participants diagnosed diabetes mellitus type 2	3 g per day of each for 16 weeks	The cinnamon extract has a moderate effect in reducing	[136]

Table 2.5: Studies and Clinical Trials on the Effects of Herbs and Spices on Metabolic Syndrome Risk Factors (continued)

Herbs	**Target/ Groups**	**Dose / Duration**	**Main outcome**	**Study Reference**
Cinnamon (*Cinnamomum*)	-Control group: placebo, n=39 -Intervention group: cinnamon powder, n=40		Fasting plasma glucose concentrations in diabetic patients.	
A combination of *Cissus quadrangularis* (CQ) and *Irvingia gabonensis* (IG)	Overweight and obese participants -Control group: placebo, n=36	Intervention group: 300 mg CQ + 500 mg IG =800 mg of compound per day Control group: 800 of placebo per day	Significant reduction in Cholesterol and LDL of FBG levels Significant decrease in body weight, body fat percent and waist size in both groups	[137]

Table 2.5: Studies and Clinical Trials on the Effects of Herbs and Spices on Metabolic Syndrome Risk Factors (continued)

Herbs	**Target/ Groups**	**Dose / Duration**	**Main outcome**	**Study Reference**
A combination of *Cissus quadrangularis* (CQ) and *Irvingia gabonensis* (IG)	-Intervention group: compound of CQ and IG, n=36	Duration: 10 weeks		
Terminalia arjuna tree-bark powder	Coronary heart disease (CHD) patients Group I: control group, n=35 Group II: vitamin E group, n=35	Group I: placebo capsules; Group II: vitamin E capsules 400 units per day;	Significant antioxidant action in the vitamin E group and *T. arjuna* tree group Significant hypo-cholesterolemic effect in the *T. arjuna* tree group	[138]

Table 2.5: Studies and Clinical Trials on the Effects of Herbs and Spices on Metabolic Syndrome Risk Factors (continued)

Herbs	**Target/ Groups**	**Dose / Duration**	**Main outcome**	**Study Reference**
Terminalia arjuna tree-bark powder	Group III: *T. arjuna* tree bark-powder group, n=35	Group III received finely pulverized *T. arjuna* tree bark-powder (500 mg) per day For 30 days		
Ginger (*Zingiber officinale*)	Diabetic adults -Control group: placebo, n=44 -Intervention group: ginger powder, n=44	3 g of each per day for 8 weeks	Reduction in FBS and HbA1c Improvement in insulin resistance	[139]

Table 2.5: Studies and Clinical Trials on the Effects of Herbs and Spices on Metabolic Syndrome Risk Factors (continued)

Herbs	**Target/ Groups**	**Dose / Duration**	**Main outcome**	**Study Reference**
Black seed (*Nigella stevia*) and turmeric (*Curcuma longa L*)	Males with MetS N=250 (randomly distributed -Control group: n=64 Turmeric group, n=62 Black seed group, n=62 Combination group, n=62	Black seeds (1.5 g/day) Turmeric (2.4 g/day) combination (900 mg Black seeds and 1.5 g Turmeric/day) placebo (2 g) for 8 weeks	Black seeds reduced lipids and FBG, while turmeric reduced LDL-cholesterol and C-reactive protein (CRP).	[140]

Table 2.5: Studies and Clinical Trials on the Effects of Herbs and Spices on Metabolic Syndrome Risk Factors (continued)

Herbs	**Target/ Groups**	**Dose / Duration**	**Main outcome**	**Study Reference**
Cinnamon, cardamom, saffron (*Crocus sativus*) and ginger (*Zingiber officinale*)	Type 2 diabetes participants -Control group: Placebo, n=39 -Treatment groups: Cinnamon, n=40 Cardamom, n=42 Saffron, n=42 Ginger, n=41	For 8 weeks 3 glasses of black tea and either 3 g/day of cardamom, or cinnamon, or ginger, or 1 g saffron. Control group received 3 tea glasses without any treatment	Significant beneficial effects on cholesterol, but not on measures of glycemic control, oxidative stress, and inflammation.	[141]

2.5.4.1 Ginger, Cinnamon, and Black Seed Usage

Ginger (*Zingiber officinale*), cinnamon (*Cinnamomum*), and black seed (*Nigella sativa*) are annual plants that have been traditionally used internationally, particularly on the Indian subcontinent, Europe, and Arabian countries such as the UAE [141]. These spices were used for food preparation and medicinal purposes, as a cure for many diseases and conditions including diabetes, asthma, hypertension, inflammation, cough, bronchitis, headache, eczema, fever, dizziness, and influenza. Additionally, black seed is used as a diuretic, lactagogue, and vermifuge, while ginger and cinnamon are used as an anti-tumor agent, and cinnamon is also used to decrease muscle soreness in athletes. These spices are also used in food as aromatic spices, carminatives, and condiments [141-147].

2.5.4.2 Chemical Analysis and Active Components of Ginger, Cinnamon, Black Seed, and Other Spices

In terms of chemical composition, a study published in 2010 analyzing ginger powder found that the ginger powder moisture content was 76.86%, while it contained 8.75% crude protein, 5.62% crude fat, 2.93% crude fiber, and 2.54% total ash. The moisture content varied significantly from study to study. A previous study of the chemical composition of ginger reported a moisture content of 6.67% [148]. The differences in the results from the previous studies in the proximate analysis and mineral analysis of ginger powder was theorized to be a result of different soil types and geographical locations of the ginger growth, which has an effect on the nutrient composition [149]. Another study analyzed ginger root and found that it has a moisture content of 15%, and also 5% protein, 3.72% fat, 38.35% carbohydrates, 25.5% soluble fiber, 23.5% insoluble fiber, and 3.85% total ash [17]. Various authors reported other values for

ginger composition as following: protein, 7.2%–8.7%; fat, 5.5%–7.3%; and ash, 2.5%–5.7%. Ginger also contains many different vitamins and minerals such as vitamin C, calcium, phosphorous, zinc, and iron [148, 150]. And is also a good source of antioxidants due to its content of total polyphenols, tannin, and flavonoids, as reported by Prakash et al. in 2010 [17].

Furthermore, 6-paradol and 6-shogaol are chemicals that are presented in ginger that give the ginger its pungent smell and taste and potential anti-glycemic effect. In 2017, a study was published by Wei et al. [151] stating that 6-paradol and 6-shogaol are proved to have an effective activity in stimulating glucose usage by adipocytes and myotubes in high-fat diet-fed mice. The effects were accredited to the elevation in adenosine monophosphate-activated protein kinase (AMPK) phosphorylation in adipocytes [151]. Additionally, Li et al. showed that the activity of (S)-(8)-gingerol was correlated with an elevation of the surface distribution of the glucose transporter type 4 (GLUT4) protein, which is responsible for glucose uptake in the plasma membrane, and it also enhanced glucose and insulin uptake [152]. Figure 2.5 features the chemical structure of 6-gingerol and 6-shagaol.

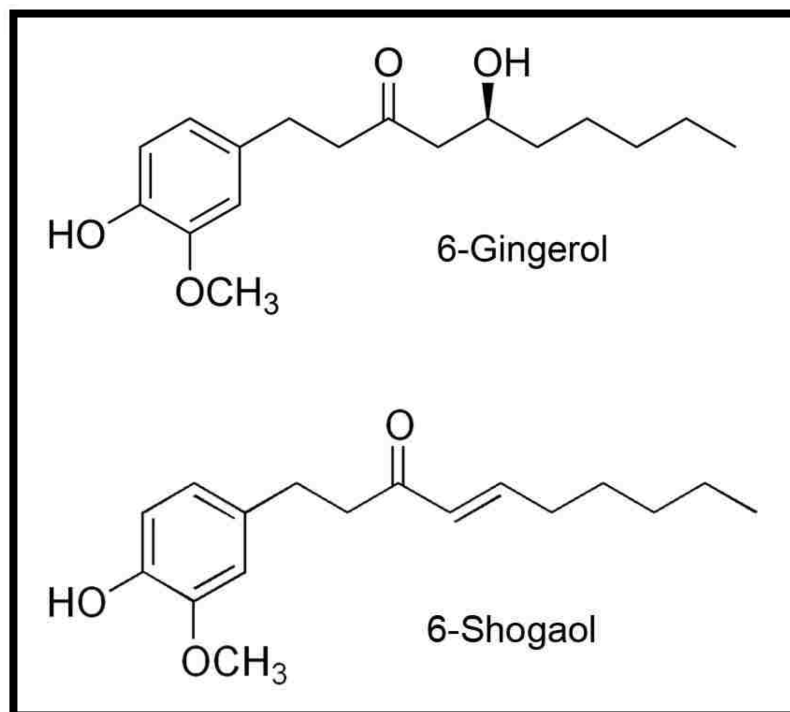

Figure 2.5: Chemical Structure of 6-Gingerol and 6-Shogaol

A study published in 2009 reported that cinnamon (*Cinnamomum*) contains the following: crude protein, 3.5%; crude fat, 4%; carbohydrates, 52%; crude fiber, 33%; and total ash, 2.4%. Cinnamon also contains several different vitamins and minerals such as potassium, copper, phosphate, zinc, and iron [153]. A systematic review published in 2015 by Kawatra et al. extensively discussed the active compounds of cinnamon (cinnamaldehyde and cinnamic acid) [18].

Cinnamaldehyde and some of its derivatives (2′-hydroxycinnamaldehyde) and (2′-benzoyl-oxycinnamaldehyde) show a substantial role in increasing the level of reactive oxygen species and in inducing apoptosis by stopping proteasome activity to make the carcinogenic cell more prone to oxidative stress [18, 154, 155]. Moreover, cinnamaldehyde and cinnamic acid together play an important role in preventing CVD because they both have the ability to produce nitric oxide and both have anti-

inflammatory effects [156]. The antioxidant property of cinnamon results from activity of the eugenol component, which stops peroxynitrite-induced nitration and also lipid peroxidation [157]. Polyphenols that are found in cinnamon are also considered to improve insulin sensitivity [158]. Figure 2.6 shows the effects of cinnamon on health.

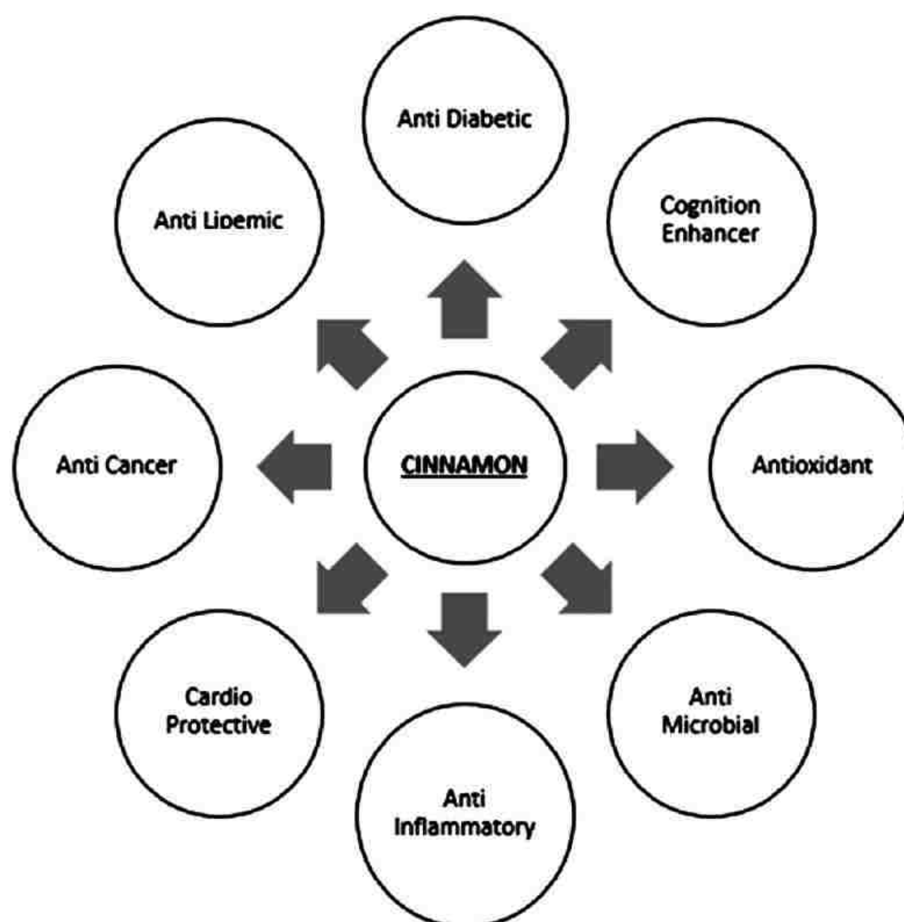

Figure 2.6: Effects of Cinnamon on Health [18]

Moreover, in 2003, Ali et al. demonstrated that black seed contains the following: protein, 26.7%; fat, 28.5%; carbohydrates, 24.9%; crude fiber, 8.4%; and total ash, 4.8%. Black seed also contains copper, phosphate, zinc, iron, and essential (volatile) and fixed oil. Black seed essential oil contains a major bioactive component, which is thymoquinone (TQ; 30%–48%) [142]. TQ is a chemical compound that is known for its therapeutic potentials, and most black seed positive effects are mainly accredited to

TQ. TQ therapeutic potentials have been investigated in some studies, which showed that TQ had an anti-oxidant, anti-inflammatory, immunomodulatory, anti-histaminic, anti-microbial, and anti-tumor effects as well as gastroprotective, hepatoprotective, nephroprotective, and neuroprotective activities [19]. Figure 2.7 is a graphic abstract of TQ's therapeutic potentials.

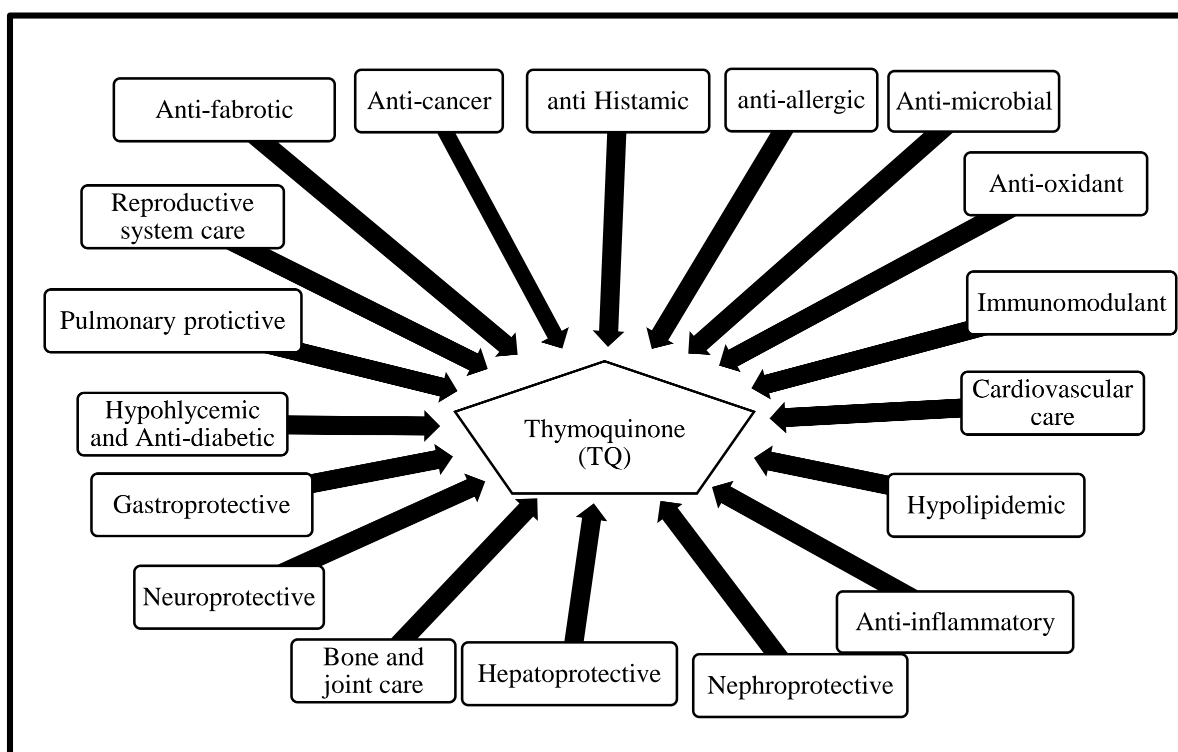

Figure 2.7: Therapeutic Potentials of TQ [19]

In 2016, a review by Amin and Hosseinzadeh stated that black seed and its primary active component, TQ, have been assigned to many pharmacological activities [159].

Black seed can be added to different types of food such as tea, coffee, casseroles, or breads, and used in canning. Additionally, its extract is used in wine [160].

Another herb, fenugreek (*Trigonella foenum graecum*), a legume seed that belongs to the Fabaceae family is widely cultivated and produced in Mediterranean countries and

Asia. Fenugreek seed is commonly used as medicine in India and Iran. A study published in 2007 examined the chemical composition of fenugreek and found that fenugreek composition was as follows: protein, 28.4%; crude fiber, 9.3%; crude fat, 7.1%; moisture, 6.87%; ash, 3.28%; and carbohydrate, 47.4% [161, 162]. Another study reported that it had 11.44% moisture, 3.9% ash, 27.57% protein, 6.71% fat, soluble dietary fiber 30.6%, and 20.6% insoluble dietary fiber [163]. Fenugreek is known to have pharmacological effects such as hypoglycemic, chemoprotective, antioxidant and hypolipidemic effects [20, 164-166] plus contains alkaloids, flavonoids, salicylate, and nicotinic acid as active compounds, and these give fenugreek its properties [167-169].

Jessie et al. tested the effects of commonly used herbs and spices on health using human and animal models. Saffron (*Crocus sativus*) was investigated in Jessie et al. study due to its hypoglycemic, hypolipidemic, and antioxidant properties. Kang et al. showed that saffron also increased glucose uptake and insulin sensitivity. Moreover, saffron was also reported to inhibit platelet aggregation and membrane lipid peroxidation in a study published by Samarghandian et al. [170-172].

A study by Mohammadi et al. in 2013 discussed the chemical composition of saffron. The results of the study were as follows: moisture, 12.50%; ash, 9.5%; crude fiber, 7.4%; crude fat, 5.8%; crude protein, 23.6%; and total carbohydrate; 20%. The study also reported that saffron is a decent minerals source, as it contained potassium (57, 460 ppm), magnesium (3, 357.5 ppm), sodium (1, 100 ppm), calcium (600 ppm), zinc (100.75 ppm), iron (194 ppm), copper (53.2 ppm), and manganese (48.5 ppm) [21].

Cardamom, is another commonly used spice that has been extensively investigation in the last few years. Cardamom is a recognized spice on the Indian subcontinent and is used for culinary and medical purposes [22, 141, 173]. In a study on rats, cardamom was reported to have an anti-hypercholesteremic influence [173] plus significant beneficial effects on cholesterol, but not on measures of oxidative stress, glycemic control, and inflammation [141]. A recent study reported that cardamom powder consumption protects against obesity, improves glucose levels, inflammation, and oxidative stress in the liver of high carbohydrate-high fat diet-induced obese rats [22] plus was active in improving the lipid profile in diabetic rats [174].

Furthermore, Pruthi et al. reported the chemical composition of large cardamom as follows: moisture, 8.49%; protein, 6%; total ash, 4%; crude fiber, 22% [175]. In comparison, small cardamom contains the following: moisture, 8.3%; protein, 10.3%; crude fiber, 9.2%; and total ash, 5% [176].

On the other hand, the essential oil of cloves (*Eugenia aromaticum*), which is isolated from the clove buds is widely used and well known for its medicinal properties. Cloves are used in the food industry because of their special aroma and their health benefits [177, 178]. Cloves can significantly reduce blood sugar and increase lipid peroxidation in diabetic rats [23] and reported to contain 5.98% protein, 20.04% fat, 61.22% carbohydrate, and 5.88% ash [179, 180]. Another study reported that cloves contains 12.1% moisture, 7.8% protein, 9.3% fat, 68.6% total carbohydrate, 1.1% crude fiber, and 1.1% total ash [181].

2.5.5 Effects of Ginger, Cinnamon and Black Seed on Metabolic Syndrome Risk Factors

2.5.5.1 Effect on Glycemic Control

A 2-month randomized double-blind placebo-controlled trial was conducted by Mahluji et al. on participants with type 2 diabetes mellitus to examine the effects of ginger powder on glycemic parameters, and the results showed that ginger significantly increased insulin sensitivity, but had no effect on FBG and HbA1c [182]. A meta-analysis concluded that ginger consumption in different forms (tablet, capsules, powder, or rhizomes) substantially lowered FBG and TG, and elevated HDL levels [183]. Another clinical trial tested the effects of 2 g of ginger powder on 40 women with obesity and their findings revealed ginger treatment had a non-significant reducing effect on serum glucose, slight positive effect of ginger powder consumption on serum glucose and significant effect on TG when compared to the placebo [184].

A study published in 2003 by Khan et al. examined the effects of cinnamon when given in three different doses for three different groups (group 1, 1 g/day; group 2, 3 g/day; and group 3, 6 g/day) of diabetic people for 40 days. The study showed that cinnamon powder decreased FBG levels significantly [144]. However, a 2008 meta-analysis of randomized controlled trials where cinnamon was administered concluded that the ingestion of cinnamon had no significant effect on improving HbA1c or FBG [185]. A meta-analysis for 10 randomized controlled trials that included a total of 543 diabetic patients showed that consuming cinnamon at a dose from 120 mg/day to 6 g/day for around 4 months causes a significant reduction in FBG levels [186].

Additionally, a study by Heshmati et al. reported that supplementation with black seed oil (3 g/day) significantly improved FBG, HbA1c, total cholesterol, TG, HDL, and

LDL levels in the blood in the treatment group when compared to the placebo group after 12 weeks of consumption [187]. Another study demonstrated that taking 2 g/day of black seeds for 3 months in individuals with type 2 diabetes mellitus decreased FBG, 2-hour post-prandial glucose (2-hPG), HbA1c, and increased insulin sensitivity without any renal or hepatic side effects [188]. Additionally, many researchers have reported that black seed has anti-diabetic and hypoglycemic activity because the components of black seed decreases oxidative stress and thus preserves pancreatic beta cell integrity [189].

2.5.5.2 Effect on Blood Pressure

A randomized controlled clinical trial was on individuals with type 2 diabetes who were randomly distributed to four interventional groups. Each intervention group received 3 g each of cinnamon, cardamom, and ginger powder and 1 g of saffron powder. The participants were asked to consume the spices with three glasses of black tea every day. The control group consumed only three glasses of tea without any spice powder for 8 weeks. The study showed that none of the spice powders had significant effect on improving blood pressure [141].

Torabi et al. concluded that ginger have no significant effect on blood pressure but also reported that ginger could be offered as a natural alternative dietary supplementation to anti-hypertensive factors in animal studies. Unfortunately, there is not enough evidence to support the same outcome in human studies [190, 191].

Furthermore, in a randomized, placebo-controlled, double-blind clinical trial, 58 individuals with type 2 diabetes were randomly assigned to consume either 2 g/day of cinnamon or placebo for 12 weeks and a significant decrease in systolic and diastolic

blood pressure was reported [192]. Similarly, a systematic review discussed the effects of cinnamon on blood pressure in individuals suffering from diabetes mellitus and reported that the short term consumption of cinnamon is linked to a significant decrease in systolic and diastolic blood pressure [193]. A double-blind randomized controlled trial by Datau et al. in 2010 enrolled 62 patients with MetS. The study stated that the supplementation with 3 g/day of black seed powder for 3 months significantly reduced systolic BP [194]. Additional evidence supports the positive effects of black seed on blood pressure. One hundred fifty-nine participants were assigned into two groups: 78 participants in the control group and 81 in the black seed group. The former group received two capsules daily for 6 weeks, each with 250 mg of black seed powder. Participants also received oral hypoglycemic and antihypertensive drugs with dietary modification including a low-fat diet and physical activity such as walking (60–90 minutes per day) on an empty stomach for 6 days every week. This intervention showed a significant decrease in blood pressure when compared to the placebo group [195]. Another study included patients with mild hypertension who were randomly assigned into three groups: placebo and two other test groups. One of the test groups received 100 mg and the other received 200 mg of black seed extract twice per day in the form of capsules for 8 weeks. Systolic and diastolic blood pressure were lowered significantly in a dose-dependent manner [196].

2.5.5.3 Effect on the Lipid Profile

In 2013, Mahluji published a randomized double-blind placebo-controlled trial and showed that ginger had significantly decreased LDL and TG in participants with type 2 diabetes mellitus [182]. A meta-analysis showed that ginger consumption (tablet, capsules, powder, or rhizomes) had a significant effect on decreasing TG and elevating

HDL [183]. Moreover, a randomized double-blinded placebo-controlled clinical trial examined the effects of 2 g/day of ginger powder on 40 women with obesity showed that ginger treatment significantly reduced TG levels in the blood compared with the placebo group [184]. Another randomized double blinded study examined the effects of 3 g of ginger powder for 45 days on patients with CVD in Iran, and concluded that ginger powder had significant effect of reducing in TG, cholesterol, LDL, and very low-density lipoprotein (VLDL) levels in the blood [197]. An earlier study that tested the effects of cinnamon given in three different doses people with diabetes for 40 days showed that cinnamon powder significantly decreased TG, LDL, and total cholesterol levels in the blood [144]. Additionally, amore recent meta-analysis established that cinnamon significantly lowered total cholesterol, LDL, and TG and improved HDL concentrations significantly while having no significant effect on HbA1c levels in the blood [186]. Similarly, another meta-analysis of randomized controlled trials of cinnamon was published by Baker et al. and concluded that cinnamon consumption did not improve any lipid parameters significantly [185].

Moreover, studies conducted by Heshmati and Namazi in 2015 showed that 1 g/day of black seed powder for 12 weeks increased HDL levels, and 2 g of black seed powder decreased total cholesterol, LDL concentrations, and TG levels. Additionally, increasing the dosage from 2 to 3 g/day did not further improve the lipid profile status. However, the most effective dose was between 2 g and 3 g per day to improve total cholesterol, TG, LDL, and HDL concentrations [198]. A randomized controlled trial by Ibrahim et al. in 2014 studied the effects of black seed consumption on menopausal women for 2 months. This study showed an improvement in the lipid profile (decrease in total cholesterol, LDL, and TG and an elevation in HDL) [199].

Additionally, a double-blind randomized controlled study was performed by Amin et al. (2015). The intervention group received 2 g/day of black seed for 4 weeks and showed a significant effect of black seed on lowering total cholesterol, LDL, and TG levels [140].

2.5.5.4 Effect on Weight and Waist Circumference

Mansour et al. examined the short-term effects of hot ginger beverages on feelings of satiety, energy expenditure, and metabolic risk factors in thirty men who were overweight. Ginger consumption in a beverage form had no significant effect on blood glucose, insulin, lipid profile, or inflammatory markers but improved thermogenesis and increased feeling of satiety suggesting a potential role of ginger consumption in managing weight [200]. Additionally, a randomized controlled clinical trial that examined the effects of each cinnamon, cardamom, saffron, and ginger powder for 8 weeks on diabetic individuals concluded that none of the spices powders had a significant effect on improving weight or WC [141]. Another study by Nayebifar et al. [201] tested the influence of ginger combined with high intensity training on inflammation on thirty healthy women who were overweight. Participants consumed 3 g/day of ginger in the first group; 3 g/d of ginger + high intensity training in the second, and the third group consumed 3 g/d of placebo + high intensity training for 10 weeks. This study showed that interval exercise, by itself or combined with a ginger supplement, improved the maximum oxygen consumption but did not significantly lower the body fat percentage or the waist-to-hip ratio [201]. Similarly, Whitfield et al. tested the effects of a cinnamon, chromium, and magnesium-formulated honey on blood glucose, weight, and lipid profile in individuals with diabetes [202]. After 40 days of the intervention, there was no difference in FBG or HbA1c, and no significant

improvement of the lipid profile or weight was reported, however, there was a tendency towards elevating HDL and lowering systolic blood pressure in the treatment group [202]. Additionally, a study in 2012 suggested that cinnamon could be an effective tool to moderate postprandial glucose in normal weight and obese adults, which will help in weight management [203]. Moreover, a 2008 study tested the effects of cinnamon on insulin sensitivity in diabetic adults. Significant improvement was reported in the FBG level, lipid profile, blood pressure, and body fat percentage and it elevated lean body mass for participants who consumed cinnamon when compared to the placebo group [158].

Datau et al. reported that the consumption of 3 g of black seeds in men with central obesity can significantly decrease waist circumference [194]. In this study, the subjects were divided into two groups: treatment and control. Both groups were evaluated weekly for 3 months. The study showed a significant decrease of WC when comparing to the placebo group [194]. Additionally, a double-blind randomized controlled trial by Amin et al. found that consuming 1.5 g/day of black seed powder for 4 weeks significantly reduced WC [140]. Furthermore, Shah et al. found that the consumption of 250 mg of black seeds for 6 weeks, along with dietary modification (cholesterol-free diet) and 60–90 minutes of walking 6 days per week provided protection against MetS and significantly lowered waist circumference [195]. A prospective randomized controlled study was carried out by Najmi et al. in 2008 on 60 participants with MetS to study the effects of 2.5 mL black seed oil twice per day along with atorvastatin 10 mg once a day for 6 weeks. This study proved that black seed oil was significantly effective in lowering weight and waist circumference of the participant who consumed the black seed oil when compared to the control group [16].

A review study by Qidwai and Ashfaq [204] reported that black seed does not have a direct effect on reducing body weight. However, it affects food intake via an anorexic effect that causes a reduction in the food consumption, and thereby a decrease in body weight [204]. A randomized, double-blind, placebo-controlled study by Heshmati et al. on patients with diabetes showed that the ingestion of 3 g/day of black seed oil for 12 weeks did not cause a significant change in body weight [187]. Another interventional prospective randomized controlled study was conducted by Haque et al. in 2011 on 161 participants. The participants were asked to take 2.5 mL of black seed twice a day for 6 weeks. The results showed that there was an improvement in some parameters including body weight and BMI in the treatment group and the placebo group, and the improvement was greater in the black seed group when compared to the placebo group [205]. Additionally, the results of the study of Najmi et al. in 2008 on 60 participants studied the effects of black seed oil on body weight, and the results showed a decrease in the body weight in both groups (the intervention and placebo). This proposes that the effect of black seed on reducing body weight is not significant [16].

2.6 Summary

MetS history, different definitions, diagnostic criteria, and methods of management and treatment were extensively reviewed in this chapter. The use of herbal therapy, chemical analysis of spices, and the active compounds in spices were also discussed. In conclusion, the effects of ginger, cinnamon, and black seed on parameters related to MetS and CVD are promising and controversial. Many studies are needed to confirm their effect in humans, especially studies related to MetS and CVD risk factors.

Chapter 3: Materials and Methods

3.1 Introduction

This chapter outlines and discusses the research design, methodology and analyses followed in the clinical trial presented in this dissertation. The purpose of the current study was to test the hypothesis that seven locally consumed spices have different nutrient composition and that consumption of ginger, cinnamon and black seed powder lowers the risk factors of metabolic syndrome and therefore decreases the risk of developing CVD. Two primary objectives were formulated for the study, the first objective is to determine the nutrient composition of seven commonly used spices, and the second objective is to assess the effects of three selected spices namely ginger, cinnamon and black seed powders on fasting blood glucose, Hb levels, HbA1c levels, blood pressure, blood lipid profile levels and waist circumference among participants at risk of CVD.

3.2 Ethical Approval

This study was carried out according to the Declaration of Helsinki guidelines. United Arab Emirates University Scientific Research Ethics Committee approved all procedures concerning human subjects (UAEU, Protocol Number: 15/22; Reference Number: DT/bb/15-22. Participants who approved to take part in the study were asked to sign a written informed consent in order to participate in the study.

3.3 Study Protocol

3.3.1 Nutrient Composition of Spices

3.3.1.1 Sample preparation

Seven locally consumed spices were purchased from the local market (Alyahar Market) in Al Ain city. The selected spices were: ginger (*Zingiber officinale*), cinnamon (*Cinnamomum*), black seed (*Nigella sativa*), fenugreek (*Trigonella foenum graecum*), cardamom (*Elettaria cardamomum*), cloves (*Eugenia aromaticum)* and saffron (*Crocus sativus*). Part of the purchased spices was used for the chemical analysis and the rest was used for the interventional study. Spices used for chemical analysis were purchased as a whole spice and were ground in the laboratory using a coffee and spices grinder machine (Moulinex Coffee Grinder, MC300161, France). Spices were prepared in triplicate for the proximate and micronutrient analyses.

3.3.1.2 Proximate Analysis

The seven spices were analyzed chemically according to the Association Official Analytical Chemist procedure (AOAC) [206] for their moisture, protein, fat, fiber and ash content according to the following procedures:

3.3.1.2.1 Moisture Content Determination

Oven drying was used to determine the moisture content of the seven spices. As water evaporates, it will leave the dry matter. The dry matter was used to calculate the moisture content. In order to calculate the dry matter, three aluminum dishes for each spice were dried at 105 °C for two hours and were placed in a desiccator to cool down, thus, avoiding any moisture from the room. After cooling, the electrical balance Scaltec® SBA 31 (Scaltec®Instruments, Heiligenstadt, Germany) was used to weigh

the dishes. 1 gram of each spice powder was weighed and spread uniformly in the aluminum dishes. By using a forced air drying oven Mommert® (Schutzart DIN 400-50-IP20, Schwabach, Germany) samples were dried for a further 16 hours at 105 °C ± 3 °C and then were returned to the desiccator to cool down to room temperature. Samples were weighed to the nearest 0.01 mg. The equations used to calculate the percentage of total dry matter and total moisture are in Table 3.1 [207].

Table 3.1: Proximate Analysis Equations

Component	Equation
% Total dry matter	$\frac{(weight\ of\ dry\ sample\ and\ dish\ in\ grams - weight\ of\ dish\ in\ grams)}{initial\ weight\ of\ sample\ in\ grams} \times 100$
% Total Moisture	$100 - \%\ Total\ dry\ matter$
% Ash	$\frac{(weight\ of\ crucible\ and\ ash\ in\ grams - weight\ of\ crucible\ in\ grams)}{weight\ of\ sample\ in\ grams} \times 100$
% Protein	$\%\ Nitrogen \times Protein\ factor\ (6.25)$
% Crude fat	$\frac{(weight\ of\ cup + fat\ residue\ in\ grams) - (weight\ of\ empty\ cup\ in\ grams)}{Initial\ sample\ weight\ in\ grams} \times 100$
% Carbohydrate	$100 - (\%\ total\ moisture + \%Ash + \%Protein + \%Crude\ fat + \%\ Total\ dietary\ Fiber)$

3.3.1.2.2 Ash Determination

Labeled ashing crucibles were placed in a forced air drying oven Mommert® (Schutzart DIN 400-50-IP20, city, country) at 500 °C for four hours, then placed in the desiccator to cool to room temperature after which they were weighed to the nearest 0.01 mg. Around 1 gram of the sample was weighed in the crucibles and placed in a muffle furnace oven (Carbolite ELM, 11/6) at 500 °C for four hours. The crucibles

were then allowed to cool to less than 200 °C and weighed to the nearest 0.01 mg. The equation used to calculate the percentage of ash is in Table 3.1 [208].

3.3.1.2.3 Protein Content Determination

The Kjeldahl method was applied to decide the nitrogen content in the spice samples. The protein content was estimated using a factor of 6.25. Using the Foss Tecator 2020 digester (Foss Tecator, Hoganas, Sweden) 0.5 gram of each sample was digested using 27 mL of H2SO4 (96%) and a catalyst (Kjedahl selenium tablets) in a digestion tube for 45 minutes at 410 °C. At the end of the digestion, nitrogen in the samples was converted to ammonia. Then, a Foss 2300 Kjeltec Analyzer Foss (Technologies Co., Ltd., Höganaös, Sweden) was used to determine ammonia and protein content in the samples [209-211]. The equation used to calculate the percentage of protein is detailed in Table 3.1 [212].

3.3.1.2.4 Fat Determination

Fat content was determined using Soxhlet extraction as recommended by AOAC [206]. The procedure starts by drying the extraction cups at 105 °C for two hours. After weighing the cups to the nearest 0.01 mg, two grams of each sample were positioned in a 33 mm × 80 mm extraction thimble and extracted with 50 mL n-hexane/acetone (1:1, v/v) in boiling solvent for one hour using the Soxhlet extraction in a Sotex system 2050 (Foss, Hillerod, Denemark). Thimbles were left to allow for maximum evaporation of the solvent, meanwhile the extraction cups were removed from the extractor to be placed in a fume hood to permit the solvent to evaporate at low temperature. After evaporation, the extraction cups were placed in an oven to be dried at 105 °C for 30 minutes, then were let to cool to reach room temperature in the

desiccator to be weighed afterwards to the nearest 0.01 mg [213]. The equation used to determine percentage of crude fat is listed in Table 3.1 [206].

3.3.1.2.5 Fiber Content Determination

The ANKOMTDF Dietary Fiber Analyzer (Dietary Fiber Analyzer, ANKOM, Macedon NY, USA, Figure 3.1) was used to measure the fiber content of each spice, using the AOAC 991.43 TDF method [206], and following the procedure listed in previous research [214]. ANKOM filter bags (DF-S, DF-FT, ANKOM Technology) were used to analyze dietary fiber. The bags were labeled, weighed and then placed in the ANKOM dietary fiber analyzer to begin the analysis. Filter bags were rinsed with acetone solution and left to dry thoroughly. Once the filtered bags were dry, they were sealed with a heat sealer (1915, ANKOM Technology) and placed in an oven at 105 °C for 90 minutes. Afterwards, their weight was recorded to the nearest 0.01 mg. One filtered sealed bag of each spice sample was sent for the protein content determination and another one was sent for the ash content determination. The percentage of total dietary fiber content was decided using the dietary fiber data spreadsheets provided by the manufacturer on the ANKOM Technology website [215].

Figure 3.1: ANKOMTDF Dietary Fiber Analyzer (Dietary Fiber Analyzer, ANKOM, Macedon NY, USA)

3.3.1.2.6 Carbohydrate Content Determination

After the calculation of all other components, the carbohydrate content was calculated by subtracting the mean percentage values of the sum of moisture, ash, protein, lipids, and dietary fiber from 100 as shown in Table 3.1.

3.3.1.2.7 Energy Calculation

The energy content of the spice samples were calculated according to Atwater's plan [216], as this method was used in literature and considered most suitable for the calculation of the energy content of the spices [153, 217, 218]. Energy content was calculated by multiplying the percentage of protein with 4, carbohydrate percentage

with 4 and fat percentage with 9. Then, values were converted to kilo calories per 100 gm of the sample weight.

Energy content = (protein%*4) + (carbohydrate%*4) + (fat%*9)

3.3.1.3 Mineral Content Determination

The procedure for measuring minerals in plants and spices by Inductively Coupled Plasma Optical Emission Spectrometer (ICP-OES) was followed for the micronutrient analysis of the spices [219].

The CEM Mars 5 microwave digestion method (Mars5, CEM, Matthews, USA) was used for elements extraction from the spice samples. The procedure of digestion was founded upon the USEPA method 3015A guidelines recommendations [219]. This microwave digestion method was designed to simulate extraction using conventional heating with nitric acid and hydrochloric acid. The spice samples were accurately prepared by placing a weighed 0.50 grams of sample into the microwave digestion vessels, then 10 mL of concentrated nitric acid and 2 mL hydrochloric acid were added. The vessels were capped and placed in the microwave digestion system. After the digestion and cooling the samples to room temperature, de-ionized water was added to the sample solution to reach 50 mL. It was then aspirated through a nebulizer. The resulting solution was transported to a plasma torch for excitation [220].

Element specific emission spectra were produced by radio-frequency inductively coupled plasma. The spectra were detached by a grating spectrometer, and intensities of the line spectra were monitored at specific wavelengths by a charged coupled detector.

A fitted background correction was used to correct the blank signal and matrix effect. Background correction was not required in case of line broadening where a background correction measurement would actually degrade the analytical result. The machine used for the analysis was an Inductively Coupled Plasma - Optical Emission Spectrometer (ICP-OES) (710-ES, Varian, USA).

3.3.1.4 Sugar Content Determination

High-performance liquid chromatography (HPLC) (Waters, Milford, MA, USA) was used to determine monosaccharides, disaccharides and trisaccharides. Sample preparation and the analysis procedure were adopted with slight modification from the research of J.S Smith et al. and Yuan et al. [221, 222]. HPLC was equipped with Binary pump 1525, auto injector /auto sampler waters 717 plus and Refractive Index Detector 2414. The chromatographic separation was achieved using column oven model code LAC and Column µ Bondapak NH2 10 µm, 125 A°, 3.9 *300 mm (Waters Associates, Milford, MA, USA). The mobile phase consisted of acetonitrile and water (83:17, v/v), while the flow rate was 1.5 mL/minute and the temperature was kept at 35 °C.

3.3.1.5 Lipid Content Determination

Fatty acid composition analysis was carried out using a Young Lin 6500 gas chromatograph (YL-6500 GC, Gyeonggi-do, South Korea, Figure 3.2), fitted with a SP-2380 Fused Silica Capillary Column (30 m × 0.25 mm I.D × 0.20 µ film (2-4110), Sigma Aldrich, St. Louis, MO). The analytical column was heated at 50 °C for two minutes. Then it was raised to 250 °C at 4 °C/minute, and held for 15 minutes. Helium was the carrier gas used for analysis, (20 cm/second) at 150 °C. The Supelco 37 constituent Fatty Acid Methyl Esters (FAME) mix standard was utilized for the recognition of key fatty acids in the spice samples. The Fatty Acid Methyl Esters

(FAMEs) were prepared following AOAC Method 969.33 [206]. The analysis procedure followed was as described in the application notes of the manufacture (Sigma Aldrich) [223].

HPLC (Waters, Milford, MA, USA) was estimate to calculate the cholesterol content. The HPLC system is composed of a Waters 2487 Dual λ Absorbance Detector, operated with Breeze software. Cholesterol was analyzed in to a reversed phase XTerra C18 column, 4.6 mm inner diameter by 150 mm, 5 μm (Waters Associates, Milford, MA, USA). The mobile phase consisted of methanol and 2-propanol (70:30, v/v), and the flow rate was set at 1.0 mL/minutes, while the oven temperature was kept at 25 °C. An ultra violet (UV) detector was used to detect cholesterol, the UV detector wavelength was of 212 nm [224, 225].

Figure 3.2: Young Lin 6500 Gas Chromatograph (YL-6500 GC, Gyeonggi-do, South Korea)

3.3.1.6 Water Soluble Vitamin Determination

Seven water soluble vitamins were analyzed using HPLC (Walters, Milford, MA, USA) [226]. The system was equipped with a binary pump 1525, auto injector /auto sampler Waters 717 plus and Dual λ absorbance Detector 2487. The chromatographic separation was achieved using Column XTeera C18 (4.6 * 150 mm, 5 μm) from Waters (Walters Associates, Milford, MA, USA). The mobile phase consisted of 50 mM K_2HPO_4 (pH7): methanol, gradient: 1% methanol for five minutes, 1-30% methanol (liner gradient) over 15 minutes, 30% methanol for five minutes with flow rate of 1.0 mL/minute. The column temperature was kept at 35 °C, and the injected volume was 10 μl. The analytical column effluents were monitored at a wavelength of 220 nm as recommended by Supelco Application Note 148 [227].

3.3.1.7 Fat Soluble Vitamin Determination

Waters ACQUITY UPLC system (Waters, Milford, MA, USA) was used to analyze fat soluble vitamins. The system operated by Empower software, is composed of three main parts: ACQUITY sample manager, ACQUITY binary solnet manager and ACQUITY PDA eλ detector. The concept of fat soluble analysis was based on a reversed-phase ACQUITY BEH C18 column (2.1 mm inner diameter by 100 mm, 1.7 μm) from Waters (Waters Associates, Milford, MA, USA).

The temperature was set at 35 °C. The mobile phase consisted of solvent A:Water: Acetonitrile (90:10), and solvent B: methanol and acetonitrile (50:50, v/v). A flow rate of 0.7 mL/minute and injection volume of 5 μl was used. For vitamin E, the analytical column effluents were monitored at a wavelength of 285 nm. For vitamin K1, K2, D2, D3 it was kept at a wavelength of 265 nm and at 325 nm for vitamin A acetate [228].

3.3.1.8 Caffeine Content Determination

The analysis of caffeine method was adopted from previous research published by Erickson et al. with modification to adapt to the equipment available in the laboratory [229]. HPLC (Waters, Milford, MA, USA) was utilized to estimate the caffeine content in the spices. HPLC was equipped with a binary pump 1525, auto injector /auto sampler waters 717 plus and Dual λ absorbance detector 2487. The chromatographic separation was achieved using the Column XTeera C18 column (4.6 * 150 mm, 5 µm) from Waters (Waters Associates, Milford, MA, USA) and was operated with Breeze software. The mobile phase consisted of acetonitrile and water (10:90, v/v), and the flow rate was 1.0 mL/minute. An UV detector was used to detect caffeine and was set at a wave length of 265 nm.

3.3.1.9 Shogoals, Gingerols and Curcumin Content Determination in Ginger Powder

Gingerols are thermally unstable and could form many derivatives at high temperatures, during gas chromatograph. HPLC is the most favored method for a more accurate analysis of gingerols. It does not involve high temperature during the analysis of gingerols.

HPLC was used to determine the 6-gingerol content in the spice powders (Waters, Milford, MA, USA). The 6-gingerol standard was dried over silica gel for three hours. Then, sufficient HPLC-grade methanol was added to 5 mg of 6-gingerol standard to produce a solution of 1000 µg/mL. Serial dilutions of the solution were made to produce different working standards ranging from 1 to 750 µg/mL. All 6-gingerol standards were capped and stored at 4 °C. An Inertsil ODS-3 column with a dimension of 250 x 4.6 mm, 5-µm particles was used (Waters Associates, Milford, MA, USA).

The mobile phase consisted of methanol: water was run for five minutes at a flow rate of 1 mL/min, while the PDA detector was set at a wavelength of 282 nm. The method was adopted from previous research with modifications [230].

Shogoals are derivatives of gengerols and are more thermally stable. Shogoals form after gengerols undergo changes under heat and they are much more pungent than gengerols [231, 232]. GC (YL-6500 GC, Gyeonggi-do, South Korea) was used to determine the shogoals content in the ginger powder. After the extraction of ginger oil, its analysis was carried out using a Shimadzu GC-2010 gas chromatograph equipped with QP 2010 mass spectrometer and RTX–5 column (30 m × 0.25 mm, 0.25 μm). At a flow rate of 1.67 mL/min, helium was used as the carrier gas. The injection port was 250 °C and the detector temperature was 220 °C. Meanwhile, the oven temperature was 60 °C for 5 min and then the temperature was elevated to 110 °C at the rate of 5 °C /min, then increased to 170 °C at the rate of 3 °C/min and finally to 220 °C at the rate of 5 °C/min. The split ratio was 1:40 and ionization energy 70 eV. The preparation of the ginger sample and the determination of shogoals in ginger method, was adopted with modifications from the research of Kizhakkayil et. al. [233].

Curcumin was determined in ginger using HPLC (Waters, Milford, MA, USA). The isocratic reversed HPLC method using RP C18 column, was used for the simultaneous determination of the curcumin in the ginger powder. The mobile phase consisted of acetonitrile: 0.1% trifluro-acetic acid (50:50). The flow rate was 1.5 mL/min and elution was monitored at a wave length of 420 nm.

3.4 Statistical Analysis

Statistical Package for Social Sciences (SPSS) version 23.0 (IBM Corp, Armonk, NY, USA) for windows was used for the analysis of the nutrient composition data. Kruskal Wallis test was used to carry out the analysis of the data as it is considered the nonparametric alternative to the ANOVA test. Kruskal Wallis test was used for comparison of medians of measurements of macronutrients and micronutrients of the spices due to the lack of normality assumption of ANOVA. Statistical analysis was set at P-value of <0.05.

3.5 Intervention Study

3.5.1 Study Population

The study was a controlled, randomized, single blind, parallel-design study conducted during the academic year 2015/2016 at United Arab Emirates University (UAEU) in Al Ain, United Arab Emirates. The study population included UAEU students, staff and faculty members aged between 18 and 50 years, who were at risk of metabolic syndrome or had metabolic syndrome. Participants were recruited through face-to-face interviews, printed advertisements and via email to voluntarily participate in the study. Participants who agreed to participate were asked to read the study information sheet thoroughly and all their questions that are related to the study were answered before taking part.

A total of 372 participants who showed interest in the study were initially screened for eligibility at the Nutrition Clinic of UAEU. 252 out of these were excluded from the study for the following reasons: 203 did not meet the metabolic syndrome diagnostic criteria nor were at risk for developing metabolic syndrome, 12 were smokers, 6 were

pregnant or lactating, 3 had a liver or kidney diseases, 7 were on a strict diet, 1 was bulimic, 9 did not want to sign the consent form and 11 refused to give blood sample. Therefore, the final number of participants was 120 between the age of 18 and 50 years old (Figure 3.3).

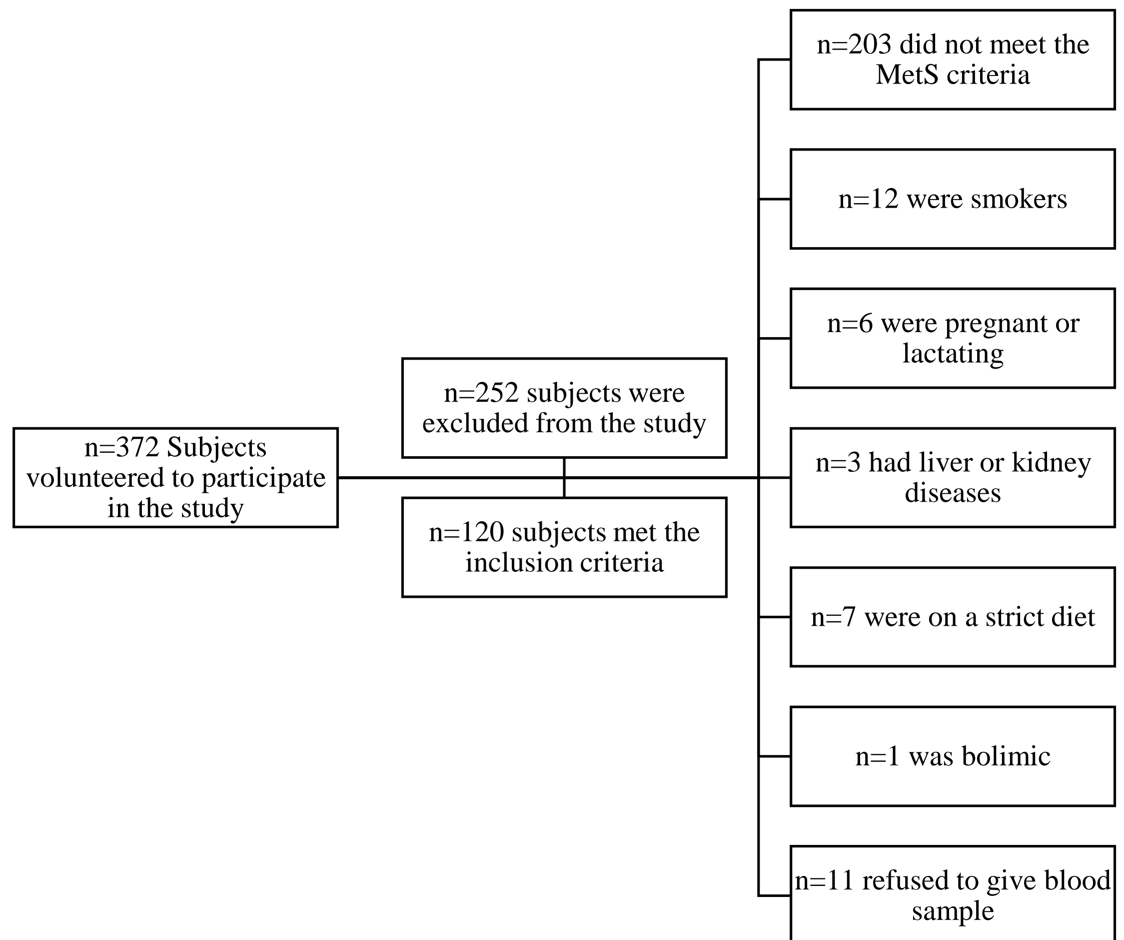

Figure 3.3: Number of Participants who were Excluded from the Study

An identification number was allocated to each participant to preserve anonymity, which confirmed confidentiality and helped link the participant to their clinical measurements and blood samples. Only cumulative data was reported to protect the privacy of all participants.

3.5.2 Inclusion and Exclusion Criteria

Participants were considered eligible to take part in the study after meeting the following inclusion criteria: age (18-50 years) and had 2 or more of MetS diagnostic criteria; high waist circumference (>80 cm for female and >94 cm for males), elevated blood pressure (equal to or greater than 130/85 mm Hg or use of medication for hypertension), high fasting blood glucose (equal to or greater than 100 mg/dL {5.6 mmol/L} or use of medication for hyperglycemia), lowered HDL cholesterol (less than 40 mg/dL {1.03 mmol/L} for men and less than 50 mg/dL {1.29 mmol/L} for women) and increased triglycerides (equal to or greater than 150 mg/dL {1.7 mmol/L}). Participants who had at least three risk factors out of five, or had two risk factors and one in the borderline level were included in the study.

Participants were excluded if they did not meet the following inclusion criteria, older than 50 years old or younger than 17 years old and did not meet the metabolic syndrome diagnostic criteria. Moreover, participants were excluded if they were allergic to spices, current smokers, pregnant or lactating women, currently taking medication or if they refused to provide a blood sample. Also, participants with any acute illnesses or any chronic diseases such as; kidney, liver, cardiovascular and gastrointestinal diseases were excluded from the study. During the study period, participants were asked to bring the remaining spice powder to each visit. The amount left was calculated to make sure that the participants have consumed 80% of the total amount or more. Those who consumed less than 80% of the treatment powder were excluded from the study.

3.5.3 Screening Measurements

To ensure that the selected study population was eligible to participate in the study, screening measurements were conducted for the MetS diagnostic criteria including: blood pressure (BP), waist circumference (WC), fasting blood glucose (FBG), high density lipoprotein (HDL) and triglycerides (TG). Figure 3.4 illustrate the screening measurement of the study.

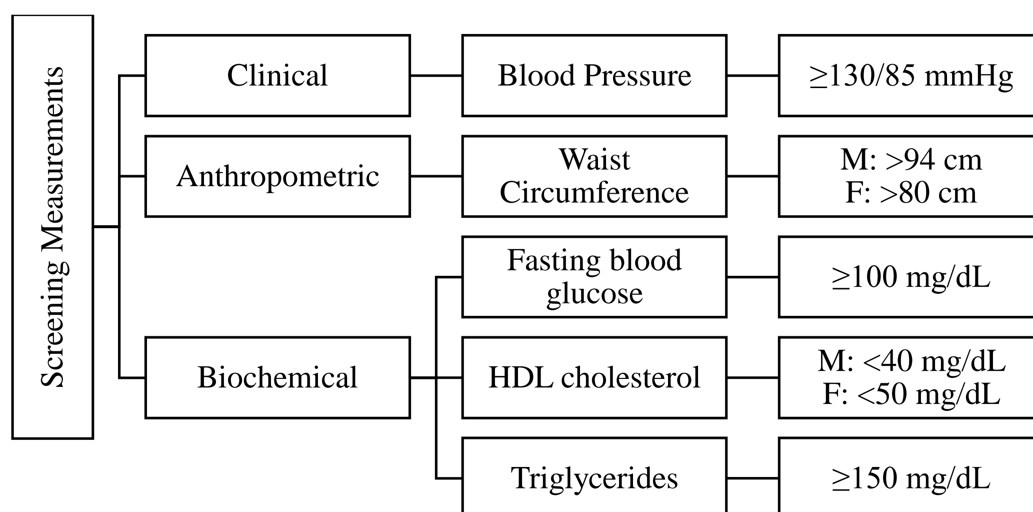

Figure 3.4: Screening Measurement of the Intervention

In addition, participants were asked to fill a health screening questionnaire which contains questions about medical conditions and medications that might influence glucose regulations, appetite and energy expenditure (Appendix 1).

Of the 120 participants, 18 were excluded from the study due to failing to comply with the study requirements: consuming less than 80% of the allocated powder amount, dieting, increasing their physical activity levels and 5 dropped out from the study for personal reasons. A total of 97 participants completed the 12-week intervention.

Participants were divided into control (n=30), ginger (n=30), cinnamon (n=30) and black seed (n=30) as shown in Figure 3.5.

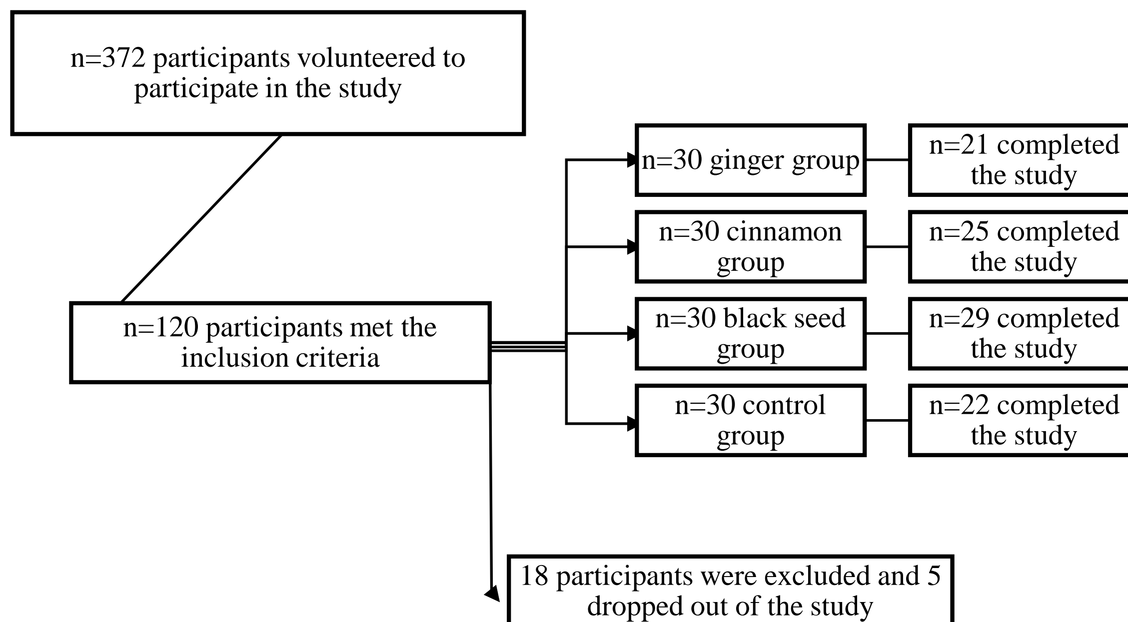

Figure 3.5: Number of Participants during Screening and Intervention

3.5.4 Intervention Study Protocol

A 12-week clinical randomized intervention was conducted by comparing participants from three treatment groups (ginger, cinnamon and black seed) with those from the control group (placebo). Participants were divided randomly into four groups; participants were asked to consume three grams per day, on separate occasion, of the allocated spice or corn starch powder for 12 weeks. In a normal day, each participant was asked to consume one gram in the morning, one gram at the middle of the day and one gram at the end of the day, preferably with hot water. This was recommended to eliminate heartburn or any gastrointestinal irritation that may result from the consumption of high dose of spices. As not all participants liked the pungent taste and smell of some spices like the ginger, it was recommended to consume the spice powder

combined with a hot beverage, or to be added to their favorite. Participants were asked not to change any of their dietary or physical activity habits through the study period. Data were collected from participants at three points: baseline, at midpoint (sixth weeks) and at endpoint (twelfth weeks) of the study period. Midpoint collection of data was considered to ensure participant's compliance to the study protocol and to follow up their progress and feedback.

Three spices out of the seven analyzed spices were used for the intervention (ginger, cinnamon and black seed). The three studied spices were chosen due to the fact that fenugreek consumption could lead to undesirable body odor, along with the highly expensive price of saffron. Therefore, fenugreek and saffron were eliminated to increase the enrollment rate of participant and to meet the study budget. Accordingly, 3 spices were chosen among the remaining spices (5 in total), taking into consideration the research budget limitation. In contrast, corn starch was used as a placebo for the control group to eliminate the psychological factor [234].

The spices were purchased from a local spices shop in Al Ain city (Alyahar Market), with the whole amount purchased at once to minimize any error. Part of the purchased spices was used for the chemical analysis and the rest was used for the interventional study. Spices were freshly ground into a powder for the intervention study. Pure corn starch powder was purchased from a local supermarket in 400 g packages.

In a clean and sanitized area, spices powder and starch powder were weighted into one gram portions and were packed in small zip lock plastic bags for the convenience of the participant's usage. Each participant received 300 grams of each powder (3 g/day * 7 days/week * 12 weeks of the intervention=252 g and by adding 20% of the amount (50 g) the total amount was 300 g).

Once participants met all of the inclusion criteria, they were asked to maintain the same dietary habits and physical activity levels for 12 weeks. They were asked to record their dietary intake using a three-day food record (Appendix 2) and to report their physical activity level by using the International Physical Activity Questionnaire (IPAQ) (Appendix 3). The mentioned records were submitted by participants at each visit to ensure that there were no changes on dietary and physical activity habits introduced through the study period.

3.5.5 Anthropometric Measurements

Anthropometric measurements are a practical to evaluate the development of human body through various ages, as it provides an evaluation of nutritional and health status of population groups [235]. Anthropometric indicators may not be as accurate as clinical and biochemical techniques. However, they provide important participant information regarding undernutrition and overweight/obesity, and also contribute to the development of proper food and nutrition policies [236]. Anthropometric measurements includes the measurement of the physical properties of the human body. These physical descriptions include body size, shape and body composition [237, 238].

All anthropometric measures in this research were taken in a 30-minute visit at each of baseline, midpoint and endpoint of the study period. All measures were taken by a trained and skillful researcher who had a received a training on anthropometric measurements. Participants were asked to attend each visit in a fasted state for 10-12 hours prior to testing. Readings of measures were recorded in triplicate immediately and the average of the three readings was calculated and used in the study. Measures included: height, weight, body composition and waist circumference. Cognizant of culture norms, anthropometric measurements were taken with participants wearing

minimal clothes and with no shoes on. Daily calibration of all the devices helped to insure the precision of data.

At each visit, participants were asked to rest for 15 minutes to relax and to adjust to climatic changes. During this period, participants were asked to complete a physical activity questionnaire with a research assistance available to clarify and answer any questions.

3.5.5.1 Height

The measurement of height considered to be one of the heritable human traits. Fetal growth, nutrition and infections during childhood and adolescence are essential factors of height variations during adulthood [239].

Data collected of height and height trends can assist the understanding of health impacts during human life cycle and its relation to nutrition [240]. Height was collected in many previous research projects to assist the development of human body as it provides an evaluation of nutritional and health status of population groups [241, 242].

In this study, height was recorded to the nearest centimeter using a Stadiometer (Seca Stadiometer, Seca Ltd, Birmingham, UK), with participants standing straight and without wearing shoes, heavy outer garments, hair cover or hair accessories were removed. Taking into account that the posture of the participants at the time of measurement may influence the accuracy of the measurement, each participant stood erect with their head in the Frankfort plane with ears and cheekbones at the same level, and the arms at the sides, feet positioned close together, knees straight, heels, buttocks,

and shoulder blades touching the vertical surface of the stadiometer as recommended by the WHO STEPS protocol [243].

3.5.5.2 Body Weight and Composition

Body weight and body composition varies between individuals and across population. Weight measurement and body composition were considered to be a tool for assessing health risk factors [244]. Since, obesity has appeared as a main public health concern, weight measurement is needed to assess obesity and to calculate body mass index (BMI). Previous studies evaluated the connection between body weight and body composition in relation to cardiovascular diseases and related higher weigh and higher fat composition to cardiovascular diseases [245-247].

In this study, body weight and body composition were recorded to the nearest 0.1 kg using the InBody 270 (Body Composition Analyzer) and body composition was measured using the Hologic Discovery Dual energy X-ray Absorptiometry (DXA) system, with participants wearing light clothing (due to cultural limits) and with no shoes or socks on.

The InBody 270 (InBody Ltd., Seoul, South Korea) is a non-invasive body composition analyzer that delivers a comprehensive breakdown of body weight in terms of muscle, fat, and water. The device predicts body weight, fat percentages, fat mass, fat free mass, skeletal muscle mass and body water by measuring the resistance of a small, water- accompanied electrical signal that is sent through the body. InBody 270 scale considers individual's age, height, weight and gender to estimate body composition [248].

Participants were asked to stand unassisted on the weighing platform (with no shoes or socks on), place their heels on the posterior electrodes, and the front part of the feet in contact with the anterior electrodes. Participants were asked to hold the grips with both hands and wait 15-120 seconds until the device competed the measurement.

DXA Hologic Discovery (Hologic Ltd., Toronto Ontario, Canada) is an advanced body composition assessment device that is considered tehe golden standard in measuring body composition. DXA produces color images of lean mass, bone and fat mass. This information is provided in a report for enhanced patient management and counseling. Moreover, DXA system proposes one of the latest innovations in bone densitometry technology as it uses the one pass single sweep scanning [249]. DXA system was calibrated every time before usage to insure maximum precision.

A certified radiology technologist conducted all DXA Hologic Discovery measurements. Participants were asked to remove all objects from pockets (e.g., wallet, cell phones, keys). False teeth, hearing aids, jewelry, and watches did not have to be removed. Before moving the table control arm (C-Arm), the runner area of the table and the table scan area were cleared of objects that might interfere with table movement.

Women that met the inclusion criteria were asked to take a pregnancy test and to self-report that they were not pregnant. If they were pregnant they were automatically excluded from the study for the safety of the embryo.

3.5.5.3 BMI Calculation

Body mass index (BMI) is derived from the individual's weight and height in attempt to classify each individual weight to height distribution [250] and used as a tool to screen populations for relative weight status [251].

BMI was calculated from weight and height using the following formula: (weight (kg)/height (m^2)) [252]. Table 3.2 list the classification of BMI.

Table 3.2: BMI Classification [264]

Category	**BMI range – kg/m^2**
Very severely underweight	less than 15
Severely underweight	from 15.0 to 16.0
Underweight	from 16.0 to 18.5
Normal (healthy weight)	from 18.5 to 25
Overweight	from 25 to 30
Obese Class I (Moderately obese)	from 30 to 35
Obese Class II (Severely obese)	from 35 to 40
Obese Class III (Very severely obese)	over 40

3.5.5.4 Waist Circumference

WC is considered to be the best tool to predict abdominal visceral obesity [253] and a high waist circumference denotes an increased risk for CVD [254]. A study published in 2004 concluded that WC is a better tool than BMI to explain obesity-related health risks [255]. Another research recommended the use of WC in health promotion programs to recognize individuals who should pursue help in managing their weight

[256]. Waist circumference cutoff points as reported by IDF, AHA/NHLBI are >80 cm for female and >94 cm for males Caucasian [257].

Measurement of WC was carried out using a stretch resistant tape that provides a constant 100 g of tension and was recorded to the nearest centimeter. Participants were asked to stand up right with the arms at the sides, feet positioned close together and weight equally distributed on the feet. The tape was placed at the approximate midpoint between the lower margin of the last palpable rib and the top superior border of the iliac crest or at umbilicus level for participants with obesity. The WHO STEPS protocol states that the tape should be snug around the body, but not pulled so tight that it is constricting [243]. Three measurements were obtained and the average of the two readings were recorded.

3.5.6 Diet and Physical Activity Assessment

3.5.6.1 Dietary Assessment

Participants were asked to maintain their dietary habits during the 12 weeks of the study. A three-day food record was collected from each participant on each visit (baseline, midpoint and endpoint), providing nine days of food records for each participant. At the beginning of the study, the researcher sat with each participant and demonstrated on how to fill the food record using food models, visual aids and measurements tools.

Details of the food and drinks consumed were very important. Participants were taught how to record their three day food record, accurately and in detail (example: brand name, fat percentage, fortification, etc.). Food records were analyzed carefully using Food Processor Nutrition Analysis software (ESHA). When traditional Emirati and

local food were consumed, Emirati and Kuwaiti food composition table were used [258].

3.5.6.2 Physical Activity Assessment

Participants were asked sustain their physical activity habits through the study. A physical activity questionnaire was collected from each participant on each visit. The International Physical Activity Questionnaire (IPAQ) was used to monitor physical activity habits during the study period. IPAQ was developed to be an international measure for physical activity. It started in Geneva in 1998, the IPAQ was followed by a wide reliability and validity testing that took place in 12 countries (14 sites) during year of 2000 [259]. The instrument evaluates total physical activity where the recommendations are based on activity (leisure-time or recreational) over and above typical individual activities. This suggests that IPAQ is the best tool available at present to measure physical activity level. Total duration and the number of day/sessions are to be recorded in the IPAQ. Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ) were used to analyze the IPAQ [260]. Three levels of physical activity are proposed for categorizing population activity as described in Table 3.3.

Table 3.3: Physical Activity Category Classification

Physical activity category	**Inactive (category 1)**	**Minimally active (category 2)**	**Health enhancing physical activity (HEPA) (category 3)**
Category characteristics	a) No activity is reported, OR	a) 3 or more days of vigorous activity of at least 20 minutes per day, OR	a) vigorous-intensity activity on at least 3 days achieving a minimum of at least 1500MET -minutes/week OR
	b) Some activity is reported but not enough to meet category 2 or 3	b) 5 or more days of moderate-intensity activity or walking of at least 30 minutes per day, OR	b) 7 or more days of any combination of walking, moderate-intensity or vigorous
		c) 5 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least	intensity activities to achieve a minimum of at least 3000 MET-minutes/week
Category characteristics		600 multiples of the resting metabolic rate (MET) -min/week.	

3.5.7 Biochemical Parameters

Nutritional status evaluation is crucial for all dietary and nutritional interventions. Evaluation of nutritional status constitutes a combination of data which includes clinical evaluation, dietary history, anthropometric evaluation and biochemical evaluation [261]. Biochemical measures have the potential of providing the most neutral and quantitative assessment of the nutritional status [262]. In order to collect such quality of information about nutritional status, biological fluids (urine or blood) must be collected [263].

All instruments used in the current research project were calibrated (if needed) and daily checked for correction before use. Therefore, a higher level of sensitivity, accuracy and a better reproducibility in analyzing the biochemical parameters was granted

3.5.7.1 Blood Collection

In this research, two methods of blood collection were followed, and blood collection was undertaken after 10 - 12 hours of fasting. The first is the finger-prick (capillary blood) method with fresh capillary blood used immediately after collection to measure TG and HDL using Reflotron® Plus Dry - chemistry analyzer (Roche® Diagnistics GmbH, Mannheim, Germany) during the screening measurements. Fresh Ethylene diamine tetraacetic acid (EDTA) plasma was used immediately after capillary blood collection and centrifusion was completed to measure the high density lipoprotein (HDL). Furthermore, capillary blood was used to measure hemoglobin (Hb) and glycated hemoglobin (HbA1c) during the study period.

Finger pricks were collected by a registered phlebolomist according to the WHO guidelines on drawing blood [264]. The hand of the participant was positioned with the palm-side up and the fingertip of the ring, middle, index finger or thumb was chosen for the prick: whichever had the least hardened skin. The fingertip was cleaned with alcohol before pricking and pressure was applied to the finger to assist blood flow. The registered nurse collecting the blood sample, started in the middle and worked the finger to the fingertip not to re-contaminate the area. The finger was air dried. A new sterile lancet (Life scan- Johnson and Johnson®, One touch, Ultra soft, UK) was used for each person. Each new lancet shown to the participants for reassurance. The lancet was placed off-center on the fingertip and pressed firmly to puncture the skin. Each lancet was disposed of in a biohazard sharps container. The first drop of blood was wiped with a disinfected cotton ball. To assist the blood flow, sometimes the finger was held lower than the elbow, following this, the blood drop was collected for analysis.

The second form of blood collection was the vinous blood collection (5 mL). A registered phlebotomist collected the blood samples in a selected clean area using a sterile butterfly needle and winged bonded to a flexible tubing with a luer connector (Vacuette®, 2015, Bangnomko, Thailand) was used each time to withdraw blood. A blood sample was collected from participants after a 10 - 12 hours of fasting in a vacutainer yellow tube 5 mL (Vacutainer®, 2014, UK) with clot activator and gel for serum separation. Two drops of the collected vinous blood (8 μ) was used to analyze hemoglobin (Hb) and glycated hemoglobin (HbA1c). The used needles were disposed in a biohazard sharps container. Sterilized nitrile powder free gloves were worn at all times during venipuncture to minimize exposure hazard and to assure sterilized environment.

After blood collection, tubes were placed in a centrifuge (Heraeus®, Biofuge Primo R, Kendro, Germany) with 1500 round per minute for 15 minutes, the serum was collected from the blood tubes and placed in triplicates in a 1 mL Eppendorf tube (eppendorf®, Safe- Lock micro test, 2015, Hamburg, Germany). Eppendorf tubes were identified using participant identification numbers and then placed in a -80 freezing system. To analyze the samples, they were thawed in ice at room temperature (25 °C) for 30 minutes before processing.

3.5.7.2 Analytical System

Reflotron® Plus Dry - chemistry analyzer (Roche® Diagnistics GmbH, Mannheim, Germany) was used to analyze TG and HDL during participant screening, while HemoCue® Glucose 201+ System (Hemocue, Dongan-gu, Korea) was utilized to assess FBG.

The Refletron® Plus Dry is an in vitro diagnostic device designed to quantitatively determine clinical chemical parameters. Reflotron® test reagent strips are used to assess the chemical measurements. Reflotron® Plus Dry uses whole blood (vinous or capillary), plasma and serum. As for this study, capillary blood was collected. A 32 µl capillary tube was inserted to an applicator device and was used to collect blood sample, then was placed directly over the pad of the desired test strip and the plunger was pushed down gently to eject the blood sample on the strip. Refletron®'s test strip was then immediately inserted into the measuring chamber and a measurement appears on the device monitor screen after three minutes.

Since Refletron® HDL analysis requires EDTA plasma, capillary blood was collected (0.8 mL) in a 1 mL Eppendorf tube (eppendorf®, Safe- Lock micro test, 2015, Hamburg, Germany) and centrifuged in a Spectrum® Mini Centrifuge (Spectrum

Chemical MFG CORP, NY, USA) 6000 round per minute. Whole EDTA plasma was applied to the reagent strip, LDL fractions were precipitated by means of magnesium ions and dextram sulphate to conduct the test. Daily maintenance of Refletron® was done using Clean and Check strips and no calibration was required.

The HemoCue Glucose 201+ System is based on glucose dehydrogenase method. A small analyzer and a disposable microcuvette are the two constitutes of the system. HemoCue Glucose 201+ microcuvettes (Hemocue, Dongan-gu, Korea) serves as a pipette and as a measuring microcuvette capillary blood (5 μL) was collected in the cavity of HemoCue Glucose 201+ microcuvette for analysis. HemoCue Glucose 201+ is factory calibrated and requires no extra calibration and no coding. Reading of the measurement appeared on the device monitor screen after 40 seconds to 4 minutes.

Hemoglobin (Hb) was analyzed using the HemoCue® Hb 201+ System (HemoCue® Ltd, UK,). In order to perform a test, whole blood (4 μL) was loaded into the HemoCue Hb 201+ microcuvette's cavity, in one continuous process. All excess blood outside was wiped with a clean lint-free wipe and no air bubbles were present in the microcuvette. The filled mirococuvette was placed in the cuvette holder during the first ten minutes after loading the microcuvette. Measurement reading appeared on the monitor screen of the device after 15-60 seconds.

Glycated hemoglobin (HbA1c) was analyzed using the HemoCue® HbA1c 501 System (HemoCue® Ltd, UK, Figure 3.6). HemoCue® HbA1c 501 System consists of the HemoCue device and cartridge HemoCue® HbA1c 501 (HemoCue®, Ängelholm, Sweden). Daily check cartridge (HemoCue® HbA1c 501 Daily Check Cartilage). Monthly check cartridge (HemoCue® HbA1c 501 Monthly Check Cartilage) were used on regular basis for quality control purposes. After blood

collection, 4 μL of blood sample were loaded into the HemoCue® cartridge reagent compartment and it was placed into the cartridge in the device (any excess blood was not wiped as the manufacturer manual instructed).

Figure 3.6: HemoCue® HbA1c 501 System (HemoCue® Ltd, UK)

After screening of the participants and during the study period visits, fasting blood glucose (FBG), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL) and total cholesterol were measured using the Cobas C111 analyzer® (Roche Diagnostics Ltd, Mannheim, Germany, Figure 3.7). Cobas C111 requires the use of blood serum, where serum samples can be loaded and unloaded uninterruptedly into eight positions on the device. Serum samples for each participant from the three phases (baseline, midpoint and endpoint) were measured together, in the same run, to minimize the chance of error. Reagents, controls and calibrations of the Cobas C111 were used according to manufacturer guidance manual and training

protocol. The research attended a training offered by the manufacturer company and carried out all the blood samples analyses.

After switching on the device, it performs an automatic check to precisely meet all the preconditions of calibration and system automated running process as displayed on its monitor. As a second step, reagents of the designated parameters (FBG, TG, HDL, LDL and total cholesterol) were loaded into the reagent disk and calibrated according to the manufacturer's recommendation. Different calibrators were needed for each parameter. f.a.s Lipids® was used to calibrate HDL and LDL, while f.a.s® was used to calibrate FBG and TG. Furthermore, Cobas C111 asks for a quality control test using PreciControl ClinChem Multi 1® and PreciControl ClinChem Multi 2®. Moreover, a daily maintenance that checks cuvettes, loading reagent desk and external fluid containers was performed. After calibration, maintenance and checkup of the device, labeled serum samples were loaded uninterruptedly into eight chambers for test performance. All labeled serum samples were thawed at room temperature before the analysis.

Figure 3.7: Cobas c111 Analyzer® (Roche Diagnostics Ltd, Mannheim, Germany)

3.5.7.3 Lipid assessment

Since metabolic syndrome diagnostic criteria included two important lipids measures (HDL and TG), it was crucial in this study to test the influence of treatment on lipid profile. Total cholesterol, LDL, HDL and TG were measured in this study at each visit (baseline, midpoint and endpoint). Dyslipidemia, a multifactorial disorder of lipoprotein metabolism is defined as high levels of total cholesterol, low-density lipoprotein (LDL), and non-high-density lipoprotein cholesterol, decreased levels of high-density lipoprotein (HDL) and increased triglyceride levels which are correlated with higher risk of cardiovascular disease [265].

The National Cholesterol Education Project (NCEP) Adult Treatment Panel III (ATP III) defined the following levels: [266]:

- LDL levels "Ideal" when less than 100 mg/dL and "high" as 160 mg/dL or more
- Total cholesterol (TC) levels "ideal" as less than 200 mg/dL and "high" when 240 mg/dL or more
- HDL levels "low" when less than 40 mg/dL
- Elevated triglycerides (TG) when greater than 150 mg/dL

Elevation in lipid profile is considerably related to increased risk of coronary heart diseases, type 2 diabetes, high blood pressure and renal diseases [267-271].

3.5.7.4 Total Cholesterol

Previous research demonstrated the direct relationship between elevated total serum cholesterol and cardiovascular diseases [272, 273]. In this study, total cholesterol was measured using Cobas® C111. 2 µ of serum was used to measure total cholesterol using a measuring range of 9.7-800 mg/dL. 47 µL of the testing reagent was used at each run. The acceptable value for normal range is <190 mg/dL [274].

3.5.7.5 Low Density Lipoprotein

Elevated levels of LDL cholesterol is one of the characteristics of dyslipidemia [275]. Compared to HDL, LDL particles are smaller, more dense, and have a high atherogenic effect. Lowering increased LDL cholesterol levels has confirmed a significant decrease in cardiovascular occasions in patients with cardiovascular diseases and diabetes [276]. According to NCEP/ATP III, the cut-off point valus is >160 mg/dL and the normal value is anywhere less than 120 mg/dL [31, 266]. Cobas® C111

required 2 μL of blood serum for the test to be measured at 3.86-548 mg/dL measuring range. For each test run, 200 μL of the reagent was used.

3.5.7.6 High Density Lipoprotein

High density lipoprotein is considered to be a predictor of and a protective factor in detecting coronary heart diseases [277, 278]. HDL cut-off point level is <40 mg/dL for men and <50 mg/dL for women [7].. Using the Cobas® C111, 2.5 μL of the serum was required to measure HDL at a range of 3-120 mg/dL [274]. 200 μL of reagent was used for each test run. The acceptable value for normal range is >40 mg/dL and ≤60 mg/dL for both men and women [31].

3.5.7.7 Triglycerides

Elevated levels of triglycerides are associated with higher risk of heart diseases, and diabetes [47, 279, 280]. According to American Heart Association (AHA), serum triglycerides is a reliable assessment of coronary heart diseases [281]. The cut-of value of triglycerides is ≥150 mg/dL to be considered as the inclusion criteria of metabolic syndrome, while the normal range value was <115 mg/dL [7]. Triglycerides were measured in this study using Refletron® during screening tests and Cobas® C111 during the study period. 32 μL of capillary blood was collected and used for the Refletron® for the TG test as instructed by the manufacturer. For Cobas® C111 2 μL of serum was used at a measuring range of 8.85-885 mg/dL. 120 μL of triglyceride reagent was needed for each test run.

3.5.7.8 Blood Glucose Assessment

Hyperglycemia is considered to be a very important diagnostic criteria of the metabolic syndrome. As one of the study objectives was to assess the influence of spice powder

on metabolic syndrome, FBG and HbA1c were measured. FBG was assessed during the screening visits and was considered as an inclusion criterion for the participants. FBG was measured using HemoCue® Glucose 201+ System (Hemocue, Dongan-gu, Korea) during the screening visits. Moreover, during baseline, midpoint and endpoint. FBG and HbA1c were measured using Cobas c111 analyzer® (Roche Diagnostics Ltd, Mannheim, Germany, Figure 3.7), while HemoCue® HbA1c 501 System was used to analyze HbA1c.

3.5.7.8.1 Fasting Blood Glucose

Fasting blood glucose (FBG) is the measurement of blood glucose level after fasting for eight hours [282]. Impaired fasting blood glucose was correlated with type 2 diabetes and cardiovascular diseases [283]. Cut-off value of FBG is equal to or greater than 100 mg/dL, while the target level of FBG in the blood is 70-100 mg/dL [32]. Cobas® C111 was used to measure FBG at range of 1.98-720 mg/dL. 2 μL of serum was used with 180 μL of reagent for each test run. Analysis process was done according to the manufacturer instruction.

3.5.7.8.2 Glycated Hemoglobin

Glycated hemoglobin (HbA1c) differs from FBG in definition, HbA1c is a form of hemoglobin that measures the cumulative status of plasma glucose for the last three months (due to the hemoglobin life span (120 days)) [284]. HbA1c is a screening tool for detecting type 2 diabetes as it provides a better insight to the history of blood glucose level [285]. High levels of HbA1c >5.7% are connected to type 2 diabetes, cardiovascular diseases and diabetes complications such as retinopathy [286]. 4-5.6% is the normal level of HbA1c [287]. 4 μL of whole blood was used to analyze HbA1c

using HemoCue® HbA1c 501 System (HemoCue® Ltd, UK, Figure 3.4) as manufacturer manual instructed.

3.5.7.9 Hemoglobin Assessment

Hemoglobin (Hb) is the protein portion of the red blood cell that carries oxygen in the blood [288]. Hb protein makes up to 35% of the red blood cells [289]. Low levels of hemoglobin (Hb) in blood (anemia) is an independent risk factor of cardiovascular consequence in individuals with heart failure and coronary artery disease. Moreover, in patients with myocardial infraction, reduced levels of Hb is are associated with higher short-term mortality rate [290]. Hb normal levels in blood varies according to age, race, pregnancy and gender [291]. According to the Wolrd Health Organization (WHO), cut-off value of Hb for an adult women and men is <8 g/dL, while normal values for adult women is 12 g/dL or higher and for adult men 13 g/dL or higher [292]. Hb was measured in this study using HemoCue® Hb 201+ System (HemoCue® Ltd, UK). 4 μL of whole blood was used to conduct the analysis. Blood was loaded to the microcuvette cavity and processed for analysis.

3.5.8 Blood Pressure Measurement

High blood pressure (BP) is a leading cause of cardiovascular diseases [293]. Moreover, morbidity rate is higher in people with high blood pressure after a stroke [294]. 1.13 billion people worldwide are affected by high blood pressure [295]. Normal level of BP is <120/<80 mmHg according to the American Heart Association (AHA), while cut-off point is >140/85 mmHg (Table 3.4) [7].

BP was measured using Omron professional blood pressure monitor (HEM 907, Tokyo, Japan). Omron HEM 907 is a validated device for measuring blood pressure

as it fulfilled the accuracy criteria of the Association for the Advancement of Medical Instrumentation (AAMI) for non-invasive blood pressure monitoring devices [296, 297]. Moreover, using an automated blood pressure measuring device such as Omron HEM 907 have been associated with eliminating the office effect [298]. Participants were given 15 minutes of rest to adjust to the climate changes. At the beginning of the measurement, the cuff suitable to the size of the participant's arm was chosen. The participant was asked to remove any heavy clothing surrounding the upper part of his/her arm. The right hand of the participant was placed with the palm of hand facing upward and the cuff was wrapped snuggly, using both hands and secured with Velcro tape. At this time, the lower edge of the cuff was placed 1.2 cm to 2.5 cm above the inner side of elbow joint. The level of the cuff was kept at the level of the heart during the measurement of the blood pressure. The measurement was taken twice with 5 minutes break between measures, and the average measurement was recorded.

Table 3.4: Classification of Blood Pressure [32]

Category	**SBP mm Hg**		**DBP mm Hg**
Normal	<120	and	<80
Prehypertension	120-139	or	80-89
Hypertension, Stage 1	140-159	or	90-99
Hypertension, Stage 2	≥160	or	≥100

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure

3.5.9 Power Analysis

Using the power of 80% and referring to previous articles that studied the effect of similar spices [197, 299, 300], and considering Alpha=0.05, the sample size required for the experiment was calculated using the Minitab software. Minitab® 15 software (Minitab Inc., Pennsylvania, USA) assumes an equal standard deviation (SD) for all groups of intervention and the control. For that reason, another way to calculate the sample for greater precision was used using the link below:

http://homepage.stat.uiowa.edu/~rlenth/Power/#Download_to_run_locally

Due to the significant difference in the SD between the intervention and the control group (specifically in the article [300]) for fasting blood glucose and the HbA1c), and by using the power of 80% and Alpha=0.05, the highest sample size calculated of the parameters (FBG and HbA1c, TG, Cholesterol, HDL and LDL) was considered.

By choosing the highest sample size, the sample size required for the experiment was set at 17. In addition, to account for a 75% attrition, the sample size number required was 30 participants for each group; with a total of 120 participants.

3.5.10 Statistical Analysis

RAND function from the Microsoft excel was used to randomize participants into four treatment groups: ginger, cinnamon, black seed and control group.

Data analysis was carried out using the IBM Statistical Package for Social Sciences SPSS® software (version 23.0) (IBM Corp, Armonk, NY, USA) for windows. Descriptive statistics were computed and summarized; continuous variables were summarized using means and standard deviations (SD). Differences of the measurements were calculated separately using the Microsoft excel 2016 (Windows

8.1, Jones, Chicago, USA), then transferred to the SPSS software for applying the normality test on data distribution. After testing the normality of the data distribution, the significancy of difference was calculated either with comparing means through the independent t-test when data is normally distributed or using the test of Mann-Whitney U in case of the abnormality of the data distribution. Data was trimmed in some tests due to extreme abnormalities in the distribution of the data (minimums or maximums), which explains the different number of participants in some tests.

Mixed models test of linear equation was applied to find interactions of gender with intervention group, gender with age and gender with the phase of the research period for the dependent variables: WC, FBG, HDL, TG and BP. All statistical significances were assessed at the 5% significance level.

Chapter 4: Results and Discussion

4.1 Results and Discussion of Spices Chemical Analysis

4.1.1 Proximate Analysis

Seven locally consumed spices were analyzed chemically according to the Association Official Analytical Chemist procedure (AOAC). The proximate analysis data were expressed as mean and standard derivations (Table 4.1).

Moisture content ranged from 6.40 g/100 g for black seed to 8.92 g/100 g for saffron. Protein content was lowest in cinnamon at 3.50 g/100 g and highest in fenugreek at 24.99 g/100 g. Fat content was remarkably highest in black seed powder reaching 36.21 g/100 g, while it was lowest in cinnamon powder 0.05 g/100 g. Ash content varied from 0.02 g/100 g for fenugreek and saffron powder, to 5.68 g/100 g for clove powder. Low moisture content of black seed increases its shelf life when compared to other spices [301].

Fiber analysis showed that cinnamon powder had the highest fiber level at 45.40 g/100 g, whereas ginger powder had the lowest level at 3.01 g/100 g. On the other hand, carbohydrate content ranged from 13.55 g/100 g for black seed powder to 69.61 g/100 g for ginger powder.

Moisture content results of ginger (8.11 g/100 g) was lower than that reported by Ereifej et al. (10.9 g/100 g) and Prakash el al (15 g/100 g) and higher than what was reported by Adeyeye et al. (1.62 g/100 g) [17, 302, 303]. Fat (3.13 g/100 g) and ash (5.63 g/100 g) content were consistent with the previous studies, while fiber content (3.01 g/100 g) was remarkably lower than what Ereifej et al. and Prakash et al. reported. On the other hand, protein and carbohydrate content reported by Ereifej et

al. (9.4 g/100 g and 21.1 g/100 g, respectively), Prakash el al. (5 g/100 g and 38.3 g/100 g, respectively) and Adeyeye et al. (5 g/100 g and 62.88 g/100 g, respectively) were lower than the current study findings (0.51 g/100 g and 69.61 g/100 g, respectively) [17, 302, 303]. Protein content of cinnamon (3.5 g/100 g) was similar to that reported by Gul et al. (3.5 g/100 g) and Ereifej et al. (4.2 g/100 g) [153, 302], while fiber, moisture and ash content (45 g/100 g, 8.24 g/100 g and 4.6 g/100 g, respectively) were higher than the results of Gul et al. (33 g/100 g, 5.1 g/100 g and 2.4 g/100 g, respectively), and lower than the results reported by Ereifej et al. (52 g/100 g for fiber and 16.2 g/100 g for moisture). While ash content of the current study (4.6 g/100 g) was similar to the ash content that Ereifej et al. reported (4.5 g/100 g). In contrast, energy result reported by Gul et al. (258 Kcal) was significantly higher than the energy results of the current study (169.78 Kcal) due to a higher fat content [153, 302]. Moisture, protein, fat and ash content (6.4 g/100 g, 18.97 g/100 g, 36.21 g/100 g, 4.2 g/100 g, respectively) of the black seed in the current study are in consistent with the findings of Al-Jassir et al. (4.64 g/100 g, 20.85 g/100 g, 38.20 g/100 g and 4.37 g/100 g, respectively), Nergiz et al. (6.4 g/100 g, 20.2 g/100 g, 32 g/100 g and 4 g/100 g, respectively) and Cheikh-Rouhou et al. (8.65 g/100 g, 22.6 g/100 g, 40.35 g/100 g and 4.41 g/100 g, respectively) [304-306]. Fiber content of the current study for black seed (20.67 g/100 g) was higher than those reported previously, while carbohydrate content (13.55 g/100 g) was lower than the literature [304-306].

Naidu et al. reported a higher moisture content (11.44 g/100 g) of fenugreek than the findings of the current study (7.33 g/100 g) [33], while Al Jasass et al. and El Nasri et el. reported similar moisture content to the current study findings (7.71 g/100 g and 6.87 g/100 g, respectively) [162, 307]. Protein content (24.9 g/100 g) was consistent

with the study results of El Nasri et al. (28.4 g/100 g) and Naidu et al. (27.57 g/100 g) and higher than Al Jasass et al. (12.91 g/100 g). Fat, ash and carbohydrate content (4.36 g/100 g, 0.02 g/100 g and 33.43 g/100 g, respectively) were lower than what the previous studies, while it was higher for the fiber content [162, 163, 307]. Moreover, Cardamom moisture and ash content (7.52 g/100 g and 0.04 g/100 g, respectively) results were lower than what was reported by Ereifej et al. (14.7 g/100 g), Pruthi et al. (8.49 g/100 g) and Singh et al. (83 g/100 g). While protein content result of this study (10.67 g/100 g) was consistent with the results of Ereifej et al. (9.9 g/100 g) and Singh et al. (10.3 g/100 g), and higher than what Pruthi et al. reported (6 g/100 g) [175, 302, 308]. Ereifej et al. reported a higher content of ash and fiber (10.2 g/100 g and 40.9 g/100 g, respectively), while Pruthi et al. and Singh et al. reported lower fiber content (22 g/100 g and 9.2 g/100 g respectively), and a higher ash content (4 g/100 g and 5 g/100 g respectively). Carbohydrate content (47.23 g/100 g) was higher than what was reported in literature [162, 163, 302].

Al Jasass et al. Adeyeye et al. and Tainter et al. reported a similar protein content for cloves (6.9 g/100 g, 5.7 g/100 g and 5.98 g/100 g, respectively) to the current study findings (6.96 g/100 g) [179, 303, 307]. Moisture content of cloves in previous studies varied from 7.44 g/100 g for Al-Jasass et al. to 16.4 g/100 g for Ereifej et al.. Our result was on the lower limit (7.87 g/100 g) and was consistent with Al Jasass et al. findings [302, 303, 307]. Carbohydrate content of cloves (44.5 g/100 g) was lower than what previously reported by A-Jasass et al., Tainter et al., Adeyeye et al. and Parthasarathy et al. (51.3 g/100 g, 61.12 g/100 g, 65.12 g/100 g and 68.6 g/100 g, respectively). In contrast, Ereifej et al. reported lower carbohydrate findings than the current study (31.3 g/100 g) [179, 180, 303, 307]

Saffron’s moisture, fat and ash content (8.92 g/100 g, 4.4 g/100 g and 0.02 g/100 g, respectively) were lower than what Mohamadi et al. Srivastava et al. and Fahim et al. reported [21, 309, 310]. Protein content (11.33 g/100 g) was in the same range when compared to the study of Srivatava et al. and Fahim et al. (10.2 g/100 g and 12 g/100 g, respectively) [21, 309, 310]. Fiber and carbohydrate content (12.23 g/100 g, 63.1 g/100 g, respectively) were higher than what Mohamadi et al. (7.4 g/100 g, and 20 g/100 g, respectively), Srivatava et al. (5 g/100 g for fiber) and Fahim et al. (8.8 g/100 g for fiber) reported (Table 4.1) [21, 309, 310].

The differences in nutrient composition of spices reported by scientists is theorized due to the different soil and geographical locations of the source of planting and growing plants, and due to the difference in environmental conditions, which has an effect on the nutrient composition [17, 162, 163, 306, 307, 311]. Moreover, different grinding and storing techniques were proved to have a major effect on the spices nutrient composition [312, 313].

As an example, a previous study investigated the nutrient content of five different sizes of ginger powder particles that were produced using a micronizer machine. They found that protein content increased significantly when the size of ginger powder particles decreased [312]. In an attempt to explain the differences in the nutrient composition in spices between previous studies and the current research findings, it is hypothesized that the superfine grinding of dried spices produces narrow and uniform particle size and that will increase the surface area and therefore increase the amount available for analysis [312]. Hence, previous studies that used different ways of grinding the spices (micronizer machines [312], all glass mortars [303] and grinders [17]) had a different nutrient composition findings. In the current study, dried whole spices were grinded

using a coffee grinding machine, with big particles of spices powder that were produced and analyzed. Grinders can have different intensity levels, different blades and different durations. Therefore, different particle sizes could be produced using different grinders, hence, different nutrient composition findings as well [314, 315].

Table 4.1: Proximate Analysis of the Seven Spices (mean ± SD)

	Ginger	**Cinnamon**	**Black seed**	**Fenugreek**	**Cardamom**	**Clove**	**Saffron**	**P-value***
Moisture (g/100 g)	8.11 ± 0.26	8.24 ± 0.20	6.40 ± 0.13	7.33 ± 0.16	7.52 ± 0.09	7.86 ± 0.04	8.92 ± 0.19	<0.001
Protein (g/100 g)	10.51 ± 0.26	3.50 ± 0.02	18.97 ± 0.13	24.99 ± 0.04	10.67 ± 0.08	6.96 ± 0.04	11.33 ± 0.05	<0.001
Fat (g/100 g)	3.13 ± 0.20	0.55 ± 0.05	36.21 ± 0.11	4.36 ± 0.09	4.40 ± 0.27	5.04 ± 0.12	4.40 ± 0.07	<0.001
Ash (g/100 g)	5.63 ± 0.04	4.60 ± 0.17	4.20 ± 0.05	0.02 ± 0.00	0.04 ± 0.00	5.68 ± 0.23	0.02 ± 0.00	<0.001
Fiber (g/100 g)	3.01 ± 0.05	45.40 ± 0.89	20.67 ± 0.59	29.87 ± 0.78	30.13 ± 1.50	29.97 ± 1.99	12.23 ± 1.31	<0.001
Carbohydrate (g/100 g)	69.61 ± 0.21	37.69 ± 0.49	13.55 ± 0.54	33.43 ± 0.61	47.23 ± 1.12	44.50 ± 1.81	63.10 ± 1.46	<0.001
Energy (Kcal)	348.65 ± 2.00	169.78 ± 2.36	455.98 ± 2.80	272.95 ± 2.99	271.20± 7.11	251.19 ± 7.23	337.32 ± 6.20	<0.001

Data is expressed as g/100 g of spice powder,

*Significant at P-value ≤ 0.05

4.1.2 Minerals Composition Analysis

4.1.2.1 Major Elements

Results of the chemical analysis of the spices showed that these spices contain major elements in significant amount. For example, cinnamon had the highest calcium content (1414.82 mg/100 g), while ginger had the lowest calcium content (125.21 mg/100 g) as shown in Table 4.2. Moreover, potassium content ranged from 460.78 mg/100 g for cinnamon to 1125.91 mg/100 g for saffron. Magnesium content ranged from 42.42 mg/100 g for cinnamon to 375.71 mg/100 g for cloves. On the other hand, sodium content was the lowest in cinnamon, clove and saffron 1.74, 2.26 and 8.82 mg/100 g respectively. Phosphorous ranged from 45.81 mg/100 g for cinnamon to 675.52 mg/100 g for ginger. Sulfur content did not exceed 310.58 mg/100 g (black seed) in any of the analyzed spices.

4.1.2.2 Trace Elements

Cobalt, copper, iron, manganese and zinc are trace minerals that play major role in metabolism. The seven commonly used spices were assessed for their trace mineral content in the current research study. Trace minerals were found in smaller amount when compared to major minerals as shown in Table 4.3. None of the trace minerals exceeded 640 mg/100 g. Moreover, Cobalt level was the highest in ginger (4.52 mg/100 g) while copper was the highest in black seed (16.52 mg/100 g). Iron levels ranged from 624.77 mg/100 g for saffron to 90.24 mg/100 g for cinnamon powder. Manganese content was the highest in clove powder (360.85 mg/100 g) and the lowest in fenugreek (23.90 mg/100 g), while zinc content did not exceed 56.24 mg/100 g (black seed powder) in any of the spice powders.

The results of this study were not in agreement with Abd- Alrahman et al., Okwu et al. and Ogbuewu et al., who reported different mineral content of ginger powder [301, 316, 317]. Another study conducted by Prakaash et al. in 2010 concluded that ginger powder contained 9.41 mg/100 g of iron, 104.02 mg/100 g of calcium and 204.02 mg/100 g of phosphorous [17]. Findings from Prakash et al. study are in agreement with the finding of the current study considering the calcium content only (125.21 mg/100 g) [17].

An earlier study published by Gopalan et al. showed that spices have the following amounts of calcium, phosphorous and iron (mg/100 g) respectively: Cardamom (229, 130 and 160), dried clove (740, 100 and 11.7), fenugreek (160, 370 and 6.5) and fresh ginger (20, 60 and 3.5) [318]. Moreover, Al-Numair et al. analyzed Chinese cinnamon and found that calcium content was the highest among the other identified elements. (Ca:1157.36 mg/dL, Mg: 74.89 mg/dL, and P: 66.31 mg /100 g, respectively). None of the minerals results of this study was consistent with the findings of the research undertaken by Al-Numair et al. [311]. In 2014, Khan et al. concluded that the manganese content for cinnamon, cardamom and clove was 879.8 µg/g, 758.1 µg/g and 649.9 µg/g, respectively [319]. Findings of the current study were not in agreement with the findings of Khan et al. as well. It is of note that cinnamon in most of these studies, had a high level of calcium content when compared to the other minerals.

Additionally, Maghrabi and his colleagues analyzed the commonly used spices in Saudi Arabia, including fenugreek and black seed. The study stated that fenugreek contains 3.36, 0.70, 16.15, 34.45 and 8.23 µg/g and black seed contains 0.525, 0.525, 20, 85, 41.14 and 13.80 µg/g of selenium, chromium, manganese, zinc and copper

respectively [320]. Manganese, zinc and copper content of the current study is not in agreement with Maghrabi et al. On the other hand, Al-Jassir et al. indicated that potassium, phosphorus, sodium and iron were the major elements presented in black seed powder. While, zinc, calcium, magnesium, manganese and copper were found at minor amounts. However, lead, cadmium and arsenic were not detected in the seeds as Al-Jassir et al. reported [304]. Al-Jassir et al. study results are not consistent with the current study.

Moreover, mineral analysis results of black seed reported by Cheikh and his colleages matches with the finding of the current study in term of calcium and sodium content (5.75 mg/100 g and 20.4 mg/100 g, respectively), while the other mineral content values varies widely [306]. Furthermore, Negriz et al. reported a lower level of all minerals in black seed when compared to the current study, except for sodium and potassium (85.3 mg/100 g and 1180 mg/100 g, respectively) as they were at high content when compared to the findings of the current study (23.62 mg/100 g and 633.3 mg/100 g, respectively) [305].

Al-Jasass et al. and Adeyeye et al. mineral composition analysis of clove were not in agreement with the findings of this study [303, 307]. Adeyeye et al. reported remarkably higher levels of phosphorous, calcium and sodium (546 mg/100 g, 400 mg/100 g and 60 mg/100 g, respectively), while Al-Jasass et al. reported lower mineral content of clove powder in all minerals when compared to this study due to the usage of different analytical techniques [307].

Based on the findings from Al-Jasass et al., fenugreek had lower levels of all minerals content when compared to the current study [307], whereas higher levels of minerals

is shown when compared with Naidu at el. findings. This is continue to be true except for zinc and copper, as they were at lower levels than the current research study findings [163].

Additionally, a study published by Mohamadi el al. reported that saffron is a good source of minerals such as potassium, magnesium, sodium, calcium, zinc, iron, copper and manganese. [21]. Results of Mohamadi et al. were not in agreement with the results of the current study due to lower mineral content of saffron when compared to the current study as demonstrated in Table 4.2 and Table 4.3. In conclusion, mineral levels fluctuate with species, and the difference in mineral content may increase due to the different colorimetric or qualitative analytical methods used, as well as this might be owing to the differences in the spices origins [21, 180, 321].

Table 4.2: Major Elements Composition of the Spices (mean ± SD)

Spice	Ca (mg/100 g)	K (mg/100 g)	Mg (mg/100 g)	Na (mg/100 g)	P (mg/100 g)	S (mg/100 g)
Ginger	125.21 ± 0.12	1071.13 ± 40.05	271.35 ± 2.3.00	69.80 ± 0.15	675.52 ± 4.84	176.40 ± 1.36
Cinnamon	1414.82 ± 8.11	460.78 ± 26.68	42.42 ± 0.15	1.74 ± 0.01	45.81 ± 0.53	76.13 ± 0.16
Black seed	578.24 ± 10.03	633.3 ± 54.60	263.60 ± 2.81	23.62 ± 0.35	649.15 ± 8.61	310.58 ± 4.84
Fenugreek	203.74 ± 2.95	853.95 ± 89.86	139.68 ± 2.95	35.13 ± 0.74	399.26 ± 6.68	237.91 ± 3.80
Cardamom	619.71 ± 20.55	873.30 ± 24.91	266.60 ± 12.41	316.79 ± 14.74	84.83 ± 4.12	130.54 ± 6.61
Clove	354.58 ± 3.50	1485.28 ± 72.12	375.71 ± 3.33	2.26 ± 0.01	125.84 ± 0.81	91.72 ± 0.15
Saffron	175.85 ± 2.85	1125.91 ± 13.62	222.32 ± 3.38	8.82 ± 0.18	391.83 ± 5.97	237.39 ± 3.63

Data is expressed as mg/100 g
Ca: Calcium; K: Potassium; Mg: Magnesium; Na: Sodium; P: Phosphorous; S: Sulfur

Table 4.3: Trace Elements Composition of the Spices (mean ± SD)

Spice	Co (mg/100 g)	Cu (mg/100 g)	Fe (mg/100 g)	Mn (mg/100 g)	Zn (mg/100 g)
Ginger	4.52 ± 0.09	0.28 ± 0.01	149.05 ± 1.15	230.65 ± 0.05	14.17 ± 0.15
Cinnamon	0.28 ± 0.10	2.70 ± 0.03	90.24 ± 0.36	171.52 ± 2.37	12.36 ± 0.10
Black seed	0.25 ± 0.01	16.52 ± 0.18	110.87 ± 1.11	30.64 ± 0.31	56.24 ± 0.78
Fenugreek	1.03 ± 0.06	9.28 ± 0.12	343.81 ± 2.60	23.90 ± 0.19	34.29 ± 1.00
Cardamom	0.52 ± 0.02	5.20 ± 0.07	421.37 ± 12.63	182.66 ± 5.46	12.98 ± 0.82
Clove	0.25 ± 0.06	7.06 ± 0.08	114.54 ± 0.89	360.85 ± 4.19	46.70 ± 0.62
Saffron	0.76 ± 0.02	9.85 ± 0.09	624.77 ± 7.43	32.05 ± 0.45	43.58 ± 1.33

Data is expressed as mg/100 g

Co: Cobalt; Cu: Copper; Fe: Iron; Mn: Manganese; Zn: Zinc

4.1.3 Vitamin Composition Analysis

4.1.3.1 Water Soluble Vitamins

Nine water soluble vitamins and all fat soluble vitamins (Vitamin C), Vitamin B1 (Thiamin), Vitamin B2 (Riboflavin), Vitamin B3 (Niacin), Vitamin B5 (Pantothenic acid), Vitamin B-6, Vitamin B7 (Biotin), Vitamin B9 (Folic acid), Vitamin B-12, Vitamin A, Vitamin K1 (phytonadione), Vitamin K2 (menaquinone), Vitamin D2, Vitamin D3 and Vitamin E (alphatocopherol)) were consecutively found in the seven spices using the High-Performance Liquid Chromatography (HPLC) method.

Vitamin C and niacin were found to be the highest water soluble vitamins present in all seven spices (Table 4.4). Vitamin B1 (thiamin) was detected in all spices, except in black seed. Vitamin B1 (thiamin) was the highest in saffron (237.63 mg/100 g) followed by cinnamon (60.21 mg/100 g). Vitamin B2 content ranged from 0.71 mg/100 g for cardamom to 93.27 mg/100 g for clove powder. Low levels of vitamin B1 and B2 are due to the lack of animal product presented in the spices, sense all the spices were plant based.

Vitamin B7 (biotin) was only detected in ginger powder (127.09 mg/100 g). However, vitamin B12 and vitamin B5 (pantothenic acid) were not detected in any of the spice powders. Vitamin B9 (folic acid) was found in all spices except for the cardamom powder as demonstrated in Table 4.4.

4.1.3.2 Fat Soluble Vitamins

Fat soluble vitamins were analyzed in the seven spices using the High-Performance Liquid Chromatography (HPLC) method and date were presented as mean and standard deviations in Table 4.5. Vitamin A was found in ginger, cinnamon, fenugreek and clove (4.38, 0.15, 0.09 and 7.23 mg/100 g, respectively). However, vitamin A was not detected in black seed, cardamom and saffron.

In contrast, vitamin K1 and K2 were present in all spices in low levels. Vitamin K1 ranged from 0.6 mg/100 g for ginger to 7.08 mg/100 g for black seed. Whereas, vitamin K2 ranged from 1.54 mg/100 g for cardamom to 3.51 mg/100 g for black seed. Vitamin D2 and D3 were not detected in any of the spices. Vitamin E was not found in ginger, however, it was the highest in saffron, followed by clove and black seed (52.97, 24.34 and 21.43 mg/100 g, respectively) as shown in Table 4.5.

The findings of the current study were consistent with the values reported by the United States Department of Agriculture's (USDA) food composition data base for ginger, fenugreek and cinnamon [322]. Additionally, the results reported in the current research study are supported by Gul et al., Mohamadi et al., Hussain et al., Nwinuka et al. and Parthasarathy et al. with a slight variation in vitamin C and E levels [21, 148, 150, 153, 179, 180].

Table 4.4: Water Soluble Vitamin Composition of the Seven Spices (mean ± SD)

Vitamin	Ginger	Cinnamon	Black seed	Fenugreek	Cardamom	Clove	Saffron
Vitamin C (mg/100 g)	1715.84 ± 142.95	5268.06± 156.48	83.89 ± 25.83	9501.10 ± 466.90	4623.31 ± 33.98	2365.23 ± 38.71	3267.65 ± 120.39
Thiamin (mg/100 g)	6.96 ± 0.05	60.21 ± 4.18	ND	18.23 ± 0.41	6.04 ± 0.95	7.46 ± 0.59	237.63 ± 5.37
Riboflavin (mg/100 g)	4.62 ± 0.05	67.42 ± 4.20	6.06 ± 1.32	3.57 ± 0.15	0.71 ± 1.22	93.27 ± 1.74	33.56 ± 10.91
Niacin (mg/100 g)	2100.73±77.16	435.32 ± 20.05	711.17± 152.93	2960.94 ± 88.56	254.04 ± 14.34	414.71 ± 19.31	4394.98 ± 39.63
Pantothenic acid (mg/100 g)	ND	ND	ND	ND	ND	ND	ND
Vitamin B6 (mg/100 g)	2.44 ± 0.16	21.35 ± 0.80	1.66 ± 0.26	0.08 ± 0.02	2.69 ± 0.26	12.33 ± 0.19	3.42 ± 0.17
Biotin (mg/100 g)	127.09 ± 10.96	ND	ND	ND	ND	ND	ND
Folic acid (mg/100 g)	4.01 ± 0.60	0.65 ± 0.00	31.98 ± 0.96	133.98 ± 19.69	ND	62.00 ± 7.39	298.37 ± 14.05
Vitamin B12 (mg/100 g)	ND	ND	ND	ND	ND	ND	ND

Data is expressed as mg/100 g of the spice powder

Table 4.5: Fat Soluble Vitamin Composition of the Seven Spices (mean ± SD)

Sample Name	**Ginger**	**Cinnamon**	**Black seed**	**Fenugreek**	**Cardamom**	**Clove**	**Saffron**
Vitamin A (mg/100 g)	4.38 ± 0.10	0.15 ± 0.00	ND	0.09 ± 0.01	ND	7.23 ± 0.35	ND
Vitamin K1 (mg/100 g)	0.60 ± 0.46	3.50 ± 0.05	7.08 ± 0.07	5.56 ± 0.14	3.44 ± 0.08	4.99 ± 0.13	1.72 ± 0.22
Vitamin K2 (mg/100 g)	2.20 ± 0.07	1.85 ± 0.03	3.51 ± 0.03	1.80 ± 0.24	1.54 ± 0.00	1.87 ± 0.07	3.43 ± 0.10
Vitamin D2 (mg/100 g)	ND	ND	ND	ND	ND	ND	ND
Vitamin D3 (mg/100 g)	ND	ND	ND	ND	ND	ND	ND
Vitamin E (mg/100 g)	ND	3.21 ± 0.03	2.18 ± 0.05	21.43 ± 0.16	5.89 ± 0.03	24.34 ± 0.08	52.97 ± 0.03

Data is expressed as mg/100 g of the spice powders
ND: not detected

4.1.4 Sugar Composition Analysis

Sugars provided by carbohydrates are found in many foods and are major component of our diet with sucrose (table sugar) being the main type. Sucrose is added to drinks and found in many processed foods, including cakes and soft drinks [323]. Glucose and fructose are found naturally in many fruits, some vegetables and in small amounts in some spices [324].

In the current study, ribose, fructose, glucose and sucrose were detected in all spices. Ribose was found to be highest in saffron (1217.55 mg/100 g) and the lowest in fenugreek (4 mg/100 g). Whereas cinnamon had the highest level of fructose followed by ginger and cardamom (496.8 mg/100 g, 326.07 and 323.67 mg/100 g, respectively). On the other hand, glucose level was the highest in saffron and cinnamon (1075.57 and 611.93 mg/100 g, respectively) and the lowest in fenugreek (52 mg/100 g).

Sucrose content varied from 7.33 mg/100 g for ginger to 443.8 mg/100 g for fenugreek. While, xylose was detected only in ginger, black seed and clove (4.93, 0.53 and 7.33 mg/100 g, respectively). Additionally, maltose was found only in black seed, fenugreek and in saffron (21.6, 310.2 and 205.74 mg/100 g, respectively) as demonstrated in Table 4.6. Arabinose was detected only in saffron (87.21 mg/100 g) and mannose was not detected in any of the spices. Total sugar content was the highest in saffron (2536.37 mg/100 g) followed by cinnamon (1166.47 mg/100 g) and cardamom (1122.2 mg/100 g). Saffron, cinnamon and cardamom are capable to deliver a natural sweet taste, hence, the usage of these spices in many Emirati local sweet dishes such as: khabisa, batheetha, habba hamra and balaleet [325].

According to USDA food composition data base, cinnamon contained 2.2 g/100 g of sugar and ginger root 1.7 g/100 g, and cloves, fenugreek, saffron and cardamom had no significant amount of sugar [322]. These results are not consistent with the findings of the current study. Additionally, Khazaei et al. reported lower level of total sugar content of saffron when compared to the findings of the current study (Table 4.6) [326]. In contrast, Deepa et al. reported similar content of total sugar of cardamom (1064 mg/100 g), however, cinnamon content in Deepa et al. study was not in agreement with the finding of the current study [327]. There is a general paucity of literature that deals with sugar composition of spices, hence comparison between similar spices were difficult. Therefore, more studies are needed to examine the nutrient content of sugar in the spices.

Table 4.6: Sugar Composition Analysis of the Seven Spices (mean ± SD)

Spice	Ribose (mg/100 g)	Xylose (mg/100 g)	Fructose (mg/100 g)	Glucose (mg/100 g)	Sucrose (mg/100 g)	Maltose (mg/100 g)	Arabinose (mg/100 g)	Mannose (mg/100 g)	Total Sugars (mg/100 g)
Ginger	9.53 ± 1.5	4.93 ± 0.83	326.07 ± 2.01	137.2 ± 1.2	7.33 ± 1.3	ND	ND	ND	485.07 ± 3.97
Cinnamon	35.53 ± 1.45	ND	496.8 ± 12.51	611.93 ± 17.39	22.2 ± 2.82	ND	ND	ND	1166.47 ± 30.65
Black Seed	1.8 ± 0.53	0.53 ± 0.5	190.47 ± 1.15	238 ± 1.59	195.2 ± 4.85	21.6 ± 1.03	ND	ND	647.6 ± 5.82
Fenugreek	4 ± 1.4	ND	136.93 ± 2.27	52 ± 1.78	443.8 ± 2.46	310.2 ± 17.19	ND	ND	946.93 ± 22.5
Cardamom	8.67 ± 1.72	ND	323.67 ± 1.53	383.6 ± 14.1	406.27 ± 12.72	ND	ND	ND	1122.2 ± 23.85
Clove	11.47 ± 1.4	7.33 ± 1.33	164 ± 0.8	250.2 ± 1.44	40.87 ± 2.27	ND	ND	ND	473.87 ± 4.08
Saffron	1217.55 ± 4.58	ND	154.93 ± 1.17	1075.57 ± 1.67	156.04 ± 1.45	205.74 ± 1.34	87.21 ± 0.45	ND	2536.37 ± 2.58

Data is expressed in mg/100 g of the sample powder

ND: not detected

4.1.5 Lipids and Caffeine Composition Analysis

Table 4.7 illustrates the lipid and caffeine composition data for the seven commonly used spices. Total saturated fatty acid was the highest in black seed oil (6.451 g/100 g), followed by clove oil (1.800 g/100 g) and cardamom oil (1.692 g/100 g). Total monounsaturated fatty acids content ranged from 9.341 g/100 g for black seed oil to 0.138 g/100 g for cinnamon oil. In contrast, among all the spices, black seed oil had the highest content of total polyunsaturated fatty acids (20.279 g/100 g), while cinnamon oil had the lowest content of total polyunsaturated fatty acids (0.268 g/100 g). Cholesterol is rarely found in plants: such as green bean leafs and etiolated bean leaves [328]. No cholesterol was detected in the seven spices analyzed. Moreover, caffeine was not detected in any of the spices (Table 4.7).

Monounsaturated fatty acid percent was the highest component of lipid in ginger oil (56.074%) and the lowest in fenugreek oil (7.29%). While the total saturated fatty acid percent was the highest in cardamom oil (38.45%) followed by saffron oil (36.12%) and clove oil (35.73%), and the total percentages of polyunsaturated fatty acids was the highest in fenugreek oil, followed by black seed oil and saffron oil (68.25%, 56% and 52.69%, respectively) as shown in Table 4.8.

Analysis of fatty acid methyl esters presented in Table 4.9 indicated that the highest fatty acid percent presented in ginger is palmitoleic acid (29.64%) and γ-linoleic acid (29.63%), followed by elaidic acid (11.92%) and stearic acid (11.32%). Lower percentages of myristoleic acid, pentadecanoic acid, oleic acid, linoleic acid, α-linolenic acid and nervonic acid were found in ginger as well. Palmitic oil was remarkably high in all spices except ginger, since palmitic oil was not detected.

Linoleic fatty acid was detected in high percentages in cinnamon oil, black seed oil, fenugreek oil, cardamom oil and saffron oil.

The highest fatty acid percent for cinnamon was linoleic (32.04%) followed by elaidic acid (22.7%) and palmitic acid (11.83%). Moreover, low traces of acids were presented in cinnamon oil such as capric acid, undecanoic acid, lauric acid, tridecanoic acid, myristic acid, pentadecanoic acid, palmitoleic acid, stearic acid, linolelaidic acid, arachidic acid, cis-11-eicosenenoic acid, α-linolenic acid, cis-8, 11, 14-eicosatrienoic acid and more as shown in Table 4.9.

Furthermore, black seed's highest fatty acid content was linoleic acid (53.89%), followed by oleic acid (25.79%), palmitic acid (15.49%), stearic acid (3.32%) and cis-11, 14-eicosadienoic acid (2.11%), while no other fatty acids were found in black seed. Additionally, among all the fatty acids found in fenugreek oil, linoleic acid (50.4%) exhibited the highest percentage followed by palmitic acid (19.99%) and γ-linoleic acid (13.92%). Other fatty acids were found in trace amounts in fenugreek oil as well (Table 4.9). Oleic acid (52.3%) was the highest fatty acid detected in cardamom, followed by palmitic acid (30.37%). Other fatty acids found in cardamom oil did not exceed 5.41% (stearic acid).

Additionally, tricosanoic acid (0.55%) and palmitoleic acid (0.34%) along with a variety of other fatty acids were presented in trace amounts in clove oil, while linoleic acid was found in higher percentage (40.54%) followed by palmitic acid (21.22%). Furthermore, palmitic acid (28.10%), lenoleic acid (25.81%) and cis-11-eicosenoic acid (19.36%) had the highest fatty acid percentages in saffron. Other fatty acids presented in saffron did not exceed 8.41% (oleic acid).

Table 4.7: Lipid Profile Composition of the Spice Oils (mean ± SD)

Spices oils	**Total Saturated (g/100 g)**	**Total Monounsaturated (g/100 g)**	**Total Polyunsaturated (g/100 g)**	**Cholesterol (mg/100 g)**	**Caffeine (mg/100 g)**
Ginger oil	0.401 ± 0.05	1.755 ± 0.03	0.939 ± 0.01	ND	ND
Cinnamon oil	0.147 ± 0.12	0.138 ± 0.18	0.268 ± 0.23	ND	ND
Black seed oil	6.451 ± 2.43	9.341 ± 1.36	20.279 ± 1.26	ND	ND
Fenugreek oil	1.055 ± 0.02	0.318 ± 0.31	2.978 ± 0.24	ND	ND
Cardamom oil	1.692 ± 0.01	2.376 ± 0.34	0.332 ± 0.37	ND	ND
Clove oil	1.800 ± 0.3	0.661 ± 0.03	2.562 ± 0.09	ND	ND
Saffron oil	1.589 ± 0.22	0.498 ± 0.06	2.319 ± 0.05	ND	ND

Data is expressed per 100 g of the spice oils
ND: not detected

Table 4.8: Percentage of Fatty Acids of the Spice Oils (mean ± SD)

Spices oil	Total Saturated %	Total Monounsaturated %	Total Polyunsaturated %
Ginger oil	12.8225 ± 0.75	56.074 ± 0.98	30.0275 ± 1.01
Cinnamon oil	26.645 ± 0.23	24.895 ± 1.02	48.375 ± 2.05
Black seed oil	17.815 ± 0.43	25.795 ± 0.32	56 ± 0.33
Fenugreek oil	24.18 ± 0.33	7.295 ± 0.69	68.25 ± 0.92
Cardamom 0il	38.45 ± 1.34	54 ± 1.22	7.55 ± 0.65
Clove oil	35.73 ± 0.23	13.13 ± 0.43	50.865 ± 0.49
Saffron oil	36.12 ± 0.87	11.33 ± 0.84	52.69 ± 0.71

Table 4.9: Percentage of Fatty Acid Methyl Esters in Spice Oils

Components (Fatty Acid Methyl Esters)	Ginger oil %	Cinnamon oil %	Black seed oil %	Fenugreek oil %	Cardamom oil %	Clove oil %	Saffron oil %
C4:0 (Butryic)	0.00	0.00	0.00	0.00	0.00	0.00	0.00
C6:0 (Caproic)	0.00	0.00	0.00	0.00	0.00	0.41	0.00
C8:0 (Caprylic)	0.00	0.00	0.00	0.00	0.00	0.00	0.00
C10:0 (Capric)	0.00	0.59	0.00	0.00	0.00	0.32	0.00
C11:0 (Undecanoic)	0.00	0.20	0.00	0.00	2.67	0.00	0.00
C12:0 (Lauric)	0.00	0.84	0.00	0.88	0.00	0.67	0.00
C13:0 (Tridecanoic)	0.00	0.45	0.00	0.00	0.00	0.00	0.00

Table 4.9: Percentage of Fatty Acid Methyl Esters in Spice Oils (continued)

Components (Fatty Acid Methyl Esters)	Ginger oil %	Cinnamon oil %	Black seed oil %	Fenugreek oil %	Cardamom oil %	Clove oil %	Saffron oil %
C14:0 (Myristic)	0.00	1.96	0.00	0.85	0.00	3.51	0.00
C14:1 (Myristoleic)	1.69	0.00	0.00	0.00	0.00	0.00	0.00
C15:0 (Pentadecanoic)	1.50	0.45	0.00	0.00	0.00	0.00	0.00
C15:1 (cis-10-Pentadecenoic)	0.00	0.06	0.00	0.97	0.00	0.00	0.00
C16:0 (Palmitic)	0.00	11.83	14.50	20.00	30.37	21.23	28.11
C16:1 (Palmitoleic)	29.64	1.07	0.00	0.34	1.62	0.35	0.00
C17:0 (Heptadecanoic)	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Table 4.9: Percentage of Fatty Acid Methyl Esters in Spice Oils (continued)

Components (Fatty Acid Methyl Esters)	Ginger oil %	Cinnamon oil %	Black seed oil %	Fenugreek oil %	Cardamom oil %	Clove oil %	Saffron oil %
C17:1 (cis-10-Heptadecenoic)	0.00	0.00	0.00	0.00	0.00	0.00	0.00
C18:0 (Stearic)	11.33	8.14	3.32	0.80	5.41	6.69	3.40
C18:1n9c (Oleic)	2.98	0.00	25.80	5.48	52.38	12.79	8.41
C18:1n9t (Elaidic)	11.92	22.75	0.00	0.00	0.00	0.00	2.92
C18:2n6t (Linolelaidic)	0.39	1.76	0.00	0.00	0.00	0.00	0.51
C18:2n6c (Linoleic)	0.00	32.04	53.89	50.40	0.00	40.55	25.81
C18:3n6 (γ-Linolenic)	29.64	0.00	0.00	13.92	0.00	0.00	0.00

Table 4.9: Percentage of Fatty Acid Methyl Esters in Spice Oils (continued)

Components (Fatty Acid Methyl Esters)	Ginger oil %	Cinnamon oil %	Black seed oil %	Fenugreek oil %	Cardamom oil %	Clove oil %	Saffron oil %
C20:0 (Arachidic)	0.00	1.64	0.00	0.00	0.00	2.37	0.93
C18:3n3 (cis-11-Eicosenoic)	0.00	5.65	0.00	0.00	2.12	6.09	19.37
C20:1n9 (α-Linolenic)	8.98	1.03	0.00	0.00	0.00	0.00	0.00
C20:2 (cis-11, 14-Eicosadienoic)	0.00	0.00	2.11	0.00	3.52	0.59	0.61
C20:3n6 (cis-8, 11, 14-Eicosatrienoic)	0.00	2.68	0.00	0.00	0.00	0.00	0.00

Table 4.9: Percentage of Fatty Acid Methyl Esters in Spice Oils (continued)

Components (Fatty Acid Methyl Esters)	Ginger oil %	Cinnamon oil %	Black seed oil %	Fenugreek oil %	Cardamom oil %	Clove oil %	Saffron oil %
C20:3n3 (cis-11, 14, 17-Eicosatrienoic)	0.00	2.25	0.00	0.00	0.00	2.44	1.71
C20:4n6 (Arachidonic)	0.00	0.00	0.00	2.21	0.00	0.00	1.61
C20:5n3 (cis-5, 8, 11, 14, 17-Eicosapentaenoic)	0.00	2.63	0.00	0.00	0.83	0.00	0.00
C21:0 (Henicosanoic)	0.00	0.00	0.00	1.17	0.00	0.00	0.00
C22:0 (Behenic)	0.00	0.22	0.00	0.00	0.00	0.00	0.00

Table 4.9: Percentage of Fatty Acid Methyl Esters in Spice Oils (continued)

Components (Fatty Acid Methyl Esters)	Ginger oil %	Cinnamon oil %	Black seed oil %	Fenugreek oil %	Cardamom oil %	Clove oil %	Saffron oil %
C22:1n9 (Erucic)	0.00	0.00	0.00	0.00	0.00	0.00	0.00
C22:2 (cis-13, 16-Docosadienoic)	0.00	0.31	0.00	1.72	0.00	0.00	3.08
C22:6n3 (cis-4, 7, 10, 13, 16, 19-Docosahexaenoic)	0.00	1.07	0.00	0.00	1.08	1.20	0.00
C23:0 (Tricosanoic)	0.00	0.17	0.00	0.50	0.00	0.56	2.26
C24:0 (Lignoceric)	0.00	0.18	0.00	0.00	0.00	0.00	1.44
C24:1n9 (Nervonic)	0.86	0.00	0.00	0.51	0.00	0.00	0.00

In 1992, Al-Jassir et al. concluded that linoleic and oleic acids were the major unsaturated fatty acids in black seed, while palmitic acid was the main saturated fatty acid [304]. Additionally, Cheikh-Rouhou et al. stated that the major unsaturated fatty acids in black seed were linoleic fatty acid (50.3–49.2%), followed by oleic fatty acid (25.0–23.7%), while the main saturated fatty acid was palmitic acid (17.2–18.4%) (17.2–18.4%) [306]. The current research study results were in agreement with the findings of Al-Jassir et al. [304] and Cheikh-Rouhou et al. [306].

Hamden et al. reported that the total saturated fatty acids percent in fenugreek seeds was 17.7% of the total lipids and palmitic acid percentage was 11.0%. Additionally, linoleic acid was the highest (43.2%) in fenugreek followed by linolenic (22%) and then oleic (16.7%) acids as reported by Hamdan et al. [329]. Hamden et al. findings varied remarkably from the results of the current study.

The percentage of linolenic acid in fenugreek oil or the current study differ from the results previously presented by Shahat et al. as it was reported to be 13.8% of the Egyptian fenugreek oil [330]. Whereas, Zafar et al. reported a linolenic acid percentage of 7% for Indian fenugreek oil, which is considered significantly lower than the currents study result [331]. In contrast, Sulaiman et al. compared fenugreek fatty acids content in previous studies, Sulaiman et al. found that temperature, atmosphere and the origin of fenugreek seed are the main factors that are responsible of variations in the reported results, especially in linolenic acid [332].

On the other hand, palmitoleic, oleic, elaidic, linoleic, linolenic, cis-11-eicosenoic and erucic acids content in ginger and cinnamon varied in previous studies. Sing et al. and Kim et al. analysis of the fatty acids content of cinnamon and ginger were not

consistent with the findings of the current study as the values presented in their studies varies significantly from the outcomes of the current study. These differences are due to the different storage techniques and the different preparation methods followed for analysis as Sing et al. and Kim et al. reported [308, 313].

Additionally, cardamom content of oleic acid (49.2%), palmitic acid (26.87%) and palmitoleic acid (1.6%) as reported by Parry et al. [333], were consistent with results of this research. In addition, Al-Jasass et al. reported a clove content of linoleic acid (44.73%) and this result was in agreement with the findings of our study [307].

Moreover, saffron content of ursolic, oleanolic, palmitic, palmitoleic and oleic acids that were reported by Rios et al., Sampathu et al. and Christodoulou et al. were not in agreement with the findings from our study (Table 4.9) [334-336].

According to Al-jasass et al. [307] and Parry et al. [333], the differences in the results attained and that reported in earlier studies are possibly due to environmental factors that conquer in production areas of spices, different planting fertilizers used and due to the different methods followed for the preparation of the spices for analysis.

4.1.6 Shogaols, Gingerols and Curcumin Composition Analysis in Ginger Powder

Shogaols, paradols, gingerols and curcumin are chemicals that are presented in ginger that give the ginger its pungent smell and taste and are believed to give ginger its hypoglyceamic, hypolipidimic and anti-inflammatory effect [337-340]. In 2017, a study reported that 6-shogaol showed potent activity in stimulating glucose utilization by adipocytes and myotubes in a high fat diet fed to mouse. The effects were attributed to the increased phosphorylation in adipocytes [151]. In addition, a study conducted in

2012, showed that the activity of (S)-(8)-gingerol was found to be correlated with an elevation in surface distribution of glucose transporter type 4 (GLUT4) protein. GLUT4 is responsible for glucose uptake on the plasma membrane that enhances glucose uptake and insulin sensitivity, therefore, improves levels of glucose on the blood [152]. Moreover, Kunchandy et al. reported the ability of curcumin to scavenge reactive oxygen radicals which are associated in inflammation, hence the high anti-inflammatory effect of curcumin [338]. Additionally, a study conducted by Ramirez-Tortosa et al. concluded that the consumption curcumin inhibited the LDL oxidation and improved lipid profile [340]. Therefore curcumin was considered to be a protective tool against atherosclerosis and cardiovascular diseases [340, 341].

Shogaols, paradols, gingerols and curcumin presence in significant amounts in ginger were reported by previous studies [337-340, 342], while cinnamon and black seed did not contain shogaols, paradols, gingerols and curcumin as reported by literature [343, 344].

Therefore, as a step further in analyzing the ginger powder, 6-gingerols, 8-gingerols, 6-shogaols and curcumin were investigated. 6-shogaols had the highest value followed by 6-gingerols and 8-gingerols 56.10, 30.21, 7.92 mg/100 g respectively. Curcumin content was very low (0.01 mg/100 g) in ginger powder as shown in Table 4.10.

Heat was applied in the process of drying ginger root before grinding, hence for chemical analysis. 6-gingerols convert to shogaols under heat and this explains the high content of shogaols in the powder form of ginger when compared to gingerols [345]. Chen and his colleagues, analyzed ginger root and found that 6-gingerol had the highest value (11.8%) of the wet weight among the pungent compounds identified in

raw ginger such as 8-gingerol (1.67%) and 10-gingerol (2.38%) of the body weight. Shogaols were found in trace amounts as ginger was analyzed in its raw form and did not go under heat treatment [345]. Results of previous studies were similar to the findings of this study [337, 345].

Table 4.10: Ginger powder Composition of Shogaols, Gingerols and Curcumin (mean ± SD)

Samples mg/100 g	Ginger Powder
6- Gingerol	30.21 ± 0.14
6- Shogaol	56.10 ± 0.30
8- Gingerol	7.92 ± 0.28
Curcumin	0.01 ± 0.00

4.1.7 Conclusion

Ginger, cinnamon, black seen, fenugreek, cardamom, clove and saffron were extensively analyzed in this study. Findings of this current study proved that these seven spices have different macronutrient, micronutrient and sugar content. Many previous studies were in agreement with the findings of this current study [163, 302, 305-307], however, findings of some studies in the literature were not in consistence with the findings of this study [153, 175, 179, 303].

The differences in macronutrient composition of spices reported by scientists is theorized due to the different soil and geographical locations of the source of planting

and growing plants, and due to the difference in environmental conditions, which has an effect on the nutrient composition [17, 162, 163, 306, 307, 311]. Moreover, different grinding and storing techniques were proved to have a major effect on the spices nutrient composition [312, 313].

Moreover, mineral and vitamin levels fluctuate within species, this difference may increase due to the different colorimetric or qualitative analytical methods used, as well as this might be owing to the differences in the spices origins [21, 180, 321].

Additionally, Saffron, cinnamon and Cardamom had the highest total sugar content, and are capable to deliver a natural sweet taste, hence, the usage of these spices in many Emirati local sweet dishes such as: khabisa, batheetha, habba hamra and balaleet [325]. However, unfortunately, there is a general scarcity of literature that deals with sugar composition of spices, hence comparison between similar spices were difficult. Therefore, more studies are needed to examine the nutrient content of sugar in the spices.

Furthermore, the differences in the lipid profile results obtained in this current study and that reported in previous studies are possibly due to environmental factors that conquer in production areas of spices, different planting fertilizers used and due to the different methods followed to prepare spices for analysis [307].

Lastly, this current study concludes that these tested seven spices while providing aroma and improving the taste of food, also have some essential nutrients. Therefore, the use of these spices's macronutrients, essential oils and active compounds such as

gingerols and shogaols could be applied nutritional supplements and for treatments considering their decent source of valuable nutrients.

4.2 Intervention Treatment of Spices

4.2.1 Population Characteristics

Clinical and demographic characteristics of the study population are presented as mean ± standard deviation in Table 4.11. The mean age of study population was 26.1 ± 9.56, 27.84 ± 12.04, 26.59 ± 8.06 and 28.82 ± 11.7 years old for the ginger, cinnamon, black seed and placebo groups, respectively, ranging from 19 to 49 years old. The range of the population age was (19 – 44), (20 – 42), (21 – 47) and (21 – 45) years old for ginger, cinnamon, black seed and placebo, respectively. The mean age of population in the ginger, cinnamon, black seed groups was not significantly different from the placebo group (P-value > 0.05). The mean body mass index (BMI) of participants was 36.07 ± 6.466, 33.53 ± 9.96, 34.78 ± 9.27 and 33.94 ± 5.84 kg/m² in the ginger, cinnamon, black seed and placebo groups, respectively. No significant difference in the mean BMI value was observed between ginger, cinnamon, black seed groups and the placebo group (P-value > 0.05).

All participants had two or more of the metabolic syndrome risk factors. Waist circumference (WC) was 105.46 ± 14.93, 96.55 ± 13.76, 98.6 ± 17.64 and 102.07 ± 11.91 cm for the ginger (P-value=0.415), cinnamon (P-value=0.125), black seed (P-value=0.43) and placebo groups, respectively. Systolic blood pressure mean values were 119.04 ± 17.74, 121.68 ± 15.64, 115.48 ± 17.72 and 122.5 ± 16.79 mmHg in ginger (P-value=0.516), cinnamon (P-value=0.863), black seed (P-value=0.158) and placebo groups, respectively, and 83.47 ± 13.41, 81.36 ± 11.24, 76.72 ± 13.43 and

81.86 ± 9.52 mmHg for the Diastolic blood pressure in ginger (P-value=0.651), cinnamon (P-value=0.871), black seed (P-value=0.134) and placebo groups, respectively. Fasting blood glucose (FBG) mean value was 89.35 ± 12, 99.1 ± 44.43, 93.7 ± 8.1 and 88.58 ± 26.87 mg/dL for the ginger (P-value=0.515), cinnamon (P-value=0.055), black seed (P-value=0.35) and placebo groups, respectively. High density lipoprotein (HDL) mean values ranged from 34.4 ± 8.52 mg/dL for ginger group to 41.23 ± 11 mg/dL for cinnamon group, with no significant difference between ginger, cinnamon and black seed groups and the placebo group (P-value ≥ 0.05). Triglycerides mean value was the highest in cinnamon group 116.76 ± 80.30 mg/dL and the lowest in black seed group 100.01 ± 33.4 mg/dL. No significant difference was found between ginger, cinnamon and black seed groups and the placebo group for triglycerides (P-value > 0.05).

Participants had no significant difference between each treatment group and the placebo group in term of their age, height, BMI, WC, BP, FBG, HDL and TG (P-value > 0.05). On the other hand, weight mean value of the participants ranged from 92.77 ± 25.44 kg for the black seed group and 100.6 ± 21.12 kg for the ginger group. Significant difference was observed in weight mean values between placebo group and ginger group (P-value=0.04), and between placebo group and cinnamon group (P-value=0.048) as demonstrated in Table 4.11. Inclusion of the participants was based on age, WC, FBG, BP, HDL and Triglycerides. Only these factors were taken into consideration during the random distribution of the population into four treatment groups. Therefore, it was impossible to distribute the population randomly without having some significant differences between the placebo group and treatment groups in some parameters (non- inclusion criteria parameters).

Table 4.11: Population Characteristics of the Intervention Study

Parameter	Ginger group, n=21 f=12, m=9 (19-44 years)	P-value of Independent sample t- test	Cinnamon group, n=25 f=16, m=9 (20-42 years)	P-value of Independent sample t- test	Black seed group, n=29 f=20, m=9 (21-47 years)	P-value of Independent sample t- test	Placebo group, n=22 f=11, m=11 (21-45 years)
Age (years)	26.1 ± 9.56 [(b)]	0.81	27.84 ± 12.04[(b)]	0.768	26.59 ± 8.06[(b)]	0.59	28.82 ± 11.7
Weight (kg)	100.6 ± 21.12[(a)]	0.04	98.05 ± 20.17[(a)]	0.048	92.77 ± 25.44[(b)]	0.871	93.77 ± 19.17
Height (cm)	166.8 ± 8.74[(b)]	0.54	165.2 ± 11.36[(b)]	0.60	164.2 ± 9.11[(b)]	0.84	167.5 ± 9.93
BMI (kg/m2)	36.07 ± 6.466[(b)]	0.26	33.53 ± 9.96[(b)]	0.87	34. 78 ± 9.27[(b)]	0.713	33.94 ± 5.84
WC (cm)	105.46 ± 14.93[(b)]	0.41	96.55 ± 13.76[(b)]	0.15	98.6 ± 17.64[(b)]	0.431	102.07 ± 11.91
FBG (mg/dL)	89.35 ± 12[(b)]	0.51	99.1 ± 44.43[(b)]	0.06	93.7 ± 8.1[(b)]	0.35	88.58 ± 26.87
Systolic BP (mmHg)	119.04 ± 17.74[(b)]	0.51	121.68 ± 15.64[(b)]	0.86	115.48 ± 17.72[(b)]	0.158	122.5 ± 16.79
Diastolic BP (mmHg)	83.47 ± 13.41[(b)]	0.65	81.36 ± 11.24[(b)]	0.87	76.72 ± 13.43[(b)]	0.134	81.86 ± 9.52
HDL (mg/dL)	34.4 ± 8.52[(b)]	1.0	41.23 ± 11[(b)]	0.087	36.62 ± 9.01[(b)]	0.556	34.68 ± 12.32
TG (mg/dL)	115 ± 31.97[(b)]	0.73	116.76 ± 80.30[(b)]	0.39	100.01 ± 33.4[(b)]	0.97	102.34 ± 30.02

Data are presented as (mean ± standard deviation)
(a) Mean value differs significantly from placebo group at P-value ≤ 0.05. (b) Mean value does not differ significantly from placebo group at P-value ≤ 0.05

4.2.2 Clinical, Anthropometric and Body Composition Assessments

Blood pressure (BP), waist circumference (WC), body fat mass (BFM), weight, skeletal muscle mass (SMM), body mass index (BMI) and percent body fat (PBF) were assessed during the study period (baseline, midpoint, and endpoint) to examine the effect of the spice powders on blood pressure, abdominal obesity and body composition, and therefore understand how they influence the cardiovascular risk factors.

4.2.2.1 Baseline Assessments

At baseline, systolic blood pressure was 119.05 ± 17.75, 121.68 ± 15.65, 115.48 ± 17.72 and 122.50 ± 16.79 mmHg and diastolic blood pressure was 83.48 ± 13.42, 81.36 ± 11.25, 76.72 ± 13.44 and 81.86 ± 9.53 mmHg for the ginger, cinnamon, black seed and placebo groups respectively.

Waist circumference (WC) was measured as part of the inclusion criteria. WC mean values were 105.46 ± 14.93, 96.56 ± 13.77, 98.61± 17.64 and 11.92 ± 102.08 cm for the ginger, cinnamon, black seed and placebo groups respectively. The average WC of participants of ginger, cinnamon, black seed groups did not differ significantly from the average WC of the placebo group (P-value ≥ 0.05).

For the ginger group, the mean value of the participants' weight was 100.61 ± 4.93 kg and their body mass index (BMI) was 36.0 ± 6.47 kg/m^2. Participants were considered to be severely obese (obese class II) [252]. The mean value of their skeletal muscle mass (SMM) was 31.34 ± 7.35 kg, body fat mass (BFM) was 44.65 ± 13 kg while percent body fat (PBF) was 44.04 ± 7.24%. No significant difference between the

ginger group and the placebo group was observed among the aforementioned parameters prior to the investigation (P-value > 0.05), except for the mean value of weight (P-value=0.027).

On the other hand, cinnamon group participant's weight mean value was 99.06 ± 20.18 kg and the BMI mean value was 33.53 ± 9.96 kg/m2. Furthermore, Participants had a BFM mean value of 42.23 ± 14.54 kg, while the PBF mean value was 41.6 ± 8.22% and the SMM mean value was 27.58 ± 7.56 kg. The difference between the cinnamon group and the placebo group were not significant for BP, WC, BFM, SMM, BMI and PBF (P-value ≤ 0.05). Moreover, the difference in the weight mean value between the cinnamon group and the placebo group was significant (P-value=0.048).

Black seed group participant weight mean value was 92.74 ± 24.44 kg and BMI was 34.78 ± 9.28 kg/m^2. Their SMM was 28.82 ± 7.31 kg, BFM 40.96 ± 17.26 kg and their PBF was 43.21 ± 9.24%. Mean value of the weight of the placebo group was 93.77 ± 19.17 kg, BMI was 33.94 ± 5.84 kg/m^2, SMM was 31.23 ± 6.99 kg, BFM was 38.30 ± 14.65 kg and PBF was 40.52 ± 10.32% as shown in Table 4.12. No significant difference between the three treatment groups was found when comparing the mean values of the clinical, body composition and anthropometric measures (P-value > 0.05).

Table 4.12: Clinical, Anthropometric and Body Composition Assessment of the Treatment Groups with the Placebo Group at Baseline (Mean ± SD)

Parameter	Ginger group n=21	P-value of Independent sample t- test	Cinnamon group n=25	P-value of Independent sample t- test	Black seed group n=29	P-value of Independent sample t- test	Placebo group n=22
Systolic BP (mmHg)	119.05 ± 17.75(b)	0.516	121.68 ± 15.65(b)	0.863	115.48± 17.72(b)	0.158	122.50 ± 16.79
Diastolic BP (mmHg)	83.48 ± 13.42(b)	0.651	81.36 ± 11.25(b)	0.870	76.72± 13.44(b)	0.134	81.86± 9.53
WC (cm)	105.46 ± 14.93(b)	0.415	96.56 ± 13.77(b)	0.152	98.61± 17.64(b)	0.431	102.08± 11.92
BFM (kg)	44.65 ± 13.00(b)	0.147	42.23 ± 14.54(b)	0.162	40.96± 17.26(b)	0.563	38.30± 14.65
Weight (kg)	100.60 ± 21.12(a)	0.027	92.06 ± 20.18(a)	0.048	92.74± 24.44(b)	0.871	93.77± 19.17
SMM (kg)	31.34 ± 7.35(b)	0.267	27.58 ± 7.56(b)	0.094	28.82± 7.31(b)	0.239	31.23± 6.99
BMI (kg/m^2)	36.07 ± 6.47(b)	0.272	33.53 ± 9.96(b)	0.867	34.78± 9.28(b)	0.713	33.94± 5.84
PBF %	44.04 ± 7.24(b)	0.206	41.6 ± 8.22(b)	0.791	43.21± 9.24(b)	0.340	40.52± 10.32

Data are presented as (mean ± standard deviation)
(a)Mean value differs significantly from placebo group at P-value ≤ 0.05. (b) Mean value does not differ significantly from placebo group at P-value ≤ 0.05
BP: Blood Pressure; WC: Waist Circumference; BFM: Body Fat Mass; SMM: Skeletal Muscle Mass; BMI: Body Mass Index; PBF: Percent Body Fat.

4.2.2.2 Midpoint Assessments

Table 4.13 demonstrates all the clinical, anthropometric and body composition values at midpoint. At the sixth week of the intervention period, systolic blood pressure was 115.86 ± 15.40, 115.80 ± 12.81, 114.66 ± 17.70, 120.05 ± 14.80 mmHg and diastolic blood pressure was 78.38 ± 11.13, 79.72 ± 8.94, 75.83 ± 13.15 and 75.64 ± 14.58 mmHg for the ginger, cinnamon, black seed and placebo groups respectively. No significant difference was detected between the treatment groups and the placebo group for the systolic and diastolic blood pressure as shown in Table 4.14.

WC mean values for the ginger, cinnamon, black seed and placebo were 101.32 ± 15.20, 90.35 ± 13.91, 95.84 ± 16.75 and 101.34 ± 12.49 cm, respectively. WC mean values reduction varied from -6.21 cm for the cinnamon group and -2.77 cm for the black seed group. The reduction was significant for the ginger (P-value < 0.001), cinnamon (P-value < 0.001) and black seed (P-value < 0.001) groups when compared to the placebo group as shown in Figure 4.1.

Moreover, mean value of weight for the participants was 99.41 ± 21.58, 91.45 ± 13.38, 93.13 ± 24.27 and 95.51 ±19.23 kg for the ginger, cinnamon, black seed and placebo groups, respectively. There was no significant difference in the mean value of the weight of the participants in ginger and black seed groups when compared to placebo group at P-value > 0.05, while the difference of weigh was considered significant for the cinnamon group when compared to placebo group (P-value=0.001).

BMI and Skeletal muscle mass (SMM) did not change significantly in all groups at midpoint (P-value > 0.05).

BFM and PBF mean values did not change significantly (P-value > 0.05) for ginger and black seed group when compared to placebo group. Changes of note were identifiable and significant in body fat mass (40.85 ± 10.15 kg) and percent body fat (41.33 ± 8.25%) in the cinnamon group when compared to placebo group with P-value < 0.001 and P-value=0.038 respectively (Table 4.13).

Weight mean value was significantly different (P-value=0.048) from the placebo mean value at baseline, with placebo group having a lower weight mean value than the cinnamon group at baseline as demonstrated in Table 4.12. Moreover, Weight mean value of the cinnamon group at midpoint was significantly different (P-value=0.001) from the placebo weight mean value, as shown in Table 4.14 and Figure 4.1. Therefore, a regression test was conducted at midpoint of the study to test the relevance of the significancy of the weight change in the cinnamon group. The regression test took into consideration the different treatment groups, weight mean values at baseline and the interaction between the treatment and weight mean values at baseline. For the cinnamon group, no significant difference was detected (P-value=0.626). This means that the difference in weight mean value for the cinnamon group is significant at midpoint when compared to placebo group.

Moreover, ginger weight mean value at baseline was significantly different (P-value=0.027) from the placebo weight mean value at baseline as demonstrated in Table 4.12. However, no significant difference was detected in the weight mean values of the ginger group when compared to the placebo group at midpoint (P-value=0.836) as shown in Table 4.14. Therefore, no further analysis was required.

Table 4.13: Clinical, Anthropometric and Body Composition Assessment of the Treatment Groups with the Placebo Group at Midpoint (Mean ± SD)

Intervention group	Ginger group n=21	Cinnamon group n=25	Black seed group n=29	Placebo group n=22
Systolic BP (mmHg)	115.86 ± 15.40	115.80 ± 12.81	114.66 ± 17.70	120.05 ± 14.80
Diastolic BP (mmHg)	78.38 ± 11.13	79.72 ± 8.94	75.83 ± 13.15	75.64 ± 14.58
WC (cm)	101.32 ± 15.20	90.35 ± 13.91	95.84 ± 16.75	101.34 ± 12.49
BFM (kg)	43.88 ± 13.69	40.85 ± 10.15	40.68 ± 17.31	39.54 ± 15.70
Weight (kg)	99.41 ± 21.58	91.45 ± 13.38	93.13 ± 24.27	95.51 ± 19.23
SMM (kg)	33.30 ± 11.17	27.84 ± 7.41	29.29 ± 7.23	32.74 ± 6.55
BMI (kg/m^2)	35.86 ± 6.49	33.01 ± 10.40	35.05 ± 9.82	34.19 ± 6.11
PBF %	43.9 ± 7.34	41.33 ± 8.25	43.16 ± 9.09	40.58 ± 10.45

BP: Blood Pressure; WC: Waist Circumference; BFM: Body Fat Mass; SMM: Skeletal Muscle Mass; BMI: Body Mass Index; PBF: Percent Body Fat.

Table 4.14: Clinical, Anthropometric and Body Composition Assessment Comparison of the Treatment Groups with the Placebo Group at Midpoint (Week 6 – Week 0)

Parameter	Ginger group n=21	P-value	Cinnamon group n=25	P-value	Black seed group n=29	P-value	Placebo group n=22
Systolic BP (mmHg)	-3.19 ± 10.14	0.452	-5.88 ± 11.79	0.676	-0.83 ± 14.21	0.182	-2.45 ± 11.70
Diastolic BP (mmHg)	-5.10 ± 10.41	0.77	-1.64 ± 7.28	0.212	-0.90 ± 13.27	0.072	-6.23 ± 16.28
WC (cm)	-4.14 ± 3.38	0.000*	-6.21 ± 10.91	0.000*	-2.77 ± 2.96	0.000*	-0.74 ± 2.37
BFM (g)	1.62 ± 6.06	0.610	-0.84 ± 1.14	0.000*	0.38 ± 1.84	0.997	0.15 ± 1.94
Weight (kg)	3.78 ± 16.12	0.836	-0.64 ± 1.19	0.001*	0.86 ± 2.14	0.628	2.05 ± 6.20
SMM (kg)	3.46 ± 15.64	0.670	0.26 ± 0.38	0.856	0.47 ± 0.66	0.219	1.50 ± 1.58
BMI (kg/m^2)	1.51 ± 6.42	0.626	-0.52 ± 6.45	0.593	0.27 ± 2.63	0.901	0.25 ± 0.93
PBF %	1.96 ± 7.92	0.932	-0.2 ± 0.90	0.038*	-0.04 ± 9.09	0.356	0.06 ± 1.95

*significant at p-value=0.05
BP: Blood Pressure; WC: Waist Circumference; BFM: Body Fat Mass; SMM: Skeletal Muscle Mass; BMI: Body Mass Index; PBF: Percent Body Fat.

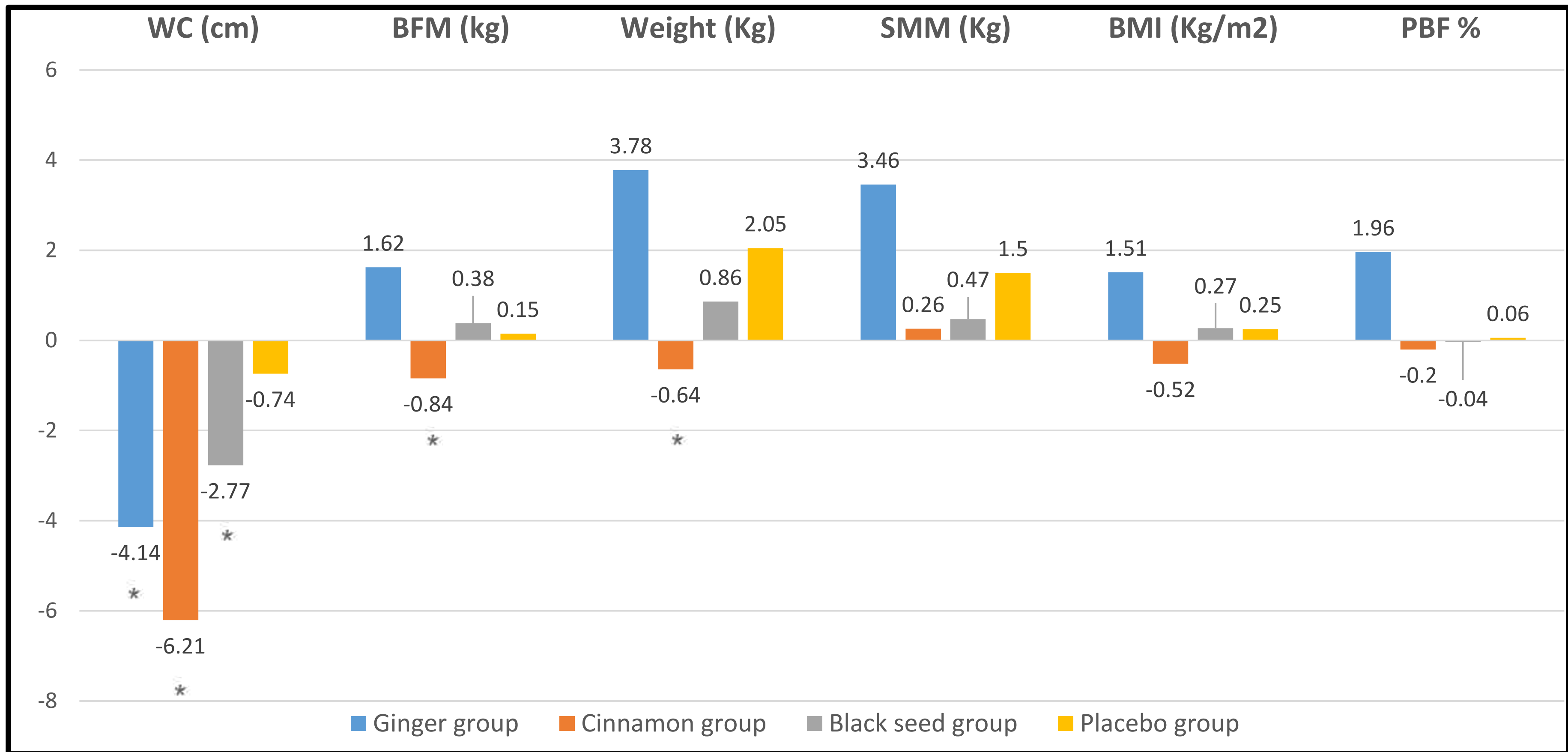

Figure 4.1: The Effect of Spice Powders on Clinical, Anthropometric and Body Composition after Six Weeks of the Intervention when Compared to the Placebo Group

WC: Waist Circumference; BFM: Body Fat Mass; SMM: Skeletal Muscle Mass; BMI: Body Mass Index; PBF: Percent Body Fat.

4.2.2.3 Endpoint Assessment

At the twelfth week, participants attended the third and last visit and all the clinical, anthropometric and body composition assessments were taken for the four treatment groups. Systolic blood pressure mean values varied from 113.63 ± 16.88 mmHg for the black seed group to 122.55 ± 16.07 mmHg for the placebo group (Table 4.15). Diastolic blood pressure mean values ranged from 77.78 ± 13.52 mmHg for the black seed group to 80.73 ± 11.74 mmHg for the placebo group. Table 4.16 shows the difference between baseline and the twelfth week for the parameters measured in this study. For the blood pressure measurements, changes from the baseline for the three treatment groups were not statistically significant when compared to the placebo group. Table 4.16 shows the difference between baseline and the twelfth week for all the clinical, anthropometric and body composition parameters measured in this study.

A significant reduction was observed in ginger, cinnamon, black seed groups in comparison with the placebo group over the twelfth weeks results for the mean values of WC (P-value ≤ 0.05). The ginger group WC reduction mean value was -6.17 cm ± 4.10 (P-value=0.000) and the cinnamon group's reduction mean value was -7.13 ± 4.93 cm (P-value=0.000), while the black seed group had the highest WC reduction among the interventional groups with a mean value of -10.56 ± 26.47 cm (P-value < 0.001), as shown in Figure 4.2.

BFM, weight, BMI and PBF reductions were only significant for the cinnamon group when compared to the placebo group (-1.3 ± 1.41, P-value=0.001; -2.01 ± 6.53 kg, P-value=0.011; -2.70 ± 9.01 kg/m^2, P-value=0.001; and -2.82 ± 1.14, P-value=0.027, respectively). BFM, weight, BMI and PBF changes mean values of the ginger and the black seed groups were considered not significant when compared to the placebo group

(P-value > 0.05). SMM increased in the cinnamon group by 0.12 ± 0.99 kg and in the ginger group by 2.18 kg ± 5.73. However, the increase was not significant when compared to the placebo group (P-value > 0.05), while it decreased non-significantly in the black seed group (-0.52 ±1.33 kg) when compared to the placebo group (P-value > 0.05) (Table 4.16).

Weight mean value was significantly different (P-value=0.048) from the placebo mean value at baseline, with placebo group having a lower weight mean value than the cinnamon group at baseline as demonstrated in Table 4.12. Therefore, a regression test was conducted at end point of the study to test the relevance of the significancy of the weight change for the cinnamon group. The regression test took into consideration the different treatment groups, weight mean values at baseline and the interaction between the treatment and weight mean values at baseline. For the cinnamon group, no significant difference was detected (P-value=0.732). This means that the difference in weight mean value for the cinnamon group is significant at endpoint when compared to placebo group, though there was a significant difference at baseline in the mean value of weigh of the cinnamon group when compared to placebo group. Moreover, ginger weight mean value at baseline was significantly different (P-value=0.027) from the placebo weight mean value at baseline as demonstrated in Table 4.12. However, the significant difference was detected in the weight mean values of the ginger group at endpoint when compared to the placebo group (P-value=0.22), as shown in Table 4.16 and Figure 4.2. Therefore, no further analysis was required.

Table 4.15: Anthropometric and Clinical Assessment of the Treatment Groups with the Placebo Group at Endpoint (Mean ± SD)

Intervention group	Ginger group n=21	Cinnamon group n=25	Black seed group n=29	Placebo group n=22
Systolic BP (mmHg)	116.86 ± 13.65	114.64± 15.12	113.63± 16.88	122.55± 16.07
Diastolic BP (mmHg)	79.38± 9.85	77.80± 10.35	77.78± 13.52	80.73± 11.74
WC (cm)	99.29± 14.73	89.43± 13.10	88.05± 29.45	102.36± 12.25
BFM (kg)	44.14± 13.20	40.83± 9.85	41.34± 17.81	38.44± 15.37
Weight (kg)	99.59± 21.41	90.08± 15.23	93.60± 25.39	95.82± 18.19
SMM (kg)	32.02± 7.26	27.59± 7.56	30.02± 7.28	31.77± 6.82
BMI (kg/m^2)	35.65± 6.67	32.12± 9.86	34.94± 9.35	34.60± 6.17
PBF %	43.60± 7.28	17.55± 20.74	42.69± 9.31	40.81± 10.53

BP: Blood Pressure; WC: Waist Circumference; BFM: Body Fat Mass; SMM: Skeletal Muscle Mass; BMI: Body Mass Index; PBF: Percent Body Fat.

Table 4.16: Clinical, Anthropometric and Body Composition Assessment Comparison of the Treatment Groups with the Placebo Group at Endpoint (Week 12 – Week 0)

Parameter	Ginger group n=21	P-value	Cinnamon group n=25	P-value	Black seed group n=29	P-value	Placebo group n=22
Systolic BP (mmHg)	-2.19 ± 10.84	0.601	-7.04 ± 11.75	0.186	-9.69 ± 28.98	0.536	0.05 ± 14.38
Diastolic BP (mmHg)	-4.10 ± 9.05	0.991	-3.56 ± 9.32	0.965	-4.31 ± 23.55	0.668	-1.14 ± 9.59
WC (cm)	-6.17 ± 4.10	0.000*	-7.13 ± 4.93	0.000*	-10.56 ± 26.47	0.000*	0.29 ± 4.92
BFM (kg)	1.36 ± 5.82	0.274	-1.3 ± 1.41	0.001*	-0.38 ± 1.36	0.070	1.25 ± 3.65
Weight (kg)	3.60 ± 15.67	0.220	-2.01 ± 6.53	0.011*	0.39 ± 1.38	0.304	1.73 ± 6.45
SMM (kg)	2.18 ± 5.73	0.601	0.12 ± 0.99	0.550	-1.91 ± 6.94	0.753	0.53 ± 1.89
BMI (kg/m^2)	1.30 ± 5.67	0.105	-2.70 ± 9.01	0.001*	0.16 ± 0.48	0.107	0.66 ± 1.52
PBF %	1.67 ± 8.00	0.307	-2.82 ± 1.14	0.027*	-0.52 ± 1.33	0.726	0.29 ± 1.08

*Significant at P-value ≤ 0.05
BP: Blood Pressure; WC: Waist Circumference; BFM: Body Fat Mass; SMM: Skeletal Muscle Mass; BMI: Body Mass Index; PBF: Percent Body Fat.

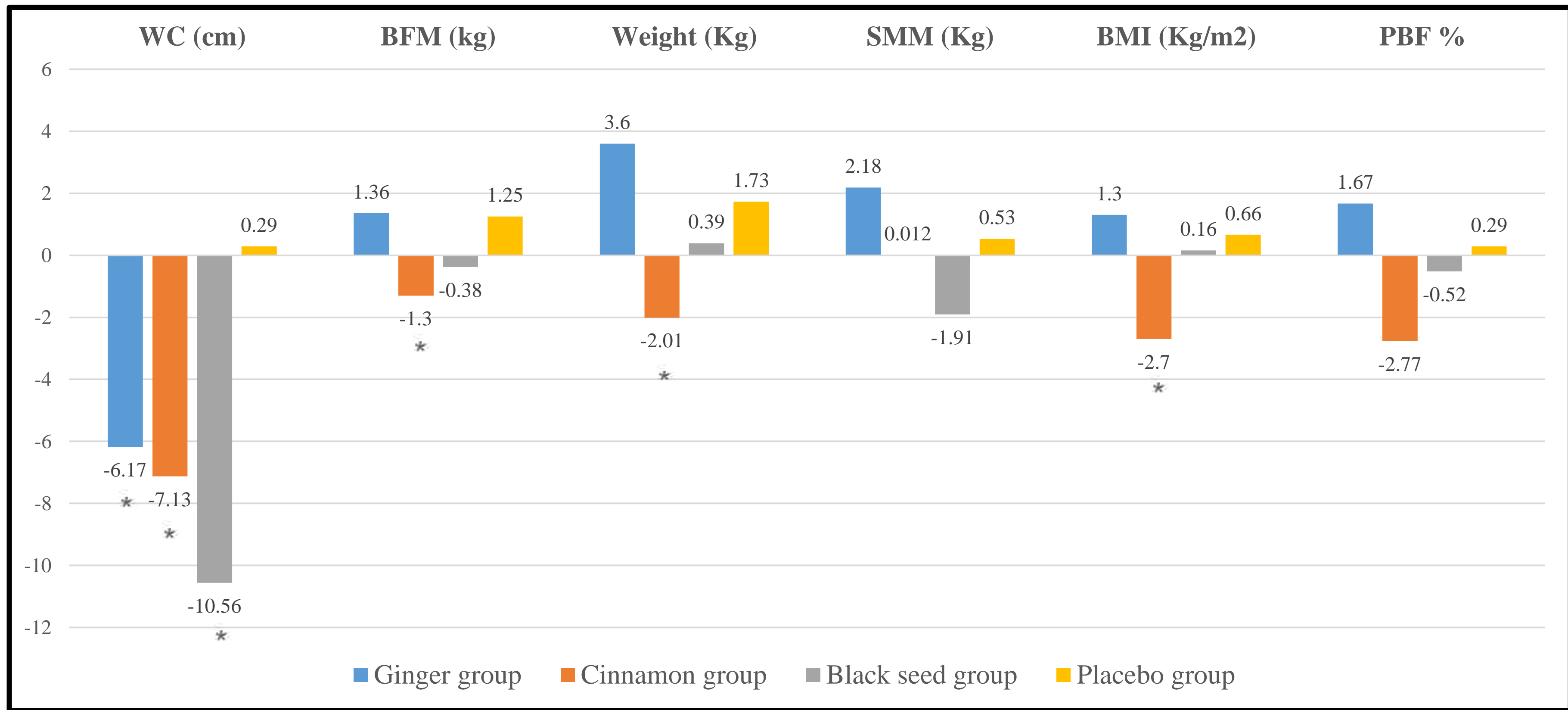

Figure 4.2: The Effect of Spice Powders on Body Composition after Twelve Weeks of the Intervention when Compared to the Placebo Group

WC: Waist Circumference; BFM: Body Fat Mass; SMM: Skeletal Muscle Mass; BMI: Body Mass Index; PBF: Percent Body Fat.

4.2.3 Dietary Assessment

In order to accurately test the effect of the spices, participants were asked to uphold their regular dietary habits and not to change their food intake. Participants who changed their eating habits or tried to lose weight by following a certain diet during the study period were excluded.

Three days of food records were collected from each participant at every visit (baseline, midpoint and endpoint). The food records were distributed before each visit and participants were asked to complete the food record with their intake of food and beverages over two days during the week (working days) and one day of the weekend. Participants were asked to bring the food record at each visit. Each participant filled a total of nine days of food records during the 12 weeks of study

4.2.3.1 Baseline Dietary Assessment

At baseline, participants consumed a total energy of 2499.74 ± 1067, 2430.55 ± 1244.16, 2492.20 ± 1136.71 and 2454.21 ± 1255.87 Kcal per day for the ginger, cinnamon, black seed and placebo groups respectively (Table 4.17). No significant difference was observed between ginger, cinnamon, black seed groups and the placebo group (P-value ≤ 0.05). Carbohydrate consumption was 358.05 ± 151.92, 350.39 ± 168.60, 358.43 ± 152.37 and 353.62 ± 150.68 grams per day for the ginger, cinnamon, black seed and placebo groups respectively. Mean value of carbohydrates consumption did not differ significantly between ginger, cinnamon and black seed groups and the placebo group (add P-value). Fat consumption was the highest in placebo group (102.45 ± 61.87 grams per day) while the other groups did not exceed 96.48 ± 62.95 grams per day. No significant difference was observed between ginger, cinnamon and black seed groups and the placebo group (P-value > 0.05). Protein consumption was

103.77 ± 49.57, 103.21 ± 36.19, 102.47 ± 34.41 and 104.16 ± 33.69 grams per day for the ginger, cinnamon, black seed and placebo groups respectively. No significant difference was observed between ginger, cinnamon, black seed group and the placebo group (P-value > 0.05). Differences in macronutrients or calories consumption between groups was not significant (P-value ≥ 0.5) as shown in Table 4.17.

Table 4.17: Macronutrient Consumption for the Treatment Groups and the Placebo Group at Baseline (Mean ± SD)

Intervention group	Ginger group n=21	P-value of Independent sample t- test	Cinnamon group n=25	P-value of Independent sample t- test	Black seed group n=29	P-value of Independent sample t- test	Placebo group n=22
Calories (kcal)	2499.74 ± 1067 [(b)]	0.762	2430.55 ± 1244.16[(b)]	0.983	2492.20 ± 1136.71[(b)]	0.863	2454.21 ± 1255.87
Carbohydrates (g)	358.05 ± 151.92[(b)]	0.292	350.39 ± 168.60[(b)]	0.545	358.43 ± 152.37[(b)]	0.679	353.62 ± 150.68
Fat (g)	94.25 ± 52.19[(b)]	0.061	95.14 ± 67.33[(b)]	0.056	96.48 ± 62.95[(b)]	0.087	102.45 ± 61.87
Protein (g)	103.77 ± 49.57[(b)]	0.532	103.21 ± 36.19[(b)]	0.652	102.47 ± 34.41[(b)]	0.591	104.16 ± 33.69

*Significant at P-value ≤ 0.05
(a)Mean value differs significantly from placebo group at P-value ≤ 0.05. (b) Mean value does not differ significantly from placebo group at P-value ≤ 0.05

4.2.3.2 Midpoint Dietary Assessment

At midpoint, participants consumed a total energy of 2516.49 ± 979.85, 2454.91 ± 1222.11, 2494.93 ± 1118.69 and 2459.44 ± 1249.48 Kcal per day for the ginger, cinnamon, black seed and placebo groups respectively (Table 4.18). No significant difference was detected between the ginger, cinnamon and black seed groups and the placebo group (P-value > 0.05). Participants consumed 353.9 ± 979.85, 349.86 ± 162.91, 357.01 ± 149.21 and 347.13 ± 143.60 grams of carbohydrate per day for the ginger, cinnamon, black seed and placebo groups respectively. Carbohydrate consumption of the three treatment groups did not differ significantly (P-value > 0.05) at the sixth week when compared with the first week and the placebo group as shown in Table 4.19.

Moreover, fat consumption was 97.35 ± 48.40, 93.62 ± 59.94, 94.27 ± 56.48 and 99.59 ± 59.49 grams per day for the ginger, cinnamon, black seed and placebo groups respectively. Fat consumption did not change significantly during the first six weeks of the study (P-values > 0.05) for the three treatment groups when compared to the placebo group and to the baseline results.

Protein consumption did not exceed 105.83 ± 45.40 grams per day for all groups, as well as did not differ significantly. The P-values of the ginger (P-value=0.264), cinnamon (P-value=0.839) and black seed (P-value=0.932) groups when compared to the placebo group and to the baseline results (Table 4.19). This suggests that participants maintained the same level of macronutrient consumption until the sixth week of the study period.

Table 4.18: Macronutrients Consumption for the Treatment Groups and the Placebo Group at Midpoint (Mean ± SD)

Intervention group	Ginger group n=21	Cinnamon group n=25	Black seed group n=29	Placebo group n=22
Calories (kcal)	2516.49 ± 979.85	2454.91 ± 1222.11	2494.93 ± 1118.69	2459.44 ± 1249.48
Carbohydrates (g)	353.96 ± 137.81	349.86 ± 162.91	357.01 ± 149.21	347.13 ± 143.60
Fat (g)	97.35 ± 48.45	93.62 ± 59.94	94.27 ± 56.48	99.59 ± 59.49
Protein (g)	105.83 ± 45.40	102.85 ± 33.80	101.47 ± 32.94	102.64 ± 30.09

Table 4.19: Macronutrients Consumption for the Treatment Groups and the Placebo Group at Midpoint (Week 6 – Week 0)

Intervention group	Ginger group n=21	P-value	Cinnamon group n=25	P-value	Black seed group n=29	P-value	Placebo group n=22
Calories (kcal)	16.75 ± 171.03	0.576	24.36 ± 91.49	0.411	6.18 ± 375.33	0.834	5.23 ± 175.18
Carbohydrates (g)	-4.08 ± 29.70	0.331	-0.53 ± 15.50	0.564	-1.42 ± 83.17	0.962	-6.50 ± 24.78
Fat (g)	3.10 ± 8.78	0.174	-1.52 ± 9.05	0.286	-2.21 ± 17.17	0.812	-2.86 ± 8.88
Protein (g)	2.07 ± 9.68	0.264	-0.36 ± 7.71	0.839	-1.00 ± 16.35	0.932	-1.52 ± 9.34

*Significant at P-value ≤ 0.05

4.2.3.3 Endpoint Dietary Assessment

At the twelfth week, participants consumed 2563.17 ± 965.13, 2474.45 ± 1231.05, 2525.22 ± 1124.20 and 2476.86 ± 1269.73 Kcal per day of their total energy intake for the ginger, cinnamon, black seed and placebo groups respectively. Carbohydrate consumption did not exceed 360.31 ± 144.39 grams per day for all four groups and did not differ significantly for the ginger, cinnamon, black seed groups when compared to the placebo group and against the baseline results (P-value > 0.05), as shown in Table 4.20 and Table 4.21

Fat consumption was the highest in placebo group (102.74 ± 61.44 grams per day) while the remaining groups did not exceed 97.25 ± 48.76 grams per day. No significant difference was detected between the three treatment groups and the placebo group (P-value > 0.05). Protein consumption was 104.67 ± 45.18, 101.81 ± 32.32, 100.77 ± 30.64 and 105.12 ± 31.93 grams per day for the ginger, cinnamon, black seed and placebo groups respectively with no significant difference between the three treatment groups and the placebo group.

As shown in Table 4.21, there were no significant differences between the treatment groups for calories, carbohydrates, fat and protein consumption when compared with the placebo group and against baseline results (P-value > 0.05).

Maintaining the same level of macronutrient consumption is a crucial key to the success of the study. At the end of the research period, participant who committed to the study protocol and did not change their macronutrient consumption, were offered a nutritional consultation to help them manage their calories intake and to improve their dietary habits.

Table 4.20: Macronutrients Consumption for the Treatment Groups and the Placebo group at Endpoint (Mean ± SD)

Intervention group	Ginger group n=21	Cinnamon group n=25	Black seed group n=29	Placebo group n=22
Calories (kcal)	2563.17 ± 965.13	2474.45 ± 1231.05	2525.22 ± 1124.20	2476.86 ± 1269.73
Carbohydrates (g)	353.03 ± 137.42	351.09 ± 164.80	360.31 ± 144.39	355.25 ± 155.53
Fat (g)	97.25 ± 48.76	95.24 ± 62.07	96.15 ± 57.87	102.74 ± 61.44
Protein (g)	104.67 ± 45.18	101.81 ± 32.32	100.77 ± 30.64	105.12 ± 31.93

Table 4.21: Macronutrients Consumption for the Treatment Groups and the Placebo Group at Endpoint (Week 12 – Week 0)

Intervention group	Ginger group n=21	P-value	Cinnamon group n=25	P-value	Black seed group n=29	P-value	Placebo group n=22
Calories (kcal)	63.42 ± 214.32	0.296	43.90 ± 123.46	0.201	-49.46 ± 639.02	0.805	22.65 ± 149.25
Carbohydrates (g)	-5.01 ± 43.41	0.923	0.69 ± 14.94	0.717	-8.12 ± 96.24	0.909	1.62 ± 17.18
Fat (g)	3.00 ± 10.65	0.152	0.09 ± 7.96	0.616	-0.33 ± 12.18	0.819	0.28 ± 13.14
Protein (g)	0.90 ± 7.46	0.382	-1.41 ± 8.47	0.873	-1.71 ± 11.10	0.819	-3.82 ± 22.28

*Significant at P-value ≤ 0.05

4.2.4 Physical Activity Assessment

Participants were asked to sustain their normal lifestyle and not to change their current physical activity level, thus reducing the variable effect. To ensure that the participants did not change any of their physical activity level, a physical activity questionnaire was collected from the participants on each visit using the international physical activity questionnaire (IPAQ) [260]. A total of three physical activity questionnaires were collected from each participant during the study period.

4.2.4.1 Baseline Physical Activity Assessment

At baseline, participants of the ginger, cinnamon and black seed groups were considered to be inactive as they did not engage in a vigorous physical activity (30 minutes/three times per week) nor any moderate physical activity (five times/per week). On the other hand, the placebo group was considered to be moderately active, as the participants were engaged in a moderate physical activity for more than 30 minutes every day of the week (31.2 ± 13.33 minutes every day). However, no significant difference for moderate activity was considerable between the three treatment group and the placebo group at baseline (P-value ≥ 0.05). All groups performed light physical activity for less than 45 minutes per day and participated in a sedentary activity for around ten hours every day (9.61 ± 2.35. 9.7 ± 2.7, 9.93 ± 2.87 and 9.56 ± 2.24 hours for ginger, cinnamon, black seed and placebo groups, respectively). Participants spent their sedentary time using electronic devices such as computers and smartphones, as well as with friends and family. The three treatment groups had no significant difference in their light physical activity and their sedentary activity when compared to placebo group (P-value > 0.05) as demonstrated in Table 4.22.

Table 4.22: Physical Activity Assessment at Baseline (Mean ± SD)

Physical Activity Level	Ginger group n=21	P-value of Independent sample t- test	Cinnamon group n=25	P-value of Independent sample t- test	Black seed group n=29	P-value of Independent sample t- test	Placebo group n=21
Vigorous Physical Activity (minutes / day)	7.38 ± 13.28[b]	0.629	7.4 13 ± 13.85[b]	0.741	7.58 ± 14.244[b]	0.428	7.72 ± 13.33
Moderate Physical Activity (minutes / day)	28.8 ± 30[b]	0.836	28.2 ± 29.4[b]	0.842	28.8 ± 43.8[b]	0.198	31.2 ± 13.33
Light Physical Activity (minutes / day)	41.66 ± 23.73[b]	0.981	43.4 ± 21.73[b]	0.657	40.68 ± 22.5[b]	0.293	42.27 ± 22.87
Sedentary Physical Activity (hours / day)	9.61 ± 2.35[b]	0.757	9.7 ± 2.7[b]	0.761	9.93 ± 2.87[b]	0.119	9.56 ± 2.24

*Significant at P-value ≤ 0.05

(a)Mean value differs significantly from placebo group at P-value ≤ 0.05. (b) Mean value does not differ significantly from placebo group at P-value ≤ 0.05

4.2.4.2 Midpoint Physical Activity

At the midpoint, participants of the following three groups: ginger, cinnamon and placebo were considered to be inactive as they did not engage in a vigorous physical activity (30 minutes/three times per week) nor any moderate physical activity (five times per week). No significant difference was detected when comparing the two treatment groups with the placebo group (P-value ≤ 0.05). On the other hand, the black seed group was considered to be moderately active, as the participants were engaged in a daily moderate physical activity (30 ± 58.2 minutes per day). This difference was not significant as well when compared with the placebo group (P-value=0.701). All the treatment groups performed light physical activity for less than 45 minutes per day and had a sedentary activity for around ten hours every day, which were spent in using electronic devices and spending leisure time with friends and family as shown in Table 4.23. Although there were some changes in the activity of the groups, this change was not considered to be significant (P-value=0.05). The changes of physical activity between the treatment groups and the placebo group (week 6 – week 0) did not show any significant differences, as all P-values were ≥ 0.05 (Table 4.24). This means that the activity of each group did not change significantly from the starting point of the study until week six, and the changes in the physical activity in the three treatment groups were not significantly different from the placebo group.

Table 4.23: Physical Activity Assessment at Midpoint (Mean ± SD)

Physical Activity Level	**Ginger group n=21**	**Cinnamon group n=25**	**Black seed group n=29**	**Placebo group n=22**
Vigorous Physical Activity (minutes / day)	7.72 ± 12.62	7 ± 13.69	5.34 ± 12.38	7.5 ± 13.07
Moderate Physical Activity (minutes / day)	28.8 ± 34.8	27.6 ± 38.4	30 ± 58.2	28.2 ± 44.4
Light Physical Activity (minutes / day)	40.95 ± 20.40	40.6 ± 19.27	38.96 ± 21.79	40 ± 20.93
Sedentary Physical Activity (hours / day)	9.9 ± 2.53	9.92 ± 2.17	10.41 ± 2.52	9.77 ± 1.99

Table 4.24: Physical Activity Assessment Differences between Treatment Groups and Placebo Group at Midpoint (Week 6 – Week 0)

Physical Activity Level	Ginger group n=21	p-value	Cinnamon group n=25	p-value	Black seed group n=29	p-value	Placebo group n=22
Vigorous Physical Activity (minutes / day)	0.04 ± 3.39	0.694	-0.4 ± 2.46	0.982	-2.24 ± 10.14	0.953	0.04 ± 3.39
Moderate Physical Activity (minutes / day)	0 ± 0.37	0.758	-0.01 ± 0.48	0.482	0.01 ± 0.81	0.701	-0.4 ± 2.46
Light Physical Activity (minutes / day)	-0.71 ± 9.52	0.599	-2.8 ± 7.37	0.809	-1.72 ± 9.28	0.556	-2.24 ± 10.1
Sedentary Physical Activity (Minutes / day)	0.35 ± 1.54	0.678	0.22 ± 1.76	0.785	0.48 ± 1.99	0.742	-0.22 ± 1.06

*Significant at P-value ≤ 0.05

4.2.4.3 Endpoint Physical Activity Assessment

At the endpoint, participants of the ginger, cinnamon, black seed and placebo were considered to be inactive, as they did not engage in a vigorous physical activity (30 minutes/three times per week) nor any moderate physical activity (five times per week). Mean values of vigorous physical activity level and moderate physical activity level had no significant differences in the treatment groups when compared to the placebo group (P-value > 0.05). All groups performed light physical activity for less than 45 minutes per day (41.42 ± 22.97, 41.4 ± 19.81, 40.68 ± 22.5 and 40.68 ± 20.60 minutes per day for the ginger group, cinnamon group, black seed group and placebo group, respectively). Moreover, participants had a sedentary activity for around ten hours every day using their electronic devices and spending leisure time with friends and family as demonstrated in Table 4.25.

Although there were some minor changes in the activity of the groups (Table 4.25), the change was not considered to be significant at P-value=0.05. When analyzing the results of the physical activity differences (week 12 – week 0) between treatment groups and the placebo group, all P-values were > 0.05 as indicated in Table 4.26. This means that the activity of each group did not change significantly from the starting point of the study till the twelfth week, and the changes in the physical activity in the treatment groups were not significantly different from the placebo group.

Therefore, it is concluded that physical activity level did not change significantly during the study period.

Table 4.25: Physical Activity Assessment at Endpoint (Mean ± SD)

Physical Activity Level	**Ginger group n=21**	**Cinnamon group n=25**	**Black seed group n=29**	**Placebo group n=22**
Vigorous Physical Activity (minutes / day)	7.61 ± 13.38	7.4 ± 13.54	7.75 ± 14.67	7.72 ± 13.33
Moderate Physical Activity (minutes / day)	28.2 ± 1.8	28.8 ± 9.4	28.2 ± 13.8	29.9 ± 10.3
Light Physical Activity (minutes / day)	41.42 ± 22.97	41.4 ± 19.81	40.68 ± 22.5	40.68 ± 20.60
Sedentary Physical Activity (hours / day)	9.71 ± 2.49	9.92 ± 2.81	9.93 ± 2.8	9.81 ± 2.59

Table 4.26: Physical Activity Assessment Differences between Treatment Groups and Placebo Group at Endpoint (Week 12 – Week 0)

Physical Activity Level	Ginger group n=21	p-value	Cinnamon group n=25	p-value	Black seed group n=29	p-value	Placebo group n=22
Vigorous Physical Activity (minutes / day)	0.23 ± 3.34	0.545	0.00 ± 2.88	1.00	0.17 ± 0.92	0.384	-3.33 ± 0.24
Moderate Physical Activity (minutes / day)	-0.012 ± 0.16	0.678	0.01 ± 0.19	0.971	-.008 ± 0.1	1.00	0.002 ± 0.11
Light Physical Activity (minutes / day)	-0.23 ± 2.94	0.432	-2.00 ± 6.29	0.496	0.00 ± 0.00	0.101	-1.59 ± 6.43
Sedentary Physical Activity (hours / day)	0.09 ± 0.43	0.981	0.22 ± 1.25	0.948	-0.03 ± 0.18	0.499	0.25 ± 1.19

*Significant at P-value ≤ 0.05

4.2.5 Biochemical Assessment

Vinous blood sample was collected from the participant of the Treatment groups in all the three visits. Hemoglobin (Hb), glycated hemoglobin (HbA1c), fasting blood glucose (FBG), total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides (TG) were analyzed to examine the effect of the spices powder on hemoglobin, blood glucose and lipid profile.

4.2.5.1 Baseline Biochemical Assessment

At baseline, the mean values of Hb were 13.93 ± 1.87, 14.04 ± 2.28, 14.72 ± 1.78 and 13.78 ± 2.20 g/dL for the ginger, cinnamon, black seed and placebo groups respectively (Table 4.27). No significant difference was detected when comparing the treatment groups Hb mean values with the placebo group Hb mean value (P-value > 0.05). HbA1c mean values were all above the cut-off point 5.7% [7]. HbA1c mean values ranged from 5.91 ± 0.69% for the ginger group to 6.45 ± 1.83% for the cinnamon group. HbA1c mean values for ginger and cinnamon groups had no significant difference when compared to the placebo group (P-values > 0.05). Whereas, black seed group mean value of HbA1c had a significant difference (P-value=0.039) when compared to placebo group.

Total blood cholesterol values varied from 121.51 ± 37.95 mg/dL for the placebo group to 160.86 ± 33.04 mg/dL for the black seed group. All treatment groups mean value of total cholesterol were significantly different from the placebo group mean value with a P-value ≤ 0.05 as shown in Table 4.27.

FBG mean value level approached 100 mg/dL for the cinnamon group (99.06 ± 42.62 mg/dL) and was 82.63 ± 15.03, 93.69 ± 8.47, 89.30 ± 30 mg/dL for the ginger, black seed and placebo groups respectively. No significant difference was observed when comparing the treatment groups mean value of FBG to the placebo group mean value. P-values were 0.259, 0.34 and 0.33 for ginger, cinnamon and black seed, respectively.

The LDL mean value level was 94.28 ± 33.14, 110.32 ± 33.39, 95.52 ± 22.61 and 70.52 ± 28.25 mg/dL for the ginger, cinnamon, black seed and placebo groups, respectively. Only the ginger group mean value had no significant difference when compared to the placebo group (P-value=0.15), whilst cinnamon group and black seed group mean values were significantly different when compared to the placebo group mean value (P-values=0.00 and 0.001, cinnamon group and black seed group, respectively).

Furthermore, the average HDL value ranged from 34.71 ± 12.88 mg/dL for the placebo group to 41.36 ± 12.76 mg/dL for the cinnamon group. No significant difference was detected when comparing the mean value of the treatment groups to the mean value of the placebo group (P-values > 0.05).

Moreover, TG mean values were 113.50 ± 91.97, 116.63 ± 79.37, 101.29 ± 33 and 102.34 ± 34 mg/dL for ginger, cinnamon, black seed and placebo group, respectively. The average values of TG had no significant difference at P-value ≤ 0.05 as shown in Table 4.27.

As participants were randomly distributed into four treatment groups considering age and metabolic syndrome criteria (high blood pressure, large waist circumference, elevated fasting blood glucose, increased triglycerides and low high density

lipoprotein), some significant differences between treatment groups in the other parameters were expected at baseline as observed in Table 4.27. If the parameters of the significant difference at baseline were significantly different at midpoint or endpoint, further analysis were be taken into consideration.

Table 4.27: Biochemical Assessment of the Treatment Groups and the Placebo Group at Baseline (Mean ± SD)

Intervention group	**Ginger group n=21**	**P-value of Independent sample t- test**	**Cinnamon group n=25**	**P-value of Independent sample t- test**	**Black seed group n=29**	**P-value of Independent sample t- test**	**Placebo group n=22**
Hb (g/dL)	13.93 ± 1.87[b]	0.817	14.04 ± 2.28[b]	0.702	14.72 ± 1.78[b]	0.09	13.78 ± 2.20
HbA1c %	5.91 ± 0.69[b]	0.816	6.45 ± 1.83[b]	0.79	5.92 ± 0.59[a]	0.039*	6.33 ± 1.16
Total Cholesterol (mg/dL)	153.23 ± 47.38[a]	0.02*	158.15 ± 33.19[a]	0.001*	160.86 ± 33.04[a]	0.00*	121.51 ± 37.95
FBG (mg/dL)	82.63 ± 15.03[b]	0.259	99.06 ± 42.62[b]	0.34	93.69 ± 8.47[b]	0.33	89.30 ± 30.00
HDL (mg/dL)	34.81 ± 10.05[b]	1.00	41.36 ± 12.76[b]	0.08	36.81 ± 10.60[b]	0.545	34.71 ± 12.88
LDL (mg/dL)	94.28 ± 33.14[b]	0.15	110.32 ± 33.39[a]	0.00	95.52 ± 22.61[a]	0.001*	70.52 ± 28.25
TG (mg/dL)	113.50 ± 91.97[b]	0.59	116.63 ± 79.37[b]	0.42	101.29 ± 33.00[b]	0.90	102.34 ± 34

*Significant at P-value ≤ 0.05
(a)Mean value differs significantly from placebo group at P-value ≤ 0.05. (b) Mean value does not differ significantly from placebo group at P-value ≤ 0.05
Hb: Hemoglobin; HbA1c: Glycated hemoglobin; FBG: Fasting blood cholesterol; HDL: High density lipoprotein cholesterol; LDL: Low density lipoprotein cholesterol; TG: Triglyceride

4.2.5.2 Midpoint Biochemical Assessment

At the sixth week of the intervention, hemoglobin (Hb) mean values did not change dramatically. Hb mean values were 13.98 ± 1.81, 14.10 ± 2.26, 14.74 ± 1.77 and 13.66 ± 2.14 g/dL for the ginger, cinnamon, black seed and placebo groups respectively, while HbA1c mean values were above the cutoff point (5.7%) for all treatment groups [7]. HbA1c mean values were 5.73 ± 0.50, 6.21 ± 2.02, 5.8 ± 0.56 and 6.35 ± 1.24% for the ginger, cinnamon, black seed and placebo groups, respectively. Only cinnamon group HbA1c mean value were significant when compared to the placebo group mean values (P-value=0.04). Fasting blood glucose mean values were below 100 mg/dL for the ginger, cinnamon, black seed and placebo groups 86.00 ± 12.34, 96.21 ± 48.94, 90.72 ± 8.65 and 94.57 ± 19.33 mg/dL, respectively. Fasting blood glucose reduction was considered significant for ginger group (P-value=0.012), cinnamon group (P-value=0.002) and black seed group (P-value=0.001) in comparison with placebo group at the sixth week of the study.

Lipid profile did not change significantly either. For instance, cholesterol mean values ranged from 159.06 ± 45.71 for the ginger group to 145.13 ± 38.03 mg/dL for the placebo group, as shown in Table 4.28. HDL increased remarkably in the black seed group with a mean value of 41.84 ± 10.76 mg/dL, however the increase was not considered significant (P-value=0.63). No remarkable changes were noticed in LDL mean values as well (P-value > 0.05).

Furthermore, TG mean values were reduced significantly in ginger group (108.89 ± 85.09 mg/dL, P-value=0.05), cinnamon group (112.71 ± 84.59 mg/dL, P-value=0.006) and black seed group (93.58 ± 34.40 mg/dL, P-value=0.000) when compared to the placebo group as shown in Table 4.28, Table 4.29 and Figure 4.3.

Table 4.28: Biochemical Assessment of the Treatment Groups and the Placebo Group at Midpoint (Mean ± SD)

Intervention group	Ginger group n=21	Cinnamon group n=25	Black seed group n=29	Placebo group n=22
Hb (g/dL)	13.98 ± 1.81	14.10 ± 2.26	14.74 ± 1.77	13.66 ± 2.14
HbA1c %	5.73 ± 0.50	6.21 ± 2.02	5.58 ± 0.56	6.35 ± 1.24
Total Cholesterol (mg/dL)	159.06 ± 45.71	148.25 ± 29.81	153.79 ± 28.55	145.13 ± 38.03
FBG (mg/dL)	86.00 ± 12.34	96.21 ± 48.94	90.72 ± 8.65	94.57 ± 19.33
HDL (mg/dL)	36.24 ± 9.04	40.89 ± 12.32	41.84 ± 10.76	35.02 ± 13.16
LDL (mg/dL)	98.30 ± 32.17	113.74 ± 30.27	92.12 ± 21.71	86.66 ± 30.09
TG (mg/dL)	108.89 ± 85.09	112.71 ± 84.59	93.58 ± 34.40	91.08 ± 43.49

Hb: Hemoglobin; HbA1c: Glycated hemoglobin; FBG: Fasting blood cholesterol; HDL: High density lipoprotein cholesterol; LDL: Low density lipoprotein cholesterol; TG: Triglyceride

Table 4.29: Biochemical Assessment Comparison of the Treatment Groups with the Placebo Group at Midpoint (Week 6 – Week 0)

Parameter	Ginger group n=21	P-value	Cinnamon group n=25	P-value	Black seed group n=29	P-value	Placebo group n=22
Hb (g/dL)	0.05 ± 0.45	0.074	0.07 ± 0.23	0.063	0.01 ± 0.24	0.092	-0.12 ± 0.17
HbA1c %	-0.18 ± 0.69	0.632	-0.23 ± 0.71	0.04*	-0.12 ± 0.57	0.000	0.22 ± 0.31
Total Cholesterol (mg/dL)	5.83 ± 22.72	0.120	-9.90 ± 27.69	0.396	-7.07 ± 29.71	0.415	23.62 ± 33.76
FBG (mg/dL)	-0.91 ± 5.27	0.012*	-2.85 ± 12.10	0.000*	-2.97 ± 5.85	0.000*	5.26 ± 9.72
HDL (mg/dL)	1.43 ± 4.49	0.128	-0.46 ± 7.97	0.991	4.26 ± 5.83	0.063	6.14 ± 8.98
LDL (mg/dL)	4.02 ± 18.39	0.444	3.42 ± 26.03	0.296	-3.40 ± 21.62	0.831	16.15 ± 23.06
TG (mg/dL)	-4.61 ± 32.78	0.05*	-3.92 ± 31.78	0.006*	-7.71 ± 13.53	0.000*	19.10 ± 25.46

*Significant at P-value ≤ 0.05

Hb: Hemoglobin; HbA1c: Glycated hemoglobin; FBG: Fasting blood cholesterol; HDL: High density lipoprotein cholesterol; LDL: Low density lipoprotein cholesterol; TG: Triglyceride

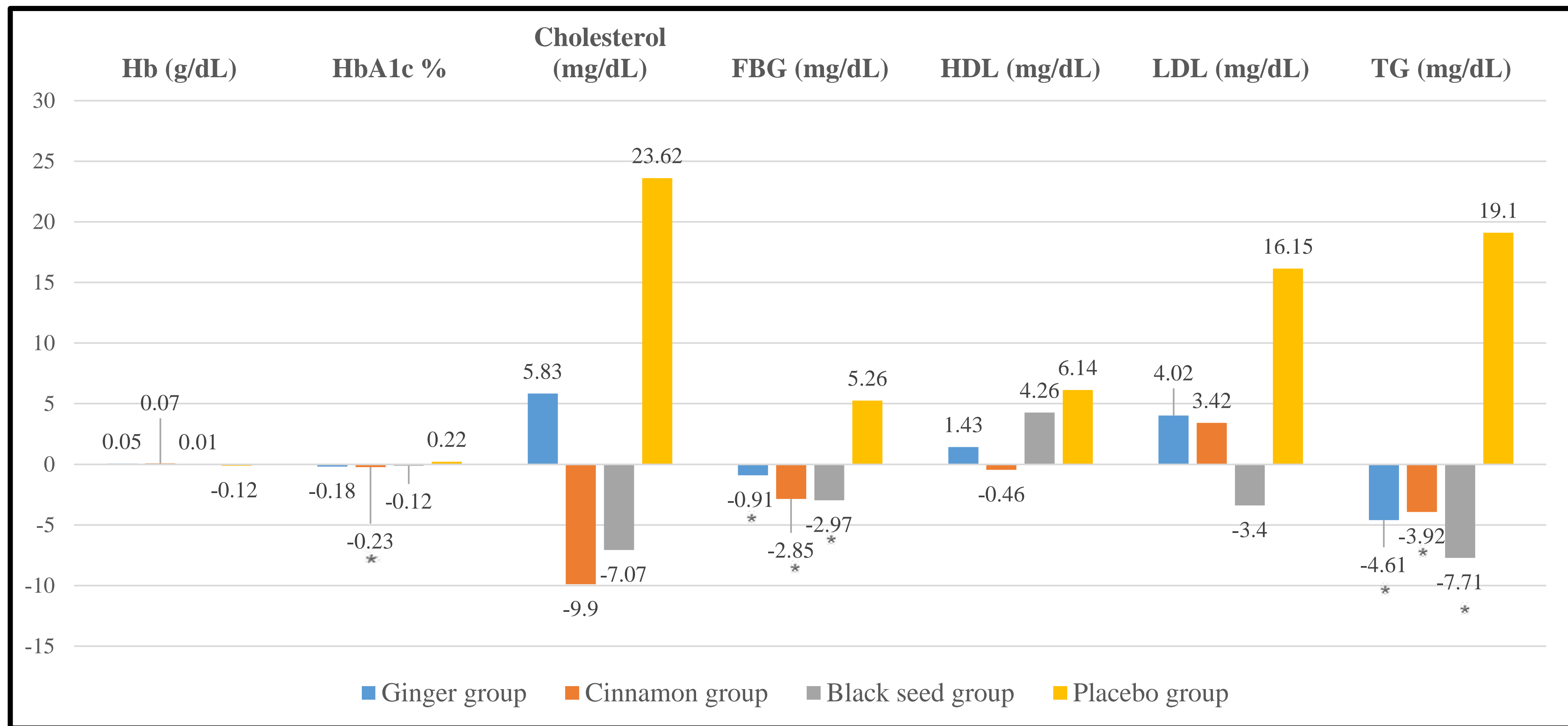

Figure 4.3: The Effect of Spice Powders on Hb, Blood Sugar and Lipid Profile after Six Weeks of the Intervention when Compared to the Placebo Group

*Significant at P-value ≤ 0.05

Hemoglobin; HbA1c: Glycated hemoglobin; FBG: Fasting blood cholesterol; HDL: High density lipoprotein cholesterol; LDL: Low density lipoprotein cholesterol; TG: Triglycerides

4.2.5.3 Endpoint Biochemical Assessment

At the end point of the study period, participants with significantly abnormal levels of blood parameters, which were tested during the study, were informed. They were advised to visit their physician and were offered appropriate advices to help them manage their blood glucose and lipid profile.

Through the statistical analysis of the data, some data were trimmed due to their extremely high values in order to normalize the distribution of the data. One participant had an extremely high cholesterol value in the placebo group, therefore the participant cholesterol reading was removed (trimmed).

Hb mean values of all groups were in the normal range with mean values ranging from 13.60 ± 2.16 g/dL for the placebo group to 14.69 ± 2.15 g/dL for the black seed group. HbA1c level was below the cut-off point (<5.7%) [7] for the ginger group (5.62 ± 0.52%) and black seed group (5.56 ± 0.51%). HbA1c decreased dramatically for the cinnamon group (-0.6 ± 0.94) to reach 5.85 ± 1.65%. The reduction in the mean value of HbA1c was significant for the cinnamon (P-value=0.003) and black seed (P-value=0.009) groups when compared to the placebo group, as illustrated in Table 4.31. FBG mean values were 79.23 ± 14.12, 97.79 ± 37.64, 86.27 ± 25.24 and 92.40 ± 13.93 mg/dL for the ginger, cinnamon, black seed and placebo group respectively, as shown in Table 4.30. The decrease in FBG was significant for the ginger, cinnamon and black seed groups at P-values 0.012, 0.048 and 0.007 respectively, when compared to the placebo group.

Blood lipid profile had a remarkably improving results in HDL, LDL and TG levels, although cholesterol level did not change remarkably in the treatment groups. Total

cholesterol mean value ranged from 129.37 ± 27.31 mg/dL for the placebo group to 157.84 ± 50.42 mg/dL for the cinnamon group. No significant reduction was observed in the total cholesterol mean values for the treatment groups when compared to placebo group (P-value > 0.05). HDL mean values increased in all groups at the twelfth week. HDL mean values were 35.42 ± 9.51, 49.12 ± 18.87, 41.03 ± 17.23 and 36.51 ± 12.09 mg/dL. The increase was considered significant only in the cinnamon group (7.76 ± 13.88 mg/dL, P-value=0.012) when compared to the placebo group.

Mean values of LDL ranged from 76.92 ± 23.26 mg/dL for the placebo group to 96.25 ± 22.89 mg/dL for the cinnamon group. LDL mean values decreased in ginger, cinnamon and black seed groups as shown in Table 4.30 and Table 4.31. This reduction was only significant in the cinnamon group when compared to the placebo group with a P-value of 0.004.

LDL mean value of black seed group was significantly different (P-value < 0.001) from the placebo group mean value at baseline, and placebo group had a lower LDL mean value than the cinnamon group at baseline as well (Table 4.27). Therefore, a regression test was conducted at end point of the study to test the relevance of the significancy of the LDL change in the cinnamon group. The regression test took into consideration the different treatment groups, LDL mean values at baseline and the interaction between the treatment and LDL mean values at baseline. For the cinnamon group, no significant difference was detected (P-value=0.505). This means that the difference in LDL mean value for the cinnamon group is significant at end point when compared to placebo group, though there was a significant difference at baseline in the mean value of LDL of the cinnamon group when compared to placebo group as shown in Table 4.31.

Additionally, black seed mean value of LDL at base line was significantly different (P-value=0.001) from the placebo LDL mean value at baseline as demonstrated in Table 4.30, nonetheless, no significant difference was detected in the LDL mean values of the black seed group when compared to the placebo group at endpoint (P-value=0.447) as shown in Table 4.31. Therefore, no further analysis was required.

In contrast, TG was reduced remarkably in the ginger, cinnamon and black seed groups as shown in Figure 4.4. TG mean values were: 95.87 ± 57.99, 112.32 ± 62.76, 93.20 ± 28.56 and 112.67 ± 40.45 mg/dL for ginger, cinnamon, black seed and placebo groups, respectively. The reduction was significant for the ginger (P-value=0.029), cinnamon (P-value=0.046) the black seed (P-value=0.001) group when compared to placebo group as shown in Table 4.31 and Figure 4.4.

Table 4.30: Biochemical Assessment of the Treatment Groups and the Placebo Group at Endpoint (Mean ± SD)

Intervention group	Ginger group n=21	Cinnamon group n=25	Black seed group n=29	Placebo group n=22
Hb (g/dL)	13.98 ± 2.08	14.16 ± 1.83	14.69 ± 2.15	13.60 ± 2.16
HbA1c %	5.62 ± 0.52	5.85 ± 1.65	5.56 ± 0.51	6.37 ± 0.89
Total Cholesterol (mg/dL)	141.74 ± 40.14	157.84 ± 50.42	147.80 ± 55.02	129.37 ± 27.31
FBG (mg/dL)	79.23 ± 14.12	97.79 ± 37.64	86.27 ± 25.24	92.40 ± 13.93
HDL (mg/dL)	35.42 ± 9.51	49.12 ± 18.87	41.03 ± 17.23	36.51 ± 12.09
LDL (mg/dL)	88.97 ± 33.17	96.25 ± 22.89	93.38 ± 30.06	76.92 ± 23.26
TG (mg/dL)	95.87 ± 57.99	112.32 ± 62.76	93.20 ± 28.56	112.67 ± 40.45

Hb: Hemoglobin; HbA1c: Glycated hemoglobin; FBG: Fasting blood cholesterol; HDL: High density lipoprotein cholesterol; LDL: Low density lipoprotein cholesterol; TG: Triglycerides

Table 4.31: Biochemical Assessment Comparison of the Treatment Groups with the Placebo Group at Endpoint (Week 12 – Week 0)

Parameter	**Ginger group n=21**	**P-value**	**Cinnamon group n=25**	**P-value**	**Black seed group n=29**	**P-value**	**Placebo group n=22**
Hb (g/dL)	0.05 ± 1.48	0.401	0.13 ± 1.85	0.949	-0.03 ± 1.36	0.834	-0.19 ± 0.15
HbA1c %	-0.29 ± 0.72	0.134	-0.60 ± 0.94	0.003*	-0.21 ± 1.18	0.009*	0.04 ± 0.81
Total Cholesterol (mg/dL)	-11.49 ± 34.74	0.099	-0.31 ± 43.94	0.565	-13.05 ± 66.52	0.300	7.86 ± 29.76
FBG (mg/dL)	-3.40 ± 8.97	0.012*	-2.27 ± 11.96	0.048*	-7.43 ± 23.87	0.007*	3.10 ± 15.94
HDL (mg/dL)	0.62 ± 6.19	0.375	7.76 ± 13.88	0.012*	4.22 ± 16.85	0.138	1.71 ± 9.42
LDL (mg/dL)	-5.32 ± 22.89	0.950	-14.07 ± 28.92	0.004*	-2.14 ± 38.18	0.447	6.41 ± 18.36
TG (mg/dL)	-17.63 ± 48.73	0.029*	-9.14 ± 67.59	0.046*	-8.08 ± 12.12	0.001*	10.64 ± 36.07

*Significant at P-value ≤ 0.05.

Hb: Hemoglobin; HbA1c: Glycated hemoglobin; FBG: Fasting blood cholesterol; HDL: High density lipoprotein cholesterol; LDL: Low density lipoprotein cholesterol; TG: Triglyceride

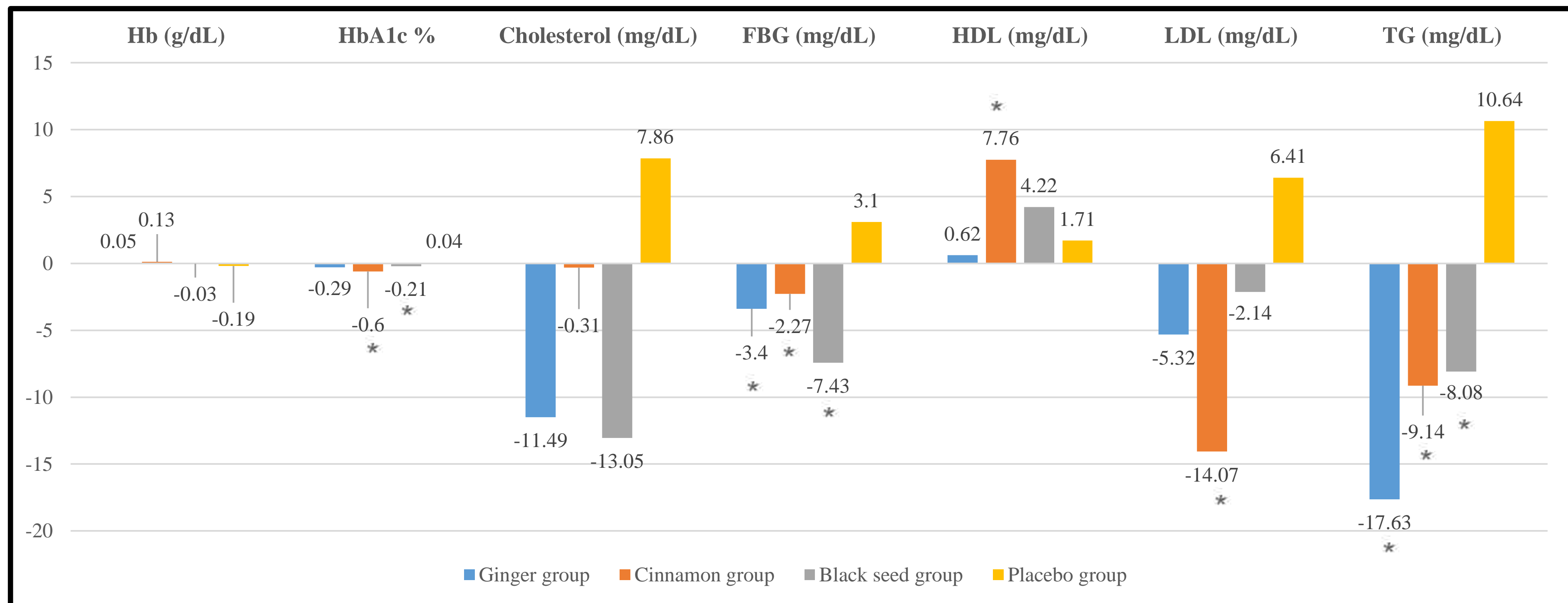

Figure 4.4: The Effect of Spice Powders on Hb, Blood Sugar and Lipid Profile after Twelve Weeks of the Intervention when Compared to the Placebo Group

*Significant at P-value ≤ 0.05.
Hb: Hemoglobin; HbA1c: Glycated hemoglobin; FBG: Fasting blood cholesterol; HDL: High density lipoprotein cholesterol; LDL: Low density lipoprotein cholesterol; TG: Triglycerides

4.2.6 Further Analysis

The SPSS® program mixed models test of linear equation was applied to find if there was any effect of the interactions of gender with treatment group, gender with age and gender with the phase of the research period. Dependent variables were the metabolic syndrome risk factors: blood pressure (BP), waist circumference (WC), fasting blood glucose (FBG), high density lipoprotein (HDL) and triglycerides (TG).

Results proves that there was a significant difference in WC (P-value=0.019), HDL (P-value=0.003) and TG (P-value=0.05) between males and females response to the intervention in the treatment groups.

Moreover, there was no difference between males and females mean values with age on WC, FBG, HDL, TG and BP (P-values > 0.05) as demonstrated in Table 4.32. On the other hand, the difference between males and females mean values of WC, FBG, HDL and TG over time is significant (P-value < 0.05). This means that the reaction of males was different from the reaction of females to the treatment at each phase in the three phases of the research (baseline, midpoint and endpoint).

Table 4.32: Type III Test For Fixed Effect Model Results for Gender Differences

Interaction	WC p-value	FBG p-value	HDL p-value	TG p-value	Systolic BP p-value	Diastolic BP p-value
Gender * Group	0.019*	0.07	0.003*	0.05*	0.902	0.871
Gender * Age	0.082	0.09	0.13	0.06	0.681	0.998
Gender * Phase	0.001*	0.000*	0.09	0.042*	0.212	0.843

WC, FBG, HDL, TG and BP are dependent variables
*Significant at P-value ≤ 0.05
WC: Waist circumference; FBG: Fasting blood glucose; HDL: High density lipo protein cholesterol; TG: Triglycerides; BP: Blood pressure.

Table 4.33 illustrates the mean values of the difference between males and females reaction to treatments over 12 weeks of intervention. Table 4.34, Table 4.35, Table 4.36 and Table 4.37 demonstrates the differences between males and females in reaction to the four treatment groups through the 3 study phases.

Male participants at the ginger group had significantly more elevated systolic blood pressure at baseline (P-value=0.02), midpoint (P-value=0.000) and endpoint (P-value=0.000) when compared to females, while diastolic blood pressure mean value for males was significantly higher than females only at endpoint (P-value=0.004). WC mean values of males had a significant difference when compared to females at midpoint (P-value=0.005) and endpoint (P-value=0.004), where males had higher mean values. Moreover, FBG mean values of males were significantly higher than females at baseline (P-value=0.010), with females having a lower FBG. Furthermore, no significant difference between males and females for HDL mean values were observed through the study phases (P-value > 0.05). Instead, TG mean value of males were significantly higher than females at baseline (P-value=0.0.028), midpoint (P-value=0.04) and endpoint (P-value=0.015) (Table 4.34).

For the cinnamon group, male participants had significantly higher systolic blood pressure at baseline (P-value=0.002) and endpoint (P-value=0.001) when compared to females, while diastolic blood pressure and FBG mean values did not differ significantly between males and females through the study phases (P-value > 0.05). WC mean values of males were significantly higher when compared to females at midpoint (P-value=0.026) and endpoint (P-value=0.021). Moreover, significant difference between males and females HDL mean values was observed. Females HDL mean values were significantly higher at baseline (P-value=0.015) and midpoint (P-

value=0.11). Furthermore, TG mean value of males were significantly higher from the mean value of females at midpoint (P-value=0.007) and endpoint (P-value=0.001) as shown in Table 4.35.

In addition, male participants at the black seed group had significantly higher systolic blood pressure at baseline (P-value=0.012), midpoint (P-value=0.002) and endpoint (P-value=0.001) when compared to females. Diastolic blood pressure mean value for males were significantly higher at midpoint (P-value=0.026) and endpoint (P-value=0.010). WC mean values of males were significantly higher when compared to females at baseline (P-value=0.019), midpoint (P-value=0.008) and endpoint (P-value=0.017). Furthermore, FBG and TG did not differ significantly between males and females through the study phases (P-value > 0.05). Moreover, significant difference between males and females HDL mean values was detected. Females HDL mean values were significantly higher than males at baseline (P-value=0.030) and midpoint (P-value=0.031) as Table 4.36 demonstrates.

Male participants of the placebo group had significantly more elevated systolic blood pressure at baseline (P-value=0.001), midpoint (P-value=0.000) and endpoint (P-value=0.002) when compared to females. Diastolic blood pressure, WC, HDL and TG mean values did not differ significantly between males and females through the study phases (P-value > 0.05). FBG mean values of males were significantly higher when compared to females at midpoint (P-value=0.017) and endpoint (P-value=0.016) (Table 4.37).

Overall, males tended to have a higher systolic blood pressure, diastolic blood pressure, WC, FBG, LDL and TG mean value levels than females in all treatment groups. While females were more likely to have higher HDL mean values than males.

Table 4.33: Difference between Males and Females Reaction to Treatments Over 12 Weeks of Intervention (Mean ± SD)

	Ginger group			**Cinnamon Group**			**Black seed Group**			**Control group**		
	Males	Females	(M-F)	Males	Females	(M-F)	Males	Females	(M-F)	Males	Females	(M-F)
Systolic BP (mmHg)	127.55 ± 12.88	108.83 ± 7.37	18.72	126 ± 12.68	107.81 ± 11.95	18.19	127.88 ± 16.19	106.5 ± 12.28	21.38	132.27 ± 9.11	112.81 ± 15.84	19.46
Diastolic BP (mmHg)	86 ± 9.11	74.41 ± 7.3	11.59	81.66 ± 10.59	75.62 ±9.87	6.04	86.85 ± 15.31	73.22 ± 10.16	13.63	82.90 ± 9.65	78.54 ± 13.62	4.36
WC (cm)	109.22 ± 14.8	91.83 ± 9.67	17.39	97.29 ± 9.78	85 ± 12.85	12.29	107.07 ± 20.89	78.48 ± 29.07	28.59	105.48 ± 12.44	99.24 ± 11.78	6.24
FBG (mg/dL)	85.34 ± 17.6	74.64 ± 9.13	10.7	112.52 ± 39.80	89.49 ± 34.89	23.03	94.96 ± 6.80	82.35 ± 29.44	12.61	92.94 ± 17.54	80.68 ± 12.50	12.26
HDL (mg/dL)	34.07 ± 6.7	36.43 ± 11.35	-2.36	41.46 ± 9.88	53.42 ± 21.51	-11.96	43.61 ± 6.98	39.87 ± 20.30	3.74	33.97 ± 9.20	39.04 ± 14.41	-5.07
TG (mg/dL)	130.07 ± 69.79	76.21 ± 29.94	53.86	162.48 ± 58.75	84.09 ± 45.84	78.39	92.18 ± 32.23	93.66 ± 27.63	-1.48	94.43 ± 56.37	70.81 ± 42.78	23.62

(M-F): Males - Females

WC: Waist circumference; FBG: Fasting blood glucose; HDL: High density lipoprotein cholesterol; TG: Triglycerides; BP: Blood pressure.

Table 4.34: Differences between Males and Females Reaction to Ginger Powder Treatment through the Intervention Three Phases.

	Baseline				Midpoint				Endpoint			
	Males	Females	(M-F)	P-value	Males	Females	(M-F)	P-value	Males	Females	(M-F)	P-value
Systolic BP (mmHg)	131.77 ± 15.74	109.5 ± 12.66	22.27	0.02*	128.88 ± 12.82	106.25 ± 8.76	22.63	0.000*	127.55 ± 12.88	108.83 ± 7.37	18.72	0.000*
Diastolic BP (mmHg)	88.77 ± 1231	79.5 ± 13.29	9.27	0.113	84.11 ± 12.82	74.08 ± 7.65	10.03	0.037*	86 ± 9.11	74.41 ± 7.3	11.59	0.004*
WC (cm)	114 .9± 14.16	98.3 ± 11.36	16.7	0.007	111.48 ± 15.06	93.69 ± 10.35	17.79	0.005*	109.22 ± 14.8	91.83 ± 9.67	17.39	0.004*
FBG (mg/dL)	91.94 ± 16.15	75.65 ± 9.84	16.29	0.010*	92.68 ± 12.77	80.99 ± 9.7	11.69	0.014	85.34 ± 17.6	74.64 ± 9.13	10.7	0.085
HDL (mg/dL)	35 ± 6.48	34.65 ± 12.37	0.35	0.940	35.1 ± 6.78	34.7 ± 12.37	0.4	0.940	34.07 ± 6.7	36.43 ± 11.35	-2.36	0.585
TG (mg/dL)	163.24 ± 116.79	76.18 ± 36.89	87.06	0.028*	152.24 ± 111.93	76.37 ± 36.89	75.87	0.040*	130.07 ± 69.79	76.21 ± 29.94	53.86	0.015*

(M-F): Males – Females
*Significant at P-value ≤ 0.05
WC: Waist circumference; FBG: Fasting blood glucose; HDL: High density lipoprotein cholesterol; TG: Triglycerides; BP: Blood pressure

Table 4.35: Differences between Males and Females Reaction to Cinnamon Powder Treatment through the Intervention Three Phases

	Baseline				Midpoint				Endpoint			
	Males	Females	(M-F)	P-value	Males	Females	(M-F)	P-value	Males	Females	(M-F)	P-value
Systolic BP (mmHg)	133.77 ± 15.02	114.87 ± 11.58	18.9	0.002*	122.22 ± 11.30	112.18 ± 12.98	10.04	0.058	126 ± 12.68	107.81 ± 11.95	18.19	0.001*
Diastolic BP (mmHg)	83.33 ± 8.84	80.25 ± 12.52	3.08	0.522	83.88 ± 5.55	77.37 ± 9.74	6.51	0.080	81.66 ± 10.59	75.62 ±9.87	6.04	0.166
WC (cm)	101.81 ± 10.83	93.60 ± 14.65	8.21	0.156	98.42 ± 10.45	85.81 ± 13.79	12.61	0.026*	97.29 ± 9.78	85 ± 12.85	12.29	0.021*
FBG (mg/dL)	113.86 ± 47.51	90.72 ± 38.69	23.14	0.199	108.08 ± 46.27	89.52 ± 50.57	18.65	0.364	112.52 ± 39.80	89.49 ± 34.89	23.03	0.145
HDL (mg/dL)	33.34 ± 8.25	45.87 ± 12.79	-12.53	0.015*	38.44 ± 7.65	47.9 ± 11.56	-9.46	0.011*	41.46 ± 9.88	53.42 ± 21.51	-11.96	0.131
TG (mg/dL)	`158.49 ± 104.9	93.08 ± 50.66	65.41	0.109	170.38 ± 106.39	80.27 ± 47.88	90.11	0.007*	162.48 ± 58.75	84.09 ± 45.84	78.39	0.001*

(M-F)=Males - Females

*Significant at P-value ≤ 0.05

WC: Waist circumference; FBG: Fasting blood glucose; HDL: High density lipoprotein cholesterol; TG: Triglycerides; BP: Blood pressure

Table 4.36: Differences between Males and Females Reaction to Black Seed Powder Treatment through the Intervention Three Phases

	Baseline				Midpoint				Endpoint			
	Males	Females	(M-F)	P-vale	Males	Females	(M-F)	P-value	Males	Females	(M-F)	P-value
Systolic BP (mmHg)	127.44 ± 15.36	110.1 ± 16.28	17.44	0.012*	129.22 ± 14.58	108.1 ± 15.03	21.12	0.002*	127.88 ± 16.19	106.5 ± 12.28	21.38	0.001*
Diastolic BP (mmHg)	78.88 ± 11.64	75.75 ± 14.34	3.13	0.570	83.77 ± 11.75	72.25 ± 12.37	11.52	0.026*	86.85 ± 15.31	73.22 ± 10.16	13.63	0.010*
WC (cm)	109.77 ± 22.71	93.58 ± 12.47	16.19	0.019*	107.70 ± 21.49	90.5 ± 11.05	17.2	0.008*	107.07 ± 20.89	78.48 ± 29.07	28.59	0.017*
FBG (mg/dL)	95.80 ± 7.81	92.74 ± 8.77	3.06	0.378	93.14 ± 6.79	89.63 ± 9.31	3.51	0.320	94.96 ± 6.80	82.35 ± 29.44	12.61	0.219
HDL (mg/dL)	30.54 ± 7.72	39.62 ± 10.64	-9.08	0.030*	35.74 ± 5.27	39.72 ± 16.74	-3.98	0.031*	43.61 ± 6.98	39.87 ± 20.30	3.74	0.597
TG (mg/dL)	`96.14 ± 31.35	103.60 ± 34.24	-7.46	0.572	88.57 ± 34.91	95.83 ± 34.82	-7.26	0.612	92.18 ± 32.23	93.66 ± 27.63	-1.48	0.900

(M-F)=Males - Females

*Significant at P-value ≤ 0.05

WC: Waist circumference; FBG: Fasting blood glucose; HDL: High density lipoprotein cholesterol; TG: Triglycerides; BP: Blood pressure

Table 4.37: Differences between Males and Females Reaction to Placebo Treatment through the Intervention Three Phases

	Baseline				Midpoint				Endpoint			
	Males	Females	(M-F)	P-value	Males	Females	(M-F)	P-value	Males	Females	(M-F)	P-value
Systolic BP (mmHg)	133.09 ± 14.11	111.90 ± 12.09	21.19	0.001*	129.9 ± 12.62	110.18 ± 71.09	19.72	0.000*	132.27 ± 9.11	112.81 ± 15.84	19.46	0.002*
Diastolic BP (mmHg)	85.36 ± 9.88	78.36 ± 8.12	7	0.085	80.18 ± 8.63	71.09 ± 18.07	9.09	0.148	82.90 ± 9.65	78.54 ± 13.62	4.36	0.396
WC (cm)	106.03 ± 12.35	98.12 ± 10.54	7.91	0.122	105.46 ± 12.95	97.21 ± 11.07	8.25	0.124	105.48 ± 12.44	99.24 ± 11.78	6.24	0.241
FBG (mg/dL)	85.99 ± 33.37	70.52 ± 16.12	15.47	0.232	104.8 ± 21.9	83.24 ± 12.36	21.56	0.017*	92.94 ± 17.54	80.68 ± 12.50	12.26	0.016*
HDL (mg/dL)	30.93 ± 8.07	38.67 ± 15.82	-7.74	0.164	31 ± 8.51	38.77 ± 17.2	-7.77	0.189	33.97 ± 9.20	39.04 ± 14.41	-5.07	0.337
TG (mg/dL)	90.65 ± 21.6	69.87 ± 33.19	20.78	0.872	113.45 ± 36.61	68.70 ± 39.09	44.75	0.509	94.43 ± 56.37	70.81 ± 42.78	23.62	0.688

(M-F)=Males - Females
*Significant at P-value ≤ 0.05
WC: Waist circumference; FBG: Fasting blood glucose; HDL: High density lipoprotein cholesterol; TG: Triglycerides; BP: Blood pressure

4.2.7 Discussion and Conclusion

This study is the first to examine the effect of ginger, cinnamon and black seed powder on individuals at high risk of developing cardiovascular disease in the United Arab Emirates. It is also one of the few studies to have measured the effect of ginger, cinnamon and black seed powder on people who are at risk of developing heart diseases and have two or three out of five metabolic syndrome risk factors.

Ginger, cinnamon and black seed powder effect on MetS risk factors and body compositions was thoroughly investigated in the undertaken study. Among the three spices, only cinnamon had a significant effect on body composition (PBF, BFM and weight) and HDL. While all of the three spices had a positive significant effect on FBG, TG and WC. However, none of the three spices had a significant effect on systolic and diastolic blood pressure.

The findings from the current study indicate that the consumption of 3 g/day of ginger powder for 12 weeks in individuals at risk of CVD significantly reduced WC (P-value=0.000), FBG (P-value=0.012) and TG levels (P-value=0.046).

Jafarnemjad and colleagues published a meta-analysis and concluded that ginger supplementation (tablet, capsules, powder or rhizomes) significantly lowered FBG and TG, and significantly improved HDL [183]. Moreover, a randomized double-blinded placebo clinical trial explored the effect of two grams of ginger powder on 40 obese women. Their findings revealed a slight but non-significant positive effect of ginger powder supplementation on serum blood glucose a significant effect on TG levels when compared to placebo [184].

The glyceamic effect of ginger is believed to be due to its high content of gingerols, paradols and shogaols. 6-Paradol and 6-Shogaol are chemicals present in ginger that give the ginger its pungent smell and taste. In 2017, Wei et al. published a research stating that 6-paradol and 6-shogaol stimulated glucose use by adipocytes and myotubes in a high fat diet fed mouse. The effects were credited to the upsurge in 50 adenosine monophosphate-activated protein kinase (AMPK) phosphorylation that are found in adipocytes [151]. In addition, Li et al. concluded that the activity of (S)-(8)-gingerol was correlated with an incline in surface distribution of glucose transporter type 4 (GLUT4) protein, a protein which enhances the glucose uptake and insulin sensitivity [152].

Ginger was believed to lower lipid levels due to its ability to increase pancreatic lipase and amylase [346]. Furthermore, ginger consumption inhibits lipid hydrolyze in intestines, which results in a lower lipid absorption and therefore a lower lipid profile [347]. Moreover, findings of Hashimoto et al. concluded that 6-shogaol, found in ginger, increases intestinal efficient movement which could contribute to the improvement of lipid profile levels [348, 349].

Fuhrman et al. reported that the ingestion of 250 mg/day of ginger extract for 10 weeks reduced the TG levels and that ginger extract lowers total cholesterol levels and inhibits LDL oxidation, hence improves lipid profile and lowers risk for CVD [350, 351]. In contrast, Bhandari et al. examined the effect of ginger extract on cholesterol fed rabbits for 10 weeks and reported that ginger reduced total cholesterol and triglycerides level in blood, while the reduction was only significant for the triglycerides [352]. Similarly, Verma et al. examined the effect of daily consumption of four grams of ginger powder on rabbits for three months. Their work showed that

ginger powder had no effect on reducing total cholesterol, LDL and triglycerides [353]. Findings of the current study were consistent with the studies of Jafarnemjad et al., Attari et al., Fuhrrman et al. and Bhandari et al. [183, 184, 350, 352, 353]. However, different from Verma et al.

Findings of the current study confirmed that ginger, cinnamon and black seed reduced WC (-6.17 ± 4.10, -7.13 ± 4.93 and -10.56 ± 26.47 cm, respectively) significantly without any significant reduction in weight or BFM. Ginger and cinnamon also increased SMM (2.18 ± 5.73 and 0.12 ± 0.99 kg, respectively), however the difference was not significant at P-value > 0.05. This slight increase in SMM could explain the stability in the body weight of the participants in ginger group, regardless the reduction in WC.

High fat mass in the upper body portion is significantly correlated with higher serum glucose [354]. While, decreased levels of serum glucose were significantly associated with lower abdominal fat accumulation [355]. Therefore, the lower level of fasting blood glucose in our recent findings could be behind the lower waist circumference. Moreover, Feldman et al. found that diabetics, especially females had a significant shift toward central accumulation of fat due to male/ female hormonal imbalances, causing the typical masculine centripetal fat distribution and therefore increasing the waist circumference [356]. It is suggested that the decrease in FBG in the recent study findings caused a correction in male/ female hormonal imbalances and consequently lead to the redistribution of fat from centripetal to peripheral without affecting the total BFM. To further analyze this observation, it is recommended that further studies should examine into details the fat distribution after consuming ginger, cinnamon and black seed powder. Moreover, participants in this study reported a positive feedback

regarding better bowel movement, less bloating and a relief from distention after consuming spice powder, consistent with findings of Hashimoto et al., Harada et al. and Randhawa et al. [348, 357, 358]. This would lead to a lower WC measurements, as a bloated abdomen can measure more than a flat relieved abdomen [359, 360].

Furthermore, the current research study concluded that the consumption of 3 g/day of cinnamon powder for 12 weeks resulted in a significant decrease in WC (P-value < 0.001), BFM (P-value=0.001), weight (P-value=0.011), BMI (P-value=0.001), PBF (P-value=0.027), HbA1c (P-value=0.003), FBG (P-value=0.048), LDL (P-value=0.004) and TG (P-value=0.046). Additionally, a significant increase in mean HDL mean value was observed (P-value=0.012).

In 2006, Ziegenfuss et al. concluded that ingestion of 500 mg/day of cinnamon extract for 12 weeks led to improvement in FBG and body composition [15]. Another study by Khan et al. (2003), examined the effect of cinnamon when given in three different doses for three different groups (group 1 (1 g/day), group 2 (3 g/day) and group 3 (6 g/day)) of diabetic people for 40 days. Their study showed that cinnamon powder significantly decreased FBG, total cholesterol, triglycerides and LDL levels [144]. On the other hand, a meta-analysis of randomized controlled trials of cinnamon conducted by Baker et al. concluded that cinnamon consumption did not significantly improve HbA1c or FBG [185]. A meta-analysis for 10 randomized controlled trials that observed the effect of ingesting cinnamon in a dose of 120 mg/day to 6 g/day for 4 months, on a total of 543 diabetic patients has proven that consuming cinnamon led to a significant reduction in the levels of FBG, total cholesterol, LDL, and triglyceride and an improvement in HDL levels. However, cinnamon had no significant effect on HbA1c [186]. On the contrary, a randomized controlled trial conducted by Crawford

et al. to examine the effect of consuming 1 gram per day for 90 days on diabetics resulted in a significant lower HbA1c levels [361]. The current study findings are consistent with Ziegenfuss et al., Khan et al., Allen et al. and Crawford et al. findings. However, Baker et al. study findings were not in agreement with the findings of the current study.

Cinnamaldehyde and cinnamic acid, found in cinnamon, play an important role in preventing CVD as they both have the ability to produce nitric oxide and both have anti-inflammatory effect [156]. Camacho and his colleagues examined the effect of cinnamon on obese mice for five weeks with a diet containing cinnamaldehyde. Camacho et al. found that cinnamaldehyde significantly decreased body weight increase and enhanced glucose tolerance [362]. Similarly, Saifudin et al. stated that cinnamaldehyde inhibited protein tyrosine phosphatase-1B (PTP-1B), which helped in preventing type 2 diabetes and obesity. In addition, a recent study (2016) proved that cinnamon supplementation reduced only the insulin resistance index. [363]. Furthermore, an earlier study (2012), suggested that cinnamon could have a positive effect on normalizing postprandial glucose response in normal weight and obese adults and, in turn assist will help in weight management [203]. Similarly, another study examined cinnamon's effect on insulin sensitivity in diabetic adults demonstrated significant improvement of FBG, lipid profile, blood pressure, body fat percent, with an elevation in lean body mass [158]. A double blind, randomized, placebo controlled clinical trial conducted on 44 diabetic patients who consumed three grams per day of cinnamon supplement for 8 weeks reported that cinnamon supplement significantly decreased the levels of fasting blood glucose, HbA1c, triglyceride, weight, BMI and

body fat mass when compared to baseline, however, this finding was not significant [364].

Cinnamon stimulates glucose uptake by regulating the expression of GLUT4 and by acting as an insulin mimetic that leads to the stimulation of the translocation of GLUT4 and therefore a reduction in blood glucose levels [365, 366]. Moreover, polyphenols, found in cinnamon improve insulin sensitivity and this effect could help in controlling blood glucose level [158]. Jarvill et al. concluded that cinnamon extracts activate insulin receptor kinase and inhibits dephosphorylation of insulin receptors, causing maximal phosphorylation of the insulin receptors. This phosphorylation is associated with improved insulin sensitivity, and linked to improved lipid profile and glyceamic response [366]. Moreover, cinnamon have the ability to inhibit hepatic reductase activity, hence lower lipid profile [136].

Additionally, chromium (Cr) and polyphenols found in cinnamon have significant effects on insulin signaling and glucose control. Cr was shown to improve all metabolic syndrome risk factors signs in human participants and decreases cortisol concentration [367], which is important for weight management, as it increases insulin circulation and fat accumulation [368]. Therefore, consuming cinnamon supplements may reduce PBF, BFM, WC and body weight. A meta-analysis published in 2003 reported a significant reduction in body weight caused by Cr supplements consumption [369]. Similarly, Anderson et al. reported that 500 mg of water-extract supplementation of cinnamon for 6 weeks lowered fasting blood glucose, total cholesterol and LDL, and enhanced insulin sensitivity of diabetic individuals [370]. Findings of Jarvill et al. and Anderson et al. are in agreement with the findings of the

current research study [366, 370]. Previous studies findings are in agreement with the finding of the current study when administrated in similar dosage and duration.

Findings of this current study concluded that ingesting 3 g/day of black seed powder for 12 weeks significantly reduced WC (P-value=0.000), HbA1c (P-value=0.009), FBG (P-value=0.007) and TG (P-value=0.001) when compared to placebo group.

Earlier research concluded that black seed oil contains the major bioactive component, thymoquinone (TQ) at 30% - 48% [142], a chemical compound known for its therapeutic potential. Most of the positive effects of black seed on health are believed to be due to TQ as it inhibits the electrogenic intestinal absorption of glucose and therefore improves glucose levels [371]. The fixed oil of the black seed accompanied with TQ supplements had anti-eicosanoid and antioxidant activity, which can inhibit eicosanoid generation and therefore lower lipid profile [372].

A study by Heshmati et al. showed that supplementation of 3 g/day of black seed oil changed significantly the FBG and HbA1c, total cholesterol, TG, HDL and LDL levels in the blood in the intervention group after 12 weeks [187]. In addition, multiple researchers have reported that black seed has anti-diabetic and hypoglycemic activity as the components of black seed decreases oxidative stress and thus preserve the pancreatic beta cell integrity [189].

Similarly, other research has confirmed that the black seed improves lipid profiles significantly [189, 198]. For example, studies by Heshmati and Namazi showed that 1 g/day of black seed powder for 12 weeks increased HDL levels and 2 g of black seed powder decreased total cholesterol, LDL concentrations and TG levels [198]. A randomized controlled trial was conducted by Ibrahim et al. (2014), to examine the

effect of black seed consumption on menopausal women for 2 months. The study reported an improvement in the lipid profile (decrease in total cholesterol, LDL and TG and an elevation in HDL levels) [199]. In addition, a double blind randomized controlled study undertaken by Amin et al. (2015). In this case, intervention group received two g/day of black seed for the duration of four weeks. The study confirmed the significant effect of black seed on lowering total cholesterol, LDL and TG levels. Reduction of TG is a result of the presence of nigellamin that act like a clofibrate (hypolipidimic agent) [373].

Additionally, this study concluded that there was a decline in total cholesterol and LDL levels when consuming ginger and black seed powder. While, the reduction was not significant, it is still could be explained throughout the antioxidative action of thymoquinone in black seed and gengerols and shogaols in ginger [374, 375]. The reduction could also be due to the ability of black seed to increase the secretion of cholesterol in the bile and hence excretion in feces [376] and lowering the total cholesterol level in the blood.

In contrast, Najmi et al. tested the effect of black seed consumption on body composition, WC, lipid profile and blood glucose. 60 participants at risk for CVD, consumed 2.5 mg of black seed oil twice daily for six weeks. This study reported that only FBG, total cholesterol and LDL levels reduced significantly, while black seed oil had no significant effect on body composition, nor WC [16]. Another study conducted by Shah et al. tested the effect of black seed on metabolic syndrome risk factors and reported a significant improvement on HDL, LDL and FBG, while it had no significant effect on blood pressure, TG and WC [195]. Previous studies are consistent with the findings of this current study when administrated in similar dosage and duration.

The increase in body weight, FBG, cholesterol, LDL and TG measurements in the placebo group when compared to the spice groups, could be due to the increase in dietary consumption of fat among the same group. However, the mentioned increase was not statistically significant. Correspondingly, previous studies reported the positive correlation between fat consumption and body weight, lipid profile, blood sugar and WC [377-379].

Moreover, corn starch that was used for the placebo group and administered in small amounts (3 grams per day), was proved to have no significant effect in body weight, FBG, cholesterol, LDL and TG according to earlier research findings [299, 380]. Therefore, the increase in the placebo group measurements mentioned above was not due to the corn starch consumption

Moreover, there was a significant difference in WC (P-value=0.019), HDL (P-value=0.003) and TG (P-value=0.05) between males and females in the response to the intervention in the treatment groups. Males tend to have a higher BP, WC, FBG and TG through the intervention period in all the treatment groups, while females had an increased level of HDL when compared to males. These differences could be due to the tendency for males in general to have a higher blood pressure than females [381]. A previous study emphasized that elevated WC in males is correlated with increased BP in males than in females [382]. On the other hand, an earlier study concluded that impaired fasting glucose incidence is more common in males than in females [383]. Another study indicated that adult females have better metabolism of blood glucose than males, therefore better glyceamic control [384]. A systematic review discussed gender differences and their role in cardiovascular diseases and found that higher abdominal fat motivates increased synthesis of very low density cholesterol (VLDL)

that leads to higher levels of triglycerides in males than females, which increases the possibility of abnormalities in males lipid profile [385]. These previous studies in agreement with our findings in terms of higher levels of fasting blood glucose in males than in females. Together, all of these factors increase the possibility of higher incidence of cardiovascular diseases in men than in women [385]. Therefore, a study that examines the effect of the treatment groups for each gender separately is recommended.

Previous studies investigated the effect of ginger, cinnamon and black seed powder on CVD risk factors using different dosage. Dosage of these spices varied from 1 gram per day to 3 grams per day [182, 198], while the duration varied from 6 weeks to 16 weeks [182, 192]. Mahluji et al. reported no significant effect of ginger powder on FBG, TG, HDL and HbA1c when investigating the effect of 2 g/d of ginger for 12 weeks on blood glucose and lipid profile [182]. In contrast, Arablou et al. assessed the effect of 1.6 g/day of ginger powder for 12 weeks on inflammatory markers, blood glucose and lipid profile to find that ginger powder decreased FBG, HbA1c, TG, total cholesterol and CRP significantly, while it had no significant effect on HDL and LDL [386]. Moreover, Mozaffari and his colleagues proved that the consumption of 3 g/day of ginger powder for 8 weeks exhibited a significant decrease in FBG and HbA1c, while no significant effect was noted for weight and BMI [139]. Similarly, cinnamon had a significant effect only on FBG when ingested in 3 g/day for 16 weeks, though, no significant effect was reported in terms of HbA1c and lipid profile as Mang et al. reported [136]. A study conducted by Vanschoonbeek et al. concluded that the consumption of 1.5 g/day of cinnamon powder for 6 weeks had no significant effect on FBG nor lipid profile [387]. Moreover, Akilen et al. reported a significant effect of

cinnamon powder when consumed in 2 g/day for 12 weeks in HbA1c and blood pressure. While WC, FBG, weight, BMI and lipid profile demonstrated no significant difference [193]. On the other hand, black seed powder was proved to show a significant effect on FBG, HbA1c, TG and HDL when consumed in 3 g/day for 12 weeks. However, it exhibited no significant effect on total cholesterol and HDL as Hashmati et al. reported. In contrast, Qidwai et al. examined the effect of 1 g/day of black seed powder for 6 weeks on blood glucose, lipid profile, WC and blood pressure and concluded there was no significant effect of black seed powder on the previously mentioned parameters [204]. Previous studies that administrated less than 12 weeks or less than 2 grams of the spice powder in their intervention, recommended longer interventional periods and a higher dose of the spice powders to exhibit a significant effect of spice powders consumption on lipid profile, blood glucose, WC and body composition (weight, PBF and BMI) [139, 193, 198, 386, 387].

In contrast, ginger, cinnamon and black seed powder have been found to have a reverse health effects when consumed in large amounts, however, toxicity, irritation, diarrhea, inflammation and damage can be caused due to misuse of these spices [388, 389]. Safety and tolerability of ginger, cinnamon and black seed was proved when consumed in 3 g/day in previous studies [204, 390, 391].

Therefore, to increase the possibility of achieving significant findings in this current study and to assure safety, 3 grams per day of the treatment for 12 weeks were administered.

Moreover, due to hormonal and body composition differences between males and females [392], different reaction to treatments was observed in the undertaken study over time. Considering that males had higher WC, BP, TG and FBG measurements

when compared to females, the duration or dose of the treatment could be modified for each gender, as males and females have a different cut-off points (WC and HDL) [36].

Strengths and limitations of this study also should be noted. As strength points, this study was done on human sample rather than animals and thus the results reflect the effect on human directly, subjects were from both genders and different adult ages, both dietary intake and physical activity level were taken into consideration to not be changed during the study so as to show the effect of spices powder only, and body composition was measured by (In body 720 and DEXA) to monitor body changes. As for limitations, randomization of the participants into four groups was applied during the screening phase which took into consideration the age and the diagnostic criteria of the MetS only without the inclusion of all the measured parameters. Consequently, significant differences in some of the parameters (that were not part of the screening) at baseline were observed. Such differences were impossible to avoid between treatment groups and placebo group after randomization at baseline.

Additionally, self-reporting of food intake and physical activity was considered as a limitation. Some of participants were either under/overestimating their food intake and physical activity levels, which were mainly due to difficulty in recalling these information. Moreover, participants were not familiar with food portion sizes, which took more time for explanations by the researcher in order to ensure correct record of information in the food dairy record. The stability in body fat mass, percent body fat and body weight with significant change in WC for ginger and black seed group, maybe contributed to fat redistribution Therefore, exact explanation for WC reduction was not accurate due to lack of fat redistribution measures.

In conclusion, previous studies findings are in consistence with our recent study results. This study indicates that consumption of three g/d of ginger, cinnamon and black seed powders daily for 12 weeks, had a significant effect on improving WC, body composition, blood glucose and lipid profile.

Chapter 5: Summary and Recommendations

5.1 Summary

The number of deaths caused by non-communicable diseases (NCDs) is increasing worldwide according to the World Health Organization (WHO). In 2015, 70% of global deaths were caused by NCDs, where the majority were caused due to the complications from the main four NCDs; namely cardiovascular diseases (CVDs), cancers, diabetes and chronic lung diseases [1].

Of these four, the highest cause of death is CVDs. Of 40 million NCD deaths annually, 17.7 million (45%) are attributed to CVDs [1], with the main cause attributed to obesity, type 2 diabetes, hypertension and high blood lipids [2-4].

Metabolic Syndrome (MetS) is a combination of medical illnesses that consists of, high fasting blood glucose (FBG), high blood pressure, central obesity, elevated blood triglycerides (TG), increased blood low density lipoprotein (LDL) and decreased blood high density lipoprotein (HDL) [5]. The diagnostic criteria of MetS are controversial, although all definitions agreed on three common characteristics namely, decreased HDL, elevated blood pressure and increased insulin resistance [5-7]. MetS management aims to reduce the risk of clinical factors that could lead to CVDs. Changing lifestyle could help in treating and improving the quality of life of people at risk of CVDs [8, 9].

The dietary factor includes improving the nutritional habits of an individual's diet. Reducing fat intake in the diet and managing the carbohydrate intake could improve blood glucose, insulin sensitivity and blood lipids [10, 11]. On the other hand, herbal therapy is broadly used in many countries as a treatment or as a preventive measure to

manage cardiovascular diseases risk factors, including, blood glucose, blood pressure and blood lipids [12-16].

In order to understand the positive effect of herbs and spices on people at risk for CVDs, chemical analysis could help in breaking down the components of individual spice and understand the nutritional value of each.

Moreover, spices such as Ginger (*Zingiber officinale*), Cinnamon (*Cinnamomum*), black seed (*Nigella sativa*), fenugreek (*Trigonella foenum graecum*), cardamom (*Elettaria cardamomum*), cloves (*Eugenia aromaticum)* and saffron (*Crocus sativus*) were examined in prior studies that demonstrated a positive effect of spices on blood glucose, body composition, lipid profile, inflammation markers, tumor necrosis and the level of oxidation in blood and tissues. These positive effects were due to the availability of active compounds and their higher content of vitamins and minerals [17-23]. Therefore, the current research study chemically analyzed the above seven spices to understand their effects on health and to explore the possibility of their usage as supplements in the management of CVDs risk factors.

The effect of spice consumption (ginger, cinnamon and black seed) on blood glucose, lipid profile, WC and body composition in people at risk for cardiovascular diseases was investigated for a period of 12 weeks. The investigation concluded that consumption of 3 grams per day of ginger, cinnamon and black seed powders daily for 12 weeks, had a significant effect on improving WC, body composition, blood glucose and lipid profile.

Summary of the key outcomes of the two studies of this dissertation is listed below:

1- Macronutrients and lipid composition analysis of ginger (*Zingiber officinale*), cinnamon (*Cinnamomum*), black seed (*Nigella sativa*), fenugreek (*Trigonella foenum graecum*), cardamom (*Elettaria cardamomum*), cloves (*Eugenia aromaticum*) and saffron (*Crocus sativuswere*) was relatively consistent with previous research. While micronutrient and sugar content of the spices were not in agreement with the findings from previous published assessments.
2- When analyzing ginger powder for gingerols and shogaols, 6-shogaols had the highest value followed by 6-gingerols and 8-gingerols 56.10, 30.21, 7.92 mg/100 g respectively.
3- Consumption of 3 g/day of ginger powder for 12 weeks for people at risk of CVD has significantly reduced WC (P-value=0.000), FBG (P-value=0.012) and TG levels (P-value=0.046).
4- Consumption of 3 g/day of cinnamon powder for 12 weeks for people at risk of CVD has resulted in a significant decrease in WC (P-value < 0.001), BFM (P-value=0.001), body weight (P-value=0.011), BMI (P-value=0.001), PBF (P-value=0.027), HbA1c (P-value=0.003), FBG (P-value=0.048), LDL (P-value=0.004) and TG (P-value=0.046), and contributed to a significant elevation in HDL blood levels (P-value=0.012).
5- Consumption of three g/day of black seed powder for 12 weeks for people at risk of CVD has significantly reduce WC (P-value=0.000), HbA1c (P-value=0.009), FBG (P-value=0.007) and TG levels (P-value=0.001).
6- There was a significant difference in WC (P-value=0.019), HDL (P-value=0.003) and TG levels (P-value=0.05) of males and females in the response to the intervention in the four different treatment groups.

7- Males tend to have a higher BP, WC, FBG and TG through the intervention period, while females had a more elevated level of HDL when compared to males.

8- The change of WC, FBG, HDL and TG levels over time (in the three phases of the research: baseline, midpoint and endpoint) differs between males and females (P-value < 0.05).

5.2 Recommendations

After analyzing extensively seven commonly consumed spices, and after studying the effect of three spices (ginger, cinnamon and black seed) on cardiovascular diseases risk factors, the recommendations of this research are:

1- Spices extracts and oils could be widely used in nutritional supplements and for treatments considering their decent source of valuable nutrients and active compounds.

2- Longer-term interventional research studies are required to investigate the effect of the spice on cardiovascular disease risk factors. Difference in some tested parameters such as HbA1c and BP was remarkable but not significant, therefore, longer duration of the intervention could demonstrate their efficiency in managing cardiovascular diseases risk factors.

3- Future intervention studies are needed for examining the effect of fenugreek powder, cardamom powder, clove powder and saffron powder on cardiovascular diseases risk factors and investigating the effect of ginger, cinnamon and black seed powder mixture on cardiovascular diseases risk factors is warranted.

4- To minimize participant dropout, administration of spices in capsule form would be more efficient and practical, especially that it can eliminate the pungent taste of some spices.

5- Investigation of the effect of the treatment groups for each gender separately is recommended, as males tend to have higher BP, WC, FBG and TG through the intervention period in all the treatment groups and control group, while females had a more elevated level of HDL when compared to males.
6- Investigating the effect of spices intake along with physical activity modifications for an optimum results.
7- Monitoring of fat distribution and bowel distention is required for such interventional study along with fat redistribution assessment to better understand the effect of spice powder on WC reduction.
8- Physical activity health benefits awareness campaign is essential for the UAE community, as participants of this study had a sedentary lifestyle.

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List of Publications

Research was published in July 2017 to the Journal of Clinical Nutrition.

Sellmann C, Degen C, Jin CJ, Nier A, Engstler AJ, Alkhatib DH, De Bandt JP, Bergheim I. Oral arginine supplementation protects female mice from the onset of non-alcoholic steatohepatitis. Amino acids. 2017 Jul 1;49(7):1215-25.

Appendices

Appendix 1: Screening Questionnaire Sheet

SCREANING QESTIONNAIRE SHEET

The Effect of Spices Powder on Blood Glycaemia, Blood Lipidemia and Body Composition on Adults at Risk for Cardio vascular Diseases: A controlled, randomized, single blind, parallel-design study

Name	
Weight (kg)	
Height (m)	
Gender (M/F)	
Age (years)	

Please tick yes / no in answer to the following questions:		No	Yes	If yes, please give details, where appropriate:
1.	Do you suffer from any heart / blood related conditions?			
2.	Do you suffer from any kidney-related conditions?			
3.	Do you suffer from any gastro-intestinal conditions?			
4.	Do you suffer from any metabolic conditions, e.g. diabetes?			
5.	Are you on any medication?			
6.	Are you on any special diet or suffer from any food allergies?			

7.	Are you currently trying to lose weight by means of dietary restriction and / or exercise?			
8.	Has your weight fluctuated within the last 3 months by more than 3 kg?			
9.	Do you suffer from any other medical condition not covered here?			
10.	Did you ever make yourself sick after having eaten in order to lose weight or not to gain weight?			
11.	Do you smoke?			
12.	Female Participants – Are you Pregnant?			

Appendix 2: Food Diary

FOOD DIARY

Subject code:

Diary dates

Day 1: ________

Day 2: ________

Day 3: ________

Do you think that you have eaten as you would do usually?

YES ☐ NO ☐

If No, then why not? i.e. were you ill, on holiday, etc.

....

....

....

Thank you for agreeing to fill in a food diary. It is an important part of the study and your help is really appreciated. A food diary enables us to learn what foods and drinks you prefer and normally eat.

1. It is important to record **everything** you **eat and drink**, no matter how small the amount.

2. Give as much information as possible about the foods and drinks you eat. It is very useful if you include:

- Brand name e.g. *Walkers* crisps, *Dairy Milk* chocolate bar
- Food weight where known – often detailed on the packaging
- How the food was cooked e.g. fried, grilled, raw, etc.
- Extra ingredients eg. Tsp of grated cheese on spaghetti bolognaise or dressings/sauces/ butter/margarine added to potatoes, salads or pasta

3. Estimating food weights:

- Recording quantities of food is important.
- Household measures may help;
- A general recording of whether portions are small, medium or large is also helpful.

REMEMBER

Remembering later is often more difficult than we initially envisage, so it is often easier for most people to try to record as you go through the day, where possible.

Day and date: ....
(Please start each day on a new sheet

Time	Food and drink. Please include: brand name, flavour *Enter each food item on a new line*	Cooking method e.g. fried, grilled, toasted	Amount eaten	Office use Weight	Office use Food code				
8:15am	Hovis granary bread	Toasted	2 slices						
	Tesco sunflower margarine	On toast	Thin spread						
	Chicken egg	Boiled	1 large						
10:30am	Ban[illegible]		Small						
	Water		Medium glass						
12:15pm	Heinz mushroom soup, 300 g tin	Micro waved	All						
	Whole meal roll from local bakery		All						
	Sainsbury's low fat fruit yoghurt		1, 125 g pot						
	Granny smith apple		1 medium						
	Glass of water		Large glass						

SAMPLE PAGE

Appendix 3: International Physical Activity Questionnaire

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (August 2002)

SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ
The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ
Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation
Translation from English is supported to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ
International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information
More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective*. Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

_____ **days per week**

☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

_____ **days per week**

☐ No moderate physical activities → ***Skip to question 5***

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you have done solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking → ***Skip to question 7***

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

This is the end of the questionnaire, thank you for participating.

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002.

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