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The Effect of Cinnamon Supplementation for Patients with Type II Diabetes Mellitus

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Objective: The study aimed to dictate the capability of cinnamon supplements in reducing fasting blood sugar levels (FBS mg/dl) and glycated hemoglobin (HbA1c %) for patients with diabetes mellitus II (DMII). Comparing pre and post-intervention glycemic markers with aloe vera, ginseng, and anti-diabetic medication to determine if herbal supplements are an effective complementary alternative medicine (CAM) treatment for DMII.

Methods: The range of articles gathered consisted of 175 through MEDLINE and 510 through Google Scholar; these platforms allowed access to MEDLINE and ScienceDirect articles but were reduced to 40 based on search terms such as *"Cinnamomum cassia."* " *Cinnamomum verum,*" "Diabetes Mellitus II," "fasting blood sugar, and "glycated hemoglobin." The meta-analysis consisted of sixteen clinical trials from 2006-2022. The study designs were randomized, placebo-controlled, double-blind, and triple-blind trials.

Results: The data collection showed variability of methodology techniques such as distinctive dose ranges (500mg, 1g, 1.5g, 2g, 3g, and 6g), study lengths, anti-diabetic medication use, and cinnamon species. Post-intervention trials had sparse reduction ranges from -3mg/dl to -21.78mg/dl and A1C of <1.2%; the most significant reduction was performed on newly diagnosed patients with an FBS decrease of -111.23mg/dl and -1.18% A1C.

Conclusion: Cinnamon supplements can reduce FBS and A1C levels, although these results are not sustainable for a chronic patient with DMII, making it a non-reliable treatment option for

DMII. More research clinical trials should be performed on cinnamon supplements to conclude more accurate, evidence-based recommendations.

Keywords and phrases: Diabetes Mellitus II, cinnamon supplement, chronic disease prevention, glycemic markers, complementary alternative medicine (CAM), herbal medicine, anti-diabetic medication, aloe vera, ginseng.

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The Effect of Cinnamon Supplementation for Patients with Type II Diabetes Mellitus

Using herbal supplements is an ancient tactic among different cultures to treat multiple illnesses. The recent use of supplements to treat acute and chronic illnesses in this 21st century has become a more convenient alternative than pharmaceuticals. Advertisement, manufacturing, and social media are factors contributing to the increase in supplements, along with a lack of education, personal preference, and availability of healthcare. Seeking new treatment alternatives is encouraged to maintain optimal longevity, but most individuals fail to inform healthcare professionals about supplement use. However, there is a lack of clinical research on complementary alternative medicine (CAM) involving herbal supplements and their effectiveness in treating illness; an in-depth evaluation should be performed to verify supplement effectiveness in the human body and avoid misleading information. Cinnamon is a herbal supplement widely used among individuals at high risk of developing diabetes mellitus type II (DMII), pre-diabetics, or chronic diabetics. The study aims to decipher whether cinnamon and other supplements, such as aloe vera and ginseng, can alter the disease progression of DMII by looking at glycemic markers and comparing results with anti-diabetic medication.

Prevalence of Herbal Medicine Use

Complementary and Alternative Medicine (CAM)

Unfortunately, there is still little research examining the efficacy and safety of herbal supplements; this poses a problematic issue among diverse populations because herbal products continue to gain popularity and are consistently introduced in the market or within social media platforms. Supplements are highly advertised through social media or recommended by family members or friends; this influences the individual to blindly purchase supplements without properly investigating or discussing them with their primary care physicians. One of the reasons

is failed treatments, which cause patients to take matters into their own hands by pursuing a more alternative historical approach; this allows a sense of independence to improve their general well-being. The alternative therapy of herbal supplementation is based on synthetic versus traditional medicine, affordability, availability of resources, and health promotion. Herbal medicine is often considered safe and natural, with promising results. However, this is not necessarily true because scientific evidence and knowledge of adverse effects still require further research.

Herbal supplements are greatly used among patients with chronic illnesses to help control and maintain their health status. The elderly population has a higher rate of chronic illnesses that take prescription medication and commonly use nonprescription herbal medicine (Rashrash et al., 2017). Herbal supplements pose a potential risk for drug interactions due to polypharmacy and risk for toxicity due to decreased organ function. The U.S. population is well known for using herbal supplements, traditional medicine, and complementary and alternative medicine (CAM) that is not yet integrated into the healthcare system; therefore, physicians and pharmacists must be cautiously aware of the high use among specific populations and educate them properly to prevent adverse effects or detrimental toxic effects. The utilization of herbal self-medication among patients can also be related to a lack of trust in their healthcare providers. The healthcare team must be open and accommodating to patients' needs, giving them freedom of choice when choosing alternative treatments and herbal remedies. Serving as the patient's advocate and honoring treatment options based on their faith backgrounds and personal preferences will benefit their chronic illness treatments.

Poly Supplements

The public must also be cautious of supplements that combine multiple herbal supplements into one dose. Many supplements claim to help decrease the disease process of diabetes and lower glycemic levels. However, it poses dangerous risks if mixed without acknowledging their chemical component effects and herbal compatibility. Researchers have begun investigating combinations of herbal additives with cinnamon by using a set dose of each herb ingredient within a capsule to accelerate its potential effect. For example, Liu et al. (2015) concluded a study within a four-month treatment using a micronutrient supplement that contained Saigon (cassia) cinnamon, chromium, and carnosine. The participants were overweight pre-diabetics with FBS ranges of 99mg/dl-126mg/dl and BMIs greater than 25. In conclusion, the dietary supplement lowered the FBS by -3.6mg/dl at the end of the trial, while the control group showed an increase of +1.8mg/dl, indicating a mean difference of 1.8mg/dl between these two groups. The BMI of both of these groups increased by <1%. Depending on the characteristics and medical history of the patient, the presented values show a potential benefit for non-diabetic subjects to prevent DMII and the risk of cardiovascular disease as well as help pre-diabetics prevent the development of related micro and macrovascular complications of DMII. Patients with chronic DMII would not benefit as nearly due to their progressive stage and higher glycemic markers; they require additional diabetic treatment, such as anti-diabetic medication, to create long-term therapeutic effects (Liu et al., 2015).

Another study by Parha et al. (2020) also incorporated other herbal supplements within a single 750mg capsule based on its therapeutic effects; this included a specific percentage of nettle leaf, berry leaf, onion, garlic, fenugreek seed, walnut leaf, and Ceylon cinnamon bark. The three-month study consisted of DMII participants with an FBS greater than 130mg/dl; they were not on a current medication regimen but had a history of oral anti-diabetic medication use. The

study concluded that participants taking the dietary supplement had a reduced A1C from 9.72% to 8.39% (-1.33) and an FBS from 210.61mg/dl to 178.25mg/dl (-32.36). While the control group displayed a reduction in A1C from 9.26% to 8.66% (-0.6) and FBS from 192.72mg/dl to 178.96mg/dl (-13.76). The mean FBS difference between these two groups is 18.6mg/dl, with an A1C difference of 0.73% (Parha et al., 2020). The herbal combination in the study helped lower glycemic markers based on the end results of the two groups, but their levels are still considered high. Continuation of therapy for 6 months-1 year can be implemented to further analyze its potential outcomes. It would also be beneficial to evaluate the effectiveness of the herbal supplement combination in the initial treatment of diabetes for pre-diabetics or newly acute diagnosed DMII.

These types of supplement research use strategic methods to strengthen potential efficiency to help acute and chronic stages of DMII. However, there are no consistent clinical trials with similar drug ingredients to conclude a definite and consistent data outcome. Study results like this can intrigue the public to mix multiple supplements and take more than the recommended dose, placing them at a higher risk of having an adverse reaction by taking individual doses of each herbal supplement.

The Interrelationship Between Diabetes Mellitus II and Cinnamon

Pathophysiology of DMII

Cinnamon contains anti-inflammatory properties and antioxidants, primarily for blood sugar regulation and reducing cholesterol levels, which is an effective treatment for DMII. Hyperglycemia is elevated blood glucose levels within the blood system and is characterized as DMII, a heterogeneous metabolic disease. DMII can lead to organ metabolic dysfunction in multiple body systems without appropriate intervention (Banday et al., 2020). This disease

progresses at a slow rate and causes irreversible damage to organs, whether symptomatic or asymptomatic. Known factors contributing to this diagnosis include genetic dispositions, age, race, ethnicity, or environmental factors of modern lifestyles, such as limited exercise, stress, and unhealthy diets that can lead to obesity.

Pancreatic β-cells produce insulin when released into the body after meals causing a spike in glucose levels; this helps regulate glucose metabolism and cell absorption necessary for energy. Hormone dysfunction occurs when there are high amounts of sugar in the body; this causes β-cells to be released to compensate for low insulin levels or decreased insulin sensitivity in the bloodstream. Initially, the β-cells and insulin production increase to adjust to the high sugar levels in the blood. However, due to insulin sensitivity, β-cell production declines, eventually leading to insulin resistance in which the body does not supply enough insulin in proportion to its blood concentration resulting in too much glucose in the blood concentration (Banday et al., 2020). Although insulin is not working efficiently, it still activates the liver and muscles to store excess sugar, which is eventually stored as fat (CDC, 2022). Also, insulin acts as an adipogenic hormone that enhances triglyceride synthesis and increases circulating fatty acids caused by carbohydrate breakdown resulting in an accumulation of subcutaneous fat and ectopic fat in the main organs such as the liver, muscle, pancreas, heart, and other tissues (Gastealdelli et al., 2017). The hormone imbalance of insulin or β-cell dysfunction causes micro- and macrovascular changes to the eyes, kidneys, heart, nerves, and blood vessels, and an overall disruption of organs that can increase morbidity and mortality rates (Banday et al., 2020). Due to the pathophysiological changes, it is crucial to innate early intervention to prevent further health decline and permanent damage.

Treatment for DMII

When a patient is diagnosed with DMII, the usual treatment across the country is to prescribe metformin or other anti-diabetic medications. DMII patients are educated on lifestyle modifications that include increasing physical activity, consuming a diet low in carbohydrates, sugary foods, and drinks, and incorporating an increase in protein, whole grains, healthy fats, and vegetable intake (Marin-Peñalver et al., 2016). If the patient demonstrates a poor response to this treatment, additional drugs or insulin therapy is initiated. A large number of people do not think of DMII as a dangerous illness; assessing their knowledge is necessary to implement an appropriate education plan based on their age and education level. This will increase medication adherence and the ability to choose healthier food options based on availability and affordability. Without proper education, clients resume their old diets, continue their sedentary lifestyle, or are uncompliant with their medication increasing morbidity risks due to the unawareness of the long-term consequences of untreated DMII (Kohei, 2010). According to the American Diabetes Association, the goal for diabetic patients is to maintain a hemoglobin A1C of <7%, a blood sugar of 80-130mg/dL before meals, and less than 180mg/dL two hours after meals (ADA, n.d). The aim of primary care providers is to secure patients with a good quality of life and prevent the progression of cardiovascular complications such as coronary heart disease, hypertension, valvular heart disease, and cardiomyopathy because all of these medical conditions can increase the risk of heart attacks.

Cinnamon Chemical Compounds

Individuals buy cinnamon supplements without knowing the types of cinnamon and the pharmacodynamics of its chemical components; knowing its exact mechanism can help the person choose the best optimal supplement. Cinnamon is considered a metabolic modulator of

antioxidants and anti-inflammatory properties that have an effect on diabetes, as well as neurological, microbial, and cardiovascular illnesses based on different free-radical scavenging flavonoids, camphene, eugenol, linalool, salicylic acid, and epicatechin. These components stop harmful free radicals in the body system and block oxidative stress. One of its bicomponents, called cinnamaldehyde, has an inhibitory effect with the potential to act against the production of nitric oxide (NO) and removes this type of inducible nitric oxide (Rao & Siew Hua Gua, 2014). This is important because NO synthase activation is controlled by insulin, and DMII causes insulin resistance which can disturb the generation and the regulation of NO metabolism (Tessari et al., 2010). Also, DMII can cause an increased overproduction of nitric oxide concentrations in the bloodstream affecting insulin-mediated postprandial glucose disposal and furthering the development of insulin resistance. High amounts of NO can also become cytotoxic for pancreatic β-cells by inhibiting insulin secretion, lipid peroxidation, and apoptosis, causing hyperglycemia-induced oxidative stress (Assmann et al., 2016).

Cinnamaldehyde also decreases the production of interleukin (IL)-1b, IL-6, and tumor necrosis factor (TNF)-a in lipopolysaccharide (LPS) that can aid in neuroinflammatory issues with diabetic neuropathy issues. Its anti-diabetic effects *in vitro* stimulate insulin release and potentiate insulin receptor activity due to its insulin-mimetic properties on rising glucose uptake due to methydroxychalone polymer (MHCP) within cinnamon. A purified polymer of hydroxychalcone stimulates glucose oxidation and holds polyphenol type-A that acts like insulin-like molecules; this is a beneficial effect for diabetic patients because it causes an imbalance between free radicals, the oxidative stress impairs glucose tolerance and increases insulin resistance (Yaseen & Mohammed, 2020).

Ceylon Cinnamon *(Cinnamomum verum)*, otherwise known as “true” cinnamon, has bioactive compounds comprised of benzoic acid, (E)-cinnamaldehyde, trans-cinnamic acid, eugenol, and o-methoxy-cinnamaldehyde. In vitro studies have determined the stimulation of glycolysis and glycogenesis, inhibiting glucogenesis in the liver and kidneys. The water extract of Ceylon cinnamon contains benzoic acid, trans-cinnamic acid, eugenol, and O-methoxycinnamaldehyde have the capability to interrupt the α-amylase and α-glucosidase enzymes process in the digestive tract. These enzymes hydrolyze carbohydrates preventing hyperglycemic blood spikes after meals by slowing digestion. Cinnamaldehyde is also known to be more effective than metformin; it plays a crucial role in reducing glucose transport and insulin signaling while regulating dyslipidemia. This bioactive component also inhibits enzyme activity to prevent glucose absorption in the bloodstream; it restores altered plasma enzymes by regulating aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, alkaline phosphate, and acid phosphate levels (Błaszczyk et al., 2021).

On the meta-analyses, six studies declared they used Cassia cinnamon for their trial, while only two studies used Ceylon cinnamon, one study purchased fresh cinnamon bark from a local Iranian market, and the rest of the trials did not specify what species they used. Based on the pre and post-intervention FBS and A1C levels, no significant data claims one cinnamon species works best; it is also difficult to determine this because there were not enough Ceylon cinnamon treatments to compare with Cassia cinnamon, and for the rest of the trials, the cinnamon powder species were unknown. These two cinnamon species require further investigation because they are essential factors in determining cinnamon effectivity.

Coumarin Levels

The species of cinnamon determines its level of coumarin; consumption of high amounts of coumarin can cause serious health problems, including hepatotoxicity and hemorrhage. It is particularly important for individuals with chronic diabetes, given that a large percentage of the population already suffers from non-alcoholic liver disease caused by hyperlipidemia, hypertension, and hyperglycemia. The combination of fatty liver disease, obesity, and insulin resistance are co-factors that cause liver damage (Hazlehurst et al., 2016). In Cassia and Ceylon cinnamon species, the main toxicity risk is derived from overconsumption of coumarin content; understanding appropriate doses is crucial to prevent acute liver injury or failure in DMII patients.

Most of the population already incorporates cinnamon powder with their everyday meals; this fine powder has a potent aroma and flavor and is used as an ingredient for many homemade dishes across various cultures. Some cultures incorporate cinnamon in their diet more than others and could exceed their daily recommended amount of 1-4g (1,000-4,000mg), increasing their toxicity risk (Al-Samydai et al., 2018). To detect the overall consumption recommendations, an average teaspoon of cinnamon powder weighs 2.6g giving a better perspective on how much a person uses for cooking measurements. Most commercial ground cinnamon sold in stores is classified as Cassia cinnamon since it is a widely available and inexpensive spice, but it still contains higher coumarin levels that can negatively affect the body compared to Ceylon cinnamon. Each kilogram of Cassia cinnamon powder contains 700-12,230mg/kg of coumarin content; therefore, 4g (0.004kg) of cinnamon would contain roughly 2.8mg-48.92mg for each gram (0.001kg); a total of 4g indicates a range of 11.2mg-195.68mg (Bandara et al., 2012). Ceylon cinnamon only has 190mg of coumarin for each kilogram of powder, a rough estimation

of 0.76mg; an individual ingesting a limit of 4g would have 3.6mg of coumarin; these concentration ranges were below the detection limit (Bandara et al., 2012). Fotland et al. (2012) dictated that a new tolerable daily intake of coumarin is based on how much an individual weighs; this consisted of 0.07mg/kg bw/day. Based on the information, an individual weighing 77.3kg (170lbs) can only have 5.4mg of coumarin to avoid toxicity risks; this individual is limited to only 1.2 grams of Cassia cinnamon, close to one teaspoon a day.

In most cases, people are unaware of what products they purchase and consume; therefore, it is unlikely that they also know the potential risks associated with Cassia cinnamon, especially if they rarely consume it. Also, people are mostly exposed to cassia cinnamon because it is commonly used in many foods, whereas if an individual takes capsules for health purposes, they can purchase either Cassia or Ceylon cinnamon. Exceeding this dosage on a daily basis can increase hepatic toxicity; symptoms can include abdominal pain, headache, nausea, discolored skin, diarrhea, and dark urine. Symptoms for decreased blood coagulability include bleeding gums, bruising, nosebleeds, hematuria, and hematochezia; individuals taking prescription anticoagulants such as warfarin, aspirin, or heparin should be cautious or refrain from consuming cassia cinnamon. Patients can also experience these symptoms if they have drug-drug interactions with prescription medications. Precautions must be taken to decrease toxicity and coagulability adverse effects if taking cefazolin, rifampin antibiotics, miconazole antifungals, and NSAID (ibuprofen, Advil, Aleve) anti-inflammatories, sulfinpyrazone uricosuric agents, and carbamazepine anticonvulsants (Harder & Thürmann, 1996). Also, there are interactions with cardiovascular and antilipidemic drugs that are coadministered with coumarins such as amiodarone, propafenone, and fibrates. These drugs are potent inducers of coumarin metabolism

that enhance the hypoprothrombinemia response to coumarin caused by various mechanisms (Harder & Thürmann, 1996).

The patient response to coumarin also depends on several acquired factors, including age, dietary intake, intercurrent illnesses, or genetic framework that affect coumarin metabolism breakdown, thus requiring frequent monitoring of coumarin doses. In particular, genetic determinants such as VKORC1 and the CYP2C9 genes lead to interindividual differences in response to coumarin dose variability. The VKORC1 gene expresses subunit one of the vitamin K cycle and the molecular target of coumarin derivatives, and the CYP2C9 gene encodes the enzyme cytochrome P450 2C9 that takes part in the hepatic metabolism of coumarin derivates; these two genes have variant alleles that increase coumarin sensitivity causing the patient to be more prone to experience adverse effects (Rakicevic et al., 2013). Therefore, patients with these genes should limit or avoid consuming cinnamon supplements because it increases bleeding risks; they are still at risk even if a recommended coumarin dosage is followed. Also, the frequency of VKORC1 and the CYP2C9 alleles differs between ethnic groups and populations; the use of genotyping is a more accurate test to dictate appropriate therapy and improve patient safety (Rakicevic et al., 2013).

Most of the studies used Cassia cinnamon for their clinical trials, and the participants did not claim any side effects or adverse effects; this can be due to them not exceeding 3g a day. Due to its low coumarin levels, it will be more optimal for studies and the general public to purchase Ceylon cinnamon. For example, the 77.3kg individual taking Ceylon cinnamon can consume a higher quantity of 5.32g since there are 0.76mg of coumarin in one gram of cinnamon, and his daily coumarin limit remains 5.4mg. A maximum of two teaspoons daily is recommended, even though consuming this amount daily is unlikely. A more accurate way to determine is to base the

daily intake on body weight; a higher set dose range can help prevent toxic effects. Having foods in moderation is key, along with proper education to purchase only Ceylon cinnamon powders and capsules to limit risks and have higher beneficial effects for patients with chronic diabetes and the general public. Taking a reasonable dose of Ceylon cinnamon can be safe and effective for most patients. However, considering their age, sex, ethnicity, past medical history, family history, current medications, and genetic factors is always necessary before recommending these supplements.

In vivo Cinnamon Research Findings

Clinical Study Characteristics

The biochemical components of cinnamon claim to treat the DMII pathophysiology; positive results on continuous supplement use can lower fasting blood glucose (FBS), A1C levels, and LDL cholesterol. At the same time, improving HDL levels and increases insulin production and circulation. Most of these clinical trials focus on the probability of decreasing FBS and A1C levels with diabetes since the disease process is related to hyperglycemia levels circulating in the blood leading to micro and macrovascular changes. Many clients are overweight with a body mass index (BMI) greater than 24; the normal range is typically between 18.5 and 24.9 (CDC, 2022). A tool used to identify health risks by calculating weight and height to estimate body fat percentage. Research has shown that a J-curve relationship exists between BMI and chronic diseases, which researchers used as a guideline in these clinical trials. Individuals with a high BMI, especially those above 30, are more likely to develop chronic diseases. DMII increases the risk for high cholesterol levels, which can lead to cardiovascular disease; their interrelationship led clinical researchers to measure low-density-lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) (Zare et al., 2019). LDL is known as “bad”

cholesterol and should be maintained at less than 100mg/dL, and HDL is known as the “good” cholesterol and should remain above 40mg/dL. These specific determinants were mentioned in most studies to verify their potential effect before and after supplement intervention; other readings included blood pressure, triglycerides, total cholesterol, and insulin.

The clinical studies used for this meta-analysis were randomized, placebo-controlled, double-blind trials performed from 2006 to 2022. The sample size ranged from 36 to 200 participants, consisting of early middle to late middle adulthood age groups (35-64) already diagnosed with DMII. Each clinical research used similar yet different treatment intervention strategies; this included the type of cinnamon species, capsule versus extract, milligram dosages, the number of times taken per day, study duration, and the usage of anti-diabetic medications and diet plans. These components are essential in determining whether cinnamon supplements can be used as an alternative method to improve blood sugar levels. The participants continued following their usual daily routine and diet; this allows unbiased data collection because if a healthier diet and active lifestyle with exercises were implemented, it could affect the outcome results. Most clinical studies, except for Sharma et al. (2012) and Ziegenfuss et al. (2006), allowed all participants to use their daily anti-diabetic medications. This is important information to consider because these are already diagnosed patients who have been on a daily medication regimen that should be lowering their glucose levels. Along with medication administration, the duration of their DMII diagnosis helps to determine cinnamon efficiency; this is pertinent data, but none of the cinnamon studies reported this information. Although it can be hypothesized that if cinnamon supplements help chronic diabetic patients, there is the likelihood of it helping in the preventative stages for high-risk individuals, pre-diabetic stages, or newly diagnosed diabetics.

Table 1

Meta-analysis evaluating the effects of Cinnamon supplements with patients with DMII

References	Study design	Sample Size	Cinnamon Intervention: Dose, Duration, Administration	Antidiabetic Medication
Mang et al. (2006)	Randomized, placebo-controlled, double-blind trial.	DMII, 65 subjects -Females, and males, average age of 63 and BMI of 25.9.	3g (1g capsule each meal) for 4 months. Cinnamon powder (species not specified), formulated with 112mg of aqueous cinnamon extract TC112	Yes, and/or following a diet (medications and diet plans were unknown)
Ziegenfuss et al. (2006)	Randomized, placebo-controlled, double-blind trial.	DMII, 22 subjects -Females, and males, average age of 46 and BMI of 33.4.	500mg (one 250mg capsule with breakfast & lunch) for 3 months. Specific aqueous extract of cinnamon (Cinnulin PF®) *(Cinnamomum cassia)*	None, only a multivitamin.
Blevins et al. (2007)	Randomized, placebo-controlled, double-blind trial.	DMII, 58 subjects -Females, and males, average age of 60.8 and BMI of 32.3.	1g (one 500mg with breakfast and dinner) for 3 months. Cinnamon powder (*Cinnamomum cassia*)	Yes, but subjects were withdrawn if anti-diabetic medicines were initiated, discontinued, or adjusted during the study.
Akilen et al. (2010)	Randomized, placebo-controlled, double-blind trial.	DMII, 58 subjects -Females, and males, the average age is 54 and BMI of 38.9.	2g (500mg x4, one at breakfast, two at lunch, one at dinner) for 3 months 100% Cinnamon bark powder (*Cinnamomum cassia*)	Yes, Metformin, Sulphonylureas, or both.
Mohammadi et al. (2012)	Randomized, placebo-controlled, double-blind trial.	DMII, 37 subjects -Females, and males, the average age is 55 and BMI 30.7.	3g (500mg x6, two at breakfast, lunch, & dinner) for 2 months. Cinnamon powder *(Ceylon Cinnamomum)*	Yes, hypoglycemics only.
Sharma et al. (2012) 3g/day	Randomized, placebo-controlled, double-blind trial	DMII, 37 subjects -Females, and males, with age >30 years old, and an average BMI of 26.6	3g (1g capsule after breakfast, lunch, & dinner) for 3 months. Cinnamon powder (species not specified)	None, oral hypoglycemic agents, and insulin therapy were not accepted.
Sharma et al. (2012) 6g/day	Randomized, placebo-controlled, double-blind trial	DMII, 37 subjects -Females, and males, with age >30 years old and an average BMI of 26.6.	6g (2g capsule after breakfast, lunch, dinner) for 3 months. Cinnamon powder (species not specified)	None, oral hypoglycemic agents and insulin therapy were not accepted.

Hasanzade et al. (2013)	Randomized, placebo-controlled, double-blind trial	DMII, 70 subjects -Females, and males, the average age was 54, and an average BMI of 27.9.	1g (one 500mg before breakfast and dinner) for 2 months. Cinnamon powder *(Cinnamomum cassia)*	Yes, and/or following a diet. (Medications and diet plans were unknown)
Anderson et al. (2015)	Randomized, placebo-controlled, double-blind trial	DMII, 137 subjects -Females, and males, the average age was 61, and an average BMI of 25.3.	500mg (250mg 2x/daily) for 2 months. Dried water extract of cinnamon. *(Cinnamomum cassia)*	Unspecified
Sensuk et al. (2016)	Randomized, placebo-controlled, double-blind trial	-DMII, 99 subjects -Females and males, the average age was 57.05, and an average BMI of 24.7.	1.5g (500mg after breakfast, lunch, & dinner) for 2 months. Cinnamon powder (Species unknown)	Yes (medications unknown) -Subjects were educated on a healthy diet.
Zare et al. (2019) >27BMI	Randomized, placebo-controlled, triple-blind trial. -Four subgroups	DMII, 120 subjects -Females and males, the average age of 52 and an average BMI of 29.6.	1g (one 500mg on fasting/breakfast and before bedtime) for 3 months. Fresh cinnamon bark was purchased from a local market in Iran.	Yes (medications unknown)
Zare et al. (2019) <27 BMI	Randomized, placebo-controlled, double-blind trial. -Four subgroups	DMII, 120 subjects -Females and males, the average age of 52, and an average BMI of 29.6.	1g (one 500mg on fasting/breakfast and before bedtime) for 3 months. Fresh cinnamon bark was purchased from a local market in Iran.	Yes (medications unknown)
Hendre et al. (2019)	Randomized, placebo-controlled, double-blind trial.	DMII, 200 subjects -Females and males, ages 35-65, BMI unknown.	500mg (post-lunch) for months. Cinnamon powder (species unknown)	Yes, Metformin only
Davari et al. (2020)	Randomized, placebo-controlled, double-blind trial.	DMII, 44 subjects -Females and males, the average age of 57 and an average BMI of 27.70.	3g (1g with three meals) for 3 months Cinnamon powder (species unknown)	Yes, Metformin only
Lira Neto et al., (2022)	Randomized, placebo-controlled, triple-blind trial.	DMII, 160 subjects -Females and males, the average age of 61.5, BMI unknown	3g (two 750mg capsules 30mins before breakfast & lunch) for 3 months Cinnamon bark powder (*Ceylon Cinnamomum*)	Yes, Metformin & Sulfonylureas (glimepiride & glibenclamide)
Rachid et al., (2022)	Randomized placebo-controlled trial	DMII, 36 subjects -Females and males, the average age of 62.8, and an average BMI of 30.8.	6g/100ml 120mins (BG measured before intervention and after 30mins; t0, t30, t60, t90, & t120) Cinnamon aqueous extract *(Cinnamomum burmannii/cassia)*	Yes, Metformin & Sulfonylureas (glipizide, glimepiride, and glyburide)

Table 2

Cinnamon Pre vs. Post FBS (mg/dl) and A1C (%) Results

References	FBS (mg/dl)	A1C (%)
Mang et al. (2006)	166.68 to 146.7 (-19.98)	6.86 to 6.83 (-0.03)
Ziegenfuss et al. (2006)	116.3 to 106.5 (-9.8)	n/a
Blevins et al. (2007)	132.9 to 142.7 (+9.8)	7.2 to 7.0 (-0.2)
Akilen et al. (2010)	158.76 to 144.72 (-14.04)	8.22 to 7.86 (-0.36)
Mohammadi et al. (2012)	139.28 to 126.47 (-12.81)	7.35 to 6.9 (-0.45)
Sharma et al. (2012) 3g/day	226.73 to 115.5 (-111.23)	8.47 to 7.29 (-1.18)
Sharma et al. (2012) 6g/day	216. 94 to 112.26 (-104.68)	8.10 to 7.25 (-0.85)
Hasanzade et al. (2013)	177 to 174 (-3)	8.9 ±1.7 to 8.9 ±1.6 (0)
Anderson et al. (2015)	159.3 to 147.2 (-12.1)	n/a
Sensuk et al. (2016)	153.54 to 131.76 (-21.78)	8.0 to 7.6 (-0.4)
Zare et al. (2019) >27BMI	162.6 to 143.2 (-19.37)	7.36 to 6.94 (-0.42)
Zare et al. (2019) <27 BMI	162.6 to 156.8 (-5.8)	7.36 to 6.43 (-0.93)
Hendre et al. (2019)	154 to 143 (-11.3)	n/a
Davari et al. (2020)	183.85 to 172.20 (-11.66)	10.04 to 10.11 (+0.07)
Lira Neto et al., (2022)	185.94 to 175.86 (-10.08)	10.98 to 10.64 (-0.34)
Rachid et al., (2022)	t0: 145.99 t30: 257.13 t60: 297.48 t90: 313.33 t120: 275.15 (+111.16)	n/a

Cinnamon Effects According to BMI Factor

Being overweight has been associated with type two diabetes; excess fatty tissue causes muscle and other cells to become resistant to insulin. The interrelationship between a higher BMI and diabetes with the use of cinnamon supplements requires an analysis. Zare et al. (2019) performed a randomized, triple-blind study and concentrated their study methods criteria based on the participant's BMI. A three-month study administering 1g/day of cinnamon divided participants into four subgroups; the cinnamon and placebo consisted of two groups, participants with a BMI less than 27 and a BMI greater than 27. The results concluded that having a higher BMI would produce the most noticeable results in reducing FBS levels, triglycerides, total cholesterol, and low-density lipoprotein (LDL) while improving high-density lipoprotein(HDL) compared to patients with a lower BMI. The baseline range for the cinnamon group with a BMI of 27≥ consisted of an FBS of 162.6mg/dL, triglycerides of 168.1, total cholesterol of 167.8, LDL of 103.8mg/dL, and HDL of 42.4mg/dL. By the end of the three-month clinical trial, it demonstrated decreased FBS of -19.37md/dL, triglyceride of -19.05, Total cholesterol of -17.4md/dl, LDL of -9.2, and an increase of +2.83 in HDL levels. While the BMI <27 groups only had a -5.8 FBS reduction and minimal changes in their lipid profile.

According to the Centers for Disease Control and Prevention (CDC), the standard range for BMI is 18.5-24.9 and is indicated by dividing an individual's weight by their height; a BMI over 25 correlates with an individual as overweight (CDC, 2022). Most of the studies had participants with a BMI of 25≥ but displayed a wide range of FBS reduction. For example, based on the Table 1 reference, 14 of the 16 trials showed variable decreased FBS levels. Mang et al. (2006) had an average BMI of 29.6, with a -19.99mg/dl reduction, Akilen et al. (2010) had a BMI

average of 33.36 but only had a -14.04mg/dl, and finally, Anderson et al. concluded a reduction of -12.1md/dl at a 24.8 BMI. In conclusion, having a BMI greater than 25> will decrease FBS based on the research data collection; it contributes as an indicative factor to see FBS changes based on the possible oxidative mechanism of cinnamon in the body. Although, incorporating other factors will dictate the final FBS results as well.

The mechanism of cinnamon can be explained by how it affects the uncoupling oxidative phosphorylation (UCP3) gene, which the body uses as a protein transporter in the mitochondria; this creates a permeable membrane within the adipose muscle tissue enabling lipid and carbon metabolism oxidation for energy consumption. Implementing cinnamon increases the oxidative metabolism caused by the insulin-regulated glucose transporter reaction and increases insulin receptors. The participants from Zare et al. (2019) had BMIs of 27≥, indicating greater adipose muscle mass creating a heightened oxidative mechanism, thus explaining why this particular group had better glycemic outcomes.

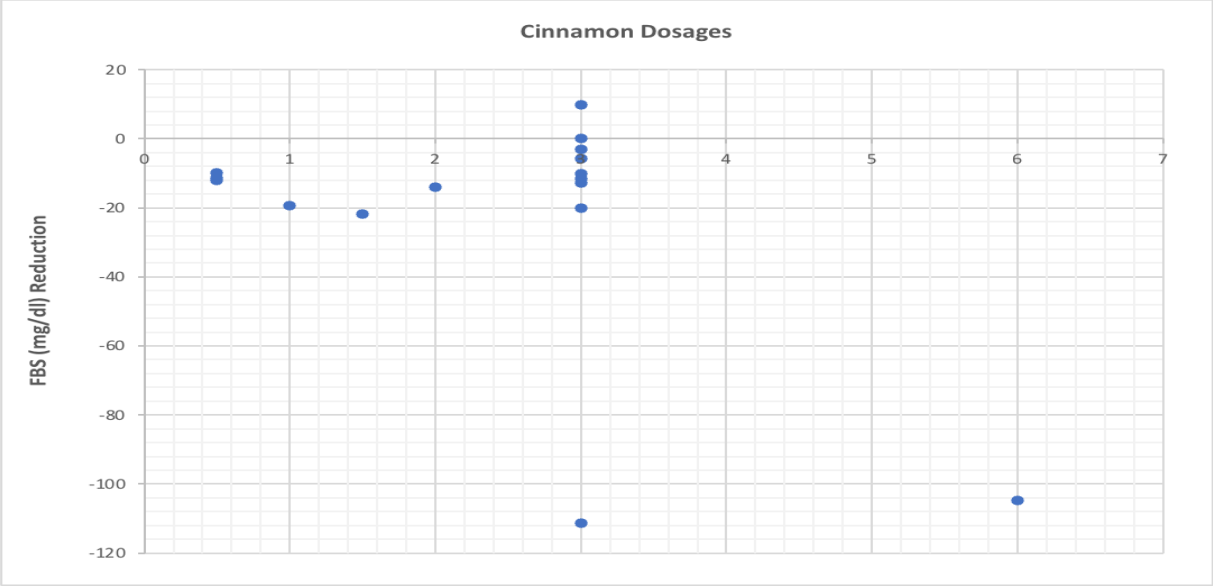
Factors such as age, sex, muscle mass, and ethnicity can affect BMI and body fat percentage; therefore, overweight and obesity issues can increase the risk of DMI. BMI measurements are a simple, inexpensive, and noninvasive method to measure fat. However, BMI fails to distinguish between excess fat, muscle, or bone mass and does not indicate the distribution of fat (CDC, 2011). It is essential to take into consideration, especially for ethnic groups, because it can influence BMI interpretations; hence specific cutoff of BMI should be incorporated for ethnic groups. For example, individuals of South Asian descent have a smaller body structure with a higher body fat distribution of visceral fat compared to subcutaneous fat (Nair, 2018). A Caleyachetty et al. (2021) study stated evidence of a high prevalence of DMII in Asian populations at lower BMI compared to the White population; lowering the BMI cutoff

would best optimize the identification of cardiometabolic risks for this group. Their results concluded that the risk of developing DMII for South Asian individuals occurred at a BMI of 23.9kg/m² while the White population had an equivalent BMI risk of 30.0 kg/m². The study also found that Black ethnic groups had a DMII incidence equivalent to the White population at lower BMI values (Caleyachetty et al., 2021). This concept can also be incorporated with age and sex factor differences because older adults have more body fat than younger adults, and women tend to have higher amounts of total body fat than men for an equivalent BMI; thus, identifying an appropriate BMI should range based on the individuals internal and external factors is necessary (CDC, 2011).

Due to the ethnic differences in BMI and waist circumference (WC) relationships with body fat distribution, it is important to validate BMI for different ethnic groups with set appropriate cutoff levels (Nair, 2018). It is still unclear whether lower BMI cutoffs in non-White populations are based on different body composition, biomechanical characteristics, lifestyle factors, the genetic architecture of DMII, or lifestyle-gene interactions, so further examination of these possible contributing mechanisms is required. Still, clinical limitations of BMI need to be acknowledged by healthcare professionals due to the diverse BMI factors to best treat DMII patients.

Figure 1

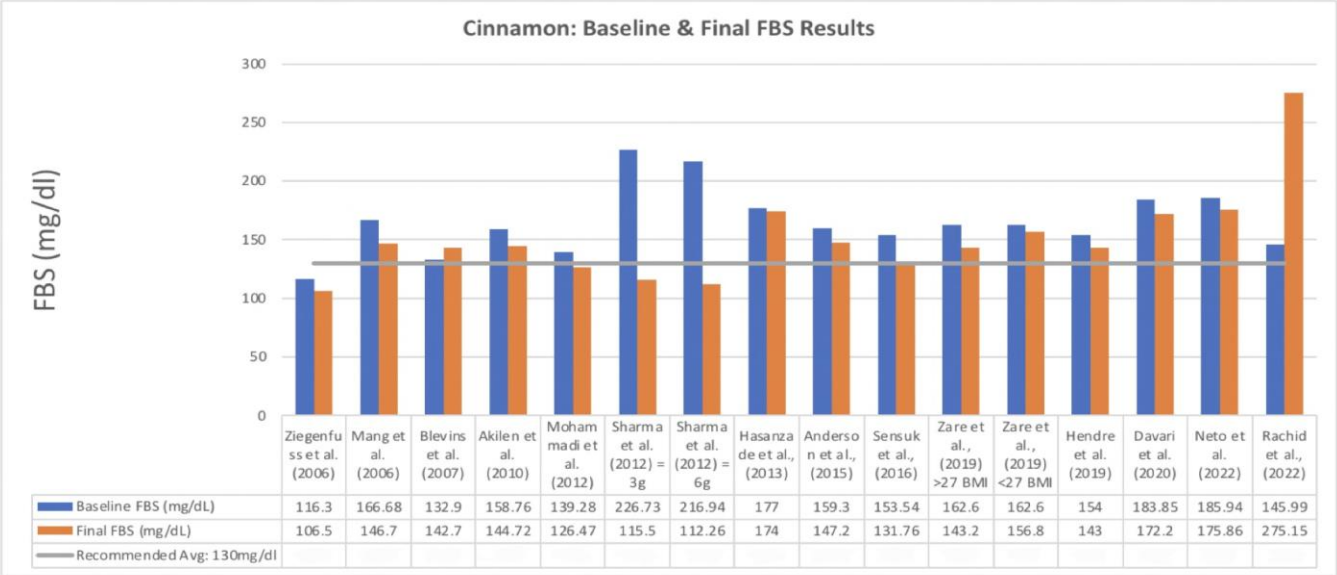
Decrease of FBS (mg/dl) according to the dosage given per day (500mg, 1g, 1.5g, 2g, 3g, 6g)



Note: Comparing the different dosages (500mg, 1g, 1.5g, 2g, 3g, 6g) used in the clinical trials on fasting blood sugar levels (FBSmg/dl).

Figure 2

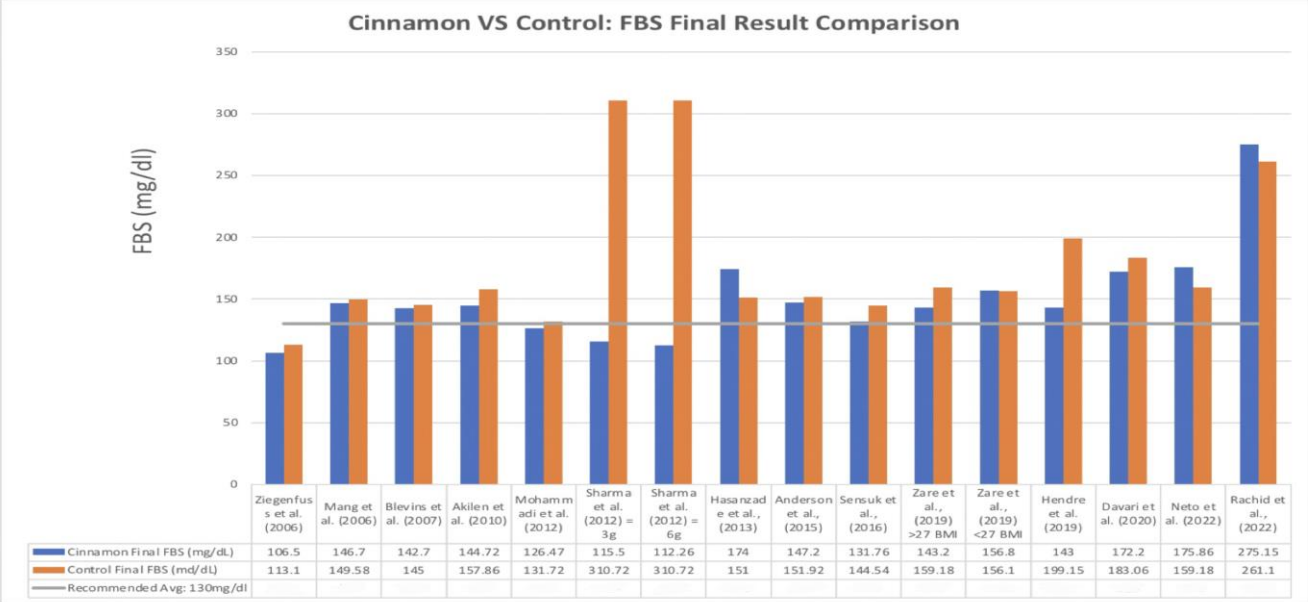
Cinnamon baseline vs. final FBS (mg/dl) results



Note: Comparing the baseline fasting blood sugar (FBS mg/dl) before intervention and the final FBS mg/dl after cinnamon supplementation with a recommended FBS average of 130mg/dl per American Diabetes Association (ADA).

Figure 3

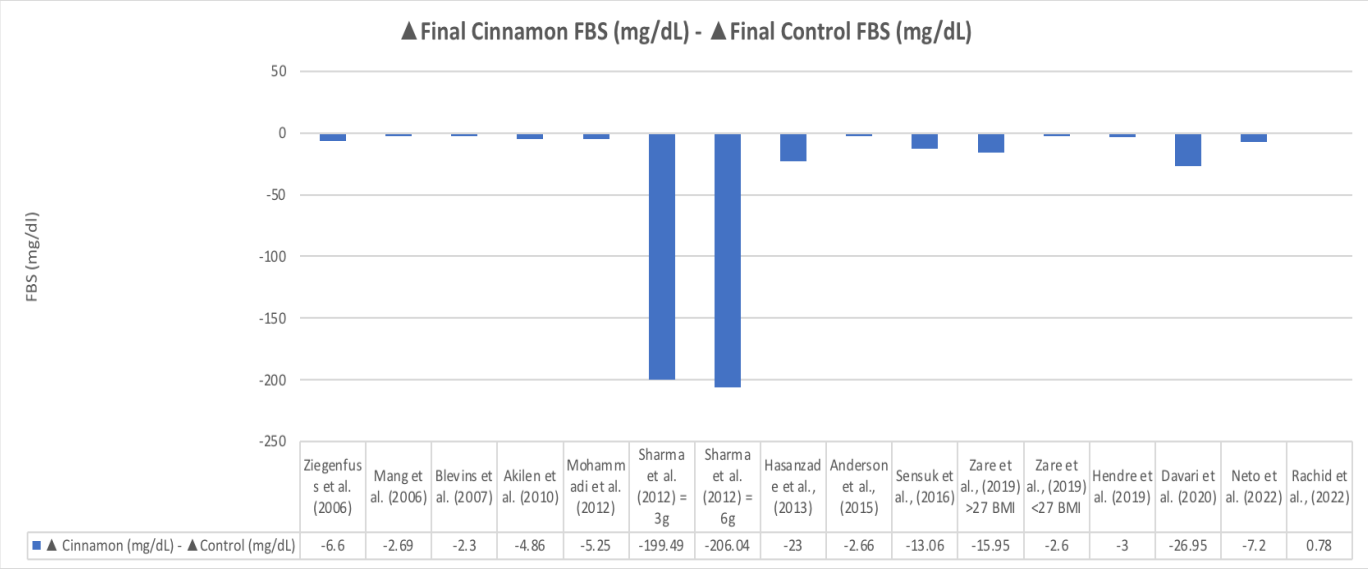
Cinnamon vs. control FBS (mg/dL) final result comparison



Note: Comparing the final fasting blood sugar (FBS mg/dl) for the cinnamon and control group. A recommended FBS average of 130mg/dl per American Diabetes Association (ADA, n.d).

Figure 4

▲Final cinnamon FBS (mg/dL) - ▲Final control FBS (mg/dL)



Note: Comparing the mean significant difference between the cinnamon and control group after the end of the clinical studies.

Figure 5

Cinnamon baseline & final A1C Results

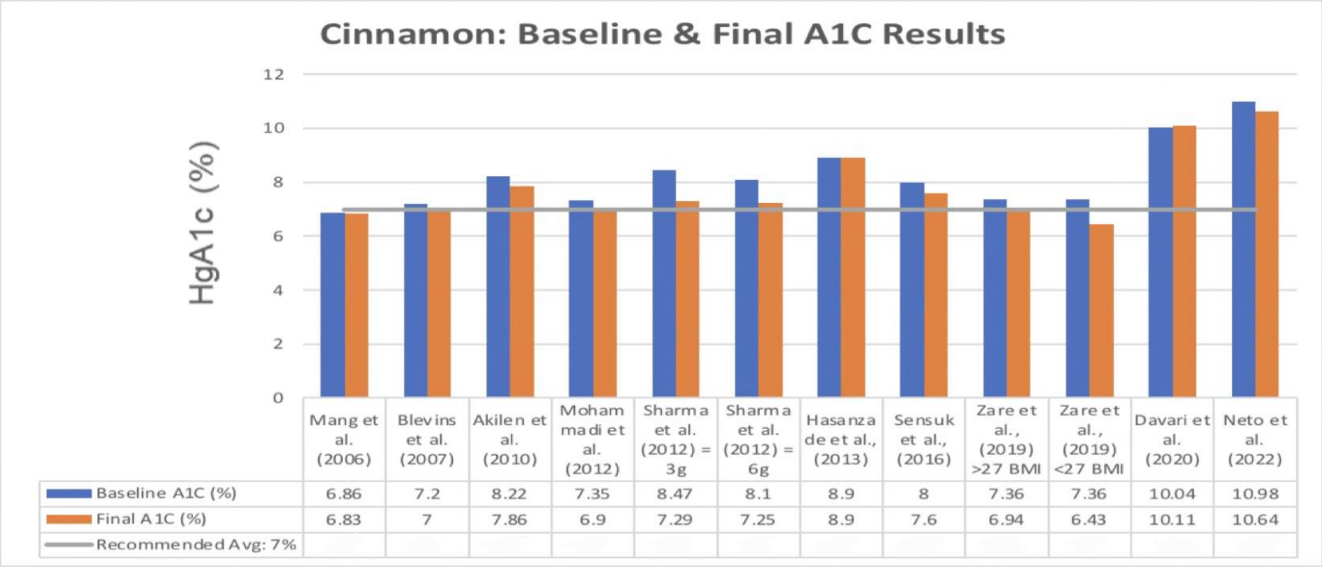
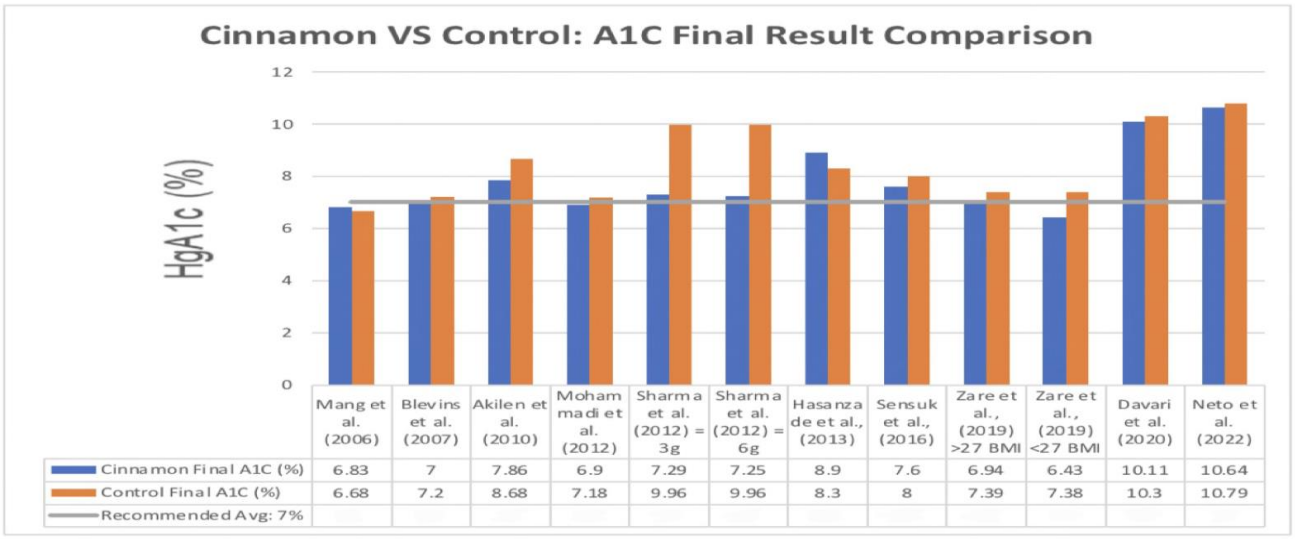


Figure 6

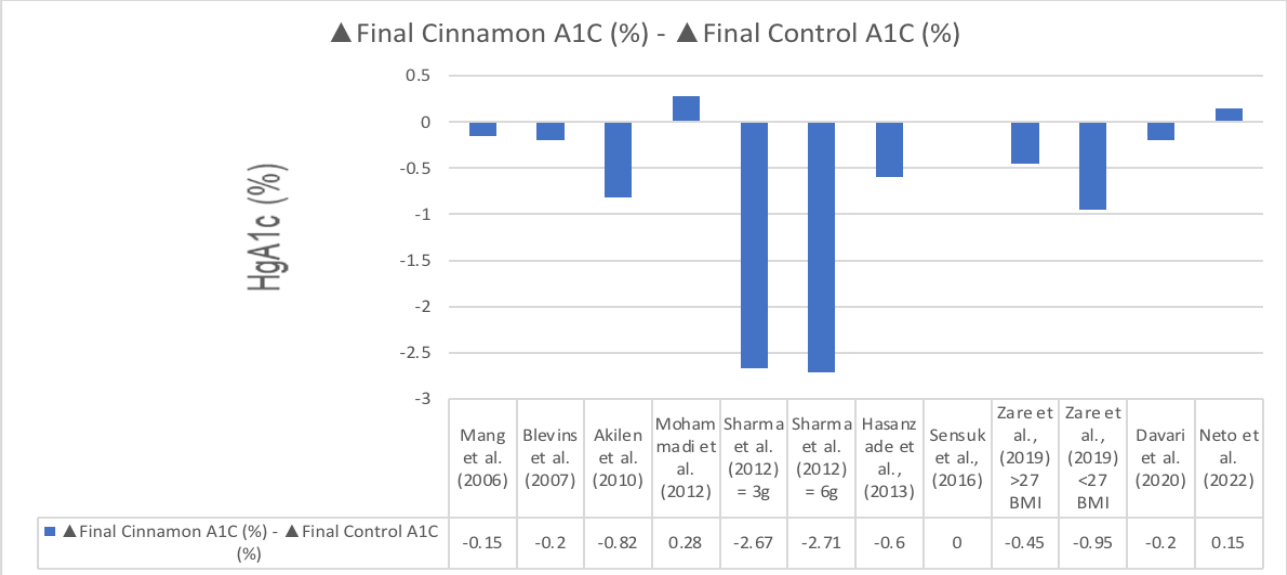
Cinnamon vs. control A1C final result comparison



Note: Comparing the final Hemoglobin A1C(%) for the cinnamon and control group. A recommended A1C average of <7% per American Diabetes Association (ADA, n.d).

Figure 7

▲*Final cinnamon A1C (%)* - ▲*Final control A1C (%)*



Note: Comparing the mean significant difference between the cinnamon and control group after the end of the clinical studies.

FBS (mg/dl) Reduction with Cinnamon Supplementation

The FBS is one of the main focuses of cinnamon effectivity; based on the results of the studies, multiple factors would affect the decrease of FBS. The final FBS results after a two or three-month intervention with cinnamon showed a minimal reduction; there is insufficient evidence to conclude whether the lower or higher dosages of cinnamon provide the most reduction of sugar levels in the blood. Sharma et al. (2012) had the most positive effect on FBS; this particular study compared the difference between administering 3g versus 6g of cinnamon supplementation against the placebo group. The 3g group's baseline started at 226.73mg/dl, and at the end of the three-month intervention, it decreased to 115.5mg/dl, indicating a (-) 111.23 difference from the baseline and final results. The 6g group also had a similar decrease in FBS with a difference of (-) 104.68; both groups had a p-value of <0.001 (Figure 2). There is a common presumption that a higher quantity of grams per day will produce better outcomes. However, this study demonstrates that this concept is unrelated and that maximizing the dosage does not provide higher-quality results (Figure 1). The intervention therapy effectiveness can be related to the study's inclusion criteria of patients; they only recruited patients with newly onset type 2 diabetes that were not taking any hypoglycemic agents or insulin therapy and other medications for other health conditions.

Along with the cinnamon supplementation given as the first line of treatment, the patients were also educated to follow a conventional treatment that consisted of a standard diet and exercise. Making dietary changes and following an exercise routine is proven to decrease FBS levels in diabetic patients, and adding the cinnamon regimen increased the results. The placebo

group might have also benefited from the conventional therapy because they were required to follow the standard diet and exercise, but surprisingly their FBS levels increased, showing a difference of (+) 83.8 (Figure 3). It can indicate that adding a cinnamon regimen has a positive effect or is related to diet and exercise regimen.

Dosages for the other clinical studies consisted of 500mg, 1g, 1.5g, 2g, and 3g, with no significant pattern indicating that higher dosages would supply greater results. The general rule is incorporating a three-month supplement intervention to determine more accurate results. For example, Sensuk et al. (2016) completed their research study within two months and only gave 1.5g per day, resulting in a (-) 21.78 difference. Whereas the following two studies implemented a 3g cinnamon supplement a day, Mang et al. (2006) reported a (-) 19.98 difference within four months, and Zare et al. (2019) reported a (-) 19.37 difference within three months for subjects with a BMI greater than 27 (Figure 1). According to Figure 1, other studies had a minimal reduction of FBS levels at a 3g and three-month interval; the final results concluded only a 10.8mg/dl reduction from the Neto et al. (2022), 3mg/dl reduction from the Hasanzade et al. study and 5.8mg/dl reduction from the Zare et al. (2019) with subjects having a BMI less than 27. The mean differences between all of these studies are within a similar range; thus, other factors potentially manipulate the outcome results, concluding that dosage and length of supplemental regimen do not affect the FBS outcomes. These other factors can include BMI, cinnamon species, or patient related. Also, when compared with the control group, there were FBS differences at the end of the clinical trial suggesting that cinnamon can potentially improve glycemic markers (Figures 3 & 4).

It is normally advised to take prescription medications and dietary supplements during breakfast, lunch, and supper. However, there was no correlation between the timing of taking

cinnamon supplements before, during, or after meals. As Yaseen & Mohammed (2020) claimed, cinnamon mimics insulin production caused by the activation of glucose rise after meals; the enzymatic activity also prevents glucose absorption when ingesting carbohydrate meals. Therefore, as long as the cinnamon supplement is taken with a meal, it should provide beneficiary effects. Although according to Zare et al. (2019), they determined that taking it during fasting hours in the morning and before bedtime can decrease FBS levels, indicating that taking it with a meal is nonessential.

Only two clinical trials used Ceylon cinnamon; evaluating the FSB and A1C differences of the reported species is still a crucial factor within this meta-analysis. In one of the studies, Mohammadi et al. (2012) had a total FBS reduction of 12.81mg/dl and 0.45% A1C reduction after a two-month intervention. In the second study, by Lira Neto et al. (2022), the FBS decreased by 10.08mg/dl and A1C by 0.34% in three months; both studies administered 3g a day. The clinical trials that used cassia cinnamon had similar results; for example, Akilen et al. (2010) had a 14.04mg/dl reduction and 0.36% A1C reduction. Ziegenfuss et al. (2006) only tested FSB levels after the three-month intervention, is only decreased by 9.8mg/dl (Figures 2 & 5). The analyzed data from either species did not show any significant differences, and the research findings with the largest reported FBS and A1c reductions did not specify which specific cinnamon powder was used in their study. No clear indications can verify that the specific species in this meta-analysis of studies have great significance in supplement effectiveness and result outcome; however, based on the coumarin content in Cassia cinnamon, it is recommended to use Ceylon cinnamon supplements instead.

A1C (%) Reduction with Cinnamon Supplementation

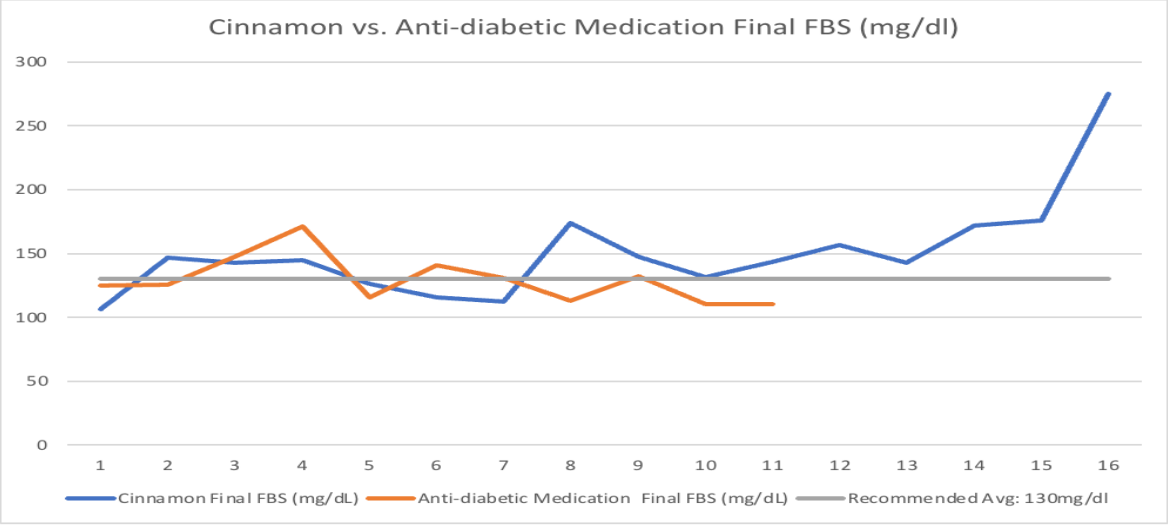
According to the American Diabetes Association, the standard range for a hemoglobin A1C test should be <6.5% for a healthy individual, but an individual with DMII should have an A1C of <7%. This blood sugar test analyzes the average sugar levels in the blood within three months; it is a baseline for DMII patients on how well they are monitoring their blood sugar levels. Therefore, evaluating A1C levels in these clinical trials is crucial to determine whether there was a more stabilized long-term change in sugar levels compared to a simple FBS level taken during fasted periods after two to three-month gaps. This determines if using cinnamon within three months truly improves A1C levels and if the change is significant enough to decrease the progression of diabetes. All the studies presented participants with A1C levels of 6.5> and up to 10.98%; these levels are dangerously high, placing the patients at risk for long-term developments like kidney failure and nerve damage.

Table 1 shows studies that only performed two-month interventions indicating that these A1C levels are inconclusive; however, it does give a generalized assumption of the participant's range after completing their cinnamon regimen. However, it is evident that the three-month groups had slightly decreased A1C reduction; thus, individuals who want to implement cinnamon supplements into their diet should follow a three-month period. Also, four of the studies did include A1C testing in their studies; these trials mainly focused on FBS readings, which is not a big portion of the total analyzed research articles. Still, comparing the A1C and FBS does grant a direct positive correlation between both administered tests. This is because A1C measures the exact amount of glucose attached to hemoglobin in red blood cells; after three months of cinnamon therapy intervention having a lower A1C percentage can dictate a lower FBS level and vice versa.

The most significant A1C reduction occurred in the clinical study by Sharma et al. (2012); after three months, it decreased from 8.47% to 7.29%; these participants were newly diagnosed with DMII with no past prescription therapy, so having a 1.18% difference is significant (Figure 5). As stated previously, they were told to practice healthier food options and incorporate an active lifestyle; these changes can positively impact the health of any individual. Table 2 and Figure 5 show that the final A1C results had a minimal reduction of less than 1.2%, and compared to the cinnamon and control groups, the control group had slightly higher A1C readings (Figure 6). The A1C differences in the cinnamon and control groups are demonstrated in Figure 7; it dictates the actual effect of cinnamon created between the two groups. Still, the data is insignificant to support the possibility that it decreases the disease progression long-term. These chronically diagnosed patients take daily antidiabetic drugs to prevent their glucose from spiking, consistently monitoring their sugar levels and having an appropriate drug therapy, diet, and active lifestyle is necessary. Another suggestion is comparing two A1C levels after six months of intervention to see any level fluctuation changes for individualized patients, resulting in an optimized treatment plan.

Figure 8

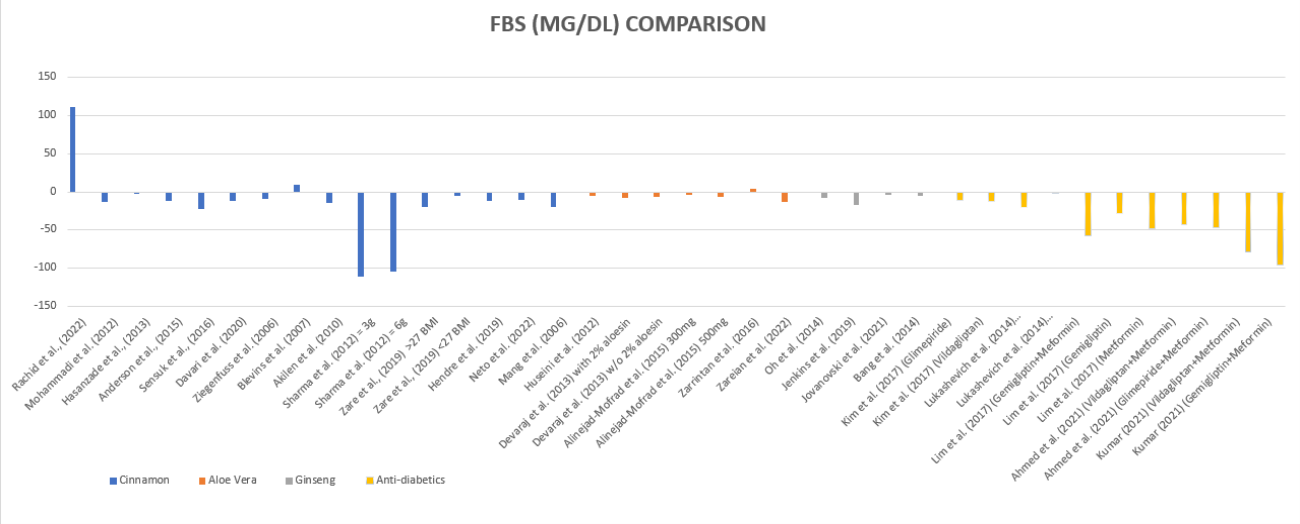
Final cinnamon vs. anti-diabetic medication



Note: Comparing the final fasting blood sugar level (FBS mg/dl) results of the cinnamon nnd anti-diabetic clinical medication trials. A recommended FBS average of 130mg/dl per American Diabetes Association (ADA, n.d).

Figure 9

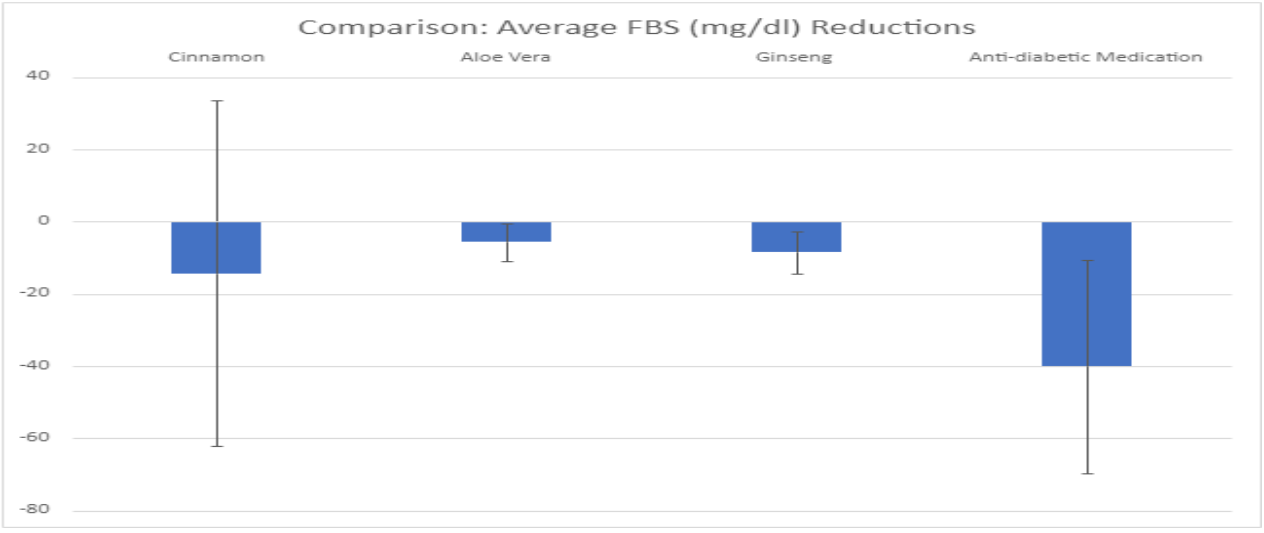
FBS (mg/dL) comparison between all supplements and anti-diabetic medication



Note: Comparing the final fasting blood sugar level (FBS mg/dl) results of the cinnamon, aloe vera, ginseng supplements, and anti-diabetic clinical medication trials.

Figure 10

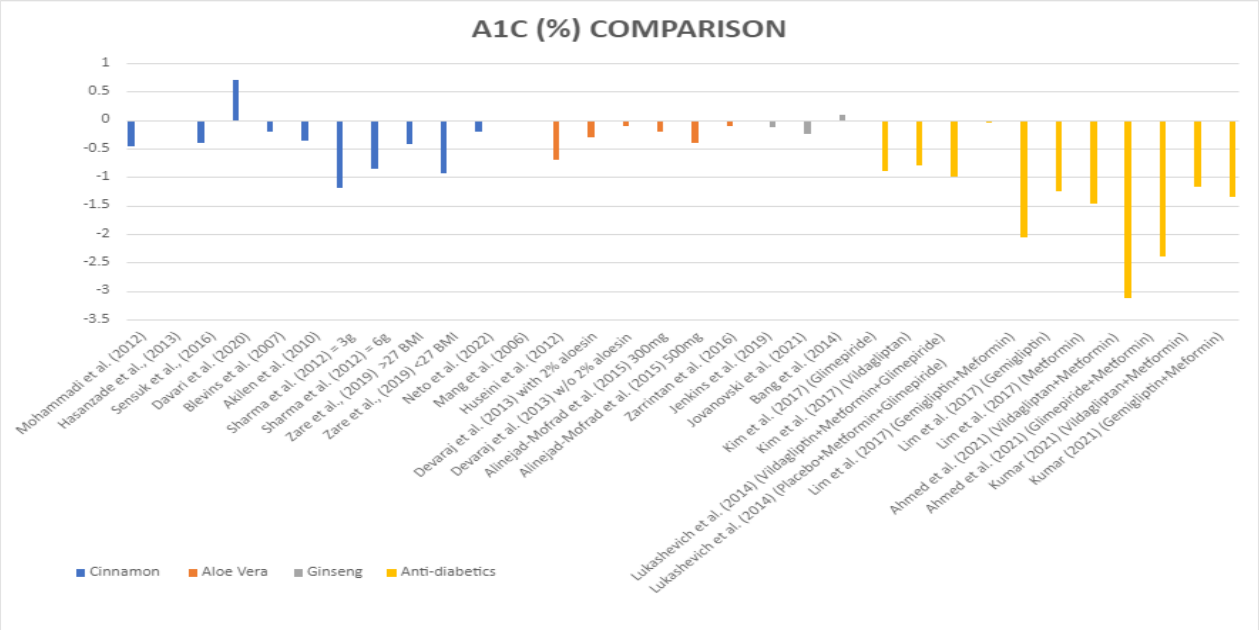
Average FBS (mg/dl) reduction in all supplements and anti-diabetic medication



Note: Comparing the average reduction of fasting blood glucose (mg/dl) of cinnamon, aloe vera, ginseng, and anti-diabetic medication.

Figure 11

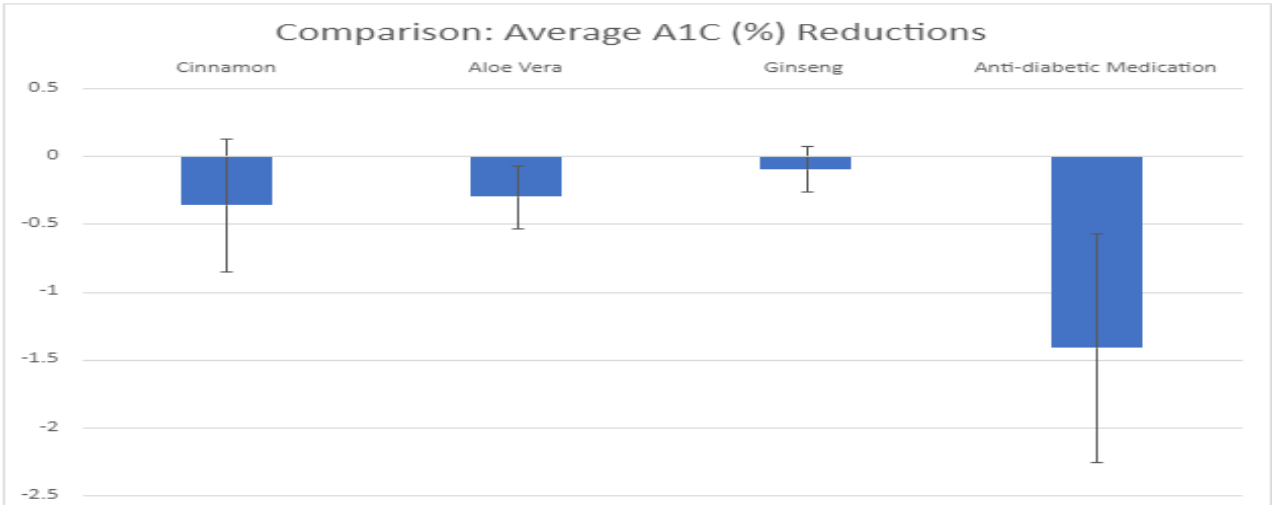
A1C (%) comparison between all supplements and anti-diabetic medication



Note: Comparing the final hemoglobin A1C (%) results of the cinnamon, aloe vera, ginseng supplements, and anti-diabetic clinical medication trials.

Figure 12

Average A1C (%) reduction in all supplements and anti-diabetic medication



Note: Comparing the average reduction of hemoglobin A1C (%) of cinnamon, aloe vera, ginseng, and anti-diabetic medication.

Aloe Vera, Ginseng, and Anti-diabetic Prescription Comparison

Aloe Vera and Ginseng for DMII

Aloe vera has antioxidant, anti-inflammatory, and anticancer properties with severity-five active components of vitamins, enzymes, minerals, salicylic acid, and amino acids that can help diabetic patients by reducing their blood glucose and lipid panel. Aloe vera works by controlling the metabolism of lipids in the liver, removing free radicals, and decreasing fatty acids in the blood. It also claims to improve the responsiveness of body tissues toward insulin and regulates glucose metabolism (Alinejad-Mofrad et al., 2015). Ginseng extract also has similar bioactive components and ginsenosides, which help reduce oxidative stress and inflammation, resulting in its anti-diabetic effect and improving glycemic control. Ginseng also goes through a steaming process to increase its potential effect and is labeled red ginseng (Oh et al., 2014). The chemical mechanism of these herbal plants provides an alternative method to help DMII, and comparing clinical trials with every single supplement can grant the reader information about effective properties based on the FBS and A1C reduction.

Supplement FBS & A1C Result

The aloe vera clinical studies were performed within two months and only had an FBS reduction of less than 15 mg/dL and less than 1% of A1C levels, as shown in Table 3. While the Ginseng clinical studies had an FBS reduction of less than 20 mg/dL and an A1C level of less than 1% (Table 4). They had similar study components to cinnamon, consisting of different dosages, a continuation of anti-diabetic medication, and taking it with a meal. Patients taking aloe vera and ginseng did not experience any adverse side effects, but people should avoid

ginseng if they have insomnia, bipolar or schizophrenia disorder, and are pregnant. These herbal supplements were used to dictate whether they had similar result outcomes as cinnamon; comparing the results of all three supplements based on the post-intervention levels did not provide significant reduction and therefore is not considered an effective treatment option for patients with DMII.

Table 3

Aloe vera supplement meta-analysis for DMII patients

References	Study design	Sample Size	Aloe Vera Intervention: Dose & Duration	FSB (mg/dL) & A1C (%) Results
Huseini et al. (2012)	Randomized double-blind placebo-controlled trial.	67 subjects	Freshly harvested whole aloe leaves into resultant gel to make pure powder capsules. One 1,000mg tablet daily for 2 months.	Decrease of the fasting plasma glucose levels from 173 to 167.8 Slight reduction of A1C from 7.3 to 6.6.
Devaraj et al. (2013)	Randomized, double-blind, placebo-controlled trial.	45 subjects	Aloe vera inner leaf gel powder standardized with 2% aloesin. 500mg two times a day for 2 months.	Decrease of the fasting plasma glucose levels from 173 to 167.8 Minimal reduction of A1C from 7.3 to 6.6.
Devaraj et al. (2013)			Aloe vera inner leaf gel powder	Decrease of the fasting plasma glucose levels from 111 to 105. Minimal reduction of A1C from 6 to 5.9.
Alinejad-Mofrad et al. (2015)	Randomized, double-blind, placebo-controlled trial.	72 subjects	Aloe vera extract powder Two 300mg capsules daily, after breakfast & dinner for 2 months.	Decrease of the fasting plasma glucose levels from 112 to 108. Minimal reduction of A1C from 6 to 5.8.
Alinejad-Mofrad et al. (2015)			Aloe vera extract powder Two 500mg capsules daily, after breakfast & dinner for 2 months.	Decrease of the fasting plasma glucose levels from 111 to 104. Minimal reduction of A1C from 6 to 5.6.
Zarrintan et al. (2016)	Randomized, double-blind, placebo-controlled clinical trial.	44 subjects	Aloe vera extract powder One 1,000mg tablet two times a day for 2 months.	Increase of the fasting plasma glucose levels from 181.05 to 184.9. Increase of A1C from 8.53 to 8.63.
Zareian et al. (2022)	Randomized, double-blind, placebo-	60 subjects	Aloe vera powder (Aloe barbadensis species). Subjects were placed on an isocaloric standard diabetic diet.	Decrease of the fasting plasma glucose levels from 137.2 to 123.8. A1C was not measured.

	controlled clinical trial.	Two 500mg capsules after breakfast & dinner for 2 months

Table 4

Ginseng supplement meta-analyses for DMII patients

References	Study design	Sample Size	Gingseng Intervention: Dose & Duration	FSB (mg/dL) & A1C (%) Results
Bang et al. (2014)	Randomized, double-blinded, placebo-controlled trial.	60 subjects	Korea Red Ginseng Three 500mg capsules after breakfast, lunch, & dinner. 3 months	Decrease of fasting plasma glucose levels from 127.9 to 122.33. Increase of A1C from 6.21 to 6.3.
Oh et al., (2014)	Randomized, double-blinded, placebo-controlled trial.	42 subjects	Fermented red ginseng extract Three 900mg capsules a day. 1 month	Decrease of fasting plasma glucose levels from 117 to 109.8. A1C was not measured.
Jenkins et al. (2019)	Randomized, double-blind, placebo-controlled, cross-over design.	24 subjects	American ginseng dried powder Two 500mg with breakfast, lunch, & dinner (3,000mg/3g) 2 months	Increase of the fasting plasma glucose levels from 164.88 to 147.78. Minimal reduction of A1C from 7.13 to 7.01.
Jovanovski et al. (2021)	Randomized controlled trial.	80 subjects	Combined American ginseng (P. quinquefolius) and Rg3-enriched Korean Red Ginseng (P. ginseng). Three 500mg AG a day & Three 250mg Rg3-KRG before each main meal. Three months	Decrease of fasting plasma glucose levels from 143.8 to 137. Increase of A1C from 6.86 to 7.07

Anti-diabetic Prescriptions

Diagnosing and treating DMII early is highly important because they have already lost 50% of β-cell function by the time they are diagnosed. Patients are immediately placed on oral antidiabetics to rapidly reduce the chances of treatment activity and HbA1c levels and improve the function of β-cells in the pancreas (Ahmed et al., 2021). Appropriate intervention must be quickly implemented for newly diagnosed diabetics to prevent loss of ß-cell functions and long-

term secondary complications. Healthcare providers recommend using a combination of therapies depending on the severity of the diagnosis to create a more positive approach within the patient's long-term therapeutic care. Many of these medications are cost-effective and quick to manage FBS and A1C levels. There are also medication combinations that are effective in antihyperglycemic effects with early initiation of treatment, and patients will need education on the potential side effects, including hypoglycemic events, urinary tract infection (UTI), headaches, and nasopharyngitis.

Table 5 and Figure 8 show that the anti-diabetic medication intervention helped reduce FBS and A1C levels significantly in six months. These clinical trials had different ranges of participants; there were patients newly diagnosed with DMII, while other studies consisted of patients chronically diagnosed for four to seven years. Therefore, a recent and long-term diabetic will have different outcomes, mainly because new diabetics have not received any treatment before. The medications will begin to work quickly and efficiently; this is a similar concept that happened with the cinnamon clinical trial from Sharma et al. (2012). Newly diagnosed patients that were treated with medications had an FBS decrease of -42.89, -46.76, -77.94, and -96.06, while chronic DMII patients had FBS reductions of -20, -13.3, -11.4, -56, -28.6 and -47.6 (Table 5 & 6). These reductions are higher than those of the three herbal supplements, as shown in Figures 9, 10, 11, and 12, demonstrating that medication use works as the best treatment for chronic DMII because its more sustainable, and dosage can be adjusted based on disease progression and patient medical history. There is enough research to back up that prescription medication will work more efficiently, and all are FDA regulated. Compared to cinnamon supplements, it only has a p-value of <0.001, potentially causing beneficial results.

Table 5

Anti-diabetic medication meta-analysis for DMII patient

References	Study design	Sample Size	Antidiabetic Medication: Dose & Duration	FSB (mg/dL) & A1C (%) Results
Lukashevich et al. (2014)	Multicentre, randomized, double-blind, placebo-controlled study.	Average DMII diagnosis of 7 years, 246 subjects	Combination of Metformin 1500mg, Glimepiride 4mg, and Vildagliptin 50mg once a day for 6 months.	Decrease of fasting plasma glucose levels from 167.4 to 147.4. A slight reduction of A1C from 8.7 to 7.7.
Lukashevich et al. (2014)			Combination of Metformin 1500mg, Glimepiride 4mg, and a placebo capsule once a day for 6 months.	Slight increase in fasting plasma glucose levels from 171 to 171.36. A slight reduction of A1C from 8.8 to 8.55.
Kim et al. (2017)	Randomized, open-label, parallel study.	Average DMII diagnosis of 6 years, 34 subjects	Vildagliptin 50mg twice daily for 3 months.	Decrease of fasting plasma glucose levels from 137.8 to 124.5. A slight reduction of A1C from 7.6 to 6.8.
Kim et al. (2017)			Glimepiride 2mg once daily for 3 months.	Decrease of fasting plasma glucose levels from 136 to 124.6. A slight reduction of A1C from 7.5 to 6.6.
Lim et al. (2017)	Multinational, multicentre, randomized, parallel-group, double-blind, phase III trial.	Average DMII diagnosis of 4 years, 433 subjects	Gemigliptin 50 mg once daily and Metformin 1000 to 2000 mg once daily with dose titration for each patient or the respective monotherapies for 6 months.	Decrease of fasting plasma glucose levels from 171.7 to 115.7. Significant reduction of A1C from 8.7 to 7.7.
Lim et al. (2017)			Gemigliptin 50 mg once daily for 6 months.	Decrease of fasting plasma glucose levels from 169.7 to 141.1. A slight reduction of A1C from 8.66 to 7.42.
Lim et al. (2017)		.	Metformin 1000 to 2000 mg once daily with a matching placebo for 6 months.	Decrease of the fasting plasma glucose levels from 178.6 to 131. A slight reduction of A1C from 8.73 to 7.26.
Ahmed et al. (2021)	Randomized, comparative, interventional study.	Newly diagnosed DMII, 180 subjects	Combination of Vildagliptin Metformin, dosage unknown for 6 months.	Decrease of the fasting plasma glucose levels from 156.22 to 113.33. A slight reduction of A1C from 10.56 to 9.92.
Ahmed et al. (2021)			Combination of Glimepiride and Metformin, dosage unknown for 6 months.	Decrease of the fasting plasma glucose levels from 163.36 to 116.6. Slight increase of A1C from 10.45 to 11.2.
Kumar (2021)	Single-center, prospective, comparative, observational study	Newly diagnosed DMII, 100 subjects	Combination of Vildagliptin 50mg BID and Metformin 500mg BID for 6 months.	Decrease of the fasting plasma glucose levels from 188.4 to 110.46. Significant reduction of A1C from 8.14 to 6.98.
Kumar (2021)			Combination of Glimepiride 2mg BID and Metformin 500mg BID for 6 months.	Decrease of the fasting plasma glucose levels from 206.58 to 110.52. Significant reduction of

A1C from 8.33 to 6.99.

Table 6

Anti-diabetic medication effects on newly diagnosed and chronically diagnosed DMII patients

References	Newly Diagnosed		Chronically Diagnosed (1yr>)
	FBS (mg/dl)	A1C (%)	FBS (mg/dl)
Lukashevich et al. (2014)			-20
Lukashevich et al. (2014)			+0.36
Kim et al. (2017)			-13.3
Kim et al. (2017)			-11.4
Lim et al. (2017)			-56
Lim et al. (2017)			-28.6
Lim et al. (2017)			-47.6
Ahmed et al. (2021)	-42.89	-0.64	
Ahmed et al. (2021)	-46.76	-0.75	
Kumar (2021)	-77.94	-1.16	
Kumar (2021)	-96.06	-1.34	

Diet and Exercise for DMII

Healthier Diet

Body weight control is crucial for DMII management. A moderate diet-induced weight loss involves a 5-10% reduction from baseline body weight, improving glycemic control, and increasing inulin production and sensitivity in the liver, adipose tissue, and muscle while correcting β-cell function (Franz, 2012). Weight loss in patients with chronic DMII can be challenging to achieve, and targeting weight itself is not suitable for all of these patients. Incorporating interventions of longer duration with specific target goals of weight loss, nutrition,

and physical activity can lead to more significant changes in blood sugar levels, blood pressure, cholesterol, and weight loss. Targeting just one issue is unsuitable for chronic diabetic patients; therefore, using multiple health behaviors through decisional support and tailored goal setting can greatly impact the disease progression.

Medical nutrition treatment is one of the cornerstones in diabetic management by incorporating individualized diet and nutritional recommendations to maintain balanced blood glucose levels, lipid levels, and reasonable body weight. Neuhouser et al. (2002) concluded that patients with diet-modifiable disorders reported personal motivation to consume less fat to prevent chronic diseases but had difficulty implementing this diet. Dietary change and maintenance are difficult to achieve, especially for chronic diabetics that require long-term treatment. New strategies are needed to identify successful methods to adopt and maintain healthier dietary practices. Healthcare providers can help by referring patients to qualified nutrition professionals. Al-shookri et al. (2011) concluded a study with two groups; the usual nutritional care group followed nutritional care with a dietician for one hour once a week, while the second group followed a practice guideline nutritional care consisting of three appointments, approximately 2.5 hours in total. There were significant improvements in FBS levels, with a mean 11.2% reduction and an A1C reduction of 8.2%; this guided nutritional group had more noticeable improvements ($p < 0.05$). It can be related to the frequency of appointments which kept patients on a better track with their dietary and health goals. Approximately 57% of the 200 participants achieved their target goal of FSB and A1C levels, and some participants were receiving dietary intervention only, while others were on oral agents or insulin therapy (Al-Shookr et al., 2012). After a dietary intervention, there needs to be ongoing follow-up with a dietitian to maintain long-term metabolic control and prevent increased trends of glucose values.

Making changes seems easy in the beginning, but maintaining dietary adjustments while keeping their prescription regimen and incorporating an exercise plan can become mentally and physically draining (Lin et al., 2004).

Physical Activity

Making healthier dietary changes within an appropriate caloric deficit to achieve weight loss is crucial for diabetics, but adding a regular exercise routine is also essential for DMII management. Much research has concluded that progressive aerobic and resistance training reduces total body fat, visceral adipose tissue, and cardiometabolic risks and helps regulate glucose homeostasis. There are recommended types of exercise for people with diabetes; one of these exercises is known as resistance training (RT). Researching a series of RT clinical trials is suggested to dictate how effective resistance training is in treating DMII compared to cinnamon supplements.

The length of the studies consisted of one year, six months, and eight weeks to examine differences in end results. Balducci et al. (2004) was the only study that reported the duration of their DMII diagnosis; their average was 9.8 years, while the other studies did not report this information. Dunstan et al. (2002) participants were given a healthy eating plan with two separate 3-day food records performed at baseline, Balducci et al. (2004) only reported to use of 3-day food records at baseline and then every three months for one year while keeping their current diet, and the rest of the studies did not implement any dietary strategy. Most participants consisted of middle-aged and older adults living sedentary lifestyles and following pharmaceutical therapies. Lastly, the exercise interventions were performed three times a week until the end of the study length for all trials except for Hazley et al. (2010); this study consisted of two 45-minute sessions on nonconsecutive days, totaling 16 sessions (Table 7).

Balducci et al. (2004) was a one-year RT study that showed the most significant results; the difference between the baseline and final results showed a difference of -36 in FBS levels, -1.21 in A1C levels, and a BMI of -1.3. The six-month Dunstan et al. (2002) study consisted of a group performing high-intensity progressive resistance training, while the control group followed a low-impact flexibility exercise. The RT group showed better results consisting of -25.3 FBS, -1.2 A1C, and -2.5 BMI reductions a the end of the study, while the flexibility program only had a difference of -10.9 FBS, -0.4 A1C, and -3.1 BMI reductions. The eight-week RT study from Amouzad Mahdirejei et al. (2014) concluded a -23 FSB, -0.33, and -1.1 BMI reduction, while the second 8-week study, Hazley et al. (2010) had no changes in any measured parameters. The data for the control groups for the rest of the clinical trials did not show significant changes; most stayed within their baseline values or had increased FBS, A1C, and BMI results (Table 7). None of the studies reported side effects in the RT programs, and the participants tolerated it well; hence, incorporating an exercise routine like resistance training is feasible and safe.

Compared to the gathered RT data and cinnamon supplement results, the RT interventions worked best to decrease glycemic markers. There were differences in the duration of the RT and cinnamon clinical studies, but based on the eight-week study from Amouzad Mahdirejei et al. (2014) it still showed similar and better results compared to the cinnamon trial duration of 2, 3, and 4 months. The highest difference in FBS and A1C reduction for chronic DMII was the two-month study by Sensuk et al. (2016); taking 1.6g/day of cinnamon supplements resulted in reductions in FSB of -21.78mg/dl and A1C of -0.4% (Figures 13 & 14). These two studies demonstrated glycemic markers within range at the end of the intervention. Thus, both of these alternative therapies can create a positive outcome. However, it also depends on the type of pharmaceutical therapy they receive and whether they comply with dietary

changes. It is ideal for trials to perform 6-month to 1-year studies to visualize the consistency of interventions and how they can affect the results. The cinnamon studies failed to conduct longer trials; therefore, comparing the rest of the trials with the RT studies will not demonstrate reliable information. If the 6-month and 1-year participants continue this exercise regimen, glycemic markers will continue to lower along with their weight, decreasing the need for anti-diabetic medication or herbal supplements; compared to patients just taking cinnamon supplements would still require medications to treat their chronic DMII.

Based on the given data, physical exercise and a healthier diet will promote better outcomes because patients are eliminating food options that are causing blood sugars to rise, and exercising helps increase glucose uptake and decreases BMI. Thus targeting the root of the problem will prevent glycemic markers from increasing, providing a more sustainable diabetic lifestyle without the possible use of anti-diabetic medication and herbal supplements. Depending on the disease progression of DMII, exercise, and diet can reduce the use of anti-diabetic medication or lead to DMII remission. A Malmö 6-year feasibility study from 1991 provided long-term data on DMII remission that solely focused on increasing physical activity. Forty-one overweight, diabetic participants received physical training sessions of 60mins two times a week; exercise intensity increased progressively with the guidance of a physiotherapist. Within six months to two years of the study, there was a weight reduction and improvement in physical performance; by the end of the study, participants had an average weight loss of 3kg, a reduction in glucose, and an improved insulin response. More than half of the participants (~54%) with DMII were in remission and no longer met the diagnostic criteria with DMII. Similar studies showed a 37-80% remission after 3-10kg weight loss at 0.5-5 years (Eriksson & Lindgarde, 1991). The key to reaching DMII remission is to achieve a weight loss of 10-15kg; factors like

carbohydrate restriction, increased physical activity, and incorporating healthier fats, proteins, and vegetables will maximize these achieved metabolic effects (Magkos et al., 2020).

Adding exercise and a diet plan can significantly improve glycemic levels; exercise reduces free fatty acids, minimizes abdominal fat, and improves insulin-sensitive skeletal muscle because insulin sensitivity causes an increase in muscle cells during contractions to use glucose and even after the physical activity has ended. Choosing healthier food options is less likely to spike blood sugar levels and will ultimately lower FBS within a healthy range. Incorporating these habits can lower the use of medications or result in a remission of diabetes. Cinnamon supplements could not demonstrate this because they still had to continue taking their prescribed anti-diabetic medication, and even with both therapies, their FSB levels decreased from 3mg/dl-20mg/dl. Exercise and diet are more sustainable interventions that can limit disease progression compared to cinnamon supplements, but most patients with chronic diabetes have difficulty making these lifestyle changes.

Table 7

Meta-analysis resistance training exercise program for DMII patient

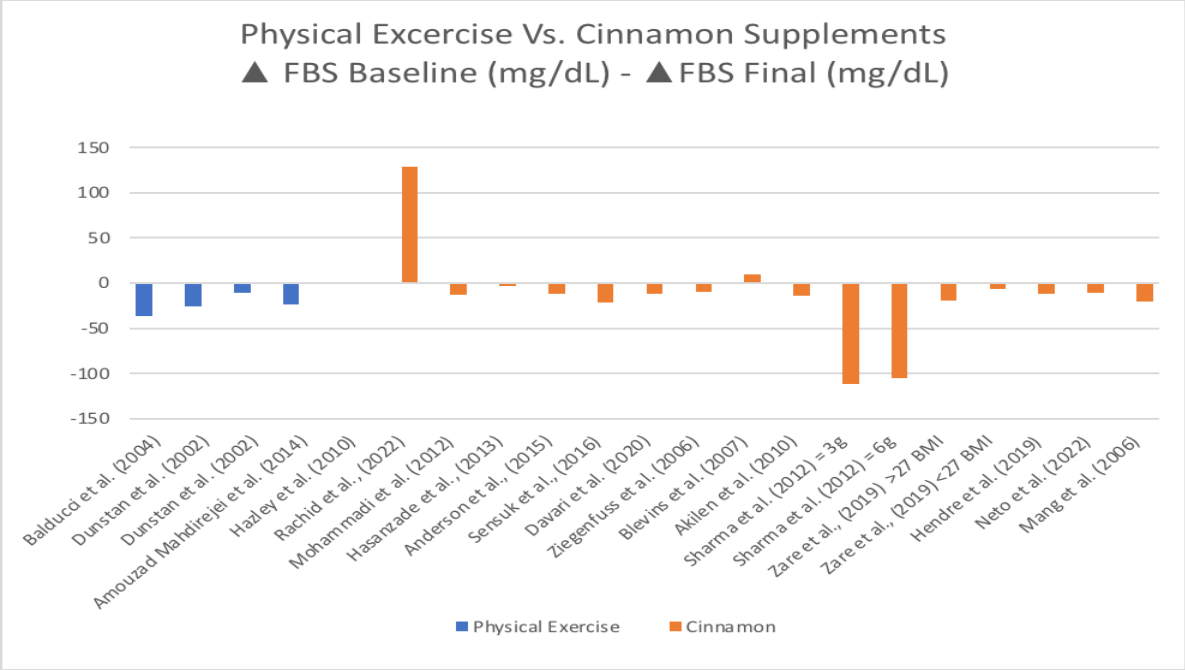
References	Study design	Sample Size: DMII	Intervention	Anti-diabetic Medication	FSB (mg/dL), A1C (%), & BMI Results
Balducci et al. (2004)	Randomized controlled clinical trial	62 subjects out of 120. Average mean age of 60.	Aerobic plus resistance training (ART) program. 30 min aerobic training following a 30 min resistance training 3x/week. A 3-day food record was obtained at baseline and every 3 months for 1 year. Participants were to continue their current diet. 1 year	Participants continued their pharmaceutical therapy.	Decreased fasting plasma glucose levels from 165 to 129. A1C reduction from 8.31 to 7.1. BMI lowered from 30.1 to 28.8.
Balducci et al. (2004)		58 subjects out of 120.	Participants were asked to continue their current	Participants continued their	Baseline values consist of 162 FBS,

(Control Group)			diet and pharmacological therapy. A 3-day food record was obtained at baseline and every 3 months for 1 year. Participants were to continue their current diet. 1 year	pharmaceutical therapy.	8.28 A1C, and a BMI of 30. The final results were not reported; the study stated there were no statistically significant changes in the measured parameters.
Dunstan et al. (2002)	Randomized controlled clinical trial	29 subjects out of 42. Average mean age of 66.5.	High-intensity progressive resistance training consisting of dynamic concentric and eccentric exercises 3x/week with a moderate weight loss plan. Training workload regularly increased as tolerated. Healthy eating plan incorporated. Use of two separate 3-day food records performed at baseline. 6 months	Participants continued their anti-diabetic and anti-hypertensive therapies.	Decreased fasting plasma glucose levels from 171.2 to 145.9. A1C reduction from 8.1 to 6.9. BMI lowered from 31.5 to 29.
Dunstan et al. (2002) (Control Group)		13 subjects out of 42	Flexibility exercise program consisting of low-impact exercises 3x/week with a moderate weight loss plan. Healthy eating plan incorporated. Use of two separate 3-day food records performed at baseline. 6 months	Participants continued their anti-diabetic and anti-hypertensive therapies.	Decreased fasting plasma glucose levels from 169.4 to 158.5. A1C reduction from 7.5 to 7.1. BMI lowered from 32.5 to 29.4.
Amouzad Mahdirejei et al. (2014)	Quasi-experimental study	9 subjects out of 18. Average mean age of 48.	Resistance training program consisting of 3 circuits of 10 exercises per session 3x/week. No specific diet was followed. 8 weeks	Participants were allowed to continue their anti-diabetic medication; the dosages were maintained throughout the study.	Decreased fasting plasma glucose levels from 187.4 to 164.4. A1C reduction from 8.33 to 8. BMI lowered from 28 to 26.9.
Amouzad Mahdirejei et al. (2014) (Control		9 subjects out of 18	Participants were to continue their current lifestyle. No specific diet was	Participants were allowed to continue their anti-diabetic medication; the	Increase of fasting plasma glucose levels from 153.3 to 159.1. A1C increased from 7.6 to 8.6. Slight BMI

Group)			followed. 8 weeks	dosages were maintained throughout the study.	increase from 26.3 to 26.4.
Hazley et al. (2010)	Self-selected quasi-experimental study	6 subjects out of 12. Average mean age of 54.	Resistance training program, two 45min sessions on nonconsecutive days, 16 total sessions. No specific diet was followed. 8 weeks	Unspecified	No changes in any measured parameters. Fasting plasma glucose levels remained at 193.2. A1C from 7.7 to 7.6, and BMI remained at 32.

Figure 13

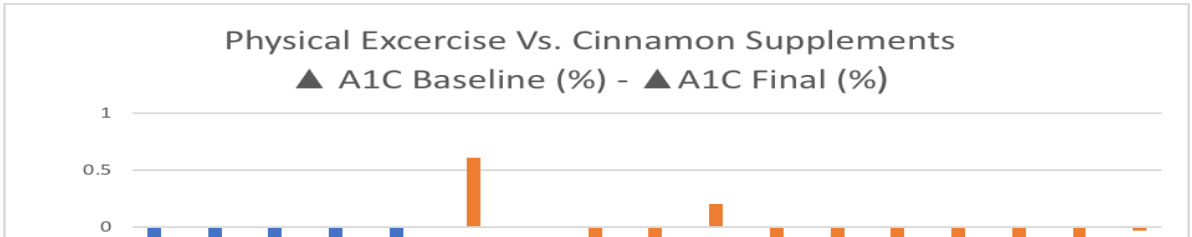
FBS (mg/dl) comparison of physical exercise vs. cinnamon supplement



Note: Comparing the final FBS (mg/dl) results of physical exercise intervention and cinnamon supplement administration.

Figure 14

A1C (%) comparison of physical exercise vs. cinnamon supplements



Note: Comparing the final A1C (%) results of physical exercise intervention and cinnamon supplement administration.

Discussion

The meta-analysis was conducted to determine cinnamon's efficacy in reducing FBS and A1C levels for patients with chronic diabetes and to evaluate factors that could affect the outcomes. Patients considering starting a cinnamon regime into their treatment plan can make decisions based on the gathered information and data to create an optimal plan that best fits their lifestyle. Healthcare teams can provide the patient with all details, which allows them to rationalize their options and decide whether this treatment will benefit them. They should first be educated on the likelihood that taking cinnamon supplements alone will not resolve their DMII; it has the potential to decrease FBS and A1C levels, but it is not significant enough to decrease morbidity risks because their levels will continue to be high or stay within a consistent range. Diabetics type II require anti-diabetic medications like metformin, glimepiride, or vildagliptin, along with changing eating habits and implementing exercises to improve glucose levels. If the patient still wants to continue cinnamon supplementation, they will require education on the

appropriate dosage, time of administration, duration of the therapy, potential side effects, keeping their adjunctive medication with anti-diabetics, attending follow-up appointments, making dietary changes, and increasing their physical activity. Patients must be involved in their health and treatment; this helps them feel listened to and in control. Advocating for their needs and concerns will improve their diabetes management and decrease morbidity risks.

Upon analysis of the gathered data, the dosage administration can range from 1g to 3g a day; the exact dose cannot be determined because, as mentioned before, patients saw similar results if they had a 1g, 1.5g, 2g, or 3g (Figure 1). Therefore it can be started at a low dose; if there are no signs of improvement, the patient has the choice to discontinue or increase their dose up to the recommended limit of 4g a day. The healthcare provider must also consider the patient's demographics, physical assessment of BMI, history of long-term use of anti-diabetics, and the duration of their DMII diagnoses. The patient will be advised to can take it around breakfast, lunch, or dinner hours, with or without a meal. After a three-month regimen, a comparison of the pre and post-FBS and A1C results are evaluated with the patient to determine if it created any beneficial effects. The majority of clinical trials claim that participants did not suffer any side effects; this may be due to the exclusion criteria used in the trials, which excluded patients who would be at a high risk of developing an adverse effect. For example, subjects with thyroid disease, hypogonadism, and a history of musculoskeletal, autoimmune, renal, hepatic, or neurologic disease were excluded from the study; healthcare members need to take this into consideration before making cinnamon supplement recommendations. One of the potential side effects that can occur is hypoglycemia if cinnamon and anti-diabetics are taken simultaneously. There were no drug interactions between both, as confirmed by the clinical studies, but the patient should still be cautioned of this potential adverse side effect. Another risk is

hepatotoxicity, but according to the findings, if Ceylon cinnamon is consumed and they do not consume passed their recommended weight-based dose or a 4g limit, they should not experience negative effects.

The patients will also be educated on the importance of continuing their anti-diabetic medications because poor medication adherence is common in DMII, and having them maintain their follow-up appointments to chart their progress, make adjustments, or have a further assessment. Maintaining an active lifestyle and a healthy diet that includes fruits, vegetables, lean meats, and low-fat, low-carb, and low-sugar food alternatives will be one of the patient's most difficult tasks; however, this significantly lowers their FBS and A1C levels. Lastly, individuals must find a herbal supplement company that uses wholesome ingredients at reasonable prices.

Cost-effectiveness is determining whether a product is worth buying based on its price and the results that the product was able to achieve. A high-quality cinnamon supplement can range up to twenty-five dollars per bottle; each bottle can contain 60, 100, or 120 capsules. To continue this alternative therapy, an individual purchases a bottle every 2-4 months costing less than a hundred dollars a year. The long-term use of cinnamon of longer than four months has not been researched yet; it is uncertain whether the cinnamon will continue to decrease glycemic markers after a certain time frame or if it will maintain levels within a reasonable range for a diabetic patient. Clients can pay roughly a hundred dollars within a year, but cinnamon effectivity varies on the individual; consistent blood sugar levels must be monitored at least every three months to determine if the product is worth taking. Although cinnamon supplements are more cost-friendly than other alternative therapies, they do not produce promising results compared to antidiabetic medication after a three-month intervention. It will be up to the patient

to determine if they can afford supplemental therapy and whether they are content with the end results, but ultimately chronic diabetics should not rely only on this form of therapy.

Herbal supplements are highly advertised to treat chronic diseases and common acute conditions. However, most of these herbal alternatives are not actively being investigated or approved by the Food & Drug Administration (FDA). There are concurrent uses of herbal supplements with prescribed medication that can cause drug-drug interactions and toxicity risks; older adults are at higher risk, thus outweighing the benefits. Also, if a patient lacks appropriate education about their chronic illness, it can lead to the misuse of herbal supplements. They tend to discontinue their medications and substitute them with herbal supplements. If chronic diabetics only rely on cinnamon supplements, there is a possibility of reduced FBS and A1C levels, but it is not effective enough to stop the disease from progressing, increasing morbidity and mortality risks. This particular group of diabetics would not benefit from this treatment alone. Another potential scenario involves the use of conjunctive therapy of cinnamon and anti-diabetic medication, which is more appropriate and can further bring down FBS and A1C levels, but constant monitoring of their blood sugar levels is necessary to prevent hypoglycemic events. Treatment intervention is individualized, and incorporating these conceptual factors is mandatory to ensure the patient understands the risks and the importance of following their treatment plan to treat their chronic disease properly.

Conclusion

The use of herbal supplements will continue to be a popular complementary alternative medicine (CAM) to treat acute and chronic illnesses; conducting continuations of herbal research can further guide healthcare members to make appropriate treatment recommendations. Based on cinnamon's chemical composition and mechanism of action, an investigation was performed to

dictate its effect in treating DMII. Patient criteria, along with supplement administration components, are factors that can influence the efficiency of cinnamon supplements. The patient criteria should include their total years of diagnosis with DMII, up-to-date medication list, past and current treatments, medical nutrition therapy, and physical exercise history. Also, a physical assessment focusing on their BMI, lipid panel, and trending glycemic markers. The supplement components include an exact dosage recommendation, the type of herbal species used, duration of intervention, side effects, toxicity risks, and supplemental education for patients. The articles within this meta-analysis missed the necessary components to fully comprehend how supplements can adequately treat DMII. The gathered data supported the hypothesis of lowering FBS and A1C levels, although the range reduction after intervention does not provide enough evidence to prove it can decrease the disease progression of DMII. Properly formulating a research trial by incorporating detailed components might provide more accurate results; hence further research is essential. Even though there is insufficient data to support the use of cinnamon supplements, healthcare providers must acknowledge it as an alternative therapy commonly used among individuals looking to treat their disease. Providers must properly implement educative strategies and individualized treatments. These patient-focused individualized treatment plans must incorporate a patient's internal and external factors emphasizing educative supplement treatment, anti-diabetic medications, diet, and physical activity. The meta-analysis for anti-diabetic medication use and a consistent exercise plan such as resistance training and a dietary intervention has been proven to help according to the end results. Finally, patients should be assessed if they can afford treatments because refilling prescription medications and cinnamon supplements can be costly, not to mention purchasing healthier food options or having insurance coverage to make frequent follow-up visits with their primary care provider.

Limitations

The majority of the clinical trials gathered participants fitting specific criteria that generally focused on subjects with a history of chronic DMII and gathered information based on their age, gender, concurrent anti-diabetic drug therapy, and anthropometric measurements consisting of height, weight, and BMI. These are requisite data gatherings, but they lacked other specific variables like ethnicity, diet, the date extent of their diagnosis, and socio-economics because the effects of cinnamon affect each person differently, and it will lead to more conclusive results. Table 1 demonstrates that out of the sixteen studies, six did not mention what cinnamon species was used for their trial, another six trials used Cassia cinnamon, and only two trials conducted their study with Ceylon Cinnamon. This information is important because the species is a factor that will determine if a specific species works better to improve glycemic markers. This same table also demonstrates the longevity of the studies, five studies were only two months, and the ideal intervention needs at least three months or longer to have an accurate A1C reading. None of the studies followed up with their participants during the intervention and after cinnamon supplementation to determine whether participants felt an improvement in their physical health. The clinical trials needed to follow up with the participants to determine if they would continue the cinnamon therapy. This data would have been optimal to better assess and understand the effects of cinnamon.

Based on the information gathered from the meta-analysis, research recommendations would be to study three groups: a placebo, cinnamon treatment only, and cinnamon with antidiabetic drug therapy for six months with a set dosage administration. The participants would not change their diet or physical activity and log daily food logs. After the six months, implement an individualized plan for each subject and have them follow a healthier diet and start

an exercise regimen with the help of a dietician for another six months. By the end of the trial, comparing the four data values from each separate three-month intervention period would provide better information on how cinnamon works. Monitoring combination medication therapy is essential due to its potential to create a synergistic effect that can result in a positive or negative outcome; a positive result is related to the combined effect improving glycemic markers more efficiently, but health professionals and patients need to monitor for an increase negative adverse effects such as hypoglycemia and toxicity symptoms. These treatment intervention therapies would be optimal in treating chronic diabetics by creating long-term effects that decrease the disease progression of DMII.

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