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Cover Page Footnote

The purpose of this review of literature was to evaluate the effects of cinnamon on hemoglobin A1C (HbA1c) and fasting blood glucose/fasting plasma glucose (FBG/FPG) in various populations that have type II diabetes, prediabetes, metabolic syndrome, and are overweight or obese. A comprehensive literature review was done with the Cumulative Index to Nursing and Allied Health Literature (CINAHL) database using the keywords cinnamon, type II diabetes, diabetes, HbA1c, and FBS. References used in previous meta-analyses were also searched and reviewed for inclusion. Studies were included in this review if they evaluated cinnamon effects on HbA1c and/or FBS/FPG. A total of 15 trials were incorporated in this literature review, 10 studied cinnamon's effect on HbA1c levels and 13 studied cinnamon's effect on the FBG. Six trials showed significant reductions in the HbA1c levels and 10 trials showed significant reductions in the FBG. Based on this review of literature, cinnamon can be recommended as effective therapy for reducing HbA1c and FBG levels in type II diabetes. To reduce FBG and HbA1c levels, cinnamon can be dosed at 1 g to 6 g daily with meals (i.e. one to four 500 mg tablets BID or TID with meals).

Cinnamon in the Treatment of Type II Diabetes

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Abstract

The purpose of this review of literature was to evaluate the effects of cinnamon on hemoglobin A1C (HbA1c) and fasting blood glucose/fasting plasma glucose (FBG/FPG) in various populations that have type II diabetes, prediabetes, metabolic syndrome, and are overweight or obese. A comprehensive literature review was done with the Cumulative Index to Nursing and Allied Health Literature (CINAHL) database using the keywords cinnamon, type II diabetes, diabetes, HbA1c, and FBS. References used in previous meta-analyses were also searched and reviewed for inclusion. Studies were included in this review if they evaluated cinnamon effects on HbA1c and/or FBS/FPG. A total of 15 trials were incorporated in this literature review, 10 studied cinnamon's effect on HbA1c levels and 13 studied cinnamon's effect on the FBG. Six trials showed significant reductions in the HbA1c levels and 10 trials showed significant reductions in the FBG. Based on this review of literature, cinnamon can be recommended as effective therapy for reducing HbA1c and FBG levels in type II diabetes. To reduce FBG and HbA1c levels, cinnamon can be dosed at 1 g to 6 g daily with meals (i.e. one to four 500 mg tablets BID or TID with meals).

Cinnamon in the Treatment of Type II Diabetes

Diabetes affects people of all races, ethnicities, ages, and genders and can significantly alter quality of life, especially when not well controlled. Conditions such as metabolic syndrome and prediabetes often result in diabetes within a few years. Controlling these syndromes and diabetes becomes a dilemma when it is coupled with the cost of medications, for those with health insurance as well as for those without. The United States Census Bureau stated that 42 million Americans did not have health insurance in 2013 (Smith & Medalia, 2014). These individuals have the full burden of paying for their own health care costs. The average cost of diabetic medications, supplies, and provider appointments, etc., is estimated at $13,700 per year (American Diabetes Association, 2015). Individuals suffering from the aforementioned prediabetic conditions and diabetes are often started on medications such as Metformin and are seen quarterly by their providers, and therefore have increasing medical expenses. Piette, Heisler, and Wagner (2004) stated, "Out-of-pocket medication costs pose a significant burden to many adults with diabetes" (p. 384). As a result, 20% of individuals with diabetes forgo taking their medications, as prescribed, in an effort to reduce their out-ofpocket expenses (Piette, Heisler, & Wagner, 2004). If diabetes is not well controlled, the long term effects can be costly, as well as deadly, as diabetes can lead to comorbidities such as neuropathy, retinopathy, nephropathy, hypertension, dermatological problems, and amputations, etc. It is imperative that prediabetic states and diabetes be well controlled to improve the quality of life within these disease processes and to reduce the long term cost of comorbidities associated with these illnesses. New cost effective alternatives, such as cinnamon supplementation, need to be identified to help reduce long term side effects and the out-of-pocket expenses for prediabetic states and diabetes.

Cinnamon has been widely used for decades as a dietary supplement for diabetes, especially in countries like China. Due to both the costs and side effects associated with traditional pharmaceuticals in the United States, there has been a growing awareness of natural and/or alternative supplements. Their use is increasing even though the Food and Drug Administration (FDA) does not regulate or manage the manufacturing of herbal remedies. Shane-McWhorter (2013) found that 67% of diabetics used herbal supplements such as cinnamon to lower their blood glucose levels, which may imply a desire to self-treat their diabetes. Lu et al. (2012) found that "cinnamon supplementation is able to significantly improve blood glucose control in Chinese patients with type II diabetes" (p. 1). Cinnamon has been shown to reduce insulin resistance, reduce blood glucose and lipid levels, reduce inflammation, and increase antioxidant activity (Qin, Panicker, & Anderson, 2010). Despite these benefits and wide spread use of cinnamon and other natural supplements, most traditional providers in the United States do not prescribe or recommend cinnamon or other natural supplements. This may be due to the lack of regulation and approval by the FDA and the lack of evidence of efficacy, or may be due to their own belief or perceptions about cinnamon and other natural supplements. Whatever the reason, there may not be enough information to influence providers to act. Increased studies that show support for cinnamon use in the treatment of type II diabetes, metabolic syndrome, and prediabetes may be the cue to action that is needed.

There are only a handful of studies that have been done on the effects of cinnamon in treating type II diabetes and not all show positive results. A few studies have been done on the effects of cinnamon on other disease processes as well as on healthy individuals. Wang et al. (2007) studied the effects of cinnamon on women with Polycystic Ovary Syndrome (PCOS). Results showed significant reductions in insulin resistance in the cinnamon group but not in the

placebo group. Solomon and Blannin (2007 & 2009) examined the effects of cinnamon on healthy individuals using an oral glucose tolerance test (OGTT). Their trials showed that cinnamon 5 g and 3 g, respectively, can reduce glucose responses to OGTT and improve insulin sensitivity in healthy individuals. Hlebowicz, Darwiche, Björgell, and Almér (2007) and Hlebowicz et al. (2009) also showed the efficacy of cinnamon in healthy individuals on postprandial blood glucose, gastric emptying, satiety, serum insulin, GLP-1 concentrations, GIP, gherlin, and GER. Prior meta-analyses have focused primarily on the type II diabetic population or have excluded studies that did not report specific biochemical markers like fasting blood sugar (FBS) (Davis & Yokoyama, 2011). There is a need for a more comprehensive review of the effects of cinnamon on multiple biochemical measures as well as multiple disease processes. The purpose of this review of literature was to evaluate the effects of cinnamon on hemoglobin A1C (HbA1c) and fasting blood glucose/fasting plasma glucose (FBG/FPG) in various populations, including those with type II diabetes, prediabetecs, metabolic syndrome, and are overweight or obese.

Theoretical Framework

The theoretical framework utilized for this research proposal was the Health Belief Model applied mostly from the perspective of the provider. This model theorizes that belief and perceptions influence actions (Glanz, & Rimer, 2005). The researcher has predicted that there is a relationship between cinnamon therapy and reduction of some biochemical measures; however, providers do not currently prescribe or recommend its use.

The Health Belief Model describes how modifiable variables and perceived ideas such as severity of consequences, susceptibility, benefits versus barriers, and cues to action can bring about the likelihood of engaging in actions that can promote health (Glanz, & Rimer, 2005).

Providers are aware of the susceptibility and severity of type II diabetes. They can be educated about the perceived benefits of cinnamon, i.e., efficacy in lowering HbA1c levels and blood glucose levels, low cost, and no side effects (unless there is an allergy to cinnamon). The perceived barriers to prescribing cinnamon are the lack of FDA regulation of cinnamon, lack of recommendation by the American Diabetic Association (ADA), lack of knowledge of the efficacy of cinnamon in lowering some biochemical measurements, and presumed lack of research to support its use. Cues to action may be evidence-based trials that show benefits and effectiveness of cinnamon in the treatment of type II diabetes and other disease states, while reducing variables such as the dosing amount of cinnamon. With knowledge of such trials, primary care providers may be influenced to act and prescribe this supplement. Providers, therefore, will be promoting health and self-sufficiency in their patients, as their patients will be less dependent on multiple medications and have fewer medication-induced side effects.

Materials and Methods

A comprehensive literature review was done with the Cumulative Index to Nursing and Allied Health Literature (CINAHL) database using the keywords, cinnamon, type II diabetes, diabetes, HbA1c, and FBS. References used in previous meta-analyses were also searched and reviewed for inclusion. Studies were included in this review if they evaluated cinnamon effects on HbA1c and/or FBS/FPG. Studies on type I diabetes were excluded because individuals diagnosed with type I diabetes have a deficiency of insulin rather than insulin resistance, and this literature review is focused on insulin resistance. Another study excluded was done by Wainstein et al. (2011) on individuals diagnosed with type II diabetes because the cinnamon tablets contained cinnamon, zinc gluconate and tri-calcium phosphate. Also not included in this review were studies done on rats.

A total of 15 trials were incorporated in this literature review. Thirteen of the trials studied the effects of cinnamon on individuals with type II diabetes, one trial assessed the effects of cinnamon on prediabetic and metabolic syndrome individuals, and one trial studied the efficacy of cinnamon use in overweight or obese individuals. Of these trials, 10 measured HbA1c levels and 13 measured FBG. Other biochemical markers were measured but are not part of this review.

Results

HbA1c

The HbA1c level measures the average blood sugars over a three-month period, and is important in diabetic management because higher HbA1c levels denote greater risk of developing diabetes-related complications. Crawford (2009) studied whether 1 gram of cinnamon cassia taken daily for 90 days would lower HbA1c levels in poorly controlled type II diabetes. Cinnamon 1 g daily was found to have lowered HbA1c levels by 0.83% ($p < 0.001$). Usual care alone without cinnamon, lowered the HbA1c 0.37% ($p < 0.16$). Crawford concluded that cinnamon does lower HbA1c for this population. Lu et al. (2012) also studied the effect of cinnamon on HbA1c levels for participants with type II diabetes. Cinnamon extract prepared from the bark of Chinese Cinnamomum aromaticum was used. In this study, they compared a placebo, low dose cinnamon (120 mg), and high dose cinnamon ($_{360}$ mg). The cinnamon or placebo tablets were taken every morning before breakfast for three months. After three months, they found that for those in the low dose group, HbA1c was reduced an average of 0.67% (8.90 ± 1.24 to 8.23 ± 0.99), ($p = .003$), and in the high dose group an average of 0.92% (8.92 ± 1.35 to 8.00 ± 1.00), ($p = 0.0004$). In this study, the higher dose was more effective than the lower dose.

The effect of cinnamon supplementation was again studied by Sharma, Sharma, Agrawal, Agrawal, and Singhal (2012) in individuals with newly diagnosed type II diabetes. One hundred fifty individuals newly diagnosed with type II diabetes were stabilized with diet and exercise for one month prior to beginning the cinnamon supplementation. The participants were randomized into a 3 g cinnamon group, a 6 g cinnamon group, a placebo group. After three months, the 3 g group's (taking 1 g after each meal) HbA1c went from 8.47 ± 1.02 at baseline to 7.29 ± 0.83 post intervention, $p < 0.005$. In the 6 g group (taking 2 g after each meal), the HbA1c went from 8.10 ± 0.84 at baseline to 7.25 ± 0.81 post intervention, $p < 0.005$. Both doses had equivalent efficacy. Vafa et al. (2012) treated type II diabetes with Cinnamomum zeylanicum. Participants took two 500 mg tablets of Cinnamomum zeylanicum at each main meal for eight weeks, for a total of 3 grams daily. The researchers concluded that cinnamon significantly decreased HbA1c ($p = 0.008$), of the treatment group, compared to the placebo group. It is noted that even though the HbA1c levels of these participants were well controlled at baseline (7.35 ± 0.51), the Cinnamomum zeylanicum was still effective in significantly reducing the mean level overall.

Al-Yasiry, Kathum, and Al-Ganimi (2014) studied the hypoglycemic effect of cinnamon on 40 male participants with type II diabetes. The participants were given 0.5 g of ground crude cinnamon 15 minutes after each meal for a total of 1.5 g daily for three months. They found that using 1.5 g of ground cinnamon daily decreased the HbA1c which went from 9.54 + 0.96 pretreatment to 8.22 + 0.65 posttreatment, ($p < 0.01$).

Cinnamon cassia usage in individuals diagnosed with type II diabetes was studied by Akilen, Tsiami, Devendra, Robinson (2010). Participants were given one 500 mg tablet of cinnamon cassia with breakfast and dinner and two 500 mg tablets with lunch, for a total of 2 g daily. The ingestion of 2 g of cinnamon each day was found to significantly reduce the HbA1c

level, 8.22 ± 1.16 to 7.86 ± 1.42, $p < 0.05$. A moderate positive correlation was found between the baseline HbA1c level and the significant drop of the HbA1c level suggesting that cinnamon supplementation for individuals with poorly controlled diabetes may play a positive role in managing their disease, $r = 0.567$, $p = 0.008$.

Four studies found no significant difference in the HbA1c levels with the use of cinnamon. Vanschoonbeek, Thomassen, Senden, Wodzig, and van Loon (2006) investigated the effects of 1.5 g per day of cinnamon cassia on HbA1c levels of 25 postmenopausal women with well controlled type II diabetes over a six week time frame. No significant changes were found. It must be noted that an appropriate amount of time was not given for a change to be properly noted in the HbA1c level as this trial was done over six weeks instead of three months. Blevins, Leyva, Brown, Wright, Scofield, and Aston (2007) also showed no significant results of cinnamon on HbA1c levels. For three months, cinnamon cassia 1 g was given daily. It was found that this dosage of cinnamon given daily for three months produced no significant change in HbA1c levels ($p > 0.05$). Mang et al. (2006) studied the effects of 3 g cinnamon daily on 79 individuals diagnosed with type II diabetes over four months. Their study showed no significant decrease in the HbA1c levels posttreatment. Suppapitiporn and Kanpaksi (2006) examined the efficacy of cinnamon cassia 1.5 g daily on reducing the HbA1c levels of 60 individuals with type II diabetes. After 12 weeks of intervention, it was found that the HbA1c levels decreased in both the placebo group and the cinnamon group. There was a greater reduction of the HbA1c level in the cinnamon group, and more patients in the cinnamon group achieved a HbA1c level of < 7% as compared to the placebo group; however, the reductions were not statistically different, $p > 0.05$.

The participants in the Vanschoonbeek et al., 2006 trial, the Blevins et al., 2007 trial, and the Mang et al., 2006 trial were all individuals with well controlled diabetes with baseline HbA1c levels of 6.86 to 7.4. DeFronzo, Stonehouse, Han, and Wintle (2010) did a meta-analysis of 59 trials with a total of 8,479 patients on the relationship of baseline HbA1c levels and the effectiveness of 10 different classes of hyperglycemic medications and produced a weighted R2 of 0.35 ($p < 0.0001$). These results showed a positive correlation between the baseline HbA1c levels and magnitude of change of the HbA1c level after treatment with glucose-reducing therapies regardless of drug classification. They further stated that, "These observations should be considered when assessing clinical efficacy of diabetes therapies derived from clinical trials, particularly when evaluating data from clinical trials of patients with relatively low baseline HbA1c levels, 7.0 – 8.0% (DeFronzo, Stonehouse, Han, & Wintle, 2010, p.309, 314)." Lower baseline HbA1c levels prior to intervention produce smaller and less significant changes in the HbA1c levels post intervention.

FBG/FPG

The most common test used to diagnose diabetes is the fasting blood glucose level. This test is more definitive than random blood glucose tests because it measures the blood glucose level after a period of at least eight hours of fasting (no food or liquids except water), eliminating the chance that the results have been influenced by recent food or beverage intake (OneTouch, no date). Khan, Safdar, Ali Khan, Khattak, and Anderson (2003) conducted the first in vivo study on the use of cinnamon in improving FBG levels. Cinnamon cassia was given 1 g daily as one 500 mg tablet taken at lunch and dinner, 3 g daily as two 500 mg tablets taken at breakfast, lunch, and dinner, or 6 g daily as four tablets taken at breakfast, lunch, and dinner. The

researchers found that all three doses of cinnamon reduced the mean FBG serum levels (18-29%, $p < 0.05$) of the participants in the treatment groups after 20, 40, and 60 days.

Anderson et al. (2010) studied the effects of cinnamon cassia 250 mg given twice a day to participants with type II diabetes. After two months it was found that the FBS decreased from 8.85 ± 0.32 pretreatment to 8.19 ± 0.29 mmol/L posttreatment, $p < 0.001$. Mang et al. (2006) evaluated the usage of cinnamon cassia 1 g daily for individuals diagnosed with type II diabetes. Participants took the cinnamon as prescribed for four months. The cinnamon group was found to have a significant reduction in the FBG between baseline and post intervention levels (9.26 ± 2.26 to 8.15 ± 1.65 mmol/L, $p < 0.001$). Ziegenfuss, Hofheins, Mendel, Landis, and Anderson (2006) evaluated the effects of Cinnulin PF 500 mg once a day (which is equivalent to 10 g whole cinnamon powder) on the FBG of prediabetic and metabolic syndrome participants. After 12 weeks, the FBG levels decreased –8.4% from 116.3 ± 12.8 mg/dl to 106.5 ± 20.1 mg/dL, $p < 0.01$. The efficacy of Cinnulin PF was also studied by Roussel, Hininger, Benaraba, Ziegenfuss, and Anderson (2009) in reducing the FBG of individuals who were overweight or obese. Cinnulin PF 250 mg was taken twice a day for 12 weeks. The FBG dropped from 114 ± 2.2 to 102 ± 4.3 mg/dL, $p < 0.05$, between pre- and posttreatment with Cinnulin PF. Khan, Khan, and Shah (2010) studied the effects of ground cinnamon 1.5 g on the FBG of participants with type II diabetes. For 30 days the participants ingested 0.5 g of cinnamon three times a day with meals. A significant reduction of the FBG was found with the use of cinnamon (216.3 ± 52.7 to 163.3 ± 44.9 mg/dL, $p < 0.05$). In a three month trial, Lu et al. (2012) examined the efficacy of cinnamon cassia 120 mg and 360 mg daily in reducing the FBS in 60 Chinese participants who were diagnosed with type II diabetes. Results showed a statistically significant decrease in both

groups. Baseline FBG levels decreased from 9 to 7.99 mmol/L in the 120 mg group, and from 11.21 to 9.59 mmol/L in the 360 mg group, ($p = 0.00008$).

The effects of cinnamon in individuals newly diagnosed with type II diabetes was studied by Sharma, Sharma, Agrawal, Agrawal, and Singhal (2012). One hundred and fifty participants were divided into three groups and given a placebo, 3 g cinnamon, or 6 g cinnamon daily spread out over three meals. FBG levels were drastically reduced in both cinnamon groups. Baseline FBG levels decreased 49% in the 3 g cinnamon group from 226.73 ± 21.43 to 115.5 ± 23.03, and 48% in the 6 g cinnamon group from 216.94 ± 26.27 to 112.26 ± 22.85, ($p < 0.001$). The effectiveness of Cinnamomum zeylanicum in the reduction of FBG was assessed by Vafa et al. (2012). Two 500 mg tablets were given to 37 participants three times daily for eight weeks. Cinnamomum zeylanicum, also known as true cinnamon, significantly reduced the FBG in the cinnamon group 139.28 ± 9.11 to 126.47 ± 17.73, ($p < 0.05$). Al-Yasiry, Kathum, and Al-Ganimi (2014) determined the hypoglycemic effects of cinnamon on 40 poorly controlled male individuals diagnosed with type II diabetes. Participants were given 1.5 g of cinnamon daily for three months. Cinnamon cassia produced a 27.5% decline in the FBG of the participants, 174.70 ± 19.83 to 126.25 ± 17.85, ($p < 0.01$).

In contrast, some trials found no significant reduction in FBG levels after cinnamon supplementation. Vanschoonbeek, Thomassen, Senden, Wodzig, and van Loon (2006) investigated the effects of cinnamon 1.5 g on FBG levels of 25 postmenopausal women with well controlled type II diabetes over six weeks. Although there was some decline of the FBG in the cinnamon group, 8.37 ± 0.59 to 7.91 ± 0.71, it was not statistically significant, ($p > 0.05$). Suppapitiporn and Kanpaks (2006) evaluated the effects of cinnamon cassia 1.5 g daily, taken over 12 weeks, on individuals with type II diabetes. No statistical significance was found in the

FBG. Blevins et al. (2007) explored the effects of 1 g of cinnamon cassia on 57 non-insulin dependent individuals diagnosed with type II diabetes. After a three month intervention phase, no significant change was noted in the FBG.

Discussion and Implications for Practice

Type II diabetes is a preventable disease. Choosing a healthy lifestyle with well balanced meals and plenty of exercise can mean the difference between a life of health and a life of illness. The global prevalence of diabetes was estimated at nine percent in 2014 in individuals 18 and over. That is over 350 million people worldwide (World Health Organization, no date) (WHO). Diabetes significantly affects quality of life and leads to death when not well controlled. Over three million people die of diabetes and its comorbidities yearly, mainly because of poor health choices. The Centers for Disease Control and Prevention (2014a, 2014b) (CDC) stated that diabetes was the seventh leading cause of death in 2010. As stated in the introduction, the American Diabetic Association estimates the cost of diabetes at $13,700 yearly per person, making diabetes costly as well as deadly. Controlling diabetes and its predecessor diseases, prediabetes and metabolic syndrome, is imperative to improving the health of our country and reducing health care expenditures. Finding safe, efficacious, and cost effective alternative treatments for diabetes is a must. Cinnamon is a promising alternative treatment that has been used for decades as a dietary supplement for diabetes, and is much less expensive than some of the traditional pharmaceuticals used to treat diabetes. Some type II diabetic medications costs $200 - $300 a month or more, while cinnamon costs $20 - $30 a month depending on what dosage is taken.

Cinnamon was found to be effective in lowering FBG levels in individuals who are diagnosed as prediabetic, overweight, or obese. Cinnamon cassia, Cinnamomum zeylanicum,

and Cinnulin PF have been shown to have similar efficacy in these populations; however, Cinnamomum zeylanicum may be more advantageous when diabetes is more controlled (Akilen, Tsiami, Devendra, and Robinson, 2010) with baseline HbA1c levels less than 8. As stated previously, there is a moderate positive correlation between the baseline HbA1c level and the significant drop of the HbA1c level. The participants of the trials that showed no significant drop in the HbA1c levels after cinnamon intervention all had baseline HbA1c levels of 6.86 – 7.4. The only trial that showed a significant drop in HbA1c levels that were well controlled at baseline (7.35 ± 0.51) was Vafa et al. (2012). This trial used Cinnamomum zeylanicum (true cinnamon).

This review of literature recommends cinnamon as an efficacious and cost effective treatment of uncontrolled type II diabetes which may potentially have some cardiovascular benefits. To reduce FBG and HbA1c levels, cinnamon can be dosed at 1 g to 6 g daily with meals (i.e. one to four 500 mg tablets BID or TID with meals). No adverse effects were seen with any of the cinnamon doses. Patients should be watched for cinnamon allergies, although none were reported in any of the studies reviewed.

Conclusion

Based on this review of literature, cinnamon can be recommended as effective therapy for reducing HbA1c levels and FBG levels in individuals diagnosed with type II diabetes. The majority of the trials reviewed in this meta-analysis showed that cinnamon cassia, Cinnamomum zeylanicum (verum), and Cinnulin PF significantly reduced HbA1c and FBS, and is effective in treating type II diabetes. Cinnamomum zeylanicum (verum) was most effective in treating lower baseline levels of HbA1c. The combined trials in this meta-analysis showed that cinnamon decreased the HbA1c levels between 0.44% - 1.32%, which is as effective as traditional pharmaceuticals used to treat type II diabetes.

Further research needs to be done to evaluate if cinnamon is as equally effective in reducing the HbA1c level and FBG level in the individual with stable type II diabetes (HbA1c level ≤ 8.0 or FBG ≤ 183) versus the individual with unstable type II diabetes (HbA1c ≥ 8.0 or FBG ≥ 183), as well as the effectiveness of various types of cinnamon such as cinnamon cassia, Cinnamomum zeylanicum, and Cinnulin PF.

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