

## Review Article

# Pharmacology and evidence for cinnamon supplementation in patients with Type 2 diabetes: rationale for consideration in Native Americans

Brian D. Fox<sup>1</sup>, Sunny A. Linnebur<sup>1</sup>, Connie A. Valdez<sup>1,2</sup>, Richard Chien<sup>1</sup>

<sup>1</sup>University of Colorado Skaggs School of Pharmacy & Pharmaceutical Sciences, USA

<sup>2</sup>Denver Indian Health Services and Family Services, Denver, USA

**\*Corresponding author**

Sunny A. Linnebur, Pharm.D, BCPS, FCCP, CGP, Associate Professor, University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, 12850 E. Montview Blvd, Campus Box C238 Aurora, CO 80045, Phone: 303-724-2621, Fax: 303-724-0979, Email: sunny.linnebur@ucdenver.edu

Submitted: 28 August 2015

Accepted: 15 October 2015

Published: 18 October 2015

ISSN: 2333-7079

Copyright

© 2015 Fox et al.

OPEN ACCESS

**Keywords**

- Cinnamon
- Type 2 Diabetes Mellitus
- Native American
- North American Indians

**Abstract**

**Objective:** Cinnamon supplementation can increase insulin sensitivity and activate glucose transporter 4. These features make it an attractive supplement, particularly in populations seeking natural therapies, such as Native Americans with diabetes. The aim of this review is to discuss the pharmacology and evidence regarding cinnamon supplementation in type-2 diabetes (T2DM) and the possible rationale for use Native Americans.

**Data Sources and Selection:** PubMed and Ovid Medline databases were searched from 1946 through August 28, 2015 using the MESH terms “cinnamon” and “Diabetes Mellitus, Type 2”. A total of 51 citations were generated, which were filtered to include only clinical trials and studies involving human subjects (n=11). Two of the 11 citations were excluded from review and three additional citations were identified from references.

**Data Synthesis:** A total of twelve studies met inclusion for review. All studies were randomized and placebo-controlled. Three trials evaluated cinnamon's effect on insulin sensitivity and nine trials investigated the influence of cinnamon supplementation on fasting blood glucose and/or HbA1C values. Of these, eight studies showed a benefit from cinnamon supplementation while four failed to demonstrate any clinical benefit. The cinnamon dose varied from 120-6000 mg per day for duration of 6 hours to 4 months. There was substantial heterogeneity in trials, making broad conclusive statements difficult.

**Conclusion:** Current evidence for the role of cinnamon in the general T2DM population appears inconclusive. However, based upon its proposed mechanism of action cinnamon may be an economical, safe, and potentially effective natural option for Native Americans with diabetes.

**ABBREVIATIONS**

**US:** United States; **T2DM:** Type 2 Diabetes Mellitus; **IRS:** Insulin Receptor Substrate; **PI:** Phosphatidylinositol; **IR:** Insulin Receptor; **FRAP:** Ferric Reducing Antioxidant Power; **SH:** Thiol; **MDA:** Malondialdehyde; **OGTT:** Oral Glucose Tolerance Tests; **FDA:** Food and Drug Administration; **DSHEA:** Dietary Supplement Health and Education Act; **USP:** U.S. Pharmacopeia; **HbA1C:** Hemoglobin A1C

**INTRODUCTION**

The World Health Organization estimates that 347 million people worldwide are living with diabetes, and 29.1 million of those affected reside in the United States (US) [1,2]. Unfortunately, not all people with diabetes are aware of their diagnosis. Of the 29.1 million US cases, it is estimated 21 million

are diagnosed while 8.1 million are undiagnosed. In 2012, the estimated cost of treating type 2 diabetes mellitus (T2DM), and associated complications, in the US was \$176 billion. This cost is projected to increase to \$192 billion by 2020 [2]. As the population ages and becomes more overweight, the epidemic of diabetes will continue to accelerate, because age and obesity are two primary risk factors for developing T2DM. This increase is particularly concerning for certain ethnic groups, such as Native Americans, who have the highest prevalence of diabetes in the US and in the world [2]. In fact, one study found that 50% of the Pima Indian population in southern Arizona over 35 years of age had diabetes [3]. Interestingly, diabetes was uncommon among Native Americans until the 1940s, when loss of traditional land and food resulted in a more Westernized-type of diet. This sudden change in diet, coupled with a more sedentary life style,

has resulted in a significant increase in the number of Native Americans diagnosed with T2DM and obesity.

### Insulin Resistance and T2DM

Obesity is thought to drive rates of diabetes by increasing insulin resistance and decreasing tissue absorption of glucose. Although it is well described how insulin resistance contributes to T2DM, it is not well understood how ethnic differences impact the severity of insulin resistance and prevalence of T2DM. When comparing ethnic populations over the age of 20 who are currently diagnosed with T2DM, Native Americans have over a two-fold prevalence of T2DM compared to Caucasians (15.9% vs 7.6%) [2]. This difference poses the question: Do Native Americans possess a genetic factor that predisposes them to insulin resistance and a higher risk of developing T2DM? To understand the difference in prevalence rates, Lillioja et al. performed a metabolic comparison between Pima Indians and Caucasians. Plasma insulin concentrations were 50% higher in Pima Indians 3-5 minutes after IV glucose administration ( $P < 0.0001$ ), 38% higher after the end of a meal ( $P < 0.0001$ ), and 20% higher 30 minutes after an oral glucose load ( $P < 0.006$ ) when compared to their Caucasian counterparts [4]. During a hyperinsulinemic-euglycemic clamp at physiological insulin concentrations, Pima Indians were 17% more insulin resistant than Caucasians, after accounting for obesity ( $P < 0.0001$ ). The authors suggested that development of insulin resistance precedes a decrease in insulin secretion [4]. These findings suggest that Pima Indians have risk factors (e.g. genetic component) which may be contributing to the increase in insulin resistance as compared to Caucasians.

Previous studies have evaluated genetic factors associated with insulin resistance in Pima Indians. One such factor is the Insulin Receptor Substrate 1 (IRS-1), which is a signaling protein. When IRS-1 signaling is reduced, glucose uptake and utilization is diminished via the insulin receptor substrate (IRS)-1/phosphatidylinositol (PI) 3-kinase pathway [5]. Baier et al. found a significant effect between variations in IRS-1, mapped to chromosome 2q36, and the development of T2DM which may explain some of the increased risk of insulin resistance in Pima Indians [6]. Kovacs et al. also noted an association between variants in expression of IRS-1 in adipocytes and skeletal muscle and T2DM in Pima Indians [7]. Although studies related to IRS-1 have been limited to Native Americans who are of Pima Indian descent, Lee et al. evaluated the association of Native American ancestry with rates of diabetes in numerous Native American tribes or communities in Arizona, Oklahoma, and North and South Dakota. After controlling for obesity, the prevalence of diabetes was significantly higher ( $P < 0.0001$ ) in individuals with 50% or more Native American ancestry compared to those who had less than 50% Native American ancestry [8]. These findings suggest that Pima Indians, and possibly other Native Americans, may be predisposed to diabetes due to genetic factors, possibly differential expression of IRS-1, leading to higher rates of insulin resistance and diabetes. Thus, treatments targeting insulin resistance may have greater efficacy in Pima Indians, and possibly Native Americans in general, compared to other ethnic groups. Since many Native Americans still rely upon traditional medicine and natural approaches to attenuate and treat medical

conditions, it would follow that a natural product may be more preferred in the management of T2DM.

### Cinnamon Pharmacology

Cinnamon, also known as Chinese cinnamon, is a natural herb believed to have insulin-sensitizing capabilities. Cinnamon cassia is sold under the culinary name of cinnamon in supermarkets all across the United States. Cinnamon is one of the oldest and most well-known spices used by many cultures, and its use can be traced back 4,000 years to the Chinese where it was used to treat "thirsty disease," or diabetes.

Cinnamon cassia (*Cinnamomum aromaticum*), has shown to be more insulin-sensitizing compared to cinnamon bark (*Cinnamomum zeylanicum*) [1]. The mechanism by which cinnamon sensitizes the body to insulin is thought to be due, in part, to the active component cinnamaldehyde. *In vitro*, cinnamon enhances glucose uptake through activation and phosphorylation of the insulin receptor (IR) as well as enhancing glycogen synthase activity. *In vivo*, cinnamon enhances insulin-stimulated tyrosine phosphorylation of (IR)- $\beta$ , IRS-1, and IRS-1 phosphatidylinositol (PI) 3-kinase [9]. Based on the pharmacology of cinnamon and the proposed pathophysiology of insulin resistance in Native Americans, the use of cinnamon in this population may provide additional targeted benefits in this population.

The purpose of this review is to evaluate the pharmacology and effects of cinnamon supplementation in the management of T2DM. We will also discuss how the use of cinnamon may be incorporated into the management of Native Americans with T2DM who request natural products.

### METHODS

Using the MESH terms "Indian, North American," "cinnamon," and "Diabetes Mellitus, Type 2," in the PubMed and Ovid Medline databases from 1946 through August 28, 2015 produced no citations. However, a total of 51 citations were generated using the MESH terms "cinnamon" and "Diabetes Mellitus, Type 2" in the same databases and time frame. These citations were then filtered to include only clinical trials and human subjects and to exclude citations related to *Cinnamomum zeylanicum*. These limitations resulted in 11 citations from studies in non-Native American populations for review by the authors. Two of the eleven citations were excluded from review because they did not evaluate patients with insulin resistance ( $n=1$ ) or they were not specific to cinnamon supplementation ( $n=1$ ). Additional citations were gathered by reviewing the references of the nine publications. A total of twelve clinical trials remained for review: three studying cinnamon supplementation and insulin resistance and nine studying cinnamon supplementation and T2DM. These trials describe the relationship between cinnamon supplementation and insulin resistance, fasting blood glucose and/or hemoglobin HbA1C values.

### RESULTS

#### Cinnamon and insulin resistance

Three trials evaluated the influence of cinnamon supplementation on insulin resistance. Roussel et al. studied twenty-two overweight and obese patients who received

either placebo or 250 mg of an aqueous extract of cinnamon twice daily for 12 weeks. Since oxidative stress is a trigger for insulin resistance, the authors used markers of oxidative stress to determine the ability of cinnamon to decrease insulin resistance. These markers included ferric reducing antioxidant power (FRAP) assay, plasma thiol (SH) groups, erythrocyte Cu-Zn superoxide activity, and plasma malondialdehyde (MDA) concentrations. At the completion of the 12-week study period, FRAP and plasma thiol (SH) groups were increased, and MDA levels were decreased in the cinnamon group. Additionally, a significant positive correlation was observed between MDA and plasma glucose levels ( $r = 0.74$ ;  $p = 0.014$ ). Finally, subjects in the cinnamon group had a greater decline in plasma glucose levels compared to those in the placebo group (baseline = 114 mg/dL  $\pm$  2.2; post-12 weeks = 102 mg/dL  $\pm$  4.3;  $p = <0.05$ ) [10].

Solomon et al. studied seven lean, healthy, male volunteers (aged  $26 \pm 1$  year) after administration of three 2-hour oral glucose tolerance tests (OGTT) in a randomized, crossover design. The three study conditions included concomitant glucose with either a 5 gram placebo or 5 grams of cinnamon (conditions 1 and 2) or 5 grams of cinnamon administered 12 hours before the glucose load (condition 3). Results indicated that cinnamon (taken 12 hours before or concomitantly with a glucose load) can significantly improve insulin sensitivity and reduce the total plasma glucose response 30 minutes following the OGTT [11].

A second study by Solomon et al. compared the influence of 14 days of cinnamon supplementation (3 grams/day) versus placebo in eight male volunteers [12]. This crossover study performed OGTTs on day 0 (prior to initiation of cinnamon) and days 1 and 14 (following the initiation of cinnamon). OGTTs were again performed on study days 16, 18 and 20 (equivalent to 2, 4, and 6 days after the cessation of cinnamon). Cinnamon supplementation resulted in a decreased plasma glucose response to OGTT ( $-13.1 \pm 6.3\%$ ,  $P < 0.05$ ) when comparing day 1 of cinnamon to day 0. The authors also found a significant difference in plasma glucose responses ( $-13.9 \pm 3.9\%$ ,  $P < 0.05$ ) when comparing day 1 of cinnamon to day 1 of placebo. Cinnamon supplementation reduced insulin responses to OGTT on day 14 compared to day 0 ( $-27 \pm 6.2\%$ ,  $p < 0.05$ ) and improved insulin sensitivity (day 14 vs day 0). These improvements, however, were not sustained after discontinuation of cinnamon supplementation [12].

### **Cinnamon and fasting blood glucose and hemoglobin HbA1C values**

Nine trials evaluated the efficacy of cinnamon on fasting blood glucose and/or HbA1C values (Tables 1 and 2). The majority of these trials were small (average number of subjects was 67) and of short duration (average study duration of 2.7 months) which may have contributed to the conflicting results.

Five trials provide evidence to support the efficacy of cinnamon and are summarized in Table 1 [9,13-16]. These trials included adult patients with Type 2 diabetes ( $n = 61-151$  patients per trial) who received a variety of cinnamon doses (120mg to 6000 mg/day) for 2 to 4 months. All trials were prospective and randomized, and four trials included a placebo group. Cinnamon forms evaluated included cassia powder and aqueous cinnamon

extract.

Four trials failed to demonstrate a benefit from cinnamon supplementation and are summarized in Table 2 [17-20]. These negative trials tended to be smaller ( $n = 9-60$  patients per trial) and shorter in duration (6 hours- 3months) than the positive trials. The dosage of cinnamon administered in these trials varied between 1000 mg to 3000 mg per day. Similar to the trials with positive results, these trials were all prospective, randomized and placebo-controlled, and other than the study by Markey et al, all of the subjects had Type 2 diabetes.

### **Safety**

Many Americans believe that herbs and nutritional supplements are safe and effective due to their "natural" origin and wide commercial availability within the US market place. Furthermore, surveys of the public indicate that most believe these products are tested by the U.S. Food and Drug Administration (FDA) for safety [21]. In fact, both assumptions are mistaken.

In 1994, Congress passed the Dietary Supplement Health and Education Act (DSHEA). This Act exempted dietary supplements and botanicals from rigorous FDA review and regulation [22]. As a result, the US experienced a rapid expansion of dietary supplements from 4,000 marketed products in 1994 to 75,000 in 2008. With the expansion of dietary supplement use, there has also been an increase in reported adverse events. A one year prospective surveillance study of dietary supplement-related poison control center calls found that of 275 calls, two-thirds were rated as probably or possibly related to supplement use [23]. Most adverse events were minor, but eight required hospital admission. Because dietary supplements and herbal products are not regulated by the FDA in the same manner as prescription drugs and adverse event reporting is not uniformly mandated, the actual numbers of adverse events are likely grossly underestimated.

Many adverse events associated with nutritional supplements and herbals are the result of unknown or poorly understood drug-drug or drug-disease interactions. For example, one component found in cinnamon products is coumarin. Coumarin is natural flavor/scent that has been linked to potential liver damage and could adversely affect patients when administered at high doses [24]. Mild side effects associated with coumarin include dizziness and diarrhea. It is not until higher doses (50-7000 mg/day) that vomiting and potential liver damage occur [24]. Thus, in patients with pre-existing hepatic dysfunction, it is important to remember that cinnamon products could potentially contain high levels of coumarin.

In addition to the adverse event concerns, the lack of product standardization may result in adulteration, variable amounts of active ingredients from bottle to bottle and the presence of harmful chemicals. Woehrelin et al. evaluated the quantity of coumarin found in cinnamon cassia [25]. The results confirmed previous studies and showed a great variation between samples, even within the same trees themselves, for the level of coumarin: mean (2680 mg/kg), median (2920 mg/kg), minimum (less than the level of detection), maximum (8790 mg/kg) [25]. These results illustrate the importance of product standardization and

**Table 1:** Summary of clinical trials which support efficacy of cinnamon on blood glucose and/or HbA1C.

Year	Author	Trial design and Specific Aim	N	Cinnamon Regimen	Study Duration	Main Findings
1993	Kahn et al [13]	Prospective, randomized, placebo controlled trial to evaluate if cinnamon reduces serum glucose	60	1, 3, or 6 grams of cinnamon cassia powder daily or placebo	60 days	Significant decrease in serum glucose at 40 days with the use of 1, 3, and 6 grams of cinnamon cassia powder ( $P < 0.05$ ).  No dose-response effect observed at 20 days. Only the group taking 6 grams of cinnamon retained significant glucose lowering effects.  Serum glucose decreases ranged from 18-29%.
2006	Mang et al [9]	Prospective, randomized, double-blind, placebo-controlled trial to compare the effects of cinnamon vs placebo on reducing fasting plasma glucose levels and HbA1C	79	112 mg aqueous cinnamon extract (correlates to 1 gram of cinnamon) three times daily or placebo	4 months	Significant reduction in fasting plasma glucose from baseline to post-intervention ( $-1.11 \pm 1.59$ vs. $-0.35 \pm 1.29$ , $P = 0.038$ ).  No significant differences in HbA1C values from baseline to post-intervention ( $-0.05 \pm 0.43$ and $-0.03 \pm 0.61$ in the cinnamon vs. placebo groups, respectively).
2009	Crawford [14]	Prospective, randomized trial to determine if cinnamon reduces HbA1C values	109	1 gram daily of cinnamon cassia or usual care	90 days	Modest decrease in HbA1C levels by 0.83% (95% CI, 0.46 – 1.20) over 90 days compared to usual care where HbA1C was 0.37% (95% CI, 0.15–0.59).
2010	Akilen et al S[15]	Prospective, double-blind, placebo-controlled trial to evaluate if cinnamon decreases fasting blood glucose and HgA1C	151	2 grams cinnamon daily or placebo	12 weeks	Significant reduction in HbA1C (8.22% to 7.86% vs. 8.55% to 8.68%, $P = 0.002$ ) in the cinnamon vs. placebo groups, respectively.  Fasting blood glucose was reduced from 8.82 mmol/L to 8.04 mmol/L in the cinnamon group versus 8.77 mmol/L to 8.74 mmol/L in the placebo group; however, this was not statistically significant ( $P > 0.05$ ).
2012	Lu et al [16]	Prospective, randomized, double-blind, placebo-controlled trial to evaluate if cinnamon reduces fasting blood glucose and HbA1C	66	Low dose (120mg) or high dose (360mg) of cinnamon cassia before breakfast or placebo	3 months	Statistically significant difference in fasting blood glucose (9.00 to 7.99 mmol/L and 11.21 to 9.59 mmol/L, $p = 0.002$ and $p = 0.00008$ ) and HbA1C values (8.9% to 8.23% and 8.92% to 8%, $p = 0.003$ and $p = 0.004$ ) in the low- and high-dose groups, respectively.

quality assurance. The U.S. Pharmacopeia (USP) establishes strict standards to verify ingredients within supplements which are distributed across the US. As such, when a cinnamon supplement is to be considered, it is important for the clinician to recommend brands which have been standardized for purity, quality and quantity. This can be ensured by recommending a brand that has been verified by the USP or has a seal of quality assurance [26].

Most providers may prefer to follow national guidelines and initiate prescription medication (such as metformin) to control T2DM. However, some patients with specific cultural beliefs may prefer to take supplements or herbal products rather than initiate prescription medication. For these patients, cinnamon could be considered. Although the likelihood of harm from cinnamon is rare, side effects and hepatic damage due to coumarin ingestion must be considered, particularly in patients predisposed to hepatic damage. The healthcare practitioner should also take into consideration drug interactions and monitoring requirements prior to recommending this product. If cinnamon is selected for a patient, then the clinician should recommend a reputable

product which is standardized for purity. Based upon efficacy data, an acceptable starting dose would be 1000-2000mg daily, taken with a meal. The dose can be titrated up to 6000mg daily in two divided doses. Patients may experience a decrease in fasting blood glucose and/or HbA1C values, but this effect might not be observed in everyone. Monitoring should include baseline liver function tests, HbA1C and fasting blood glucose [27]. Patients should be advised to monitor their blood sugar on a daily basis and when symptoms are consistent with a hypoglycemic episode.

## DISCUSSION

A Cochrane review from 2012 found there was insufficient evidence to support the general use of cinnamon for T2DM [27]. The authors found high or unclear bias in the most of the 10 clinical trials that they reviewed, but observed that adverse effects were typically mild and infrequent. Overall, the Cochrane review suggested that further research eliminating the limitations of the current research (e.g. issues of allocation concealment and blinding, incorporation of other important outcomes such as

**Table 2:** Summary of clinical trials which do not support efficacy of cinnamon on blood glucose and/or HbA1C.

Year	Author	Trial design and Specific Aim	N	Cinnamon regimen	Study duration	Main Findings
2006	Suppakitiporn et al [17]	Prospective, single blind, randomized, placebo-control trial to determine effects of cinnamon vs placebo on reducing HbA1C	60	1.5 g/day of cinnamon cassia powder or placebo	12 weeks	Similar, non-significant HbA1C reductions (8.14% to 7.76% vs. 8.06% to 7.87%) in the cinnamon vs. placebo groups, respectively. Proportion of patients reaching a goal HbA1C of $\leq 7\%$ was not statistically different.
2006	Vanschoonbeek et al [18]	Prospective, double-blind, randomized, placebo-controlled trial to evaluate the effects of cinnamon vs placebo on plasma glucose and HbA1C	25	1.5 g/day of cinnamon cassia or placebo	6 weeks	Arterial blood samples and oral glucose tolerance tests performed after 2 and 6 weeks failed to show a difference in plasma glucose levels and HbA1C between the groups ( $P > 0.05$ ).
2007	Blevins et al [19]	Prospective, randomized, double-blind, placebo-controlled trial to compare the effects of cinnamon vs placebo on lowering fasting plasma glucose levels and HbA1C	60	500 mg of cinnamon cassia twice daily or placebo	3 months	No significant reduction in fasting glucose values or changes in HbA1C values when compared to placebo.
2011	Markey et al [20]	Prospective, single-blind, crossover trial to determine if cinnamon reduces postprandial glucose concentrations	9	3 grams of cinnamon orally post high fat meal	6 hours	No statistical differences in postprandial glucose concentrations when compared to placebo.

health-related quality of life, diabetic complications, and cost) is needed. This is consistent with our findings: approximately one-half of the studies we reviewed demonstrated positive effects in patients with T2DM taking cinnamon. However, only three studies found HbA1C reduction with cinnamon [14-16, 28]. To find significance, in addition to correcting the above methodological concerns, further research with cinnamon may need to target larger study populations and those ethnic groups, like Native Americans, who have a pharmacologic reason to benefit from cinnamon.

## CONCLUSION

Over the past decade, researchers have evaluated the influence of cinnamon on insulin resistance, fasting plasma glucose and HbA1C values. Current data suggest that cinnamon may have a role in lowering blood glucose and HbA1C, yet not all data are consistent. Heterogeneity amongst the trials, including dose and duration of cinnamon, has decreased the ability to make strong conclusions surrounding the role of cinnamon in patients with T2DM. However, since cinnamon is unlikely to cause patient harm, and in fact may aid the control of T2DM, it is plausible to consider the addition of cinnamon for patients considering a natural approach to disease modification. Further research is needed to determine if cinnamon has greater efficacy in Native Americans compared to other ethnic groups secondary to the potential ability of cinnamon to affect the variations in IRS-1 expressions observed in the Native American population.

## REFERENCES

- World Health Organization. Diabetes. Accessed August 28, 2015.
- Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States 2014. Accessed August 28, 2015.
- Bennett PH, Burch TA, Miller M. Diabetes mellitus in American (Pima) Indians. *Lancet*. 1971; 2: 125-128.
- Lillioja S, Nyomba BL, Saad MF, Ferraro R, Castillo C, Bennett PH, et al. Exaggerated early insulin release and insulin resistance in a diabetes-prone population: a metabolic comparison of Pima Indians and Caucasians. *J Clin Endocrinol Metab*. 1991; 73: 866-876.
- Draznin B. Molecular mechanisms of insulin resistance: serine phosphorylation of insulin receptor substrate-1 and increased expression of p85alpha: the two sides of a coin. *Diabetes*. 2006; 55: 2392-2397.
- Baier LJ, Hanson RL. Genetic studies of the etiology of type 2 diabetes in Pima Indians: hunting for pieces to a complicated puzzle. *Diabetes*. 2004; 53: 1181-1186.
- Kovacs P, Hanson RL, Lee YH, Yang X, Kobes S, Permana PA, et al. The role of insulin receptor substrate-1 gene (IRS1) in type 2 diabetes in Pima Indians. *Diabetes*. 2003; 52: 3005-3009.
- Lee ET, Howard BV, Savage PJ, Cowan LD, Fabsitz RR, Oopik AJ, et al. Diabetes and impaired glucose tolerance in three American Indian populations aged 45-74 years. The Strong Heart Study. *Diabetes Care*. 1995; 18: 599-610.
- Mang B, Wolters M, Schmitt B, Kelb K, Lichtinghagen R, Stichtenoth DO, et al. Effects of a cinnamon extract on plasma glucose, HbA, and serum lipids in diabetes mellitus type 2. *Eur J Clin Invest*. 2006; 36: 340-344.
- Roussel AM, Hininger I, Benaraba R, Ziegenfuss TN, Anderson RA. Antioxidant effects of a cinnamon extract in people with impaired fasting glucose that are overweight or obese. *J Am Coll Nutr*. 2009;

28: 16-21.

11. Solomon TP, Blannin AK. Effects of short-term cinnamon ingestion on in vivo glucose tolerance. *Diabetes Obes Metab.* 2007; 9: 895-901.
12. Solomon TP, Blannin AK. Changes in glucose tolerance and insulin sensitivity following 2 weeks of daily cinnamon ingestion in healthy humans. *Eur J Appl Physiol.* 2009; 105: 969-976.
13. Khan A, Safdar M, Ali Khan MM, Khattak KN, Anderson RA. Cinnamon improves glucose and lipids of people with type 2 diabetes. *Diabetes Care.* 2003; 26: 3215-3218.
14. Crawford P. Effectiveness of cinnamon for lowering hemoglobin A1C in patients with type 2 diabetes: a randomized, controlled trial. *J Am Board Fam Med.* 2009; 22: 507-512.
15. Akilen R, Tsiami A, Devendra D, Robinson N. Glycated haemoglobin and blood pressure-lowering effect of cinnamon in multi-ethnic type 2 diabetic patients in the UK: A randomized, placebo-controlled, double-blind clinical trial. *Diabet Med.* 2010; 27: 1159-1167.
16. Lu T, Sheng H, Wu J, Cheng Y, Zhu J, Chen Y. Cinnamon extract improves fasting blood glucose and glycosylated hemoglobin level in Chinese patients with type 2 diabetes. *Nutr Res.* 2012; 32: 408-412.
17. Suppapitiporn S, Kanpaksi N, Suppapitiporn S. The effect of cinnamon cassia powder in type 2 diabetes mellitus. *J Med Assoc Thai.* 2006; 89: 200-205.
18. Vanschoonbeek K, Thomassen BJ, Senden JM, Wodzig WK, van Loon LJ. Cinnamon supplementation does not improve glycemic control in postmenopausal type 2 diabetes patients. *J Nutr.* 2006; 136: 977-980.
19. Blevins SM, Leyva MJ, Brown J, Wright J, Scofield RH, Aston CE. Effect of cinnamon on glucose and lipid levels in non insulin-dependent type 2 diabetes. *Diabetes Care.* 2007; 30: 2236-2237.
20. Markey O, McClean CM, Medlow P, Davison GW, Trinick TR, Duly E, et al. Effect of cinnamon on gastric emptying, arterial stiffness, postprandial lipemia, glycemia, and appetite responses to high-fat breakfast. *Cardiovasc Diabetol.* 2011; 10: 78.
21. U.S. Food and Drug Administration (FDA). Health and Diet Survey. 2008. Accessed August 28, 2015.
22. National Institute of Health: Office of Dietary Supplements. Dietary Supplement Health and Education Act of 1994. Accessed August 28, 2015.
23. Haller C, Kearney T, Bent S, Ko R, Benowitz N, Olson K. Dietary supplement adverse events: report of a one-year poison center surveillance project. *J Med Toxicol.* 2008; 4: 84-92.
24. Felter SP, Vassallo JD, Carlton BD, Daston GP. A safety assessment of coumarin taking into account species-specificity of toxicokinetics. *Food Chem Toxicol.* 2006; 44: 462-475.
25. Woehrlin F, Fry H, Abraham K, Preiss-Weigert A. Quantification of flavoring constituents in cinnamon: high variation of coumarin in cassia bark from the German retail market and in authentic samples from indonesia. *J Agric Food Chem.* 2010; 58: 10568-10575.
26. U.S. Pharmacopeial Convention. Accessed August 28, 2015.
27. Natural Medicines Comprehensive Database. Cassia cinnamon. Accessed August 28, 2015.
28. Leach MJ, Kumar S. Cinnamon for diabetes mellitus. *Cochrane Database Syst Rev.* 2012; 9: CD007170.

**Cite this article**

Fox BD, Linnebur SA, Valdez CA, Chien R (2015) Pharmacology and evidence for cinnamon supplementation in patients with Type 2 diabetes: rationale for consideration in Native Americans. *J Pharmacol Clin Toxicol* 3(5):1060.