Bioactivity of cinnamon with special emphasis on diabetes mellitus: A review

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Abstract

Cinnamon is the oldest spice and has been used by several cultural practices for centuries. In addition to its culinary uses, cinnamon possesses a rising popularity due to many stated health benefits. Out of the large number of cinnamon species available, *Cinnamomum aromaticum* (Cassia) and *Cinnamomum zeylanicum* have been subjected to extensive research. Available *in vitro* and *in vivo* evidence indicates that cinnamon may have multiple health benefits, mainly in relation to hypoglycaemic activity. Furthermore, the therapeutic potential of cinnamon is stated also to be brought about by its anti-microbial, anti-fungal, antiviral, antioxidant, anti-tumour, blood pressure-lowering, cholesterol and lipid-lowering and gastro-protective properties. This article provides a summary of the scientific literature available on both *C. aromaticum* and *C. zeylanicum*. All studies reported here have used cinnamon bark and its products. Although almost all the animal models have indicated a pronounced anti-diabetic activity of both cinnamon species, conflicting results were observed with regard to the few clinical trials available. Therefore, the necessity of evaluating the effects of cinnamon for its therapeutic potential through well-defined and adequately powered randomized controlled clinical trials is emphasized, before recommendations are made for the use of cinnamon as an effective treatment for humans.

Keywords: Cinnamomum zeylanicum, Cinnamomum aromaticum, Cassia, blood glucose, cholesterol

Introduction

Cinnamon is one of the well-known and oldest spices, which has been used for centuries in several cultures (Gruenwald et al. 2010). Chinese literature 4000 years ago has cited the traditional use of cinnamon in naturopathic medicine (Qin et al. 2003). It has been traditionally used in Ayurvedic and Chinese medicine as a treatment for diabetes (Modak et al. 2007). Cinnamon was reported to be employed as a stomachic and carminative for gastrointestinal complaints as well as other ailments in many countries (Teuscher 2003).

About 250 species are included in the genus *Cinnamomum* (Lauraceae). These species are shrubs and small to medium-sized trees (Jantan et al. 1995) and found in tropical rain forests where they grow at various altitudes from highland slopes to lowland forests and occur in both marshy places and on well-drained soils. The four principal *Cinnamomum*

species are *Cinnamomum zeylanicum* (*C. verum*: 'True cinnamon', Sri Lanka cinnamon or Ceylon cinnamon), *C. loureirii* (Saigon cinnamon or Vietnamese cinnamon), *C. burmanni* (Korintje or Indonesian cinnamon) and (*Cinnamomum aromaticum* (Cassia or Chinese cinnamon). The bark of mainly *C. aromaticum* and *C. zeylanicum* enters the trade as cinnamon, although the European Union has labelled *C. aromaticum* as Cassia.

The bark of cinnamon is widely used as a spice. It is used in cookery as a condiment and flavouring material. It is used in the preparation of chocolate, in many desserts recipes (apple pie, doughnuts and cinnamon buns), spicy candies, tea, hot cocoa and liqueurs (especially in Mexico, the main importer of true cinnamon). In the Middle East, it is often used in savoury dishes of chicken and lamb. In the United States, cinnamon (mainly cassia) and sugar are often

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used to flavour cereals, bread-based dishes and fruits. Cinnamon is further used in pickling. Cinnamon powder is used as a spice in Persian cuisine in a variety of thick soups, drinks and sweets. It is also used in 'Sambar powder' or 'BisiBelebath powder' in Karnataka, in India. It has a rich aroma and tastes unique. Cinnamon is used as an insect repellent. It has been found that cinnamon leaf oil is very effective in killing mosquito larvae. The medicinal value of cinnamon is brought about by its anti-microbial, anti-fungal, antiviral, antioxidant, anti-tumour, blood pressurelowering, cholesterol and lipid-lowering, hypoglycaemic and gastro-protective properties. Cinnamon has traditionally been used to treat toothache and fight bad breath and its regular use is believed to stave off the common cold and aids digestion. More than 600 formulations of cinnamon are mentioned in Indian traditional medicine (Ayurveda). It is stated to be useful in conditions such as flatulence, piles, amenorrhoea, diarrhoea, toothache, amoebiasis, heart diseases, fever, cough, cold, headache, etc. but statements are mainly based on folklore with little clinical trials.

This paper aims to provide a comprehensive summary of the scientific literature on the effects of cinnamon species on health centred on its hypoglycaemic activity.

Methodology of search

A database search was carried out using the databases PubMed, Medline and Google Scholar. 'cinnamon', 'cinnamomum', 'cinnamomum zeylanicum', 'cinnamomum cassia', cinnamon combines with 'blood glucose', 'cholesterol', 'hypoglycaemic', 'antimicrobial', 'anti-oxidant', 'anti-tumour', 'lipid lowering', 'cholesterol lowering' and 'diabetes' were the search terms used. The literature search was confined to articles in the English language. Due to inability to access the full articles of some studies, only their abstracts were evaluated.

Published findings

An interest in the therapeutic potential of cinnamon has been growing for almost 20 years (Khan et al. 1990). Both *C. aromaticum* and *C. zeylanicum* possess numerous health benefits. Extensive literature is available on *C. aromaticum* while the biological activities of *C. zeylanicum* have not been studied in any great detail up to now.

Animal studies on unspecified cinnamon

Hypoglycaemic properties

A major problem in the literature is that many publications do not specify the species used. Most of them are related to the anti-diabetic and lipidlowering activities. Khan et al. (1990) have shown the insulin-sensitizing property of 'cinnamon' in the rat epididymal fat cell assay. Berrio et al. (1992) have used the insulin secretary effect of 'cinnamon' to evaluate the influence of bovine serum albumin on insulin activity. According to Jarvill-Taylor et al. (2001) a hydroxychalcone derived from 'cinnamon' could function as a mimetic for insulin in adipocytes. Results of the research conducted by Qin et al. (2003) have suggested that 'cinnamon' extract would improve insulin action via enhancing glucose uptake in vivo at least in part through an insulin signalling pathway in skeletal muscles. Research conducted in 2004 by the same group has suggested that early administration of 'cinnamon extract' to high-fructose diet-fed rats prevents the development of insulin resistance at least in part by enhancing insulin signalling.

Several animal experiments were conducted in 2010 to evaluate the anti-diabetic effects of 'cinnamon'. Ping et al. (2010) have reported that cinnamon oil could significantly reduce the fasting blood glucose in diabetic mice. The effects of 'cinnamon extract' on insulin resistance and body composition have been studied by Couturier et al. (2010) using Wistar rats of induced metabolic syndrome. Their results also concluded that 'cinnamon' alters the body composition in association with improved insulin sensitivity.

Lipid-lowering properties

Ping et al. (2010) have observed significant declines in plasma C-peptide, serum triglycerides, total cholesterol and blood urea nitrogen with a significantly increased serum high-density lipoprotein levels, after 35 days of treatment of 'cinnamon' oil to diabetic mice.

Effects of 'cinnamon extract' on the regulation of plasma levels of adipose-derived factors and expression of multiple genes related to carbohydrate metabolism and lipogenesis in adipose tissue in fructose-fed rats have also been studied (Qin et al. 2010). Results of this study have suggested that cinnamon extract could effectively ameliorate the circulating levels of adipokines partially mediated via regulation of the expression of multiple genes involved in insulin sensitivity and lipogenesis in the epididymal adipose tissue. The effects of 'cinnamon extract' on postprandial apolipoprotein B-48 production in fructose-fed rats and the secretion of apo B-48 in freshly isolated intestinal enterocytes of fructose-fed hamsters have been studied (Qin et al. 2009a,b). The results of this study have shown that cinnamon improves the postprandial overproduction of intestinal apo B-48-containing lipoproteins by ameliorating intestinal insulin resistance and therefore may be beneficial in the control of lipid metabolism. Furthermore, the effect of 'cinnamon extract' on TNFalpha-induced intestinal apo-B-48 overproduction by Qin et al. (2009a,b) have suggested that a water extract of 'cinnamon' reverses TNF-alpha-induced overproduction of intestinal apoB48 by regulating

Animal studies on Cinnamomum aromaticum

Hypoglycaemic properties

Verspohl et al. (2005) have studied the anti-diabetic effect of both cinnamon species *in vivo* and *in vitro*. They have used the bark extracts of both cinnamon species and evaluated the blood glucose and plasma insulin levels in rats. This study has concluded that cassia extract is superior to that of the *C. zeylanicum* extract. They have observed an elevation of insulin secretion by using insulin-secreting cell lines and have concluded the direct anti-diabetic potency of *C. aromaticum* extract.

Kim and Choung (2010) evaluated the antihyperglycaemic and insulin-sensitizing activities of C. aromaticum bark extract in C57BL/Ks db/db mice by measuring the blood glucose levels and serum insulin levels. Results of this study have shown that C. aromaticum extract significantly increases the insulin sensitivity and improves hyperglycaemia.

Lipid-lowering properties

Kim and Choung (2010) have also studied the effects of *C. aromaticum* bark extract on adiponectin levels, serum and hepatic lipids, PPARalpha mRNA expression in liver and PPARgamma mRNA expression in adipose tissue in C57BL/Ks db/db mice. Their study has concluded that *C. aromaticum* extract significantly reduces serum and hepatic lipids and improves hyperlipidaemia possibly by regulating the PPAR-mediated glucose and lipid metabolism.

Other bioactivities

C. aromaticum also exhibits anti-inflammatory and cancer chemo-protective potential. *C. aromaticum* bark extracts has shown potent inhibition of cyclo-oxygenase-2 activity in lipopolysaccharide-induced mouse macrophage cells (Hong et al. 2002). Furthermore, cinnamaldehyde derivatives isolated from the bark of *C. aromaticum* has significantly inhibited lipopolysaccharide-induced nitric oxide production and NF-kappaB transcriptional activity in a dosedependent manner (Lee et al. 2005).

Oussalah et al. (2006) have studied the mechanism of the anti-microbial action of the essential oil of C. aromaticum against cell membranes and walls of bacteria by measurement of intracellular pH and ATP concentration. Results have suggested that the action on the cytoplasmic membrane is involved in the toxic action.

According to Premanathan et al. (2000) *C. aromaticum* bark extract is highly effective against HIV-1 and HIV-2 replication in terms of inhibition of virus-induced cytopathogenicity in MT-4 cells infected with HIV.

Lin et al. (2003) have found that ethanol extracts of dry bark of *C. aromaticum* exhibit a greater inhibition of lipid peroxidation of rat liver homogenate *in vitro* than alpha-tocopherol, high superoxide anion scavenging activity, strong anti-superoxide formation activity (P < 0.05) and excellent antioxidant activity in enzymatic and non-enzymatic liver tissue oxidative systems.

Animal studies on Cinnamomum zeylanicum

Hypoglycaemic properties

Roffey et al. (2006) have found that water extract of *C. zeylanicum* has insulin-mimetic action in adipocytes in terms of glucose uptake. They have used 3T3-L1 adipocytes for their study. However, they have reported that the secretion of adiponectin was adversely affected concurrently.

Subash Babu et al. (2007) have studied the effects of cinnamaldehyde from C. zeylanicum on blood glucose levels of streptozotocin-induced diabetic rats. Bioassay-guided fractionation has been used for isolation and purification of putative compounds. They found a significant decline in plasma glucose and glycosylated haemoglobin. Furthermore, there had been a significant increment in plasma insulin and hepatic glycogen levels after the treatment period. At the same time cinnamaldehyde was able to restore the altered plasma enzyme (aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, alkaline phosphatase and acid phosphatase) levels to near normal levels. This study has confirmed the definite hypoglycaemic effects of C. zeylanicum in STZ-induced diabetic rats.

Effects of cinnamaldehyde from C. zeylanicum on transcriptional regulation of pyruvate kinase, phosphoenolpyruvate carboxykinase and GLUT4 translocation have been studied in experimental diabetic rats (Anand et al. 2010). Oral administration of cinnamaldehyde (20 mg/kg BW) for 2 months significantly improved the hepatic and muscle glycogen content. Further in vitro incubation of pancreatic islets with cinnamaldehyde (CND) has been shown to enhance the insulin release in comparison to glibenclamide. The insulinotropic effect of CND has been found to increase the glucose uptake through glucose transporter (GLUT4) translocation in peripheral tissues. This treatment has also showed a significant improvement in altered enzyme activities of pyruvate kinase and phosphoenolpyruvate carboxykinase and their mRNA expression levels. These results indicate the therapeutic potential of C. zeylanicum as a candidate for the treatment of diabetes.

The ameliorative effect of the cinnamon oil from *C. zeylanicum* on the early stages of diabetic nephropathy has also studied. Cinnamon oil has been extracted by hydro-distillation of the dried bark. The results have shown that cinnamon can confer a dose-dependent significant protection against alloxan-induced renal damage (Mishra et al. 2010).

Lipid-lowering properties

Subash Babu et al. (2007) have further studied the effects of cinnamaldehyde from *C. zeylanicum* on lipid levels of streptozotocin-induced diabetic rats. They have observed a significant reduction in serum total cholesterol and triglyceride levels. Furthermore, there had been a significant increment in plasma high-density lipoprotein-cholesterol levels after the treatment period.

Antioxidant properties

It has been suggested that antioxidant properties of both *C. zeylanicum* and *C. aromaticum* could influence diabetic complications. The polyphenolic compounds found in both species have demonstrated the reduction of oxidative stress in dose-dependent manner through inhibition of 5-lipoxygenase enzyme (Anderson et al. 2004). Dudonné et al. (2009) have also found a high level of antioxidant properties in *C. zeylanicum* and postulated that it would be a good source of natural antioxidants.

Human studies on unspecified cinnamon

It has been reported that ingestion of 6 g of 'cinnamon' bark together with rice pudding has reduced the postprandial blood glucose and gastric emptying rate (GER) in healthy subjects (Hlebowicz et al. 2007).

Human studies on Cinnamomum aromaticum

Hypoglycaemic properties

Khan et al. (2003) have investigated the effects of *C. aromaticum* (finely ground and capsulated bark) on blood glucose levels of the patients with type 2 diabetes. They have included a total of 60 patients in this study. This study has indicated that the intake of 1, 3 or 6 g of *C. aromaticum* per day could reduce serum glucose levels significantly (by 18-29%) after 40 days. They have suggested that inclusion of cinnamon to the diet of the patients with type 2 diabetes would reduce the risk factors associated with diabetes and cardiovascular diseases.

Mang et al. (2006) have studied the effect of cassia on plasma glucose and HbA_1c in type 2 diabetics. They have used an aqueous cinnamon purified extract. For this double-blind study, a total of 79 type 2 diabetic patients who are not on insulin therapy but treated with oral anti-diabetic drugs were included. Their results have indicated a significant difference in the mean absolute and percentages between the preand post-intervention fasting plasma glucose levels of the cinnamon and placebo groups. There had been a significantly higher reduction in the cinnamon group (10.3%) than in the placebo group (3.4%). However, no significant differences were observed regarding HbA₁c concluding a moderate effect of *C. aromaticum* in reducing fasting plasma glucose levels in diabetic patients.

Suppapitiporn et al. (2006) have investigated the effect of cinnamon cassia powder in type 2 diabetic patients. Sixty type 2 diabetic patients were included in this study. The patients were on their conventional metformin and sulphonylurea treatment. The treatment period was for 12 weeks. Their results have indicated that the treatment was ineffective in reducing fasting blood glucose or HbA1c. Vanschoonbeek et al. (2006) have estimated the effects of C. aromaticum supplementation on insulin sensitivity and/or glucose tolerance in 25 postmenopausal patients with type 2 diabetes. The test group has been treated with 1.5 g of cinnamon per day over a period of 6 weeks. This study has concluded that cinnamon supplementation could not improve wholebody insulin sensitivity or oral glucose tolerance in postmenopausal patients with type 2 diabetes.

Furthermore, Blenin et al. (2007) have reported that ingestion of cassia at a dose of 1 g daily for a period of 3 months could not produce any significant change in fasting glucose, HbA₁c or insulin levels. This is reported to be the first study conducted in the United States to evaluate the effect of cinnamon on type 2 diabetes.

Solomon and Blanin (2007) have investigated the effect of cassia on lean healthy male volunteers. They have included only eight male volunteers in this study. It has been found that cassia ingestion (3 g/day) could significantly reduce the total plasma glucose responses to oral glucose ingestion. They have concluded that cassia supplementation may be important to *in vivo* glycaemic control and insulin sensitivity in humans. According to them, its effects are lost following cessation of treatment.

Naturally occurring substances such as chromium and polyphenols have been shown to improve the insulin sensitivity (Anderson 2008). These compounds could exert similar effects on insulin signalling and glucose control (Anderson 2008). Cinnamon polyphenols activate insulin receptors by increasing their tyrosine phosphorylation activity and by decreasing phosphatase activity that inactivates the insulin receptor (Imparl-Radosevich et al. 1998). Based on these facts, Anderson (2008) has suggested that some of the beneficial effects brought about by cinnamon in relation to blood glucose lowering in humans are due to polyphenols in cinnamon.

However, a review article published by Baker et al. (2008) has concluded that cinnamon does not appear

to improve fasting blood glucose or HbA_1c in patients with either type 1 or type 2 diabetes.

Hlebowicz et al. (2009) have re-investigated the effects of 1 and 3 g C. aromaticum on gastric emptying, satiety, and postprandial blood glucose, insulin, glucose-dependent insulinotropic polypeptide, glucagon-like peptide 1 and ghrelin concentrations in healthy subjects. This study has indicated that the ingestion of 3g of cinnamon reduced postprandial serum insulin and increased glucagon-like peptide-1 concentrations without affecting postprandial GER, satiety or blood glucose, glucose-dependent insulinotropic polypeptide, or ghrelin concentrations in healthy subjects. This study has also shown a relationship between the amount of cinnamon consumed and the decrease in insulin concentrations in healthy subjects and concluded that higher doses of cinnamon are required to influence GER and postprandial blood glucose concentrations (Hlebowicz et al. 2009).

Akilen et al. (2010) have conducted a prospective, randomized, placebo-controlled, double-blind clinical trial to determine the effects of cassia powder in type 2 diabetic patients. Fifty-eight type 2 diabetic patients have included in the study. It has been observed that intake of 2 g of cinnamon for 12 weeks could significantly reduce HbA₁c, systolic blood pressure and diastolic blood pressure among poorly controlled type 2 diabetes patients. This study has concluded that cinnamon could be considered an additional dietary supplement option to regulate blood glucose and blood pressure levels along with conventional medications to treat type 2 diabetes.

Lipid-lowering properties

Khan et al. (2003) have investigated the effects of C. aromaticum on lipids of patients with type 2 diabetes. This study has indicated that the intake of 1, 3 or 6g of C. aromaticum per day could reduce serum triglyceride, Low density lipoprotein (LDL) cholesterol and total cholesterol levels significantly. Mang et al. (2006) have also studied the effect of cassia extract on serum lipids in type 2 diabetics. They have found that the treatment with cassia extract could not affect the lipid profiles of type 2 diabetic patients significantly. Suppapitiporn et al. (2006) have also reported that the treatment of cassia powder in type 2 diabetic patients was ineffective in reducing serum lipid levels. Vanschoonbeek et al. (2006) have estimated the effects of C. aromaticum supplementation on lipid profiles in postmenopausal patients with type 2 diabetes. This study has concluded that cinnamon supplementation could not modulate blood lipid profile in postmenopausal patients with type 2 diabetes. Furthermore, a review article published by Baker et al. (2008) has concluded that cinnamon does not appear to improve lipid parameters either in type 1 or type 2 diabetic patients.

Antioxidant properties

The antioxidant effect of cassia extract (a dried aqueous extract) has been analysed in patients with impaired fasting blood glucose that are overweight and obese (Roussel et al. 2009). Twenty-two subjects have been included in this study. The treatment used was 250 mg of cinnamon extract twice a day for a period of 12 weeks. They have measured the plasma malondialdehyde concentration, plasma antioxidant status, erythrocyte Cu–Zn superoxide activity and erythrocyte glutathione peroxidase activity. This study has supported the hypothesis that ingestion of cassia could reduce the risk factors associated with diabetes and cardiovascular diseases due to its antioxidant properties.

Human studies on Cinnamomum zeylanicum

Quale et al. (1996) have conducted a pilot study to investigate the activity of *C. zeylanicum* against fluconazole-resistant and -susceptible *Candida* isolates. They used a small sample size (five patients with HIV infection and oral candidiasis). Subjects had confirmed pseudomembranous candida infection. Patients have been treated with eight lozenges of a cinnamon candy daily and three of the five patients had improvement of their oral candidiasis.

Data of the human studies on the effects of *C. zeylanicum* were not found in relation to hypo-glycaemic and lipid-lowering potentials.

Chemical composition of cinnamon species

Volatile oils obtained from the leaf, bark and root bark of C. zeylanicum and C. aromaticum have reported to be varying significantly in chemical composition. Hence, it is obvious that there must be variations in their pharmacological effects (Wijesekera 1978; Shen et al. 2002). The oils of three different parts of the plant possess the same array of monoterpene hydrocarbons in different proportions. However, in bark oil the primary constituent is cinnamaldehyde which is about 95% in cassia and 40-65% in C. zeylanicum (Wijesekera 1978). According to Chericoni et al. (2005), the other components of the bark of C. zeylanicum are eugenol and linalool with as many as 50 other volatile substances. Cinnamaldehyde and eugenol have also been found to be the major components of cinnamon extract (Usta et al. 2003). The stem bark of C. aromaticum contains in addition cinnamic acid, cinnamyl alcohol and coumarin (Gruenwald et al. 2010).

Cinnamon toxicity due to coumarin

Coumarin is a natural substance, a known phytochemical found in cinnamon, which can cause liver and kidney damage in rats, mice and in a proportion of the human population, when tolerable daily intake (TDI) was exceeded (Lungarini et al. 2008; Woehrlin et al. 2010). TDI for coumarin is 0.1 mg/kg body weight (Abraham et al. 2010). The chemical composition of the *C. zeylanicum* and *C. cassia* is markedly different, with respect to their coumarin levels. According to Miller et al. 1995, coumarin concentration of *C. zeylanicum* is below the detection limit to 190 mg/kg, whereas in cassia the level is 700-12,230 mg/kg.

Discussion

The documented health benefits of cinnamon appear to be its glucose-lowering activity. In addition, cinnamon possesses anti-microbial, anti-fungal, antiviral, antioxidant, anti-tumour, blood pressurelowering, cholesterol and lipid-lowering properties. Research on the anti-diabetic activity of cinnamon extends over a period of 20 years. Much more literature is available on cassia and lesser number of publications are available on C. zeylanicum which is known to be the 'true cinnamon' (endemic Sri Lankan species). Therefore, comparison is difficult. The potential glucose-lowering effect and the underlining pharmacological mechanisms of cinnamon species have been studied in vitro and in vivo animal studies. Almost all the animal models have indicated a pronounced anti-diabetic activity. However, conflicting results were reported with regard to the few clinical trials available. This leaves room for considerable doubt. The variability of results of the available publications could be due to the species used, the sampling techniques (collection, storage and method of grinding, etc.), methodological differences of extractions, differences in the controls used and their glucose-lowering drugs, the cinnamon dose administered, duration of the treatment, the number and type of the patients included and their inclusion and exclusion criteria, baseline blood glucose levels, body mass index that has a bearing on both hypoglycaemic and hypolipidaemic effects and the ethnicity of the patients. Furthermore, the climatic and edaphic features of the point of collection of samples may affect the bioactivity and very often these details have not specified. In the case of C. zeylanicum in Sri Lanka, there are different grades and the bioactivity can be varied with different grades. The ethnicities of patients will naturally give different genetic factors that may influence the effects of cinnamon doses even when all the other parameters are kept well under control. The other major failure in cinnamon research is the absence of dose curves.

Hence, the necessity of evaluating the effects of cinnamon for its therapeutic potentials through a welldefined and adequately randomized controlled clinical trial is emphasized, before recommending cinnamon as an effective treatment for humans.

Conclusion

Based on the evidence in the literature which has a number of details that are not mentioned, it appears that cassia is more potent than *C. zeylanicum* with regard to the lowering of blood glucose and its hypolipidaemic effects. However, clearly triangular clinical trials involving the most popular types of cassia and *C. zeylanicum*, taking all precautions to ensure that the history of sampling, sample preparation and controls are taken into account are needed.

So far the data appear to indicate that cinnamaldehyde may be the key compound in at least some of the bioactivities of cinnamon. This may explain why cassia may appear to be more potent than *C. zeylanicum*. However, *C. zeylanicum* commands a premium price over cassia in export market due to its more rounded flavour.

The recent studies on the relatively high coumarin content of cassia unlike *C. zeylanicum* could also prove to be a deciding factor in some western markets. Therefore, it is also important that the work on coumarin be repeated on all varieties of cassia and all types of barks of *C. zeylanicum* in order to confirm beyond any doubt the advantage of *C. zeylanicum*.

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