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THE UTILIZATION OF CINNAMON (CINNAMOMUM CASSIA) AS A NATURAL MEDICINE FOR DIABETES MELLITUS TYPE 2: SYSTEMATIC REVIEW



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ABSTRACT

Introduction: Diabetes mellitus is a metabolic disorder characterized by high blood glucose levels because the body cannot release or use insulin adequately. Diabetes mellitus has become a health problem whose prevalence continues to increase in society. WHO estimates an increase in the number of people with diabetes mellitus in Indonesia from 8.4 million in 2000 to about 21.3 million in 2030. One of the natural remedies that can be used to lower blood sugar levels is cinnamon (Cinnamomum cassia). Purpose: This systematic review aims to find out the effectiveness of cinnamon use against blood sugar reduction in people with diabetes mellitus. Methods: Journals are derived from electronic databases such as Google Scholar, PubMed and Science Direct, published from 2017 to 2021. Keywords used: cinnamon, diabetes mellitus, and benefits. Discussion: Bioactive content in cinnamon, flavonoids, can lower blood sugar levels by affecting glucose and insulin function in the body. The action mechanism of cinnamon by increasing the sensitivity of insulin receptors includes activating 3-kinase P1 receptors and inhibiting tyrosinfosfatase, increasing the concentration of the fossilized IRS-1 substrate and its binding to 3-kinase PI, activating syntaseglyogen, stimulating glucose uptake, and activating kinase from insulin receptors. Conclusion: After a review of 7 journals, it can be concluded that the administration of cinnamon has the potential to lower blood sugar levels in patients with type-2 diabetes mellitus.

Keywords: Cinnamon, diabetes mellitus type 2, and benefits.

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INTRODUCTION

One of the non-communicable diseases that become a health problem in Indonesia and even in the world is Diabetes Mellitus (DM). The incidence and prevalence of the disease continue to increase especially in developing countries and countries that have entered a culture of industrialization (Arisman, 2013). It is estimated that there are 463 million people in the world in 2019 (aged 20 - 79years) or equivalent to the prevalence rate of 9.3% of the total population at the same age. As the population ages, the prevalence of the disease is expected to increase to 19.9% or 111.2 million people by the age of 65 - 79vears and will continue to increase to reach 578 million in 2030 and 700 million in 2045 (International Diabetes Federation, 2019). In Indonesia, almost all provinces except East Nusa Tenggara showed an increase in prevalence from 2013 to 2018. Yogyakarta, DKI Jakarta, North Sulawesi, and East Kalimantan became the provinces with the highest prevalence in 2013 and 2018 (R&D Agency; Ministry of Health, 2019).

Diabetes Mellitus (DM) is a group of diseases with characteristic metabolic hyperglycemia that occurs due abnormalities of insulin secretion, insulin work, or both (Indonesian Endocrinology Association, 2015). This disease is a serious chronic disease that occurs because the glucose regulatory hormone insulin is not produced sufficiently by the pancreas or when insulin is used ineffectively by the body so that blood glucose levels become high. Generally, diabetes mellitus classified into DM type 1, which is caused

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Received: 02-07-2022 Approved: 17-07-2022 Published: 03-08-2022 by heredity and DM type 2, which is caused by lifestyle. DM type 1 or Insulin Dependent Diabetes Mellitus (IDDM) is insulindependent diabetes. In this type, pancreatic beta cells that under normal circumstances produce the hormone insulin, which is then destroyed by an autoimmune process (Smeltzer & Bare, 2013). Meanwhile, DM type 2 or Non-Insulin Dependent Diabetes Mellitus (NIDDM) is caused by a decrease in insulin resistance or caused by a decrease the amount of insulin formation. Approximately 90-95% of all diabetic patients are people with DM type 2 (Syamsiyah, 2017). The main contributing? factors of DM are obesity and an unhealthy lifestyle that can be overcome by diet and regular exercise (Damayanti, 2015).

Patients with diabetes mellitus often experience complications due to hyperglycemic. These complications are classified into microvascular (retinopathy), kidney (nephropathy), and (dermopathy)) and macrovascular skin disease, (heart infarction, stroke. hypertension, neuropathy, and cardiovascular disease) (Lewis et al., 2011). DM is one of the leading causes of kidney disease and blindness under the age of 65 also amputation (Marshall Flyvbjerg, 2006 in Hill, 2011). Another impact of diabetes is that it can reduce life expectancy by 5 to 10 years. The life expectancy of DM type 2 sufferers with mental illnesses, schizophrenia, is even 20% lower compared to the general population (Goldberg, 2007 in Garnita, 2012). In addition, people with diabetes and their families also suffer economic losses, ranging from components of hospital costs, outpatient care, the cost of insulin analog 1 which is widely prescribed, and loss of jobs and income.

Efforts to control diabetes mellitus are one of the minimum services that must be done by the local government. Every patient with diabetes mellitus will receive services according to the standard at least once a month which includes blood sugar level measurement, education, pharmacological therapy, and referral if needed (Government Regulation No. 2 of 2018, Regulation of the Minister of Home Affairs No. 100 of 2018, and Regulation of the Minister of Health No. 4 of 2019). In addition, the inculcation of healthy living behaviors for the entire

community, including people with risk factors for non-communicable diseases (NCD) and diabetes mellitus, is also encouraged by Presidential Regulation Number 1 of 2017 concerning Community Movement (Germas). With this statement, it is hoped that people with diabetes mellitus can be well-controlled so as to avoid complications and premature death and to reduce the cost burden as well as the prevalence of diabetes mellitus and risk factors. However, DM type 1 cannot be prevented by medical science at this time, while for DM type 2, an effective approach is needed to prevent the risks that will occur. Prevention of complications and severity that occur due to diabetes mellitus can be done with 4 pillars including medicine (pharmacological therapy), regular physical exercise, food planning (diet), and education (Indonesian Endocrinology Association. 2015). One of the natural remedies that can be used to lower blood glucose levels for people with DM type 2 is cinnamon (Cinnamomum cassia).

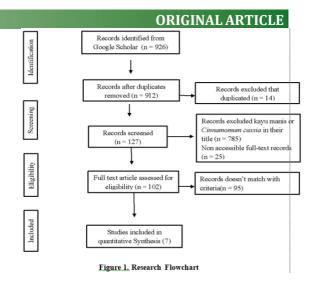
Generally, the treatment of DM type 2 has been done medically using synthetic drugs and insulin injections that have a variety of risks, such as the occurrence of long-term complications and abnormalities of some organs. However, herbal or natural medicine is currently growing rapidly in society. DM type 2 can also be overcome by natural treatment by utilizing nutritious plants, such as cinnamon or Cinnamomum cassia that can be used to lower blood glucose levels. Cinnamon is native to Sri Lanka and grows in Southeast Asia. This plant grows in areas with temperatures of 10-23oC with an altitude of 100-1200 m above sea level. Other cinnamon species such Cinnamomum aromaticum, Cinnamomum verum, Cinnamomum zeylanicum from China, and Cinnamomum burmannii are found in Indonesia, especially in Java and Sumatra (Hermansyah, 2014).

Cinnamon has active ingredient components cinnamate, including cinnamaldehyde, polyphenols, and flavonoids. Some studies said that cinnamaldehyde can increase glucose transport by GLUT 4 in seladiposa and skeletal muscles so as to significantly lower blood glucose (Gaber, 2012). The action mechanism of cinnamon is by sensitivity increasing the of insulin receptors, namely by activating 3-kinase P1

receptors and inhibiting tyrosinfosfatase, increasing the concentration of the fossilized IRS-1 substrate and its binding to PI3kinase. activating syntaseglyogen, stimulating glucose uptake, and activating kinase from insulin receptors. Other content such as polyphenols can activate insulin receptors bv increasing insulin phosphorylase activity and inhibiting tyrosine phosphatase-1 protein (PTP-1) which will decrease insulin receptor activity in adipose tissue (Sangal, 2011). Some in vitro studies have also shown that methlhydroxychalone polymer (MHCP) contained in cinnamon can increase insulin activity more than 20 times compared to other contents. MHCP stimulates insulin autophosphorylation receptor and glucose inhibits the activity uptake, glycogensintase $3-\beta$, and activates glycogensintase. A study conducted by Hardiyani in 2013 showed administration of cinnamon steeping at a dose of 4 g/day for 7 days was able to lower sugar levels in mice-induced localization. It can be concluded that the administration of cinnamon with the right dose and time frame has the potential to lower blood glucose levels in people with DM type 2. This systematic review aims to find out the effectiveness of the use of (Cinnamomum Cassia) cinnamon reducing blood glucose in people with DM type 2.

METHOD

The design used in this study was a systematic review. The journals in this study were obtained from an electronic database published in Google Scholar, PubMed, and Science Direct published from 2017 to 2021. This method was carried out using reviews, studies, structured evaluations, classifications, and categorizations that were previously generated evidence-based. The structure of the keywords in the search is "cinnamon" or "Cinnamomum cassia", "diabetes mellitus", and "benefits". The inclusion criteria in this study are articles of the last 5 years, in English, available in full text, research articles, and administration of cinnamon with the right dose and time period has the potential to reduce blood sugar levels in people with diabetes mellitus.



The number of journals obtained from the Google Scholar database is 926 journals, PubMed is 14, and Science Direct is 95. Doublepublished journals by Google Scholar, PubMed, and Science Direct were instantly selected and deleted. Based on the inclusion criteria, there were 912 journals that met the criteria. The selection was carried out again by looking at the journal titles so that 127 journals were obtained according to the title of this systematic review. Furthermore, the journals were re-selected by looking at the completeness of the journal and the suitability of the journal with the title of a systematic review so that 95 journals were obtained. After being re-selected, the researchers looked at the abstracts from each journal to look at variable indicators, evaluated and selected articles that met the inclusion criteria that showed the potential of cinnamon (Cinnamomum cassia) to reduce the prevalence of diabetes so that 7 journals were obtained. There were 7 journals that met the inclusion criteria found previously.

RESULT

Based on the results of Roghayeh Zare's research in 2018, it can be proven that the administration of cinnamon supplements (500 mg capsules twice a day) to patients with type-2 diabetes mellitus can increase the parameters of anthropometry, glycemic index, and lipid profiles of patients with type 2 diabetes. This benefit is much more prominent in patients with higher BMI (BMI \geq 27). This study is also in line with the results of a study from Azadeh Najarzadeh in 2020 which stated supplementation with one gram a day of cinnamon for three months led to improvements in glycemic indices (FPG and HbA1C) and insulin resistance compared to placebo. All results were improved in patients with wet

syndrome compared to dry syndrome.

Lebin Weng's research (2021) illustrates that onion, cinnamon, and tea blend extracts have potential therapeutic value for the treatment of diabetes in human clinical trials. Polyphenols contained in cinnamon can affect the function of glucose and insulin in the body. Polyphenols will stimulate the auto-fosforization of insulin receptors through increased activity forforization of tirosin and decrease the process of defosphosization??. One of the other components of cinnamon methylhydroxychalcone polymer (MHCP). which is a purification polymer that can stimulate the oxidation of glucose. Based on research, when MHCP enters the cell and interacts with the intracellular part of kinase, MHCP will produce insulin-like properties. In diabetes mellitus, insulin present in the body is reduced, experiencing resistance, and may not even be produced in the body. The presence of insulin-like MHCP seems to replace the work of insulin that is lacking in the body and activate the provision of insulin information.

According to an article from Behrouz Talaei's research (2019) to date, cinnamon is proven to lower blood sugar. The dosage and duration of cinnamon supplementation in the trial varied between 0.5 to 6gr/day for 1 to 4 months. Cinnamon supplementation at a dose of 500 mg/day for three months up to 3gr /day for four months has been found to cause a significant decrease in blood sugar levels.

DISCUSSION

Diabetes mellitus (DM) a disease characterized bv the occurrence of hyperglycemia and impaired metabolism of carbohydrates, fats, and proteins associated with absolute or relatable deficiencies of the work and or secretion of insulin. Symptoms complained of in people with DM are polydipsia, polyuria, polyphagia, weight loss, and tingling. Meanwhile, DM type 2 is a metabolic disorder characterized by a rise in blood sugar due to a decrease in insulin secretion by pancreatic beta cells and or insulin function (insulin resistance). DM type 2 is one of the chronic diseases that has characteristics of hyperglycemia. Hyperglycemia or elevated blood sugar levels are uncontrolled effects of diabetes and in the long run, there can be serious damage to body systems, especially in the blood vessels of the heart that can cause coronary heart disease, in the eyes can cause blindness, in the kidneys can cause kidney failure, and in nerves can occur

stroke (Restyana, 2015).

The American Diabetes Association (ADA) states that DM is associated with irrefiable and irrefiable?? risk factors. Risk factors that can not be changed include family history with DM (first-degree relative), age ≥ 45 years, and the history of giving birth to babies with birth weight of infants > 4000 grams or a history of suffering from gestational DM. Changeable risk factors include obesity where at the rate of overweight BMI \geq 23 can lead to an increase in blood glucose levels to 200 mg??, lack of physical activity, hypertension, dyslipidemia, and an unhealthy diet. Based on International Diabetes Federation (IDF) data in 2011, there are 329 million people in the world with DM type 2 with 4.6 million deaths. Indonesia, in 2011, ranked tenth in the world with the number of DM type 2 sufferers as many as 6.6 million people (IDF, 2011).

DM type 2 in women is higher than in men. Women are more at risk of diabetes because physically women have a greater chance of increasing their body's mass index. Basic Health Research results show the prevalence of DM in Indonesia increased to 57%, in 2012 the incidence of diabetes mellitus in the world is as much as 371 million people, where the proportion of the incidence of DM type 2 is 95% of the world population who suffer from diabetes mellitus and only 5% of the number have DM type 1 (Restyana, 2015). A study conducted by Kusniawati (2011) on self-care conducted in one of the hospitals in Indonesia, mentioned that selfcare is still not biased done by DM type 2 patients. The 4 domains in self-care, DM type 2 patients do not obey in terms of treatment due to the saturation factor. Similarly, when it comes to diet control, when at home, DM type 2 patients are unable to control their diet. DM type 2 patients are also unable to perform regular foot care due to a lack of knowledge about foot care. Patients also rarely do physical exercise (Kusniawati, 2011).

Treatment of diabetes mellitus disease has been carried out with medical and clinical treatment with the consumption of drugs. Prolonged use of the drug can cause side effects on the health of other organs, such as the kidneys. Based on this, it is necessary to find alternative treatments that are safe, cheap, and easy to get, namely through herbal medicine derived from plants. One of the herbal plants that are believed to lower blood sugar is cinnamon. Cinnamon is a dried bark derived from a tree of the genus Cinnamonum (Ghofar, 2012).

From the results of the seventh systematic review of the journal, it can be known that cinnamon can decrease blood sugar levels in diabetics. The content of flavonoids in cinnamon works by increasing glucose metabolism and converting glucose into energy. The process increases the sensitivity of cells to insulin so that blood glucose levels decrease. The cinnamon plant is an alternative in the healing of DM disease because this plant contains chemical compounds such as safrole, essential oil eugenol, tenin, cinnamaldehyde, resin, potassium oxalate and tanner, as well as flavonoids (Hastuti, 2014). Based on the results of research conducted by Hananti (2012), stated that cinnamon bark ethanol extract dose of 50, 100, and 200 mg/kg bb?? is able to decrease blood glucose levels in male mice induced glucose 2 g/kg bb?? with glucose tolerance test method. Decreased blood glucose levels are caused by the presence of flavonoid compounds that can increase the sensitivity of β-pancreatic cells to release insulin (Hananti, 2012).

The results of the linear regression test conducted by Syafriani and Besti in 2017 showed that there is a significant influence in the administration of the cinnamon extract to decrease blood sugar levels. The results showed that there was a decrease in respondents' blood sugar levels after cinnamon extract intervention, which is 37,75 mg/dl, which blood glucose levels before intervention by 263.40 mg/dl and after the intervention of 225.65 mg/dl. The results of this study are also in line with research conducted by Ramadhona (2016) in the working area of the Public health center (Puskesmas) Pauh Padang City in 2015. Based on the Paired T-Test test there was a decrease in blood sugar levels of patients with DM type 2 before and after the administration of steeping cinnamon powder with a value of p 0.000. This indicates that the administration of cinnamon can lower blood sugar levels of patients with DM type 2.

CONCLUSION

DM type 2 is diabetes caused by a decrease in insulin resistance or caused by a decrease in the amount of insulin formation. The main factors that cause it are obesity and an unhealthy lifestyle. People with diabetes mellitus often have complications due to hyperglycemic and life expectancy reduction by 5 to 10 years. Prevention of complications and severity that occur due to diabetes mellitus type 2 disease can be done

by changing lifestyle to a healthy one and using natural remedies, for example, cinnamon (Cinnamomum cassia). Bioactive content in cinnamon, flavonoids, can lower blood sugar levels by affecting glucose and insulin function in the body. The action mechanism of cinnamon by increasing the sensitivity of insulin receptors, namely activating 3-kinase P1 receptors inhibiting tyrosinfosfatase, increasing the concentration of the fossilized IRS-1 substrate and its binding to 3-kinase PI, syntaseglyogen, activating stimulating glucose uptake, and activating kinase from insulin receptors. Based on the results of a systematic review. consumption cinnamon in people with type 2 diabetes mellitus can be used as an alternative solution to reduce blood glucose levels.

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ORIGINAL ARTICLE

Table 1. Extraction Results Data

Title	Author	Method	Respondent/ Sample	Research Site	Research Results	Conclusion
A Nutraceutical Combination of Cinnamon, Purple Onion, and Tea Linked with Key Enzymes on Treatment of Type 2 Diabetes.	Lebin Weng, Ting- Hsu Chen, Liyue Huang, Dong Lai, Yaw-Syan Fu, Ching- Feng Weng.	Experimentation and analysis of statistics with oral glucose starch tolerance test	Mice with high-fat diabetes.	Xiamen Medical College, China.	Compared to acarbose, a mixture of extracts (purple onions, cinnamon, and tea) is indicated lower blood glucose in oral starch tolerance test. In oral glucose tolerance test, the extract mixture showed greater efficacy for hypoglycemia when compared to metformin.	Decrease in blood glucose with a combination extract of cinnamon, shallot diet, and tea, involves prospective nutraceuticals that may improve hyperglycemia in diabetes.
Analysis of The Effectiveness of Cinnamon (Cinnamomum verum) in The Reduction of Glycemic and Lipidic Levels of Adults with Type 2 Diabetes	José Claudio Garcia Lira Neto, MDa, Marta Maria Coelho Damasceno, PhDa, Márcia Aparecida Ciol, PhDb, Roberto Wagner Junior Freire de Freitas, PhD, Márcio Flávio Moura de Araujo, PhD, Carla Regina de Souza Teixeira, PhDd, Gerdane Celene Nunes Carvalho, PhDe,	Quantitative research method with <i>pre-experimental</i> design of one group test and statistical analysis	130 type-2 diabetes mellitus patients	Parnaíba, Piauí state, Brazil.	After 3 months of administration of cinnamon capsules (placebo), obtained: (1) Decreased lipid levels (LDL cholesterol, triglycerides, and total cholesterol); (2) Increase HDL cholesterol levels. (3) Reduction of anthropometry measurements.	Cinnamon can be used as an alternative or supplement the drug in cases where only oral antidiabetic agents are used. Its use can minimize the occurrence of complications of diabetics.

GINAL ARTICLE	V Waldin J					
	Kenya Waléria de Siqueira Coelho Lisboa, PhDf, Danilo Ferreira de Souza, MDg, Jéssica de Menezes Nogueira, PhDh, Regina Lucia Lino Marques, Ana Maria Parente Garcia Alencar Phd.					
The Effects of Cinnamon on Diabetes Mellitus.	Behrouz Talaei, Shohreh Bahreini.	Methods of literature studies and journal reviews from PubMed, Web of Science, Science Direct, and Google Scholar (2006-2017).	Cinnamon (Cinnamomum sp).	Kerman University of Medical Science, Iran.	Supplementation cinnamon at a dose of 500 mg/day for three months to 3gr/day for four months was found to cause a decrease in blood sugar levels significantly.	The use of cinnamon as an anti-diabetes therapy may potentially lower blood sugar levels, but depending on population differences, dosage range, dosage form, and duration of treatment.
Simultaneous Natural Deep Eutectic Solvent- Based Ultrasonic- Assisted Extraction of Bioactive Compounds of Cinnamon Bark and Sappan Wood as a Dipeptidyl Peptidase IV Inhibitor.	Islamudin Ahmad, Ayun Erwina Arifianti, Aditya Sindu Sakti, Fadlina Chany Saputri, and Abdul Mun'im	Research method and experimentation by conducting In Vitro Dipeptidyl Peptidase IV Activity Assay and In Silico Molecular Docking Analysis.	Cinnamon bark (Cinnamomum burmannii) and sappan wood (Caesalpinia sappan).	Faculty of Pharmacy, University of Indonesia.	The results showed that NADES (with choline composition Extraction of chloride-glycerol) from cinnamon and sappan wood has DPP IV inhibition activity of 205.0 and 1254.0 µg/mL.	Extraction of NADES-based choline chloride-glycerol from cinnamon bark and sappan wood has DPP IV inhibition activity. However, cinnamon bark (trans cinnamaldehyde, coumarin, and trans-cinnamic acid) has no significant DPP IV inhibitory activity.
Efficacy of Cinnamon in Patients with Type II Diabetes Mellitus: A Randomized Controlled Clinical	Roghayeh Zare, Azadeh Najar zadeh, Mohammad Mehdi Zarshenas, Altar Shams, Mojtaba Heydari.	The research method with randomized clinical trials was controlled using a parallel design.	140 patients with type 2 diabetes mellitus.	Yazd University of Medical Sciences, Iran.	Cinnamon supplementation leads to an increase in all anthropometry and lipid yield (Total Cholesterol, LDL-c,	Cinnamon can increase the parameters of anthropometry, glycemic index and lipid profile of patients with diabetes type 2, especially in patients with higher initial

				ORICINAL AR	TICLE	
Trial				ORIGINALA	and fDL-c) (except triglyceride levels). All changes are observed (except for Total Cholesterol and LDL-c).	BMI (BMI ≥ 27).
Effects of Cinnamon Consumption on Glycemic Indicators, Advanced Glycation End Products, and Antioxidant Status in Type 2 Diabetic Patients	Behrouz Talaei, Atieh Amouzegar, Shamim Sahranavard, Mehdi Hedayati, Parvin Mirmiran, Fereidoun Azizi	Experimental Research Methods are randomized, double-blind.	44 patients with type 2 diabetes mellitus aged ± 57 years.	Iran	Results showed three grams of cinnamon supplements in patients had no beneficial effect on FPG, insulin glucose levels, HbA1c, HOMA-IR, carboxymethyl lysine, total antioxidant capacity, and MDA after eight weeks of intervention.	It was concluded that the 8-weeks-intervention as much as three-gram cinnamon supplements per day have no beneficial effect on FPG, insulin levels, HbA1c, HOMA-IR, lysine carboxymethyl, total antioxidant capacity, and MDA levels.
Analysis of the Efficacy of Cinnamon for Patients with Diabetes Mellitus Type II Based on Traditional Persian Medicine Syndrome Differentiation: A Randomized Controlled Trial	Roghayeh Zare, Altar shams, Mojtaba Heydari, Azadeh Najarzadeh, Mehdi Zarshenas.	The trial method was a randomized, triple- blindly, placebo- controlled trial based on a parallel design.	140 patients with type-2 diabetes mellitus	Yazd University of Medical Sciences, Iran.	Glycemic index increased in patients receiving cinnamon supplementation compared to the placebo group (-13.1 ± 1,7, -1.7 ± 1.9, P <0.001 for FPG change and -0.27 ± 0.039 vs. 0.001 ± 0.019, P<0.001 for changes respectively in HbA1C).	In this study, supplementation with one gram a day of cinnamon sausage for three months led to improvements in glycemic index (FPG and HbA1C) and insulin resistance compared to placebo. All results were improved more in patients with wet <i>syndrome</i> compared to <i>dry syndrome</i> .



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