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Possible Benefits of the *Coriandrum sativum* in the Management of Diabetes in Animal Model: A Systematic Review

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Abstract

Diabetes mellitus (DM) is a group of a metabolic disease characterized by chronic hyperglycemia and disturbances of carbohydrate, lipid, and protein metabolism, resulting from defects in insulin secretion, or action or both. DM caused at least 12% of global health expenditure is spent on diabetes ($ USD 673 billion). The control of diabetes with fewer side effects is a challenge. Authors have reported that herbal medicine would be an alternative to manage DM. *Coriandrum sativum* (Coriander) is a plant that has been used in the management of the diabetes. The purpose of this study was to review the published research concerning the use of coriander in the treatment of DM in animal models using a database. The papers were searched in the PubMed. It was verified a strong interest in studies involving diabetes. It is also observed that about 6.92% of the articles with the keyword "*Coriandrum sativum*" are related to diabetes. Five studies have reached the inclusion criteria to be analyzed. In all these investigations a reduction of the plasma level of glucose was detected in the animals treated with coriander. In conclusion, putting together the findings described in this study and considering the results in the publications, it is possible to conclude and to suggest that the use of coriander could be suitable to try to decrease plasma glucose level of diabetic animals. However, it is important to consider the limited number of publications available in the PubMed involving searches evaluating the antidiabetic effect of coriander.

Keywords: *Coriandrum sativum*; Diabetes; PubMed; Experimental model; Glucose

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Introduction

Diabetes mellitus (DM) is a group of a metabolic disease characterized by chronic hyperglycemia and disturbances of carbohydrate, lipid, and protein metabolism, resulting from defects in insulin secretion, or action or both [1,2]. There are mainly three forms of diabetes: Type 1 DM, Type 2 DM, and gestational diabetes [3]. Briefly, Type 1 DM results from the body's failure to produce insulin; Type 2 DM is due to insulin resistance, and gestational diabetes develops during pregnancy [4]. The International Diabetes Federation (IDF) predicts that 415 million people world-wide have diabetes and by 2040 this will rise to 642 million. It is also predict that 77% of people with diabetes live in low- and middle-income countries. DM caused at least 12% of global health expenditure is spent on diabetes ($ USD 673 billion) [5]. The control of diabetes with fewer side effects is a challenge

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[6]. Due the increasing prevalence of the disease, the significant morbidity associated with diabetic complications [7] and the side effects associated with the use of insulin and oral hypoglycemic agents, there is an increasing demand by patients to use natural products with antidiabetic activity [8], through their free radical-scavenging activity [9].

Increased free radical generation and oxidative stress play an important role in the pathogenesis of DM and its late complications. In DM the efficiency of the antioxidant properties is altered. Antioxidants act against the free radicals and protect the human body from various diseases [10]. Ramadan et al. [11] have reported that DM is associated with overproduction of free radicals and diminution of antioxidants. Free radicals mediate activation of signal transduction cascades and transcriptional factors leading to expression of specific genes that produces tissue damage and ultimately to diabetes complication [12]. Several studies have revealed that a strong part of the antioxidant activity may be found in chemical compounds such as flavonoids, flavones, isoflavones, anthocyanin, catechin, and other phenolic compounds [13,14].

Authors have reported that herbal medicines are good source of antioxidants [15,16]. In addition, medicinal plants have been used in various countries in the treatment of various diseases [17,18], as the diabetes [19-21]. One of these is *Coriandrum sativum* (Coriander) [19].

Coriandrum sativum (Coriander) is a plant that has been used in the management of the diabetes [22,23]. It is an herbaceous plant originally from the Mediterranean and Middle Eastern regions, belonging to family *Apiaceae* [24]. Furthermore, it is successfully grown in a wide range of conditions [25]. It is cultivated for its aromatic leaves and seeds in North Africa, Central Europe and Asia as a spice and medicine [26]. There is a large number of compounds isolated from coriander, including flavonoids (quercetin and isoquercetin), polyphenols (rutin, caffeic acid derivatives, ferrulic acid, gallic acid and chlorogenic acid), β -caroteinoids, anethole, borneol, camphene, camphor, carvone, cineole, citronelol, coriandrol, coriandrin, coumarins and hydroxy-coumarins (umbelliferone and scopoletin). Furthermore, the p-cymene, euginol, geraniol, geranyl acetate, limonene, d (+)-linalool, myrcene, α- and β-phellandrene, α- and β -pinenes, α - and γ -terpinene, 5- and 8-methoxypsoralens, tannins, and many others [27-29].

Coriander is known to possess antifungal, antibacterial [30], free radical scavenging, and lipid per oxidation activities [31]. In traditional medicine, it is used for the treatment of diabetes, gastrointestinal complications such as dyspepsia, flatulence, diarrhea, vomiting [32] and as an antiseptic and emmenagogue [33].

Some authors have demonstrated the antidiabetic effect of coriander [12,19,22,23]. Therefore, the purpose of this study was to review the published research concerning the use of coriander in the treatment of DM in animal models using a database. Considering the findings described in the literature, it is hypothesized a decrease of the glucose in the diabetic animals treated with coriander.

Methods

Search strategy and selection of the studies

This systematic review of scientific studies followed the guidelines of the *Transparent Reporting of* Systematic Reviews and Meta-Analyses (PRISMA statement) [34]. One database was systematically searched for experimental trials *in vivo* and *in vitro*. The papers were searched in the PubMed, (http://www.ncbi.nlm.nih.gov/pubmed) on January 15th, 2016. The search was performed using the keyword "*Coriandrum sativum*" and diabetes.

Inclusion and exclusion criteria

A systematic selection of the articles was carried out by three independent examiners based on the following inclusion criteria: (i) Biological activity: antihyperglycemic or antidiabetic activity of *Coriandrum sativum*; (ii) Plant material: extract from *Coriandrum sativum*; (iii) Study design: experimental trials *in vitro* and/or *in vivo* (with coriander and diabetic animals); (iv) Language: articles written in English. In addition, ethnobotanical and ethnopharmacological surveys, case reports, expert opinion or consensus statements were excluded, as those have used *Coriandrum sativum* mixed with other product.

Table 1 Number of publications (database PubMed) involving "*Coriandrum sativum*" and diabetes.

Keyword	Number of publication
Coriandrum	302
"*Coriandrum sativum*"	231
Coriander	475
"*Coriandrum sativum*" AND diabetes	16
"*Coriandrum sativum*" AND "diabetes mellitus"	9
Coriander AND diabetes	17
Coriander AND "diabetes mellitus"	9
Diabetes	533 489
"Diabetes mellitus"	387 100

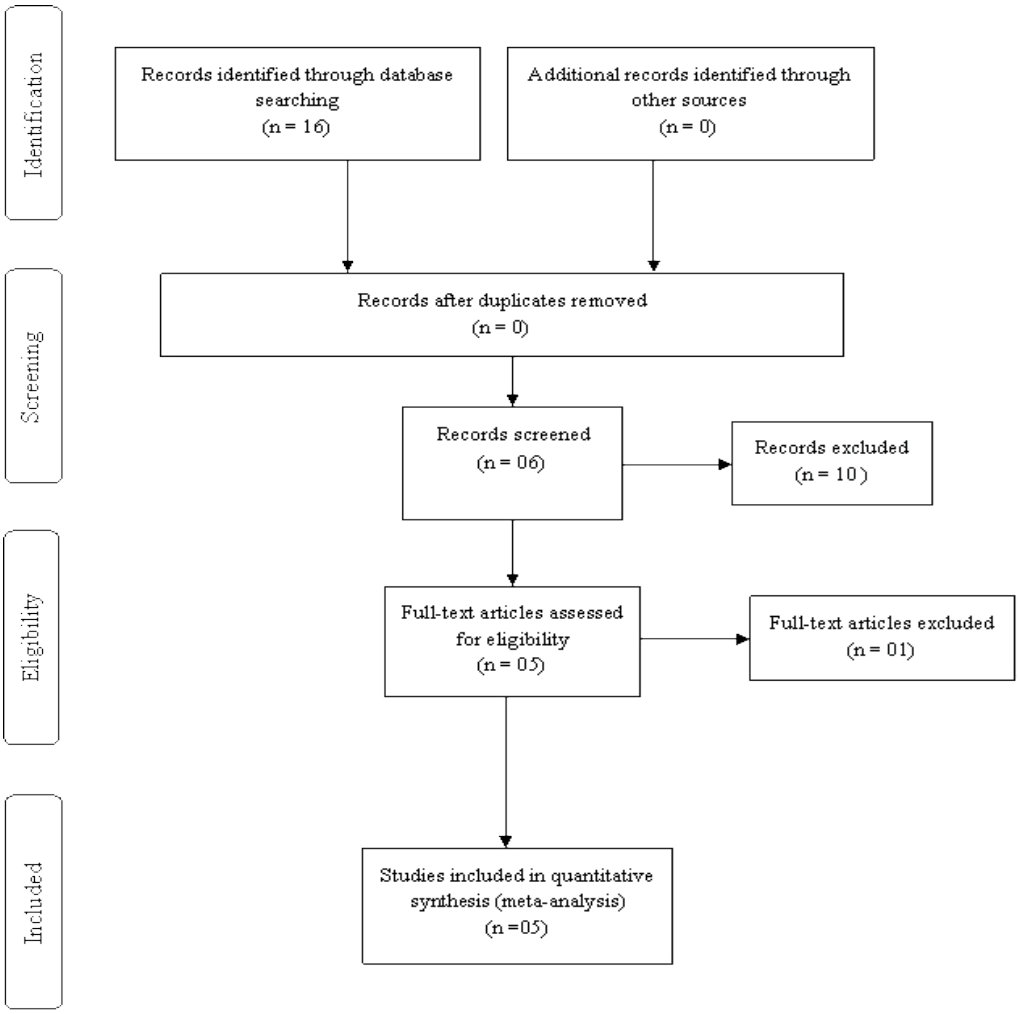

Figure 1 Flow diagram of the search strategy comprising the identification of potentially relevant material, and preliminary screening and final selection of the studies included in this review (based on PRISMA statements).

Table 2 Information about the animals and plant material used on the selected studies.

		Animal			*Coriandrum sativum* (CS)	
Animal used	**Number**	**Weight**	**Age**	**Source**	**Preparation of the extract**	**Reference**
Rat	30	150-180 g	N/I	in natura	Coriander leaves and stem (450 g) were finely chopped before extraction with aqueous ethanol (80%) for 24 h. After the removal of the solvent in vacuo, the crude extract (18 g) was suspended in distilled water and extracted with 150 mL portions of ethyl acetate until the extracts were nearly colorless. Solvents were removed in vacuo, and the yield of 6.5 g and 4.4 g, respectively, were obtained.	[22]
Rat	18	120-150 g	12-14 weeks	in natura	CS was ground into a fine powder. 50 g of the seed powder was suspended in distilled water (500 mL) and heated to boil under reflux for 30 min. The decoction obtained was centrifuged, filtered, frozen at −20 °C and lyophilized to give a residue (yield = 10% w/w).	[19]
Rat	24	180-200 g	7-8 weeks	commercial	The seeds were ground into a fine powder. Powder material (1 g) was boiled for 30 min in 40 ml cold distilled water-cooled. This suspension was filtered and the volume was made up to 40 ml with distilled water	[12]
Rat	30	200-250 g	N/I	in natura	60 g of dried ground seeds was extracted with 300 mL ethanol (80%). After extraction, the mixture was filtered and evaporated to give a final weight of extract of 5 g.	[35]
Mice	10-14	N/I	N/I	commercial	Dried leaves of CS was supplied as infusions prepared by adding 1 g of plant material to 400 ml of boiling water and infusing for 15 min.	[36]

N/I – Non informed, CS - *Coriandrum sativum*

Results

Table 1 shows the number of publications searched in the PubMed involving the keywords coriander and diabetes. It is possible to verify a strong interest in studies involving diabetes. It is also observed that about 6.92% of the articles with the keyword "*Coriandrum sativum*" are related to diabetes.

According to a previously set strategy, literature searches resulted in 16 articles. Five publications met the inclusion criteria and were included in the final review after thorough analysis **(Figure 1).** It is possible to see in **Table 2** that there is a predominance of trials with rats, more than with mice. The number of animals used in these studies varied from 10 up to 30 and the weight body follows a variation between 120-250 g. Despite not having information of the age of the animals in all the studies, it is possible to verify the range is 7-14 weeks considering two studies [12,19]. Furthermore, most of works use coriander collected in natura, which have influence in the method of preparation of the extract, when compared the process with coriander obtained from commercial source.

It is possible to see in **Table 3** the diabetes induction procedure, protocol experimental, outcomes and conclusion. The three different procedures of diabetes induction: (i) by a single intra-peritoneal (i.p) injection of Streptozotocin (STZ), (ii) a single i.p of Alloxan monohydrate and (iii) submitted to a Hypercaloric diet. Overall, the majority of studies in this review (60%) tested STZ, followed in lower proportions by Alloxan and Hipercaloric diet studies (20% each). The studies have shown a very similar protocol, with a control group, an induced-diabetic group and a group treated with coriander. Three of the five studies used a standard antidiabetic drug (Glibenclamide, GLZ) as positive control. All the studies observed an antidiabetic activity of coriander.

It is possible to see in **Table 4** the influence of the treatment of animals with diabetes with extract of *Coriandrum sativum* in the plasma profile of some biomarkers. In all the five studies was observed an antidiabetic activity of coriander, decreasing the blood glucose level. Two studies [12,35] reported an increase on plasma insulin level of animals treated with coriander. Sreelatha

Table 3 Diabetes induction procedure, protocol experimental, outcomes and conclusion.

Induction of diabetes	Protocol	Outcomes	Conclusion	Reference
Alloxan	Control Diabetic control (150 mg/kg) Alloxan+ CS Leaf extract (200 mg/kg) Alloxan+ CS Steam extract (200 mg/kg) Alloxan Glibenclamide	The leaf and stem extract of CS showed a significant reduce in the blood glucose levels and blood lipids as the total cholesterol, TC, VLDL, LDL	The data obtained in this study point out that CS leaves and stem possess a significant antidiabetic effect.	[22]
Hipercaloric diet	Control (Water) Diabetic and Normal rats -Baseline -6 h post-dose CS-extract (20 mg/kg) Diabetic and Normal rats -Baseline -6 h post-dose Glibenclamide (2.5 mg/kg) Diabetic and Normal rats -Baseline -6 h post-dose	CS-extract group reduce the blood glucose levels from Diabetic rats (highly significant) and normal. In addition, decrease the lipids levels and insulin resistance in Diabetic rats.	This study demonstrates that administration of CS in diabetics rats normalized glycemia and decreased the elevated Insulin Resistance, levels of insulin, total cholesterol, LDL-cholesterol, and triglycerides and could decreased hyperglycemia as well as prevent or reduce Cardiovascular complications.	[19]
Streptozotocin	Control Streptozotocin (45 mg/kg) STZ + CS (10 g/100 g feed) Control + CS (10 g/100 g feed)	The CS produced significantly decrease in blood glucose levels and significantly increase in plasma insulin level and reduction in glycated hemoglobin, when compared with diabetic rats.	The results indicate that coriander seeds possess beneficial action on kidney and pancreas.	[12]
Streptozotocin	Control STZ + CS (100 mg/kg) STZ + CS (200 mg/kg) STZ + CS (250 mg/kg) Glibenclamide (600 µg/kg)	The CS extract at doses of 100, 200 and 250 mg/kg significantly decreased serum glucose. In addition, increased the insulin releasing activity.	The results have shown that CS possesses a hypoglycaemic effect on Streptozotocin-induced hyperglycemic rats and thus validates to some extent the folk use of this plant.	[35]
Streptozotocin	Control + Agrimony or Alfalfa or Coriander or Eucalyptus or Juniper. STZ (200 mg/kg) + Agrimony or Alfalfa or Coriander or Eucalyptus or Juniper.	Treatment with coriander consistently lowered mean values for basal plasma glucose concentrations in the diabetic mice.	This study suggests that treatment with CS does not significantly affect plasma insulin concentrations.	[36]

Table 4 Effects of *Coriandrum sativum* in some blood biomarkers.

Biomarkers	*Coriandrum sativum* effects	References
Glucose	Decrease	[12,19,22,35,36]
Plasma Insulin Level	Increase	[12,35]
Total Cholesterol	Decrease	[22]
HDL- cholesterol	Increase	[22]
LDL- cholesterol	Decrease	[22]
VLDL- cholesterol	Decrease	[22]
Triglycerides	Decrease	[22]

and Inbavalli, [22] have pointed out an improvement on blood lipid profile.

Discussion

The investigations about diabetes mellitus have relevant due to various clinical disorders associated with this disease, as well as the cost involved with its management [5]. These considerations justify the elevated number of publications in PubMed with the keywords diabetes or diabetes mellitus **(Table 1).** The relevance of the experimental models with natural products that could be used in the management of diabetes reveals the importance of the coriander **(Table 1).** About 6.92% of the publications with the keyword "*Coriandrum sativum*" involve diabetes. Five studies have reached the inclusion criteria to be analyzed. In all these investigations a reduction of the plasma level of glucose was detected in the animals treated with coriander. Due the side effects associated with the use of insulin and oral hypoglycemic agents, there is an increasing demand by patients to use natural products with antidiabetic activity [8]. Coriander have stood out as a promising natural source with relevant effects in treatment of diabetes [19,22], despite the small number of publications in the PubMed database involving the keyword *Coriandrum sativum* AND diabetes, as shown in **Table 1.**

Following, the findings of the selected papers are discussed. The procedures to prepare the extract of the coriander are different due the source of this medicinal plant (commercial or in natura) **(Table 2).** Certainly, it would be preferable, if and when possible, to compare studies homogeneous in terms of species and age of animals. As it was shown in **Table 2**, two species of animal with different ages and weights were used in the studies. The main findings of the selected papers reveal the importance of the coriander in improving the clinical conditions of the diabetic animals.

The current study has several limitations that must be considered in the interpretation of the findings in this systematic review [36]. It is suggested to take care in generalizing these results due to the analyzed publications have methodological variations concerning to the specie of the animals, the kind of source of *Coriandrum sativum*, type of the protocols. In addition, although we tried to retrieve the articles following the selected keywords, it may not be sure that it was retrieved all the papers identified for inclusion, including articles that were not published in English and articles published in journals that were not indexed in the PubMed database.

Although it possible to verify limitations in this study, it was verified that considering the publications that were analyzed, all of them have reported a decrease in blood glucose level of the diabetic animals due to the treatment with an extract of *Coriandrum sativum*. The reason of these results may be due to the higher rate of glycolysis, probably by the high activity of hexokinase and phosphoglucomutase, two of the key enzymes of glycolysis, that are increased in the liver of animals administered with coriander [37].

Conclusion

Putting together the findings described in this study and considering the results in the publications, it is possible to conclude and to suggest that the use of coriander could be suitable to try to decrease plasma glucose level of diabetic animals. However, it is important to consider the limited number of publications available in the PubMed involving searches evaluating the antidiabetic effect of coriander.

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