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The availability and validity of safety information of over the counter herbal products for use in diabetes in Sri Lanka: A cross sectional study

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ABSTRACT

Aims: There is an increase of over-the-counter (OTC) herbal products for use in diabetes mellitus. The aim of this study is to evaluate the safety information provided with OTC herbal remedies intended for diabetic patients in Sri Lanka and to assess the completeness of the information provided. **Methods:** Inclusion criteria consisted of OTC herbal remedies meant for use in diabetes. They were bought from local Sri Lankan supermarkets and non-ayurvedic pharmacies and product information regarding the risk of hypoglycemia, precautions for use, adverse events, dose, and interactions were assessed using a scoring system. The accuracy of the information was then compared against published data. **Results:** 11 products fulfilled the inclusion criteria. Five products contained a single constituent and five contained more than one. None had complete and accurate safety information according to our criteria. None specifically warned against the risk of hypoglycemia. 9 out of 11 products (81.8%) carried ≤3 items of the five essential factual information we expected. Hypoglycemic coma, gastrointestinal symptoms, hepatotoxicity, carcinogenesis, and interactions causing elevated drug levels of Carbamazepine were some of the safety information that was missing. **Conclusions:** Key safety information was absent in most products. Regulation of sale, provision of key safety information and adverse event reporting should be a priority.

KEY WORDS: Complementary and alternative medicine, diabetes mellitus, herbal remedies, safety information

INTRODUCTION

Diabetes mellitus is a major cause of morbidity and mortality worldwide with an increasing prevalence. The WHO estimates a prevalence of 347 million people with diabetes worldwide in 2013 [1].

There is an emerging trend worldwide for patients with chronic illnesses such as diabetes to use complementary and alternative medicine (CAM) in an attempt to improve the outcomes of their illnesses. Biologic therapies such as herbal remedies are popular [2], and can broadly be divided into commercialized over-the-counter (OTC) preparations and preparations that are locally sourced and prepared.

Consumers of commercially available herbal products need access to reliable and accessible information to ensure safe and appropriate use. This should preferably be in the form of printed material supplied alongside the product, similar to what's available with conventional medications [3]. This is particularly important, as it has been shown that the staff knowledge on the products sold in community pharmacies and health food shops is sub-optimal elsewhere [4]. In addition, there appears to be reluctance on the patient's part in informing about herbal remedies to their respective physicians. One UK study found that a vast majority did not inform their physicians regarding herbal use [5]. In India, 59.9% of CAM users were not willing to disclose CAM use to their physician [6]. In Taiwan, 75.4% did not disclose CAM use [7]. This is of critical importance as many unrecognized interactions may occur between herbal remedies and conventional medicines. Similarly, many patients believe that herbal products are safe and devoid of adverse effects [8].

Although there is an absence of data for Sri Lanka, these observations may be valid locally as well.

To enable the appropriate and safe use of OTC herbal products, availability of relavant information to the consumer is essential. Particularly information on precautions, adverse events and interactions with conventional medications is critical. Although sale and use of conventional medicine are well regularized globally, herbal medicines (HM) are still largely sold without registration or regulatory supervision.

The European Medicines Agency (EMA) Committee on HM products implemented the development of community

herbal monographs for herbal products in 2004. Community herbal monographs collected scientific data on two aspects of a product, namely the well-established use and traditional use. For some plants, the monograph covers the well-established use, as well as traditional use. Traditional use indication gives credentials to a plant based on its long history of traditional use, well-established use indication also implies innovation and research on a plant [9].

This key directive adopted by the European Parliament in (Directive 2004/24/EC 2004) 2004 enabled the non-prescription use of traditional medicines following assessment of suitability. An important outcome of this was a sharp increase of the HM registrations from 2 in 2005 to 265 in 2012 [9]. The existence of such a legal framework is critical in registering products based on scientific evidence and well-established safety. However, at consumer level there should be legislation or industry concurrence in making available information to the consumer that enables its safe and effective use.

In most instances, herbal products tend to be registered with their respective regulatory authorities under the "traditional use" category as opposed to the "well-established" category, which is more evidence-based. Although there is some evidence of efficacy for few HM, most lack readily reproducible evidence of efficacy, sufficient to meet regulatory standards [3,9]. Further, insufficient research is generated within the use of these medications to make them more likely of obtaining regulatory standards [9].

Nevertheless, the UK sets a valuable example by requiring products registered as traditional herbal registration (THR) to carry essential safety information in the form of a leaflet [10]. In 2011, Raynor *et al*. reported that in the UK the majority (93%) of OTC herbal products were unlicensed [3].

The World Health Organization traditional medicines strategy of 2002 [11] also highlighted the need for reliable information as a key item to enable the safe and effective use of traditional medicines. In 2003, the WHO addressing the use of HM in developing countries strongly recommended the implementation of national advisory committees and guidelines on herbal remedies. It further emphasized the need of a body for monitoring adverse drug reactions for HM [12].

At present, there is no legislative framework for registering or regulating the use of OTC herbal products in Sri Lanka.

Essential information that would enable safe use of herbal products includes (1) precautions, (2) interactions, and (3) adverse events such as allergic reactions.

Very few published research studies are available on the safety related issues in dispensing and use of HM.

In a previous publication, we reported a high prevalence of herbal remedy use among Sri Lanka diabetic patients [13]. These were locally sourced plants that were prepared at home. However, at present, herbal remedies are commercially marketed as capsules, tea bags and syrups, targeting the Sri Lankan diabetic population. There is no published data on the type of products and whether they provide essential information on safe use to consumers.

The aim of this study is to critically evaluate the safety information provided with OTC herbal remedies intended for use among diabetic patients in Sri Lanka and to assess the completeness of the information provided.

MATERIALS AND METHODS

We performed a cross-sectional survey between 20th June and 31st July 2014, using the printed and internet-based information provided with the OTC herbal products in two major cities in Sri Lanka.

Obtaining the Products

Samples of commercially available OTC herbal remedies intended for use by diabetic patients fulfilling the inclusion criteria were bought from supermarkets and pharmacies in the cities of Colombo and Kandy, Sri Lanka. The 2 cities were selected on convenience of access. Six supermarkets were visited ensuring that at least one outlet from each chain of supermarkets in these cities was included. The 10 pharmacies were randomly selected from the city centers of both cities, from a total of 96 that dispensed western medicines and OTC herbal products. When products were bought from supermarkets, those fulfilling the inclusion criteria were picked off the shelves. When products were procured from pharmacies, the authors requested for OTC products intended for use by diabetes patients for glycemic control to the pharmacy staff and those that fulfilled the inclusion criteria were selected. Inclusion criteria included labeling stating, use for diabetes, being of herbal origin and availability as an OTC product.

These products were then re-scrutinized to confirm adherence to inclusion criteria once they were purchased. Herbal products that stated diabetes as the sole indication, as well as those that mentioned diabetes as an indication among others were also included.

In Sri Lanka, ayurvedic medicine is a separately registered stream of practice with its own regulatory authority for practice and sale of medication. Pharmacies that dispense ayurvedic medicines are distinct from those dispensing conventional medications. We intentionally did not include products available at the ayurvedic pharmacies, as it was not our intention to scrutinize the safety of herbal products dispensed in these, but rather the safety of those available to the general public as OTC herbal products.

Evaluation Criteria

The labeling, the package insert and where available websites appearing on the label were scrutinized to gather information about the product. The manufacturer, the active ingredient (s), precautions for use, adverse effects, interactions, indication for use, dose and duration, preparation of the product (tablet, powder, liquid, tea bag, etc.) were recorded as stated by the manufacturer.

We assessed each product to see if they carried information on (1) warning of possible hypoglycemia, (2) Information on adverse events, (3) precautions for use, (4) interactions and, and (5) dose recommendations. A point was awarded for each category of information provided and a score out of 5 was used to assess the completeness of the safety information.

Each category of information (e.g., adverse events) provided for each individual product was then compared against published data to assess if the information provided was complete and accurate.

At present, there is no complete and authoritative reference available to gather information on herbal products. Natural Medicines Comprehensive Database [14], Stockley's HM interactions [15], The EMA [16], the US National Centre for CAM [17] and online searches on PUBMED using constituent names were used for cross-referencing the information. However, it has to be borne in mind that natural products do not conform to the same stringent scrutiny in relation to adverse event reporting, interactions, etc., as conventional medications and many clinically significant events, therefore, may not be on record at present. We limited our search for adverse events and interactions to those reported in humans.

Accuracy was checked by cross-referencing the stated information against the published data stated above. If all parameters were supplied and were accurate, the product was categorized as complete and accurate.

RESULTS

Product Analysis

Eleven products that fulfilled the inclusion criteria were bought from the local supermarkets and pharmacies and analyzed. The manufacturer was mentioned in all the products. Five products contained a single constituent and five more contained more than one. One product failed to mention its constituent(s). Five were marketed as an herbal drink, 3 as herbal tea, 1 as herbal syrup and 2 products were in capsule form. All products stated in the labeling that they were intended for glycemic control. In addition to glucose control, 7 products mentioned additional indications for use; these included diabetic neuropathy, enhancement of memory and cure of circulatory problems.

Package inserts were available in 5/11 (45%) products. Nine products (81.8%) carried telephone numbers or a website for help regarding the product.

Utilizing our scoring system, 9/11 (81.8%) products scored ≤3 on the presence of essential safety information. 2 (18.1%) products scored 4/6.

Table 1 illustrates the summary of the products and the completeness of the safety information.

A complete list of the constituents and their frequency in the products are tabulated in Table 2.

Assessment of Safety Information

None of the products had complete and accurate safety information according to our criteria. None specifically stated the risk of hypoglycemia. However, 2 products containing bitter gourd advised patients on regular blood glucose monitoring. Information regarding adverse events was available in only 3 (27%) of the products. Interactions were mentioned in only 1 (8.1%) product. Precautions for use were mentioned by 5 (45%) products. Pregnancy and lactation, heartburn and age <18 years were some mentioned. The dose was mentioned in all the products, but the duration for use was not mentioned in any. One product contained nutritional information of its contents. The amount of each constituent in weight or volume was mentioned in only 2 products. Details of adverse events and precautions for use as given by the manufacturer are given in Table 1.

When the information provided under different categories were assessed for accuracy against published data, none of the products carried information that was accurate and complete. Reported adverse events and interactions of the key constituents of the products are summarized in Table 3.

DISCUSSION

Diabetic patients use CAM with the expectation of improving their blood glucose levels [2]. Patients should be able to expect full disclosure of safety information on purchasing herbal products [18]. Most patients perceive less adverse events from herbal products than from conventional medicines [8]. However, most diabetic patients use herbal therapies in conjunction with conventional medications raising the possibility of interactions [13].

The products we examined, which were specifically marketed for use among diabetic patients contained little or no information on precautions for use, the risk of developing hypoglycemia, interactions or adverse events.

Adverse event information was available in only 3 (27.2%) products. Since most of the products studied contained more than one constituent [Table 1], the situation is complex in adverse event reporting. Ideally, the manufacturer should mention adverse events for any of the constituents contained in the product. Cinnamon, which was a constituent of two products is known to contain Coumarins [19]. Coumarins are hepatotoxic and carcinogenic, and Cinnamon already carries a caution from health authorities against prolonged and continued use [20]. Fenugreek taken orally can cause mild gastrointestinal disturbances like diarrhea, dyspepsia, abdominal bloating and flatulence [21]. Black seed (*Nigella sativa*) may cause hepatotoxicity in animals, but clinical evidence is lacking [22]. *In vitro* studies have shown inhibition of platelet aggregation, making bleeding a possibility with black seed oil [23]. However, no clinical evidence is available at present. Bitter gourd is known to cause abdominal cramps in some [24]. Dans *et al*. reported the incidence of hypoglycemic coma in children given bitter melon tea [25].

Table 1: Summary of the products, product information provided and the score depicting completeness of the safety information

Product number	Type of product	Number of constituents (n)	Hypoglycemic potential mentioned	Adverse events mentioned (captioned from product)	Interactions (captioned from product)	Precautions mentioned	Dose mentioned (yes=Y, no=N)	Score out of 5
1	Herbal drink	7	No	Yes (devoid of adverse events)	Not mentioned	None	Yes	2
2	Capsules	1	No	No	Not mentioned	Caution in pregnancy gastritis	Yes	2
3	Herbal drink	8	No	No	No mentioned	Caution in pregnancy, lactating mothers, people <18 years	Yes	2
4	Herbal syrup	NA	No	No	Not mentioned	None	Yes	1
5	Herbal tea	2	No	No	Available (none)	None	Yes	2
6	Herbal tea	1	No	No	Not mentioned	None	Yes	1
7	Herbal drink	1	No	No	Not mentioned	None	Yes	1
8	Herbal drink	1	No	No	Not mentioned	None	Yes	1
9	Herbal drink	13	Blood glucose monitoring advised	Yes (Heart burn)	Not mentioned	Caution in non-diabetics, pregnancy, age <12 years, presence of heart burn	Yes	4
10	Capsules	2	No	No	Not mentioned	Caution in pregnancy	Yes	2
11	Herbal tea	1	Blood glucose monitoring advised	Yes (devoid of adverse events)	Not mentioned	Caution in pregnancy	Yes	4

Table 2: Complete list of the constituents and their frequency of inclusion in the products

Constituents		Number of products
Common name	Scientific name	
Tanner's cassia	*Cassia auriculata*	4
Kothala himbutu	*Salacia reticulata*	3
Black tea	*Camellia sinensis*	3
Ceylon cinnamon	*Cinnamomum zeylanicum*	2
Black seed oil	*Nigella sativa*	2
Black plum	*Eugenia jambolana*	2
Indian gooseberry	*Phyllanthus emblica*	2
Bitter gourd	*Momordica charantia*	2
Guduchi	*Tinospora cordifolia*	1
Yellow vine	*Coscinium fenestratum*	1
Java grass/nut grass	*Cyperus rotundus*	1
Wood apple	*Aegle marmelos*	1
Lemon grass	*Cymbopogon citratus*	1
Indian sarsaparilla	*Hemidesmus indicus*	1
Ivy gourd	*Coccinia grandis*	1
Bush passion fruit	*Passiflora foetida*	1
Beleric	*Terminella berelica*	1
Indian fig	*Ficus racemosa*	1
Weeping fig	*Ficus benjamina*	1
Devil's thorn	*Tribulus terrestris*	1
Sickle wild sensitive plant	*Cassia tora*	1
Indian lilac	*Azadirachta indica*	1
Arjuna (tree)	*Terminalia arjuna*	1
Balloon plant	*Cardiospermum halicacabum*	1
Fenugreek	*Trigonella foenum-graecum*	1

Some clinically relevant adverse events and interactions of selected herbal constituents are given in Table 3. Unfortunately, none of these published adverse events were included in the manufacturer's product information. The absence of a formal method for reporting adverse events, non-recognition of adverse events by patients and clinicians and the small sample sizes of previous studies further confound the situation.

None of the products specifically cautioned the user against the possibility of hypoglycemia. Two products, however, recommended frequent blood glucose monitoring. Most of the individual constituents of each product had published evidence of their potential to lower blood glucose. Cinnamon has the largest pool of evidence to date [26]. *Selacia reticulata* has evidence for inhibition of intestinal alpha glucosidase and may have clinical significance in reducing postprandial and fasting plasma glucose (FPG) values [27-29]. Evidence of efficacy for bitter melon is similar with some studies showing improvements in FPG and postprandial plasma glucose [30,31]. Although a common constituent of many anti-diabetic herbal products, Tanners cassia (*Cassia auriculata*) has not been studied widely in humans. Although it has hypoglycemic effects in experimental rat models [32] evidence for safety and efficacy in humans is not available.

As the hypoglycemic potential of the commonly used herbal constituents is evidence backed, we believe an appropriate warning on hypoglycemia is essential with these products. Previous studies have demonstrated that CAMs are often used alongside conventional hypoglycemic agents [7,13,33] probably increasing the risk of a serious hypoglycemic event.

Only 1 (8.1%) product had information on interactions. Interactions may occur with the conventional medications or within herbal constituents where more than one constituent is present. Only 4 products had a single constituent whereas 6 products contained at least 2 constituents. Tanners Cassia the constituent in 4 of the products studied is known to cause significant elevation of Carbamazepine levels with continued use [34].

The commonest precautions stated were use during pregnancy and in individuals less than 18 years.

Using the scoring system we devised, 9/11 products (81.8%) had ≤3 items of the essential items of safety information. Only 2 products (18.1%) had 4 items of information, and none had complete and accurate information.

Table 3: Reported adverse events and interactions of commonly used selected constituents

Constituent		Number of products	Reported adverse events/interactions	Mentioned in product-(Y) or not- (N)
Common name	Scientific name			
Tanner's cassia	*Cassia auriculata*	4	Elevated levels of carbamazepine [34]	N
Ceylon cinnamon	*Cinnamomum zeylanicum*	2	Potential for hepatotoxicity and carcinogenesis based on coumarin levels [19]	N
Black seed oil	*Nigella sativa*	2	*In vitro*: Inhibition of platelet aggregation: No reported clinical evidence [23]	N
Bitter gourd		2	Hypoglycemic coma [24] Abdominal pain [25] Diarrhoea [25]	N
Fenugreek	*Trigonella foenum-graecum*	1	Dizziness [25] Increased urinary frequency [24] Diarrhoea [21] Dyspepsia [21] Hypokalaemia [24]	N

Raynor *et al*., studying 68 preparations of 5 commonly purchased OTC herbal products in the UK found that three-quarters of these preparations contained no safety information and only 3 preparations had complete information [3]. Two-thirds of the products failed to mention interactions.

A study performed in Canada revealed that consumers expect pharmacy staff to be knowledgeable about herbal products [35]. However, others have recognized that pharmacists where herbal remedies are commonly sold lack knowledge regarding herbal products. There is also evidence that most consumers need help from the pharmacy staff to select a suitable herbal product [3]. Therefore, the presence of crucial product information is essential to ensure safe dispensing and use.

Most of the databases or texts cited as references [14-17] contained little or no information on the types of herbal products available in the Sri Lankan market. This study provides the evidence supporting to strengthen the regulation of HM locally. The need for developing a sound database, establishing regulatory authority for products that target a specific population of patients should, therefore, take priority considering the number of individuals who consume these products. In Sri Lanka, complementary remedies were used by 76% [13], in India by 67% [36] and in Malaysia by 48% [2] of diabetes patients. In the western countries the prevalence of use varied between 30% and 57% [37]. In Sri Lanka, all the patients studied continued to use their conventional medications together with herbal use.

The implementation of the "Directive 2004/24/EC" - So called, "traditional HM products directive" resulted in most member countries accepting it with a sharp increase in the registration of herbal products from 2 in 2005 to 265 in 2012 [9].

There seems to be a welcome trend globally toward uniform registration and safe use of traditional herbal remedies. In Brazil, proposed legislation seeks to separate HM into two categories: HM and traditional herbal product. In 2004, the UK created the new category of THR with a 7-year grace period for all the herbal remedies to be registered under this scheme. This scheme required the consumer to be presented with a leaflet similar to that found on conventional registered products [10] detailing product information that would enable safe use. A similar strategy needs to be adopted by Sri Lanka if safe practice of herbal therapies were to be implemented.

European directive of 2004 allows a non-EU product to be registered if an HM has been in use for a minimum period of 15-year in the EU. Alternately, generating scientific evidence favoring a product may be used to obtain registration [38]. Creation of herbal product monographs in the EU has largely simplified the registration of products enabling them to be registered under "well-established use" or traditional use. A similar method of product registration can be utilized in Sri Lanka for products with long-standing history of traditional use, thereby simplifying the process of registration through which legislation can be implemented to promote safe use. In the United Kingdom where herbal medications needed to be registered as THR, 85% of the expected safety information was found to be included within the product [3]. While these legislative measures would regularize registration, sale, and consumer issues to a large extent, still there would be natural remedies that would not fall within the purview of licensed or regulated products such as garlic, which have been traditionally called food supplements [3].

Strengths and Limitations

The strength of this study is that it opens up a new field of research regarding the provision of safety information together with herbal products. Limitations include the limited number of herbal products available to us through supermarkets and pharmacies allowing only 11 products to be analyzed. Although there is no data on the purchasing patterns of this community with regard to herbal products, we believe our mode of sampling reflects the pattern of the community studied.

CONCLUSION

There is a definite deficiency in providing key safety information of the products we studied. At present, Sri Lanka lacks a sound system for OTC herbal product registration and regulation. Since the use of these medications in Sri Lanka is common,

it is essential that legislation be enacted to make essential safety information be available in printed form and to set up a regulatory body for product registration and monitoring. Education of the public and conventional medical practitioners may also enable safe use of OTC herbal products.

AUTHORS' CONTRIBUTIONS

AM conceptualized the study, collected the samples, analyzed the data and wrote the manuscript.
HW: Collected the samples and analyzed the data.
TP: Collected the samples and analyzed the data.

REFERENCES

1. World Health Organization. WHO Diabetes Fact Sheet No 312. Available from: http://www.who.int/mediacentre/factsheets. [Last accessed on 2013 Oct 2015].
2. Ching SM, Zakaria ZA, Paimin F, Jalalian M. Complementary alternative medicine use among patients with type 2 diabetes mellitus in the primary care setting: A cross-sectional study in Malaysia. BMC Complement Altern Med 2013;13:148.
3. Raynor DK, Dickinson R, Knapp P, Long AF, Nicolson DJ. Buyer beware? Does the information provided with herbal products available over the counter enable safe use? BMC Med 2011;9:94.
4. Cramer H, Shaw A, Wye L, Weiss M. Over-the-counter advice seeking about complementary and alternative medicines (CAM) in community pharmacies and health shops: An ethnographic study. Health Soc Care Community 2010;18:41-50.
5. Vickers KA, Jolly KB, Greenfield SM. Herbal medicine: Women's views, knowledge and interaction with doctors: A qualitative study. BMC Complement Altern Med 2006;6:40.
6. Bhalerao MS, Bolshete PM, Swar BD, Bangera TA, Kolhe VR, Tambe MJ, *et al.* Use of and satisfaction with complementary and alternative medicine in four chronic diseases: A cross-sectional study from India. Natl Med J India 2013;26:75-8.
7. Chang HY, Wallis M, Tiralongo E. Use of complementary and alternative medicine among people with Type 2 diabetes in Taiwan: A cross-sectional survey. Evid Based Complement Alternat Med 2011;2011. pii: 983792.
8. Hasan SS, See CK, Choong CL, Ahmed SI, Ahmadi K, Anwar M. Reasons, perceived efficacy, and factors associated with complementary and alternative medicine use among Malaysian patients with HIV/AIDS. J Altern Complement Med 2010;16:1171-6.
9. Cranz H, Anquez-Traxler C. TradReg 2013: Regulation of herbal and traditional medicinal products – European and global strategies – International Symposium. J Ethnopharmacol 2014;158:495-7.
10. Herbal Medicines. Available from: http://www.webcitation.org/query.php?url=http://www.mhra.gov.uk/Howweregulate/Medicines/Herbalmedicines/index.htm&refdoi=10.1186/1741-7015-9-94. [Last accessed Oct 2015].
11. WHO Traditional Medicines Strategy 2002-2005. Available from: http://www.whqlibdoc.who.int/hq/2002/who_edm_trm2002.1.pdf%5D. [Last accessed Oct 2015]
12. World Health Oganization. Guidelines for the Regulation of herbal MedicinesIn the South-East Asia Region. New Delhi: World Health Organization Office for South East Asia; 2003.
13. Medagama AB, Bandara R, Abeysekera RA, Imbulpitiya B, Pushpakumari T. Use of complementary and alternative medicines (CAMs) among Type 2 diabetes patients in Sri Lanka: A cross sectional survey. BMC Complement Altern Med 2014;14:374.
14. Natural Medicines Comprehensive Database. Available from: http://www.naturaldatabase.com. [Last accessed Oct 2015].
15. Williamson EM, Driver S, Baxter K, editors. Stockley's Herbal Medicines Interactions. 2nd ed. London, UK: Pharmaceutical Press; 2013.
16. Agency EM. Community herbal monographs. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000212.jsp&mid=WC0b01ac058003380a.
17. Herbs at a glance. Available from: https://www.nccih.nih.gov/health/herbsataglance.htm. [Last accessed Oct 2015].
18. Routledge PA. The European herbal medicines directive: Could it have saved the lives of Romeo and Juliet? Drug Saf 2008;31:416-8.
19. Wang YH, Avula B, Nanayakkara NP, Zhao J, Khan IA. Cassia cinnamon as a source of coumarin in cinnamon-flavored food and food supplements in the United States. J Agric Food Chem 2013;61:4470-6.
20. European Food Safety Association. Coumarin in flavourings and other food ingredients with flavouring properties. EFSA J 2008;793:1-15.
21. Gupta A, Gupta R, Lal B. Effect of *Trigonella foenum-graecum* (fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes mellitus: A double blind placebo controlled study. J Assoc Physicians India 2001;49:1057-61.
22. Tennekoon KH, Jeevathayaparan S, Kurukulasooriya AP, Karunanayake EH. Possible hepatotoxicity of *Nigella sativa* seeds and *Dregea volubilis* leaves. J Ethnopharmacol 1991;31:283-9.
23. Awad EM, Binder BR. *In vitro* induction of endothelial cell fibrinolytic alterations by *Nigella sativa*. Phytomedicine 2005;12:194-202.
24. Medagama AB, Bandara R. The use of complementary and alternative medicines (CAMs) in the treatment of diabetes mellitus: Is continued use safe and effective? Nutr J 2014;13:102.
25. Dans AM, Villarruz MV, Jimeno CA, Javelosa MA, Chua J, Bautista R, *et al.* The effect of *Momordica charantia* capsule preparation on glycemic control in type 2 diabetes mellitus needs further studies. J Clin Epidemiol 2007;60:554-9.
26. Medagama AB. The glycaemic outcomes of Cinnamon, a review of the experimental evidence and clinical trials. Nutr J 2015;14:108.
27. Koteshwar P, Raveendra KR, Allan JJ, Goudar KS, Venkateshwarlu K, Agarwal A. Effect of NR-Salacia on post-prandial hyperglycemia: A randomized double blind, placebo-controlled, crossover study in healthy volunteers. Pharmacogn Mag 2013;9:344-9.
28. Jayawardena MH, de Alwis NM, Hettigoda V, Fernando DJ. A double blind randomised placebo controlled cross over study of a herbal preparation containing *Salacia reticulata* in the treatment of type 2 diabetes. J Ethnopharmacol 2005;97:215-8.
29. Medagama AB. *Salacia reticulata* (Kothala himbutu) revisited; a missed opportunity to treat diabetes and obesity? Nutr J 2015;14:21.
30. Ahmad N, Hassan MR, Halder H, Bennoor KS. Effect of *Momordica charantia* (Karolla) extracts on fasting and postprandial serum glucose levels in NIDDM patients. Bangladesh Med Res Counc Bull 1999;25:11-3.
31. Welihinda J, Karunanayake EH, Sheriff MH, Jayasinghe KS. Effect of *Momordica charantia* on the glucose tolerance in maturity onset diabetes. J Ethnopharmacol 1986;17:277-82.
32. Gupta S, Sharma SB, Bansal SK, Prabhu KM. Antihyperglycemic and hypolipidemic activity of aqueous extract of *Cassia auriculata* L. leaves in experimental diabetes. J Ethnopharmacol 2009;123:499-503.
33. Khalaf AJ, Whitford DL. The use of complementary and alternative medicine by patients with diabetes mellitus in Bahrain: A cross-sectional study. BMC Complement Altern Med 2010;10:35.
34. Thabrew I, Munasinghe J, Chackrewarthi S, Senarath S. The effects of *Cassia auriculata* and Cardiospermum halicacabum teas on the steady state blood level and toxicity of carbamazepine. J Ethnopharmacol 2004;90:145-50.
35. Kwan D, Boon HS, Hirschkorn K, Welsh S, Jurgens T, Eccott L, *et al.* Exploring consumer and pharmacist views on the professional role of the pharmacist with respect to natural health products: A study of focus groups. BMC Complement Altern Med 2008;8:40.
36. Kumar D, Bajaj S, Mehrotra R. Knowledge, attitude and practice of complementary and alternative medicines for diabetes. Public Health 2006;120:705-11.
37. Bell RA, Suerken CK, Grzywacz JG, Lang W, Quandt SA, Arcury TA. Complementary and alternative medicine use among adults with diabetes in the United States. Altern Ther Health Med 2006;12:16-22.
38. Qu L, Zou W, Zhou Z, Zhang T, Greef J, Wang M. Non-European traditional herbal medicines in Europe: A community herbal monograph perspective. J Ethnopharmacol 2014;156:107-14.

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