Functional herbal food ingredients used in type 2 diabetes mellitus

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ABSTRACT

From many reports it is clear that diabetes will be one of the major diseases in the coming years. As a result there is a rapidly increasing interest in searching new medicines, or even better searching prophylactic methods. Based on a large number of chemical and pharmacological research work, numerous bioactive compounds have been found in functional herbal food ingredients for diabetes. The present paper reviews functional herbal food ingredients with regards to their anti-diabetic active principles and pharmacological test results, which are commonly used in Asian culinary system and medical system and have demonstrated clinical or/and experimental anti-diabetic effectiveness. Our idea of reviewing this article is to give more attention to these functional food ingredients as targets medicinal foods in order to prevent or slow down the development of type 2 diabetes mellitus.

Key words: Anti-diabetic, functional herbal food, type 2 diabetes mellitus

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a global epidemic with an estimated worldwide prevalence of 6% (246 million people) in 2007, and forecast to rise to 7.3% (380 million) by 2025.[1] The health, social, and economic burden is great;[2,3] consequently, T2DM presents a major challenge to healthcare systems around the world.

Based on current understanding of the pathophysiology of T2DM, multiple pharmacological and non-pharmacological interventions have been developed over the past five decades with the aim of improving glycemic control and hopefully slowing disease progression.[4] To an extent, there has been some disappointment, in that most of the observed initial improvements in glycemic control are not sustained because of the progressive nature of the disease.[5,6] With the presence of more approaches to improve glycemic control using treatments, the target on food conservation for people becomes even more important.

This article particularly explores the demonstrated clinical or/and experimental anti-diabetic functional food ingredients that prevents or slows down the development of T2DM. Especially T2DM requires the adoption and maintenance of multiple self-care behaviors to achieve and sustain glycemic control. These behaviors include monitoring blood glucose, exercising regularly, and adhering to a recommended eating regimen. Eating is a major aspect of daily living, one that may influence the development of diabetes and its subsequent progression.[7] Therefore we suggest that it is important to pay close attention to these review functional food ingredients for preventive and curative of T2DM and its complications.

TYPE 2 DIABETES

Most patients, previously called as non-insulin-dependent diabetes mellitus (NIDDM), belong to this category. In this type, the mass of pancreatic β cells and their function are preserved to some extent, and insulin injection is seldom needed to sustain life.[8,9] Ketoacidosis could occur, however, in the presence of severe infection or other stress. This type also decreases insulin secretion and decreased insulin sensitivity (insulin resistance) is involved in its pathogenesis. Insulin resistance may not always be present. The relative role of these two factors varies between patients. With regard to insulin secretion, the acute insulin response to a glucose load is characteristically defective. The majority of patients is obese or has been obese in the past.

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Typically, this type of diabetes develops after middle age, but may occur in younger people. Screening by urinalysis of large numbers of schoolchildren has revealed that T2DM has been steadily increasing since the 1970s.[10]

Complimentary medicine aspects of diabetes

Nowadays, besides conventional approaches, comprehensive complementary medicine (CAM) modalities are attaining more and more popularity in the world.[11] More than 2000 years ago, symptoms such as polyuria and polydipsia were regarded as important morbid manifestations in ancient China and some other parts of the world, which spurred people to learn about diabetes.[12,13] It has long been utilized across the long Chinese history to treat a complex of symptoms, which manifests the disease of "diabetes mellitus" as Western medicine terms it.[14,15] Thus the ancient disease "wasting thirst" (xiao-ke), which probably equates to the term "diabetes" in Western medicine, was formed in that special way.[16] T2DM was recognized as xiaokezheng (a disease with symptomatic polydipsia) in ancient China.[17]

Symptoms that included polyuria and polydipsia were described in the Egyptian Ebers papyri, Greek Epidemics Book III of Hippocrates, and the Chinese Nei Ching.[18,19] Hindu writings in the Ayurvedic texts used these same symptoms and others including glucosuria and the smell of breath acetone to differentiate two main types of diabetes mellitus: One inherited and another acquired through obesity.[20] Recorded treatments for these disorders included largely diet- and plant-based remedies.[20,21]

Concepts of functional foods

The term "functional food" was first introduced in Japan in the mid-1980s and refers to foods containing ingredients that aid specific bodily functions in addition to being nutritious.[22] Generally, they are considered as those foods intended to be constituted as part of a normal diet, and that contain biologically active components, which offer the potential of enhanced health or reduced risk of disease.[23]

Research has demonstrated that nutrition plays a crucial role in the prevention of chronic diseases like diabetes, as most of them can be related to diet.[23] Functional food enters the concept of considering food not only necessary for living but also as a source of mental and physical well-being, contributing to the prevention and reduction of risk factors for several diseases or enhancing certain physiological functions.[24] A food can be regarded as functional if it is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects, in a way which is relevant to either the state of well-being and health or reduction of the risk of a disease. The beneficial effects could be either maintenance or promotion of a state of well-being or health and/or a reduction of risk of a pathologic process or a disease.[25] The increasing interest in functional food reflects the fact that epidemiological studies indicating a specific diet or component of the diet is associated with a lower risk for a certain disease like diabetes.

Functional herbal food ingredients used in diabetes

Allii Sativi Bulbus

The bulbs of *Allium sativum* L., has a very long folk history of use in a wide range of ailments. It is also alleged to help regulate blood sugar levels. It can reduce glucose metabolism in diabetics, slows the development of arteriosclerosis and lowers the risk of further heart attacks in myocardial infarct patients.[26] Garlic has been found to be effective in lowering serum glucose levels in STZ-induced as well as alloxan-induced diabetic rats and mice. Most of the studies showed that garlic can reduce blood glucose levels in diabetic mice, rats, and rabbits.[27] Aged garlic extract was also effective in preventing hyperglycemia in mice hyperglycemic by immobilization stress.[28] In addition, Liu *et al* 2005 reported that both garlic oil and diallyl trisulfide improved glycemic control in STZ-induced diabetic rats.[29] Intake of garlic juice resulted in better utilization of glucose in glucose tolerance tests performed in rabbits, while allicin at a dose of 250 mg/kg was 60% as effective as tolbutamide in alloxan-induced diabetic rabbits.[30]

Mechanism of garlic has previously suggested that allicin can enhance serum insulin by effectively combining with compounds like cysteine, which would spare insulin from SH group reactions that are a common cause of insulin inactivation.[30] Another mechanism proposed that the antioxidant effect of S-allyl cysteine sulfoxide, an isolated product from garlic, may contribute to its beneficial effect in diabetes.[31] Another researcher postulated that garlic may act as an antidiabetic agent by increasing either the pancreatic secretion of insulin from the β cells or release of bound insulin.[32] Therefore the hypoglycemic action of garlic could possibly be due to an increase in pancreatic secretion of insulin from β cells, release of bound insulin or enhancement of insulin sensitivity [Figure 1].

Allii Cepa Bulbus

The bulbs of *Allium cepa* L. or common onion has a long history of medicinal and culinary use.[33] Also it has been used for many centuries for their pungency and flavoring value, for its medicinal properties.[34] Many people in Asian and African countries use plants for the treatment of diabetes.[35] Onion feeding improved the metabolic status in diabetic conditions, probably because of hypoglycemic and hypo-cholesterolemic effect,[36] mediated diabetic nephropathy by lowering blood cholesterol levels and decreasing lipid peroxidation.[37] Its active principles showed that allyl propyl disulfide and S-methyl cysteine sulfoxide have an anti-diabetic and anti-hyperlipidemic effect, the latter being analogous to glibenclamide and insulin [Figure 2].[38-40]

Trigonella foenum-graecum (L.)

Trigonella foenum-graecum L. (fenugreek) is cultivated throughout India and in certain regions of China. Its seeds are used as condiment in India, a supplement to wheat and maize flour for bread-making in Egypt, and one of the staple foods in Yemen. Its seeds are also used as herbal medicine in many parts of the world for their carminative, tonic, and aphrodisiac effects. Various reports have demonstrated that fenugreek seeds extracts, powder, and gum of seeds and leaves can lower blood glucose

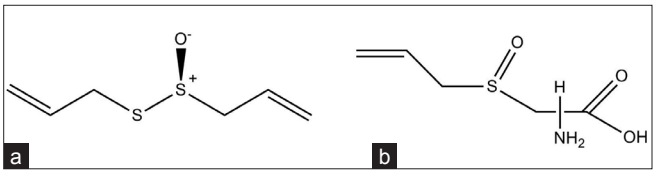

Figure 1: Chemical components in Allium sativum L. which involve in anti-hyperglycemic activity. (a) Allicin; (b) S-allyl cysteine sulfoxide

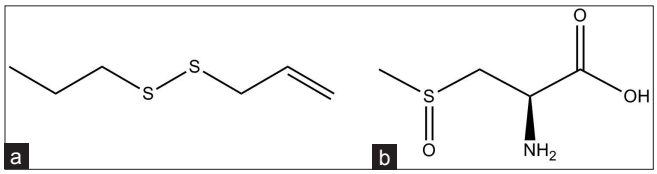

Figure 2: Chemical components in Allium cepa L. which involve in anti-hyperglycemia. (a) Allyl propyldisulfide; (b) S-methyl cysteine sulfoxide

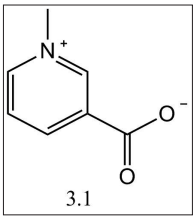

Figure 3: Chemical components in Trigonella foenum-graecum L. which involve in anti-hyperglycemia. (a) Trigonelline

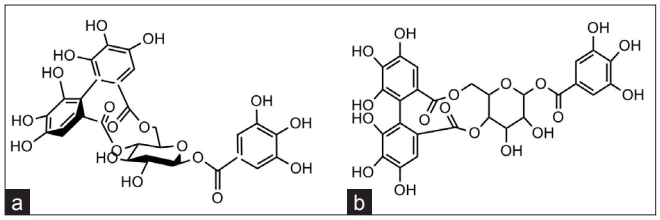

Figure 4: Chemical components in Psidium guajava L., which involve in anti-hyperglycemia. (a) Strictinin; (b) Pedunculagin

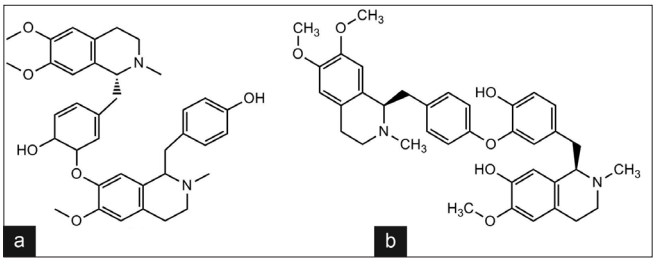

Figure 5: Chemical components in Nelumbo nucifera Gaertn. which involve in anti-hyperglycemia. (a) Liensinine; (b) Daurisoline

and cholesterol levels in human and experimental diabetic animals.[41-45] Its activity has been attributed largely to saponins,[46] high-fiber content,[47] the amino acid 4-hydroxyisoleucine,[48] and the major alkaloid trigonelline [Figure 3].[49]

Psidium guajava (L.)

Psidium guajava L. is a semi-deciduous tropical tree and is widely grown throughout India for its fruit called Guava. Its fruits are rich in dietary fiber associated with natural antioxidant compounds.[50] The fruit contains a high percentage of vitamin C, carotene, vitamin B1, B2, B6, and pectin.[51] The extract of the whole plant of *P. guajava* excluding roots was reported to be devoid of any antibacterial, antifungal, antiviral, anti-fertility, hypoglycemic, diuretic, and anti-inflammatory activities.[52] Recently, the ripe fruit peel has been found to possess hyperglycemic activity in diabetic patients.[53] Antidiabetic activity based on higher concentration of Mg in the raw fruit peel of *P. guajava* had been found.[54] The leaves of *P. guajava* inhibit the increase of plasma sugar level in alloxan-induced diabetic rats, during glucose tolerance test.[55] Flavonoid glycosides such as strictinin, isostrictinin, and pedunculagin are the effective constituents, which have been used in clinical treatment of diabetes to improve the sensitivity of insulin [Figure 4].[55]

Nelumbo nucifera (Gaertn.)

Nelumbo nucifera Gaertn. is a useful medicinal culinary plant. It has been reported that rhizome extract showed anti-diabetic and anti-inflammatory effects.[56,57] On the other hands; it has recently been used as plain extraction or blend tea to treat obesity in China.[57,58] Alkaloids isolated from *Nelumbo nucifera*, including liensinine, daurisoline, neferine, and flavonoids are the main compounds that give medicinal effects [Figure 5].[59-61]

Stevia rebaudina (Bert.) Hemsl.

Stevia rebaudina (Bert.) Hemsl. has been used in the treatment of diabetes for many years in China and some other parts of the world. In China this plant is used in medicinal teas for treating heartburn and other ailments also. Plant contain stevioside sweetener that reduces postprandial blood glucose levels in T2DM patients, indicating beneficial effects on the glucose metabolism.[62] The plant contain stevioside with the mechanism to stimulate insulin secretion via a direct action on β cells of pancreatic islet, which is considered to have the potential of becoming a new anti-diabetic drug for use in T2DM [Figure 6].[63,64]

Prunella vulgaris (L.)

Dried *Prunella vulgaris* L., is used to make herbal drink to help restore the body to a natural state after eating too many fried foods. It can be used in salads, soups, stews, or boiled as a pot herb. For medicinal purposes, the whole plant is gathered when the flowers bloom, and dried. It has been reported that there is anti-hyperglycemic effect of the ethanol extract of *Prunella vulgaris* L. in mice.[65] Compound Jiangtangsu had been isolated from this plant and confirmed to have a remarkable effect to lower blood sugar levels in mice with diabetes mellitus induced by alloxan.[66] The possible mechanism of Jiangtangsu is to repair β cells of pancreatic islet to release insulin. Constituents in the *P. vulgaris* have been identified, such as, phenolic acids (rosmarinic, caffeic.), triterpenoids (methyl oleanolate, methyl ursolate, methyl maslinate),[67-69] flavonoids (quercetin, campherol, rutin),[70] tannins, and polysaccharide.[71,72] The anti-hyperglycemic activity of the *P. vulgaris* may be due to any one or more of the above constituents [Figure 7].

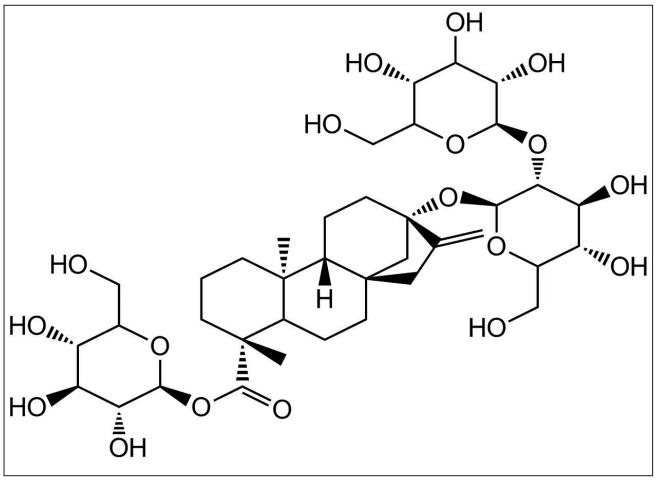

Figure 6: Chemical components in Stevia rebaudina (Bert.) Hemsl., which involve in anti-hyperglycemia, Stevioside

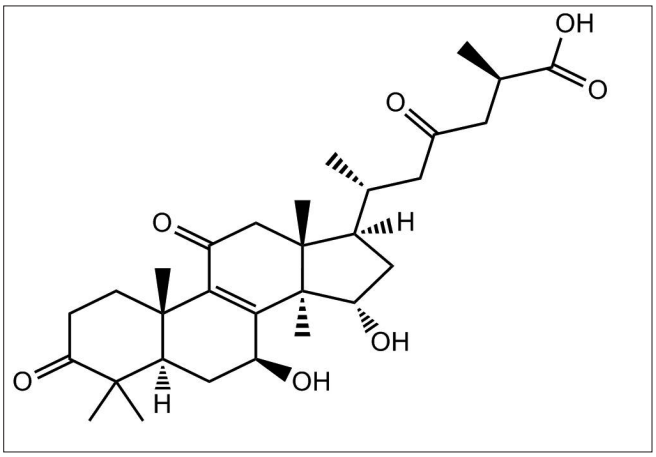

Figure 8: Chemical components in Ganoderma lucidum (Leyss. Ex Franch.), which involve in anti-hyperglycemia, Ganoderic acid

Ganoderma lucidum (Leyss., ex. Fr.)

Mushrooms have a notable place in the folklore throughout the world and in the traditions of many cultures.[73] *Ganoderma lucidum* is commonly known as a medicinally potent mushroom. It has been widely used in China and other oriental countries for hundreds of years for the treatment of various diseases, including diabetes and cancer. The sporophore of *Ganoderma lucidum* is used as both tonic nourishment and medicine for care of diabetic patients. Some research results showed that polysaccharides are the active principles for anti-diabetes.[74,75] Ganoderans A and B have been isolated and confirmed to have a hypoglycemic activity [Figure 8].[76,77]

Punica granatum (L.)

Punica granatum (Pomegranate) is a fruit-bearing deciduous shrub or small tree with diverse pharmacological and therapeutic effects.[78] Pericarpium Granati is used to treat diabetes mellitus in some parts of China. Male abortive flowers of *Punica granatum* are also used for the treatment of diabetes mellitus in India. Oral administration of the aqueous ethanolic extract of *Punica granatum* flowers led to a significant blood glucose lowering effect in normal, glucose fed and alloxan-induced diabetic rats.[79] The extract of *Punica granatum* seeds was also reported to have antidiabetic activity; ursolic acid may be the active constituent [Figure 9].[80]

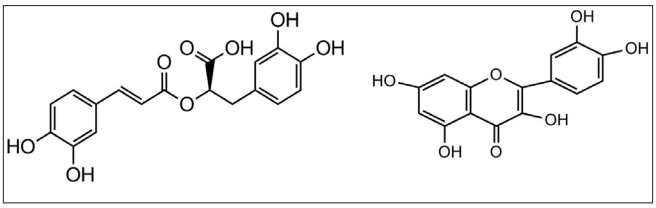

Figure 7: Chemical components in Prunella vulgaris L., which involve in anti-hyperglycemia. (a) Rosmarinic acid; (b) Quercetin

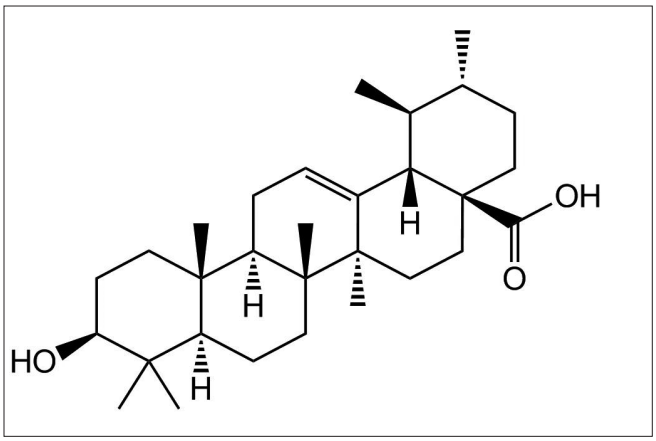

Figure 9: Chemical components in Punica granatum L., which involve in anti-hyperglycemia, Ursolic acid

Dioscorea opposita (Thunb.)

Dioscorea opposite, "Chinese yam", is native to China. The rhizomes of *Dioscorea opposita* Thunb., was traditionally used in diets to control Xiaokezheng (diabetes) in China. Researches confirmed that the water decoction of *Dioscorea opposita* has an anti-hyperglycemic effect to experimental diabetic mice.[81] Polysaccharides were considered to be the active constituents. Chemical component of *Dioscorea opposite,* dioscin and diosgenin may be the cause for medicinal effects [Figure 10].[82]

Momordica charantia (L.)

Momordica charantia L. is not only a nutritious vegetable, but is also used in traditional medical practices to treat T2DM. Experimental studies with animals and humans suggested that the vegetable has a possible role in glycemic control. Oral administration of the extract, fruit juice or seed powder of *Momordica charantia* caused a significant reduction in fasting blood glucose and improved glucose tolerance in normal and diabetic animals and in humans.[83-89] A wide range of compounds have been isolated from *Momordica charantia*, of which, a polypeptide (p-insulin, was named as "plant insulin"), the sterol glucoside mixture charantin and the pyrimidine nucleoside vicine have been identified as the orally anti-diabetic principles for humans and animals [Figure 11].[90,91]

Murraya koenigii (L.)

Murraya koenigii L. is promising as it is widely and regularly used as a spice for food flavoring and as such it appears to be without any side effects and toxicity. It is also popular in medical usage. Eating, fully-grown curry leaves is beneficial in controlling diabetes and in weight loss. The leaves of *Murraya koenigii* are also used as a herb in Indian medicine. Their properties include much value as an anti-diabetic and antioxidant.[92,93] The aqueous extract of *Murraya koenigii* leaves has been taken to evaluate the hypoglycemic activity in normal and alloxan-induced diabetic rabbits. The findings from this study suggested that the aqueous extract of these leaves may be prescribed as adjunct to dietary therapy and drug treatment for controlling diabetes mellitus.[94] An intense search of the literature has revealed that the stems, leaves, roots, and seeds are potential sources of carbazole alkaloids, which provide the medicinal effect. Some identified alkaloids are Koenimbine, Koenine, Koenigine, Koenidine, Mahanimbine and Mahanine[Figure 12].[95-98]

Artocarpus heterophyllus (Lam.)

Artocarpus heterophyllus Lam. (jackfruit) is an integral part of common Indian diet and is freely available in Indian and adjoining continents, its medicinal properties are also mentioned in Indian medicine. The plant is reported to possess antibacterial, anti-inflammatory, anti-diabetic, antioxidant and immunomodulatory properties.[99]

Hot water extract of mature jack leaves is recommended by Ayurvedic and traditional medical practitioners as a treatment for diabetes mellitus.[100] Previous studies have indicated that an extract of *Artocarpus heterophyllus* improves the glucose tolerance in normal human subjects and diabetic patients.[101] Its leaves contains hypoglycemic and hypolipidemic principles that have the potential to be developed further for the treatment of diabetes.[102] The leaves and stem show the presence of sapogenins, cycloartenone, cycloartenol, β-sitosterol, and tannins [Figure 13].[103]

Mangifera indica (L.)

Mangifera indica is one of the most popular of all tropical fruits. Most parts of the tree [Fruit, seeds, pulp, stem bark, roots, and leaves] have medicinal properties.[104] It is native to tropical Asia. The leaves of *Mangifera indica* were proven for antidiabetic properties using normoglycemic, glucose-induced hyperglycemia and streptozotocin (STZ)-induced diabetic mice.[105] The natural C-glucoside xanthone mangiferin has been reported in various parts of *M. indica*, which gives the medicinal property.[106] In KK-A^y mice, an animal model of type 2 diabetes, mangiferin (90 mg/kg), 7 h after oral administration, decreased the baseline glucose level by 56%.[107] In the same model, mangiferin (30 mg/kg, p.o., once daily followed 30 min. later by exercise (120 min motorized treadmill) for 2 weeks) reduced the blood cholesterol (~40%) and triglyceride levels (~70%) [Figure 14].[108]

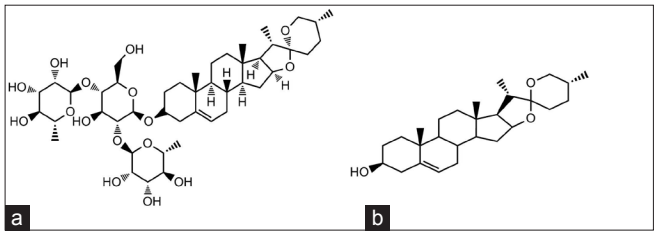

Figure 10: Chemical component in Dioscorea opposita Thunb., which involve in anti hyperglycemia. (a) Dioscin; (b) Diosgenin

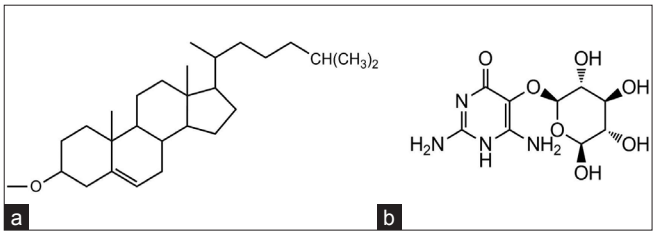

Figure 11: Chemical components in Momordica charantia L., which involve in anti-hyperglycemia. (a) Charantin; (b) Vicine

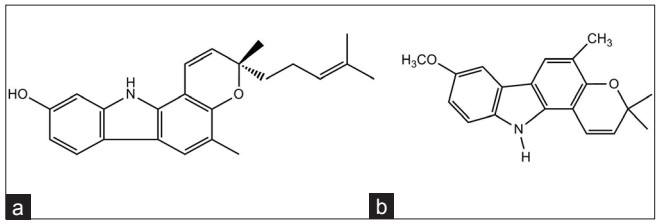

Figure 12: Chemical components in Murraya koenigii L., which involve in anti-hyperglycemia. (a) Mahanine; (b) Koenimbine

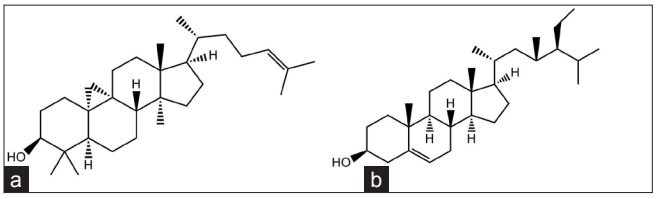

Figure 13: Chemical components in Artocarpus heterophyllus Lam., which involve in anti-hyperglycemia. (a) Cycloartenone; (b); β-sitosterol

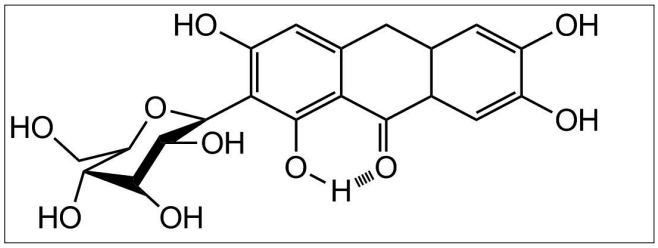

Figure 14: Chemical component in Mangifera indica Lam., which involve in anti-hyperglycemia, Mangiferin

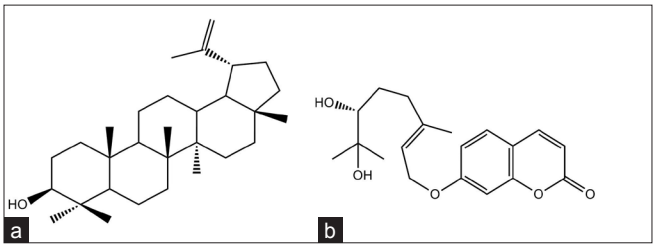

Figure 15: Chemical components in Aegle marmelos L., which involve in anti-hyperglycemia. (a) Lupeol; (b) Marmin

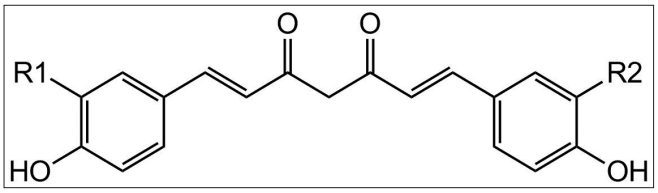

Figure 16: Chemical components in Curcuma longa L., which involve in anti-hyperglycemia, Curcumin

Aegle marmelos (L.) Corr.

Aegle marmelos (bael tree) fruit is eaten fresh or dried. As for other parts of the plant, the leaves and small shoots are eaten as salad greens in many Asian countries. It is a popular medicinal plant in the Ayurvedic and Siddha systems of medicine and folk medicines used to treat a wide variety of ailments.[109,110] The leaves, fruits, and stems contain skimianinc, sterol and aegelin, lupeol, marmin. In pharmacological trials, both the fruit and root showed anti-amoebic and hypoglycemic activities.[111-113] *A. marmelos* would act like insulin in the restoration of blood sugar and body weight to normal levels in rat and was therefore recommended as a potential hypoglycemic agent [Figure 15].[113]

Curcuma longa (L.)

Curcuma longa L., commonly known as turmeric, has been used as spice and coloring agent with long history. Its rhizomes have been reported to possess anti-diabetic properties in experimental animal models.[114-116] Researches reported that active ingredient curcumin is the response for anti-diabetic action [Figure 16].[116]

CONCLUSIONS

The development of T2DM is strongly influenced by eating practices. Also once diagnosed, a critical part of treatment is the modification of a lifetime of food and eating habits.[117] Functional herbal foods might have a particularly high impact for prevention or treatment of overweight and diabetes for which, more than in many other fields. Many of the elements found in the present review were identified in previous research about diabetes and functional food ingredients. However, the present research provided assistant for selecting of specific functional herbal food ingredients in the lives of people with T2DM and our normal day-to-day food consuming system to prevent such diseases.

REFERENCES

1. IDF (2006). The Diabetes Atlas. Available from: http://www.eatlas.idf.org/media/.
2. de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complications: A meta-analysis. Psychosom Med 2001;63:619-30.
3. Jacobson AM. Impact of improved glycemic control on quality of life in patients with diabetes. Endocr Pract 2004;10:502-8.
4. Tahrani AA, Piya MK, Kennedy A, Barnett AH. Glycaemic control in type 2 diabetes: Targets and new therapies. Pharmacol Ther 2010;125:328-61.
5. Kahn SE, Haffner SM, Heise MA, Herman WH, Holman RR, Jones NP, *et al*. Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. N Engl J Med 2006;355:2427-43.
6. Del PS, Bianchi C, Marchetti P. Beta-cell function and anti-diabetic pharmacotherapy. Diabetes Metab Res Rev 2007;23:518-27.
7. Groop LC, Tuomi T. Non-insulin dependent diabetes mellitus a collision between the thrifty gene and an affluent society. Ann Med 1997;2:937-53.
8. Facchini FS, Hua N, Abbasi F, Reaven GM. Insulin resistance as a predictor of age related diseases. J Clin Endocrinol Metab 2001;86:3574-8.
9. Stumvoll M, Goldstein BJ, van Haeften TW. Type 2 diabetes: Principles of pathogenesis and therapy. Lancet 2005;365:1333-46.
10. Kuzuya T, Nakagawa S, Satoh J, Kanazawa Y, Iwamoto Y, Kobayashi M, *et al*. Report of the Committee on the classification and diagnostic criteria of diabetes mellitus. Diabetes Res Clin Pract 2002;55:65-85.
11. Gill GV, Redmond S, Garratt F, Paisey R. Diabetes and alternative medicine: Cause for concern. Diabetic Med 1994;11:210-3.
12. Christopoulou-Aletra H, Papavramidou N. 'Diabetes' as described by Byzantine writers from the fourth to the ninth century AD: The GraecoRoman influence. Diabetologia 2008;51:892-6.
13. Ahmed AM. History of diabetes mellitus. Saudi Med J 2002;23:373-8.
14. Maggie BC. Traditional Chinese medicine in the treatment of diabetes. Diabetes Spectrum 2001;14:154-9.
15. Liu JP, Zhang M, Wang WY, Grimsgaard S. Chinese herbal medicines for type 2 diabetes mellitus. Cochrane Database Syst Rev 2004;3:CD003642.
16. Jun Y, Hanjie Z, Jianping Y. Traditional Chinese medicine in treatment of metabolic syndrome. Endocr Metab Immune Disord Drug Targets 2008;8:99-111.
17. Gu Y, Zhang Y, Shi X, Li X, Hong J, Chen J, *et al*. Effect of traditional Chinese medicine berberine on type 2 diabetes based on comprehensive metabonomics Talanta 2010;81:766-72.
18. Rezabek KM. Medical nutrition therapy in type 2 diabetes. Nurs Clin North Am 2001;36:203-16.
19. Cheung BM. The Cardiovascular Continuum in Asia-A New Paradigm for the Metabolic Syndrome. J Cardiovasc Pharmacol 2005;46:125-9.
20. Vuksan V, Sievenpipera LJ. Herbal remedies in the management of diabetes: Lessons learned from the study of ginseng. Nutr Metab Cardiovasc Dis 2005;15:149-60.
21. Cheng JT. Review: Drug therapy in Chinese traditional medicine. J Clin Pharmacol 2000;40:445-50.
22. Swinbanks D, O'Brien J. Japan explores the boundary between food and medicine. Nature 1993;364:180.
23. Toma MM, Pokrotnieks J. Probiotics as functional food: Microbiological and medical aspects Acta Universitatis Latviensis 2006;710:117-29.
24. López-Varela S, Gonzαlez-Gross M, Marcos A. Functional foods and the immune system: A review. Eur J Clin Nutr 2002;56:S29.
25. Roberfroid MB. What is beneficial for health? The concept of functional food. Food Chem Toxicol 1999;37:1034-41.
26. Duke JA, Ayensu ES. Medicinal Plants of China. Algonac : Reference Publications Inc.; 1985
27. Jamison JR. Garlic (Allium sativum). In: Clinical Guide to Nutrition and Dietary Supplements in Disease Management. London: Churchill Livingstone; 2003.
28. Kasuga S, Ushijima M, Morihara N, Itakura Y, Nakata Y. Effect of aged garlic extract (AGE) on hyperglycemia induced by immobilization stress in mice. Nippon Yakurigaku Zasshi 1999;114:191-7.
29. Liu CT, Hse H, Lii CK, Chen PS, Sheen LY. Effects of garlic oil

and diallyl trisulfide on glycemic control in diabetic rats. Eur J Pharmacol 2005;516:165-73.

30. Mathew PT, Augusti KT. Studies on the effect of allicin (diallyl disulphide-oxide) on alloxan diabetes I. Hypoglycaemic action and enhancement of serum insulin effect and glycogen synthesis. Indian J Biochem Biophys 1973;10:209-12.
31. Augusti KT, Sheela CG. Antiperoxide effect of S-allyl cysteine sulfoxide, a insulin secretagogue, in diabetic rats. Experientia 1996;52:115-20.
32. Jain RC, Vyas CR. Hypoglycemic action of onion and garlic. Am J Clin Nutr 1975;28:684-5.
33. Gruenwald J, Brendler T, Jaenicke C. PDR for Herbal Medicines. 2nd ed. Montvale, NJ: Medical Economics Company; 2000.
34. Rshaad B, Azaizeh H, Said O. Tradition and perspectives of Arab herbal medicine: A review. Evid Based Complement Alternat Med 2005;2:475-9.
35. Baldé NM, Youla A, Baldé MD, Kaké A, Diallo MM, Baldé MA, *et al*. Herbal medicine and treatment of diabetes in Africa: An example from Guinea. Diabetes Metab 2006;32:171-5.
36. Babu PS, Srinivasan K. Influence of dietary capsaicin and onion on the metabolic abnormalities associated with streptozotocin induced diabetes mellitus. Mol Cell Biochem 1997;175:49-57.
37. Babu PS, Srinivasan K. Renal lesions in streptozotocin-induced diabetic rats maintained on onion and capsaicin containing diets. J Nutr Biochem 1999;10:477-83.
38. Augusti KT, Roy VC, Semple M. Effect of allyl propyl disulfide isolated from onion (Allium cepa) on glucose tolerance of alloxan diabetic rabbits. Experientia 1974;30:1119-20.
39. Sheela CG, Kumud K, Augusti KT. Antidiabetic effects of onion and garlic sulfoxide amino acids in rats. Planta Med 1995;61:356-7.
40. Kumari K, Mathew BC, Augusti KT. Antidiabetic and hypolipidemic effects of S-methyl cysteine sulfoxide isolated from Allium cepa Linn. Indian J Biochem Biophys 1995;32:49-54.
41. Khosla P, Gupta DD, Nagpal RK. Effect of Trigonella foenum graecum (Fenugreek) on blood glucose in normal and diabetic rats. Indian J Physiol Pharmacol 1995;2:173-4.
42. Puri D, Prabhu KM, Murthy PS. Hypocholesterolemic effect of the hypoglycemic principle of fenugreek (Trigonella foenum graecum) seeds. Indian J Clin Biochem 1995;9:13-6.
43. Puri D, Prabhu KM, Murthy PS. Mechanism of action of a hypoglycemic principle isolated from fenugreek seeds. Indian J Physiol Pharmacol 2002;4:457-62.
44. 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.
45. Vats V, Grover JK, Rathi SS. Evaluation of anti-hyperglycemic and hypoglycemic effect of Trigonella foenum-graecum Linn, Ocimum sanctum Linn and Pterocarpus marsupium Linn in normal and allox- anized diabetic rats. J Ethnopharmacol 2002;79:95-100.
46. Petit PR, Sauvaire YD, Hillaire-Buys DM, Leconte OM, Baissac YG, Ponsin GR, *et al*. Steroid saponins from fenugreek seeds extraction, purification, and pharmacological investigation on feeding behavior and plasma cholesterol. Steroids 1995;60:674-80.
47. Ali L, Kalam A, Khan A, Hassan Z, Mosihuzzaman M, Nahar N, *et al*. Characterization of the hypoglycemic effects of Trigonella foenum-graecum seed. Planta Medica 1995;61:358-60.
48. Sauvaire Y, Petit P, Broca C, Manteghetti M, Baissac Y, Alvarez, JF, *et al*. 4-Hydroxyisoleucine: A novel amino acid potentiator of insulin secretion. Diabetes 1998;47:206-10.
49. Raghuram TC, Sharma RD, Sivakumar B, Sahay K. Effect of fenugreek seeds on intravenous glucose disposition in non-insulin dependent diabetic patients. Phytotherapy Res 1994;8:83-6.
50. Jimenez-Escrig A, Rincon M, Pulido R, Saura-Calixo F. Guava fruit (*Psidium guajava* L.) as a new source of antioxidant dietary fiber. J Agric Food Chem 2001;49:5489-93.
51. Mishra K, Seshadri TR. Chemical components of the fruits of Psidium guajava. Phytochemistry 1967;7:641-5.
52. Adsule RN, Kadam SS. In: Handbook of fruit science and technology. Production, composition storage, and processing. New York: M. Dekker; 1995.
53. Rai PK, Singh SK, Kesari AN, Watal G. Glycaemic evaluation of Psidium guajava in rats. Indian J Med Res 2007;126:224-7.
54. Rai PK, Rai NK, Rai AK, Watal G. Role of LIBS in elemental analysis of P. guajava responsible for glycemic potential. Instrum Sci Tech 2007;35:507-22.
55. Maryuma Y, Matsuda H, Matsuda R, Kubo M, Hatano T, Okuda T. Study on *Psidium guajava* L. (I). Antidiabetic effect and effective components of the leaf of *Psidium guajava* L. (Part I). Shoyakugaku Zasshi 1985;39:261-9.
56. Mukherjee PK, Saha K, Das J, Pal M, Saha BP. Studies on the anti-inflammatory activity of rhizomes of Nelumbo nucifera. Planta Med 1997;63:367-9.
57. Mukherjee PK, Saha K, Saha BP. Effect of Nelumbo nucifera rhizome extract on blood sugar level in rats. J Ethnopharmacol 1997;58:207-13.
58. Gao X, Dang Y. Traditional Chinese Medical Beauty Care. Peking: China Science and Technology Press; 2000.
59. Liu C, Tseng A. Chinese Herbal Medicine. Boca.Raton: CRC Press, LLC; 2005.
60. Zhou T, Luo D, Li X, Luo Y. Hypoglycemic and hypolipidemic effects of flavonoids from lotus (Nelumbo nucifera Gaertn) leaf in diabetic mice. Journal of Medicinal Plants Research 2009;3:290-3.
61. Jinmin S, Zhi Y. TLC-scanning determination of liensinine in lotus plumule. Chin J Hosp Pharm 1993;1:8-10.
62. Gregersen S, Jeppesen PB, Holst JJ, Hermansen K. Antihyperglycemic effects of stevioside in type 2 diabetic subjects. Metab Clin Exp 2004;53:73-6.
63. White JR Jr, Kramer J, Campbell RK, Bernstein R. Oral use of a topical preparation containing an extract of Stevia rebaudiana and the chrysanthemum flower in the management of hyperglycemia. Diabetes Care 1994;17:940.
64. Jeppesen, PB, Gregersen S, Alstrup KK, Hermansen K. Stevioside induces antihyperglycaemic, insulinotropic and glucagonostatic effects *in vivo*: Studies in the diabetic Goto-Kakizaki (GK) rats. Phytomedicine 2002;9:9-14.
65. Liu BL, Zhu DN, Wang G. The anti-hyperglycemic effect of ethanol extract of Prunella vulgaris L. to mice. J. China Pharm Univ 1995;26:44-6.
66. Xu SL, Hou XJ, Wu AP. Pharmacological studies on blood sugar-lowering activity of the active principle of common selfheal. Chin Tradit Herb Drugs 1989;20:358-60.
67. Kajima H, Ogura H. Triterpenoids from Prunella vugaris. Phytochemistry 1986;3:729-33.
68. Kajima H, Tominga H, Sato S. Pentacyclic tritepenoids from Prunella vulgaris. Phytochemistry 1987;4:1107-11.
69. Kajima H, Tominga H, Sato S. Two novel hexcyclic triterpenoids from Prunella vulgaris. Phtochemistry 1988;9:2921-5.
70. Dmitruk SI, Dmitruk SE, Berezovskaya TP. Flavonoids of Prunella vulgaris. Khim Prir Soedin 1987;3:449-50.
71. Natherova L, Rezacova A. Pharmacognostic studies of 3 species of the genus Prunella L. Acta Fac Pharm Univ Comeniana 1972;21:33-61.

72. Tabba HD, Chang RS, Smiths K. Isolation, purification and characterization of Prunellin: An anti-HIV component from aqueous extracts of Prunella vurgaris. Antiviral Res 1989;11:263-73.
73. Chang S, Buswell JA. Mushroom nutriceuticals. World J Microbiol Biotechnol 1996;12:473-6.
74. Kimura M, Diwan PV, Yanagi S, Kon-no Y, Nojima H, Kimura I. Potentiating effects of β-eudesmol-related cyclohexylidene derivatives on succinylcholine-induced neuromuscular block in isolated phrenic nerve-diaphragm muscles of normal and alloxan-diabetic mice. Biol Pharm Bull 1995;18:407-10.
75. Zhang LH, Xiao PG. Effect of the extract of ganoderma lucidum spores to experimental diabetes mellitus. Chin Tradit Herb Drugs 1993;24:246-7, 272.
76. Hikino H, Mizuno T, Oshima Y, Konno C. Isolation and hypoglycemic activity of Morans A. A glycoprotein of Morus alba root barks. Planta Med 1985;51:159-60.
77. Hikino H, Konno C, Mirin Y, Hayashi T. Isolation and hypoglycemic activity of ganoderans A and B. Glycans of Ganoderma lucidum fruit bodies. Planta Med 1985;51:339-40.
78. Jurenka JS. Therapeutic applications of pomegranate (*Punica granatum* L.): A review. Altern Med Rev 2008;13:128-44.
79. Jafri MA, Aslam M, Javed K, Singh S. Effect of Punica granatum Linn. (flowers) on blood glucose level in normal and alloxan induced diabetic rats. J Ethnopharmacol 2000;70:309-14.
80. Das AK, Mandal SC, Banerjee SK, Sinha S, Saha BP, Pal M. Studies on the hypoglycaemic activity of Punica granatum seed in streptozotocin induced diabetic rats. Phytother Res 2001;15:628-9.
81. Hao ZQ, Hang BQ, Wang Y. The anti-hyperglycemic effect of water decoction of Dioscorea opposita Thunb. To experimental diabetic mice. J China Pharm Univ 1991;22:158-60.
82. Huiqi S, Mingjing L, Aixin S, Xiuhua L. RP -HPLC Determination of Diosgenin in Dioscorea opposite Thunb. and D. alata L. Chinese Journal of Pharmaceutical Analysis 2004;05:1-4.
83. Raman A, Lau C. Anti-diabetic properties and phytochemistry of Momordica charantia L. (Cucurbitaceae). Phytomed 1996;2:349-62.
84. Miura T, Itoh C, Iwamoto N, Kato M, Kawai M, Park SR, *et al*. Hypoglycemic activity of the fruit of the Momordica charantia in type 2 diabetic mice. J Nutr Sci Vitaminol (Tokyo) 2001;47:340-4.
85. Fan YL, Cui FD. Comparative studies on hypoglycemic activity of different sections of Momordica charantia L. J Shenyang Pharm Univ 2001;18:50-3.
86. Srivastava Y, Venkatakrishna-Bhatt H, Verma Y, Venkaiah K, Raval BH. Antidiabetic and adaptogenic properties of Momordica charantia extract: An experimental and clinical evaluation. Phytother Res1993;7:285-9.
87. Ahmed I, Lakhani MS, Gillett M, John A, Raza H. Hypotriglyceridemic and hypocholesterolemic effects of anti-diabetic Momordica charantia (karela) fruit extract in streptozotocin-induced diabetic rats. Diabetes Res Clin Pract 2001;51:155-61.
88. Ooi CP, Yassin Z, Hamid TA. Momordica charantia for type 2 diabetes mellitus. Cochrane Database Syst Rev 2010;2:CD007845.
89. Wang, F, Zhang PP, Yu XF. A clinical observation of type 2 diabetes treated by saponins from Momordica charantia L. Pract Clin J Integrated Tradit Chin West Med 1991;4:721.
90. Zhang, PP, Wang F, Xue AQ. Experimental study on antihyperglycemic effect of “Kuguasu”. Jiangsu J Chin Tradit Med 1992;13:30-1.
91. Arulselvan P, Senthilkumar GP, Sathish Kumar D, Subramanian S. "Anti-diabetic effect of Murraya koenigii leaves on streptozotocin induced diabetic rats". Pharmazie 2006;61:874-7.
92. Arulselvan P, Subramanian SP. "Beneficial effects of Murraya koenigii leaves on antioxidant defense system and ultra structural changes of pancreatic beta-cells in experimental diabetes in rats". Chem Biol Interact 2007;165:155-64.
93. Kesari AN, Gupta RK, Watal G. Hypoglycemic effects of Murraya koenigii on normal and alloxan-diabetic rabbits. J Ethnopharmacol 2005;97:247-51.
94. Nayak A, Manda S, Banerji A, Banerji J. Review on chemistry and pharmacology of Murraya koenigii Spreng (Rutaceae). J Chem Pharm Res 2010;2:286-99.
95. Tachibana Y, Kikuzaki H, Lajis NH, Nakatani N. J Agric Food Chem 2001;49:5589-94.
96. Narasimhan NS, Paradkar MV, Chitguppi VP, Kelkar SL. Indian J Chem 1975;13:993-9.
97. Reisch J, Goj O, Wickramasinghe A, Herath HM, Henkel G. Phytochem 1992;31:2877-9.
98. Prakash O, Kumar R, Mishra A, Gupta R. Artocarpus heterophyllus (Jackfruit): An overview. Phcog Rev 2009;3:353-8.
99. Jayaweera DM. Medicinal plants used in Ceylon 4-89. Part 11. Sri Lanka, Colombo: National Science Council; 1982.
100. Fernando MR, Wickramasinghe SM, Thabrew MI, Ariyaratne PL, Karunanayake EH. J Ethnopharmacol 1991;31:277-82.
101. Chackrewarthy S, Thabrew MI, Weerasuriya M, Jayasekera S. Evaluation of the hypoglycemic and hypolipidemic effects of an ethylacetate fraction of Artocarpus heterophyllus (jak) leaves in streptozotocin-induced diabetic rats. Phcog Mag 2010;6:186-90.
102. Prakash O, Kumar R, Mishra A, Gupta R. Artocarpus heterophyllus (Jackfruit): An overview. Phcog Rev 2009;3:353-8
103. Sathyavathi GV, Gupta AK, Tandon N. Medicinal plants of India. New Delhi, India: Indian Council of Medical Research; 1987.
104. Umezawa H, Aoyagi H, Ogawa K. Diprotein A and B, inhibitors of Dipeptidyl amino peptidase IV, produced by Bacteria. J Antibiot 1984;26:422-5.
105. Muruganandan S, Gupta S, Kataria M, Lal J, Gupta PK. Mangiferin protects the streptozotocin-induced oxidative damage to cardiac and renal tissues in rats. Toxicol 2002;176:165-73.
106. Miura T, Ichiki H, Iwamoto N, Kato M, Kubo M, Sasaki H, *et al*. Antidiabetic activity of the rhizome of Anemarrhena asphodloides and active components, mangiferin and its glucoside. Biol Pharm Bull 2001;24:1009-11.
107. Miura T, Iwamoto N, Kato M, Ichiki H, Kubo M, Komatsu Y, *et al*. The suppressive effect of mangiferin with exercise on blood lipids in type 2 diabetes. Biol Pharm Bull 2001;24:1091-2.
108. Hooker JD. The flora of British India. Vol. 1. Reeve, United Kingdom: Reeve and Co. ; 1975. p. 516-7
109. Islam R, Hossain M, Karim MR, Joarder OI. Regeneration of Aegle marmelos (L.) Corr., plantlets *in vitro* from callus cultures of embryonic tissues. Curr Sci 1995;69:494-5.
110. Ponnachan PT, Paulose CS, Panikar KR. Effect of the leaf extract of Aegle marmelos (L.) Corr. in diabetic rats. Indian J Exp Biol 1993;31:345-7.
111. Kamalakkannan N, Prince PS. The effect of Aegle marmelos fruit extract in streptozotocin diabetes: A histopathological study. J Herb Pharmacother 2005;5:87-96.
112. Seema PV, Sudha B, Padayatti SP, Abraham A, Raghu KG, Paulose CS. Kinetic studies of purified malate dehydrogenase in liver of streptozotozin – diabetic rats and the effect of leaf extract of Aegle marmelos (L.) Corr Indian J Exp Biol 1996;34:600-2.
113. Shnkar TN, Shanta NV, Ramesh HP, Murthy IA, Murthy VS. Toxicity Studies on Turmeric (Cuecuma longa): Acute Toxicity studies in rats, Guineapigsand Monkeys. Ind J Exp Biol 1980;18:73-5.
114. Eshrat MH, Hussain A. Hypoglycemic, hypolipidemic and

antioxidant properties of combination of curcumin from Curcuma longa. Lnn, and partially purified product from Abroma augusta, Linn in streptozotocin induced diabetes. Indian J Clin Biochem 2002;17:33-43.

115. Tank R, Sharma N, Sharma, I, Dixit, VP. Anti-diabetic activity if C.longa in alloxan Induced diabetic rats . Indian drugs 1989;27:587-9.
116. Groop LC, Tuomi T. Non-insulin dependent diabetes mellitus a collision between the thrifty gene and an affluent society. Ann Med 1997;2:937-53.
117. Savoca M, Miller C. Food selection and eating patterns: Themes found among people with type 2 diabetes mellitus. J Nutr Educ Behav 2001; 33:224-233

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