Plants present in Mexico with studies in metabolic syndrome

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Abstract
Metabolic syndrome represents one of the major risk factors for developing cardiovascular disease, with high risk affecting most of the worldwide adult population in both sexes. In Mexico, cardiovascular diseases are the first cause of morbidity and mortality. Generally, for the therapeutic management of both diseases is using multiple drugs with different mechanisms of action, which aim to reduce risk factors, associated with metabolic syndrome. These are managed for a long time, which often represents a high economic cost. On the other hand, some patients have no adherence to treatment as this one, is ineffective, the adverse effects are situations that require change or discontinue medication immediately. Mexico has a large diversity of plants widely used in traditional medicine and with a high potential for use in treating metabolic syndrome.

Keywords: Metabolic syndrome, medicinal plants

Introduction
Metabolic syndrome (SM) is a disorder characterized by the presence of multiple risk factors, including central obesity, hyperglycemia, hypertriglyceridemia, low plasma high density lipoprotein (HDL) - cholesterol and hypertension. Concurrence of at least 3 of these factors means that an individual has MS [1]. The relation of MS with the risk of developing several chronic diseases, such as diabetes mellitus and cardiovascular diseases is well established, and it is also associated with a high mortality risk [2].

In developed countries SM appears to affect around 25% of the population. Moreover, its prevalence is increasing rapidly throughout the world, in parallel with the increasing prevalence of diabetes and obesity and becoming a major public health problem [3]. The prevalence of SM in Mexican adults was of 41 % in accordance with ENSANUT 2012. Cardiovascular disease is the primary cause of death for both sexes. This increased tendency could be associated with significant changes in lifestyle behaviour including physical inactivity, high carbohydrate diets, alcohol, and tobacco consumption [4].

Pharmacological treatment of SM in addition to lifestyle including weight loss, a targeted approach for control of individual components of the SM is often necessary. Because there are drugs proven effective in reducing specific components of SM, must be individualized.

a) An anti-obesity: such as lorcaserin is approved for its use in obese adults who have high blood pressure and cholesterol. Lorcaserin acts as a selective 5 - HT 2C receptor agonist on pro-opiomelanocortin neurons, which in turn causes release of α-melanocyte-stimulating hormone (α-MSH). Further α - MSH acts on melanocortin 4 receptor in the paraventricular nucleus in the hypothalamus, leading to a decrease in appetite and body weight.

b) Insulin sensitizers: Thiazolidinedione (TZD) is a synthetic ligand of peroxisome proliferator-activated receptor-γ (PPARγ). TZDs reduce the intracellular levels of toxic lipid metabolites, resulting in less lipotoxicity, protect against the cytostatic effect of free fatty acids and restores glucose-mediated insulin release, increase insulin sensitivity in the liver and muscle tissue, promote adipose tissue differentiation in subcutaneous adipose tissue regions, which increases the synthesis of adiponectin, thereby further reducing insulin resistance, reduce circulating levels of free fatty acids and proinflammatory cytokines as resistin, interleukin 6 (IL-6), tumor necrosis factor a (TNF-α), and intercellular adhesion molecule 1 (ICAM-1) [5].
Metformin is the only biguanide that is available in most regions of the world. Its mechanism for lowering the glucose level is based on reduction of hepatic glucose output and enhancement of insulin sensitivity in skeletal muscle and adipocytes. Metformin monotherapy is expected to decrease glycosylated hemoglobin A1c (HbA1C) by 1.0–2.0 % [9]. The major non-glycemic effect of metformin is either weight stability or modest weight loss. There are some evidences that metformin has antioxidant properties. Reported antioxidant properties of metformin are: decreasing the xanthin oxidase and lipid peroxidase activity, increasing the enzymatic antioxidants activity, chelating metal ions such as copper and iron, scavenging oxygenated free radicals generations, decreasing ROS level by activating different pathways such as AMP-protein kinase (AMPK)-mediated signaling, inhibition of advanced glycation end products (AGEs) formation, decreasing β-cell apoptosis, and also decreasing the production of TNF-α [7]. Improvement of some markers of endothelial function in patients with type 2 diabetes has been reported by metformin usage [8].

c) Lipid lowering: Statin, 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor, and fibrate, a peroxisome proliferator activated receptor a (PPARα) agonist, are pharmacologic agents for dyslipidemia, are competitive inhibitors of HMG-CoA reductase, block the rate-limiting step in cholesterol biosynthesis; so that reduced circulating total of low-density lipoprotein (LDL) cholesterol levels, via lipoprotein lipase-mediated hydrolysis of very-low-density lipoprotein (VLDL).

d) Hypertension: the renin angiotensin system have an important relationship with insulin resistance and endothelial dysfunction. Angiotensin II inhibits insulin signaling and produces oxidative stress that accelerates hyperglycemia and atherosclerosis. Angiotensin converting enzyme (ACE) inhibitor reduces the plasma levels of angiotensin-II, leading to a decrease in blood pressure by peripheral vasodilatation. The beneficial effect of ACE inhibitors on glucose metabolism is demonstrated by clinical trials such as the HOPE (Heart Outcomes Prevention Evaluation) Study, which showed a reduced rate of new onset diabetes mellitus in patients taking the ACE inhibitor ramipril although this effect has been variable. Angiotensin-II receptor blocker is also known to exert blood pressure lowering, insulin sensitizing, induce PPARγ activity, reduce serum uric acid and proinflammatory cytokines such as IL-6 and TNF-α.

e) Novel antidiabetic agents: Glucagon like peptide-1 (GLP-1) agonists improves hyperglycemia by enhancing glucose-stimulated insulin secretion through activation of cyclic adenosine monophosphate (cAMP) and upregulates protein kinase A (PKA), which leads to rapid increases in intracellular calcium and insulin exocytosis in a glucose-dependent manner, disadvantage GLP-1 agonists have the potential to reduce insulin resistance which helps reverse insulin resistance-associated defects in the failing β-cells [9]. Sodium glucose transporter-2 (SGLT-2) inhibitors: The kidney plays an important role in glucose homeostasis by mediating reabsorption of glucose from the glomerular filtrate, which happens through SGLT-2 and SGLT-1. SGLT-2 inhibitors block 90% of reabsorption of filtered glucose in the proximal tubules, leading to increased urinary glucose excretion, which eventually reduces hyperglycemia. In 2013 and 2014, the US FDA approved three drugs in this class: canagliflozin, empagliflozin, and dapagliflozin as antidiabetic medications, as reduce cardiovascular risk not only via glucose lowering effect but via beneficial effects on body weight, blood pressure and serum uric acid [10]. Phosphodiesterase inhibitor: Cilostazol a selective phosphodiesterase-3 (PDE-3) inhibitor with anti-thrombotic and vasodilating properties. Activates AMPK and causes phosphorylation of endothelial nitric oxide synthase, leading to increased production of nitric oxide, while it inhibits cytokine-induced NFkB activation and suppresses vascular cell adhesion molecule 1 (VCAM-1) gene expression. In a clinical trial, administration of cilostazol reduced triglycerides and increase in lipoprotein lipase activity [11].

These groups of drugs have proven effective for the treatment of SM, so it is often the desired effect with side effects and/or toxic arise, and would find no scope for a large segment of the population, they have made the patient leaves treatment, and resort to other alternative treatments.

Medicinal plants are used as a source of drugs for the treatment of various human health disorders all over the world from ancient times to the present day. They are important natural wealth. They provide primary healthcare services to people from all walks of life. They serve as important therapeutic agents as well as important raw materials for the manufacture of traditional and modern medicines. A total of 250,000 species of flowering plants are referred to as medicinal plants. The World Health Organization (WHO) enlisted some 21,000 medicinal plant species. The present global herbal market is worth about US$ 62 billion per annum. The annual growth of herbal market is about 15% and the global herbal market by 2050 is expected to be about US$ 5 trillion [12].

Plants are one of the most important sources of medicines. Today the large number of drugs in use is derived from plants, like morphine from Papaver somniferum, Ashwagandha from Withania somnifera, ephedrine from Ephedra vulgaris, atropine from Atropa belladonna, reserpine from Rauwolfia serpentine [13]. The medicinal plants are rich in secondary metabolites which are potential sources of drugs and essential oils of therapeutic importance.

The tendency to use traditional medicinal becomes clear with MS, given the high costs can represent treatment, and may be in some population it is inaccessible, especially in patients with low socioeconomic status and those living in rural areas, use alternative medicine, which is less costly and more accessible than a biomedical treatment. Also, patients are exposed to standard treatments, which are not only expensive but also display several side effects that eventually discourage patients. Alternative therapies, on the contrary, are believed to have few consequences for the body and their proximity to people beliefs and perception of disease and well-being make them popular [13].

Considering the need for the introduction of new drugs into the market, the plants have an added advantage when compared with synthetic ones, as their molecular diversity and consequent changes in biological function are more complex. With respect to research and development of newer potential herbal drugs, screening and evaluation of their phyto-pharmacological effect are essential [13]. The biodiversity and plant assets are often the basis for the development of synthetic drugs, which show a combination of chemical structures and yet unexplored physicochemical properties. This current review focuses on medicinal plants used in the treatment of MS in Mexico.
The bibliographies of all identified studies and review articles were reviewed to look for additional studies of interest. So, we preferably selected papers reporting recent comprehensive reviews or meta-analyses, or original clinical trials on substance with action on at least two or more components of MS.

*Psacalium decompositum* (Matarique): hypoglycemic properties of this plant have been extensively studied; extracts and fractions are effective in reducing glucose levels in normoglycemic and mildly diabetic mice [14], as well as in temporally hyperglycemic rabbits, but not in severely diabetic animals. Aqueous fraction contains a carbohydrate-type fructan (inulin), which showed hypoglycemic effect in healthy and alloxan-induced diabetic mice. Phytochemical studies revealed that contain various hypoglycemic sesquiterpenic compounds (furanoeremophilanes), such as cacalol, and the mixture of 3-hydroxyacacalolide, and epi-3-hydroxyacacalolide. Fructooligosaccharide (FOS) fraction obtained from the root of *P. decompositum* showed anti-inflammatory, anti-obesity fructose-induced in Wistar rats [15].

*Swietenia humilis* Zucc., commonly named as zopilote, gateado, cabano and caobilla; the seeds of the plant are valued as blood depurative, a popular way to raw and dried (crude drug) and decoction are consumed as antiadipogenic agents in Mexican folk medicine [16].

An aqueous extract from the seeds of *Swietenia humilis* (3.6–100 mg/kg bw) lowered blood glucose levels in nicotinamide-streptozotocin induced hyperglycemic mice [17]. Furthermore, when administered to fructose-fed rats with metabolic syndrome, decoction showed antihyperglycemic, hypoglycemic and hypolipidemic effects, as well as an augmentation of hepatic glycogen [17].

*Hibiscus sabdariffa* L. (Hs) (roselle): Mexico ranks seventh production of this plant. Several studies have showed that extracts (water and ethanolic extracts of dried calyces or leaves) decrease LDL-C, triglycerides, total cholesterol lipid peroxidation in vivo and VLDL cholesterol [18-19] along with an increase in serum level of HDL cholesterol levels [19-20]. Several groups of compounds in the extract, such as anthocyanins and protocatechuic acid, have been implicated as responsible for these effects [21-22].

Standardized (33.64 mg of total anthocyanins per each 120 mg) water extract was able to reduce weight gain in obese mice while at the same time it increases the liquid intake in healthy and obese mice [25]. This effect is probably achieved through the modulation of phosphatidylinositol 3-kinase /Akt (PI3K/Akt) and extracellular signal-regulated kinase (ERK) pathway, which play pivotal roles during adipogenesis [23].

In *vitro* and in *vivo* studies showed that *Hibiscus* extract (or tea) inhibited the activity of α-amylase, blocking sugars and starch absorption, which may assist in weight loss [24-25].

The aqueous extract was more efficient in inhibiting triglyceride accumulation when devoid of fibre and polysaccharides, but when polyphenols were fractionated and isolated, the benefits of the whole extract was greater than the sum of its parts [26].

The protective effect of a polyphenol extract of *Hibiscus* at a dose of 200 mg/kg, reduced serum triacylglycerol, cholesterol and the ratio of LDL/HDL, as well as reduced the plasma AGE formation and lipid peroxidation [27]. *Hibiscus* extract on intestinal α-glucosidase and pancreatic α-amylase activity in vitro, shown to be a potent pancreatic α-amylase inhibitor [28]. Similar results were found for hibiscus-type (2S, 3R)-hydroxyxycetid acid lactone [29], which inhibited pancreatic α-amylase and intestinal α-glucosidase enzyme [30,31].

In alloxan-induced diabetic rats was showed that an ethanolic extract of flowers (200 mg/kg) had hypolipidemic as well as antioxidant effect, which suggest that this activity might be linked to polyphenolic compounds dihydrobenzoic and protocatechuic acids [32].

Decoctions of calyces have been used traditionally in West Africa and Mexico as an anti-hypertensive remedy. The administration of 125 to 500 mg/kg of decoctions reduce systolic and diastolic pressures, heart rate [33-35]. Anti-hypertensive activity might be through inhibition of angiotensin-converting enzymes, presumably angiotensins, as delphinidin-3-O-sambubioside (hibiscin) and cyanidin-3-O-sambubioside (gossypicin) [36,37] and vasorelaxant effects through activation of the endothelium-derived nitric oxide/cGMP-relaxant pathway, or endothelium-independent through inhibition of Ca2+ influx [31].

Clinical studies randomised, double-blind, placebo-controlled clinical trial showed that tea (1.25 g of *Hibiscus sabdariffa* per 240 mL boiled water; 3 servings a day for 6 weeks) reduced blood pressure in pre- and mildly-hypertensive adults [38].

Similar effects on decreasing systolic and diastolic blood pressures were observed in mildly hypertensive type II diabetic individuals when taking green or hibiscus (sour) tea for 4 weeks (three times a day, 2 h after each meal) [39].

*Iberverila sonorae* Greene (syn. *Maximowiczia sonorae* S.Wats) (IS), popularly known as “wareque”, is one of the most widely used plant remedies for the treatment of diabetes. In previous acute studies, a single intraperitoneal administration of aqueous decoction and the raw extract (juice) showed dose-dependent hypoglycemic activity in healthy and alloxan diabetic mice and rats. Moreover, when it was intraperitoneally injected at doses as high as 850 mg/kg body weight, or orally administered at doses as high as 2000 mg/kg, no signs of toxicity were observed in healthy mice [41].

Antidiabetic properties by means of hydro soluble compounds stimulating the glucose uptake in human preadipocytes by a PI3K-independent pathway and without proadipogenic effects [42].

Murine model of obesity and hyperglycaemia, induced by a high-calorie diet, for 8 weeks simultaneous treat aqueous extracts, at doses of 100, 200, and 400 mg/kg, decreased triglycerides and glycaemia levels, prevented an increase in body weight in a dose-dependent manner, and decreased hepatic lipid oxidation at a dose of 200 mg/kg, however, high doses may induce toxicity [43].

*Medicago sativa* (Alfalfa): in various studies on animal models (e.g. rats, prairie dogs, and monkeys), as well as on human volunteers, plant seeds, root and flowering tops have displayed anti-hypercholesterolemia properties [44]. Contains glycosylated triterpenoid saponins, mainly derivatives of medicagenic acid, zanhi acid, lucernic acid, hederagenin, bayogenin and soyasapogenols, these compounds are thought to play a role in plasma cholesterol lowering activities. A saponin-enriched leaf extract has been found to modulate the expression of genes involved in hepatic cholesterol in the rat, providing some hint about the mechanism of action of saponins, and suggesting their potential usefulness in the treatment of hyperlipidemia [45].

The administration of methanolic extract (500 mg/kg), petroleum ether (32.5 mg) and butanol fractions (60 mg), aqueous extract (1 mg/mL) for 4 weeks exhibit activity antihyperlipidemic and antihyperglycemic. Characterization and identification of isolated compounds from the active fractions afforded 9 compounds: β-sitosterol and stigmasteryl from the petroleum ether fraction; 10-hydroxy-coumestrol, 10-hydroxy-coumestrol,
Apigenin, genistein, p-hydroxy-benzoic-acid, 7, 4'-dihydroxyflavone, quercetin-3-glucoside and sissotrin from the ethyl acetate fraction [46-47].

Taraxacum officinale (Dandelion) it has been considered as an herbal medicine due to its anti-diabetic, anti-obesity, and diuretic properties [48]. Hypolipidemic effects of leaf (1 % w/w) in rabbits fed with a high-cholesterol diet, (-36 % on triglycerides, -11 % on LDL values, and 29 % higher of HDL concentration) [49] additionally [50-51] showed that leaf extract (2 and 5 g/kg) on high-fat-diet-induced C57BL/6J mice improved fasting glucose, insulin resistance and reduced the body weight.

1. Aqueous extract (20 mg/kg), to alloxan or streptozotocin-induced rats, decrease serum glucose, additionally in vitro aqueous extracts, can inhibit α-glucosidase with IC50 of 2.3, 3.5, and 1.83 mg plant extract/mL [52-54].

Allium sativum (garlic), in particular alliin, is well known for its anti-diabetic, hypotensive and lipid-lowering properties suggesting a role in the management of SM [55]. Garlic extracts have mainly a significant blood pressure lowering effect [56]. The dry aged garlic extract has an inhibitory activity on ACE and acts as calcium channel blocker, which reduces the sensitivity to catecholamines; it also increases the levels of bradykinin and nitric oxide and consequently improves arterial compliance [57]. A recent meta-analysis of randomized clinical trials controlled with placebo has shown an average reduction in systolic blood pressure in the group of patients treated with garlic; moreover, in the subgroup of patients with hypertension it has been found a mean reduction in systolic blood pressure and diastolic pressure [58].

Garlic reduces the lipogenic and cholesterogenic activities of enzymes such as malic enzyme, fatty acid synthase, glucose-6 phosphate dehydrogenase, and 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase in liver cells. Enhanced the excretion of acidic and neutral steroids and exert hypocholestelemia effects in cholesterol-fed rats [59].

In a recent study of 43 subjects [60], the intake of aged garlic extract for 12 weeks has proved to be effective in increasing the levels of adiponectin, inversely associated to both body weight and cardiovascular disease risk [61].

Anti-obesity garlic is a result of its ability to activate AMP-activated protein kinase (AMPK). AMPK activation led to increase thermogenesis and decreased expression of multiple genes involved in adipogenesis, 1,2-vinlyliithium, reduced lipid accumulation by decreasing the expression of CCAAT-enhancer-binding proteins a (C/EBPa), PPARg2, and lipoprotein lipase (LPL) [62].

Allium cepa Linn (Onion) is rich in sulfur-containing compounds and is used as foodstuff, condiment, flavoring and folk medicine. Sulfur-containing compounds in onion may be volatiles and non-volatiles. When cutting onions, volatile compounds such as dialk (en)yl disulfides and dialk(en)yl trisulfides provide the characteristic flavor and odor through the action of alliinase (E.C. 4.4.1.4, S-alk(en)yl-L-cysteine sulfoxide lyase). Non-volatile cysteine sulfoxides (such as S-methyl-L-cysteine sulfoxide, S-propyl-L-cysteine sulfoxide and S-allyl-L-cysteine sulfoxide) are known as the precursors of the volatile compounds. Onion contains a considerable amount of compounds highly beneficial for human health [63].

Onion has been reported to exert moderately hypolipidemic effects on experimental animals such as healthy pigs fed a high-fat diet and consequently reduction of cardiovascular disease risk and obesity [64-65]. Among bioactive compounds involved in this effect, are quercetin that reduce serum cholesterol levels [66] and S-methyl cysteine sulfoxide with hypoglycemic effect [67-69]. It was inferred that the beneficial in hyperglycemia in part due inhibiting alpha-glucosidase activity and reduce lipid peroxidation [70].

The administration of peel hydroalcoholic extract for 3 weeks reduced the blood pressure via inhibition of calcium influx but without involving nitric oxide [71].

Persea americana (Avocado): anti-obesity effects have been reported for both the leaf and fruit. Aqueous, methanolic, hydro-alcoholic fruit and leaves extracts (10 and 100 mg/kg body weight) for 8 and 14 weeks in hypercholesterolemia albino rats and rats fed at high-fat diet (23 % fat), caused reduction in the body weight gain and body mass index compared to the control [72-73]. This effect was attributed o the up-regulation of PPAR-γ. Chemical constituent’s alkanols (aliphatic acetogenins), terpenoid glycosides, various furan ring-containing derivatives, flavonoids, and a coumarin [74]. The administration of aqueous and methanolic leaves extracts for 8 and weeks in albino rats with hypercholesterolemia improved the concentration of blood glucose and lipid profile [75-76].

Hypotensive activity: the intravenous administration of doses of leaf aqueous and methanol extract of P. americana to normotensive anesthetized rats produced dose-related hypotensive effects, vasorelaxant activity in the rings of rat aorta with intact endothelium was significantly reduced by L-NNAME and methylene blue, the vasorelaxant effect may also be produced by the inhibition of Ca2+ mobilization through voltage-dependent channels and, to a lesser extent, through receptor-operated channels [77].

Citrus fruits such as oranges (Citrus sinensis), mandarin (Citrus reticulata), grapefruit (Citrus paradisi) and lemon (Citrus limon), are especially rich in flavonoids, mainly naringenin, which according to fruits this flavonoid content varies. Administration of lemon peel for 12 weeks, rats with high fat intake, decreases body weight gain through, induce expression of enzymes involved in β-oxidation, as acyl-CoA oxidase and fatty acid synthase in the liver and adipose tissue. Administration of naringenin (0.003%, 0.006%, and 0.012%) for 6 weeks reduced adiposity, plasma triglycerides and cholesterol because it induces increased expression in liver enzymes of carnitine palmitoyltransferase 1 protein (CPT-1), and decoupling 2, 3 hydroxy-3- methylglutaryl-CoA (HMG-CoA). Citrus paradisi has been used as an aid in weight reduction, inhibiting adipogenesis in subcutaneous rat adipocytes. The consumption of fresh fruit before eating any food has an effect on body weight loss, in addition to improving insulin resistance in humans [78-80]. Other effects exhibited naringenin is prevention of lipid peroxidation and oxidative stress because it enhances the antioxidant activity of superoxide dismutase, catalase and glutathione peroxidase, which improves endothelial function through increasing the production of nitric oxide and inhibits proliferation of smooth muscle cells by TNF-α.

The administration of lyophilized C. sinensis juice at a dose of 5 g/kg in aqueous vehicle in a volume of 0.5 mL/100 g body weight for 15 days on male Wistar rats, decreased plasma levels of cholesterol, LDL and triglycerides. Microsized insoluble fibers of fruits lowered the concentrations of serum triglycerides and serum total cholesterol by means of enhancing the excretion of cholesterol and bile acids in feces [81].
The effects of citrange (C. sinensis × Poncirus trifoliate) fruit extracts in high-fat (HF) diet-induced obesity showed citrange peel extract or citrange flesh for 8 weeks. The body weight, blood glucose, serum total cholesterol and LDL cholesterol decreased levels through inhibition of PPARγ and liver X receptor (LXR) α and β, involved in lipid and glucose metabolism [82].

The drinking of commercial decreased diastolic and systolic blood pressure in healthy volunteers using 500 mL/day of orange juice twice a day during four-weeks. However, the administration of natural Citrus sinensis juice during four weeks did not have significant effects on either diastolic or systolic blood pressure [93].

Punica granatum (Pomegranate): Juice, seed oil, and flower extracts are rich in many compounds such as proanthocyanidin and ellagitannins [84]. The pomegranate seeds contain high concentration of conjugated fatty acids such as linoleic, linolenic, punicic, stearic and palmitic acid. Minor amounts of conjugated linolenic acid isomers including eleostearic and catalpic acid, are found [85].

Administration punic acid (800 mg / day), seed oil (400 mg) twice daily, for 4 weeks to patients with hyperlipidemia, they reduced the plasma concentration of triglycerides and HDL, cholesterol, LDL-C and glucose unmodified [86].

The anti-obesity effect mechanism reported for flower is at least in part, by activating hepatic expression of genes responsible for fatty acid oxidation. Other anti-obesity mechanisms reported for is inhibition of the pancreatic lipase activity, suppressing energy intake by appetite suppressant [87].

2. The anti-diabetic effect was reported that hydro-ethanolic extract of flowers at 200, 300 and 500 mg/kg/day for 18 days and 6 weeks in obese Zucker and streptozotocin-induced diabetic rats, reduced the serum glucose, cholesterol, triglycerides, LDL, urea, uric acid, creatinine, alanine amino transferase and aspartate amino transferase enzymes levels, while it increased serum HDL level in comparison to control diabetic rats [88].

The anthyptensive effect of juice (100 mg/kg) for 4 weeks decreases systolic blood pressure through to inhibit the activity of angiotensin converting enzyme [89].

Psidium guajava Linn. (guava): is native to tropical and subtropical countries. Its fruit is commonly used as food and processed as juice and aqueous leaf extract caused hypotension in the experimental animal model used via cholinergic mechanisms [90]. Moreover, acute intravenous administrations of the leaf extract (50–800 mg/kg i.v.) produced dose-dependent, reductions in systemic arterial blood pressures and heart rates of hypertensive, Dahl salt-sensitive rats [90]. The proposed mechanism for this effect is through activation of an alpha-adrenoceptor and to a lesser extent by acting via calcium ion channel [90].

Guava contains high levels of dietary fibre and could have health potential in the management of blood glucose level; administration of ethanol extract, (250 mg) decoction of leaves, aqueous leaf extract (0.01–0.625 mg/ml) or capsules (500 mg) on alloxan-induced diabetic rat or diabetic patients, reduced blood glucose level, but is devoid of hypoglycemia effect in normal and normal glucose loaded rats [91]. Tannins, flavonoids, pentacyclic triterpenoids, guaiaverin and quercetin present in the plant are speculated to account for the observed hypoglycemia and hypotensive effects leaf extract [91].

Guava is an excellent anti-LDL glycate agent [92-93] the aqueous (0.01–0.625 mg/ml) and methanol (10 mg/kg) exhibit excellent antiglycation effect, being a rather powerful and effective inhibitor of LDL glycation in both glucose and glyoxal induced models. The antiglycation activities directly related with polyphenolic content (extractable polyphenols 2.62–7.79%). In patients shown that consumption of 400 g / day guava it reduces levels of blood cholesterol and oxidative stress [94].

Malus domestica (Apples) are the fourth most widely produced fruit and approximately 20% of the freshly harvested apples are used for juice production. Apple pomace, the press residue from juice production, represents a mixture of flesh, stem, seeds and peel and is used, for example, as animal feed [95] for the production of pectin, ethanol, natural gas, or citric acid [96] But apple pomace also represents a rich and especially cheap source of polyphenolic compounds, one of the polyphenol compounds in apples is phlorizin, which is relatively stable during drying and long-term storage [97]. The main biological effect of phlorizin is the competitive inhibition of intestinal glucose uptake and renal glucose re-absorption via the sodium d-glucose co-transporters 1 and 2 (SGLT1 and SGLT2) located in the proximal renal tubule [98]. Similar to other inhibitors of SGLT, phlorizin inhibits the re-uptake of glucose in the kidneys and thus lowers the plasma glucose concentration and increases the renal excretion of glucose. Transporter-mediated uptake of glucose accounts for most intestinal glucose uptake under physiological conditions, and phlorizin effectively abolishes intestinal glucose uptake. In addition to its direct anti-hyperglycaemia effect, phlorizin mediates several other pharmacological activities. For example, phlorizin promotes lipolysis and inhibited inflammation in macrophage–adipocyte co-cultures [99-100]. Furthermore, apple polyphenols and phlorizin have been suggested as new trapping agents of reactive dicarbonyl species, which might delay the formation of advanced glycation end-products (AGEs) [100].

Procyanidin-rich apple polyphenol extract to attenuate disruptions in lipid membranes and lipid metabolism resulting from exposure to dietary cholesterol oxidation products [101]. Feeding the extract to rats for 3 wk resulted in reduction markers of lipid metabolism including reduced lipoperoxides (measured by TBARS) in serum and liver, lowered SOD activity in RBC, lower hepatic Δ6 desaturase activity, altered fecal excretion patterns, and reduced levels of oxidized cholesterol products in serum and liver. Plasma levels of HDL cholesterol increased and liver TG content decreased, although plasma TG levels were somewhat higher, so that the high procyanidin content and metabolites in the apple extract might directly interfere with cholesterol absorption in addition to modulating lipids and lipid-related processes.

In vitro work in cultured human intestinal cells suggested that apples may directly alter lipid absorption and metabolism. Caco-2/TC7 cells were exposed to apple extract, including a polyphenolic concentration equivalent to the consumption of 3apples/d. It was found that the accumulation of esterified cholesterol decreased and the secretion of apo-B (B-48 and B-100) containing lipoproteins was reduced. Similar results were found in cells exposed to an enriched extract of procyanidins (flavanols, catechin, and epicatechin). If these findings are applicable to the in vivo situation, altered intestinal lipid secretion might account for the lipid-lowering effect of AP observed in some studies and suggest one possible mechanism for reduced risk of cardiovascular disease [101].

Antihypertensive effect. On clinical trials, reported that consumption of 425.8 mg epicatechin for 2 weeks decreased blood pressure in hypertension subjects [102].

Lagenaria siceraria is known as Gourd, pumpkin pilgrim,
spoon, waist gourd, calabusa raft, acinturiao bule, itsui, pumaxkat, xical, xicale, buli, xomom, kweentu. Various parts of bottle gourd were utilized as medicines by many peoples around the world. Administration of fresh bottle gourd juice to healthy volunteers received reduced plasma glucose and cholesterol. Other studies showed that the pulp and seed extract stimulate insulin secretion of pancreatic beta cells, followed by the decrease of blood glucose\cite{103-104}.

Anti-hyperlipidemia activity: The cardioprotective effects were assayed by the methanolic extracts in hyperlipidaemic induced rats. The lipid level in rats were reduced gradually after 30 days of evaluation and observed \textit{L. siceraria} fruits have a capacity to increase the excretion of bile salts\cite{105}.

Antihypertensive activity: \textit{L. siceraria} fruit powder administered in the dexamethasone-induced rats on long term, decreased in the hypertensive activity in \textit{lagensaria} siceraria rats\cite{106}, and other study showed administration of fruit (500 mg/kg) antihypertensive and cardioprotective activity inhibition of nitric oxide synthesis induced hypertension in rats\cite{107}.

\textbf{Conclusion}

The severity of metabolic syndrome per se as well as its complications and the global rise of people affected encourage research and search for new drugs that help control. Mexican ethnobotany offers scientific study of plants used empirically to validate experimentally the effects.

\textbf{References}


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