

Eddouks M and Zeggwagh NA

Faculty of Sciences and Techniques Errachidia, Moulay Ismail University, BP 21, Errachidia, Morocco.

Abstract

This paper aims to review some medicinal plants and compounds of botanical origin which are capable to lower plasma glucose levels and blood pressure. Hypoglycemic natural products comprise flavonoids, xanthones, triterpenoids, alkaloids, glycosides, alkyl disulfides, aminobutyric acid derivatives, guanidine, polysaccharides and peptides. Hypotensive compounds include flavonoids, diterpenes, alkaloids, glycosides, polysaccharides and proteins.

Keywords: Blood pressure, hypoglycemic activity and medicinal plants.

*Corresponding Author:

Eddouks M,

Faculty of Sciences and Techniques Errachidia,
Moulay Ismail University, BP 21, Errachidia,
Morocco.

Tel: 00212535574497; Fax: 00212535574485

E-mail: mohamed.eddouks@laposte.net

Received: July 12, 2014

Accepted: July 26, 2014

Published: July 29, 2014

Citation: Eddouks M and Zeggwagh NA (2014) A Short Review of Some Medicinal Plants And Phytochemicals With Hypotensive And Hypoglycemic Activities. Int J Diabetol Vasc Dis Res. 2(5), 63-66. doi: <http://dx.doi.org/10.19070/2328-353X-1400012>

Copyright: Eddouks M © 2014. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Introduction

The serious health risks posed by hyperglycemia and hypertension need little elaboration. Diabetes mellitus, which manifests itself hyperglycemia and other symptoms, would lead, if untreated, to a myriad of complications including retinopathy, neuropathy, coronary heart disease, stroke, etc. Hypertension and hypercholesterolemia may also result in cerebrovascular accident and myocardial infarction if not well taken care of. Atherosclerosis is thickening and hardening of the vessel walls due to soft deposits of intra-arterial fat and fibrin that harden over time [1,2]. Hypertension appears if atherosclerosis increases systemic vascular resistance [3-7]. Atherosclerosis contributes to coronary artery and cerebrovascular disease.

Natural products furnish a good source for treatment of diabetes and hypertension around the world especially in developing countries. In fact, the fungal product mevinolin, a competitive inhibitor of P-hydroxy-p-methylglutaryl CoA reductase, is used to treat hypercholesterolemia, and a host of related drugs (statins) with antiatherosclerotic and antithrombotic properties have been developed [8,12]. Biguanides such as metformin, which has been in use for the treatment of non-insulin-dependent diabetes mellitus, are derived from guanidine, another natural product.

Many medicinal plants have demonstrated to exert antidiabetic and hypotensive activities in different animal models as well as in vitro and a lot of compounds responsible for this pharmacological activity have been isolated [13-16]. This non-exhaustive short review focuses on some medicinal plants and botanical compounds with hypoglycemic and hypotensive activities

Plants And Phytochemicals with Hypoglycemic Activity

Acacia arabica

Wadood *et al* demonstrated that *Acacia arabica* seeds contained substance(s) which depressed the blood glucose level in normoglycaemic but not in alloxan-diabetic rabbits, suggesting that the mechanism of action involved release of insulin from pancreatic beta-cells [17].

Artemisia herba alba

Aerial parts of *Artemisia herba alba*, which is used in Iraqi folk medicine as an anti-diabetic agent, exerted a significant hypoglycemic action on normoglycemic and alloxan-diabetic rats [5].

Cleome droserifolia

An extract of the plant suppressed the basal blood glucose level and also the postprandial hyperglycemia in rats rendered glucose-intolerant with tetracycline. Potentiation of peripheral and hepatic insulin sensitivity and reduction of intestinal glucose absorption were implicated in the mechanism of hypoglycemic action of the plant extract. Additionally, the extract might possess anti-atherogenic activity in view of its ability to elevate the ratio of high density lipoprotein-cholesterol to low density lipoprotein-cholesterol in the blood [18,19].

Eugenia jambolana

The pulp as well as the seed extract of *E. jambolana* fruits displayed hypoglycemic activity. Serum insulin level rose after oral administration of the extracts in normoglycemic and streptozotocin-induced diabetic rats. Insulin secretion from isolated islets of Langerhans from normal and diabetic rats was augmented after incubation with the extracts [20,21].

Ficus bengalensis

Similarly the bark extract of *E. bengalensis* possessed hypoglycemic activity. Insulin secretion was augmented in combination with *E. bengalensis* and *E. jambolana* pulp and seed extracts. A flavonoid of leucodelphinidin derivative isolated from *E. bengalensis* by Geetha *et al* [22] showed hypoglycemic activity in normal and alloxan-induced diabetic rats, comparable with the activity of glibenclamide [22,23].

Glossostemon bruguieri

Mucilage from *G. bruguieri* roots exerted a pronounced hypoglycemic action on diabetic rats, bringing the glucose level down to half of the pre-treatment level within 15 days. It is noteworthy that the powdered root of the plant has been traditionally used in Eastern countries because of its nutritive and therapeutic value [9].

Lagerstræmia speciosa

Colosolic acid isolated from *Lagerstræmia speciosa* can activate glucose transport into Ehrlich ascites tumor cells along with hypoglycemic activity [10].

Lythrum salicaria

The hypoglycemic activity of extracts of this plant has been studied. Lamela *et al* [11] subsequently reported that ethereal extracts of the stems and flowers induced hypoglycemia and enhanced insulin secretion in normoglycemic rats.

Momordica charantia

A polypeptide with 66 amino acid residues, designated as polypeptide-P, was isolated from the fruits and seeds of *M. charantia*, elicited hypoglycemia in gerbils, langurs and humans when administered subcutaneously [24,25]. Two polypeptides from the seeds, with a molecular weight of approximately 90,000 and amino acid compositions distinct from that of insulin, displayed insulin-like (i.e. antilipolytic and lipogenic) activities in isolated rat adipocytes. Saponin-free methanolic extract of pulp juice of this plant elicited hypoglycemia in normal rats and glucose-fed normal rats but was devoid of similar effects in streptozotocin-induced diabetic rats and glucose-fed normal rats either in the fasting or postprandial state. Similarly prepared extracts of seeds and the whole plant were ineffective [26]. The results suggest that non-sapogenin compounds in the *M. charantia* fruit pulp produced hypoglycemia by augmenting insulin secretion from beta cells or by potentiating the action of insulin.

Opuntia cactus

The plant extract of this plant can lower blood glucose level in pancreatectomized rabbits as well as normal rabbits, and was used traditionally in Mexico for treating diabetes [27].

Panax ginseng

Glycans isolated from this plant, like panaxans A to E had been demonstrated to elicit hypoglycemia in both normal and diabetic mice [28,29]. A fraction of panaxan called DPG-3-2 exerted its hypoglycemic action or provoked insulin secretion in diabetic and

glucose-loaded normal mice. Adenosine, a carboxylic acid, and a peptide with a molecular weight of 1400 inhibited catecholamine-induced lipolysis in rat epididymal fat pads. EPG-3-2, a fraction of DPG-3-2, also exhibited antilipolytic activity [30].

Petiveria alleaceae

Extracts of leaves and stems of *Petiveria alleaceae* showed over 60% reduction in blood glucose concentration one hour after oral administration in male Balb/c mice which had been fasted for 48 hours [21,31,32].

Phaseolus vulgaris

Hypoglycemic activity of the vegetal complex of *P. vulgaris* in experimental diabetes was demonstrated by Khaleeva *et al* [20].

Swertia chirayita

Swertichirin (1,8-dihydroxy-3,5-dimethoxyxanthone), a xanthone from the hexane fraction of *S. chirayita*, produced hypoglycemic activity in fasted, fed, glucose-loaded and tolbutamide-pretreated rats [21]. Centipiperalone induced hypoglycemia in normal rats, elevation of plasma immunoreactive insulin level and B-cell degranulation. It was also active in streptozotocin-induced severely diabetic rats [22].

Swertia japonica

Five xanthones with two triterpenoids were isolated from the ethyl acetate-soluble fraction of *S. japonica* with hypoglycemic activity [23]. Thysanolactone was one of that triterpene, first isolated from *S. japonica*, while a xanthone bellidifolin manifested a potent hypoglycemic activity in streptozotocin-induced diabetic rats [23].

Tecoma stans

T. stans is an allegedly antidiabetic medicinal plant in Mexico. Intravenous administration of *T. stans* infusion in normal dogs evoked an early hyperglycemic response probably due to hepatic glycogenolysis, followed by a slow decline of blood glucose level [33,34].

Teucrium polium

An aqueous decoction of the aerial parts of *T. polium* produced a decline in blood glucose level 4 hours after intravenous administration and 24 hours after intraperitoneal injection, probably by increasing peripheral metabolism of glucose and not by augmenting insulin release [25].

Among the known hypoglycemic natural products some polysaccharides have been reported such as aconitan A from *Aconitum carmichaeli* root, anemaran A from *Anemarrhena asphodeloides* rhizome, dioscoran C from *Dioscorea japonica* rhizophor, lithospermum B from *Lithospermum elythrhorizon* root, panaxan from *Panax ginseng* root and saccharan C from *Saccharum onarum* stalk; while tuber of *Amorphophallus korjaci* yielded glucomannan and seeds of *Cyamopsis tetragonolobus* showed galactomannan [35,37].

Epicatechin, a flavonoid from *Pterocarpus marsupium* heartwood; alkaloids from leaves of *Catharanthus roseus*, *Coccinia indica* and *Tecoma stans*, *Lupinus terminis* seeds; glycosides from *Ficus bengalensis*

bark, *Ficus religiosa* root bark and *Gymnema sylvestre*, leaves and aerial part of *Momordica charantia* were the other hypoglycemic products. Alkyldisulfides from *Allium cepa* and *Allium sativum* bulbs, hypoglycins (aminopropylpropionic acid derivatives) from unripe fruits of *Blighia sapida*, aminobutyric acid derivative from *Emericella quadrilimeata* fruiting bodies and guanidine from *Galega officinalis* leaves were among the other anti-diabetic compounds cited [35-37].

Of the aforementioned compounds, guanidine is toxic at high doses. However, biguanides and the antidiabetic drug metformin are derived from guanidine [2]. Alkyl disulfides lack stability and hypoglycins are toxic, hence limiting their usefulness. Hypoglycemic polysaccharides may act within the intestinal tract to retard glucose absorption but they can also suppress blood glucose level when administered parenterally, suggesting a distinct sites of action [35-37].

Plants And Phytochemicals with Hypotensive Activity

Andrographis paniculata

The *n*-butanol extract of *Andrographis paniculata* evoked a dose-dependent fall in mean arterial blood pressure without influencing the heart rate in Sprague-Dawley rats. The hypotensive action was not altered by propranolol, atropine and captopril, indicating that it was not mediated through the β -adrenoceptor, muscarinic cholinergic receptor and angiotensin-converting enzyme. The hypotensive action was mediated by α -adrenoceptors, autonomic ganglion and histaminergic receptors because of the attenuating effect of phentolamine, hexamethonium, pyrilamine and cimetidine [12].

Cadiu elliuma

The hypotensive potency of the alkaloid 13-hydroxylupanine-2-pyrrolcarboxylic acid ester from the plant was higher in anesthetized dogs, monkeys and rats than that in conscious animals. In the isolated rabbit heart with intact accelerator nerves, perfusion with the alkaloid reduced norepinephrine release from nerve endings, diminished the positive inotropic effect and decreased the rise in heart rate by electrical stimulation of the accelerator nerve. The alkaloid inhibited transmission of sympathetic impulse and attenuated sympathetic circulatory reflexes. The antifibrillatory effect of the alkaloid was also demonstrated [16].

Casimiroa edulis

An aqueous extract of the seeds suppressed rat aortic ring contractions induced by norepinephrine, serotonin and prostaglandin. An intact vascular endothelium was not required and histamine antagonists had no effect [4].

Chrysanthemum indicum

It is a traditional drug used for hypotensive activity. Chrysantheriol, a sesquiterpene, has been isolated from the plant but its hypotensive principle remains to be elucidated [8,9,38].

Coleus forskohlii

The diterpene coleonol isolated from *Coleus forskohlii* lowered blood pressure in the anesthetized cat and the spontaneously hypertensive rat due to relaxation of vascular smooth muscle. The

diterpene forskolin potentiated the effect of adenosine on coronary relaxation [11,12].

Cynomorium coccineum

Fresh juice and its water-soluble fraction blocked the entry of extracellular calcium through calcium channels and inhibited the release of intracellularly stored calcium in the vascular smooth muscle cell [14,15].

Lindera megaphylla

Dicentrine, an aporphine derivative and α -adrenoceptor antagonist, was isolated from *Lindera megaphylla*. Intravenous administration of dicentrine elicited a dose-related decrease in mean arterial pressure in anesthetized normotensive rats without affecting heart rate, cardiac output and stroke volume but markedly increasing tail blood flow [19].

Moringa oleifera

Niaziminin A, niaziminin B and 4-[(4'-O-acetyl- α -1-rhamnosyloxy) benzyl] isothiocyanate have been isolated from the ethanolic extract of *M. oleifera* leaves which has been reported to exhibit hypotensive activity [17].

Ocotea duckei

A specific platelet-activating factor (PAF) receptor antagonist, yangambin, was isolated from this plant and the pretreatment of yangambin curtailed PAP-induced cardiovascular changes and thrombocytopenia [18,19].

Phyleanthus amarus

A preparation of the entire plant showed hypotensive effects on humans with mild hypertension [39].

Conclusion

In this non-exhaustive short review, we have reported some known hypoglycemic and antihypertensive medicinal plants. In addition some known active botanical active substances have been cited. This scoop shows the growing interest toward the use of medicinal plants in the treatment of diabetes and hypertension.

Acknowledgments

The authors extend their thanks to the Moroccan Government for supporting this work.

References

1. Ai J, Yan X, Zhao L, Lu Y, Liang F, et al. (2009) The protective effect of Daming capsule on heart function in streptozocin-induced diabetic rats with hyperlipidemia. Biol Pharm Bull 32: 1354-8.
2. Ameer, O.Z., Salman, I.M., Siddiqui, M.J.A., Yam, M.F., Sriramaneni, R.N., et al. (2009) Characterization of the possible mechanisms underlying the hypotensive and spasmogenic effects of *Loranthus ferrugineus* methanolic extract. Am J Chin Med 37: 991-1008.
3. Bailey SJ, Winyard P, Vanhatalo A, Blackwell JR, Dimenna FJ, et al. (2009) Dietary nitrate supplementation reduces the O₂ cost of low-intensity exercise and enhances tolerance to high-intensity exercise in humans. J Appl Physiol 107: 1144-55.
4. Balint EE, Falkay G, Balint GA (2009) Khat - a controversial plant. Wien Klin Wochenschr 121: 604-14.

- [5]. Barceló, F., Perona, J.S., Prades, J., Funari, S.S., Gomez-Gracia, E., et al. (2009) Mediterranean-style diet effect on the structural properties of the erythrocyte cell membrane of hypertensive patients: the Prevention con Dieta Mediterranea Study. *Hypertension* 54: 1143-50.
- [6]. Baumann, M., Richart, T., Sollinger, D., Pelisek, J., Roos, M., et al. (2009) Association between carotid diameter and the advanced glycation end product N-epsilon-carboxymethyllysine (CML). *Cardiovasc Diabetol* 8: 45.
- [7]. Belmokhtar M, Bouanani NE, Ziyat A, Mekhfi H, Bnouham M, et al. (2009) Antihypertensive and endothelium-dependent vasodilator effects of aqueous extract of *Cistus ladaniferus*. *Biochem Biophys Res Commun* 389: 145-9.
- [8]. Brown, M.J (2009) Success and failure of vaccines against renin-angiotensin system components. *Nat Rev Cardiol* 6: 639-47.
- [9]. Bucarety F, de Capitani EM, Hyslop S, Mello SM, Madureira PR, et al. (2010) Compartment syndrome after *Bothrops jararaca* snakebite: monitoring, treatment, and outcome. *Clin Toxicol (Phila)* 48: 57-60.
- [10]. Chao, M., Zou, D., Zhang, Y., Chen, Y., Wang, M., et al. (2009) Improving insulin resistance with traditional Chinese medicine in type 2 diabetic patients. *Endocrine* 36: 268-74.
- [11]. Cowie, R.V., Stone, P.R., Parry, E., Jensen, E.C., Gunn, et al. (2009) Acute behavioral effects of intrapleural OK-432 (Picibanil) administration in pre-term fetal sheep. *Fetal Diagn Ther* 25: 304-13.
- [12]. Cui HZ, Choi H.R, Choi DH, Cho KW, Kang DG, et al. (2009) Aqueous extract of *Zanthoxylum schinifolium* elicits contractile and secretory responses via beta1-adrenoceptor activation in beating rabbit atria. *J Ethnopharmacol* 126: 300-7.
- [13]. Egert, S., Boesch-Saadatmandi, C., Wolfram, S., Rimbach, et al. (2010) Serum lipid and blood pressure responses to quercetin vary in overweight patients by apolipoprotein E genotype. *J Nutr* 140: 278-84.
- [14]. Eggink M, Charret S, Wijtmans M, Lingeman H, Kool J, et al. (2009) Development of an on-line weak-cation exchange liquid chromatography-tandem mass spectrometric method for screening aldehyde products in biological matrices. *J Chromatogr B Analyt Technol Biomed Life Sci* 877: 3937-45.
- [15]. Fu Y, Yuan J, Chen J, Xie Y (2009) The effects and mechanisms of *Forsythia suspense* on the expression of Foxp3 on splenocytes and level of Treg in peripheral blood in severely burnt rats. *Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi* 25: 935-7.
- [16]. Garjani A, Afroozian A, Nazemiyeh H, Najafi M, Kharazmkia A, et al. (2009) Protective effects of hydroalcoholic extract from rhizomes of *Cynodon dactylon* (L.) Pers. On compensated right heart failure in rats. *BMC Complement Altern Med* 9: 28.
- [17]. Kim T, Kim B, Kim J, Kim K, Yi S, et al. (2009) Comparison of the pharmacokinetics of ticlopidine between administration of a combined fixed-dose tablet formulation of ticlopidine 250 mg/ginkgo extract 80 mg, and concomitant administration of ticlopidine 250-mg and ginkgo extract 80-mg tablets: an open-label, two-treatment, single-dose, randomized-sequence crossover study in healthy Korean male volunteers. *Clin Ther* 31: 2249-57.
- [18]. Lei H, Ji W, Lin J, Chen H, Tan Z, et al. (2009) Effects of Ginkgo biloba extract on the pharmacokinetics of bupropion in healthy volunteers. *Br J Clin Pharmacol* 68: 201-6.
- [19]. Leong, X., Najib, M.N.M., Das, S., Mustafa, M.R., Jaarin, K (2009) Intake of repeatedly heated palm oil causes elevation in blood pressure with impaired vasorelaxation in rats. *Tohoku J Exp Med* 219: 71-8.
- [20]. McKay DL, Chen CO, Saltzman E, Blumberg JB (2010) Hibiscus sabdariffa L. tea (tisane) lowers blood pressure in prehypertensive and mildly hypertensive adults. *J Nutr* 140: 298-303.
- [21]. Mohan M, Jaiswal BS, Kasture S (2009) Effect of *Solanum torvum* on blood pressure and metabolic alterations in fructose hypertensive rats. *J Ethnopharmacol* 126: 86-9.
- [22]. Renouf M, Marmet C, Guy P, Fraering A, Longet K, et al. (2010) Nondairy creamer, but not milk, delays the appearance of coffee phenolic acid equivalents in human plasma. *J Nutr* 140: 259-63.
- [23]. Sams C, Patel K, Jones K (2010) Biological monitoring for exposure to pirimicarb: method development and a human oral dosing study. *Toxicol Lett* 192: 56-60.
- [24]. Swaggerty CL, Pevzner IY, He H, Genovese KJ, Nisbet DJ, et al. (2009) Selection of broilers with improved innate immune responsiveness to reduce on-farm infection by foodborne pathogens. *Foodborne Pathog Dis* 6: 777-83.
- [25]. Takayama S, Seki T, Watanabe M, Monma Y, Sugita N, et al. (2009) The herbal medicine Daikenchuto increases blood flow in the superior mesenteric artery. *Tohoku J Exp Med* 219: 319-30.
- [26]. Yoshimura, M., Toyoshi, T., Sano, A., Izumi, T., Fujii, T., et al. (2010) Antihypertensive effect of a gamma-aminobutyric acid rich tomato cultivar 'DG03-9' in spontaneously hypertensive rats. *J. Agric Food Chem* 58: 615-9.
- [27]. Shimada M, Hasegawa T, Nishimura C, Kan H, Kanno T, et al. (2009) Antihypertensive effect of gamma-aminobutyric acid (GABA)-rich *Chlorella* on high-normal blood pressure and borderline hypertension in placebo-controlled double blind study. *Clin Exp Hypertens* 31: 342-54.
- [28]. Perona JS, Montero E, Sánchez-Domínguez JM, Cañizares J, García M, et al. (2009) Evaluation of the effect of dietary virgin olive oil on blood pressure and lipid composition of serum and low-density lipoprotein in elderly type 2 diabetic subjects. *J Agric Food Chem* 57: 11427-33.
- [29]. Qin, Y., Wu, X., Huang, W., Gong, G., Li, D., et al. (2009) Acute toxicity and sub-chronic toxicity of steroidal saponins from *Dioscorea zingiberensis* C. H. Wright in rodents. *J Ethnopharmacol* 126: 543-50.
- [30]. Ofem OE, Eno AE, Nku CO, Antai AB (2009) *Viscum album* (mistletoe) extract prevents changes in levels of red blood cells, PCV, Hb, serum proteins and ESR in high salt-fed rats. *J Ethnopharmacol* 126: 421-6.
- [31]. Monsky WL, Pahwa A, Li C, Katzberg RW (2009) Clinical factors associated with dense and wedge-shaped nephrograms detected 24 h after chemoembolization. *Cardiovasc Intervent Radiol* 32: 1193-1201.
- [32]. Myers A, Barrueto FJ (2009) Refractory priapism associated with ingestion of yohimbe extract. *J Med Toxicol* 5: 223-5.
- [33]. Neelam, K., Mahalingam, R., Birudharaj, R., Alfredson, T., Anne, P., et al. (2009) Relative bioavailability of chlorothiazide from mucoadhesive compacts in pigs. *AAPS Pharm Sci Tech* 10: 1331-5.
- [34]. Ochiai R, Chikama A, Kataoka K, Tokimitsu I, Maekawa Y, et al. (2009) Effects of hydroxyhydroquinone-reduced coffee on vasoreactivity and blood pressure. *Hypertens Res* 32: 969-74.
- [35]. He L, Di B, Du Y, Yan F, Su M, et al. (2009) Development and validation of a high performance liquid chromatography-tandem mass spectrometry method for the rapid simultaneous quantification of aconitine, mesaconitine, and hypaconitine in rat plasma after oral administration of *Sini* decoction. *J Anal Toxicol* 33: 588-94.
- [36]. Hwang J, Kwon DY, Yoon SH (2009) AMP-activated protein kinase: a potential target for the diseases prevention by natural occurring polyphenols. *N Biotechnol* 26: 17-22.
- [37]. Hwang K, Choi HG (2009) Bleeding from posterior superior alveolar artery in Le Fort I fracture. *J Craniofac Surg* 20: 1610-2.
- [38]. Broncel M, Kozirog M, Duchnowicz P, Koter-Michalak M, Sikora J, et al. (2010) *Aronia melanocarpa* extract reduces blood pressure, serum endothelin, lipid, and oxidative stress marker levels in patients with metabolic syndrome. *Med Sci Monit* 16: CR28-34.
- [39]. Woottisin S, Hossain RZ, Yachantha C, Sriboonlue P, Ogawa Y, et al. (2011) Effects of *Orthosiphon grandiflorus*, *Hibiscus sabdariffa* and *Phyllanthus amarus*. Extracts on Risk Factors for Urinary Calcium Oxalate Stones in Rats. *J Urol* 185(1): 323-8.