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An overview of available Hypoglycemic Triterpenoids and Saponins to cure Diabetes mellitus

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Abstract

Diabetes mellitus is a condition when excess amount of sugar is excreted out in the urine. It is probably caused due to hyperglycemia; when body fails to produce sufficient amount of insulin which may utilize or help to store these excessive carbohydrates. When a body does not produce sufficient insulin or to help utilize carbohydrates, it results in the accumulation of unutilized sugar in the blood, the condition is termed as hyperglycemia whereas the condition of passing off the excess sugar in the urine is known as *diabetes mellitus*. The excretion of sugar makes a profound effect on health that may lead to disability and death. According to some studies, it may cause myocardial infarction, cardiovascular disorders and terminal nephritis. These complications are reported to be the most important causes of mortality and the principal cause of irreversible blindness. There are hundreds of millions of patients around the world suffering from this disease and the number is spreading with an alarming rate. Such a condition has inspired the therapists to develop the methods which help in controlling this malaise. In this article, we have summarized some of hypoglycemic agents from natural sources especially from plants. Since there is a vast number of plants, which are reported to be utilized traditionally in the crude form for diabetes cure in the past. This article is meant to mention only the hypoglycemic ingredients of triterpenoids origin. This information can be helpful in getting new and more effective drugs in future by utilizing unexplored plants which are reported in the literature to possess hypoglycemic activity. This current review is comprised of the relevant work done up to the year 2007 based on search from Google.

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Introduction

There are quite a large number of people who suffer from diabetes that may result from hyperglycemia. According to one estimate there were 124.7 million cases of diabetes mellitus in the recent past around the world [1-3]. Whereas another study reveals that the number is expected to increase by 2025 to 300 million from 151 million as recorded in the year 2000 [2]. With the passage of time there is an exponential growth in the number of patients with diabetes mellitus and it would be a leading cause of higher death rates in the near future. It therefore, has become a big challenge to the therapists to devise the methods to effectively control this disease. There is a need of exploring the effective ways to bring about awareness to the masses regarding prevention measures and proper ways and means to cure the disease, diabetes mellitus. If such efforts are not dealt with properly and seriously, the disease could be a leading cause of deaths. A number of drugs have been discovered in this regard. However, the disease still has a profound effect on human life. Nowadays as the phytochemical research has acquired a predominant position in the field of medicine, the interest is advanced to explore the plants which may prove to be beneficial for the control of this disease.

Methods

Search strategy and selection criteria

A systematic search was carried out from Google by entering keywords like, "Hypoglycemic Triterpenoids" and "saponins'' with no filter. We found about 36,000 results, from which only 80 relevant articles.

Discussion

Hypoglycemic constituents Role

The compound which brings the excessive sugar level towards the normal range by certain biochemical reactions is known as hypoglycemic component. There are several classes of organic compound which possess hypoglycemic activity such as terpenoids, steroids, saponins flavonoids, alkaloids, glycans proteins [2]. To cite all of them is beyond the scope of this article. Hence the compound of triterpeniod origin obtained from various plants is described. Hence the hypoglycemic compounds of triterpeniod origin reported since the beginning of systematic investigation up to the year 2007 from various plants are described. The relevant constituents are summarized in tables (1- 6) which are specified with the particular groups of triterpenoids.

Triterpenoids and saponins with hypoglycemic activity

Most of the hypoglycemic triterpenoids (Table 1) and their glycosides (Table 2-3) belong to oleanane group. Some other groups with the similar activity comprising of ursane (Table 4), lupane (Table 5) are reported to a lesser extent.

Compound name	Source	Part used	Reference
Bassic acid,2β, 3β, 23-Trihydroxy-5,12-oleanedien-28-oic acid	*Bumeliasartorum*	Root bark	[4]
Glycyrrhetinic acid, Syn.-Sumaresinoleic acid,3β-Hydroxy-11-oxo-12-oleanen-30-oic acid; (18α) – form	*Peterium Spinosum*	Roots	[5]
Hederagenin acid, 3β,23-Dihydroxy-12-oleanolic acid; (18β) –form	*Oleaeuropaea* (olive) and *Campsis grandiflora*	Leaves	[6,7]
Oleanolic acid,3β-Hydroxy-12-oleanen-28-oic acid	*Memordica Cochinchinensis,* *Olea Europaea (olive) Campsis Grandilora* *Aralia dasyphylla Mig* *Beuvardia terniflora* *Syzegium aromaticum*(Clove)	Seeds Leaves Stem Unopened flower bud	[1,8] [6,7] [9,10]
16β-Hydroxy-18β-H-oleanolic acid	*Aralia Dasyphylla Mig*	Leaves	[11]
Maytenfolic acid,3β,22α-Dihydroxy-12-oleanen-29-oic acid	*Salacia oblonga*	Roots	[12]
Sapogenol,2β,3β,23-trihydroxy-12-oleanen-28-acetate	*Bumelia santorum*	Roots and bark	[1,13]

Table 1: Hypoglycemic triterpenoids of oleanane origin

Compound name	Source	Part used	Reference
Betavulgarosides II and IV	*Beta vulgaris*	Roots	[14]
Boussingosides A_1 and C	*Baussingaultia basselloides*	Aerial parts	[15]
ElatosidesA_1, E, G, H and I	*Aralia elata*	Root cortex, bark and young shoots	[16-20]
EscinsIa, Ib, IIa, IIb (Acylated polyhydroxyoleanene-3-*O*-monodesmoside derivatives)	*Aesculus hippocastanum*	Seed	[14,17,21]
2'-*O*-β-D-GlucopyranosylmomordinIc	*Momordica cochinchinensis* and *Panex Japonicus* *Kochia scoporia*	Leaves Fruit	[14] [14,22]
Gymnemic acid II, III,IV, V and VII	*Gymnema sylvestre*	Leaves	[23-27]
Gymnemoside b	*Gymnema sylvestre*	Leaves	[14,23,25]
Momordin Ic	*Momordi cacochinchinensis* and *Panex japonicus* *Kochia scoporia* *Baussingaultia basselloides*	Leaves Fruit Aerial parts	[14] [22] [15]

Table 2: Hypoglycemic monodesmosidesaponins of oleanane origin

The plants which are reported to possess hypoglycemic activity may be taken under cconsideration for being the source of these important bioactive compounds with specific reference to being anti-hyperglycemic activity. In the literature, there are lot of plants which are used traditionally for treating diabetes mellitus [1-3]. Some of them which are mentioned, along with the antidiabetic constituents, in this article are, *Olea europea, Campsis grandiflora, Beta vulgaris, Gymnema sylvestre and Panex ginsing.*

The isolation of several monodesmoside derivatives (Table 2) and bisdesmoside derivatives (Table 3) of oleanolic acid obtained from various plant species reported to be hypoglycemic are worth noting as these groups of compounds have larger contribution in this respect.

Compound name	**Source**	**Part used**	**Reference**
Boussingosides A_2 and A_3	*Boussingalliabanelloides*	Aerial parts	[15]
Chikusetsu saponin IV	*Aralia elata* *Memordi cacochinchinensis* and *Panax japonicus*	Root cortex Leaves	[14,20]
Desacylsenega saponin a and b	*Polygala senega* var. *latifolia*	Roots/ Rhizomes	[29,30]
Gymnema saponin V and Gymnemoside f	*Gymnema sylvestre*	Leaves	[25]
E-Senega saponin a and b	*Polygala senega* var. *latifolia*	Roots/ Rhizomes	[14,30]
Z-Senega saponin a and b	*Polygala senega* var. *latifolia*	Roots/ Rhizomes	[14,30]
Z-Senegins II	*Polygala senega* var. *latifolia*	Roots/ Rhizomes	[14,30-33]
Z-Senegins III	*Polygala senega* var. *latifolia*	Roots/ Rhizomes	[14,33]
Z-Senegins IV	*Polygala senega* var. *latifolia*	Roots/ Rhizomes	[30]
Stipuleanoside R_2	*Aralia elata*	Root cortex	[18]

Table 3: Hypoglycemic bisdesmosidesaponins of oleanane origin

Compound name	Source	Part used	Reference
Asiatic acid, 2α,3β,23-Trihydroxyurs- 12-en-28-oic acid	Banaba *(Lagarstroemia specicosa*	Leaves	[34]
Corosolic acid, 2α, 3β-Dihydroxyurs- 12-en-28-oic acid	*Eriobotrya japnica* *Lagarstroemia specicosa* Banaba *(Lagarstroemia specicosa)* *Symplocos paniculata*	Leaves Leaves Leaves Leaves	[35] [36] [34] [37]
2α,19β-Dihydroxy-3-oxours-12-en-28-oic acid	*Banaba symplocos paniculata*	Leaves	[34]
Myrianthic acid, 2α, 3β,19α,23-Tetrahydroxyurs-12-en-28-oic acid	*Campsisgr andiflora*	Leaves	[7]
2α,3β,19α,-Trihydroxyurs-12-en-28-oic acid	*Campsisgr andiflora*	Leaves	[7]
3β,6α,19α,-Trihydroxyurs-12-en-28-oic acid	*Eriobotrya japonica*	Leaves	[35]
Urs-12-ene	*Agarista mexicana*	stem	[38]
Ursolic acid, Urs-12-en-28-oic acid	*Bouvardia terniflora* *Corni officinale* *Symplocos paniculata* *Oleaeuropaea (*olive*)* *Campsis grandiflora* *Thymus vulgaris*	Stem Seeds Leaves & stem Leaves Leaves	[1,9] [39] [1,9] [37] [7,34]

Table 4: Hypoglycemic triterpenoids of ursane origin

Compound name	Source	Part used	Reference
3β,6α-Dihydroxylup-20(29)-ene	*Periplocaaphylla*	Stem	[40]
Lupeol, Lup- 20(29) –en-3 –ol	*Mangeferaindica* (Mango)	Fruit pulp	[41]
Lupeol acetate, Lup- 20 (29) –en-3-acetate	*Phoenixdactylefera*	Leaves	[42]

Table 5: Hypoglycemic triterpenoids of lupane origin

Conclusion

The work by coordinating the activity of a particular plant used for treatment of diabetes, to the presence of antidiabetic agents hitherto reported may lead to very promising results. By viewing above data related to the hypoglycemic activity of the aforementioned compounds, it seems that these ingredients may be exploited for large scale supply of the drugs at industrial scale to cope with the increasing demand of such drugs. The objective can also be achieved by utilizing the constituents available in abundance, which are closely related to the framework of the active principles by bringing them in conformity to the activity positive entity by certain chemical transformations. The promising results may be achieved by exploiting the experiments which have been conducted to check the structure-activity relationship.

Compound name	Source	Part used	Reference
Cucurbitane derivatives			
5β,19-Epoxy-3β,25-dihydroxycucurbita-6,23(*E*)-diene	*Memordica charantia*	Gourds	[2]
Mogroside III, Cucurbit-5-ene-3,11,24,25-tetrol,3-*O*-[β-D-glucopyranoside,24-*O*-β-D-glucopyranosyl(1→2)-β-D-glucopyranoside]	*Siratia/Memordica grosvenori*	Fruit	[43]
Mogroside IV, Cucurbit-5-ene-3,11,24,25-tetrol,3-*O*-[β-D-glucopyranosyl(1→6)-β-D-glucopyranoside]-24-*O*-β-D-glucopyranosyl(1→2)-β-D-glucopyranoside	*Siratia/Memordica grosvenori*	Fruit	[43]
Mogroside V, Cucurbit-5-ene-3,11,24,25-tetrol,3-*O*-[β-D-glucopyranosyl(1→6)-β-D-glucopyranoside]-24-*O*-β-D-glucopyranosyl (1→2)-[β-D-glucopyranosyl(1→6))-β-D-glucopyranoside]	*Siratia/Memordica grosvenori*	Fruit	[43]
Siamenoside I, Cucurbit-5-ene-3,11,24,25-tetrol,3-*O*-β-D-glucopyranoside,24-*O*-[β-D-glucopyranosyl(1→2)-β-D-glucopyranosyl(1→6)-β-D-glucopyranoside]	*Siratia/ Memordica grosvenori*	Fruit	[43]
3β,7β,25-Trihydroxycucurbita-5,23(*E*)-dien-19-al	*Memordica charantia*	Gourds	[2]
Dammarane derivative			
GinsenosideR_{g2}, 6-*O*-[α-L-Rhamnopyranosyl-(1→2)-β-D-glucopyranoside]	*Panex ginseng*	Leaves	[44]
Friedelane derivatives			
Kotalagenin-16-acetate (16-acetoxy-26-hydroxy-1,3-friedelanedione)	*Salacia oblonga*	Roots	[14]
Hopane derivative			
Thysanolactone,1β,3β-Epoxy-2,3-seco-21α-H-hop-22(29)-ene-2,3α-olide	*Swertia japonica*	Whole plant	[45]
Lanostane derivative			
3,25-Dihydroxy 22-acetoxyl-lanosta-8,23-diene	*Scleroderma aurantium*	Fruit	[46]

Table 6: Miscellaneous Hypoglycemic triterpenoids

For example, the sugar moieties attached at position C-3 of the olenane framework enhance the hypoglycemic activity of the relevant glycoside which may be either mono- or oligoglycoside; whereas the attachment of sugar groups at position C-28 decreases or render the molecule biologically inactive [17-20,31,47].

Competing interests:

The authors declare no competing interests. Although, the sources of some known compounds may be more than those reported in the article. The incorporation of only selected plants is due to their citation as a source of isolation of respective hypoglycemic constituents.

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