

## A MINI REVIEW ON ANTIDIABETIC PLANT DERIVED ALKALOIDS

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### ABSTRACT

Diabetes is a endocrine and metabolic disease in which blood sugar level becomes very high. The inadequacy of insulin or dysfunction of insulin or both result disturbances in the metabolism of fat, carbohydrate and protein. The chronic hyperglycemia (diabetes) damage the body system. Body does not properly process blood glucose to be used as energy. The control and management of diabetes with synthetic drugs is costly. The synthetic drugs are toxic and chances of side effects are very much high. Therefore a safer and effective treatment is needed with lower cost and lesser side effects. The plant derived chemicals play very important role in the management of diabetes mellitus. The natural alkaloids have been reported to exert a wide range of anti-diabetic activities. In present review article, an attempt has been made to report the various alkaloids isolated from plants with their antidiabetic activities.

**KEYWORDS:** Diabetes Mellitus, Insulin, Photochemical, Alkaloids

Diabetes is one of the most common health problems. Diabetes is a very much dangerous to human being like cancer and cardiovascular diseases. The insulin secreted from pancreas, control sugar level. Insulin transport glucose to our body cells from blood stream. The absence or inadequate production of insulin or inability of body to use insulin properly causes diabetes. If diabetes is not controlled, our body organs mainly eyes, kidney, heart, nerves and blood vessels may be damaged. Diabetes mellitus is broadly divided into type-1 and type-2 diabetes. In type-1 diabetes the immune system causes destruction of pancreatic beta-cells and body becomes unable to produce insulin. In type-2 diabetes either body does not produce enough insulin or insulin is not used properly by body. Thus there is insulin resistance. Hence in both type of diabetes glucose level in blood becomes high.

Since the start of the human civilization, we are using plants as the important source of medicines. The phytochemicals are used now a day as drugs of interest because of the lesser side effects, low cost of treatment and their effectiveness. The plant derived chemicals have been reported to play an important role in the control and management of diabetes mellitus (Aniszews, 2015). Alkaloids isolated from several medicinal plants, have been found to possess a wide range of antidiabetic properties (Sharma *et al.*, 2010) (Rajan *et al.*, 2018) (Gidad *et al.*, 2008) (Soon *et al.*, 2013) (Aska and Pindiga, 2010). Alkaloids present in plants play the role of chemical defense. The nitrogen is in a negative oxidation state in alkaloids which are cyclic compounds. Cardell *et al.*, 2001, have reported the role of many plant derived alkaloids to control diabetes. Berberine has been found to promote insulin secretion in rat's pancreatic islets (Wang *et al.*, 2008). The following four classes of

alkaloids have been found to show anti-diabetic activity: (i) Indole alkaloids (ii) Isoquinoline alkaloids (iii) Aminoalkaloids (iv) Terpenoidal alkaloids. It is also well known that some of the alkaloids are biosynthesized in plants from precursors. Indole, piperidine, pyrrolidine, phenyl ethyl amine and imidazole alkaloids are derived from tryptophan, lysine, ornithine, tyrosine and histidine respectively.

A number of indole alkaloids, isolated from *Catharanthus roseus*, were reported to increase metabolism of glucose and beta-cell rejuvenation and regeneration. Vindogentianine shows hypoglycemic activity (Tiong *et al.*, 2015). Isoquinolene alkaloids palmatine sulphate, palmatine chloride and berberine isolated from *Coptis Japonica* were found as aldose reductase inhibitor (Lee, 2002). 8-Oxoberberine isolated from *Berberis brevissima* has inhibited protein, tyrosine phosphatase T13 (Ali *et al.*, 2013). Nonterpenoidal alkaloids from the seeds of *Nigella glandulifera* Fryen have been reported to show inhibition activity of protein of tyrosine phosphatase 1B (PTP1B) in vitro (Tang *et al.*, 2017). Mycaminose has been characterized to reduce blood sugar level (Kumar *et al.*, 2008). Aegeline an alkaloidal-amide isolated from bark of *Aegle marmelos* (Linn) corr, serr, was found to have antihyperglycemic activity in STZ induced rats (Gandhi, 2012). Piperine, piperonaline and dehydropiperonaline isolated from piper retrofraction fruits, were reported as potential antidiabetic agents (Sharma *et al.*, 2018). Trigolelline isolated from Fenugreek, was reported to increase the sensitivity of tissues to insulin action by increasing the activity of enzymes of glucose utilization (Yoshinario and Igarashi, 2014). The pyrrolidine alkaloids Radicamins A and Radicamins B isolated from *L. Chinensis* were

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reported as  $\alpha$ -glucosidase inhibitor (Shibano *et al.*, 2001). The carbazole alkaloids isolated from *Murraya koenigii* were reported as potent antidiabetic agents. The 4-Koenidine was reported to control diabetes and manage insulin resistance (Om Patel *et al.*, 2016).

The recent advancements in antidiabetic alkaloids isolated from various plants, is summarized here in this brief review.

### PLANT DERIVED ALKALOIDS AS ANTIDIABETIC AGENTS

Some important alkaloids isolated from plants with their antidiabetic properties are given in the following lines:

1. Aegeline, Marmesin and Marmelosin (*Aegle Marmelos*): Regeneration of pancreatic  $\beta$ -cells and increases insulin secretion (Kamalkkandan and Prince, 2005)
2. Berberine (*Tinospora cordifolia* *Iberberis aristata*): Activity of hexokinase and phosphofructokinase is enhanced resulting in glucose transport, carbohydrate digestion and absorption, DDP-IV inhibition (Singh *et al.*, 2003) (Al Masri *et al.*, 2009)
3. Betaine, Achyranthine,  $\beta$ -ecdysone (*Achyranthus aspera*): Carbohydrate digestion and absorption is affected (Akhtar and Iqbal, 1991)
4. Boldine and isoboldine (*Peumus boldus*): Prevent hyperglycemia in diabetic rats, renal alternations (Romina *et al.*, 2013)
5. Cantharantine, Vindoline, Vindolinine, Vindoblastine and Vincristine (*Cantharanthus roseus*, *Vinca roseus*) : Free radicals scavenging action, Reduction in blood sugar level (Jarald *et al.*, 2008) (Chattopadhyay, 1999)
6. Castanospermine, australine (*Caslanospermium australe*): DPP-IV inhibition (Bharti *et al.*, 2012)
7. Castanospermine epifagomine, Fagomine (*Xanthocercis Zambesiaca*): Carbohydrate digestion and absorption, Insulin secretion (Akhtar, 1992)
8. Cryptolepine (*Cryptolepis sanguinolenta*): Decrease in blood glucose level, increase glucose uptake in 3T3-L1 cells (Heo *et al.*, 1998)
9. Casuarine-6- $\alpha$ -glucoside (*Syzygium malaccense*): Inhibit  $\alpha$ -glucosidase activity (Kiyoteru *et al.*, 2005)
10. Calystegine B<sub>2</sub> (*Nicandra Physaloidis*): Reduce diet induced hyperglycemia and endogenous insulin secretion by inhibiting intestinal R-glucosidase (Griffiths *et al.*, 1996)
11. Caffeine, Catechins (*Camellia sinensis*): Inhibit development of insulin resistance. Decreases glucose absorption from intestine (Alam, 2016) (Tedeng *et al.*, 2010).
12. 1-Ephedrine (*Ephedra distachya* Linn): Suppression of hyperglycemia in rats (Xiu *et al.*, 2001)
13. Ginkgolide (*Ginkobiloba*): Increases insulin secretion (Pinto *et al.*, 2009)
14. 11-Hydroxypalmatine (*Steplenia glabra*): Causes reduction in blood glucose (Senwal *et al.*, 2010)
15. Harmene, norharmene (*Tribulus terrestris*): Stimulate insulin secretion by the activation of imidazoline I binding sites in the pancreatic- $\beta$ -cell (Kirtikar and Bani, 1993)
16.  $\beta$ -Carboline harmene, pinoline (*Tribulus terrestris*): Increases insulin secretion (Cooper *et al.*, 2003)
17. 1-Deoxyojirimycin (*Morus alba*) : Potent  $\alpha$ -glucosidase inhibitor (Oku *et al.*, 2006)
18. Javaberine A, Javaberine A hexa acetate, Javaberine, B hexa acetate (*Talinum paniculatum*): Inhibitors of TNF- $\alpha$ -production by macrophages and fat cells. The plant used as diet any supplement to prevent diabetes (Shimoda *et al.*, 2001) (Cattareeya *et al.*, 2013)
19. Jambosine (*Syzygium Cumini*): It checks the conservation of starch (Murlimanohar, 2011)
20. Jatrorrhizine, magnoflorine, palmatine (*Tinospora cordifolia*): Stimulated insulin secretion for RIN in 5F cell line (Patel and Mishra, 2011)
21. Lupanine, 13- $\alpha$ -hydroxylupanine, 17-Oxolupanine (*Lupinus perennis*): Enhance glucose stimulated insulin release and lower blood sugar level (Zopez *et al.*, 2004)
22. Lepidine and Semilepidine (*Lepidium sativum*): Potentiate pancreatic secretion of insulin from islet  $\beta$ -cells (Shukla *et al.*, 2012)
23. Mahanimbine (*Murray Koenigii*): Lower blood glucose level (Kumar *et al.*, 2010)
24. Nuceferine (*Nelumbo nucifera*): Stimulate insulin secretion (Nguyen *et al.*, 2012)
25. Pangomol, Karangin (*Pongomia pinnala*): Shows excess level of insulin circulating in blood (Tamarkar *et al.*, 2008) (Hyper insulinimic activity)
26. Piperumbellactum A (*Piperumbellactum*): Inhibition of glucosidase enzyme (Tabopda *et al.*, 2008)
27. Schilzeines A, B and C (*Penures Schulzes*): Inhibit  $\alpha$ -glucosidase activity (Takada *et al.*, 2004)
28. Swerchirin (*Swertia chirayita*): In fasted, Fed and glucose loaded albino rats, the blood glucose level lowering effect observed (Bajpai *et al.*, 1991)

29. Sotolon, Trigonelline, gentianine (Trigonellia foenum graecum): The activity of fructose-1, 6-biphosphatase is suppressed and its dephosphorylation checked (Khosla *et al.*, 1995)
30. Tecomine (Tecomastans): Glucose uptake rate increased (Costantino *et al.*, 2003)
31. Tetrandrine 2'-N-β-Oxide: Fangchinoline, 2'-N-methyl tetrandrium chloride (Stephania tetrandra). Reduce high blood glucose level and increase blood insulin (Tsutami *et al.*, 2003)

## CONCLUSION

The prevention and management of diabetes is still a major challenge to researchers. Hence the scientists, medical practisnors and herbalogists must try to investigate the various ways to manage and control the diabetes. Thus new class of drugs must be searched to overcome the diabetic problems. The plant derived antidiabetic alkaloids have been reported less costly, less toxic with lesser side effects. There is increasing demand to search and develop new herbal formulations and plant based antidiabetic alkaloids with their mechanism of action to diabetic problems. The control of diabetes with phytochemicals must be preferred over conventional synthetic drugs. This review justify the applications of plant alkaloids and also provide a platform for further investigations to explore the antidiabetic potentials of the plants.

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