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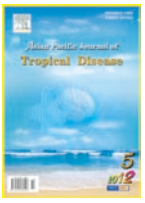

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Pharmacological and analytical aspects of gymnemic acid: a concise report

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ABSTRACT

Gymnemic acid is the main phytoconstituents of *Gymnema sylvestre* (Asclepiadaceae) found in the different parts of world. Gymnemic acid posseses different pharmacological activities including supression of taste sensitivity to sweetness, showed inhibition of intestinal glucose absorption and lower the plasma glucose levels. Various techniques have been used for the isolation and characterization of the gymnemic acid so far. In the present review data was collected in regards with pharmacological activity, analytical techniques and bioavailability of gymnemic acid. This review will be helpful to the researcher in regards to the exploration of the valuable potential of the gymnemic acid.

1. Introduction

Gymnema sylvestre(*G. sylvestre*) (Asclepiadaceae) commonly known as 'Gudmar' in Hindi is an important medicinal plant (Climber) used in different systems of medicine as a remedy for the treatment of diabetes, rheumatism, cough, ulcer, jaundice, dyspepsia, constipation, eyes pain and also in snakebite. The major phytoconstituents of gymnema sylvestra are gymnemic acids, gudmarin and saponins[1]. Gymnemic acid [(C43H68O14) (Figure 1)] is a pentacyclic triterpenoid main active phytoconstituents of *G. sylvestre*, exhibiting potent antidiabetic activity. Gymnemic acids show different physiological activities like they suppress taste sensitivity to sweetness, lower plasma glucose and insulin levels in the diabetic subjects and inhibit intestinal glucose absorption. Few reports about molecular interaction of Gymnemic acid with proteins is also found in the literature[2, 3]. More than 20 different types of gymnemic acid are found in the leaves of *G. sylvestre*. Among all, Gymnemic acid 1 has the highest anti-sweet properties. It suppresses the sweetness of most of the sweeteners including aspartame and thaumatin (sweet protein)[4].

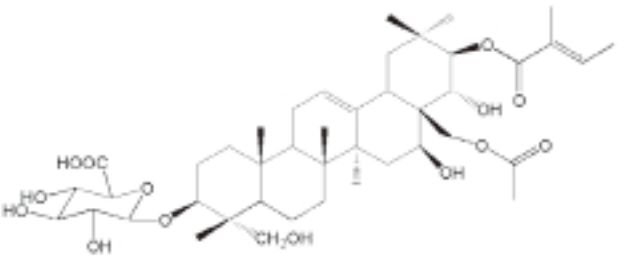

Figure 1. Chemical structure of gymnemic acid

2. Pharmacological activity of gymnemic acid

Gymnemic acid IV isolated from *G. sylvestre* leaves has antihyperglycemic, glucose uptake inhibitory, and gut glycosidase inhibitory activity[5]. Gymnemic acid of leaf and callus extracts of *G. sylvestre* significantly increases the regeneration of β-cells in treated rats compared to the control rats[6]. Effect of combination of voglibose and gymnemic acid in diabetic rats was investigated. Combinative and individual effects of voglibose and gymnemic acid on maltose absorption in small intestine were also carried out. Absorptive rate, onset time and the effective duration were significantly changed with the

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combination of voglibose[7]. Effect of triterpene glycosides (gymnemic acids I–IV) in streptozotocin–induced diabetic mice was investigated. Gymnemic acid IV reduced the blood glucose levels significantly compared to the standard drug glibenclamide, but did not change the blood glucose levels of normal mice. It also increased plasma insulin levels significantly in STZ–diabetic mice[8]. Effects of gymnemic acid on the serum glucose level of oral glucose–loaded rats were investigated. Gymnemic acids III, V, and VII showed little inhibitory activity against glucose absorption[9]. Effect of extracts containing gymnemic acids were evaluated on a high K(+)–induced contraction of guinea–pig ileal longitudinal muscles, and on glucose transport mediated by the difference of glucose–evoked transmural potential difference (delta PD) in the inverted intestine of guinea–pig and rat. From the results it was concluded that extracts containing gymnemic acids reduced the elevated blood glucose level by inhibiting glucose uptake in the intestine[10]. Interaction of gymnemic acid with glycolytic and related enzymes was investigated and found that gymnemic acid induced a band smearing of glycerol–3–phosphate dehydrogenase (G3PDH) as well as that of GAPDH in SDS–PAGE, which showed the interaction of gymnemic acid with G3PDH, an enzyme involved in glycerol metabolism[11]. Gymnemic acids inhibited rabbit muscle glyceraldehyde–3–phosphate dehydrogenase (GAPDH) activity. Binding of gymnemic acid to GAPDH was observed by surface plasmon resonance measurement[3]. Gastric inhibitory peptide release into the portal vein in response to duodenal infusion of D–glucose was studied in the presence of a gymnemic acid in the intestinal lumen. The increase in the portal immunoreactive gastric inhibitory peptide induced by glucose was significantly depressed by concomitantly infused purified gymnemic acid[12].

3. Effect of gymnemic acid on bioavailability

Effect of acarbose and gymnemic acid on maltose absorption and hydrolysis in small intestine were investigated. The total inhibitory rate of maltose absorption was improved by the combination of gymnemic acid and acarbose throughout their effective duration. There are augmented effects of acarbose and gymnemic acid, which involve pre–cellular and paracellular barriers[13]. Effect of gymnemic acids on fecal steroid excretion in rats was investigated and found that high dose of gymnemic acids increases fecal cholesterol and CA–derived bile acid excretion[14]. Gymnemic acid is known to inhibit the intestinal absorption of glucose in human and rats. It was also found that gymnemic acid potently inhibited the absorption of oleic acid in intestine by the method of intestinal perfusion[15]. The inhibitory effects of gymnemosides–c, –d, –e, and –f and principal triterpene glycosides from *G. sylvestre* on glucose uptake in rats small intestinal fragments were examined. Gymnemic acids II, III, and IV, gymnemasaponin V, and gymnemoside–f were found to exhibit the inhibitory activity against glucose uptake[16].

4. Effect of gymnemic acid on taste

It was evaluated that the sensitivity of antisweet taste of gymnemic acid was diminished by application of gamma–cyclodextrin (gamma–CD) in the mouth at the molecular level using isothermal titration calorimetry, NMR and dynamic light scattering. The physiological phenomenon that the antisweet taste effect of gymnemic acid is diminished by application of gamma–cyclodextrin (gamma–CD) in the mouth was evaluated at the molecular level using isothermal titration calorimetry, NMR and dynamic light scattering. These analyses showed that gymnemic acid specifically binds to gamma–CD[17]. The effect of a gymnemic acid rinse, which simulated a sweet–taste deficit, was measured on human taste perception and identification. Taste ratings showed that gymnemic acid reduced the intensities of sucrose and aspartame[18]. In humans and chimpanzees, gymnemic acids suppress the sweet taste of all sweeteners whereas miraculin adds a sweet taste quality to sour stimuli. Gymnemic acids also abolish miraculin–induced sweet taste[19]. In another study it was found that gymnemic acid was glycoside of triterpenes that suppress sweetness in human[4]. Whole and single fiber chorda tympani nerve recordings were obtained in 5 chimpanzees to stimulate with monosodium phosphate (MSG) and guanosine 5′–monophosphate disodium salt (GMP) alone and in combination. From the observation it was found that the response to GMP and MSG was unaffected by gymnemic acid, although it blocked the response to the sweet compounds[19]. In other study chorda tympani proper nerve recordings from the chimpanzee before and after gymnemic acid were recorded. On the chimpanzee tongue, application of 2 mL gymnemic acid completely abolished the taste responses acesulfam–K, aspartame, D–tryptophan, monellin, thaumatin, sucrose and xylitol[20]. Effect of gymnemic acid on gustatory activity of the chorda tympani proper nerve has been recorded in hamster and rat. In the hamster gymnemic acid suppressed the response to solutions of sucrose. The depression caused in the response to sucrose was directly related to the strength of the gymnemic acid and inversely to that of the sucrose solution[21].

5. Analytical and isolation techniques of gymnemic acid

G. germplasm collected from various regions of Madhya Pradesh was evaluated for its gymnemic acid content by HPLC methods. Mature leaves were hand–plucked in the month of October and June through non destructive harvesting practice and found that there is variation in the gymnemic acid content in *G. sylvestre* collected from various locations[1]. The gymnemic acid content was determined through HPTLC and HPLC using C18 (ODS) reverse phase column and water/methanol (35:65) + 0.1% acetic acid as a mobile phase[2]. An improved HPTLC method for the standardisation of *G. sylvestre* is developed. The method involves the initial hydrolysis of gymnemic acids, the active ingredients, to a common aglycone followed by the quantitative estimation of gymnemagenin[22]. Two gymnemic acid–enriched fractions of GS4 were obtained from *G. sylvestre* by size exclusion and silica gel chromatography[23]. Extraction of gymnemic acid through gymnemagenin from callus cultures of *G. sylvestre* was presented in the literature. Components were separated on pre–coated silica gel 60 GF254 plates with chloroform: methanol (8:2) as a mobile phase[24]. In another study, five antisweet principles, gymnemic acid–III, –IV, –V, –VIII, and –IX, were isolated in pure states from the hot water extract of leaves of *G. sylvestre*[25].

6. Conclusion

Medicinal plants are very ancient and only true natural medicines have been found useful in several ways. They can be used directly or in extracted forms for the management of various ailments, due to presence of many

phytochemicals. The use of plants, parts of plants and isolated phytochemicals for the prevention and treatment of various ailments has been in practice from immemorial time[26, 27]. According to WHO, about 80% of the World's population in 2001 used herbal medicine for the health need[28]. Before there were drug from companies, natural cure were used and still they can be used even today for the treatment of various type of disorder. For example medicinal plants that are effective in controlling plasma glucose level with minimal side effects are commonly used in developing countries as alternative therapy for the treatment of diabetes mellitus[29, 30]. *G. sylvestre* has an important place among such antidiabetic medicinal plants. The scientific research on gymnemic acid revealed its biological potential for the treatment of different types of disease including diabetes. The information presented in this review regarding the pharmacological activity and analytical techniques of the gymnemic acid may provide the evidence for its importance in the different system of medicines. However parameters like toxicity studies should be scientifically investigated in order to support of its uses.

Conflict of interest statement

The authors report no conflict of interest.

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