# Chapter 58 Studies on Gymnemic Acids Nanoparticulate Formulations against Diabetes Mellitus

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#### ABSTRACT

The solid dosage forms of Gymnemic acid nanoparticulate formulations developed earlier were tested for anti-diabetic activity and hypoglycemic activity. Glucose, insulin and various biochemical parameters were monitored from blood samples of rats to study the efficacy of these formulations. The nanoformulations exhibited significant anti-hyperglycemic activity and produced substantial hypoglycemia. Blood glucose levels (mg/dL) in glucose loaded hyperglycemic rats after dosing with Gymnemic acids nano-formulations were 79 to 98, as against 105 in the control after 3 hours. Hypoglycemic activity of Gymnemic acids nano-formulations ranged between 63 to 66 (Blood glucose concentration, mg/dL) as against 80 in the control. Biochemical parameters studied also supported the above observations. The study clearly shows that gymnemic acid nanoparticulate formulations developed may be a better therapeutic adjunctive option for diabetes mellitus in humans.

#### INTRODUCTION

*Gymnema sylvestre* commonly known as 'Gudmar' in Hindi is an important Indian medicinal plant used in different systems of medicine as a remedy for the treatment of diabetes, rheumatism, cough, ulcer, jaundice, dyspepsia, constipation, eyes pain

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and also in snakebite (Patel et al., 2012). The major phytoconstituents of *gymnema sylvestra* are gymnemic acids, gudmarin and saponins. Gymnemic acid ( $C_{43}H_{68}O_{14}$ ) is a pentacyclic triterpenoid and is the main active phytoconstituents of *G. sylvestre*, exhibiting potent anti-diabetic activity (Shivani Vaidya, 2011). 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 (Ankit Saneja et al., 2010). Recent times have witnessed increased incidence of diabetes across the globe, along with increased popularity of herbal products in the international market (Classen, 2012). Gymnemic acids are poorly soluble in water and thus show reduced pharmacological activity (Ankit Saneja et al., 2010). The need for new and improved approaches to increase its solubility and bioavailability remains a key focal point for many researchers (Parijat Kanetkar et al., 2007). Recently, many poorly soluble drugs have been nanonized to increase their dissolution rate, their saturation solubility and in turn to enhance their oral bioavailability (Ravichandran, 2009a,b). In this direction recently we reported the preparation and characterisation of nanosuspension of gymnemic acids (Ravichandran, 2010a) and its oral formulation (Ravichandran, 2010b). In this paper we report the pharmacokinetic and pharmacodynamic behavior of nanoparticulate gymnemic acids.

## MATERIALS AND METHODS

#### Chemicals

Gymnemic acid was purchased from Amruta Herbals Private Limited, Indore (India). Gymnemic acids nanosuspensions were prepared by high pressure homogenization method and the results of its characterization, and solid dosage form development have been recently reported by us (Ravichandran, 2010a,b). The solid dosage formulation contained GANS-A: Gymnemic acids nanocrystals 50mg + Avicel PH 101 42mg, AcDiSol5mg, Explotab0mg, magnesium stearate 2mg, Talc 1mg as Excipients; GANS-B: Gymnemic acids nanocrystals 50mg + Avicel PH 101 42mg, AcDiSol 0mg, Explotab 5mg, magnesium stearate 2mg, Talc 1mg as Excipients ; GANS-C: Gymnemic acids microcrystals 50mg + Avicel PH 101 42mg, AcDiSol 5mg, Explotab 0mg, magnesium stearate 2mg, Talc 1mg as Excipients ; and GANS-M: Gymnemic acids microcrystals 50mg + 50mg Excipients not known as it is a commercial product. The tablets were prepared using direct compression by a single punch tablet machine.

### **Experimental Animals**

Male Wistar rats weighing 250–300 g were fed with commercial pellet diet (Kamadenu Agencies, Bangalore, India) and water *ad libitum*. The animals were acclimatized to laboratory hygienic conditions for 10 days before starting the experiment. The animals were maintained in groups of six and were fasted for 8 h prior to the commencement of the study.

#### **Treatment of Animals**

Animals were fed with glucose (4 g/kg) for hyperglycemia (Parveen Kumar, 2012) following an intramuscular injection of ketamine (22.5 mg/ animal) and acepromazine (0.75 mg/kg). Insulin was administered subcutaneously as a solution prepared in Dulbecco's phosphate-buffered saline at a concentration of 1  $\mu$ U/0.2 ml. Gymnemic acids tablet formulations (Ravichandran, 2010a,b) were fed at a dose of 400 mg/kg. The samples were analysed at different intervals of time such as t=0 is immediately just after glucose loading; t=0.5 is immediately just after treatment and so on.

Alloxan-induced diabetic model was selected to confirm the utility of active anti-hyperglycemic nano-formulations in diabetic conditions. Diabetes was induced by injecting 120 mg/kg of alloxan monohydrate intraperitoneally in 0.9%w/v NaCl to overnight-fasted rats. 10% glucose solution bottles were kept in their cages for the next 24 h to prevent hypoglycemia. After 72 h of injection, fasting blood glucose level was measured. Animals which did not develop more than 300 mg/ dl glucose levels were rejected. These diabetic animals were treated with insulin and gymnemic acids tablet formulations as stated above to study 11 more pages are available in the full version of this document, which may be purchased using the "Add to Cart" button on the publisher's webpage: www.igi-global.com/chapter/studies-on-gymnemic-acids-nanoparticulateformulations-against-diabetes-mellitus/102067

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