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Interactions of Antidiabetic Herb -Antidiabetic Drug –A Review

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Zeba I Mulla*[1], Girdhar Vedantum[2], Rinky Thakur[3]

1 MD Scholar of Department of Dravyaguna, KLE Shri BMK Ayurveda Mahavidyalya Belagavi, India

2 Reader Department of Dravyaguna, KLE Shri BMK Ayurveda Mahavidyalya Belagavi, India

3 Research Officer NITI Aayog, India

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ABSTRACT

Gymnema sylvestre is told to be as one of the herbs with strong anti-diabetic properties. *Gymnema* tea is a wonderful drug for Obesity also as diabetes and obesity are almost connected to each other because both have medovaha dushti. If we look at active compound this plant gymnemic acids is one of the active components. It has been experiential that there might be a likely link between obesity, Gymnemic acids and diabetes. This reconsider will attempt to put forth an overall idea regarding the drug interaction between Ayurvedic drug and the drug metformin which is a Diabetic drug in allopathy. Hence an attempt has made to recollect the reference regarding the drug review and their interaction.

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INTRODUCTION

MESHSHRINGI

The plant is native to central and western India, tropical Africa and Australia.

Synonyms in Sanskrit: *Meshashringi*, *madhunashini*, Hindi: *Gur-mar*, *merasingi*, Marathi: *Kavali*, *kalikardori*, *vakundi*, Gujrathi: *Dhuleti*, *mardashingi*, Telugu: *Podapatri*, Tamil: *Adigam*, *cherukurinja*, Kannada: *Sannagerasehambu*

Plant description

G. sylvestre (Asclepiadaceae), a susceptible species is a slow-mounting, perennial, medicinal woody climber establish in central part of India. It is a strong antidiabetic plant and used in folk, Ayurvedic and homeopathic systems of medicine. It is also used in the management of bronchial asthma, eye disorders, in various inflammations, family planning and various snake bite management. In addition, it acts as antimicrobial, antihypercholesterolemic, hepatoprotective and sweet suppresses activities. It also acts as feed deterrents to caterpillar, *Prodenia eridania*; prevent dental caries caused by *Streptococcus mutans* and comes in various skin creams.

COMPOSITIONS

If we look at the Leaves of this plant, it contains triterpene saponins that belong to oleanane and dammarane classes. Oleanane saponins are gymnemic acids and gymnemasaponins, while dammarene saponins are gymnemasides. Besides this, other plant constituents are flavones, anthraquinones, pentatriacontane, α and β-chlorophylls, phytin, resins, *d*-quercitol, tartaric acid, formic acid, butyric acid, lupeol, β-amyrin and other glycosides and many alkaloids. Leaves of this species yield acidic glycosides and anthroquinones and their derivative.[1]

Gymnemic acids have antidiabetic, anti-sweetener and anti-inflammatory actions. The antidiabetic array of molecules has been recognized as a group of closely related gymnemic acids after it was productively remote and purified from the leaves of *G. sylvestre* [2-3]. Later, the phytoconstituents of *G. sylvestre* were remote, and their chemistry and structures were deliberate and elucidate.

Gymnema leaf extract, notably the peptide 'Gurmarin', has been found to interfere with the ability of the taste buds on the tongue to taste sweet and bitter. Gymnemic acid has a similar effect. It is believed that by controlling the sweet taste sensation, people taking it will limit their intake of sweet foods, and this activity may be partially responsible for its hypoglycemic effect.

How Gymnemic acids from *G. sylvestre* exert its hypoglycemic effects, probable reasons according to study are-

1) it increases secretion of insulin, 2) it promotes regeneration of islet cells, 3) it increases utilization of sugar: it is shown to increase the activities of enzymes responsible for the utilization of sugar by insulin-dependent pathways, an increase in phosphorylase activity, decrease in gluconeogenic enzymes and sorbitol dehydrogenase, and it causes inhibition of sugar absorption from intestine.

The gymnemic acid components are believed to block the absorption of sugar in the small intestine, the exact action being unknown. It could be involve one or more mechanisms [4].

One of the mechanisms responsible for adult-onset DM (Raised sugar level) is a form of insulin resistance, which is attributed to the inability of insulin to enter cells via the insulin receptor. *Gymnema* may overcome this resistance, but require further studies to confirm its validity and also whether the effect is clinically relevant. Should this effect be proven, *Gymnema* may prove useful in both adult onset (NIDDM) and juvenile-onset DM (Raised sugar level) (IDDM) to help insulin enter cells. In the case of IDDM, the insulin is injected by a syringe and is not secreted from the pancreas. [5]

THE DRUG METFORMIN

The drug metformin is an extensively used drug in the therapy of suffers affected by DM (Raised sugar level). Although some caution is mandatory in the very old, advanced age per se does not represent a contraindication to the drug metformin use. Even though its precise mechanism of action it is not completely elucidated, long-term treatment with this drug in monotherapy, improves sugar control and reduces heart mortality in overweight type 2 diabetic suffers. Research evidence produced over the years suggests that the drug metformin may be useful in some clinical conditions different from DM (Raised sugar level). In the present review study we have examined currently available data about the possible use of the drug metformin as an effective therapeutically agent in pathological conditions

different from type 2 DM (Raised sugar level). On the basis of our investigation, the use of The drug metformin can be suggested in obese suffers affected by impaired glucose tolerance and/or fasting hyperglycemia and in subjects affected by polycystic ovary syndrome, while further data are mandatory in order to prescribe such a drug in suffers affected by non-alcoholic state-hepatitis and in HIV suffers on antiretroviral therapy. Effective prevention is mandatory to combat the worldwide epidemic of type 2 diabetes. We investigated the long-term extent of beneficial effects of lifestyle intervention. [6-9]

MATERIAL AND METHODS

Material:

- Review of literature from modern, classics of *Ayurveda* regarding *Diabetes (Madhumeha)*, and about the drug *meshashringi*.

- Relevant modern literature, various journals, articles and previous work done will also be consulted for comparative study and drawing inferences.

- Web media will also be referred for similar matter and will be incorporated according to the need of topic.

Methods:

1. These materials are to be collected and co-related with the contemporary aspect.

2. Evaluation of drug interaction of meshashringi with metformin (antidiabetic drug) from classics literature, research papers , modern books to be done from march 2021 till February 2022.

3. Analysis will be done based on the findings from literature and later on conclusion will be done.

DISCUSSION

In one study it has been found that it helps in lowering serum cholesterol and triglycerides. The chief chemical constituents of *Gymnema* include gymnemic acid, tartaric acid, gurmarin, calcium oxalate, sugar, stigmasterol, betaine, and choline. While the water-soluble acidic fractions reported and provide the hypoglycemic action, it is not yet clear what specific constituent in the leaves is responsible for the same. Some researchers have suggested

gymnemic acid as one possible candidate, although further research is mandatory. Both gurmarin (*another constituent of the leaves*) and gymnemic acid have been shown to block sweet taste in humans. The major constituents of the plant material 3B glucuronides of different acetylated gymnemagenins, gymnemic acid a complex mixture of at least 9 closely related acidic glucosides.

The following figure could provide a diagrammatic representation for explaining the action of gymnemic acids on the intestinal receptors. The basic function of the acids is to bind to the receptor on the intestine, and help in reducing extra sugar level. if we look at the pharmacodynamics of Drug The drug metformin we can see the Research conducted on the same. The largest and longest clinical trial of the drug metformin for the prevention of diabetes is the Diabetes Prevention Program/Diabetes Prevention Program Outcomes Study (DPP/DPPOS). In this review study, we summarise data from the DPP/DPPOS, focusing on The drug metformin for diabetes prevention, as well as its long-term sugar and cardiometabolic effects and safety in people at high-risk of developing diabetes. The DPP (1996–2001) was a RCT of 3234 adults who, at baseline, were at high-risk of developing diabetes. Participants were assigned to masked placebo (n = 1082) or the drug metformin (n = 1073) 850 mg twice daily, or intensive lifestyle intervention (n = 1079). The masked the drug metformin/placebo intervention phase ended approximately 1 year ahead of schedule because of demonstrated efficacy. The primary outcome was reported at 2.8 years. At the end of the DPP, all participants were offered lifestyle education and 88% (n = 2776) of the surviving DPP cohort continued follow-up in the DPPOS. Participants originally assigned to the drug metformin continued to receive the drug metformin, unmasked. The DPP/DPPOS cohort has now been followed for over 15 years with prospective assessment of sugar, cardiometabolic, health economic and safety outcomes. After an average follow-up of 2.8 years, the drug metformin reduced the incidence of diabetes by 31% compared with placebo, with a greater effect in those who were more obese, had a higher fasting sugar or a history of gestational diabetes. The DPPOS addressed the longer-term effects of the drug metformin, showing a risk reduction of 18% over 10- and 15-years post-randomization.

INTERACTION OF GYMNEMA SLYSTRE WITH METFORMIN

According to study by P. Raja, et al revealed that there is no significant decrease in BGL (Blood glucose level) of diabetic rats on treatment with metformin in presence of Gymnema tea. Even though there was increase in plasma concentration of metformin in animals still

remained as diabetic. The above results indicate a significant drug – herb interaction between gymnema tea and metformin. In presence of gymnema tea, the antidiabetic effect of metformin was found to decrease in selected animals. The interaction may be pharmacodynamic or pharmacokinetic which needs to be evaluated through mechanistic studies. Further the interaction is to be established in human subjects to adjust the appropriate dose of metformin and gymnema tea. [10-11] Diabetes mellitus (DM) is a group of metabolic disorders, characterized by increased sugar level resulting from defects in insulin secretion, insulin action or both 1. The chronic increased sugar level or diabetes is linked with long term damage, dysfunction and failure of various organs especially the eyes, kidney, nerves, heart and blood vessels 2. The abnormalities in carbohydrate, fat and protein metabolism during diabetes is due to the deficient action of insulin on target tissues. It is also believed that the increased oxidative stress is the widely accepted factor in the expansion and development of diabetes and its complications. DM is usually accompanied by augmented making of free radicals or an impair antioxidant defence. Very high levels of free radical's cause injure to cellular proteins, membrane lipids and nucleic acids and eventually cell death. One of the important sources of free radicals in diabetes is the interaction of glucose with proteins leading to the formation of Amadori products and then advanced glycation end products (AGEs). AGEs via their receptors inactivate antioxidative enzymes and alter their structures and functions, therefore speeding up the oxidative damage to cells. The inhibition of this intracellular free radical formation would provide a therapeutic strategy to prevent oxidative stress and diabetes-related complication. We have seen antihyperglycemic activity of many herbs but very few literatures are obtainable to decide the drug – herb interaction. Susan et. al. Informed the Pharmacodynamic interaction of Momordica charantia with rosiglitazone in rats [12]. Fakeye et. al. reports the investigation of interacting effects of co-administration of *Carica papaya* leaf extract on the hypoglycemic activity of metformin and glimipiride in an animal model [9]. Metformin is an oral antihyperglycemic agent belongs to the class of biguanides, whose efficacy depends on its plasma concentration. Any drugs (synthetic or natural) or food that alters the plasma concentration of metformin can decrease its efficacy (increase in its plasma concentration above therapeutic window can lead to hypoglycemia and decrease in concentration below the therapeutic window may makes metformin ineffective). Hence when metformin is administered along with herbal drugs having anti hyperglycemic activity, dose must be adjusted suitably. Intending to evaluate the interaction between metformin and anti-hyperglycemic herbal tea, we have developed a simple RP-HPLC method for determination of metformin in rat plasma. Using the developed

method we have assessed the interaction between metformin and gymnema tea contains *Gymnema sylvestre* which is an anti hyperglycemic agent. [13-14]

CONCLUSION

Based on the literature review we can say that Metformin its the self-most of the possible drug interactions of Metformin occur through the inhibition of OCTs (organic cation transporter) and MATEs as it is not metabolized and excreted through urine as such. The risk of Metformin Linked Lactic Acidosis (MALA) enhances with the rise of plasma concentrations of Metformin. Metformin administration should be stopped and urgent medical attention given to the patients developing first signs of MALA such as severe vomiting and diarrhea. The prescribers and pharmacists should be aware of the medications inhibiting OCTs (organic cation transporter). And there is no significant decrease in blood sugar level. In presence of *Gymnema sylvesteris*, the antidiabetic effect of metformin was found to decrease in selected animals. Probable interactions might be due to simultaneous administration of two dosages forms (metformin and Gymnema tea), which can also occur in diabetic patients.

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