

NEW WORLD SYNDROME (OBESITY) GONE BY *GUGGUL*: A REVIEWKapil Deo Yadav<sup>1</sup> Anand Kumar Chaudhary<sup>2</sup>

## ABSTRACT:

**Background:** Obesity is multi factorial disease would lead to excessive or abnormal fat accumulation. Its prevalence is on continuous rise in all age groups of the developed as well as developing countries in the world and it can be described as the "New World syndrome". Among the materia medica of *Ayurveda*, *Guggul* is essential herb indicated for the management of obesity but their mechanism of action in relation to scientific parameter is lacking. **Aim & Objective:** To review effect of *Guggul* on New World Syndrome. **Materials & Methods:** References of *Guggul* are search out in classical as well as contemporary science in new world syndrome. **Observation:** During survey of *Ayurvedic* literature it was observed that different herbs, metals, minerals are used for treatment of obesity as single drug as well as in compound formulations. Among herbs *Guggul* occupied significant position and effectively used for treatment of obesity. It is oleo gum resin, obtained from *Commiphora mukul* originate in India, Bangladesh and Pakistan having anti hyperlipidemic, anti oxidant, anti inflammatory property which are important pharamcotherapeutic targets in the treatment of obesity agent of obesity. Besides this *Guggul* also act as drug delivery medium and help in transportation of anti obesity agent to target site and performing their action when used with other anti obesity drugs. **Conclusion:** *Guggul* is right choice in management of New World syndrome and probably acting by different pharmacological properties.

**Key Words:** Obesity, *Guggul*, Hyperlipidemic, Anti oxidant.

## INTRODUCTION:

Obesity can be described as "New World Syndrome", is a pathological condition in which excess body fat accumulated to the extent that it may produces an adverse effect on health, leading to reduced life expectancy and/or increased health problems<sup>[1]</sup>. It may be defined as a state of imbalance between calories ingested versus calories expended and generally measure in term of Body Mass Index (BMI) i.e. measure of weight corrected for height and which reflects the total body fat and has been the most accepted parameter for defining over weight<sup>[2]</sup> and classified based on it by WHO<sup>[3]</sup>. It is ingredient of metabolic syndrome along with dyslipidemia, hypertension & hyperglycemia and documented as risk factors for cardiovascular disease (CVD), has become one of the major public health challenges in developed and developing countries<sup>[4]</sup>.

Oleo-gum-resin, known as *Guggul* is obtained from *Commiphora mukul* (*Hook. ex stocks*) found in India, Bangladesh, and Pakistan, used for treatment of variety of disease conditions, including hypercholesterolemia, obesity and atherosclerosis. It was introduced to the scientific world in 1966 by an Indian medical researcher, G. V. Satyavati<sup>[5]</sup> inspired by the *Ayurvedic* classics which described *medohara* properties<sup>[6,7]</sup> that it was directly recommended for the treatment of a condition called "coating and obstruction of channel" which is basic pathology for hypercholesterolemia and obesity and

approved for marketing in India as a hypolipidemic drug<sup>[8,9]</sup>. *Guggul* was introduced into the Western medical literature in middle of 1990s<sup>[10]</sup> for treating or preventing hypercholesterolemia. Here an attempt has been done to show a relationship between *Ayurveda* science and contemporary science.

## MATERIALS AND METHODS:

Important manuscripts of *Ayurveda* such as *Charak Samhita*, *Sushrut Samhita*, *Bhaishjya Ratnavali* along with *Rasa Shastra* literature like *Rasa Ratna Samuchya* and *Ayurvedic* Formulary of India are the source of various preparation of *Guggul*. We search out formulation of *Guggul* which are used in treatment of *medoroga* (obesity) among these vast literatures of *Ayurveda*. Besides this, we also search out different pharmacological properties of *Guggul* in *Ayurvedic* classics as well as different search engines like pubmed, Embase, Google scholar etc. and other Pharmacological

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journals to find out probable mode of action in relation to obesity.

### OBSERVATION AND RESULTS:

Different formulations of *Guggul* are mentioned for treatment of obesity in different classical manuscripts of *Ayurveda* [Table 1]. Pharmacological properties of *Guggul* like *Medohara* (nearly correlated with hypolipidemic activity), *Shothaghna* (nearly correlated with Anti inflammatory activity) and Anti oxidant activity etc are observed in various international and national journals which may be beneficial in treatment of obesity.

**Table 1: Showing classical & contemporary references for Obesity having *Guggul***

Name Drug/ Formulations	Reference (Classical & contemporary research)
<i>Guggul</i>	Charak sutra sthan 25/40 Sushrut Chikitsa
<i>Amritadi guggul</i>	<i>Chakradatt 36/17</i>
<i>Navak guggul</i>	<i>Chakradatt 36/18</i>
<i>Dashang guggul</i>	<i>Bhava prakash 39/29</i>
<i>Trayushani guggul</i>	<i>Bhava prakash 39/31</i>
<i>Guggul</i>	Satyavati G et al. Effect Of An Indigenous Drug On Disorders Of Lipid Metabolism With Special Reference To Atherosclerosis And Obesity (Medoroga) M.D. Thesis (Doctor Of Ayurvedic Medicine). Banaras Hindu University, Varanasi 1966.
<i>Guggul</i>	Kotiyal JP, Singh DS, Bisht DB. Gum Guggul ( <i>Commiphora mukul</i> ) Fraction A In Obesity-A Double-Blind Clinical Trial. J Res Ayur Siddha 1985;6:20-35.
<i>Guggul</i>	Szapary PO, Wolfe M I, Bloedon LT, Cucchiara AJ, Demarderosian AH, Cirigliano MD et al. Guggulid For The Treatment Of Hypercholesterolemia JAMA 2003;290:765-72
	Nohr LA, Rasmussen LB, Straand J. Resin From The Mukul Myrrh Tree, Guggul, Can It Be Used For Treating Hypercholesterolemia? A Randomized, Controlled Study Complementary Therapies In Medicine 2009;17:16-22

### DISCUSSION:

Obesity is a chronic metabolic disorder results from the imbalance between energy intake and energy expenditure characterized by enlarged fat mass and elevated lipid concentration in blood. Different parts of

plants, metals and minerals are indicated for treatment of obesity as single or compound formulations in classics of *Ayurveda*. Among them *Guggul* occupied significant seat and effectively used for obesity treatment since ancient time. In classics of *Ayurveda* it is quoted that *Guggul* is superior among drugs which are used for treatment of *Medoroga* (obesity) [6] and also narrated that old *Guggul* is effectively used for treatment of *Medoroga* [7]. Pharmacological properties of *Guggul* like anti hyperlipidemic, anti oxidant activity etc. could be responsible for treatment of obesity.

### Anti Hyper lipidimic action

Guggulsterone, the bioactive constituent of *Guggul*, an antagonist at the nuclear receptor farnesoid x receptor (FXR) [11,12], a key transcriptional regulator for the maintenance of cholesterol and bile acid homeostasis [13,14,15] in body system. It removes excess cholesterol from body by converting in to bile acid through enterohepatic circulation and this is major pathway to remove excessive cholesterol from the body [16]. It is observed that *Guggul* treatment significant increase (57%) bile acid secretion through faecal route [17]. The cholesterol 7 $\alpha$ -hydroxylase (CYP7A1) is other rate-limiting enzyme of bile acid synthesis from cholesterol in the liver [18] and bile salt export pump (BSEP) expression, a rate-limiting efflux transporter for eliminating cholesterol metabolites as bile acids from the liver [19]. Guggulsterone up regulated BSEP expression and help in excretion bile and maintain harmony of cholesterol in body. The FXR antagonism and enhanced BSEP expression have been proposed as possible mechanisms for the hypolipidemic effect of guggulsterone [11]. Adipose tissue secretes adipokinines like tumour necrosis factor- $\alpha$  (TNF-  $\alpha$ ), interleukins 6 (IL-6) etc. [20,21,22], which induces marked hyperlipidemia [23]. Crude extract of *Commiphora mukul* also down regulate TNF -  $\alpha$  by inhibition of mitogen activated protein Kinase which in turn inhibit hyperlipidemia [24].

### Reduces Oxidation Status

It is generally accepted that overproduction of nitric oxide is associated with oxidative stress, that decrease Glutathione [25], superoxide dismutase (SOD) and increase xanthine oxidase which involved in the pathogenesis of hypercholesterimia, obesity, atherosclerosis and chronic inflammation [26]. The antioxidant activity of guggulsterone was first reported in the 1990s [27,28]. It exhibited potent inhibitory activity against the production of nitric oxide [29] and therapeutically beneficial to diseases associated with oxidative stress such as obesity etc. Glutathione “detoxify” reactive oxygen species such as hydrogen peroxide etc and guggulid significantly increases the levels of glutathione (GSH) suggesting inhibition of oxidative stress [30]. Xanthine oxidase promotes the

production of reactive oxygen species, whereas SOD is an important antioxidant enzyme catalyzing the conversion of superoxide anion to oxygen and hydrogen peroxide. Guggulsterone decreases Xanthine oxidase and increase SOD<sup>[31]</sup> thus reduces the production of reactive oxygen species and reducing oxidative stress which help prevention of obesity.

### Suppress inflammation

NF- $\kappa$ B is a transcription factor playing a central role in the regulation of diverse cellular processes including inflammation, immune response, differentiation, proliferation, and apoptosis. Activation of NF- $\kappa$ B can be achieved by induction with pro inflammatory molecules, such as tumour necrosis factor  $\alpha$  (TNF- $\alpha$ ), interleukin-1 $\beta$  (IL-1 $\beta$ ) etc. and increase severe hyperlipidemia<sup>[32]</sup>. The anti inflammatory activity of *Guggul* was documented in Ayurveda classics in terms of *Shothaghna* and further reported in 1960<sup>[33]</sup>, and subsequently in 1977<sup>[34]</sup>. Guggulsterone has been found to be a potent inhibitor of the nuclear factor- $\kappa$ B (NF- $\kappa$ B)<sup>[35,36,37]</sup>, a key regulator for inflammatory responses. This inhibition of NF- $\kappa$ B activation is mediated through a direct inhibition of I $\kappa$ B kinase (IKK) activation<sup>[35]</sup>. It was proposed that repression of NF- $\kappa$ B activation through inhibition of IKK activity represents a mechanism of the anti inflammatory effect of guggulsterone.

### Drug delivery medium

Solid lipid nanoparticle is an important aspect drug delivery system<sup>[38,39]</sup> having good biocompatibility, lower cytotoxicity, drug targeting, drug release<sup>[40]</sup>. Solid lipid nanoparticles of *Guggul* (GLN) have smaller particle size and related to release higher drug content due to large surface area. GLN formulations retain appreciable drug quantity despite being in lower size range which further enforces the possibility of better packing of drug<sup>[41]</sup> and showed good physicochemical parameters along with good stability and permeation.

Liposome (type of drug delivery system)<sup>[42]</sup> contains an outer mono- or bilayer of molecules surrounding hollow core which serves as storage for the therapeutic agent. It accommodates physico-chemically different drugs in liposome membrane (hydrophobic) and internal core (hydrophilic)<sup>[43,44]</sup> and enhance the bioavailability, improve elimination of rapidly metabolized drugs so it has been successfully used as vehicles for controlled drug delivery. Cholesterol is major component of various lipid based formulation and improves the stability of the liposome. The structure of cholesterol and guggulsterone are quite similar (except presence of side chain), which is an important constituents of lipid base formulation<sup>[45,46]</sup>. These formulations constitute an important category and used to influence the

absorption of active ingredients by means of modification of release of active ingredients. It was reported that Guggulusomes has mixed properties of liposome, solid lipid particles and multiple emulsions etc.<sup>[47]</sup> and represent a class of drug delivery system.

### CONCLUSION:

*Guggul* is an amazing drug used for treatment of obesity and its associated disorders mentioned in *Ayurvedic* classics. Its pharmacological properties like anti inflammatory, anti hyperlipidemic, anti oxidant activity are core mechanism for treatment of obesity. *Guggul* also act of as a type of drug delivery medium which help active constitute of formulation to reach the target site. In this way *Guggul* itself have anti obesity property and act as drug delivery medium by this activity *Guggul* will be beneficial in treatment of obesity.

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