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Review Article

MODE OF ACTION OF "*AMRITADYA GUGGULU*" IN THE MANAGEMENT OF *STHOULYA* W.S.R TO OBESITY

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ABSTRACT

Obesity (*Sthoulya*) is the major and basic cause of lifestyle disorders like Diabetes mellitus (T2DM), Coronary heart disease (CHD), Hypertension. Obesity (*Sthaulya*) is increasing at an alarming rate in developed industrialized countries which are undergoing rapid nutrition and lifestyle transition. Obesity is one of the most effective diseases which affect someone's social, physical and mental status. In Ayurveda, *Sthoulya* (Obesity) is regarded as *Medoroga,* a disorder of *Meda Dhatu*, which includes fat tissue and fat metabolism. According to Ayurveda, *Sthoulya* begins with an imbalance of *Doshas* (*Vata*, *Pitta* and *Kapha*), *Agni* (digestive fire), *Malas* (waste products) or an imbalance of S*rotas* (microcirculatory channels). This collection of imbalances then interferes with the formation of tissues or *Dhatus* and leads to a tissue imbalance that we experience as excess weight. Overweight and obesity are linked to more deaths worldwide than underweight. Overall, about 13% of the world adult population (11% of men and 15% of women) was obese in 2016. The worldwide prevalence of obesity nearly tripled between 1975 and 2016. *Amritadya Guggulu* possesses *Rasa- Katu, Tikta, Kashaya, Guna- Laghu, Ruksha* and *Virya- Ushna*, *Vipaka- Katu, Dosha Karma- Kapha Vatashamaka* is effective in the management of *Sthoulya*. By virtue of its *Rasapanchaka*, contents of drug are very well indicated in *Kapha* predominant pathologies. Due to this property, it breaks the *Samprapti* of *Sthoulya*. Hence the present attempt is done to encompass the up to date comprehensive literature to study the mode of action of *Amritadya Guggulu* in the management of *Sthoulya* w.s.r. to Ayurvedic properties and modern pharmacology.

KEYWORDS: Obesity, *Sthoulya, Amritadya Guggulu, Medoroga.*

INTRODUCTION

Normally in a Human being, the amount of energy required by the body is consumed in the various bodily functions and excess is stored, if the excess fat is much greater in proportion, then this gradually gets accumulated in the body and ultimately after sometimes leads to obesity. In present era, everyone is in mental and physical stress due to their modern living lifestyle, undisciplined to pursue the daily regimen, dietetic rules and regulations, which result in many lifestyle induced diseases and Obesity (*Sthoulya*) is one of them which is defined as the increased body weight beyond the desired health standards. A recent National Institute of Health consensus conference defined Obesity as Body Mass Index greater than 27 kg/m^2. Now a days, Obesity is defined at or greater than 25kg/m^2 BMI. Obesity may be defined as an abnormal growth of adipose tissue either in size or number of fat cells or both. Obesity is the commonest nutritional disorder in affluent societies and mostly prevalent in developed countries. The common way to find out whether you are *Sthoulya* or *Atisthoola* is ascertained by calculating the Body Mass Index (BMI). BMI is an estimate of body fat and can indicate risk for disease. BMI is a simple index and calculated by dividing person weight in kilograms by his height in square meters. The World Health Organization (WHO) defines as follows:

Table 1: **BMI Range (WHO)** [1]

Weight	BMI Range
Normal weight	18.5 to 24.9
Overweight	25.0 to 29.9
Obesity 1	30 to 34.9
Obesity 2	35 to 39.9
Extreme Obesity	>40

In Ayurvedic text *Acharya Charaka* has described eight *Nindniya prakruties* according to the body constitution and *Sthoulya* is one of them. In Ayurveda, Obesity (*Sthoulya*) is described as "*Medoroga*". In the manifestation of any diseases vitiation of certain basic components takes place

which are *Doshas, Dushya, Srotas* and *Agni.* In *Sthoulya*, due to *Avarana* (obstruction) of all the *Srotas* (channels) by the *Meda*, there is *Vriddhi* of *Kosthasthit Samana Vayu*, which in turn causes *Ati Sandhukshan* of *Jatharagni*. The increase in *Jatharagni* leads to rapid digestion of consumed food and leaves the person craving for more food. If at all due to some reason the person does not receive more food the increased *Agni* causes *Dhatu Pachana* which may lead to various complications. In this way it becomes a vicious cycle creating excessive improperly formed *Medo Dhatu*, giving various symptoms. Because of such a condition of *Srotorodha*, the other *Dhatus* are not nourished properly causing *Shaithilya* (flabbiness due to excess of water element) of *Dhatus* prior to *Meda Dhatu* and depletion of *Dhatus* next to *Medo Dhatus.*[2] According to *Sushruta, Ama Anna Rasa* is mentioned as root cause of *Sthoulya*. *Rasa* has been considered as a causative factor for *Sthoulya* and *Karshya*. *Ama Rasa* is produced due to *Kaphavardhakaahara*, *Adhysana, Avyayama, Divaswapana* etc. The *Madhura Bhava Ama Rasa* moves within the body, *Snigdhansha* of this *Anna Rasa* causes *Medovruddhi* which produces excessive stoutness.[3]

Aims and Objectives

The main aim of the article is to study the mode of action of *Amritadya Guggulu* in *Sthoulya* w.s.r. to Ayurvedic properties and modern pharmacology.

Materials and Methods

Important manuscripts of *Ayurveda* such as *Charak Samhita, Sushrut Samhita, Dravya Guna, Bhaisajya Ratnavali* along with *Rasa Shastra* literature like *Ras Ratna Samuchya* and *Ayurvedic* formulary of India are the sources of various preparation of Ayurvedic medicines. Besides this, we also search out different formulations containing ingredients of *Amritadya Guggulu* in Ayurvedic classics as well as different search engines like Pubmed, Google Scholar etc., and other pharmacological journals to find out the probable mode of action in relation to *Sthoulya*.

Ayurvedic Properties

Amritadya Guggulu is the contribution of *Chakra Dutta "Sthoulya Chikitsa Prakaran"* with its special indication in *Sthoulya.*[4] In *Amritadya Guggulu*, all the eight contents are in increasing quantity i.e., *Amrita* 1 part, *Elaichi* 2 part, *Vayvidang* 3 part, *Vatsaka* 4 part, *Vibitaki* 5 part, *Haritaki* 6 part, *Amalaki* 7 part and *Shudh Guggulu* 8 part respectively, to be taken with *Madhu* as *Anupana*.

Table 2: *Rasapanchaka* of *Amritadya Guggulu*[5]

Drug	*Rasa*	*Guna*	*Veerya*	*Vipaka*	*Karma*
Guduchi	*Tikta, Kashaya*	*Guru, Snigdha*	*Ushna*	*Madhura*	*Tridoshaghana*
Ela	*Katu, Madhura*	*Laghu, Ruksha*	*Sheeta*	*Madhura*	*Tridoshaghana*
Kutaj	*Tikta, Kashaya*	*Laghu, Ruksha*	*Sheeta*	*Madhura*	*Kaphapittashamaka*
Vayavidanga	*Katu, Kashaya*	*Laghu, Ruksha, Tikshna*	*Ushna*	*Katu*	*Kaphavatashamaka*
Vibitaki	*Kashaya*	*Laghu, Ruksha*	*Ushna*	*Madhura*	*Tridoshaghana (Kaphashamaka)*
Haritaki	*Kashaya Pradana Panchrasa*	*Laghu, Ruksha*	*Ushna*	*Madhura*	*Tridoshaghana (Vatashamaka)*
Amlaki	*Amla Pradana Panchrasa*	*Guru, Ruksha, Sheeta*	*Sheeta*	*Madhura*	*Tridoshaghana*
Guggulu	*Katu, Tikta*	*Laghu, Ruksha, Vishada, Suksham, Sara, Sugandhi*	*Ushna*	*Katu*	*Tridoshaghana*

a) On the basis of *Rasa*

Katu, *Tikta* and *Kashaya Rasa* are present in maximum drugs. *Katu Rasa* has *Deepana; Sneha-Kleda- Sweda- Abhishyandinashaka; Kapha Shamaka* and *Srotoshodaka* properties. *Katu Rasa* is formed by *Vayu* and *Agni Mahabhuta*[6] having qualities opposite to *Kapha (Prithvi* and *Jala),* thus helps in reducing excessive *Meda* deposition. *Tikta rasa* has also got *Deepana, Lekhana, Kleda-Meda-Vasa-Sweada Shoshana* and *Pachana* properties.[7] *Tikta Rasa* is a combination of *Vayu* and *Akasha Mahabhuta.*[8] Substances that are made up of *Vayu Mahabhuta* cause *Rukshta* and *Laghuta* in the body whereas *Akasha Mahabhuta* causes *Laghuta* in the body thereby reducing excessive *Meda Dhatu.*[9] These two *Mahabhuta* have qualities opposite *to Kapha. Tikta Rasa* also shows *Chedana* and *Shodhana* properties.[10] *Kashaya Rasa* is mainly formed by conjugation of *Vayu* and *Prithvi Mahabhuta*. *Vayu* is *Ruksha* in quality and dries up the excessive *Sneha* present in the body while *Prithvi* by virtue of *Kathina* and *Sthira Guna* which are opposite to *Drava* and *Sara Guna* reduces the *Shaithilta*. *Kashaya Rasa* has *Shoshana, Kledanashak* and *Sleshamaprashaman* properties.[11] So it clarifies the *Srotorodha* and scraps excess *Medodhatu* from body and dries up excessive *Vasa*.

b) On the basis of *Virya*: Contents of drug are mainly having *Ushna Virya* and rests are *Sheeta Virya*, but the most of *Sheeta Virya* drugs are *Mridu*. *Ushna Virya* suppresses the action of *Sheeta Virya* drugs and due to *Agni Mahabhuta Pradanta*, it possesses *Vata* and *Kaphahara* property.[12]

c) On the basis of *Vipaka*: Drugs having *Katu Vipaka* acts by their *Kapha Shamaka* property while drugs with *Madhura Vipaka* acts as *Rasayana* e.g., *Guduchi, Amalaki, Haritaki* etc.

d) On the basis of *Guna*: Maximum contents possess *Laghu, Ruksha* properties. *Laghu Guna* increases the *Agni* and decreases *Kapha*. It produces *Laghuta* in the body. *Ruksha Guna* may pacify vitiated *Kapha* and *Kleda* due to its *Shoshana Karma.*[13] *Laghu Guna* also pacifies the *Snigdha* and *Pichchila* properties of vitiated *Kapha* by the virtue of its *Langhana* and *Lekhana Karma.*[14] To cure *Srotodushti* caused by *Abhishyandi,* property of *Ama Shoshana Karma* is required.

So, *Amritadya Guggulu* is one of the ideal combination for the management of *Sthoulya* mentioned in Ayurveda; having maximum ingredients possessing *Katu, Tikta* and *Kshaya Rasa; Laghu, Ruksha Guna*; *Ushna Virya; Katu-Vipaka* ;*Vata-Kaphashamaka*; *Lekhaniya Medohara*, *Ama Pachana, Dhatushoshana* property which normalize the state of *Agni* and *Srotas*. Thus regulated *Agni* checked the excessive growth and accumulation of *Medodhatu* and thereby causing *Lakshana Upshamna* of *Sthoulya.*

Modern Pharmacology

a) *Guduchi*

It is a large, deciduous extensively spreading climbing shrub with several elongated twining branches. The branches bear smooth heart shaped leaves, so known by the common names Heart-leaved moonseed, *Giloy* and *Guduchi*. It is a herbaceous vine of the family Menispermaceae. Tinosporin and furanoidditerpine dilactone identical with Columbin have been isolated. Other constituents are Tinosporide, Cordifolide, Tinosporicacid, Cordifoli and quaternary alkaloids magnoflorine and Tembetarine.[15] Leaves are rich in protein and fairly rich in calcium and phosphorous. It is used as antipyretic, CNS depressant, hypoglycemic, anti-arthritic, anti-inflammatory, anti-allergic, hepato-protective, antioxidant, antistress, hypotensive, diuretic, antimicrobial were most important as most of the properties have been confined after clinical trials. Various Ayurvedic formulations such as "Ilogen-Excel", "Hyponidd" has shown significant decrease in the blood glucose levels and increase in the plasma insulin, hepatic glycogen and total hemoglobin as well as antioxidant activity.[16] The cardio protective activity of an herbal formulation "Caps HT2", which contains methanol extract of TC as a component, has antioxidant, anticoagulant, platelet antiaggregatory, lipoprotein lipase releasing, anti inflammatory and hypolipidaemic activity in rats.[17] The *Tinospora cordifolia* has potential application in food systems as an antioxidant and probably in biological systems as a nutraceutical.

b) *Ela*

Elettaria cardamomum is a pungent, aromatic, herbaceous, perennial plant, growing to about 2-4 meter in height, belongs to Zingiberaceae family. In India, the states of Sikkim and Kerala are the main producers of Cardamomum; they rank highest both in cultivated area and production. A 3-8% volatile oil contains terpine, terpinyl acetate and 3-4% starch. Oil has anti aflatoxin substance. The major constituents of the volatile oils of Cardamom include about 36% 1,8- cineol, 31% alpha terpinil acetate, 12% limonene, 3% sabinene and others.[18] Volatile components of cardamom exhibit antimicrobial activity. It has an inhibitory property against aflatoxin synthesis and caused 90% drops in aflatoxin elaboration. Cardamom tincture is used in the slimming preparations containing ephedrine. Cardamom is used in preparation of antioxidants which control ageing. Cardamom polyphenols will be able to influence thermogenesis and improve insulin resistance. Effects of 1,8 Cineole compound present in volatile oil are apoptic, the inhibiting of cytokines, prostaglandins, leukotrienes, and nitric oxide, TNF-alpha and IL-1Beta inhibition, liver necrosis reduction, cardiovascular effects as well as anti-cholinergic effects.[19]

c) *Vayavidanga*

It is a bulky shrub with long slender. Fruits are globose in shape, dull red to nearly black, wrinkled, short pedicle always present and usually one seeded. It contains Embelin, Quercitol, Tannin, Christembine, Embelic Acid, fatty ingredients, Resinoid, Volatile oils and Vilangin (Fruit); Potassium embelate; 2,5- dihydroxy; 3- undecyl- 1,4-benzoquinone (plant).[20] The fatty oil is reported to be similar to linseed and rapeseed oils in its properties. Fruits are astringent, bitter, anti-helmintic, depurative, brain tonic, digestive, carminative, stomachic, diuretic, contraceptive, rejuvenating, tonic, laxative. They are useful in helminthiasis, skin diseases, leprosy, pruritis, anemia, dyspepsia, flatulence, colic, constipation, strangury, tumors, asthma, fever, general debility. Roots are astringent, stomachic, and useful in odontalgia, colic, flatulence, and dyspepsia. Leaves are astringent, demulcent, depurative and useful in pruritis, indolent skin diseases and leprosy. Pharmacologically it is used as nematicidal, estrogenic, hypoglycemic,

antihelmintic, antibiotic, antifungal, antihyper-lipidemic, anti-diabetic, antibacterial, anti tubercular, anti-implantation, anti ovulatory, anti fertility, anti-inflammatory, hypotensive, antipyretic, diuretic, hepatoprotective, antileishmanial, resorptive**,** antiandrogenic**,** antispermatogenic, anticancer, immunestimulant etc.[21]

d) *Kutaj*

A deciduous laticiferous shrub or small tree, white flowers in cymes, grows all over India upto 900 meter elevation. Free alkaloids Conessine, Kurchine, Kurchicine, Hollarhine, Conamine, Conimine, Conkurchine, Holarricine, Holarrhimine group alkaloids and o-containing alkaloids are present in bark whereas seeds contain steroidal alkaloids Kurchiphyllamine, Kurchiphylline, Holantosine E, Trimethyl Conkirchine, Kurchessine, Holonarmine. Leaves contain Holarosine E,F, Holantosine A,B,C D; Alpha and Beta methyl derivatives, N-acetylholantosine D and N- acetyl Holarosine A, N-acetyl-L-holantosamine, whereas bark extract contains two alkaloids named Holacine and Holacimine[22]. It also shows immune-modulatory and hypolipidaemic action. Oral administration of Ethanolic extract of seeds in diabetic rats showed significant decrease in levels of blood glucose, serum cholesterol, triglycerides, aspartate transaminase, alanine transaminase, alkaline transferase, urea, creatinine, and uric acid.[23] Hydro- methanolic seeds extracts of the plants showed antioxidant/free radical scavenging property. Ethanolic seed extract showed a satisfactory 24% angiotensin- converting enzyme (ACE) inhibition.[24]

e) *Haritaki*

Haritaki; also known by *Terminalia Chebula* is a medium to large sized deciduous tree growing upto height of 25-30meter and diameter of trunk of this tree is 1 meter. This plant matures with numerous branches and rounded crown. Flowering takes place between April and August and plant bears fruits from November to January. The fruit of *Haritaki* contains Tannin, Galic acid, Chebulnic acid, Chebulogic acid, Triperpenoic acid and Mucilage.[25] Chebulin is isolated from its flower. From the bark of Terminalia chebula*,* beta-sitosterol has been isolated. Its fruits are laxative, carminative, digestive, diuretic, anti inflammatory, cardio tonic and aphrodisiac. They are used in anorexia, indigestion, hyperacidity, flatulence, constipation, jaundice, ulcers skin disease, leprosy etc. Chebulin is very useful in obesity, cardiac disease, anaemia, stomatitis, neuropathy and general debility. It lowers the VLDL and increase the HDL level.

f) *Vibitaki*

Vibitaki is a large deciduous tree found throughout India reaches height upto 30meter. Its fruit resembles to *Haritaki* but without ridges. It contains chemical constituents as Chebulagic acid, Ellagic acid (also from bark, heartwood) and its Ethyl ester, Gallic acid (also from seed coat); Fructose, Galactose, Glucose and its Galloyl derivatives, Mannitol and Rhamnose, Beta Sitosterol and Bellericanin (fruits); protein and Oxalic acid (seed); Oxalic acid and Tannins (bark); Palmitic, Oleic and Linoleic acids (kernel and its oil)[26].The fruits of *Vibhitaka* are antipyretic, anti-emetic, rejuvenating, anti inflammatory, digestive, anodyne, styptic, anti-helminthic and expectorant. They are used in vomiting, dyspepsia, flatulence, fever, leprosy and general debility. Its bark is mildly diuretics and used in anaemia and leucoderma. It exhibits antispasmodic and bronchodilator effect. It exhibit antibacterial and antifungal activities. Oil obtained from seeds is trichogenous and is useful in dyspepsia, skin diseases, leucoderma and greyness of hair.

g) *Amalaki*

Amalaki, also known as Indian Gooseberry; is a small to medium sized tree which grows to a height of 8-18meter. The plant bears subsessile leaves and greenish yellow flowers growing in clusters and appear in spring. Fruits are almost spherical and light greenish yellow in color. Its fruits contain Vitamin- C, Phyllemblin, Linolic Acid, Indole Acetic Acid, Ellagic Acid, Phyllemblic Acid, Terchebin and Corilagin. Roots contain Ellagic Acid, Lupeol, Oleanolic aldehyde.[27] Bark contains Leucodelphinidin, Procyanidin, Tannin. It shows Spasmolytic, Mild CNS depressant, Hypolipidaemic**,** Anti-atherosclerotic, Anti-mutagenic, Anti-oxidant, Immunomodulator, Anti-fungal, Anti-tumour, Hypoglycaemic**,** Anti-inflammatory, Antibacterial and Anti-ulcer properties.[28]

Gallic acid, a phenolic compound of *Triphala* also showed Antiobesity activity. Accordingly, a randomized, double-blind, placebo controlled, clinical safety and efficacy trial at Shahed University in collaboration with Endocrinology and Metabolism Research Institute (EMRI) has being conducted for evaluation of the activity of *Triphala* in obesity.[29]

h) *Guggulu*

It is about 2-3.5 meter heighted plant of Burceraceae family. The plant grows wild in the arid, rocky tracts, also in low rainy and hot areas. The part used is resin collected by tapping the barks. From the Gum -resin, Sesamin, few other steroids, essential oil containing steroidal ketones, alcohol and aliphatic triols were reported. In addition, Diterpenoid constituents - Cembrene-A and Mukulol, some fatty tetrols-Octadecan-1,2,3,4tetrols,eicosan-1,2,3,4 tetrol and Non adecan-1,2,3,4 tetrol were reported.[30] It removes excess cholesterol from body by converting

into bile acid through enterohepatic circulation and this is the major pathway to remove excessive cholesterol from the body. *Guggulu* is an oleo resin obtain from the plant *Commiphora Mukul* and is very much used in Indian system of medicine as astringent, antiseptic, expectorant, aphrodisiac, demulcent, carminative, antispasmodic and used in rheumatism. Gum resin showed different pharmacological properties uses and clinical application; astringent, expectorant, carminative, antifertility, arthritis, leprosy, impotence, sterility, liver disorders, hemiplegia, hypolipidaemic, atherosclerosis, thyroid stimulating, psoriasis and cardiac ischemia etc. Guggulsterone, the bioactive constituent of *Guggul*, an antagonist at the nuclear receptor farnesoid x receptor

(FXR) a key transcriptional regulator for the maintenance of cholesterol and bile acid homeostasis in the body system.[31] Adipose tissue secretes adipokinines like tumour necrosis factor-*α* (TNF- *α*), interleukins 6 (IL-6) etc. which induces marked hyperlipidemia.[32] Crude extract of *Commiphora mukul* also down regulate TNF - *α* by inhibition of mitogen activated protein Kinase which in turn inhibit hyperlipidemia.[33] *Guggulu* has been found to have the capacity to enhance production of thyrosine, tri-idothyroxine which also account for its lipid lowering activity. It is generally accepted that overproduction of nitric oxide is associated with oxidative stress, that decrease Glutathione, superoxide dismutase (SOD) and increase xanthine oxidase which involved in the pathogenesis of hpercholesterimia, obesity, atherosclerosis and chronic inflammation. The antioxidant activity of guggulsterone was first reported in the 1990s. It exhibited potent inhibitory activity against the production of nitric oxide and therapeutically beneficial to diseases associated with oxidative stress such as obesity etc.[34]

DISCUSSION

The disease *Sthoulya* originates due to consumption of *Kapha Vriddhikara Aahara Vihara* and *Anya Nidana*. These factors derange *Jatharagni* causing *Ama Aanarasa* which results in *Medodhatu Agnimandya*. This condition leads to excessive growth and accumulation of *Medo Dhatu* causing the disease *Sthaulya*. In Ayurveda, the action of drugs is executed in the body through its pharmaco dynamics properties like *Rasa, Guna, Veerya, Vipaka* along with these *Prabhava* is the specific property inherited by the drug which cannot be explained and the principle of treatment in Ayurveda is based on *Samprapti Vighatana* which is achieved by relieving *Dosha Dushya Sammurchana*. In the pathology of *Sthoulya, Kapha* is main *Dosha* and *Meda* is main *Dushya*, while *Agnimandya* takes place at *Medodhatvagni* level. So, drug having *Kapha* and *Medanashaka* property and efficacy to correct the function of *Medodhatvagni-mandya* is effective to control *Medoroga*. *Amritadya Guggulu* possesses *Rasa- Katu, Tikta, Kashaya, Guna-Laghu, Ruksha* and *Virya- Ushana*, *Vipaka- Katu, Kapha-Vatashamaka* property, is effective in the management of *Sthoulya*. By virtue of its *Rasapanchaka*, contents of drug are very well indicated in *Kapha* predominant pathologies.[35] Due to this property, it breaks the *Samprapti* of *Sthoulya*. As it is *Deepana* and *Pachana* it can do very well in certain other *Kapha-Vata* conditions.

CONCLUSION

According to modern science excessive adipose deposition in the body is the prime reason for manifestation of disease and natural products can play a safe and effective role with obesity specially those containing fibers, polyphenols, sterols, and alkaloids. *Amritadya Guggulu* having Antiobesity, Immunomodulatory, Prokinetic, Hypolipidemic, Thermogenesis property possesses a core mechanism for the treatment of *Sthoulya* (Obesity). In Ayurveda, as equilibrium of *Doshas* is the main aim of treatment of disease, properties like *Srotoshodhana*, *Ama Pachna Shodhana*, *Vata Shamana*, *Lekhana, Shoshara, Kleda* as well as *Meda Vilayna* will be beneficial in *Sthoulya*. So, *Amritadya Guggulu* is considered to be a safe Ayurvedic drug for the treatment of *Sthoulya* and its associated disorders mentioned in Ayurveda Classics.

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