ANTI-OBESITY POTENTIAL OF *GAVEDHUK* (*Coix lacryma-jobi* Linn.): A REVIEW

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ABSTRACT

Obesity is one of the epidemic lifestyle disorders of the 21st century which is recognized as chronic progressive disease. Presently 2.8 million people die each year due to obesity and overweight. Current statistics suggest that about 2.7 billion of global populations will suffer by 2025. In India, the sufferers are 5% of total population and male and female obesity hold the 14th and 15th position in world ranking respectively. For the prevention of the disease, the present study aims to highlight the anti-obesity potential of indigenous food grain (Coix lacryma Linn. Fam. Poaceae). Obesity has been described as Sthaulya or Medoroga in Ayurvedic texts and considered under the Santarpan-janya vikaar (a disease caused by over nourishment). In Charaka Samhita Sutrasthan-Chapter 25- in Agraya Prakrana (list of drug of choice) i.e. Gavedhukanna Karshaniyanam (Gavedhuk is best among anti-obesity drug). After thorough review literature, found that extract of coix seeds regulate neuroendocrine activity in the brain and causing reduction in body weight, fat mass, serum leptin levels and activities of neuropeptide Y (NYP). It has an inhibitory effect on synthesis of cholesterol in the liver, facilitates biliary excretion of triglyceride and accelerates phospholipid synthesis in the liver. Coix may prove helpful in obesity as per classical references as well as by pharmacological researches.

Keywords: *Obesity, Lifestyle disorders, Coix lacryma, Ayurveda, Gavedhuk.*

INTRODUCTION

Obesity and overweight are a 5th leading risk factor of global health problem in developed and developing countries [1]. Obesity is one of the epidemic lifestyle disorders of the 21st century and recognized as chronic progressive disease. Presently 2.8 million people die each year due to obesity and overweight. Health statistics suggested that about 2.7 billion of global populations will suffer by 2025. In India, the sufferers are 5% of total population and male and female obesity hold the 14th and 15th position in world ranking respectively.

Overweight and obesity are defined as abnormal or excessive fat accumulation in adipose tissue, to the extent that may impair health [2]. Overweight and obesity are diagnosed on the basis of body mass index (BMI) in a simple index of weight for height (Kg/m^2). According to WHO, BMI greater than or equal to 25 Kg/m^2 is overweight and greater than or equal to 30 Kg/m^2 is obesity [3]. Obesity has been described as *Sthaulya* or *Medoroga* in Ayurvedic texts [4]. It is described under the *Santarpan-Janya Vikar*a (Disease caused by over nourishment). Charaka has described *Atisthool* (obese and overweight) in eight *Nindnaya Purush* (eight undesirable physical constitutions) in *Ashtonindnaya Adhayaya* as Chapter 21st of *Sutrasthana*. He has also mentioned the *Chikitsa*, *Pathya* and *Vihar* for the treatment of *Sthaulya Chikitsa*. Apart from these Charaka has mentioned the special indication as *Agraya Prakarana* i.e. collection of drug of choice and the drug *Gavedhuka* has been mentioned as *Gavedhukanna Karshaniyanam* (best among anti-obesity drug) [5].

Need of the study:

Obesity is not as simple as it saw but it is an alarm for the risk of insulin resistance, diabetes, cardiovascular disease, cerebrovascular disorder, fatty liver, hypertension, sleep apnea, and sometimes psychological disorders. For the prevention of obesity one should limit the carbohydrate and fat consumption, increases fibre rich grains, pulses, fruit and vegetables and also increases regular physical activity. There are some medicines as Sibutramine, Orlistat and therapy as Lipo-section have been used for the management of the obesity but they have only effective in small population. Some medicines have serious side effects and some have causing steatorrhea, colic pain and flatulence. Therefore they have limited in use and creating a gap in the society and health care. For fulfill the gap there are many ayurvedic formulations in the market, but the situation has not been changing as required. So *Gavedhuka* as a single drug therapy described by the Charak as best anti obesity drug can prove the remedy for the obesity and overweight.

GAVEDHUK (Coix lacryma-jobi L. Fam. Poaceae):

Gavedhuk is one of the important grains of India from the Vedic period. It is commonly known as Job's tears, coix seed, Chinese Pearl Barley [6]. The plant has been mentioned in Ayurvedic classics for its best anti-obesity action. In recent researches, several other pharmacological actions came into light, such as hypoglycemic actions, antispasmodic and anti-inflammatory action, anti-neoplastic action, skin health and complexion enhancing action, antioxidant activity. Traditionally it has been used as a drug cum food supplement for obesity and overweight which contributes a major lifestyle disorder [7].

Varieties:

There are four varieties [8] -

1. *C. lachryma-jobi* L. var. *typical*
2. *C. lachryma-jobi* L. var. *stenocarpa* Stapf.

3. *C. lachryma-jobi* L. var. *monilifer* Stapf.
4. *C. lachryma-jobi* L. var. *mayuen* Stapf.

Wild Type: *Coix lacryma-jobi* var. *stenocarpa* and var. *monilifer*. These have very hard

shell pseudocarps and pearl white oval structures and have been used as beads.

Cultivated Type: *Coix lacryma-jobi* var. *mayuen* are harvested as a cereal crop, has soft

shell and cultivated in all parts of Asia.

Vernacular Names [9]:

Table: 1 Name of Gavedhuk in different languages

S.N.	Language	Names	S.N.	Language	Names
1.	Sanskrit	*Gavedhu, Gavedhuka*	2.	Kannada	*Manjutti*
3.	Bengali	*Gadagad, Dedhaan, Devaan*	4.	Malayalam	*Kaatugotampu, Kaakkappalunku*
5.	English	Adlay, Jobs tears, Coix	6.	Marathi	*Kasai*
7.	Gujarati	*Kasai*	8.	Tamil	*Kaattukuntumani*
9.	Hindi	*Garheduaa, Garahedu, Gargari*	10.	Telugu	*Adaviguruginja*

Classical Pharmacology [10]**:**

Rasa- Katu, Madhura
Vipaka- Katu
Virya- Ushna
Dosha-karma- Kaph-nashaka
Karma- Karshya-karaka, Sukranashaka

Classical uses of *Gavedhuka* in Ayurvedic texts:

Table: 2 Classical uses and indications of Coix in Ayurvedic texts [9]

Classical text	Indications and Uses	References
Charak Samhita	Causes *karshana* Parched *gavedhuka* with honey	CS.Su.2.25
	To check emesis decoction of *gavedhuka* is indicated	CS.Ci.20.94
Bhavaprakash	*Sthaulya chikitsa*	BP.Ci39.22; Ni.647
Madanpal Nighantu	Used as food grains in meal	MP.Ni. p.209
Kaiyadeva Nighantu		KD. Ni. p.321
Haritkyadi Nighantu		HK.Ni. p.266
Saligram Nighantu		S.Ni.P. p.642
Priya Nighantu		P.Ni. p.206
Bhaishajya Ratnavali	*Vatavyadhi chikitsa*	BR.26.308
Vrinda Madhava	Decoction sprinkled in *Masurika* (conjunctivitis)	VM.56.40

Morphology:

Annuals, Terrestrial, stem nodes swollen or brittle, stems erect or ascending, geniculate, decumbent, or lax, sometimes rooting at nodes, terete, round in cross section, or polygonal, branching above the base or distally at nodes, internodes solid or spongy. Culms 1-2 m tall, scapes exceeding basal leaves, Leaves mostly cauline, conspicuously 2-ranked, distichous,

sheathing at base, sheath mostly open or loose, smooth, glabrous; Leaf blades lanceolate, ovate, 1-2 cm wide, mostly flat, glabrous, Ligulate, Ligule fringed, ciliate, or lobed membranous. Inflorescence; terminal, solitary with one spike, fascicle, glomerule, head or cluster per stem or culm. Flowers unisexual, Plants monoecious, Spikelets pedicellate, dorsally compressed or terete, 3-10 mm wide, with two florets, in paired units, 1-sessile, 1-pedicellate, Pedicellate spikelet rudimentary or absent, usually sterile; Fruit- caryopsis, isodiametric, trigonous or globose, broadest at the base or beaked [11].

Fig 1: Coix (*Gavedhuk*) Seeds and plant with spikelets.

Nutritional Value:

100 gm of seed contains 380 calories, 11.2 gm Water, 15.4 gm Protein, 6.2 gm Fat, 65.3 gm Carbohydrate, 0.8 gm Fibre, 25 mg Calcium, 435 mg Phosphorous, 5.0 mg Iron, 0.28 mg Thiamine, 4.3 mg Niacin, 0.19 mg Riboflavin and 1.9 gm ash. The major protein component in Job's tears seed is a prolamin called coixin. It also contains albumins and globulins and other residual proteins [9].

Phytochemistry:

C. lacryma contains 4-ketopinoresinol, alpha coixins, alpha sitosterol, beta sitosterol, coicin, coixan A, coixan B, coixol, coix spirolactum A, coix spirolactum C, coniferyl alcohol, ferulic acid, gamma sitosterol, glucose, methyl dioxindole-3-acetate, myuenolide, palmatate, phytin, potassium chloride, stearate, stigmasterol, syringic acid, syringaresinol, vitamin B_1, peracetylated forms of glucose, maltose, maltotriose, maltotetraose, maltopentaose [9].

Pathophysiology of Obesity:

There are many mechanisms suggested for the development of obesity. The appetite pathway begins with the arcuate nucleus (specified area of the hypothalamus), which has two outputs i.e., lateral hypothalamus (LH) as feeding center and ventromedial hypothalamus (VMH) as satiety center. The arcuate nucleus contains two distinct groups of neurons, first group is Neuropeptide-Y (NPY) and Agouti-related peptide (AgRP) and second group is pro- opiomelanocortin (POMC) and cocaine-amphetamine-regulated transcript (CART). NP-Y/AgRP neurons stimulate feeding and inhibit satiety, while POMC/CART neurons stimulate satiety and inhibit feeding. Leptin mediates long-term appetitive control and also called as satiety hormone or starvation hormone, which is

produced by the adipose cells in response of stored fat. Leptin inhibits the NPY/AgRP group while stimulating the POMC/CART group. Diminished leptin signaling either via leptin deficiency or leptin resistance leads to overfeeding and getting obese. It may be due to some genetic and acquired forms of obesity[12]. Leptin deficient or leptin resistant condition mainly present in obese persons in whom high levels of leptin present but do not respond. Leptin resistance also causes hunger and the person regains their body fat. Inflammatory signaling in hypothalamus and free fatty acids in blood, interfere the leptin response and may develop resistance. Long-term lifestyle changes, soluble fibre and high protein diet help to reverse the leptin resistance. Others mechanisms are also involved in obesity like as ghrelin, insulin, orexin, PYY 3-36, cholecystokinin, adiponectin, adipokines and hormonal factors. Ghrelin produced by the stomach and modulate the short term appetite control. When the stomach is empty then need to eat and when the stomach is stretched then stop eating [13]. Intestinal flora is also involved in the generation of obesity. Some dietary polysaccharides remained undigested but increased gut-flora secrets some enzymes which fermented into the monosaccharide, short-chain fatty acids (SCFA) which increases triglycerides and energy stores [14].

Oxidative stress in obesity:

Increased leptin level leads to increase in adipocytes and respond the monocytes which are then transformed into macrophages that producing large amounts of oxidants like as peroxynitrite. Increased reactive oxygen triggers the cytotoxic reaction and damages the membrane lipids, proteins, nucleic acids and carbohydrates. Oxidative stress is the main causative factor of many complications associated with obesity i.e. insulin resistance, diabetes, hypertension, cardiovascular diseases and cerebrovascular diseases [15].

PRE-CLINICAL STUDIES:

Effects on lipid metabolism:

1. High-fat diet (HFD) induced obese rats were injected 50 mg/100g/body weight/day of crude extract of coix seed for 4 weeks. The result showed modulation of expressions of leptin and α-TNF which declined and reduced the body weights, food intake, fat size, adipose tissue mass and serum hyperlipidemia in rat [16].

2. A study was carried out to investigate the effects of ethyl acetate fraction of an ethanol extract of coix seed on glucose uptake and adipocyte differentiation in 3T3-L1 cells. Differentiation was examined by Oil red O staining activity after the treatment with extract for 6 days. The results showed that the extract phosphorylated the AMP-activated protein kinase which processes the adipose differentiation and modulated the adipocyte functions. It may be effective in improving the symptoms of obesity and another metabolic syndrome [17].

3. A study of coix on lipid metabolism by the effect on plasma, liver and fecal lipid components was carried on Sprague-Dawley male rats fed on a coix-lard diet, coix-soybean oil diet and control diets (containing 1% cholesterol) for 27 days. Plasma and liver cholesterol levels in the coix-lard diet group significantly decreased and no effect on the

fecal excretion of cholesterol as compared to the control group. The decreased liver triglyceride and the increased fecal excretion of triglyceride were found in the coix-soybean oil diet group. There were no significant changes in plasma and fecal bile acids in either coix diet group. These results suggested that coix may have an inhibitory action on cholesterol synthesis in the liver, by facilitating the biliary excretion of triglyceride and phospholipids synthesis in the liver [18].

4. A study on the effects of coix seed oil on plasma lipids, insulin and leptin in rats was carried out and found that it could decrease low-density lipoprotein cholesterol (LDL-C), insulin, leptin and thiobarbituric acid reactive substance (TBARS) concentrations after 4 weeks of feed [19].

Anti-obesity activity:

The water extract of coix seeds exhibits anti-obesity activity by regulating the neuroendocrine activity in the brain [19].

1. Obesity-induced rats (by HFD) were injected with 50 mg/100 g /body weight of water extract of coix seeds daily for 4 weeks. Optical density of Neuropeptide-Y (NPY) immunoreactivity in the paraventricular nucleus of rats was lowered by 2.6 fold. Both of NPY and LR (Leptin receptor) mRNA levels were also determined by real-time PCR and decreased in coix treated rats. The result showed that coix may regulate neuroendocrine activity in the brain and regulate fat metabolism [20].

2. A study was conducted to investigate the effect of coix extract on protein expression levels of Peroxisome proliferator-activated receptor PPARγ [2] and c/EBPα (CCAAT-enhancer-binding protein α) and obesity responses in obese mice induced by HFD. The results showed that obesity, fat accumulation, and serum cholesterol were alleviated by the coix extract. PPARγ [2] and C/EBPα, proteins are related to the adipogenesis, were also modulated by the extract [21].

3. An in vitro study was carried on to evaluate the antiadipogenic activity of coix seed on pre-adipocytes cell line 3T3-L1. The result showed that significant inhibitory activity on adipocyte differentiation, assessed by measuring fat accumulation using Oil Red O staining. Time gap interval treatment with the coix seed exerted inhibitory activity on adipocyte differentiation via acting on the early stage of adipogenesis [22].

Glycemic load reducing activity:

1. Study on streptozotocin (STZ) induced hyperglycemia in mice, the chloroform fraction of ethanol extract of coix significantly reduced blood glucose as well as gluconeogenic enzyme activities. Two compounds isolated, ß-sitosterol and stigmasterol, have been reported as hypoglycemic [23]. Another study confirmed the antidiabetic potential of dehulled seed of C. lacryma-jobi by reducing blood glucose level in streptozotocin-induced diabetic rats [24].

2. Oral administration of coixan to normal mice showed no obvious action to decrease blood glucose level. Peritoneal administration of coixan in the dosage from 50 to 100 mg/kg was

able to decrease blood glucose level significantly in normal mice, diabetic and hyperglycemic mice (P 0.05 to P 0.01) in a dose-dependent manner [25].

Effect on intestinal bacteria:

1. Study on the effect of a dietary supplement of dehulled coix on the culture counts of intestinal bacteria and their metabolism in the gastrointestinal (GI) tract of Sprague-Dawley rats. Four groups were made on the basis of a diet containing different amount of dehulled Coix in 0% (control), 5%, 20%, and 40%. All animals fed with coix had normal healthy intestinal walls and no pathogenic signs whatsoever. The culture counts of fecal lactic acid bacteria were higher in feces of rats fed with coix than in the control group. Cecal short-chain fatty acid (SCFA) content and fecal SCFA were significantly higher in the 20% and 40% groups than in the control and 5% groups. All the coix-fed rats had a significant influence on the growth of intestinal bacteria. Currently, the use of prebiotics and probiotics or gut microbiota transplant has been the new approach to control the development of obesity or insulin resistance. It can be also through the supplementation of dietary fiber [26].

CLINICAL STUDY:

Hypolipidaemic activity:

A clinical trial was done on the effects of coix on plasma lipids and LDL oxidation in hyperlipidaemic smokers and found that coix could reduce the total and low-density lipoprotein cholesterol (LDL-C) while at the same time increase the lag phase of LDL oxidation. The antioxidative effect was found to be less pronounced in smokers than in non-smokers [27].

Anti-obesity potential:

A clinical study was conducted on *Karshaniya Yavagu* to evaluate the efficacy of Anti-obesity potential. After 90-day trail weight, body mass index, waist circumference, hip circumference and waist to hip ratio of the trail group showed significant result. The study made hope for obese individuals [28].

Free radical scavenging activity:

Whole coix demonstrated higher TPC (total phenolic content) and better DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging activities than dehulled coix and roasting increases the TPC and radical DPPH scavenging activities [29]. Methanol extract of coix hull separated into the water, 1-butanol, ethyl acetate, and hexane fraction and 1-butanol-soluble fraction exhibited a greater capacity of scavenging of DPPH radical compared to water, ethyl acetate and hexane fraction. Strong antioxidant activity of six compounds i.e. coniferyl alcohol, syringic acid, ferulic acid, syringaresinol, 4-ketopinoresinol and mayuenolide were found in 1-butanol [30].

DISCUSSION:

The *Gavedhuk* seed possesses *Katu* predominant *Rasa* and *Vipaka*. It is antagonist to *Madhura Rasa, Madhura Vipaka* and *Kapha Dosha* which reduces the *Kapha* and *Meda* (similarity with the *Kapha* properties) in the body. It has also *Ushna Virya* (potency) which increases the influence of digestion power that reduces the *Kapha* and melted down the *Meda* in the body. Pacification of *Kapha* and *Meda* represent the anti-obesity potential of *Gavedhuk.* The grains have also 17 % dietary fibers and high polyunsaturated fat as 4.3g/100g of fat. These dietary fibers are amylose in nature and digested by the enzymes of the intestines which control the glycemic load. The increase in fat mass is not only due to efficient harvest of energy, but also the gut microbiota which changes the bowel permeability, insulin resistance, hormonal environment, expression of genes regulating lipogenesis, interaction with bile acids and also changes the proportion of brown adipose tissue[18]. Obese animal's microbiota are more efficient than lean animals on energy extraction from dietary intake and subsequent fat storage. Dietary fiber rich food changes the diversity of microbiota and reverses their activity. Gavedhuk dietary fiber is act as a prebiotics and decreases the glycemic load.

Coix regulate the neuroendocrine activity in the brain and causing reduction in body weight, fat mass and activities of NYP. Coix increases serum leptin levels which lowers the feeding habits. It has also inhibitory effect on synthesis of cholesterol in the liver, facilitates biliary excretion of triglyceride and accelerates phospholipids synthesis in the liver.

CONCLUSION:

Gavedhuka has been used since time immemorial for obesity and overweight. Therapeutically it has been used as *Pathya Aahar* (wholesome diet) as well as in the form of *Yavagu* (gruel) in overweight and obesity. But it becomes lesser known today due to social negligence and somehow governmental ignorance. Its proper cultivation and utilization may be the solution for large number of health problems originating from faulty lifestyle. Though there is a need for further clinical researches to validate the classical and pharmacological activities.

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