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A SYSTEMATIC REVIEW ON EVIDENCE BASED VALIDATION OF TWO MEDICINAL PLANTS FOR THE SAFE AND EFFICIENT MANAGEMENT OF OBESITY

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ABSTRACT

Obesity is a metabolic disease in which excess body fat has accumulated such that it may have an adverse effect on health. It is the major chronic health problem which has reached epidemic proportions worldwide. Its treatment includes synthetic drugs and bariatric surgery, which may entail high costs and serious complications. Plant-based medicinal agents offer an alternative approach for the management of obesity. The demand for plant-based medicines is ever growing due to their cost effectiveness and less or no side effects. This review compiles available clinical trials literature (human and animal studies) on the two most important medicinal plants *Achyranthes aspera* and *Cissus quadrangularis* in the management of obesity. In studies, significant weight loss and no adverse effects or mortality were observed. In conclusion, these herbs have an acceptable level of evidence in obesity management due to having good number of clinical trials and rich scientific background.

KEYWORDS: Obesity, bariatric surgery, *Achyranthes aspera*, *Cissus quadrangularis*.

INTRODUCTION

Obesity is rapidly rising health problem and it has affected people from all walks of life. It is a lifestyle disease. Obesity is increasing at an alarming rate throughout the world. Today it is estimated that there are more than 250 million obese people worldwide, equivalent to 7 ercent of the adult population (WHO 1998).[1] National Family Health Survey India (nfhs-2).[2]

1998-99 shows 5.8 percent obese women with BMI (Body Mass Index) 30 or more and 17.7 percent overweight women with BMI 25-30 in urban India. Due to urbanization and modernization, our lives are becoming more sedentary. Household durable goods like washing machines, cooking gas and electric ovens etc again reduce the physical activity. Many similar activities prevent people from physical activity leading to overweight and obesity. At the same time, consumption of oily and junky food also adds to the problem. Obesity is not immediate lethal disease itself, but it is a significant risk factor associated with a range of serious non-communicable diseases.[3] Cohort and cross-sectional studies have indicated that obesity may be linked with an increased risk of coronary heart disease, hypertension, diabetes mellitus and gallstone.[4] A body mass index (BMI) of over 40 has been linked to a higher chance of developing diabetes. According to the Centre for Disease Control and Prevention (CDC) a healthy BMI ranges from 18.5 to 24.9.[5]

The treatment of obesity with synthetic drugs and bariatric surgery is costly and chances of side effects are high. Long-term use of synthetic drugs has lead to side effects such as nausea, vomiting, diarrhoea, dizziness, jittery feeling, acidity, sinusitis, headache in the body which may lead to heart failure. Besides, anti-obesity drugs are a frequent adjunct, because these interventions have limited long-term success and the weight is regained when treatment is discontinued.

Herbal medicines have a strong base and potential to be useful as safe and effective drug for treating obesity. The use of natural remedies for weight loss has increased, based on reliability, safety, and cost compared with synthetic drugs or surgical procedures. Medicinal plant or their preparations may enhance satiety, boost metabolism, and speed up weight loss.[6,7] Ayurveda and other traditional medicinal system describe a number of plants used as herbal drugs for the treatment of obesity. Safe effective and inexpensive indigenous remedies are gaining popularity among the people of both urban and rural areas especially in India. They act as alternative medicine due to less side effects and low cost. The active principles present in medicinal plants have been reported to possess anti-obesity effect.

Certain herbs, have also been used by native people for their appetite suppressing effects. This includes ***Achyranthes aspera*** (Latjira) and ***Cissus quadrangularis*** (Hadjor). These plants have been used in traditional Indian medicine for thousands of years to treat various disorders. Several reviews about anti-obesity properties on these important medicinal plants have been appeared in literature. ***Achyranthes aspera*** (Amaranthaceae) is an important

medicinal herb found as a weed throughout India. Though almost all of its parts are used in traditional systems of medicines, seeds, roots and shoots are the most important parts which are used medicinally. The special property of the seeds of *Achyranthes aspera*, as an anorexient, bestows valuable effect, to cure the excessive hunger in obesity and stimulates the release of insulin from the beta-cells in human.

Achyranthes aspera

Some studies have examined role of ***Cissus quadrangularis*** (Vitaceae) in fighting obesity and symptoms of metabolic syndrome has attracted interest in other parts of the world. A significant proportion of these plants have been observed to possess potent antioxidant activity, which may contribute to anti-obesity property in animals.

***Cissus quadrangularis*.**

Keeping this in view, we surveyed *Achyranthes aspera* and *Cissus quadrangularis* for their anti obesity potential and reviewed the scientific data, including experimental methodologies, adverse effect (if any), subchronic toxicity, gentotoxicity studies, active components, animal studies, and human studies.

This review is aimed to evaluate the efficacy and safety of *Achyranthes aspera* and *Cissus quadrangularis* in the management of obesity which could be beneficial not only for researchers and academician but also for common people in selecting a herbal product to develop a healthy body.

METHODOLOGY

Data were acquired from various databases, including Science Direct, Pub-Med, Scopus, Web of Science, and from books and theses for the period from 1991 to 2014. Key search words included: *traditional medicine, medicinal herbs, plant extracts, anti-obesity, weight loss, overweight, botanical remedy, efficacy, safety, lipogenesis, Cissus, Achyranthes, adipocytes* and *anthropometric indices*. Papers on human and animal studies, clinical trials, and related to plant-based obesity medication are discussed.

RESULTS

Study of adverse effect and quantity of safe dose to intake of *C. quadrangularis* extract (CQR-300) was studied by Kothari.[8] SC *etal*. They investigated these effects of *C. quadrangularis* extract (CQR-300) in subchronic toxicity, and gentotoxicity studies. In the subchronic study no treatment related clinical signs of toxicity, mortality were reported. The results of mutagenicity studies suggested that CQR-300 is not genotoxic.

Jiji.[9] *etal*, investigated the comparative effect of ethanol extract of *Cissus quadrangularis* and *Tribulus terrestris* on lipid profile in rats. The data suggested that both plants have significantly anti hyperlipidemic effect.

Shirin HR.[10] *etal*, reviewed the efficacy and safety of effective herbal medicines in the management of obesity in humans (19) and animals (58) a total of 77 studies were included. Studies with *Cissus quadrangularis* (CQ), *Sambucus, Asparagus, Garcinia*, Ephedra, Slimax showed a significant decrease in body weight. In conclusion they reported, compounds containing ephedra, *Cissus quadrangularis* (CQ), etc. were found to be effective in the management of obesity.

Shamina & Gokilavani.[11] did the toxicological studies of aqueous extract of *Cissus quadrangularis* in female albino rats. The serum biochemical parameters of the animals treated with both acute and sub acute doses of oral extract of *C. quadrangularis*, suggest that the plant extract may be safe especially at the therapeutic dose.

Aimmanas.[12] *etal*, conducted Toxicity study to evaluate subchronic toxicity of *C. quadrangularis* powder in rats. Result showed that *C. quadrangularis* at the given doses did not produce any significant toxic effect in rats during the period of treatment for 3 months.

Oben *etal* (2006, 2007 and 2008).[13,14,15] evaluated the effects of formulations and extracts of, *Cissus quadrangularis* on weight loss in overweight and obese human subjects and reported that the extracts and formulation appeared safe and useful in the management of weight loss and metabolic syndrome.

Chidambaram and Venkatraman.[16] evaluated the protective effects of *Cissus quadrangularis* stem extract (CQEt) in rats fed high fat–high fructose diet and also tested its free-radical scavenging property *in vitro*. Results suggested that CQEt affords hepatoprotection by its antioxidant and insulin-sensitizing activities.

Rathinam Prema.[17] *etal.,* evaluated the safety of combined ethyl acetate extract of *Cissus quadrangularis* and *Aegle marmelos* by determining its toxicity after acute and chronic administration in albino rats. Study on acute toxicity of extract found to be safe.

G. Geetha.[18] *etal.,* Laxmi marotia.[19] *etal. and* Neerja Rani.[22] *etal.,* B. Pushpa Latha.[23] *etal.,* studied anti-obesity effect of various extract of *Achyranthes sp.* suggested that it may prevent obesity.

Muhammad Shoaib Akhtar.[20] and Javed Iqbal determined the blood glucose levels of normal and diabetic rabbits after oral administration of various doses of *Achyranthes aspera* extracts. The water and methanol extracts decreased blood glucose levels in normal and diabetic rabbits. Acute toxicity study did not reveal any adverse effects.

Manjunatha.[21] *etal.,* showed that the animal group treated with ethanol extract of *A. aspera* inhibited the increase in serum levels reflecting the liver protection by crude drug.

Anil Mangal and Mahesh Chandra Sharma.[24] reported that the powder of *Achyranthes aspera* stem is found to be effective in the treat.ment of obesity.

Malarvili *etal.,*.[25] reported the effect of *Achyranthes aspera* seeds on the metabolic parameters of fructose fed rats concluded that administration of *A. aspera* regulated the body weight and lipid profile.

Table: 1 Studies Considering the Antiobesity Efficacy and Safety of *Achyranthes aspera* and *Cissus quadrangular.*

S.No	Author	Title of the paper	Work	Major findings
1	Shil C. Kothari etal ., 2011	Safety assessment of *Cissus quadrangularis* extract (CQR-300): Subchronic toxicity and mutagenicity studies	In the subchronic study, Sprague Dawley rats (20/sex/group) were administered (gavage) *C. quadrangularis* extract (CQR-300) at dose levels of 0, 100, 1000, and 2500 mg/kg body weight (bw)/day for 90 days.	**No treatment related** clinical signs of abnormalities**, toxicity or mortality** were noted. Mutagenicity studies reveals non genotoxicity of CQR-300. Subchronic study shows the no-observed-adverse-effect for CQR-300 highest dose tested 2500 mg/kg bw/day.
2	Jiji *et al*. 2009	Antilipidemic activity of *Cissus quadrangularis* and *Tribulus terrestris* on obesity in high fat fed rats	Study was designed to investigate the comparative effect of ethanol extract of ***Cissus quadrangularis*** and *Tribulus terrestris* on lipid profile in rats. Plant extract was orally administered to high fat fed	Antihyperlipidemic effect was shown against high fat fed rats. The normal histopathology was reported.
3	Hasani *etal*, 2009	A systematic review of the efficacy and safety of herbal medicines used in the treatment of obesity	A Review has been made to focus on the efficacy and safety of effective herbal medicines in the management of obesity in humans and animals. 915 results were identified and reviewed, and a total of 77 studies were included (19 human and 58 animal studies).	A significant decrease in body weight and **No adverse effects** or **mortality** was reported in the case of treatment with *C. quadrangularis*
4	Shamina & Gokilavani 2012	Effect of serum biochemical markers and Haematological values in sub-acute toxicity study of C*issus quadrangularis* (stem)	Toxicological studies of aqueous extract of *Cissus quadrangularis* were conducted in female albino rats.	Results suggested that the **plant extract may be safe. No mortality** reported.
5	Aimmanas A. *etal*., 2002	Subchronic Toxicity of C*issus quadrangularis* Linn.	Toxicity study was conducted to evaluate the subchronic toxicity of *C. quadrangularis* powder in five groups of 12 wistar rats of each sex.	No **toxicity** reported in the rats during the administration period of 3 months.
6	Julius Oben et. al.,2008	The use of a *Cissus quadrangularis/Irvingia gabonensis*	To evaluate the effects of two formulations, *Cissus quadrangularis*-	***C. quadrangularis***-only group showed significant reduction ***C. quadrangularis*** and *Irvingia gabonensis* combination

		combination in the management of weight loss: a double-blind placebo controlled study	only and a *Cissus quadrangularis/Irvingia gabonensis* combination, on weight loss in overweight and obese human subjects.	resulted in even larger reductions.
7	Julius Oben et. al.,2006	The use of a *Cissus quadrangularis* formulation in the management of weight loss and metabolic syndrome	Study was designed to investigate the use of a *Cissus quadrangularis* formulation in the management of metabolic syndrome, particularly weight loss and central obesity on weight loss in overweight and obese human subjects.	Significant net reductions in weight, central obesity, blood glucose, TC, LDL, Tg, were observed after treatment.
8	Julius Oben et. al., 2007	The effect of *Cissus quadrangularis* (CQR-300) and a *Cissus* formulation (CORE) on obesity and obesity-induced oxidative stress	Study was to compare the effect of a proprietary extract of *Cissus quadrangularis* (CQR-300 =300 mg daily) to that of a proprietary formulation containing CQR-300 (CORE=1028 mg daily)) on weight, blood lipids, and oxidative stress in overweight and obese people.	CQR-300 and CORE did significant weight reductions. The increase in plasma 5-HT & creatinine was also reported which may linked to controlling appetite and weight loss effect.
9	Chidambaram and Venkatraman 2010	*Cissus quadrangularis* stem alleviates insulin resistance, oxidative injury and fatty liver disease in rats fed high fat plus fructose diet	The study evaluated the protective effects of *Cissus quadrangularis* stem extract (CQEt) on oxidant-antioxidant balance and insulin resistance (IR) in rats fed high fat-high fructose diet (HFFD) and also tested its free-radical scavenging property *in vitro*	CQEt addition improved insulin sensitivity, reduced liver damage, oxidative changes, and brought back the antioxidants and lipids towards normal.
10	Rathinam Prema *etal.*, 2012	Acute and chronic toxicity studies on combined extract of *Cissus quadrangularis* and *Aegle marmelos*	The study evaluated the safety of combined ethyl acetate extract of *C. quadrangularis* and *A. marmelos* (c-EACQAM) and combined ethanol extract of *C. quadrangularis* and *A. marmelos* (c-ECQAM) by determining its toxicity after acute and chronic administration in	safe dose= 2000mg/kg body weight (in acute toxicity study) In the chronic toxicity study result suggested that the c-EACQAM and c-ECQAM does not produce significant toxicity.

			albino rats.	
11	G. Geetha *etal.*, 2008	Hypolipidemic activity of *Achyranthes rubrofusca* linn. whole plant extracts in high fat diet induced hyperlipidemic rats	Study was aimed to evaluate the effect of ethanol and aqueous extract from whole plant of *Achyranthes rubrofusca* in high fat fed rats.	Ethanol extract at the dose 300mg/kg body weight of *A. rubrofusca* possesses significant hypolipidemic activity in high fat fed rats.
12	Laxmi marotia *etal.*, 2011	Study on the effect of methanol extract of Alkaloid rich fraction of Seeds of *Achyranthes aspera* Linn. on Rats	Study was aimed to investigate the effect of Methanol extract of alkaloid rich fraction of seeds of *Achyranthes aspera* on body weight, food intake, body temperature and serum lipids and glucose levels in rats.	Significant reduction in body weight, blood glucose and cholesterol levels. **No toxicity** and **Mortality** was observed
13	Muhammad Shoaib Akhtar, and Javed Iqbal 1991	Evaluation of the hypoglycaemic effect of *Achyranthes aspera* in normal and alloxan-diabetic rabbits	Blood glucose levels of normal and alloxan diabetic rabbits were determined after oral administration of various doses of *Achyranthes aspera* powdered whole plant and certain aqueous and methanolic extracts.	Hypoglycaemic effect in normal as well as in diabetic rabbits. Acute toxicity study **did not reveal any adverse** or **side effects**
14	Manjunatha *etal.*, 2012	Hepatoprotective Potency of *Achyranthes aspera*: An In-vivo Study	Ethanolic extract of *Achyranthes aspera* seeds was studied for its hepatoprotective potential by CCl_4 induced liver damage model in rats.	*A. aspera* (100mg/kg) inhibited the increase in serum levels reflecting **the liver protection by crude drug**.
15	Neerja Rani *etal.*, 2012	Assessment of anti-obesity potential of *Achyranthes aspera* Linn. seed	Antiobesity effect of ethanol extract of *A. aspera* seed (EAA) by employing *in vitro* and *in vivo* models.	EAA significantly suppressed the increase in body. **no observed pathological lesions**.
16	B. Pushpa Latha *etal.*, 2011	Effect of saponin rich extract of *Achyranthes aspera* on high fat diet fed male wistar rats	Anti-obesity effect of saponin rich extract of *Achyranthes aspera* on male wistar rats after feeding them for eight weeks with high fat diet was studied.	Treatment reduces excess accumulation of body fat and changing the lipid profile in blood.
17	Anil Mangal & Mahesh Chandra Sharma 2008	Evaluation of certain medicinal plants for antiobesity properties	A compound herbal drug powder *Obeloss* was prepared having one part each of ***Achyranthes aspera* (Apamarga)**, *Clerodendrum, Garcinia*	The compound herbal powder *Obeloss* was found to be effective in the treatment of obesity.

			and *Cyperus* was clinically tested on 60 patients.	
18	Malarvili *etal.*, 2011	Effect of *Achyranthes aspera* seeds on lipid profiles in selected tissues of rats fed with high doses of fructose	This study reports the effect of *Achyranthes aspera* seeds on the metabolic parameters (body weight, lipid profile in liver, kidney serum, HMG-CoA, lipase) of fructose fed rats.	Treatment with 100 mg/kg body weight of *A. aspera* twice daily for 3 weeks substantially reversed the above changes in a significant manner.
19	Sadashiv and Krishna 2011	Acute toxicity study for *Achyranthes aspera* leaves	Research work was to examine acute toxicity studies for the leaves powder and extract of *A.* in swiss mice weighing 35 to 45 gm.	There was **no abnormality** or toxicity observed in all groups.
20	Dr. Vimla Dunkwal and Indu Arora 2008	**Apamarg (*Achyranthes aspera*) as weight reducing agent**. Research work Thesis., Department of food and nutrition, College of Home science, Swami Keshwanand Rajasthan Agricultural University (SKRAU), Bikaner	Study was designed to investigate the use of edibles, nutraseuticals and tea of ***Achyranthes aspera*** in the management of metabolic syndrome, particularly weight loss and central obesity on weight loss in overweight and obese human subjects.	Studies with ***Achyranthes aspera*** showed a significant decrease in body weight. **No significant adverse effects** compared to controls were mentioned and **no mortality** was reported
21	Dr. S. Krishnakumari 2006	**Hypolipidemic Efficacy of *Achyranthes aspera* on Lipid Profile in Sesame oil fed Rats**	Research work was to evaluate the antihyperlipidemic effect of aqueous extract of *Achyranthes aspera* in rats fed with diet containing sesame oil.	Study unveiled the antihyper -lipidemic activity of *Achyranthes aspera*.

Sadashiv and Krishna.[26] examined acute toxicity studies for the extract and leaves powder of *Achyranthes aspera* in swiss mice There was no abnormality observed in all groups. The leaves powder and extract both were found to be nontoxic.

Dr. Vimla Dunkwal and Indu Arora.[27] investigated the use of edibles, nutraseuticals and tea of *Achyranthes aspera* seed powder in the management of metabolic syndrome particularly weight loss and central obesity on weight loss in human subjects. No significant adverse effects and no mortality was reported.

Krishnakumari S & Priya K.[28] evaluated the antihyperlipidemic effect of aqueous extract of *Achyranthes aspera* in experimental rats. This study unveiled the antihyperlipidemic activity of *A. aspera*.

DISCUSSION

Any pharmacological treatment should be administered only when considered safe and effective for subjects. This fact is also applicable in regard to obesity treatment. Only few drugs are available for the treatment of obesity, and some drugs have been withdrawn from the market due to serious side-effects. The need exists for anti-obesity drugs having greater effectiveness, which are better tolerated. Ideally, such type of review and further research will lead to a safer and more effective pharmacological treatment for obesity.

CONCLUSION

A good number of literature was found in the favor of anti obesity properties of *Achyranthes aspera* and *Cissus quadrangularis.* According to literature crude extracts and isolated compounds from these plants, can induce body weight reduction in safe manner. Present review summarizes the possible potential of *A. aspera* and *C. quadrangularis* to treat obesity. These plants may provide an excellent alternative approach for the development of safe and effective herbal drug against obesity.

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