

A REVIEW OF PRE-CLINICAL STUDIES ON OBESITY MARKERS USING AYURVEDIC MEDICINAL PLANTS

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ABSTRACT

Obesity is the most prevalent problem among all age group & population worldwide which is associated with increased mortality & morbidity rate. Disappointing results were seen after cessation of lifestyle modification & pharmacotherapy. This has established need for some non-invasive & safer treatment modalities. Ayurveda has given enough focus on obesity (*Sthaulya*) & its related complications. In last 2 decades many researches has been done to assess anti-obesity potential of Ayurvedic medicinal plants. As compared to human studies pre-clinical studies gives quantitatively more accurate & faster results. They contribute to the first level of evidence in the clinical applications of Ayurvedic Plants. These studies allows easy monitoring

under strict and controlled conditions and interventions. A review about efficacy of herbal medicines in the management of obesity in pre-clinical trials was carried out by searching bibliographic data bases such as, PubMed, Scopus and Google Scholar. In this paper we have reviewed pre-clinical anti-obesity studies reported during January 2000 to December 2020. We particularly reviewed anti-obesity potential of 25 Ayurvedic medicinal plants. Critical review of action of these plants on obesity markers is reviewed & summarised in this article, which will help readers to understand the mode of action of Ayurvedic plants on obesity.

KEYWORDS: Pre-clinical anti-obesity studies, Ayurvedic medicinal plants, immunomodulators (Pro-inflammatory & anti-inflammatory cytokines, hypolipidemic agents.

INTRODUCTION

Obesity is an inflammatory state, referred as subclinical chronic mild inflammation of adipocytes. It is multifactorial & most prevalent problem among all age group & population worldwide. It is associated with alarming increase in mortality & morbidity rate related to metabolic syndrome, stroke, congestive heart diseases & DM-type 2.^[1] Fat tissues are mainly comprised of adipocytes & its physio-anatomical details have provided answers to lot of questions for better understanding of complex pathophysiology of obesity. In obesity with increase in appetite & food consumption along with down regulation of calorie utilization, there is excessive fat accumulation, which results in hypertrophy & hyperplasia of adipocytes. This leads to increased production of free fatty acids & release of pro inflammatory cytokines along with leptin & ghrelin.

Disappointing results were seen after cessation of lifestyle modification or pharmacotherapy used in treatment of obesity. This has established need for other simple treatment modalities which are more acceptable to patients & have least side effects. In modern pharmaceuticals most of anti-obesity drugs are found to be inconsistently effective & are having side effects also. Therefore, in recent decades as an alternative form of medicines, vast range of crude extracts & their isolated compounds from Ayurvedic herbal plants are being used in treatment & prevention of obesity.

Ayurveda text gives detailed instruction on proper balanced diet as well as on appropriate daily & seasonal regimen as per constitution of person. In Ayurveda, *Acharya Charaka* has included obese person (*Sthool*) among most difficult to treat patients. Ayurveda texts provides a wide spectrum of herbal plants & other treatment modalities for obesity. Considering these facts we found need to review pre-clinical anti-obesity studies on Ayurvedic herbal medicinal plants.

Ways of conducting anti-obesity studies are clinical trials, preclinical studies (in-vitro & in-vivo). For this review we are keen about anti-obesity markers used in pre-clinical setup. As pre-clinical studies gives quantitatively more accurate and faster results. These studies allows easy monitoring under strict and controlled conditions and interventions.

In recent years, increasing number of in-vitro anti-obesity studies on Ayurvedic herbal plants are being conducted, so we reviewed this topic with special focus on parameters used for

these studies. Furthermore, materials and methods used in pre-clinical anti-obesity studies were also reviewed.

MATERIALS AND METHODS

A review of Anti-obesity effect of different Ayurvedic medicinal plants in-vitro & in-vivo studies, was carried out by searching bibliographic databases such as PubMed, Google scholar. The studies reported between Jan 2000 to Dec 2021 were considered for review.

Search terms were Pre-clinical Anti-obesity studies AND Ayurvedic herbal medicinal plants/ immuno-modulators (pro-inflammatory & anti-inflammatory cytokines, hypolipidemic agents. Available abstracts or full articles of publications were reviewed. All animal studies conducted on herbal medicines plants or their extract on markers of obesity & hyperlipidaemia were included.

Different markers used in pre-clinical anti-obesity studies starting from Anthropometrical markers to immunomodulatory markers are as follows.

• MARKERS FOR OBESITY

A) Physical markers

1. Weight gain
2. Food consumption
3. Energy expenditure
4. Abdominal circumference (AC)
5. Body mass index (BMI)
6. Fat mass

B) Bio-Chemical

1. Lipid profile
2. Inhibition of pancreatic enzymes activity.
3. Fasting blood sugar levels

C) Immunomodulators

- 1) Adiponectin
- 2) Leptin
- 3) Interleukin-6

D) Inflammatory cytokines**a) Pro-inflammatory cytokines**

- 1) Interleukin-1 β ,
- 2) Interleukin-6,
- 3) Interleukin-10,
- 4) TNF- α

b) Anti-inflammatory cytokines

- 1) Interleukin-4
- 2) Interleukin-10

Adipocytes are comprised of BAT (Brown adipose tissue) & WAT (White adipose tissue), of which WAT tissues are main site for calorie storage as triglycerides & is main site of inflammation in obesity. It also secretes immunomodulators (Adiponectin, Leptin, Resistin, and Ghrelin), Pro-inflammatory cytokines (IL-1 β , IL-6, IL-10, and TNF- α) & Anti-inflammatory cytokines (IL-4 and IL-10).

RESULTS

Ayurveda texts has given number of anti-obesity drugs & treatment modalities considering constitution (*Prakruti*) of each person. Complex pathophysiology of obesity has provided many assessment parameters right from weight up to immunomodulatory markers. There are some studies which mainly focussed on adipocyte differentiation as adipocytes are main site for fat deposition. Furthermore, different animal models are used for anti-obesity studies as per assessment parameters. *Wistar* albino rats, *Sprague Dawley* rat, *Zucker* rats, TSOD mice are commonly used for anti-obesity studies. 3T3 adipocytes are used for in-vitro studies of adipocyte differentiation. In last two decades many studies were conducted to assess anti-obesity potential of Ayurvedic medicinal plants and herbal plants. In this review we considered only pre-clinical anti-obesity studies.

Physical marker: (Table no 1)

Extracts of *Piper nigrum*, *Ziziphus jujube*, *Nelumbo nucifera*, *Asparagus officinale*, *Cyprus rotundus*, and *Piper longum* significantly reduced body weight, fat mass index. Along with it these plants also increased insulin sensitivity & improved abnormal glucose metabolism. Among these *Piper longum* reduced total body weight by 12-15%. *Cyprus rotundus* reduced body weight without altering food consumption.

Table no.1: Anti-obesity studies using physical markers.

Sr. No.	Plant used	Author	Method used for obesity induction	Rodent Used	Marker used	Result
1.	<i>Piper nigrum</i> ^[2] (<i>Lavanga</i>)	Parim B Et al	High fat diet	Sprague-Dawley rats	Body weight(gm), Total fat %, Fat free mass %	Reduction of all markers.
2.	<i>Salicia Reticulate</i> ^[3] (<i>Saptchakra</i>)	Tsutomu S et al	High fructose, High fat diet	TSOD mice	Body weight(gm)	Reduction
3.	<i>Ziziphus Jujube</i> ^[4] (<i>Badar</i>)	Ghanachari M S & Kumar S	High sucrose diet	Wistar rats	Body weight(gm)	Reduction
4.	<i>Nelumbo Nucifera</i> ^[5] (<i>Kamala</i>)	Huan D et al	High fat diet	Wistar Rats	Body weight(gm)	Reduction
5.	<i>Cyprus rotundus</i> ^[6] (<i>Musta</i>)	Lemaure B	High fat diet	Wistar rats	Body Weight(gm)	Reduction
6.	<i>Asparagus Officinale</i> ^[7] (<i>Shatavari</i>)	Zhu X et al	High fat diet	Wistar rats	Body Weight(gm)	Reduction
7.	<i>Piper longum</i> ^[8] (<i>Pippali</i>)	Sharma S S et al	High cholesterol diet	Albino rats	Body weight(gm)	Reduction

Lipid profile: (Table no. 2)

Extract of *Gymnema sylvestre*, *Asparagus officinale*, *Picrorrhiza kurro*, *Ocimum sanctum*, *Piper longum* & its derivative GB-N significantly reduced levels of serum LDL, VLDL, cholesterol & triglyceride along with significant increase in serum HDL levels. Whereas extracts of *Nelumbo nucifera*, *Areca catechu*, *Acorus calamus*, *Apium graveolans*, *Achyranthus aspera*, *Phyllanthus niruri*, *Curcuma longa*, *Nordostachys jatamansi* & *Pterocarpus marsupium* only reduced levels of serum LDL, VLDL, cholesterol & triglyceride levels without any effect on serum HDL levels.

Table no.2: Anti-obesity studies on lipid profile.

Sr. No.	Plant used	Author	Method used for obesity induction	Rodent Used	Marker used (mg/dl)	Result
1.	<i>Piper longum</i> ^[9] (<i>Pippali</i>)	Bao L et al	High fat diet	Albino rats	TG, Total CH, LDL, HDL	Dose dependent reduction in TG, Total CH, LDL, Increase in HDL
2.	<i>Asparagus Officinale</i> ^[7] (<i>Shatavari</i>)	Zhu X et al	High fat diet	Wistar Rats	Total cholesterol, LDL, HDL	Reduction in total cholesterol & LDL. Increase in HDL
3.	<i>Picrorrhiza kurro</i> ^[10]	Hyeung et Al	High cholesterol diet	Wistar Rats	LDL, Total CH.	Reduction In LDL, Total CH. &

	(Kutaki)				TG	TG
4.	<i>Gymnema Sylvestre</i> ^[11] (Meshashrungi)	Kumar V et al	High fat diet	Wistar Rats	Sr lipids HDL	Reduction in sr. lipids & increase in HDL levels
5.	<i>Ocimum Sanctm</i> ^[12] (Tulasi)	Sarkar A et al	High fat diet	Albino Rats	Sr.CH, TG,LDL & HDL	Reduction in sr.CH,TG,LDL Levels. Increase in HDL levels
6.	<i>Nelumbo Nucifera</i> ^[5] (Kamala)	Huan D et al	High fat diet	Wistar Rats	Total CH., LDL, TG	Reduction in all markers
7	<i>Areca catechu</i> ^[13] (Puga)	Byun S J	High cholesterol diet	Wistar Rats	Absorption of TG	Reduction in absorption of TG
8	<i>Acorus calamus</i> ^[14] (Vacha)	Parab R S	High fat diet	Wistar Rats	LDL, TG	Dose dependent hypolipidemic activity
9	<i>Apium graveolans</i> ^[15] (Ajamoda)	Tsi et al	High fat diet	Wistar rats	Sr. total CH,LDL,TG	Reduction in all markers
10	<i>Achyranthes aspera</i> ^[16] (Apamarg)	Khanna A K et al	Triton induced Hyperlipi-demia	Wistar Rats	Sr. total CH, TG	Reduction in all markers
11	<i>Phyllanthus Niruri</i> ^[17] (Bhumi-amalaki)	Khanna et al	High Choleste-rol diet	Wistar Rats	LDL, VLDL	Reduction in all markers
12	<i>Curcuma longa</i> ^[18] (Haridra)	Dixit V P et al	Triton Induced Hyperlip-idemia	Wistar Rats	Sr.total CH, TG	Reduction in all markers
13	<i>Nordistacys Jatamansi</i> ^[18] (Jatamansi)	Dixit V P et al	Triton Induced Hyperlip-idemia	Wistar rats	Sr.total CH, TG	Reduction in all markers
14	<i>Pterocarpus Marsupium</i> ^[19] (Beejak)	Jahromi M A & Ray A B	High fat diet	Wistar Rats	LDL, VLDL, TG & Sr.total CH	Reduction in all markers

(Abbreviations- CH- Cholesterol, TG- Triglyceride, LDL- low density lipoprotein, VLDL- very low density lipoprotein, HDL- high density lipoprotein, Sr- serum)

Immunomodulators of obesity: (Table no.3)

There are very few pre-clinical studies which assess effect of Ayurvedic medicinal plants on immunomodulators of obesity. *Piper nigrum* significantly reduced Leptin levels & increased Adiponectin levels. In addition to hypolipidemic effect *Gymnema sylvestre* also downregulated leptin levels. *Terminalia bellerica*, *Salicia reticulate* & 4-herbs formula containing, *Crataegus Fructus*, *Schisandrae Fructus*, milk thistle & *Momordica chirantica*

were found to increase Adiponectin level. Extract of leaves of *Carica papaya* significantly reduced IL-6 levels.

Table no. 3: Preclinical anti-obesity studies using Ayurvedic herbal medicines on immunomodulatory markers.

Sr. No.	Plants used	Author	Method used for obesity induction	Rodent used	Marker used (ng/ml)	Result
1.	<i>Piper nigrum</i> ^[2] (Lavang)	Parim B et al	High fat Diet	Sprague-Dawley Rat	Leptin, Adiponectin	Decrease in leptin levels & increase in Adiponectin levels.
2.	<i>Gymnema Sylvestre</i> ^[11] (Meshashrunji)	Kumar V et al	High fat diet	Wistar Rat	Leptin	Decrease in Leptin levels
3.	<i>Terminalia bellerica</i> ^[20] (Bhibhitaka)	Makihara H et al	High fructose, High fat diet	TSOD mice	Adiponectin	Increased
4.	<i>Salicia reticulata</i> ^[3] (Saptachakra)	Tsutomu S	High fructose, High fat diet	TSOD mice	Adiponectin	Increased
5.	4-Herb formula ^[21] (<i>Crataegus Fructus</i> , <i>Schisandrae Fructus</i> , milk thistle & <i>Momordica chirantica</i>)	Wat E et al	High fat diet	Wistar rats	Adiponectin	Increased
6	<i>Carica papaya</i> ^[22] (Erاندkarkati)	Phicitra O.	High fat diet	Wistar rats	Interleukin-6	Decreased

Pancreatic lipase inhibition:_(Table no.4)

Extracts like *Piper nigrum*, *Terminalia bellerica*, *Oroxylum indicum* were found to possess pancreatic lipase inhibitory activity. In addition to It *Oroxylum indicum* also had anti-adipogenesis activity.

Table no.4: Pre-clinical anti-obesity studies on Digestive enzyme activity.

Sr. No.	Plant used	Author	Method used for obesity induction	Rodent used	Marker used	Result
1.	<i>Piper nigrum</i> ^[2] (Lavang)	Parim B et al	High fat diet	Sprague-Dawly rat	Pancreatic Lipase	Inhibition
2.	<i>Terminalia Bellerica</i> ^[21] (Bhibhitaka)	Makihara H Et al	High fructose, High fat diet	TSOD mice	Pancreatic Lipase	Inhibition
3	<i>Oroxylum indicum</i> ^[23] (Shyonak)	Mangal P et al	High fat diet	Wistar rats	Pancreatic lipase	Inhibition

3T3-Adipocyte lipolysis

Extract of *Cyprus rotundas*^[6] (*Musta*) & *Crategus fructus*^[21] induced 3T3- Adipocyte lipolysis.

DISCUSSION

Many studies reported anti-obesity potential of different Ayurvedic herbal medicinal plants. Among the studies reviewed, plants possessing anti-obesity effects are summarized in above 4 tables. These plants are generally of *Katu-tikta rasa*, *Laghu*, *Ruksha* & *Tikshna* properties.^[24] Only few of them belongs to *Lekhaniya gana*^[25] described by *Acharya Charaka* which are *Cyprus rotundus*, *Acorus calamus* & *Curcuma longa*. However some plants like *Asparagus officinale*, *Ziziphus jujube*, *Areca catechu* & *Nelumbo nucifera*, besides being *snigdha*, *guru* possess lipid lowering & anti-obesity effect. *Nordostachys jatamansi* can used in stress induced pathology. *Piper longum* & *Achyranthes aspera* are having significant weight reducing & lipid lowering effect.

Anti-obesity effect in terms of weight reduction is seen in almost all studies. Though only weight reducing properties are not evident enough in proving anti-obesity potential of Ayurvedic herbal plants. Some studies shows significant decrease in serum lipids, only few of them showed reduction in serum lipids along with increase in high density lipoprotein. However there are very few studies which assess anti-obesity potentials of Ayurvedic herbal plants on immunomodulatory markers of obesity such as pro-inflammatory & anti-inflammatory cytokines. Whereas Ayurveda texts has given wide range of drugs for treating obesity. Most of reviewed studies has given qualitative analysis reports regarding effect of Ayurvedic herbal medicines in obesity. Furthermore there is a significant need for non-invasive treatment option to bridge gap between lifestyle modifications & surgical interventions.

CONCLUSION

Ayurvedic plants have tremendous potential to be used in regimen of obesity treatment. They have many fold anti-obesity actions, which needs to be evaluated on molecular levels. There is a need of an hour for Ayurvedic doctors to conduct studies on Anti-obesity potential of different Ayurvedic plant to establish Ayurvedic herbal plant remedy as main line pharmacotherapy not as alternative medicines. At the same time well-designed pre-clinical trials are still needed to focus on both safety and efficacy of Ayurvedic herbal medicinal plants.

REFERENCES

1. Expert panel on the identification, evaluation, and treatment of overweight in adults: Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: executive summary. *Am J Clin Nutr.*, 1998; 68: 899–917; 4.
2. Parim B. et al; Effects of *Piper nigrum* extracts: Restorative perspectives of High fat diet-induced changes on lipid profile, body composition, and hormones in Sprague–Dawley rats, *Pharmaceutical Biology*, 53(9): 1318-1328.
3. B.Makhihara H et al; Gallic Acid, the Active Ingredient of *Terminalia bellirica*, Enhances Adipocyte Differentiation and Adiponectin Secretion; *Biol Pharm Bull*, 2016; 39(7): 1137-43. doi: 10.1248/bpb.b16-00064.
4. Tsutomu shimada et al; *Salacia reticulata* has therapeutic effects on obesity; *Journal of natural medicine*, 2014; 68: 668-676.
5. Ghanachari M.S. & kumar S; Effect of *Ziziphus jujuba* leaf extract on body weight, food intake & lipid levels in sucrose induced obese Rats; *Indian Journal of Pharmaceutical sciences*, 2004.
6. Huan D et al; Antiobesity and hypolipidemic effects of lotus leaf hot water extract with taurine supplementation in rats fed a high fat diet; *Journal of Biomedical sciences*, Aug 24, 2010; 17(1): S42. doi: 10.1186/1423-0127-17-S1-S42.
7. Lemaure B et al; Administration of *Cyperus rotundus* tubers extract prevents weight gain in obese Zucker rats; *Phytotherapy Research*, Aug, 2007; 21(8): 724-30.
8. Zhu X et al; Hypolipidaemic and hepatoprotective effects of ethanolic and aqueous extracts from *Asparagus officinalis* L. by-products in mice fed a high-fat diet. *Journal of the Science of Food and Agriculture*, 01 May, 2010; 90(7): 1129-1135.
9. Sharma S S et al; Effect of piperine in the regulation of obesity-induced dyslipidemia in high-fat diet rats; *Indian J Pharmacol*, May-Jun, 2011; 43(3): 296–299.
10. Bao L et al; Hypolipidemic effects of a new piperine derivative GB-N from *Piper longum* in high-fat diet-fed rats; *Journal of pharmaceutical sciences*, 2012; 50: 8.
11. Hyeung S et al; Hypolipidemic effect of water extracts of *Picrorrhiza kurroa* in high fat diet treated mouse; *Fitoterapia*, December 2006; 77(7–8): 579-584.
12. Kumar V et al; Anti-obesity Effect of *Gymnema sylvestre* Extract on High Fat Diet-induced Obesity in Wistar Rats; *Drug Res (Stuttg)*, 2013; 63(12): 625-632.
13. Sarkar A. et al; Changes in blood lipid profile after administration of *Ocimum sanctum* leaves in normal albino rats; *Indian Journal of Physiology & Pharmacology*, 1994; 38(4): 311-312.

14. Buyn S.J. et al; Supplementation of *Areca catechu L.* Extract Alters Triglyceride Absorption and Cholesterol Metabolism in Rats; *Annals of Nutrition & Metabolism*, 2001; 45(6): 279-284.
15. Parab R.S.; Hypolipidemic activity of *Acorus calamus L.* in rats; *Fitoterapia*, October 2002; 73(6): 451-455.
16. Tsi D et al; Effect of aqueous celery (*Apium graveolens*) extract on lipid parameters of rats fed a high fat diet; *Planta Med.*, 1995; 61(1): 18-21.
17. Khanna A.K. et al; Hypolipidemic activity of *Achyranthus aspera* in normal & triton induced hyperlipidemic rats; *Indian journal of Exp Biol.*, 1992; 30(2): 128-130.
18. Khanna A.K. et al; Lipid lowering activity of *Phyllanthus niruri* in hyperlipemic rats; *J Ethnopharmacol*, 2002; 82(1): 19-22.
19. Dixit V.P. et al; Hypolipidemic effects of *Curcuma longa* & *Nardostachys jatamansi* in triton-induced hyperlipidaemic rats; *Indian Journal of Physiology Pharmacology*, 1991; 32(4): 299-304.
20. Jahromi M.A. & Ray A.B.; Anti-hyperlipidaemic effect of flavonoids from *Pterocarpus marsupium*; *J Nat Prod*, 1993; 56(7): 989-994.
21. Makihara M. et al; Preventive effect of *Terminalia bellirica* on obesity and metabolic disorders in spontaneously obese type 2 diabetic model mice; *Journal of natural medicine*, 66: 459-467.
22. Wat E. et al; An in vitro and in vivo study of a 4-herb formula on the management of diet-induced metabolic syndrome; *Phytomedicine*, Mar 15, 2018; 42: 112-125.
23. Picitra et al; Anti- obesity effect of *Carica papaya* in high- fat diet fed rats; *Biomed Rep.*, 2020; 13: 30.
24. Mangal P. et al; Screening of six Ayurvedic medicinal plants for anti-obesity potential: An investigation on bioactive constituents from *Oroxylum*; *Journal of Ethnopharmacology*, 2 February, 2017; 197: 138-146.
25. Bhavprakash nighantu by Krushnachandra Chunekar; Chaukhamba Bharati Prakashan; Varanasi, 2010.
26. Charak samhita; Kashinath Pandey & Gorakhnath chaturvedi; Chaukhamba Bharati Prakashan; Varanasi, 2011; 4: 11.