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Review Article

ROLE OF *TRIPHALA* ON GUT MICROBIOTA IN THE TREATMENT OF OBESITY AND ITS COMPLICATIONS

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ABSTRACT

Obesity is a rapidly increasing global public health concern with a prevalence of 40.3% in India. This review investigates the potential role of *Triphala* in the treatment of obesity and its complications on gut microbiota. Method: We selected relevant articles after searching Scopus, PubMed and Google Scholar using keywords *Triphala*, Obesity, DM, CVD, and Gut microbiota. Obesity and related complications are considered by definite changes within the human gut microbiome. The gut microbiota of individuals with obesity contains lower proportions of *Bacteroidetes* and greater amounts of *Firmicutes*. Gut microbiota modulation and revitalization are emerging as potential obesity prevention and/or treatment strategies via probiotics, prebiotics, synbiotics, or faecal transplants. Research showed that butyrate generating bacteria like *Faecalibacterium prausnitzii* and *Akkermansia muciniphila*, were greatest in normal people, but that *Bacteroides* were halved in diabetes patients. The host metabolic syndrome and cardiovascular risk may be influenced by lipopolysaccharides (LPS) from gut microbiota. A placebo-controlled trial concluded that *Triphala* includes a hopeful role in reducing weight, circumferential measures and body fat. *Triphala*'s prebiotic effect was studied using in vitro batch cultures, fruit fly, and a simulated model of the human alimentary tract, where *Triphala* promoted the growth of good bacteria while inhibiting pathogenic species in each model. Clinical research is still under progress on the effect of *Triphala* on Stool Microbiome Profiles and Inflammation. The action of *Triphala* in altering the gut microbiota for effective management of obesity and its complications is yet to be studied. Here we recommend the potential action of *Triphala* in managing obesity and its complications by targeting gut microbiota.

INTRODUCTION

Obesity is defined as an increase in the body's fat cell size and number. Obesity is a major risk factor for diseases like cardiac diseases, diabetes mellitus, OA, cancers and stroke. Obesity is estimated to be responsible for 5% of all worldwide mortality. South Asia has one of the world's fastest-rising obesity rates and assessed that 135 million people in India are suffering from obesity.[1]

As per the Indian National Family Health Survey, obesity increased over a 10-year period. Obesity among females and males of 15 to 49 years increased from 13% to 21% and 9.3% to 19% respectively over the same time period.[2] Obesity and its complications are caused by a wide range of mechanisms and the role of the microbiome is getting more attention in the development of obesity-related complications. Gut microbes influence metabolism of host via signalling pathways, influencing fat deposition, insulin resistance and inflammation. Obesity has been linked to significant microbial changes, according to research.[3]

Triphala is a powder made from the dried fruits of *Haritaki*, *Vibhitaki*, and *Amalaki*. *Triphala* is classified as *Tridosha shamaka* and also *Rasayana*. It is *Kapha Pittahara* and heals *Meha*, *Kushta*, and *Vishamajwara*. It helps to improve vision, digestion, and taste perception[4].

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Triphala specifically promotes general health and longevity while reducing accumulated excess fat.[5] It has antimicrobial properties[6], immunomodulatory properties[7] etc. This formulation is effective against cardiovascular disease, cancers, digestive disorders, hypertension, and a variety of other diseases.[8]

Triphala has a beneficial effect on gut microbiota as a prebiotic. It has been observed that the human gut microbiome can be modify with the help of polyphenols in *Triphala* and promotes the growth of beneficial bifidobacteria and lactobacillus and also inhibits the growth of pathogenic gut microorganisms.[9]

METHODS AND MATERIALS

Ayurvedic classics, published information from several articles, e-database viz., PubMed, Science Direct were assessed for literature search. The key words searched were *Triphala*, obesity, gut microbiota, prebiotic, probiotics.

RESULTS AND DISCUSSION

Gut Microbiota and Obesity

The gut microbiota contains a diverse community of microorganisms that benefit the host's health. Dysbiosis caused by age, diet, stress and antibiotic use contributes to diseases such as obesity, diabetes mellitus, cancer, IBS and neurodegeneration. According to recent research, a probiotic regimen combined with a prebiotic-rich diet may correct dysbiosis, improves health and wellness.[3]

Gut microbes have an important part in the extraction of energy from food. Many complex carbohydrates and plant polysaccharides are indigestible in the gut and good microbes can transform them to short chain fatty acids (SCFA) such as butyrate, acetate and propionate. Primary energy source for colonic epithelial cells is the butyrate. In the liver for lipogenesis and gluconeogenesis, propionate and acetate are needed.[10]

As per studies about germ-free mice, there is a connection between obesity and its complications with the gut microbiota. They have no microorganisms in their gut and they were raised in a sterilized environment. The conventionally raised mice even if they consume less food, have additional 40% body fat and 47% gonadal fat than germ-free mice. Besides that, transplantation of distal gut microbiota from normal mice to germ free mice, was observed that 60% gain in body fat within 2 weeks devoid of any increase in food intake, indicating that the relation between gut microbiota and its phenotypic characteristics with body mass in the host.[11]

Besides that, caloric intake was related increase in firmicutes and a decrease in bacteroidetes, which was directly proportional to increase in weight of body. Research findings have discovered that dysbiosis increases the firmicutes: bacteroidetes ratio in obese people. Factors such as diet, fasting, antibiotic use and energy content can affect gut microbial composition. More research is needed to know whether manipulating the gut microbiota will help to treat and/or prevent obesity.[12]

Dysbiosis and Obesity

Dysbiosis is defined as a microbiota imbalance. It is seen in obesity and a loss of microbiota diversity. There is a connection between the modification of the microbial pattern in the colon and the progressive increase in body weight. Specific nutrition, prebiotics, probiotics and synbiotics are effective approaches for the prevention of obesity.

Prevention of Obesity and Gut Microbiota

Particular changes in the gut microbiota may contribute to bariatric surgery's valuable effects on obesity. A study of gastric bypass surgery using a mouse model for to characterize changes in the gut microbiota, it showed significant and sustained changes in the gut microbiota that were irrespective of diet and the weight loss associated with this procedure, as mice was given a sham procedure and placed on a controlled diet.[13]

According to the findings, transplanted microbiota increased caloric release from dietary plant polysaccharides and altered host genes that affect energy deposition in adipocytes, such as fasting-induced adipocyte factor (Fiaf). It is required for microbiota-induced triglyceride deposition in adipocytes. These outcomes imply that the presence of a beneficial gut microorganisms sometimes influence the energy taken from the diet and the host's adiposity.[11] Obesity has been linked to microbiota changes, such as decreased microbial community and metabolic pathways.[14] Obese mice have a more intestinal firmicutes and less bacteroidetes and also a greater number of microbial genes involved in polysaccharide degradation.[12]

When germ-free mice were implanted with either the microbiota from obese or lean offspring, the microbiota from obese mice extracted more calories from their food and gained more total body fat than lean mice.[10] These findings indicates that differences in caloric intake efficiency from food can be decided by the microbiota and also the role of microbiota in the pathogenesis of obesity.[3] Differences in the faecal microbiota of 12 lean and 9 obese individuals during caloric content diets revealed that a change in nutrient load can cause rapid changes in the gut bacterial community.[15]

Microbiota targeting could lead to new possibilities for prevention or treatment of obesity and related disorders. Use of prebiotics, probiotics, or synbiotics, faecal microbial community transplantation are examples of these approaches.[3]

Probiotics and Obesity

Probiotics are good live microorganisms that can induce health benefits on the host.[16]

Administering multi-strain probiotics may be more beneficial than single-strain probiotics for preventing fat accumulation and metabolic disturbances in diet-induced obesity.[17] Mice fed with a high fat diet with supplementation of Lactobacillus rhamnosus NCDC 17 in fermented milk showed a significant decrease in body weight, fasting blood glucose, and serum insulin levels.[18]

Prebiotics and Obesity

A food ingredient that is a source of food for good microbes present in gut microbiota but ingestible by the host and can induce beneficial health effects on the host is called as prebiotic. The majority of the focus in this area has been on non-digestible oligosaccharides. Inulin, lactulose, and resistant starch are examples of common prebiotics. In general, all fermented dietary fibres are expected to have prebiotic effect. There are also commercially available dietary supplements containing fructo oligosaccharides, primarily inulin.[16]

In a placebo-controlled, double-blind study, intake of a prebiotic fibre like inulin was associated with a decrease in hunger and increased plasma GLP-1 compared to a placebo. The findings indicate that prebiotics can help regulate food intake.[19]

In a study, 12 volunteers were administered with inulin (10g/day) for 16 days with no other supplement intake, and bifidobacterium adolescentis increased from 0.89 to 3.9% of the total microbiota. As a result, consuming prebiotics can change the microbiota of the gut.[20]

Synbiotics and Obesity

The mixture of a probiotic and prebiotic is known as a "synbiotic".[22] Evidence suggests that synbiotics can influence the microbiota. For example, combination of an oligofructose enriched inulin (SYN1) with *lactobacillus rhammnosus GG* and *bifidobacterium lactis Bb12* for 12 weeks increased the amount of lactobacillus and *bifidobacterium* species while decreasing the numbers of *Clostridium perfringens*.[23] In vitro studies showed that synbiotics are better than prebiotics or probiotics for altering gut microflora.[24]

Gut microbiota and complications of obesity

It was discovered that in 16S rRNA gene sequencing, a leptin deficient obese mouse model has a lower abundance of the bacteroidetes phylum and increase in firmicutes levels.[12] The gut microbiota is diverse in healthy people than those with overweight, impaired insulin sensitivity and high cholesterol.

***Triphala* in Obesity**

RCT was done to observe the impact of *Triphala* in obesity in 30 obese patients divided into two equal groups who received *Triphala churna udhvartana* or *Triphaladi taila abhyanga* for 14 days. The symptoms were subjectively and objectively assessed in the patients before and after treatment. Both groups produced significant results, but *Triphaladi taila abhyanga* outperformed *Triphala churna udhvartana* in the management of *Sthaulya*.[21]

Triphala and its individual components were studied for a high fat diet caused (HFD) obesity and complications through a study with Swiss albino mice. The researchers discovered that mice fed an HFD for 10 weeks and supplemented with *Triphala* had noticeable decrease in body mass, energy consumption, and percentage body fat. *Triphala* also improved the lipid panel of the mice by lowering total blood cholesterol, TG and LDL while increasing HDL. The study also discovered that use of herbal treatment reduced blood sugar, oral glucose tolerance as measured by the OGTT, and ALT levels. Treatment with *Triphala* reduced the pathological changes in liver tissue and decreased the relative body fat in addition to its three individual components. From the current findings *Triphala* and its constituents can prevent the effects of high diet fat intake and can be used for anti-obesity treatment.[25]

***Triphala* in Complications of Obesity**

The effect of *Triphala churna* on diabetic neuropathy was studied in Streptozotocin-induced diabetic rats. It improved the motor nerve conduction velocity whereas decreasing thermal and mechanical hyperalgesia and mechanical allodynia. TGF-1, TNF-, and IL-1 levels were reduced by the treatment. A histopathology study confirmed *Triphala churna*'s neuroprotective effect. Western blotting analysis revealed that NGF expression was higher in sciatic nerves. According to the findings, *Triphala churna* slowed the development of neuropathy in diabetic rats.[26]

A network pharmacology and bioinformatics analysis were done which focused on CCVDs and action of *Triphala*. Network analysis identified 132 compounds in three individual herbal medicines. That were taken for ADME screening and 23 compounds and 65 genes forming the pathways linked to CCVDs. Furthermore, 10 compounds that have been connected to more than 3 genes. They have been identified as critical chemicals. In addition, cancer-related pathways, such as the TNF signalling pathway and neuroactive ligand-receptor interactions, were recognised. In vitro studies shown that, when compared to the control group, TNF- treatment increased the expression of PTGS2, MMP9, and IL6, whereas pre-treatment with *Triphala* significantly inhibited their expressions depending on a concentration-gradient. This uncovered some complex components and pharmacological mechanism of

Triphala, as well as some possible therapeutic targets of CCVDs, which could serve for the future research and development.[27]

A study with 32 patients who had elevated alanine transaminase combined with sonological evidence of fatty liver. They were divided into two groups who received *Pathya* alone or *Pathya* with medicines including *Triphala guggulu*. The 2nd group showed statistically significant improvement in clinical symptoms, biochemical parameters and body mass index.[28]

Triphala's anti-arthritic potential was investigated in wistar albino rats induced by intradermal injection of complete Freund's adjuvant. *Triphala* was administered intraperitoneally following arthritis induction. Arthritis induction increased the levels of reactive oxygen species, elastase, and mRNA expression of pro-inflammatory cytokines, inflammatory marker enzymes, receptor activator of nuclear factor kappa-B ligand, and transcription factors in the paw tissues of rats. The findings suggest that taking *Triphala* can help with bone and cartilage degradation in rheumatoid arthritis.[29]

Triphala in Gut Microbiota

A study was conducted using *Lactiplantibacillus plantarum, Lactobacillus fermentum*, and *Bifidobacteria infantis*, as well as polyphenol-rich, *Triphala*. The prebiotic action of *Triphala* was studied using in vitro batch cultures, drosophila melanogaster and a simulated model of the human gastrointestinal tract, in which *Triphala* promoted the growth of good bacteria while hindering growth of pathogenic species in each model. Interestingly, the probiotic and synbiotic formulations combined proved to increase motility, indicating the good variations in the gut microbiota.[30]

Another study is going on about the effects of *Triphala* and probiotic medical food VSL#3® on stool microbiome profiles and inflammation (TRIPH2017). Probiotics like VSL#3® and herbal supplements like *Triphala* have been linked to gut microbiota restoration, increased intestinal mucosal barrier function and reduced inflammation. The current study is going to look into the effects of a synbiotic (*Triphala* plus probiotic) intervention on gut microbiome profiles as measured by stool, inflammatory blood markers and questionnaires about GI health. The researchers will look at psychological and physical functioning at reference line and after 8 weeks of supplementation with synbiotic (*Triphala* and VSL#3®), only *Triphala*, or placebo.[31]

CONCLUSION

In the studies, the authors found human gut microbiota may have a potential role in obesity and its complications. To improve gut health, consume more foods high in polyphenols, and plant compounds that serve as food for the microbiome, increase bio absorption, and promote the growth of good bacteria. *Triphala* is a formulation with numerous therapeutic applications for maintaining body equilibrium as well as disease prevention and treatment. *Triphala* has been shown in recent studies to increase of good gut bacteria and inhibits the growth of harmful microorganisms. So, for correction of dysbiosis there is a need for novel therapeutical approaches. The efficacy of *Triphala* in maintaining healthy gut microbiota as well as its potential action in managing obesity and its complications is reviewed in this study.

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