

# Hypophagic and weight reducing effect of *Momardica charinta* fruit by Enhancing 5-HT neurotransmitter in rats brain

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**Abstract:** *Momardica charinta* seed as vegetable and folk medicine in Pakistan, India, China, Bangladesh and other Asian countries *Momardica charinta* also known as Kerala, bittergourd, balsam pear. It possesses many biological active constituents including glycosides, saponins, phenolic and flavonoids compound, protein, triterpenes, steroid, saponins, alkaloid. It also contains thiamine, beta carotene, folate, riboflavin, calcium, iron, potassium, zinc and fiber. Several studies have been done to show medicinal importance of its fruit which has different biological functions such as anti-diabetes, antihypertension, antiviral, antibacterial and antifungal infection, anti-tumorous as well as anti-carcinogenic effects. The present research is a big contribution of *Momardica charinta* activity as a weight reducing plant through serotonergic neurotransmitter. Decrease in body weight and food intake might be due to increased concentration of serotonin in their respective receptors in brain, which produce hypophagic effect in rats treated with water extract of *Momardica charinta*. More animal and human trials are needed to confirm the safety and anti-obesity effect of MC and the role of neurotransmitter involved in reduction of body weight.

**Keyword:** *Momardica charinta* aqueous extract (MCAE), 5-HT (5-hydroxytryptamine), 5-HIAA (5-Hydroxyindoleacetic acid), TRP (Tryptophan).

## INTRODUCTION

Many factors are involved in developing obesity such as intake of high fat diet, use of junk food and lack of exercise. Present decade researchers are highly focusing on obesity and its related complication. The use of herbs, herbal compounds and their extracts have increased day by day due to ease in their availability, low cost and fewer adverse effects. Many synthetic formula and drug are also available in market to decrease body weight.

Obesity is linked to more than 60 chronic diseases. It is responsible for increased morbidity and mortality worldwide. Cardiac disease, diabetes, and hypertension are strongly related with obesity. (Cassandra and Krista, 2016). The *Momardica charinta* plant has been used as a traditional and folk medicine since a long time (Massimo *et al.*, 2019). The effects of *Momardica* fruit, leaves and seeds are due to the presence of different phytochemicals. MC is involved in antidiabetic and hypoglycemic activity (Xu *et al.*, 2015; Wang *et al.*, 2014; Mohammady *et al.*, 2012; Lo, 2013; Peter *et al.*, 2019) also have weight reducing and hypolipidemic effect (Wang *et al.*, 2015), prevent cancer progression (Salehi *et al.*, 2018). Previous study also shown hypoglycemic and hypolipidemic effects of whole *Momardica charinta* fruit. (Farhat *et al.*, 2011).

Diabetes and its metabolic disorders are characterized by increased glucose level due to defect in insulin function or

secretion. Glycosidic compounds, namely, saponins are bioactive part of MC theorized to decrease glucose level in diabetic patient. (Amira *et al.*, 2017).

Many of the traditional medicinal herbs have been evaluated for their beneficial effect on health. Herbs and herbal extracts have been successfully used since decades. But it requires more investigation in their mode of action and their bioactive constituent responsible for their effect. In the current research study has been carried on the MCAE effect on brain indoleamine (5-HT) and their relation with food intake and body weight.

## MATERIALS AND METHODS

### Preparation of extract

*Momardica charinta* fresh fruit purchased from a local market was washed thoroughly with water. Thin pieces were dried at day sunlight. The dried fruit was powdered in a blender. The 10 gm powder was soaked in 100ml water and left for 24 hours at 37°C. The mixture was filtered and the filtrate was stored until ready to use. Identification of MC fruit was provided by an experienced Botanist from the Institute of Agriculture Department, University of Karachi. All experiments were conducted according to a protocol approved by the Local Animal Care Committee of Biochemistry department of Karachi University.

### Animal

24 Male rats weighing 260-300gms were purchased from the HEJ research center of Karachi University

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Pakistan. Each rat was kept in separate cage at room temperature (23±2°C) and continues supply of tap water and standard food. 24 rats were randomly assigned to two groups 12 rats in each. To test animals, the MCAE 2ml/day was given orally by feeding tube. The control animals were given equal amount of the tap water.

After 15-19% body weight reduction was observed in herbs treated rats were decapitated using guillotine. Brain samples were collected and stored at -70°C for the estimation of brain 5-HT, 5-HIAA and tryptophan. Plasma was also stored for estimation Trp. Estimation of neurotransmitters and their metabolites in the whole brain samples of rats was made by HPLC-EC method as reported by (Farhat *et al.*, 2015).

## STATISTICAL ANALYSIS

Data were analysis by using SPSS 16. The significance differences between the mean of the treated and untreated groups were analyzed by student's *t*-test. Values of *p* < 0.05 were considered as significant. Data expressed in figures as mean ± standard deviation (SD)

## RESULTS

### *Effect of MCAE on food intake and bodyweight*

Fig. (1, 2) shows significant decrease (*p* < 0.01) in food intake since 2<sup>nd</sup> week and body weight from 3<sup>rd</sup> week in test animal as compared to control.

### *Effect of MCAE on whole brain 5-HT and 5- HIAA*

Fig. (3, 4) shows significant increase (*P* < 0.01) in brain 5-HT and 5-HIAA levels as compared to control.

### *Effect of MCAE on whole brain and plasma TRP*

Fig. (5, 6) shows significant increase (*p* < 0.01) in brain and plasma tryptophan levels as compared to control.

## DISCUSSION

Study revealed that MCAE after 3<sup>rd</sup> week showed significant weight reducing effect in treated rats as compared to control treated with equal amount of water.

The scientific name of serotonin is 5-HT. Serotonin level in brain mediates food behavior. Obesity either due to genetic or diet both alter the concentration of 5-HT on dorsal raphe neuron and their terminal region. Genetically alter Zucker rats shown hyperexcitability in 5-HT reach neuron and exhibit greater feeding behavior level as compare to lean Zucker rats. (Lechin *et al.*, 2006; Medeiros *et al.*, 2005). Dysregulation of serotonergic pathway in hypothalamus lead to develop obesity. (Popkin *et al.*, 2009).

The role of 5-HT in feeding behavior is very well-

established. Many studies support indirect relation between 5-HT concentration and feeding behavior. 5-HT dysfunction might be biological marker for eating disorder.

Obesity is a major worldwide health problem among all age group. Obesity increase mortality rate among younger. It is known as diseases of diseases develop metabolic syndrome and two fold increase in developing CVD and cerebrovascular diseases (Engin *et al.*, 2019) due to their complication obesity increase 1.5 fold increases in overall mortality.

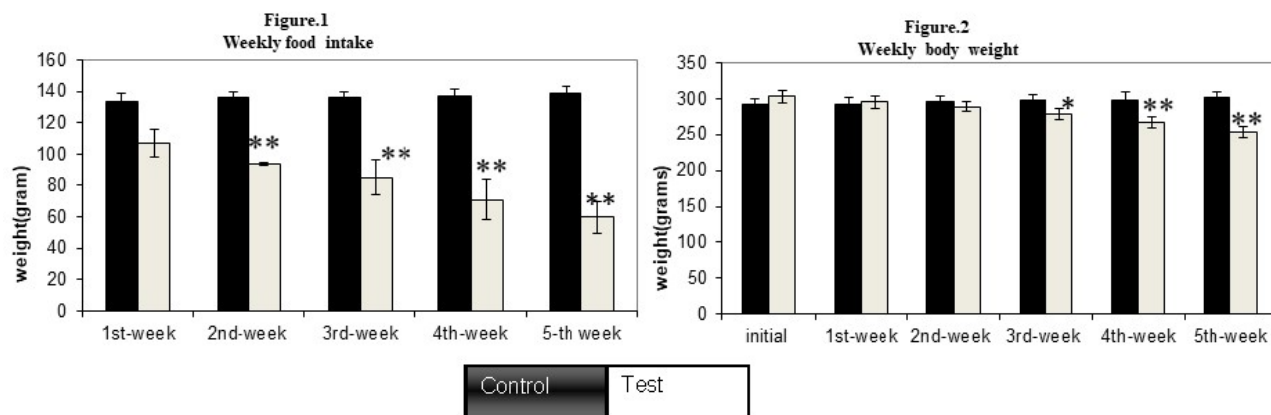
Major cause of pathogenesis of obesity is up regulation of appetite and down regulation of calories by body obesity can be control by decrease in food intake or by increasing energy utilization.

Weight reducing effect is produce and increase by different mode of action, selective serotonin re-uptake inhibitor reduce food intake (Nicholas *et al.*, 2011), lipase inhibitor decrease fat absorption (Nitin *et al.*, 2014), increasing energy expenditure (Alan *et al.*, 2016). Despite the weight reducing properties of drugs. Most of them have been withdrawn from market due their sever side effects especially bad effect on heart. (Connolly *et al.*, 1997). There is need of great attention to synthesize new drug and herb to treat obesity.

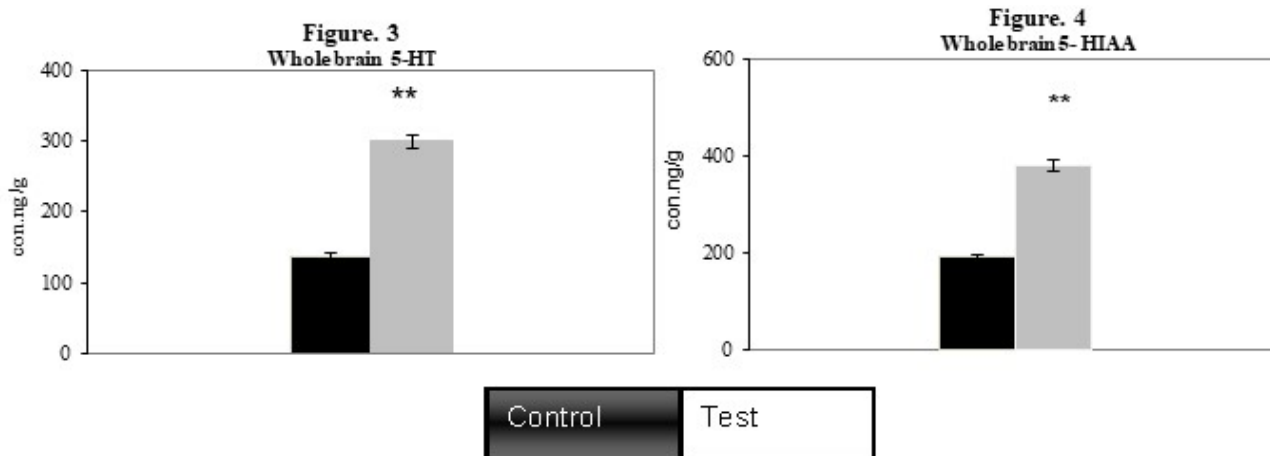
Many other herb used for reducing weight and food intake include ginseng (Liu *et al.*, 2010) capsaicin and capsiate (Ludy *et al.*, 2011) Chen Blueberry and mulberry juice (Wu *et al.*, 2013).

Previous research on herbs demonstrated the weight reducing effect of O-2 lean a herbal mixture (Farhat *et al.*, 2013), *Cinnamomi cassiae* (Lauraceae) bark aqueous extract (Farhat *et al.*, 2014) & *Anethum graveolens* seeds aqueous extract through increase brain 5-hydroxytryptamine metabolism. (Farhat *et al.*, 2015)

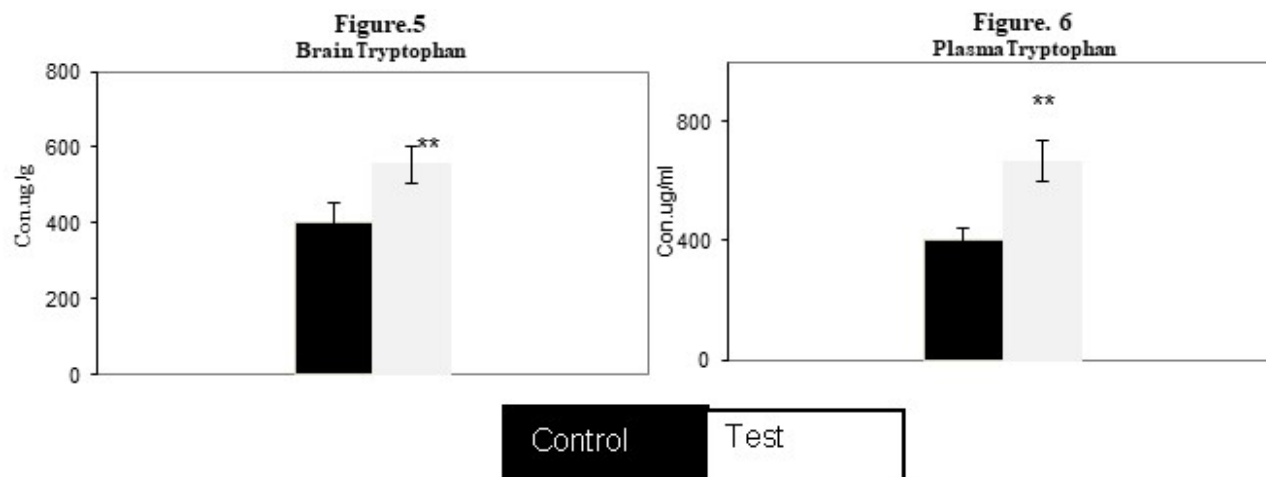
More important part of our research is estimation of 5-HT and their metabolites 5-HIAA in whole rat brain. MCAE increase the concentration of 5HT (fig. 3) and their metabolites 5HIAA (fig. 4) in brain which in turn increase satiety level and decrease body weight (fig. 2) and food intake (fig. 1) in treated rats. It has been establish that weight reducing sibuteramin and dexfenfluramine, fenfluramine suppress food intake by enhancing satiety through serotonergic pathways (Dersa *et al.*, 2012). Many researchers have reported that agonist of 5-HT increase 5-HT concentration in brain which result in increased level of serotonin, decrease food intake, while antagonist decrease 5-HT concentration and produce hyperphagic effect (Jason *et al.*, 2005). increased serotonin metabolism, which might be responsible for increase satiety and reduce body weight.



**Figs. 1,2:** Effect of MCEA on food intake and body weight in rats. Significant difference \*\* $p < 0.01$  and \* $p < 0.05$  from respective controls.



**Fig. 3,4:** Effect of MCAE on 5-HT and 5-HIAA level in rats brain. Significant difference \*\* $p < 0.01$  from respective controls.



**Fig. 5,6:** Effect of MCAE on brain and Plasma TRP in rats. Significant difference\*\* $p < 0.01$  from respective controls.

High plasma level of TRP were monitored MCAE treated rats compared to control as shown in (fig. 6). Tryptophan is an essential amino acid series of reaction required to become 5-HT. Restricted diet decrease the rate of synthesis of serotonin in brain.

The rate of biosynthesis of monoaminergic neurotransmitter 5-HT bounded by availability of TRP in brain. In our study we observed high concentration of plasma tryptophan as well as brain TRP (fig. 5). In agreement with the literature report where research has highlighted that supplementation of TRP increase serotonin (5-HT) synthesis and depletion cause opposite effect (Rizaldy *et al.*, 2018)

Above literature reports support that the weight reducing and hypophagic effect is mediated through 5-HT neurotransmitters and availability of tryptophan to brain. Researchers are more interested in herb to treat obesity with negligible adverse effect. *Garciniacambogia* effects the release and availability of 5-HT which is responsible for controlling appetite (Ohia *et al.*, 2002).

According to research result we can say that increase concentration of TRP in brain convert into 5-HT. Increase concentration of 5-HIAA indicates catabolism of 5-HT into 5-HIAA. Serotonin fulfilled satiety level and in turn decrease food intake or might be due to increase energy utilization in body result of both theories decrease in weight gain. More investigation required to investigate the active constituent of MC fruits responsible for increasing 5-HT level as well as specific area of brain and receptor involved in hypophagic effect of MCAE. Research work support MCEA as weight reducing agent which can be useful for the management of body weight.

## CONCLUSION

Obesity is a serious health problem .Different drugs already available in market to reduce body weight. The use of folk herbs, herbal combination and herbal medicines in world population increasing day by day due to less toxic effects. The main reason is that they are economically affordable. Many herbs traditionally used to reduce body weight since a long time .In current research MCAE shows significantly increases indoleamine level in whole rat brain and produce hypophagic effects which in turn reduce body mass. MCAE can be used as weight reducing herb. Further studies on individual constituent of MC fruit provide valuable information which may be helpful to treat different health issues.

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