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EVALUATION OF ANTI-OBESITY ACTIVITY OF HERBALS FORMULATION USING HIGH FAT DIET INDUCED OBESE RAT MODEL.

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Abstract:

The present study was designed to evaluate the anti-obesity activity of herbals formulation using high fat diet induced obese rat model. The obesity was induced using high fat diet. The study was carried out for 8 weeks and various biochemical parameters[cholesterol, HDL cholesterol, LDL, Triglycerides] and body weight were evaluated. On treatment with Ruta graveolens and Carica papaya 50mg/kg and 100mg/kg effectively showed decrease in body weight of obese rats when compared with disease control group. It was also observed that biochemical parameters i.e., Cholesterol, HDL cholesterol, LDL Triglycerides values were normal in Ruta graveolens and carica papaya 50mg/kg and 100mg/kg treated groups when compared with disease control group. Histopathological studies were performed where disease control group showed presence of peri portal and peri biliary inflammation, moderate degeneration of hepatocytes and foci and central lobular necrosis was observed in hepatocytes of liver and treated groups of ruta graveolens and carica papaya showed similar results to standard group [orlistat 30mg/kg] where hepatocytes appeared normal in portal, peri portal and central lobular region. Hepatic artery and portal vein appeared normal. Thus the results suggests that Ruta Graveolens and Carica Papaya possess anti-obesity activity.

Keywords : *Obesity, High fat diet, Body weight, cholesterol, HDL Cholesterol, LDL Triglycerides, Orlistat, Ruta Graveolens and Carica Papaya.*

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INTRODUCTION:

Obesity is a expression derived from the Latin word obesity which describes about fatness, plumpness, stoutness, fleshiness. [1] Obesity is also termed as corpulence and fatness, immoderate accumulation of body fat ,normally caused by consumption of high calories than the body can use.[2] Obesity primarily shows phenotypic symptoms or assertion of extreme fat deposition responsible for changing the heath conditions as well as elevates mortality level.[3] The above description was provided by WHO.[4]

Obesity is a long-term disease with a multifaceted etiology including genetics, metabolism, behavioral components and lifestyle whereas lifestyle factors include proper nutrition with regular physical activity.[5] Obesity and overweight are creating problems that lead to major health and social issues for people. Generally defined by a Body Mass Index [BMI] calculated by dividing a person's body weight by the square of the person's height. The prevalence of overweight of adult BMI between 25 and 29.9 and Obesity BMI of 30 or over.[6]

Obesity in children and adolescent have been associated with less orbit to frontal cortex gray matter volume, including poor executive functions.[7] Obesity increases chance of occurrence of various secondary diseases which includes type 2 diabetes, hypertension, dyslipidemia, ischemic heart disease, stroke, obstructive sleep apnea, asthma, polycystic ovary syndrome, Alzheimer, vascular dementia.[8]

Categorization of body fatness and corpulence in accordance with BMI as reported by World Health Organization.[9]

BMI	CATEGORY	CHANCE OF CO-MORBIDITIES
<18.5	Underweight	Mean
18.5-24.9	Normal Range	Medium
25.0-29.9	Overweight	Enhance
30.0-34.9	Obese Class I	Moderate
35.0-39.9	Obese Class II	Severe
>40	Obese Class III	Very Severe

Concept of obesity in unani medicine:

As per ancient Unani medicines texts, obesity also called as Saman-e-mufrat, kasata al-Dasam Fir al-Dam [Hyperlipidemia], Shaham, and Farbahi. While hyperlipidemia and obesity are related in various report and studies, whereas the Unani concept implies a common demonstration. obesity is a phlegmatic - balghami disease and consequently khilt -e- balgham prevails in the body of an individual. khilte -e-balgham is a leaning component in causation of obesity. In this state loss of movement of organs [Aaz'as] is due to extravagant gathered phlegm and cold nature. Consequently, the individual becomes dull and lazy. This condition is termed as arrest of body-Qaidul Badan. In this condition blood gets highly viscous [Qiwam] hence mixing with phlegm causes constriction of blood vessels-resulting in Atherosclerosis. Phlegm and accumulated fat hinder passing of oxygen [Nufuz- e-Rooh] in the organs which ultimately results in the death of obese person. [10,11,12,13]

MATERIALS AND METHODS:

Plant Material:

Dried leaves of ruta graveolens and unripe carica papaya were collected from Dr Ghousia Tabassum MD [Moalajat], [Ph. D] -JMI, Regd no. 296/U/2012 Govt. Nizamia General Hospital, Charminar. The

drug obtained was dried a nd ground into fine powder and utilized for the study.

Animals:
30 Wistar male Albino rats were used in this study. The Male Wistar albino rats of weight 150-200gm were procured from sainath agencies, musheerabad, Hyderabad, India. Animals have been kept within standard laboratory conditions in a 12 hours light-dark cycle at 25±20C. The rats were kept under standard well conditions i.e., temperature 22o [±3], humidity 50-60% throughout the expriment. The animals were provided with pellet diet and drinking water ad libitum. The animal exprimental protocol has been approved by our Institutional Animal Ethical Committee with reference no: IAEC/SUCP/2019/02.

Induction of obesity:
Obesity in rats have been induced by high fat cafeteria diet [CD]. The diet comprises of three diets, specifically 40gm of condensed milk plus 40gm of bread, 15gm of chocolate plus 30gm of biscuit plus 30gm of dried coconut, and 40 gm of cheese plus 50 gm of boiled potatoes.

METHODOLOGY:

Experimental Design:
30 healthy wistar albino rats has been involved in the study and were divided into 5 groups based upon their treatment plan. In the starting 4 weeks only cafeteria diet will be given to all groups except normal group. Later after completion of obesity inducement, treatment will be provided from 5 week to produce Anti- obesity activity .

- Group I [Normal]: will be given pellet diet and 0.5% w/v CMC by p.o.
- Group II [Negative Control]: will be given High fat cafeteria diet and water.
- Group III[Standard]: will be given high fat cafeteria diet including orlistat [30mg/kg] and water.
- Group IV [Test I]: will be given high fat cafeteria diet including Ruta graveolens and Carica papaya [50mg/kg] and water.
- Group V [Test II]: will be given high fat cafeteria diet including Ruta graveolens and carica papaya [100mg/kg] and water.

Body weight:
Body weight was recorded on 0th day, and at the end of every week throughout 8 weeks using Docbel - Braun weighing scale.

Collection of blood sample and biochemical parameter estimation:
The blood samples were collected every week from retro orbital plexus of rats under mild ether anesthesia. These blood samples were centrifuged at 4000 RPM for 10 min and serum was isolated. This serum was subjected to Total cholesterol, HDL cholesterol, LDL, Triglycerides using standard kits.

HISTOPATHOLOGICAL STUDIES:

The liver was shifted in 10% formalin solution for fixation. Following the fixation of the tissue it was embedded in paraffin wax. Later the tissue was serially sectioned [3-5µm] and stained with Hematoxylin and Eosin for evaluation of Histopathological changes in the liver tissue.

STATISTICAL ANALYSIS:

The statistical analysis was carried out using Graph pad prism 8.2.0.All results are expressed as mean ± SEM. Groups of data were compared with analysis of variance[ANOVA] to identify significance [$p<0.0001$,$p<0.001$,$p<0.01$,$p<0.5$]among groups.

RESULTS:

Body weight:
$p<0.0001$ and was significant when test was compared with standard for body weight investigation.

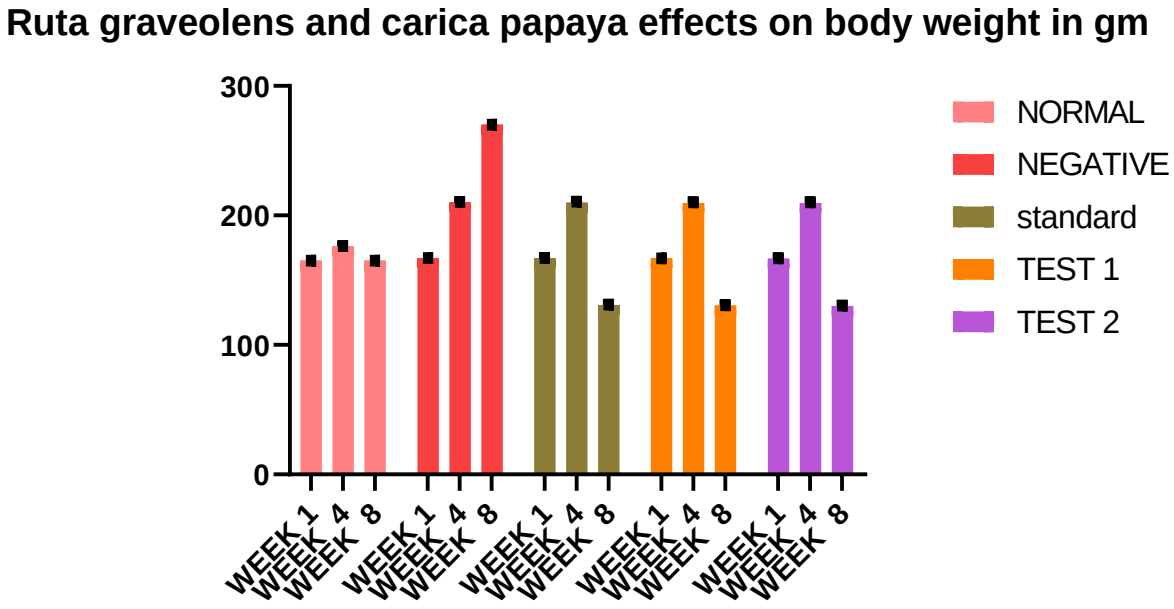

Figure No.1:- Effect of Ruta graveolens and Carica papaya shows decrease in body weight .

BIOCHEMICAL PARAMETERS:

Effect of ruta graveolens and carica papaya on lipid parameters

CHOLESTEROL:

P<0.0001 and was significant when test compared with standard for cholesterol investigation.

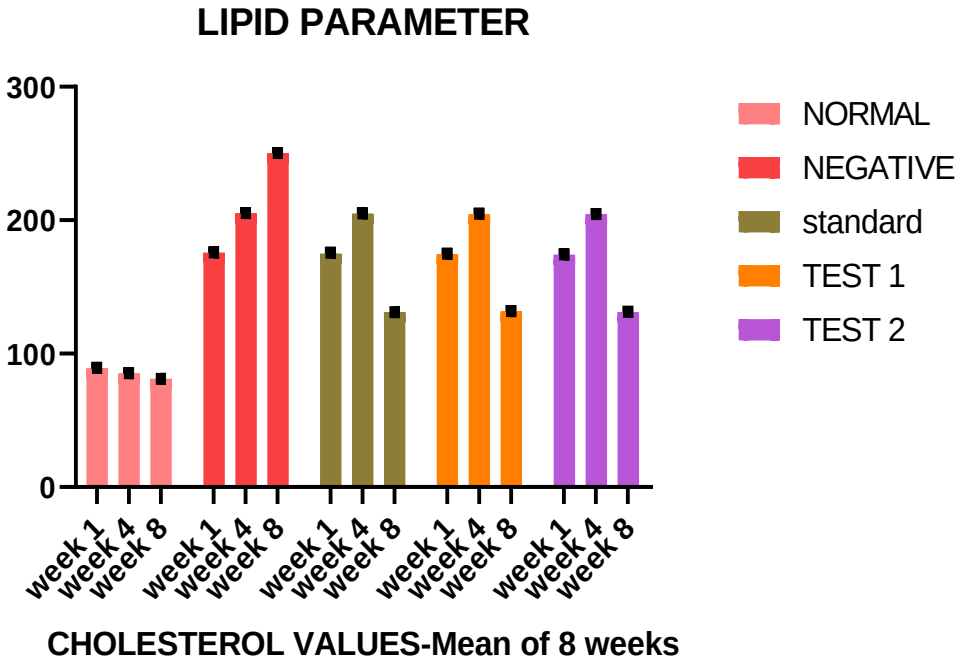

Figure No.2:- Effect of Ruta Graveolens and Carica Papaya in Cholesterol values exhibiting Anti- obesity activity.

HDL CHOLESTEROL:

p<0.0001 and was significant when test was compared with standard for HDL- Cholesterol investigation.

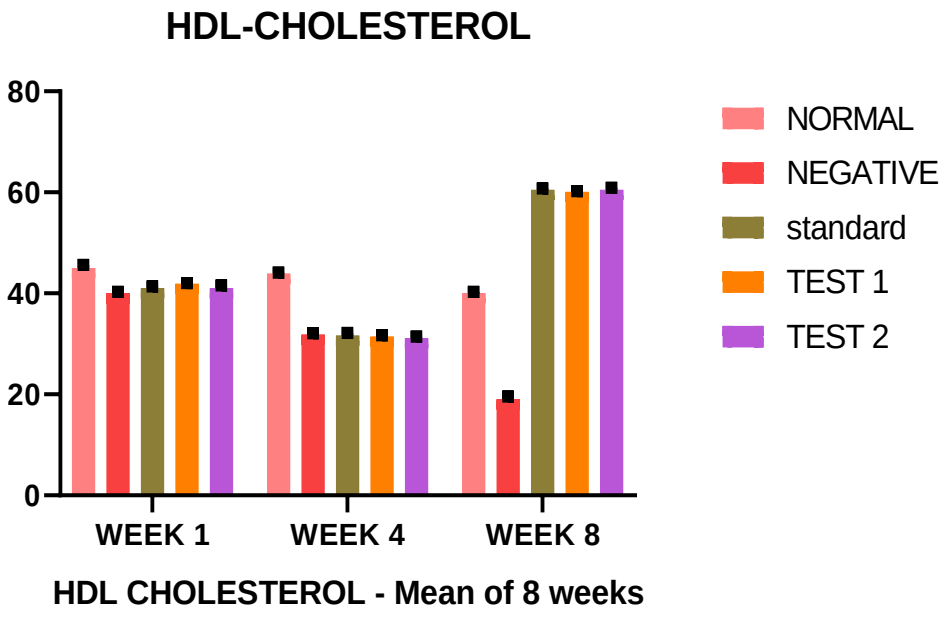

Figure No.3:-Effect of Ruta Graveolens and Carica Papaya in HDL-cholesterol values shows anti-obesity activity

LDL CHOLESTEROL:

p<0.0001 and was significant when test was compared with standard for LDL-Cholesterol investigation.

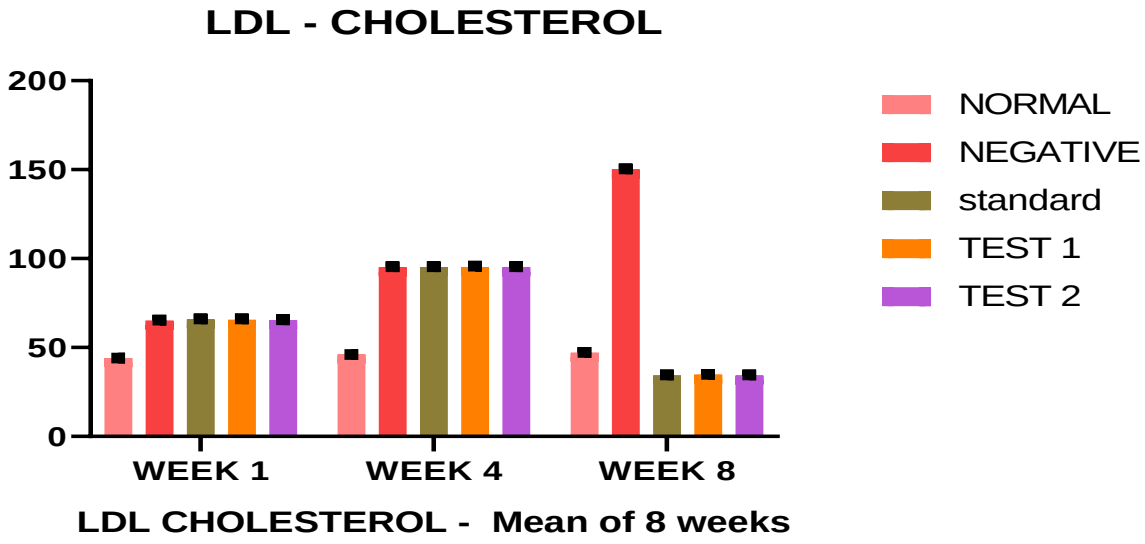

Figure No.4:-Effect of Ruta Graveolens and Carica Papaya in LDL- Cholesterol values shows anti- obesity activity.

TRIGLYCERIDES:

P<0.0001 and was significant when test was compared with standard for Triglycerides investigation.

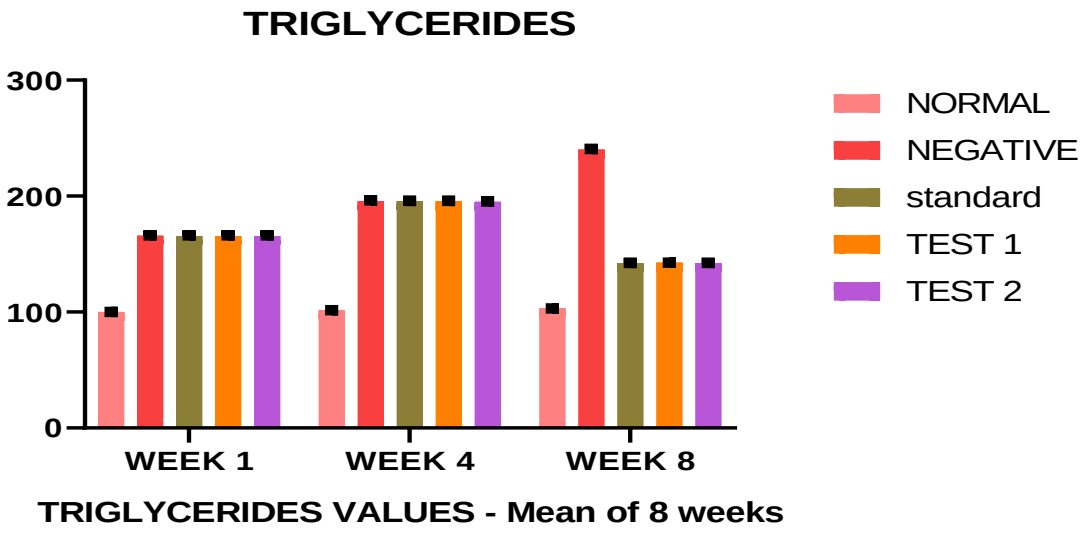

Figure No 5:-Effect of Ruta Graveolens and Carica papaya in Triglycerides values exhibiting anti-obesity activity.

RESULTS:

In this research, Evaluation of anti-obesity activity of herbals formulation using high fat diet induced obese rat model [wistar albino male rats] was done. The impact of ruta graveolens and carica papaya was noted on rats fed with high fat cafeteria diet . The research was carried out for 8 weeks. In the starting 4 weeks animals were provided with high fat cafeteria diet only . later, after completion of 4 weeks of high fat cafeteria diet, the treatment was started and given for next coming 4 weeks in conjunction with high fat cafeteria diet. Body weight of each animal from all groups was recorded on every alternate day.

High fat cafeteria diet significantly increased body weight of each rat in 4 week when compared with normal control group. After providing treatment from 5-8 week , the evalaution of parameters was done which includes the estimation of cholesterol, triglycerides , HDL-Cholesterol and LDL levels. Every week blood was collected from retro orbital plexus of rat and cholesterol, triglycerides, HDL-Cholesterol, LDL levels were evaluated and reported that all the parameters were in normal range when compared with standard group.

After completion of study i.e., on 8 week, ruta graveolens and carica papaya including both higher and lower dose exhibited substantially effective activity and also resulted in decrease in body weight when compared with standard orlistat drug + high fat cafeteria diet. Ruta Graveolens and Carica Papaya both doses 50mg/kg and 100mg/kg exhibited effective, significant and equivalent activity when compared with standard orlistat drug .

In this research, Ruta Graveolens and Carica Papaya as well as standard orlistat drug reduced the body weight when comppared with high fat cafeteria diet control. This clearly stated that Ruta Graveolens and Carica Papaya prevents the absorption of fat from intestine, resulting in decrease in body weight.

In this study investigation of Ruta Graveolens and Carica Papaya was done for anti-obesity activity and compared with standard anti-obesity drug [Orlistat] and detected that Ruta Graveolens and Carica Papaya exhibited higher activity against obesity and also reported that it can be used as potentially effective anti-obesity drug.

DISCUSSION:

Across the world, substantially more than 205 million men and 297 million women endures obesity from a total of around 600 million adult human populations. Whereas India holds 3 rank with 65,619,826 individuals experiencing obesity. As per % prevalence of obesity , Nauru Island has highest % prevalence i.e., 85% for males and 93% for female. In accordance to NFHS the % has elevated from 11% -15%. However in NFHS-2 to NFHS-3 the % increased even in married women's varying age from 15-49.

Obesity has became choice of interest of study due to its risk factors resulting in public health problems or related diseases and to overcome this, medicinal

plants are used for prevention and also for treating obesity. ethno pharmacological ways have elevated over the last few decades, and stated as important scientific mechanism for selection and finalization of plant species for in vivo research work regarding efficacy, safety and quality of anti-obesity pharmacological actions.

The blood samples of rats which was collected from retro orbital plexus after treating with suspension of Ruta Graveolens and Carica Papaya powder had substantial decrease in their lipid profile and also exhibited protection and prevention against formation of excess fat deposition which also suggests its protective impact and capability to decrease overall body fat.

The lipid profile:

- Total cholesterol values of test -week 1[174],week 4 [204].week 8[131] when compared with negative control values - week 1[175],week 4[205],week8[250] and $p<0.0001$ and was significant when compared with standard group using Annova analysis
- HDL cholesterol values of test - week 1[41],week 4[31], week 8[60] when compared with negative control values - week 1[40], week 4[31], week8[19] and $p<0.0001$ and was significant when compared with standard group using Annova analysis.
- LDL Cholesterol values of test - week 1[65],week 4[95],week 8[34] when compared with negative control values -week1[65],week 4[95] week 8[150] and $p<0.0001$ and was significant when compared with standard group using Annova analysis.
- Triglycerides values of test - week 1 [165], week 4[195], week 8 [142] when compared with negative control values - week 1[165], week 4[195], week 8 [240] and $p<0.0001$ and was significant when compared with standard values using Annova analysis.
- Body weight variation: -
- Body wt values of test group- week 1[166], week 4[209], week 8 [130] when compared with negative control group week 1[167], week 4[210], week 8[270] and $p<0.0001$ and was significant when compared with standard values using Annova analysis
- Liver samples which was sent for Histopathological evaluation portrayed the protection towards fat deposition and inflammation due to excessive fat deposition, when provided with regular high fat cafeteria diet to induce obesity.
- Histopathology of normal control group liver- normal portal triad with bile duct, normal portal vein, normal peri portal and centri lobular region, normal hepatocytes.
- Histopathology of negative control liver- moderate degeneration of hepatocytes, foci of central lobular necrosis was observed in hepatocytes, peri portal inflammation along with infiltration of lymphocytes, peri biliary inflammation of inflammatory cells are noticed.
- Histopathology of Standard group liver - Hepatocytes appeared normal in peri portal region, normal portal vein, normal bile duct, normal portal triad with bile duct, portal vein and hepatic artery.
- Histopathology of Test I liver - Hepatocytes appeared normal in portal, peri portal and central lobular region, normal peri biliary region, normal portal vein, no necrosis and inflammation.
- Histopathology of Test II liver - Hepatocytes appeared normal in peri portal region, normal portal triad with bile duct and normal portal vein, normal hepatic artery and normal liver morphology.

From the present results/outcomes, it can be concluded that Ruta Graveolens and Carica Papaya has the quality to improve the lipid profile and exhibits protective activity against obesity which might be due to its antioxidant activity as a result of phytochemical constituents for example phenols Acridone alkaloids, Coumarins, Essential oils, Flavonoids, Fluoroquinolones, Alcohols and flavanoids of ruta graveolens contains rutin and quercetin whereas Papaya includes saponins, polyphenols and cardinolides, presence of potassium, phosphorous, zinc, copper, chromium, calcium, minerals, carotene, carbhydrates, fibre, protein.

After conducting a complete study of clinical trials, these plants may be deemed as easily affordable, potent and effective herbal medicine for preventing Obesity.

CONCLUSION:

Generally, most of the people are unaware of damaging effects caused by obesity, which resulting in worsening of body and overall health. Most of the review stated that childhood obesity results in increased risk of adult obesity related morbidity, childhood obesity should be well treated to avoid adult obesity related morbidity.

Every individual should eat healthy, regular exercise, stay fit and active and must restrict diet containing calorie dense fast food and sucrose enriched drinks including sedentary lifestyle. Obesity is an infectious

disease and major risk factor for non-communicable disease.

Medicinal herbs are best substitutes for various diseases and has been used for 60,000 years ago for best curing ill health results and less negative effects.

In conclusion we have estimated that administration of ruta graveolens and carica papaya in obese animals, resulted in reduction of body weight. Lipid parameters [Total cholesterol, HDL, LDL, Triglycerides] was also evaluated and best therapeutic effects was detected using ruta graveolens and carica papaya.

Even results of liver histopathology revealed and confirmed that ruta graveolens and carica papaya is a potent and highly effective anti-obesity drug nearly equivalent to marketed standard anti-obesity drug.

In the present study, the formulation was investigated in animal model and exhibited good therapeutic results and decrease in body mass index [BMI]. Still investigations are required to be encouraged to help the inheritance of herbal drugs to accomplish more influence and acceptance. Furthermore, clinical trials should be performed for approval of these potentially active and potent Anti-obesity drugs.

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CONFLICT OF INTEREST:
There is no conflict of interest among the authors

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