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Effect of *Myristica fragrans* Extract on Food Intake and Body Weight in Experimental Models

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ABSTRACT

Introduction: *Myristica fragrans* (Mace) is one of the commonly used Indian spices. It was used in traditional medicine to treat digestive problems, rheumatism, hyperlipidaemia, diarrhoea and insomnia. More food intake than required on a daily basis, can lead to overweight Body Mass Index (BMI 25-30) or Obesity (BMI >30). Herbal supplements and diet based therapies for weight loss are among the most common in Complementary and Alternative Medicine (CAM) modalities. *Myristica fragrans* (*M. fragrans*) contains Tetrahydrofuran (THF), Lignans. Saponins, flavonoids, glycosides, tannins and terpenoids. These chemical compounds are believed to have anti-obesity properties. Hence, Mace extract was selected to observe its effect on food intake and body weight.

Aim: To evaluate the effect of *M. fragrans* extract on food intake and body weight in normal and obese wistar albino rats.

Materials and Methods: Healthy albino rats (male/female) weighing between 150-180 gm were selected and randomly divided into five groups with six rats each. Body weight of all rats was recorded on day one. From day one to day 35 (five weeks), Body weight (BW) and Food intake (FI) capacity of an individual rat per day and for 35 days was measured in all the groups before treatment with *M. fragrans* extract. Group-I (Control) was treated with standard pellet diet and normal saline, Group-II (Test 1) with *M. fragrans* extract 200 mg/kg and Group-III (Test 2) with *Myristica fragrans Extract* (MFE) 400 mg/kg for 35 days (day 36 to day 70). Group IV (Test 3) and V (Test 4) were given Cafeteria Diet (CD) to induce obesity for first five weeks and last five weeks treated with *M. fragrans* Extract in the doses of 200 mg/kg and 400 mg/kg respectively. On day 70, FI capacity and BW of each rat was measured statistically using SPSS Statistics 20.0 (IBM software) for the analysis. Animals were observed for FI capacity and BW for 70 days (first 35 days and last 35 days).

Results: Repeated measures One-way analysis of variance (ANOVA) indicated that, after 35 days of treatment (between 36-70 days), there was a significant reduction of FI capacity and BW in Group III and V, and slightly reduced in Group-II and IV in a dose dependent manner ($p<0.01$) but there was no difference in Group-I animals.

Conclusion: These results suggest that *M. fragrans* extract may have clinical value in the treatment of obesity due to its inhibitory effect on FI capacity (by inhibiting hunger sensory mechanism) and BW by inhibiting pancreatic lipase enzyme.

Keywords: Adipose tissue growth, Nutmeg, Obesity, Pancreatic lipase

INTRODUCTION

Body mass index more than 30 is considered as obesity [1]. It is the leading metabolic disorder in both developed and developing countries. Both reduced physical activity and increased energy intake are important risk factors for obesity. Triglycerides (TG) levels are increased and High Density Lipoproteins (HDL) levels are decreased in abdominal obesity [2]. Chronic untreated obesity leads to diabetes, hypertension, dyslipidaemia, Coronary Heart Disease (CHD) and malignancy.

Treatment of obesity starts with comprehensive lifestyle management (diet, physical activity and behaviour modification) followed by pharmacotherapy. Patients prefer pharmacotherapy to other modalities of treatment [3], but the results were disappointing with the existing drugs. This indicated the need for newer therapies to produce better and long-lasting results [4]. In CAM, dieting, and plant products are the commonly used methods to reduce the BW [5]. Different variety of natural products and medicinal plants (including crude extracts and isolated compounds) show potential to induce weight loss and prevent diet-induced obesity [3,6]. Medicinal plants, which form the backbone of traditional medicine, have become the subject for numerous pharmacological studies in the last few decades. They are potential sources of new compounds of therapeutic value [7,8]. For the present study, we have chosen one of the commonly used Indian spices *M. fragrans* (Mace). Its effect on FI and BW in animal models was evaluated.

Myristica fragrans, commonly known as Nutmeg, belongs to the family *Myristicaceae* [Table/Fig-1]. It is a medium sized, evergreen aromatic tree. It is distributed in India, South East Asia, and North Australia and Pacific islands [9]. The seed (Nutmeg) and its fleshy aril (Mace) are used as spices. It contains 4% Myristicin. Many bioactive compounds including camphene, elemicin, eugenol, isoelemicin, isoeugenol, methoxyeugenol, pinene, sabinene, safrol, myristic acid, myristicin, saponins and lignan were found in *M. fragrans*. Phenolic compounds belonging to the lignans group have been reported capable of scavenging 2, 2-Diphenyl-1-Picrylhydrazyl (DPPH) free radicals as well as chelating with metallic elements to form complexes [10,11]. In traditional medicine, it is used to support digestion and to treat rheumatism because of its essential oil [12]. Previous studies have shown the cholesterol lowering activity of *M. fragrans* seed extract in rabbits which contains THF [13,14], lignans, flavonoids, glycosides, saponins, tannins, and terpenoids. These chemical compounds are believed to have weight reducing and hypolipidaemic properties [15]. Saponins inhibit pancreatic lipase activity. THF regulates the body energy metabolism and prevents the growth of adipose tissue mass [16]. Due to presence of these chemical constituents and their lipid lowering property in *M. fragrans*, the present research study was undertaken to examine the effects of *M. fragrans* (Mace) extract on FI capacity and BW of normal and diet induced obese rats.

[Table/Fig-1]: *Myristica fragrans* (Mace, Nutmeg):

MATERIALS AND METHODS

An experimental study involving rats was performed in Department of Pharmacology, Santhiram Medical College, Nandyal, India, from December 2016 to February 2017. Before conducting this study, Institutional Animal Ethical Committee (IAEC) (897/PO/Re/S/05/CPCSEA) permission was taken. This study was strictly conducted according to Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines.

Collection of *Myristica fragrans* Material

Fresh and dried Mace was purchased from wholesale grocery store for the preparation of extract. Authentication was done by Dr. Suryanarayana Moorthi, PhD, Professor of Botany. Its uses were explained by Dr. Gurunath Reddy. B.A.M.S. Nandyal, Andhra Pradesh.

Preparation of *Myristica fragrans* Extract

Dried mace was ground to a fine powder. From the stock, 30 gm of powder was weighed and placed in the Soxhlet basket. The Soxhlet flask was filled with 300 mL of ethyl alcohol which acts as solvent. The Soxhlet connected with condenser and tap water was running through the inlet and outlet of the condenser. The solvent was heated to reflux. The solvent vapour travels up a distillation arm and floods into the Soxhlet basket which contains solid. The condenser ensures that any solvent vapour cools, and drips back down into the sac which was filled with mace powder in the basket. The Soxhlet basket was filled slowly with solvent. Some of the desired compounds in the powder dissolved in the warm solvent. When the basket was almost full, it was automatically emptied by a side arm, and the solvent running back down to the Soxhlet flask. This cycle was allowed to repeat many times in 24 hours. After many cycles the desired compounds were concentrated in the distillation flask. Finally, the extracted solvent was placed on the water bath for evaporation for yielding the extracted compound. The resultant solid extract was measured [17]. Out of 30 gm of dry powder, 5 gm of solid extract was obtained. The percentage of yield extract was 16. 6%. This extract was dissolved in 5 mL distilled water and administered orally by gastric intubation.

Hypercalorie/Cafeteria Diet

(It consisted of three variants): [18].

1) Condensed milk + bread + peanuts + pellet chow (4:1:4:1),
2) Chocolate + biscuits + dried coconut + pellet chow (3:2:4:1),
3) Cheese + boiled potatoes + pellet chow (4:2:1).

The different variants were fed on alternate days throughout the treatment period (10 weeks). First five weeks without treatment and last five weeks treatment with *M. fragrans* extract in Group-IV, and Group-V.

Acute Toxicity Study

Acute toxicity study was done as per OPPTS guidelines in healthy Albino rats by up and down Procedure [19]. The rats were divided into six groups of six rats each. The groups were treated with ethanolic extract of *M. fragrans* in doses of 10 mg/kg, 50 mg/kg, 100 mg/kg, 200 mg/kg, 500 mg/kg and 1000 mg/kg respectively. The animals were observed for behavioural changes and death rate. No abnormal changes were found in the first five groups up to the dose of 500mg/kg. In the sixth group (1000 mg/kg), abnormal behavioural changes were observed and two rats died. Thus, *M. fragrans* extract was found to be safe below 500 mg/kg. The doses of 200 mg/kg and 400 mg/kg were chosen for the present study.

Experimental Design

Thirty wistar Albino rats of both the sexes, weighing 150-180 gm, were selected and taken from the Central Animal House of Santhiram Medical College. They were fed with commercial standard pellet diet and water ad libitum and maintained under standard laboratory conditions with 12:12 hour light: dark cycle [20]. The rats were divided into five groups of six animals each:

Group-I-Control: Treated with Standard Pellet diet (SPD) + Normal saline.

Group-II-Test-1: Treated with Standard Pellet diet (SPD) + *M. fragrans* extract 200 mg/kg.

Group-III-Test-2: Treated with Standard Pellet diet (SPD) + *M. fragrans* extract 400 mg/kg.

Group-IV-Test-3: Treated with CD + *M. fragrans* extract 200 mg/kg.

Group-V-Test-4: Treated with CD + *M. fragrans* extract 400 mg/kg.

All the test compounds were administered orally once a day before food [16].

Experimental Procedure

The BW of all the rats were recorded on day one in the first week and last day of the 10th week. All the five groups were given standard pellet diet and water from day one to last day of the 10th week. FI per day of each rat was assessed and the average FI capacity was calculated. From first day of sixth week to last day of 10th week (five weeks of duration), the rats in Group I were given Normal saline. The rats in Group II and III were treated with SPD and *M. fragrans* extract in the doses of 200 mg/kg and 400 mg/kg respectively. These two groups were considered as weight Preventive models. Group IV and V were given CD along with pellet diet and treated with *M. fragrans* extract in the doses of 200 mg/kg and 400 mg/kg respectively. These two groups were considered as obesity treatment models. BW and FI of each rat was measured at the end of the 10th week.

Food intake: All the rats were fed with normal laboratory Pellet diet. Food was presented in the form of pellets in grams [21]. FI was measured manually. A known amount of food was given to the animal. After 24 hours, the food was weighed again and the amount consumed was calculated. FI in 24 hours by an individual rat was multiplied with 35 (for five weeks). FI was measured for first five weeks (before treatment), and the last five weeks (after treatment).

Body weight: Body weight was recorded on day one of first week and on last day of fifth week (without treatment) and at the end of the study on last day of 10th week (after treatment with the extract).

STATISTICAL ANALYSIS

The results obtained were expressed as mean±SEM and were analysed by the application of ANOVA, followed by Dunnett's t-test. Results were considered to be statistically significant at p-value <0.05.

RESULTS

In Group-I, the BW and FI was almost the same on day one and day 70 [Table/Fig-2]. The average BW on day one, on day 35 and on day 70 was 162.83±4.81, 203.66±6.24, 225.00±5.11 respectively. FI capacity on day 35 and on day 70 was 835.83±10, 893.33±12 respectively. There was slight increase in body weight. This could be attributed to the fact that as the age (10 weeks) increases, BW and FI capacity also increases. There was not much difference observed in first five weeks (1-35 days) and last five weeks (36-70 days).

Rats	Normal Body Weight (on day one)	After five weeks without treatment (day one-day 35)		At the end of 10th week with Normal Saline treatment (day 36-day 70)	
		Body Weight	Food Intake	Body Weight	Food Intake
1	171	196	875	223	920
2	153	198	770	209	820
3	176	201	805	230	860
4	155	197	880	235	975
5	166	210	775	231	820
6	156	220	910	222	965

[Table/Fig-2]: Group-I: (Control): treated with standard pellet diet and normal saline (day 36-day 70).

In Group-II, in the days 1-35, there was not much difference in the weight. In the days 36-70, there was a reduction in the BW. In the days 36-70, FI capacity was also reduced. The average BW on day one, on day 35 and on day 70 was 165.75±5.59, 194.5±5.92, 179.33±7.09 respectively. FI capacity on day 35 and on day 70 was 868.83±12, 808.66±10 respectively [Table/Fig-3].

Rats	Normal Body Weight (on day one)	After five weeks without treatment (day one-day 35)		At the end of 10th week with *M. fragrans* extract (day 36-day 70)	
		Body Weight	Food Intake	Body Weight	Food Intake
1	165	185	875	162	770
2	172	196	910	175	850
3	166	200	854	172	786
4	155	190	889	186	820
5	174	201	805	195	790
6	163	195	880	186	836

[Table/Fig-3]: Group-II: (Test-1) treated with standard pellet diet and *M. fragrans* extract 200 mg/kg (day 36-day 70).

In Group-III, the average BW on day one, on day 35 and on day 70 was 165.50±4.81, 190.00±6.23, 168.66±7.17 respectively. High dose of *M. fragrans* extract has shown more effect on BW gain than the low dose. FI capacity on day 35 and on day 70 was 900.00±10, 811.33±11respectively. From 36-70 days, food intake capacity also greatly reduced. Thus BW and FI significantly reduced in a dose dependent manner (p<0.01) when compared with control group [Table/Fig-4].

Rats	Normal Body Weight (on day one)	After five weeks without treatment (day one-day 35)		At the end of 10th week with *M. fragrans* extract (day 36-day 70)	
		Body weight	Food intake	Body weight	Food intake
1	155	194	931	165	826
2	162	205	735	168	630
3	177	193	903	158	855
4	156	210	962	166	842
5	168	196	980	175	910
6	175	190	889	180	805

[Table/Fig-4]: Group-III: (Test-2) treated with standard pellet diet and *M. fragrans* extract 400 mg/kg (day 36-day 70).

In group-IV, the average BW on day one, on day 35 and on day 70 was 169.50±2.36, 280.16±4.92, 250.83±5.63 respectively. From 1-35 days, there was great increase in BW due to high fat diet (diet induced obesity), but in the days 36-70, there was slight reduction of BW. FI capacity on day 35 and on day 70 was 895.50±0.6, 843.52±1.10 respectively. From 36-70 days, FI capacity also reduced but very less [Table/Fig-5].

Rats	Normal Body Weight (on day one)	After five weeks without treatment (day one-day 35)		At the end of 10th week with *M. fragrans* extract (day 36-day 70)	
		Body weight	Food intake	Body weight	Food intake
1	162	240	931	210	863
2	155	266	735	225	690
3	160	285	903	256	865
4	150	280	962	260	884
5	163	290	950	269	920
6	177	320	892	285	866

[Table/Fig-5]: Group-IV: (Test-3) treated with cafeteria diet and *M. fragrans* extract 200 mg/kg (day 36-day 70).

In Group-V, the average BW on day one, on day 35 and on day 70 was 164.16±1.63, 287.33±6.11, 211.45±5.23 respectively. From 1-35 days, there was great increase in BW due to high fat diet (diet induced obesity), but in the days 36-70, BW was reduced greatly. High dose of *M. fragrans* extract has shown more effect on body growth than the low dose. FI capacity on day 35 and on day 70 was 866.23±13, 774.83±3.11 respectively. From 36-70 days, FI capacity also greatly

Rats	Normal Body Weight (on day -one)	After five weeks without treatment (day one-day 35)		At the end of 10th week with *M. fragrans* extract (day 36-day 70)	
		Body weight	Food intake	Body weight	Food intake
1	165	320	931	210	820
2	159	298	740	223	660
3	171	340	920	256	840
4	169	290	840	210	760
5	166	196	980	166	845
6	155	280	785	203	724

[Table/Fig-6]: Group-V: (Test-4) treated with cafeteria diet and *M. fragrans* extract 400 mg/kg (day 36-day 70).

Groups (I-V)	Normal body weight on day one	Body weight on day 35 without treatment	Body weight on day 70 with treatment	Food intake on day 35 without treatment	Food intake on day 70 with treatment
Group-I (Control) (SPD+Normal Saline)	162.83±4.81	203.66±6.24	225.00±5.11	835.83±10	893.33±12
Group-II (Test-1) SPD+MFE-200 mg/kg	165.75±5.59	194.5±5.92	179.33±7.09**	868.83±12	808.66±10**
Group-III (Test-2) SPD+MFE-400 mg/kg	165.50±4.81	190.00±6.23	168.66±7.17***	900.00±10	811.33±11***
Group-IV (Test-3) CD+MFE-200 mg/kg	169.50±2.36	280.16±4.92	250.83±5.63**	895.50±0.6	843.52±1.10**
Group-V (Test-4) CD+MFE-400 mg/kg	164.16±1.63	287.33±6.11	211.45±5.23***	866.23±13	774.83±3.11***

[Table/Fig-7]: Comparison of body weight and food intake within and in-between the groups.
(n=6, Mean±SEM) *p<0.05, **p<0.01, ***p<0.001 compared to Control
Statistically analysed by one-way ANOVA followed by Dunnett's t-test
SPD - Standard pellet diet, MFE - Myristica fragrans extract, CD - Cafeteria diet

reduced. Thus, BW and FI significantly reduced in a dose dependent manner (p<0.01) when compared with control group [Table/Fig-6].

From [Table/Fig-7] it can be concluded that high dose of *M. fragrans* extract (400 mg/kg) has shown more effect on both BW and FI capacity of the rats at the end of 70 days.

DISCUSSION

Studies have shown that medicinal extracts (obtained from traditional medicine) can be used to obtain new compounds with potential pharmacological activity [22]. The potential of *M. fragrans* to decrease FI and reduce BW was evaluated in rats. Rats were selected for the study because they enable us to obtain answers in a short time (10 days in the life of a rat accounts for approximately one year in the life of humans) when comparing changes in BW. Furthermore, there are similarities neuroanatomically in brain areas that play role in the control of FI. It is well established that a number of different neurotransmitters and peptides produce similar effects on FI and energy homeostasis in laboratory rodents and man. As the age increases in rats, its weight and FI capacity also increase rapidly within a short period [23].

Myristica fragrans (Mace) is a commonly used spice in various dishes and food preparations. It has been shown to possess hypolipidaemic properties [24]. However, studies have not been done so far to assess its impact on FI and BW. In the present study, the effect of *M. fragrans* on FI capacity and body growth in experimental animal models were studied as per standard guidelines. According to traditional system of medicine, different parts of *M. fragrans* have different medicinal properties.

Arulmozhi DK et al., observed that hydroalcoholic extract of fruits of *M. fragrans* effectively attenuate the raised TG (47% reduction) and CH (66.7%), and at 450 mg/kg, significantly inhibited the hepatic lipoprotein secretion in high cholesterol fed rats. These results proposed that *M. fragrans* extract can be used to improve hyperglycaemia and hyperlipidaemia [25].

Nguyen PH et al., isolated the seven active compounds from the total extract of *M. fragrans* and have shown anti-obesity property [14]. The active compounds were 2,5-bis-aryl-3,4-dimethyltetrahydrofuran lignans, tetrahydrofuroguaiacin B (1), saucernetindiol (2), verrucosin (3), nectandrin B (4), nectandrin A (5), fragransin C(1) (6), and galbacin (7). In differentiated C2, C12 cells, the sole target area for the treatment of obesity and type-2 diabetes is AMP-Activated Protein Kinase (AMPK) enzyme. The active compounds from *M. fragrans* can stimulate the AMPK. THF is one of the important chemical compounds, and its preventive effect was tested on body weight in a diet-induced animal model. According to outcome of the animal study, the active compounds of the *M. fragrans* can be used for the evolution of agents to treat metabolic disorders [13].

Al-Shammary Hayfaa A et al., demonstrated the analgesic activity of *M. fragrans* seed extract in mouse model of acetic acid-induced visceral pain. It was concluded that the analgesic activity of seed extract was due to presence of various alkaloids and inhibit phospholipase A2, thus lowering the availability of arachidonic acid precursor for prostaglandin synthesis [26].

Olaleye MT et al., explained the antioxidant property of aqueous extract of *M. fragrans* in animal models of rat. The results showed that alkaloids present in *M. fragrans*, were saponins, anthraquinones, cardiac glycosides, flavonoids and phlobatanins have antioxidant property [27].

In another study, Kartika Dewi et al., demonstrated the anti-inflammatory effect of *M. fragrans* ethanolic extract by in vitro method -cell viability assay. They concluded that, anti-inflammatory effect was due to antioxidant property of Quercetin, the most commonly occurring flavonoid in *M. fragrans* seeds. Anti-inflammatory potential may be due to inhibition of TNF-α, IL-6, IL-1β and no production [28].

Jaiswal P et al., explained the biological effects of *M. fragrans* in a review article. The chemical constituents of *M. fragrans* was found to exhibit hypolipidaemic and hypocholesterolaemic effects, antimicrobial, antidepressant, aphrodisiac, memory enhancing, antioxidant and hepatoprotective properties. Recent studies revealed strong insecticidal and molluscicidal activities of *M. fragrans* [29].

In the previous animal studies, the whole fruit and seed (nutmeg) extracts have shown antioxidant, antidiabetic and hypolipidaemic properties [30,31]. The effect of Mace (fleshy covering of nutmeg) extract was not evaluated on body weight and FI capacity. Hence, mace was chosen for the present study.

The results of this study revealed that the *M. fragrans* extract can reduce FI capacity and prevent the increase in BW in a dose dependent manner. High dose (400 mg/kg) has shown maximum effect in reducing FI capacity and preventing the increase in BW in Group-III, and V (p<0.01). Low dose (200 mg/kg) has less effect on FI, BW in Group-II, and IV when compared with the high dose. The exact mechanism of action of the mace extract was not well established. Based on the observations and previous research studies, the possible mechanism for weight reducing property may be due to presence of saponins in mace extract. Saponins can inhibit the pancreatic lipase enzyme; thereby reduce the cholesterol levels [32]. Tetrahydrofuran is one of the active chemical compounds present in the Mace, also contributes to prevent weight gain by stimulating AMPK enzyme in differentiated C2, C12 cells. Its steroidal compounds reduced the FI capacity for its inhibitory effect on hunger sensory mechanism in hypothalamus [33]. This could be beneficial to the obese persons and to treat obesity associated complications. Acute toxicity study revealed that this plant extract was found to be safe for a short period. Prolonged use of *M. fragrans* extract can lead to toxic effects on various organs [27,34]. Further studies are needed for the establishment of safety.

LIMITATION

The present study was carried out in the rat models but histological study, and plasma lipid profile was not conducted to establish its weight reducing effect by observing adipose tissue mass and cholesterol levels. Its delayed effects were not studied. Further evaluation is needed on the separation of the individual compounds present in the *M. fragrans* and their effects at the molecular level.

CONCLUSION

The present experimental study indicates that the commonly used spice *M. fragrans* extract has potential inhibitory effect on body weight and FI. Hence, this extract can be used as an anti-obesity preparation in obese and overweight individuals. However, it needs further studies to prove its weight reducing property in humans.

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REFERENCES

[1] Swinburn BA, Caterson I, James WP, Seidell IC. Diet, nutrition and the prevention of excess weight gain and obesity. Public Health Nutrition. 2004;7(1A):123-46.
[2] Paccaud F, Schiuter-Fasmeyer V, Wietlisbach V, Bovet P. Dyslipidemia and abdominal obesity, an assessment in three general populations. J Clin Epid. 2000;53(4):393-400.
[3] Moro CO, Basile G. Obesity and medicinal plants. Fitoterapia. 2000;71:S73-S82.
[4] Abdollahi M, Afshar-Imani B. A review on obesity and weight loss measures. Middle East Pharmacy. 2003;11:06-10.
[5] Barnes PM, Powell-Griner E, McFann K, Nahin RL. Complementary and alternative medicine use among adults: United States, 2002. Adv Data. 2004;(343):01-19.
[6] Hanl K, Kimura Y, Okuda H. Anti-obesity effects of natural products. Studies in Natural Products Chemistry. 2005;30:79-110.
[7] Aiyelaagbe OO, Osamudiamen MP. Phytochemical screening for active compounds in Mangifera indica leaves from Ibadan, Oya State. Plant Science Research. 2009;2:11-13.
[8] Edeoga HO, Okwu DE, Mbaebie BO. Phytochemical constituents of some Nigerian medicinal plants. African Journal of Biotechnology. 2005;4(7):685-88.
[9] Bamidele O, Akinnuga AM, Alagbonsi IA, Ojo OA, Olorunfemi JO, Akuyoma MA. Effects of ethanolic extract of *Myristica fragrans* houtt. (Nutmeg) on some heamatological indices in albino rats. Int J Med Med Sci. 2011;3(6):215-18.
[10] Chatterjee S, Zareena N, Gautam S, Adhikari S, Variyar PS, Sharma A. Antioxidant activity of some phenolic constituents from green pepper (Piper nigrum L.) and fresh nutmeg mace (*Myristica fragrans*). Food Chem. 2007;101(2):515-23.
[11] Su L, Yin JJ, Charles D, Zhou K, Moore J, Yu L. Total phenolic contents, chelating capacities and radical-scavenging properties of black peppercorn, nutmeg, rosehip, cinnamon and oregano leaf. Food Chem. 2007;100(3):990-97.
[12] Peter KV. Handbook of herbs and spices. Woodhead Publishing Ltd., Cambridge. 2001;2:238-48.
[13] Sharma A, Mathur R, Dixit VP. Prevention of hypercholesterolemia and atherosclerosis in rabbits after supplementation of *Myristica fragrans* seed extract. Indian J Physiol Pharmacol.1995;39(4):407-10.
[14] Nguyen PH, Le TV, Kaug HW, Chae J, Kim SK, Kwon KL, et al. AMP-activated protein kinase (AMPK) activators from *Myristica fragrance* and its anti obesity effect. Bio Org Med Chem Lett. 2010;20(4):128-31.
[15] Rosengarten F. The book of spice. 1st ed. Livingston publishing company. 1969;pp:489.
[16] Thomas RA, Krishnakumari S. Lipid lowering effects of *Myristica fragrans*. Int J Pharmacol Pharmaceut Sci. 2016;3(3):10-13.
[17] Semiz A, Sen A. Antioxidant and chemoprotective properties of *Momordica Charantia L* (bitter melon) fruit extract. African J Biotechnol. 2007;6(3):273-77.
[18] Harris RB. The impact of high or low-fat cafeteria foods on nutrient intake and growth of rats consuming a diet containing 30% energy as fat. Int J Obes Relat Metab Disord. 1993;17(6):307-15.
[19] Health Effects Test Guidelines, Acute oral toxicity (computer program). OPPTS 870, 1100 United States Office of prevention, Pesticides and Toxic Substances Environmental Protection Agency (7101). http://www.epa.gov/opptsfrs/home/guideline.htm. (Accessed 5/6/2004).
[20] Mazidi M, Baghban Taraghdari S, Rezaee P, Kamgar M, Jomezadeh MR, Akbarieh Hasani O, et al. The effect of hydroalcoholic extract of Cannabis Sativa on appetite hormone in rat. J Complementary and Integr Med. 2014;11(4):253-57.
[21] Kylie L, Kevin G. Accurate measurement of body weight and food intake in environmentally enriched male wistar rats. Obesity. 2011;19:1715-21.
[22] Bento EB, de Brito Junior FE, de Oliveira DR, Fernandes CN, de Arauj Delmondes G, Santana Cesario FR, et al. Anti-ulcerogenic activity of the hydroalcoholic extract of leaves of *Annona muricata* Linnaeus in mice. Saudi Journal of Biological Sciences. 2016.
[23] Vickers SP, Clifton PG. Animal models to explore the effects of CNS drugs on Food intake and energy expenditure. Neuropharmacology. 2012;63(1):124-31.
[24] Ram A, Lauria P, Gupta R, Sharma VN. Hypolipidaemic effect of *Myristica fragrans* fruit extract in rabbits. J Ethnophamlacol. 1996;55(1):49-53.
[25] Arulmozhi DK, Kurian R, Veeranjaneyulu A, Bodhankar SL. Antidiabetic and antihyperlipidemic effects of *Myristica fragrans* in animal models. Pharmaceutical Biology. 2007;45(1):64-68.
[26] Al-Shammary Hayfaa A, Malik Al-Saadi Sahar AA, Al-Saeidy Awatif M. Evaluation of analgesic activity and toxicity of alkaloids in *Myristica fragrans* seeds in mice. J Pain Res. 2013;6:611-15.
[27] Olaleye MT, Akinmoladun AC, Akindahunsi AA. Antioxidant properties of *Myristica fragrans* (houtt) and its effect on selected organs of albino rats. African J Biotechnol. 2006;5(13):1274-78.
[28] Dewi K, Widyarto B, Erawijantari PP, Widowati W. In vitro study of *Myristica fragrans* seed (nutmeg) ethanolic extract and quercetin compound as anti-inflammatory agent. Int J Res Med Sci. 2015;3(9):2303-10.
[29] Jaiswal P, Sunita K, Singh VK, Singh DK. Biological effects of *Myristica fragrans*. Annu Rev Biomed Sci. 2009;11:21-29.
[30] Tripathi N, Kumar V, Acharya S. *Myristica fragrans*: a comprehensive review. Int J pharm pharm Sci. 2016;8(2):27-30.

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