Pharmacologia 3 (11): 611-616, 2012
ISSN 2044-4648 / DOI: 10.5567/pharmacologia.2012.611.616

Evaluation of Adptogenic Activity of Extracts of *Apium graveolens* on Mice and Rats

Vasanth Kumar and Chandrashekhar M. Sultanpur
Department of Pharmacology, Government College of Pharmacy, Bangalore, India

Abstract: Stress is defined as a nonspecific response of the body to any excessive demand imposed on it. Stress represents a reaction of the body to a stimulus that tends to alter its normal physiological equilibrium or homeostasis, extreme stress leads to various complications like depression, anxiety, immunosuppressant and endocrine disorder including diabetes mellitus, ulcerative colitis, obesity etc. There is extensive search for plant products for use in stress condition which is devoid of adverse effects. This study was planned to investigate the adaptogenic activity (antistress) of the ethanolic and aqueous extracts of *Apium graveolens* at various dose using experimentally induced stress models in mice and rats like anoxia stress tolerance, swimming endurance and cold stress model were used for evaluation of adaptogenic activity. *Withania sominifera* (100 mg kg^{-1}, p.o.) was used as reference standard and it showed significant adaptogenic activity in all three models of stress. The aqueous (200 mg kg^{-1}) and ethanolic (400 mg kg^{-1}) extracts concomitant administration have shown increase in anoxia stress tolarance time and swimming endurance time as compared to control group and also there was marked decrease in blood glucose, cholesterol, triglycerides and BUN level as compare to stress control group in cold stress model. The liver and adrenal gland weight were markedly decreased but no weight change was observed in spleen and testes in this model. The presents study suggests that ethanolic extract of *Apium graveolens* possess more adaptogenic property than aqueous extracts.

Key words: Adaptogenic, stress, free radicals

INTRODUCTION

Stress is defined as a nonspecific response of the body to any demand imposed on it. Stress represents a reaction of the body to a stimulus that tends to alter its normal physiological equilibrium or homeostasis. Every individual is likely to face stressful situations in day to day life (Rai *et al*., 2003). When stress becomes extreme it is harmful for the body and hence need to be treated. Stress is involved in pathogenesis of a variety of diseases and psychiatric disorder such as depression, anxiety, immunosuppressant and endocrine disorder including diabetes mellitus, male impotence, cognitive dysfunction, peptic ulcer, hypertension, ulcerative colitis (Singh *et al*., 2009) and influence on eating behavior in the humans (Gupta *et al*., 2009). Stress is a complex array of internal and external factors which influences on the appetite and consequently increases the amount and types of food intake by humans. When an acute stress is experienced, such as a threat to personal safety, there is an instant physiologic response "flight or fight" which results in the suppression of appetite. Exposure to chronic psychological stressors e.g., job pressure is reason for one of many mental health disorders that contribute to the global burden of stress associated disease. In the chronic stressful situations rather than avoiding food, individual seeks to consume energy dense foods. If stress causes some individuals to consume food in excess than requirement, this may culminate in weight gain and contribute to development of obesity. Internal factors have physiologic mechanisms that regulate appetite by hormone release such as neuropeptide-Y which stimulates food intake and hormone l Eptin reduce food intake (Torres and Nowson, 2007).

Chronic stress is one of the etiologies for obesity, the underlying physiological mechanisms explains potential link between stress and abdominal obesity. The release of glucocorticoids (e.g., cortisol) due to stress response may disrupt the food intake regulation in humans by stimulating the neuropeptide Y system (food intake stimulation) and blunting the effect of the l eptin system (food intake reduction) which leads to obesity (De Vriendt *et al*., 2009).

Obesity is a major cause of morbidity and mortality. The prevalence of obesity (BMI = 30) continues to be a health concern in individuals. Approximately 1.2 billion people in the world are overweight and at least 300 million of them are obese. According to the World Health Organization (WHO), obesity is one of the 10 most preventable health risks (Wolf and Colditz, 1998).

Corresponding Author: Vasanth Kumar, Pharmacology Division, Government College of Pharmacy, Bangalore, India Tel: +918050958077

Obesity is becoming an increasingly great threat to human health. Obesity affects nine organ systems and a major risk factor for gastroesophageal reflux disease, nonalcoholic fatty liver disease, cholelithiasis and colon cancer. The primary environmental determinants of obesity are high calorie intake and decrease in physical activity. It is a multi factorial disorder, which is often associated with a considerable burden of ill health and other disorders such as diabetes; hypertension associated cardiovascular diseases, osteoarthritis and cancer (Liu *et al*., 2010).

As there is an increased scientific research in herbals, it is clear that the medicinal herbs are equally potential in today's synthetic era. According to various studies it's evident that only 20% of the plant flora has been studied and 60% of synthetic medicines owe their origin to plants. Hence, all over the world, there is increase in search of natural system of healing (Sarah *et al*., 2000).

The available synthetic antistress drugs produce severe adverse effects like headaches, dry mouth, insomnia respiratory disturbance, constipation and trigger systemic arterial hypertension associated with cardiac arrhythmias. Herbs can be used on a long-term basis without a risk of serious side effects (Sarah *et al*., 2000).

Man approaches are put forth for treatment of stress, American ginseng is found to reduce stress, lower high blood sugar and adjust immunity. Various studies have shown that Ginsenoside, saponin, glycosides and flavonoid constituents of *Panax quinquefolius* L. (Nocerino *et al*., 2000) and *Withania somnifera* plant are responsible for adaptogenic activity.

The *Apium graveolens extracts* were traditionally used for diabetes, headache, hepatic disorder (Singh and Handa, 1995), hypercholesterolaemic (Tsi and Tan, 2000), stomach ache, CNS stimulant, antimicrobial (Momin and Nair, 2001), antioxidant (Momin and Nair, 2002), anitinflammatory, inflammation and pain (associated with sprains, bruises, wounds, spasmodic colics and rheumatic arthritis (Lewis *et al*., 1985). This study was planned to screen adaptogenic of *Apium graveolens* having the similar chemical constituents as of *Withania somnifera, Panax quinquefolius* L., *V. vinifera, Bacopamonnieri* (Rai *et al*., 2003), Zinziber officinalis, *Piper nigrum*, *Emblica officinalis* and *Terminalia bellerica* (Guevara *et al*., 1999).

MATERIALS AND METHODS

Extraction procedure: The fresh leaves were thoroughly washed and dried in shade. The dried leaves were crushed to coarse powder using a hand mill and sieved (sieve No. 10). Coarse powder was successively extracted in soxhlet apparatus with 70% ethanol (60-80°C) for 24 h and cold maceration with distilled water and added few milliliter of chloroform to avoid fungal growth in aqueous extract. The extracts were concentrated by evaporating them at room temperature and air dried. The above obtained extracts of ethanolic and aqueous extracts were dissolved in distilled water (vehicle). All preparations (doses) were freshly prepared on the day of experiment and administered to the animals.

Preliminary phytochemical analysis: Preliminary phyto-chemical studies were carried out for all the two different extracts of *Apium graveolens* to find out the presence of different phyto-chemical constituents like carbohydrates, proteins, fats and oil, alkaloids, glycosides, terpenoids, flavonoids, tannins and polyphenols (Liu *et al*., 2008; Hu *et al*., 2008).

Animal studies: Swiss albino mice of either sex (25-35 g) or male wistar rats (200-250 g) were used. The animals were obtained from Drug Testing Laboratory (DTL) Bangalore, Karnataka. Animals were maintained in suitable nutritional and environmental condition throughout the experiment. The animals were acclimatized for 10 days under standard laboratory condition i.e., room temperature 25±2°C, relative humidity 65±10%, 12 h light/dark cycle. They were fed with standard pellet diet (Venkateshwara enterprises, Bangalore) and water *ad libitum* under hygienic condition.

Acute toxicity studies (Klein *et al*., 2007): Acute oral toxicity studies were carried out for ethanolic and aqueous extracts of *Apium graveolens* using "acute toxic class method" according to OECD guidelines No. 423. Healthy adult Swiss albino mice (female) weighing between 25 to 35 g was used for the study. Animals were divided in to four groups of three animals each, fasted overnight and administered different doses 5, 50, 300, 2000 mg kg^{-1} b.wt. to each group of animals. The physiological changes in these animals like body temp, CNS activities, micturition and defecation etc were observed for 24 h.

Swimming endurance test (Rangari, 2002): Healthy adult Swiss albino mice of either sex weighing between 25 to 35 g were divided in to six groups of six animals each. Group I animals served as control were administered vehicle alone (1 mL/100 g, p.o.). Group II and III animals were administered aqueous extract of *Apium graveolens* at dose of 200 and 400 mg kg^{-1}, respectively and Group IV and V animals were administered ethanolic extracts of *Apium graveolens* at dose of 200 and 400 mg kg^{-1}. Group

VI animals were administered standard drug (*Withania somnifera* extract 100 mg kg^{-1}). All the extracts were administered orally once daily for 7 days and allowed for free access to food and water. On 7th day 1 hr after extract treatment, all the mice were subjected to swimming endurance test. The mice were allowed to swim individually in a propylene tank of dimension 37×37×30 cm, filled with water to a height of 25 cm maintained at 26±1°C temperatures. The end point was death of animals due to drowning when the animals remained at the bottom of swimming tank. The mean swimming time for each group was calculated.

Anoxia stress tolerance test (Rangari, 2002): Healthy adult Swiss albino mice of either sex weighing between 25 to 35 g were divided in to six groups of six animals each. Group I animals served as control were administered vehicle alone (1 mL/100 g, p.o.). Group II and III animals were administered aqueous extract of *Apium graveolens* at dose of 200 and 400 mg kg^{-1}, respectively and Group IV and V animals were administered ethanolic extracts of *Apium graveolens* at dose of 200 and 400 mg kg^{-1}. Group VI animals were administered standard drug (*Withania somnifera* extract 100 mg kg^{-1}). All the extracts were administered orally once daily for three weeks and were allowed for free access to food and water. At the end of 1st week (7th day), 2nd week (14th day) and 3rd week (21st day) week 1 h after the extract treatment, stress was induced in all mice by placing each animal individually in the hermetic vessel of 500 mL capacity to record anoxia tolerance time. The moment when the animal showed the first convulsions, it is was immediately removed from the vessel and resuscitated if needed. The time duration of animal entry of the animal into the hermetic vessel and the appearance of the first convulsion was taken as time of anoxia tolerance. Appearance of convulsion was very sharp end point, as delay by minute of removal of the animal from the vessel may lead to death of the animal.

Cold restraint stress (Rangari, 2002): Healthy adult Wistar rats were divided in to six groups of six animals each. Group I animals served as control were administered vehicle alone (1 mL/100 g, p.o.). Group II and III animals were administered aqueous extract of *Apium graveolens* at dose of 200 and 400 mg kg^{-1}, respectively and Group IV and V animals were administered ethanolic extracts of *Apium graveolens* at dose of 200 and 400 mg kg^{-1}. Group VI animals were administered standard drug (*Withania somnifera* extract 100 mg kg^{-1}). The extracts were administered orally once daily to respective groups for 10 days. All the animals were subjected to cold stress by exposing them to 4±1°C daily for 2 h. This procedure was repeated for 10 days between 11.00 am to 1.00 pm. On 10th day blood was collected from the hepatic portal vein under light ether anesthesia to estimate biochemical parameters like serum glucose, cholesterol, triglyceride and BUN (Blood Urea Nitrogen). Animals were sacrificed by cervical dislocation and the weight of organs such as liver, spleen, testes and adrenal gland were recorded per 100 g body weight of animal after washing them with alcohol (Hu *et al*., 2008).

Statistical analysis: Data obtained were expressed as Mean±Standard error of mean (SEM). The significance was determined by applying one-way ANNOVA using prism graph pad software. The statistical differences in the sample means were considered significant at $p<0.05$.

RESULTS

The preliminary phytochemical analysis of the ethanolic and aqueous extracts of *Apium graveolens* revealed the presence of the phyto-chemical constituents like alkaloids, carbohydrates (Reducing sugars Non-reducing Sugar), Glycosides (Coumarin Saponin Phenolic and Flavonoid), flavanoids, proteins and aminoacids in both additionally ethanolic extract contains tannins, fats, terpenoids, tannins and polyphenols.

Acute oral toxicity studies of the ethanolic and aqueous extracts of *Apium graveolens* did not exhibit any sign of toxicity up to 2000 mg kg^{-1} b.wt. Since, there was no mortality of the animals found at highest dose. In the present study dose was selected randomly i.e., 200 and 400 mg kg^{-1}.

It was found that ethanolic and aqueous extracts of *Apium graveolens* induced a striking increase in swimming endurance time in mice was found to be dose dependant. The extract shows significant increase in the percentage increase in swimming endurance time over vehicle treated animals by 26.82% in 200 mg kg^{-1} and 38.05% in 400 mg kg^{-1} of aqueous extracts of *Apium graveolens* and 48.65% in 200 mg kg^{-1} and 52.70% in 400 mg kg^{-1} of ethanolic extracts of *Apium graveolens* in the treated groups, respectively. Result are expressed as Mean±SEM (Table 1).

The effect of aqueous and ethanolic extracts of *Apium graveolens* on anoxia stress tolerance test in mice was found to be dose dependant increase (Table 2). Treatment with aqueous extract of 200 and 400 mg kg^{-1} has produced stress tolerance time 33.9±1.38 and 36.65±1.31 in 1st h, 39.76±1.16 and 43.04±1.36 in 2nd h and 46.04±1.21 and 53.59±1.58 in 3rd h. The ethanolic extracts of 200 and 400 mg kg^{-1} has produced stress tolerance time 34.03±0.27and 37.38±0.3 in 1st h, 41.22±0.7 and 46.12±0.87

in 2nd h and 52.14±0.49 and 61.86±0.62 in 3rd h. Treatment with aqueous and ethanolic extracts as shown significant increase in anoxia stress tolerance time. The result express as mean (Table 2).

The chronic stress due to the cold resulted in significant rise in serum glucose, cholesterol, triglycerides and BUN. The aqueous extracts of dose 200 and 400 mg kg^{-1} as shown reduction in the blood glucose 109.04±3.78 and 102.25±2.04, cholesterol 76.37±1.78 and 74.25±2.04, triglyceride 74.61±2.31 and 81.17±4.5 and BUN 25.06±0.67 and 24.58±0.99. Ethanolic extract of dose 200 and 400 mg kg^{-1} as shown reduction in blood glucose 91.95±1.27 and 84.66±1.57, cholesterol 68.75±2.51 and 55.22±1.61, triglyceride 79±2.01 and 77.73±1.40 and BUN 24.31±0.86 and 24.58±1.50. Concomitant treatment with ethanolic extracts has shown significant and greater extent than aqueous extracts alone in reduction of all the parameter (Table 3). The ethanolic and aqueous extracts were shown significant decrease in the cold stress induce elevated level of serum glucose, cholesterol and triglyceride with respect to Standard (*Withaniasomnifera*) activity expect BUN.

The chronic stress due to the cold resulted in significant rise of liver, adrenal gland weight and decrease in spleen and testes weight (Table 4). The aqueous extracts of dose 200 and 400 mg kg^{-1} as shown decrease in the liver weight 7.48±0.18 and 6.30±0.16 and decrease in adrenal gland weight 0.02±0.00 and 0.027±0.00 and increase in spleen weight 1.16±1.16 and 1.50±0.22 and testes weight 1.60±0.00 1.76±0.00. Ethanolic extract of dose 200 and 400 mg kg^{-1} as shown decrease in the liver weight 6.91±0.31 and 6.30±0.22 and decrease in adrenal gland weight 0.024±0.00 and 0.023±0.0 and increase in spleen weight 1.00±12.03 and 1.36±0.21 and testes weight 1.60±0.00 and 1.92±0.23. Concomitant treatment with ethanolic extracts has shown Significant and greater extent than aqueous extracts alone in reduction of all biological parameters. The ethanolic and aqueous extracts were shown significant decrease in the cold stress induced increased liver, adrenal gland weight and increase in weight of spleen and testes respect to Standard activity.

Table 1: Effect of extract of *Apium graveleons* on swimming endurance test in mice. n = 6

Treatments	Dose (mg kg^{-1})	Swimming survival time in mice (min)	Percentage increase in swimming endurance time
Control (received vehicle)	1 mL/100 g	2.10	-
Aqueouse extract	200	2.87±0.23*	26.82
Aqueouse extract	400	3.39±0.17***	38.05
Ethanolic extract	200	4.09±0.39***	48.65
Ethanolic extract	400	4.44±0.28***	52.70
Standard (*Withania somnifera*)	100	5.28±0.26***	60.22

**Significance at p<0.05, ***p<0.001 as compared to control gp

Table 2: Effect of ethanolic and aqueous extracts of *Apium graveolens* on anoxia stress tolerance test in mice n = 6

		Duration of anoxia stress tolerance time		
Treatments	Dose-II	I Week	II Week	III Week
Control (received vehicle)	1 mL/ 100 g	31.66±0.27	31.58±0.33	31.57±4.39
Aqueouse extract	200	33.9±1.38*	36.65±1.31**	39.76±1.16**
Aqueouse extract	400	43.04±1.36**	46.04±1.21*	53.59±1.58**
Ethanolic extract	200	34.03±0.27**	37.38±0.33**	41.22±0.7**
Ethanolic extract	400	46.12±0.87**	52.14±0.49***	61.86±0.62***
Standard (*Withania somnifera*)	100	61.76±9.16***	67.26±1.25***	71.89±1.10***

Significance at **p<0.01, *p<0.05, ***p<0.001 as compared to control gp

Table 3: Effect of ethanolic and aqueous extracts of *Apium graveolens* on biochemical parameters of rats in cold restraint stress n = 6

		Biochemical parameters (mg dL^{-1})			
Treatments	Dose-II (mg kg^{-1})	Glucose	Cholestrol	Triglycerides	BUN
Control (received vehicle)	1 mL/100 g	129±2.04	89.8±1.65	94.73±1.50	27.42±2.08
Aqueouse extract	200	109.04±3.78**	76.37±1.78**	74.61±2.31**	25.06±0.67
Aqueouse extract	400	102.25±2.04**	74.25±2.04*	81.17±4.5**	24.58±0.99
Ethanolic extract	200	91.95±1.27**	68.75±2.51***	79±2.01***	24.31±0.86
Ethanolic extract	400	84.66±1.57**	55.22±1.61***	77.73±1.40***	24.58±1.50
Standard (*Withaniasomnifera*)	100	91.74±1.92***	91.74±1.92***	76.59±1.87**	24.66±0.63

Significance at *p<0.05, **p<0.01, ***p<0.001 as compared to positive control gp (stress rats)

Table 4: Effect of ethanolic and aqueous extracts of *Apium graveolen on* organ weights of rats in cold restraint stress n = 6

		Biological parameters (g/b.wt.)			
Treatments	Dose-II (mg kg^{-1})	Liver (g)	Spleen (g)	Adrenal gland (g)	Testes (g)
Control (received vehicle)	1 mL/100 g	8.66±0.42	0.03466±0.001	0.6676±0.011	1.0833±0.02
Aqueouse extract	200	7.48±0.18**	1.16±1.16*	0.02±0.00***	1.60±0.00***
Aqueouse extract	400	6.30±0.16***	1.50±0.22***	0.027±0.00***	1.76±0.00***
Ethanolic extract	200	6.91±0.31**	1.00±12.03**	0.024±0.00***	1.60±0.00***
Ethanolic extract	400	6.30±0.22***	1.36±0.21***	0.023±0.0***	1.92±0.23***
Standard (*Withania somnifera*)	100	6.03±0.05***	1.52±0.22***	0.0215±0.00***	1.59±0.21***

Significance at *p<0.05, **p<0.01***p<0.001, as compared to positive control group

DISCUSSION

The swimming endurance test was conducted in mice has shown significant increase in the swimming endurance time with both doses of ethanolic and aqueous extracts. The ethanolic extract adaptogenic activity was potential than aqueous extracts. The activity produced may be possibly due to normalization of plasma levels of catecholamine and MAO, which are decreased during stress situation or by decreasing muscle glycogen and preventing accumulation of fat (Friedewald *et al*., 1972). The other possible mechanism for this adaptogenic activity may also be mediated by slowing glycogen depletion, decreases in concentrations of muscle lactic acid and ammonia. The anti-oxidant property of the *Apium graveolens* extracts has already reported and which may also contributes for the adaptogenic activity.

The anoxia tolerance test was conducted in mice has produced increase in the anoxia tolerance time with both doses of ethanolic and aqueous extracts. The anoxia tolerance test of adaptogenic property of the extracts may due to increasing succinate dehydrogenase (SDH) in the brain. This enzyme is responsible for utilization and conservation of energy in the cellular system of the organism which helps adaptive processes during stress (Bhatwadikar *et al*., 1999). The effect is probably related to an increase in cerebral resistance to anoxia and reducing the cerebral consumption of oxygen in anoxic stress. The present study has given emphasis on estimation of stress induced biochemical and biological parameters by *in vitro* method.

Stressful conditions lead to formation of excessive free radicals which are the major internal treat to cellular homeostasis of aerobic organisms. Free radicals are formed in human body both in physiological and pathological conditions in cytosol, mitochondria, lysosomes, peroxisomes and plasma membranes (Patil *et al*., 2006). These free radicals are extremely reactive and unstable chemical species which reacts with proteins, lipids, carbohydrates and nucleic acids in the body. Exposure of lipids in cell membrane to free radicals stimulates the process of lipid peroxidation. The free radical activity and the extent of tissue damage are related quantitatively to the amount of lipid peroxide level in the blood. There are reports suggesting that there is a stress induced accelerated lipid peroxidation (Han *et al*., 2005) (increased MDA) and alterations in lipid profile affecting serum total cholesterol, LDL, VLDL and triglycerides. The aqueous and ethanolic extracts were shown significant reduction in stress induced elevated levels of serum glucose, cholesterol and triglyceride levels (Kaur and Kulkarni, 2001) except BUN in a dose of 200 and 400 mg kg^{-1} with respect to standard (*withania somnifera)*. Concomitant administration of aqueous extracts and ethanolic extracts with a dose of 200 and 400 mg kg^{-1} were shown significant decrease in liver and adrenal gland weight and increase in weight of spleen and testes with respect to standard (*Withania somnifera*).

Both aqueous and ethanolic extracts has produced significant change in the reduction of stress induced biochemical and biological changes in rats. The reduction in the stress induced all the above parameters which may likely to prevent formation of excessive free radicals resulting in preventing internal treat to cellular haemostatis, thus depressing the processes of lipid peroxidation and normalizing the elevated serum glucose, cholesterol and triglycerides.

CONCLUSION

The ethanolic extract of the plant has produced significant effect in swimming endurance time, anoxia tolerance time and biochemical and biological parameters compared to aqueous extracts. Hence, extracts of *Apium graveolens* considered to be having potent antistress effect. These extracts might help in preventing stress induced complications, these results obtained in the study are encouraging to pursuing further studies on the isolated active constitute present in the extracts responsible for the activity.

REFERENCES

Bhatwadikar, A.D., S.D. Chintawon, R.S. Somani, V.S. Kasture and S.B. Kasture, 1999. Antistress activity of Butea monosperma flowers. Indian J. Pharmacol., 31: 153-155.

De Vriendt, T., L.A. Moreno and S. De Henauw, 2009. Chronic stress and obesity in adolescents: Scientific evidence and methodological issues for epidemiological research. Nutr. Metab. Cardiovasc. Dis., 19: 511-519.

Friedewald, W.T., R.I. Levy and D.S. Fredrickson, 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin. Chem., 18: 499-502.

Guevara, A.P., C. Vargas, H. Tokuda and H. Nishino and H. Sakurai *et al*., 1999. An antitumor promoter from *Moringa oleifera* Lam. Mutat. Res., 440: 181-188.

Gupta, S., T.G. Ray and I. Saha, 2009. Over weight, obesity and influence of stress on the body weight among undergraduate medical student. Indian J. Community Med., 34: 255-257.

Han, L.K., Y.N. Zheng, M. Yoshikawa, H. Okuda and Y. Kimura, 2005. Anti-obesity effects of chikusetsusaponins isolated from *Panax japonicus* rhizomes. BMC Complementary Altern. Med., Vol. 5. 10.1186/1472-6882-5-9

Hu, J.N., X.M. Zhu, L.K. Han, M. Saito and Y.S. Sun *et al*., 2008. Anti-obesity effects of escins extracted from the seeds of *Aesculus turbinata* BLUME (Hippocastanaceae). Chem. Pharm. Bull., 56: 12-16.

Kaur, G. and S.K. Kulkarni, 2001. Differential effect of polyherbal, antiobesity preparation, OB-200G in male and female mice and monosodium glutamate treated rat. Indian J. Exp. Biol., 39: 551-557.

Klein, G., J. Kim, K. Himmeldirk, Y. Cao and X. Chen, 2007. Anti-diabetes and anti-obesity activity of *Lagerstroemia speciosa*. Evidence-Based Complement Alternat. Med., 4: 401-407.

Lewis, D.A., S.M. Tharib, G. Bryan and A. Veitch, 1985. The anti-inflammatory activity of celery *Apium graveolens* L. (Fam. Umbelliferae). Pharm. Biol., 23: 27-32.

Liu, R., J.Z. Zhang, W.C. Liu, Y. Kimura and Y.N. Zheng, 2010. Anti-obesity effects of protopanaxdiol types of Ginsenosides isolated from the leaves of American ginseng (*Panax quinquefolius* L.) in mice fed with a high-fat diet. Fitoterapia, 81: 1079-1087.

Liu, W., Y. Zheng, L. Han, H. Wang and M. Saito *et al*., 2008. Saponins (Ginsenosides) from stems and leaves of *Panax quinquefolium* prevented high-fat diet-induced obesity in mice. Phytomedicine, 15: 1140-1145.

Momin, R.A. and G. Nair, 2001. Mosquitocidal, nematicidal and antifungal compounds from *Apium graveolens* L. Seeds. J. Agric. Food Chem., 49: 142-145.

Momin, R.A. and M.G. Nair, 2002. Antioxident, Cyclooxygenasa and topoisomerase inhibitory compounds from *Apium graveolens* L. seed. Phytomedicine, 9: 312-318.

Nocerino, E., M. Amato and A.A. Izzo, 2000. The aphrodisiac and adaptogenic properties of ginseng. Fitoterapia, 71: S1-S5.

Patil, R.A., S.C. Jagdale and S.B. Kasture, 2006. Anti hyperglycemic, antistress and nootropic activity of roots of *Rubia cordifolia* Linn. Indian J. Exp. Biol., 44: 987-992.

Rai, D., G. Goutam, G. Patil, R. Pal, S. Singh and H.K. Singh, 2003. Adaptogenic activity effetc of *Bacopa monniera* (Brahmi). Pharmacol. Biochem. Behav., 75: 823-830.

Rangari, V., 2002. Pharmacognosy and Phytochemistry. Career Publication, Nashik, pp: 130-134.

Sarah, H.B., B. Robert and J.B. Clifford, 2000. High body mass index for age among US children and adolescents. Asian Nat. Prod. Res., 4: 321-327.

Singh, A. and S.S. Handa, 1995. Hepatoprotective activity of *Apium graveolens* and *Hygrophila auriculata* against paracetamol and thioacetamide intoxification in rats. J. Ethnopharmacol., 49: 119-126.

Singh, A.K., S.S. Dhamanigi and M. Asad, 2009. Antistress activity of hydro alcoholic extract of *Eugenia caryophyllus* buds clove. Indian J. Pharmacol., 41: 28-31.

Torres, S.J. and C.A. Nowson, 2007. Relationship between stress, eating behavior and obesity. Nutrition, 23: 887-894.

Tsi, D. and B.K.H. Tan, 2000. The mechanism underlying the hypocholesterolaemic activity of aqueous celery extract, its butanol and aqueous fractions in genetically hypercholesterolaemic rico rats. Life Sci., 66: 755-767.

Wolf, A.M. and G.A. Colditz, 1998. Current estimates of the economic cost of obesity in the United States. Obesity Res., 6: 97-106.