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ORIGINAL ARTICLE

THE EFFECTS OF AEGLE MARMELOSON ANXIETY IN WISTAR RATS AND IT'S COMPARISON WITH DIAZEPAM

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Abstract:

The present study was designed to evaluate the neuropsychopharmacological effects (anxiolytic) of Aegle marmelos extract. These effects were compared with standard drugs of their class (Diazepam). Aegle marmelos extract showed anxiolytic activity in elevated plus-maze and Y-maze models. A. marmelos extract administration at both the doses (100 mg/Kg, 200 mg/Kg, p.o) significantly increased open arm activity in EPM by increasing time spent and number of entries into open arms and decreased the number of visits in Y-maze, as compared to those of control. Effect of higher dose was more than lower dose. This anxiolytic effect was achieved without any impairment in motor co-ordination in contrast to diazepam which has skeletal muscle relaxant activity at antianxiety dose. Present study shows that Aegle marmelos possess anxiolytic properties. All these effects could be attributed a number of phytoconstituents including flavonoids, quercetin, tannic acid, phenols, eugenol, marmesinin, ascorbic acid, skimmianine and saponin.

KEY WORDS:-

Aegle marmelos, anxiolytic effect, diazepam,

INTRODUCTION:

Anxiety is defined as a subjective sense of unease, dread or foreboding. It can indicate a primary psychiatric condition or can be a component of or reaction to a primary medical disease. The anxiety, worry and physical symptoms cause clinically significant distress or impairment in social and occupational life (Reus, 2012). Anxiety disorders include generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, post-traumatic stress disorder, social phobia, specific phobias, and acute stress (Atack, 2003). In general, symptoms of anxiety that lead to pharmacological treatment are those that interfere significantly with normal function. Symptoms of anxiety also are often associated with depression and other medical conditions.

A variety of agents and drug classes provide anxiolytic effects. The primary treatments for anxiety-related disorders include the selective serotonin reuptake inhibitors (SSRIs), Serotonin–norepinephrine reuptake inhibitors (SNRIs), benzodiazepines, the azipirone buspirone, and beta adrenergic antagonists (Atack, 2003). The SSRIs and the SNRI (venlafaxine) are well tolerated with a less side effect profile. In addition to their documented antidepressant activity, they also have anxiolytic activity on chronic treatment. The benzodiazepines are effective anxiolytics for both acute and chronic treatment. However, the clinical uses of benzodiazepines are limited by their side effects such as

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psychomotor impairment, potentiation of other central depressant drugs and dependence liability (Emamghoreishi et al., 2005). β adrenergic antagonists, particularly those with higher lipophilicity (e.g., propranolol and nadolol) are occasionally used for performance anxiety such as fear of public speaking; their use is limited due to significant side effects such as hypotension.

Now a days scientific interest in medicinal plants has burgeoned in recent times due to increased efficiency of new plant derived drugs and rising concerns about the side effects of allopathic medicines.

Aegle marmelos, commonly known as a bael, is one of the gifts of nature to mankind. Numerous pharmacological studies have been conducted on different parts of Aegle marmelos. This plant is having great potential to cure the diseases like diabetes, hyperlipidemia, peptic ulcer, diarrhoea, dysentery, cancers etc. It has also shown its effect as cardio protective, anti bacterial, anti fungal, radio protective, anti pyretic, analgesic, antioxidant, hepatoprotective, and many more.

However, there are only few studies of Aegle marmelos pertaining to central nervous system activities. Hence in the present study, Neuropsychopharmacological effects of Aegle marmelos (Bael) (including antidepressant, nootropic, anxiolytic, analgesic activities and effect on motor function) were studied in wistar rats.

Anxiety disorders, the most prevalent psychiatric illnesses in the general community, are present in 15–20% of medical clinic patients. Anxiety, defined as a subjective sense of unease, dread, or foreboding, can indicate a primary psychiatric condition or can be a component of or reaction to a primary medical disease. The principal components of anxiety are psychological (tension, fears, difficulty in concentration, apprehension) and somatic (tachycardia, hyperventilation, palpitations, tremor, sweating). Other organ systems (eg, gastrointestinal) may be involved in multiple-system complaints. Fatigue and sleep disturbances are common (Reus, 2012).

MATERIALS AND METHODS

The study was conducted in the Department of Pharmacology and Therapeutics, King George's Medical University, Lucknow (Erstwhile Chhatrapati Shahuji Maharaj Medical University). Ethical clearance was obtained from the Institutional Animal Ethics Committee before conducting the study.

EXPERIMENTAL ANIMALS & REARING CONDITIONS

Adult healthy Male Wistar rats weighing 160-200 gm had been used in study. Animals had been obtained from CPCSEA-certified animal house [Indian Institute of Toxicology Research, Lucknow (IITR)]. They were allowed to access normal rat pellet diet and water ad libitum and were kept in Institutional animal house under temperature controlled environment [25 ± 2°C] with 12 hours' light and dark cycle. The animals were housed for two weeks prior to the experiments to acclimatize to new environment.

The maintenance of the animals and the experimental procedures were in accordance with the guiding principles of Institutional Animal Ethics committee and the 'Guide for the Care and Use of Laboratory Animals', National Research Council, 1996 (Latest revision in 2011). The guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Govt. of India were followed.

Dosage Forms, Doses and Sources of the Drugs

Following drugs were used in this study.

(1)Test Drugs - Bael (Aegle marmelos)- Drug (extract form) was dissolved in normal saline and administered orally with the help of feeding cannula in a doses of 100 mg/ kgbw and 200 mg/ kgbw (Shankharananth, 2007). It was purchased from market (Aegle marmelos extract, Himalaya Drug Company).
(2)Standard drugs - Diazepam : Dose 2 mg/kgbw i.p. (Sujith et al., 2011; Kumar et al, 2011). Tablets were purchased from government authorized medical store.

EXPERIMENTAL PROTOCOL -

The present study had been designed to evaluate Neuropsychopharmacological effects of Aegle marmelos (Bael) that includes anxiolytic in male wistar rats.

Animal Groups

A total number of 24 Male Wistar rats were included in the study. They were kept in Institutional Animal House under standard conditions. All the animals received normal rat pellet diet and water ad libitum. All the animals were allowed to get acclimatised to the new environment for period of 2 weeks.

Rats were randomly divided in to 4 groups, each group containing 6 rats: all groups were used to evaluate the effect of Aegle marmelos on learning and memory and its comparison with that of piracetam. Three weeks after the evaluation of effect on learning and memory, all groups were used to evaluate the effects of Aegle marmelos on anxiety. The effects were compared with those of diazepam.

Neuropsychopharmacological Evaluation

Adult male Albino Wistar rats weighing between 160- 200 gms were used. All the animals allowed to get to acclimatize to the new environment for period of 2 weeks. They were provided with normal rat pellet diet & water ad libitum.

Following validated behavioural models of rodents were used to assess the neuropsychopharmacological effects of Aegle marmelous extract.

Assessment of Anxiotytic Activity in rats
By Elevated plus maze (EPM) model:
Grouping:
Albino Wistar rats weighing between 160- 200 gms were randomly divided into 4 groups, each group containing 6 rats.
Group 1: Rats were administered normal saline p.o (1 ml)
Group 2: Rats were administered aegle marmelous extract (100 mg/kg) p.o.
Group 3: Rats were administered aegle marmelous extract (200 mg/kg) p.o.
Group 4: Rats were administered standard drug Diazepam (2 mg/kg) i.p.

PROCEDURE:

The elevated plus-maze model is well established animal model for testing anxiolytic drugs (Pellow et al., 1985). The elevated plus-maze is based on two conflicting tendencies; the rodents drive to explore a novel environment and its aversion to heights and open spaces. The plus-maze apparatus constructed of wood consisting of two open arms (40 x 10 cm) and two closed arms (40 x 10 cm x 41) and a central platform (10 cm×10 cm), arranged in such a way that the two arms of each type were opposite to each other to give the apparatus a plus sign appearance. The entire maze was elevated to a height of 50 cm above the floor (Kulkarni and Reddy, 1996; Vogel and Vogel, 1997).

Animals were brought to the testing room 1 hr prior to testing. Each rat was placed at the centre of the elevated plus maze with its head facing the open arms. The dose administration schedule was so adjusted that each rat was having its turn on the elevated plus-maze apparatus 30 min after diazepam (2 mg/Kg, i.p.) and 60 min after the oral administration of the extracts doses and vehicle.

Each rat was observed for a total of 5 minutes at approximately 2 m distance from the apparatus. Entry into an arm was defined as the point when the animal places all four paws onto the arm. Time was recorded with the help of stop watch.

During the entire experiment, (Kulkarni , 2002), every precaution was taken to ensure that no external stimuli, other than the height of plus-maze could invoke anxiety in the animals.

Room level lighting was kept consistent during all trials.
The procedure was conducted in a sound attenuated room.
The apparatus was cleaned thoroughly between trials to eliminate the possible bias due the odour left by the previous animal.

Assessment:

During the 5 min experiment, following behavior of the rats was recorded (Pellow et al., 1985; Saivasanthi et al., 2011);

Number of entries into the open arm
Number of entries into the closed arm

Time spent in the open arm and
Time spent in the closed arm

The mean for each treated group was determined and compared.

By Y maze model:

The apparatus was constructed of plain wood and consist of identical three arms. Each arm was 44 cm x 16 cm x 24 cm (length x width x height). The maze has an equilateral triangular centre, each arm of the Y beginning from each side of the triangle and extending radially away from the centre at an angle of 120°, forming the letter Y shape of the maze. It was important that the three arms be made similar to prevent preference on the part of the animal when introduced into the maze.

Rats were treated with Aegle marmelos (100 and 200 mg / kg p.o.) or vehicle for consecutive 5 days once daily p.o. and the last dose was given on the 5th day, 60 min prior to experiment and kept individually in one arm of the apparatus. The standard drug Diazepam was given at a dose of 2 mg/kg i.p. 30 min before starting the experiment on the 5th day.

Each rat, naive to the maze, was placed at the end of one arm and allowed to move freely through the maze during an 10-min session. Rat entered in the arm of the maze with all four feet was counted as a single entry (Monique et al., 1997).

Assessment:

The total numbers of visits to different arm were measured visually. Mean of the each group was calculated and used for the comparison of control and drug treated groups.

TECHNIQUE OF INTRAPERITONEAL INJECTION:

To perform an intraperitoneal injection, the rat must be well restrained so that it cannot move during the procedure. This avoids traumatizing the organs once the needle entered the abdomen. The animal was restrained in such a way that the abdomen was exposed. An imaginary line was drawn across the abdomen just above the knees. The 26 G needle was inserted at a point on this line on the animal's right side and close to the midline after disinfecting the injection site. The needle was inserted into the abdomen at an angle of 30 degree and not more than a depth of half centimetre. The small intestines (on the right side) are less likely to be punctured by the needle. Inserting the needle too far caudally or laterally from the insertion point would risk making an injection into the rear leg which would injure the muscle tissue.

Before injecting drugs, a gentle aspiration was done to make sure that the needle had not penetrated a blood vessel, the intestines, or the urinary bladder. In case any fluid was aspirated, the contaminated solution was discarded and the procedure repeated with a new syringe and needle. After injection, the site was again cleaned and animal was observed.

ORAL DRUG ADMINISTRATION:

The desired doses of drugs were calculated on the basis of body weight and dissolved in normal saline just prior to administration. It was then loaded in a syringe fitted with a 16 G ball tipped feeding needle. The rat was restrained using a towel in the left hand. The head of the rat were restrained using the thumb and index finger whereas the tail of the rat was restrained between the ring and little finger. While the rat was lying on the left palm, the ball-tipped feeding needle was introduced from the side of mouth in to the pharynx and then let in to the esophagus when the animal was in the act of swallowing. The drug was then injected in to the esophagus of routs.

STATISTICALANALYSIS

A one-sample Kolmogorov-Smirnov test was used to investigate whether the variables were normally distributed. The one way analysis of variance (ANOVA) was used to assess the comparability of the groups assigned to the treatment groups. Independent t test/Tuke's pairwise comparison was used to compare the different parameters like immobility time, transfer latency, open arm activity, number of visits, reaction time and duration of stay on rotarod between respective treatment groups. Differences in treatment effects within groups and between the treatment and control groups were tested by a multivariate analysis of variance repeated-measures design with treatment type as a between-subject factor (2 groups) and

treatment effect (baseline compared with follow-ups) as a within-subject factor. A significant P value for the treatment effect indicated a change over time in the combined values of the groups and was further investigated by using a paired t test for each individual group. Between group differences in treatment effect were indicated by significant interactions between treatment effect and treatment type. The percent change from baseline to follow-ups was also calculated for each group. Statistical significance was based on a two-tailed P value < 0.05.

OBSERVATIONS AND RESULTS

Assessment of Antianxiety Activity

By Elevated plus maze (EPM) model:

The antianxiety effect on different treatment group (Group 1: Control, Group 2: Aegle marmelous extract 100 mg/kg, Group 3: Aegle marmelous extract 200 mg/kg, Group 4: Diazepam 2 mg/kg) have been summarized in Table-1. The time spent in open and close arm was 60.00±5.86 and 200.00±8.46 respectively in Group 1. The percentage of total time spent in open arm was 23% in Group 1. Almost similar observation was found for Group 2, 3 and 4. The %age of total time spent in open arm was higher in Group 4 than Group 3 (32%), Group 2 (30%) and Group 1 (23%).

Table 8a: Effect of *Aegle marmelous* extract on Time spent in different arms (ELEVATED PLUS MAZE):

Groups	Time spent		Percentage of total time spent	
	Open arm (Mean±SD)	Close arm (Mean±SD)	Open arm	Close arm
Group 9	60.00±5.86	200.00±8.46	23.0	76.9
Group 10	75.17±6.07	174.83±4.35	30.0	69.9
Group 11	85.19±6.02	170.17±5.99	32.0	67.9
Group 13	105.00±5.25	144.83±3.65	42.0	57.9

The average no. of entries in open and close arm was 2.00±0.90 and 9.50±1.04 respectively in Group 1. Almost similar observation was found for Group 2, 3 and 4. The percentage of open arm entries was higher in Group 4 (44.9%) than Group 3 (39.1%), 2 (28.8%) and 1 (17%) (Table-2).

Table 2: Effect of *Aegle marmelous* extract on No. of entries in different arms (ELEVATED PLUS MAZE):

Groups	No of entries (Mean±SD)		Percentage of entries	
	Open arm	Close arm	Open arm	Close arm
Group 1	2.00±0.90	9.50±1.04	17.0	82.9
Group 2	3.67±0.82	9.00±0.90	28.8	71.1
Group 3	5.50±1.04	8.50±1.04	39.1	60.8
Group 4	9.00±0.89	11.0±0.89	44.9	55.0

* Statistically significant

The time spent was significantly different between Group 1 and 2 ($p<0.01$), 3 ($p<0.001$), 4 ($p<0.001$). However, the time spent was significantly different between Group 2 and 4 ($p<0.001$). The time spent was also significantly different between Group 3 and 4 ($p<0.001$). Almost similar observation was found for no. of entries (Table-3).

Table 3: Comparison of antianxiety activity (ELEVATED PLUS MAZE) between groups

Groups		Time spent				No. of entries			
		Open arm		Close arm		Open arm		Close arm	
		Mean d/f	p-value	Mean d/f	p-value	Mean d/f	p-value	Mean d/f	p-value
Grp 9 vs	Group 10	15.17	<0.01*	25.16	<0.001*	1.66	<0.05*	0.50	.811
	Group 11	25.19	<0.001*	29.83	<0.001*	3.50	<0.001*	1.00	.313
	Group 13	45.00	<0.001*	55.16	<0.001*	7.00	<0.001*	1.50	.065
Grp10 vs	Group 11	10.02	0.46	4.66	0.53	1.83	0.01*	0.50	.811
	Group 13	29.83	<0.001*	30.00	<0.001*	5.33	<0.001*	2.00	0.01*
Grp11 vs	Group 13	19.91	<0.001*	25.33	<0.001*	3.50	<0.001*	2.50	<0.01*

* Statistically significant Mean difference - Mean d/f

By Y maze model

The percentage of number of entries was 22.7% lower in Group 2, 30.9% in group 3 and 50.5% in Group 4 than Group 1 (Table-4).

Table 4: Effect of *Aegle marmelous* extract on Average number of visits (Y MAZE):

Group	Number of visits (Mean±SD)	Mean percentage change with respect to control group 1
Group 1	32.33±1.75	--
Group 2	25.00±1.78	22.7
Group 3	22.33±2.58	30.9
Group 4	16.00±2.53	50.5

The average number of visits was significantly different between Group 1 and 2 ($p<0.05$), 3 ($p<0.05$) and 4 ($p<0.01$). The average number of visits was also significantly different between Group 2 and 4 ($p<0.01$) and Group 3 was significantly different with 4 ($p<0.01$) (Table-5).

Table 5: Comparison of antianxiety activity (Y MAZE) between groups:

Groups		No. of visits	
		Mean difference	p-value
Group 1 vs	Group 2	7.33	<0.05*
	Group 3	10.00	<0.05*
	Group 4	16.33	<0.01*
Group 2 vs	Group 3	2.66	>0.05
	Group 4	9.00	<0.01*
Group 3 vs	Group 4	9.00	<0.01*

* Statistically significant

DISCUSSION

Any mental illness significantly affects feeling, thinking and behaviour of person. Stresses of life can precipitate number of mental illnesses. Modern day life style leads to numerous stressful conditions. Anxiety and depression are widely prevalent psychiatric disorders. Moreover their prevalence is increasing day by day. Stress might influence learning-and-memory processes by suppression of adult neurogenesis or by affecting neurochemical systems (for example, catecholamines, opiates, glucocorticoids).

Due to the various side effects of allopathic drugs used for treatment of these diseases, there is continuous search for alternative treatment. So it is prudent to look for options which are efficacious & safer. Indigenous system of medicine including natural herbs are time tested way of treatment. Herbal medicines emphasize the prevention of diseases, rejuvenation of our body systems, maintain balance and harmony and extend the life span (Mahe et al., 1978). Medicinal herbs are indispensible part of traditional medicine practiced all over the world due to easy access, low cost and ancestral experience. Number of

plants have been being used for management of mental illness. Some of them are as follows:

For treatment of anxiety- Bacopa monniera (kumar, 2006), Citrus paradise (Gupta et al., 2010), Azadirachta indica, Centella asiatica;

For treatment of depression- Allium cepa (Sakakibara et al., 2008), Bacopa monniera (Sairam et al., 2002), Centella asiatica (Rajput et al., 2011) , Curcuma longa (Yu et al., 2002);

For improving learning and memory- Ginkgo biloba, Glycyrrhiza glabra, Piper longum, Bramhi, Shatavari, Shankhapushpi.

Several active constituents, which can be of immense importance as drugs, are the precursors for synthesis of many drugs (Dhankhar and Ruhil, 2011). Their effectiveness, low cost and comparative freedom from serious toxic effects make these medicines not only popular but also an acceptable mode of treating diseases even in modern times. Due to the various unavoidable adverse effects of available allopathic medicines, management of various diseases without any untoward side effects is still a challenge for modern medical science. So several herbal plants having various bioactive phytochemicals, possessing several activities and no or very less adverse effects, have been explored.

Number of studies have shown beneficial effects of Aegle marmelos as antiviral, antibacterial, antifungal, anticancer, antihyperlipidemic, antidiabetic and antioxidant agents. However, there are only few studies pertaining to neuropsychopharmacological actions of Aegle marmelos. Many phytoconstituents like flavonoids, saponins, quercetin, phenols, skimmianine and ascorbic acid have shown very important role in management of psychiatric illnesses. The herbal plants which are used for treatment of various psychiatric illnesses in traditional medicines contains these phytoconstituents. Phytochemical screening of Aegle marmelos have shown the presence of many phytoconstituents including flavonoids, saponins, quercetin, phenols, skimmianine and ascorbic acid (Patel and Sahu, 2012). Hence, we hypothesised that, due to the presence of these important phytoconstituents similar to the other herbal plants being used for many psychiatric illnesses, Aegle marmelos could have the potential place in treatment of such type of illnesses.

The present study was undertaken to explore the Neuropsychopharmacological effects of Aegle marmelos (Bael) that includes anxiolytic in wistar rats.

The dose of Aegle marmelos was based on previous studies (Shankharananth, 2007). Extract form needs less amount to be administered, previous trials and experimental studies have been mostly performed using extract (ethanolic or aqueous) forms and also they are soluble in normal saline. Therefore we have chosen the extract-form in our study.

We have chosen the oral route for administering the herbs as a drug, as this route is natural & usual route of taking herbal drugs if prescribed by a physician. This route doesn't need assistance of others and is quite easy in terms of intake.

A total number of 24 male Wistar rats were included in the study. Rats were randomly divided in to 4 groups, each group containing 6 rats. All the animals were allowed to get acclimatised to the new environment for period of 2 weeks. All group were used to evaluate the effect of Aegle marmelos on learning, memory and anxiety.

Antianxiety activity of A. marmelos in rats was assessed by Elevated Plus-Maze model. The elevated plus-maze model is based on two conflicting tendencies; the rodents drive to explore a novel environment and its aversion to heights and open spaces. Each rat was given the choice of spending time in open, unprotected maze arms or enclosed, protected arms. Animals tend to avoid the open areas, especially when they are brightly lit, favouring darker, more enclosed spaces. Thus “anxious” animals spent most of the time in the closed arms while less anxious animals explored open areas longer.

Administration of classic anxiolytic benzodiazepines and other anxiolytic treatments results in increased exploration of the open arms. These results confirm the suitability of the method used in the present study, and agree with previous literature data (Wolfman et al., 1994; Yasumatsu et al., 1994; Lister, 1987).

Results of present study showed anxiolytic activity of Aegle marmelos in elevated plus-maze model as well as Y-maze model. Aegle marmelos extract administration at both the doses significantly increased open arm activity by increasing time spent and number of entries into open arms when compared with control. Higher dose of Aegle marmelos extract (200 mg/kg p.o) showed more percentage increase in open arm activity, but less than Diazepam (Table 1, 2, 3). In Y maze, there was significant decrease in visits at both doses. Higher dose shows more decrease, but less than standard (Table 4, 5). The results were consistent with previous study (Kothari et al., 2010).

Apart from main neurotransmitters, such as monoamines (dopamine, noradrenaline and serotonin), gamma-amino-butyric acid (GABA) and glutamate, many other modulators like neuropeptides (galanin, neuropeptide Y, arginine vasopressin, tachykinin and substance P), neurosteroids and cytokines have been observed to play a modulators role in anxiety states (Anusha et al., 2012; Gilhotra and Dhingra

2010; Millan, 2003).

It has well established that anxiolytic activity of diazepam is due to its GABA facilitatory effect on GABAA receptors (Sieghart, 1994).

Since in our study the pharmacological profile of A. marmelos extract was similar to that of benzodiazepines, it is possible that A. marmelos extract might possess similar mechanism of action.

Phytochemical screening of Aegle marmelos showed presence of flavonoids (Charoensiddhi S. and Anprung, 2008; Sharma et al., 2011). Flavonoids have shown anti-anxiety activity in various studies and the anxiolytic effect of flavonoids has been attributed to its effect on benzodiazepine receptors (Griebel et al., 1999; Medina et al., 1997; Paladini et al., 1999; Wolfman et al., 1994). Therefore, flavonoids present in the extract Aegle marmelous may be responsible for the anti-anxiety activity in present study. Further studies are needed to know the exact mechanism responsible for antianxiety activity.

Beside these, flavonoids has been reported to inhibit the cyclooxygenase enzyme thereby inhibiting prostaglandin synthesis (Desai et al., 2012). Pharmacological studies indicate that flavonoids and saponin have anti-inflammatory activity by reducing the mediators of inflammation (Ramprasath , Shanthi, 2004; Sivraj and Balakrishnan, 2011).

From the results it could be concluded that the extracts exhibit anti-nociceptive activity by both central as well as peripheral mechanisms.

A. marmelos treated group showed significant anxiolytic activity as shown by standard anxiolytic drug Diazepam. This anxiolytic effect was achieved without any impairment in motor co-ordination in contrast to diazepam which has skeletal muscle relaxant activity at its anxiolytic dose.

Hence, due to the presence of a number of phytoconstituents including flavonoids, quercetin, tannic acid, phenols, eugenol, marmesinin, ascorbic acid, skimmianine and saponin etc or any other mechanisms, Aegle marmelos possesses anxiolytic properties. Aegle marmelos can be a safe and effective indigenous drug for the treatment of number of psychiatric disorders including anxiety and depression. However, a more extensive study is necessary to determine the exact mechanism of action of the extracts and its active compound(s).

CONCLUSION

The present study was designed to evaluate the neuropsychopharmacological effects (anxiolytic) of Aegle marmelos extract. These effects were compared with standard drugs of their class (Diazepam). From the results of present study following conclusions may be drawn -

Aegle marmelos extract showed anxiolytic activity in elevated plus-maze and Y-maze models. A. marmelos extract administration at both the doses (100 mg/Kg, 200 mg/Kg, p.o) significantly increased open arm activity in EPM by increasing time spent and number of entries into open arms and decreased the number of visits in Y-maze, as compared to those of control. Effect of higher dose was more than lower dose.

A. marmelos treated group showed anxiolytic activity as shown by standard anxiolytic drug Diazepam. This anxiolytic effect was achieved without any impairment in motor co-ordination in contrast to diazepam which has skeletal muscle relaxant activity at antianxiety dose.

Present study [an experimental study to evaluate the neuropsychopharmacological effect (anxiolytic) of Aegle marmelos extract] shows that Aegle marmelos possess anxiolytic properties. All these effects could be attributed a number of phytoconstituents including flavonoids, quercetin, tannic acid, phenols, eugenol, marmesinin, ascorbic acid, skimmianine and saponin. These phytoconstituents are also present in other herbal extracts which are in use since ages. These phytoconstituents are supposed to be safe without any major adverse effects. These findings are in favour of using A. marmelos as anxiolytic analgesic drug. However the results from present study have limitations in the form of short duration of study, only one or two selected models and less number of animals. The other limitation of this study is lack of measurement of various biochemical parameters at various time intervals. Large scale animal study with inclusion of more animal models and biochemical parameters will strengthen the findings of present study. If A. marmelos passes through the positive results in animal study, clinical studies may be planned in future. No wonder that A. marmelos will become a safe and effective indigenous drug for the treatment of number of psychiatric disorders including anxiety and depression.

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