EVALUATION OF ANTI DEPRESSANT ACTIVITY OF METHANOL EXTRACT OF AEGLE MARMELOS (BAEL FRUIT TREE) LEAVES IN MICE

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INTRODUCTION

▸ Depression is a most common mood disorders characterised by a feeling of worthlessness, sadness and suicidal thoughts .

▸ Affects more than 10-15% of the total population.

PATHOPHYSIOLOGY

- Genetic abnormality

- De arrangement of neurotransmitters like norepinephrine or 5-HT or both in some sites in brain.
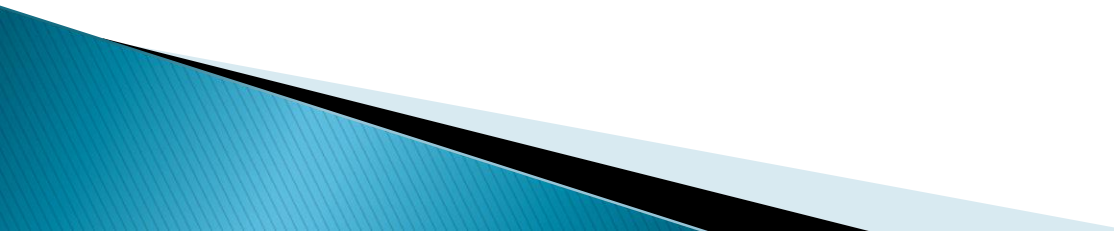
CLASSIFICATION

Depression is classified into 2 major types:

- Unipolar depression (80% of depression cases)
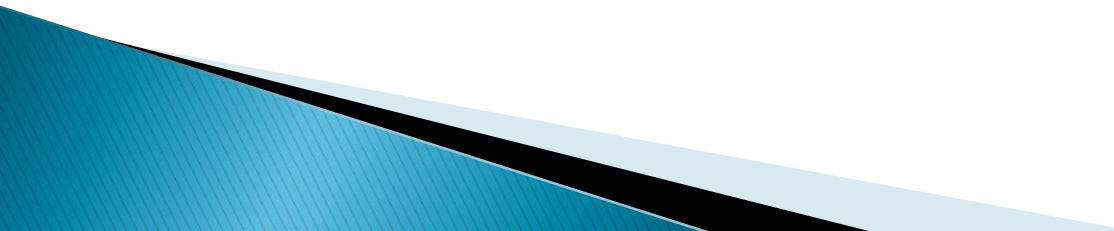- Bipolar depression (20% of cases)

Treatment

- SSRIs & Tricyclic antidepressants etc

INTRODUCTION OF PLANT

▸ *Aegle marmelos (AM)* is an ayurvedic medicinal tree commonly known as the bael fruit tree.

▸ It is found all over India and this is also known as golden apple tree, stone apple tree.

▸ The tree has various medicinal properties.

Several studies on AM showed that the plant has :

- Antidiarrheal
- Anti diabetic
- Anticancer
- Radio protective
- Antifungal
- Antimicrobial
- Anti-inflammatory
- Antipyretic and analgesic activities

- Synthetic drugs available for treatment of depression have various adverse effects like sedation, anticholinergic side effects, anxiety and insomnia.

- Drugs obtained from natural sources are known to cause fewer side effects with same ability to cure disorders in much the same way as their synthetic counterparts.

- Therefore this study is undertaken to evaluate the anti depressant property of methanol extract of *Aegle marmelos* leaves in mice.

OBJECTIVE

▶ To evaluate the antidepressant activity of the methanol extract of *Aegle marmelos* leaves in albino mice.

MATERIALS AND METHODS

Plant materials:

- The leaves of *Aegle marmelos* were collected from their natural habitat in davangere city Karnataka.

Standard drug :

- Imipramine (20mg/kg)
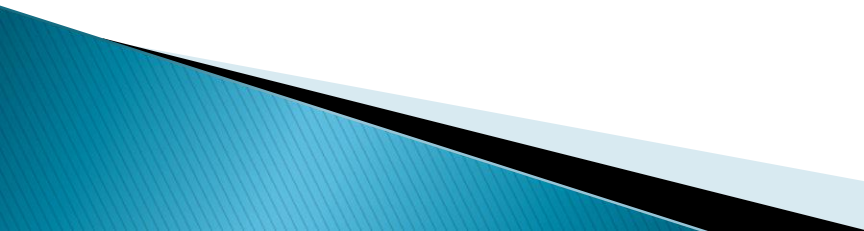
Duration of the study

- 2 months

Preparation of extract:

- The shade dried leaves were powdered (coarse) using a mechanical grinder.

- Coarse powder of 300 g was successively extracted with 1.5 L of petroleum ether, chloroform and methanol, in a soxhlet apparatus at 60–70° C temperature each for 10–12 h

SELECTION OF ANIMALS

Inclusion criteria:

- Healthy albino mice weighing 20-25g of either sex with normal behaviour and activity.
- Animals from institutional animal house (JJM Medical College, Davangere Karnataka.) were used for the study.

Exclusion criteria:

- Pregnant and diseased animals are not included in the study.
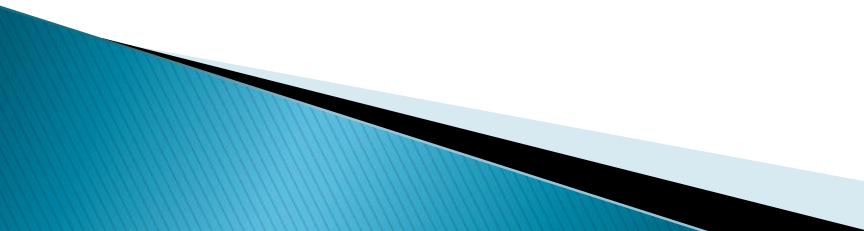- Animals used for other experiments within 4 weeks.

Screening methods :

- Tail suspension method
- Digital actophotometer

The mice weighing 20–25gms of body weight are randomly selected irrespective of sex and grouped into 5 groups so that each group consisting of 6 mice for each dose in both models.

- GA. 10ml/kg (control)
- Imipramine 20mg/kg (standard)
- AM 100 mg/kg (t1)
- AM 200 mg/kg (t2)
- AM 400mg/kg (t3)

TAIL SUSPENSION METHOD

▸ During experiment the mice are suspended on the metal rod placed 55 cm above the ground with help of stands and adhesive tape is placed approximately 1 cm from the tip of the tail.

▸ Mice are considered as immobile when they hang passively and completely motionless for at least 1 min of duration.

▸ The duration of immobility is noted for period of 6min.

DIGITAL ACTOPHOTOMETER

Principle:

- A continuous beam of light from six lights was made to fall on corresponding photoelectric cells, the photoelectric cells will get activated when an animal crossed the beam of light and thereby cuts off (crossing) the rays of light falling on it.

- These crossings are counted automatically for a period of 10 min by the machine.

- The number of cuts off was taken as a parameter of the locomotor activity of the mice.
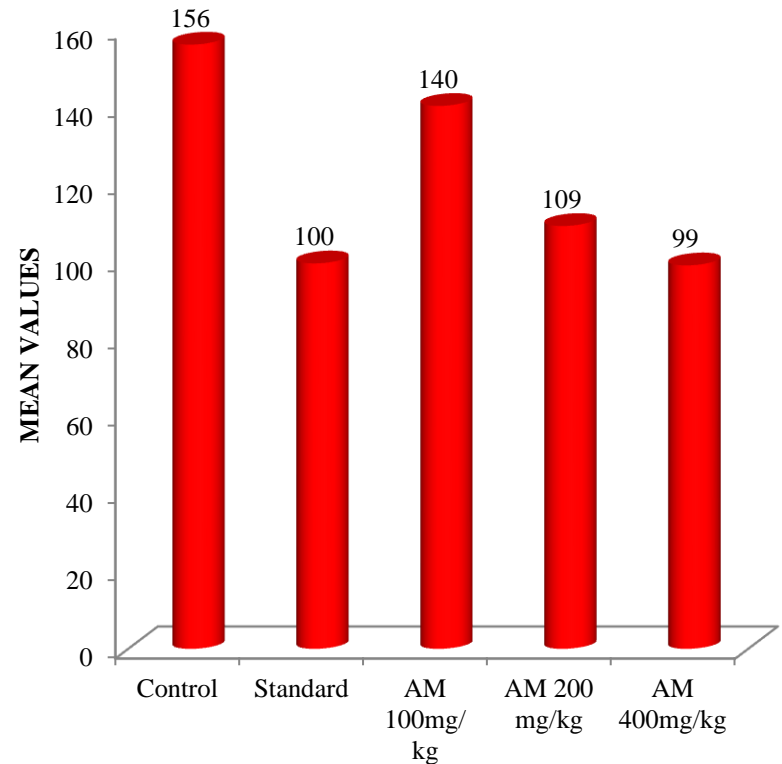
DIGITAL ACTOPHOTOMETER

Statistical analysis

▸ Results are presented as Mean $\pm$ SEM.

▸ One way **ANOVA** was used for multiple comparisons. Following that, **Tukey's post hoc test** was done for comparison between the groups.

▸ For all the tests a 'p' value of 0.05 or less was considered for statistical significance.

RESULTS

Tail suspension test (duration in seconds)				ANOVA	
Groups	DRUGS	Mean	Std. Deviation	F Value	P Value
Group -A	Control	156.17	34.66	7.28	P<0.000
Group -B	Standard	99.67	7.12		
Group -C	AM 100mg/ kg	140.33	34.30		
Group -D	AM 200 mg/kg	109.33	11.71		
Group -E	AM 400mg/kg	99.17	13.92		

Tail suspension test (duration in sec)

Tukey's Post Hoc Multiple Comparison		
Groups	P Value	Significance
A Vs B	P<0.003	HS
A Vs D	P<0.01	S
A Vs E	P<0.002	HS
B Vs C	P<0.01	S
C Vs E	P<0.03	S
S=SIGNIFICANT, HS=HIGHLY SIGNIFICANT		

Actophotometer test (locomotor activity)				ANOVA	
Group	DRUGS	Mean	Std. Deviation	F Value	P Value
Group -A	Control	436.17	35.39	11.33	P<0.000
Group -B	Standard	623.83	111.80		
Group -C	AM 100mg/ kg	508.83	88.96		
Group -D	AM 200 mg/kg	627.00	108.51		
Group -E	400mg/kg	749.33	71.04		

Actophotometer (locomotor activity)
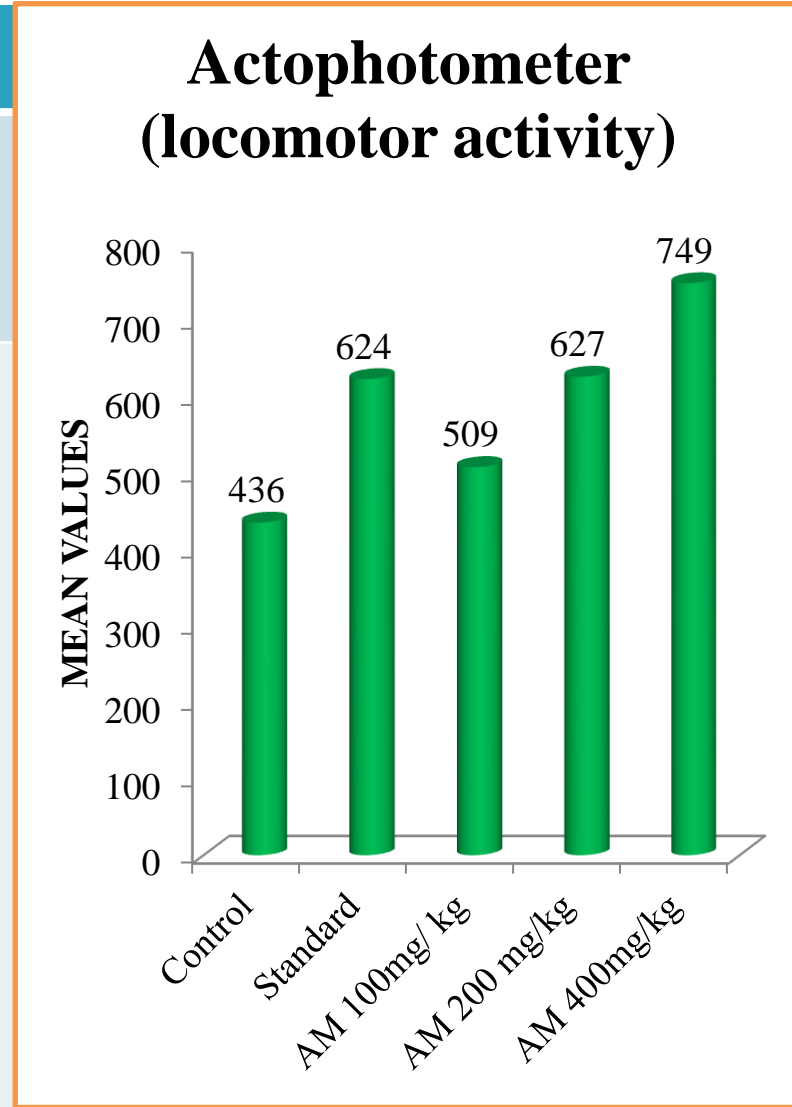
Tukey's Post Hoc Multiple Comparison		
A Vs B	P<0.008	HS
A Vs D	P<0.007	HS
A Vs E	P<0.000	HS
B Vs E	P<0.04	S
C Vs E	P<0.001	HS
D Vs E	P<0.05	S
S=SIGNIFICANT, HS=HIGHLY SIGNIFICANT		

Comparison of tail suspension and actophotometer results

MEAN VALUES

Control	Standard	AM 100mg/ kg	AM mg/kg	200	400mg/	kg

MODEL-1 values: 156.17, 99.67, 140.33, 109.33, 99.17

MODEL-2 values: 436.17, 623.83, 508.83, 627.00, 749.33

◆ MODEL-1   ■ MODEL-2
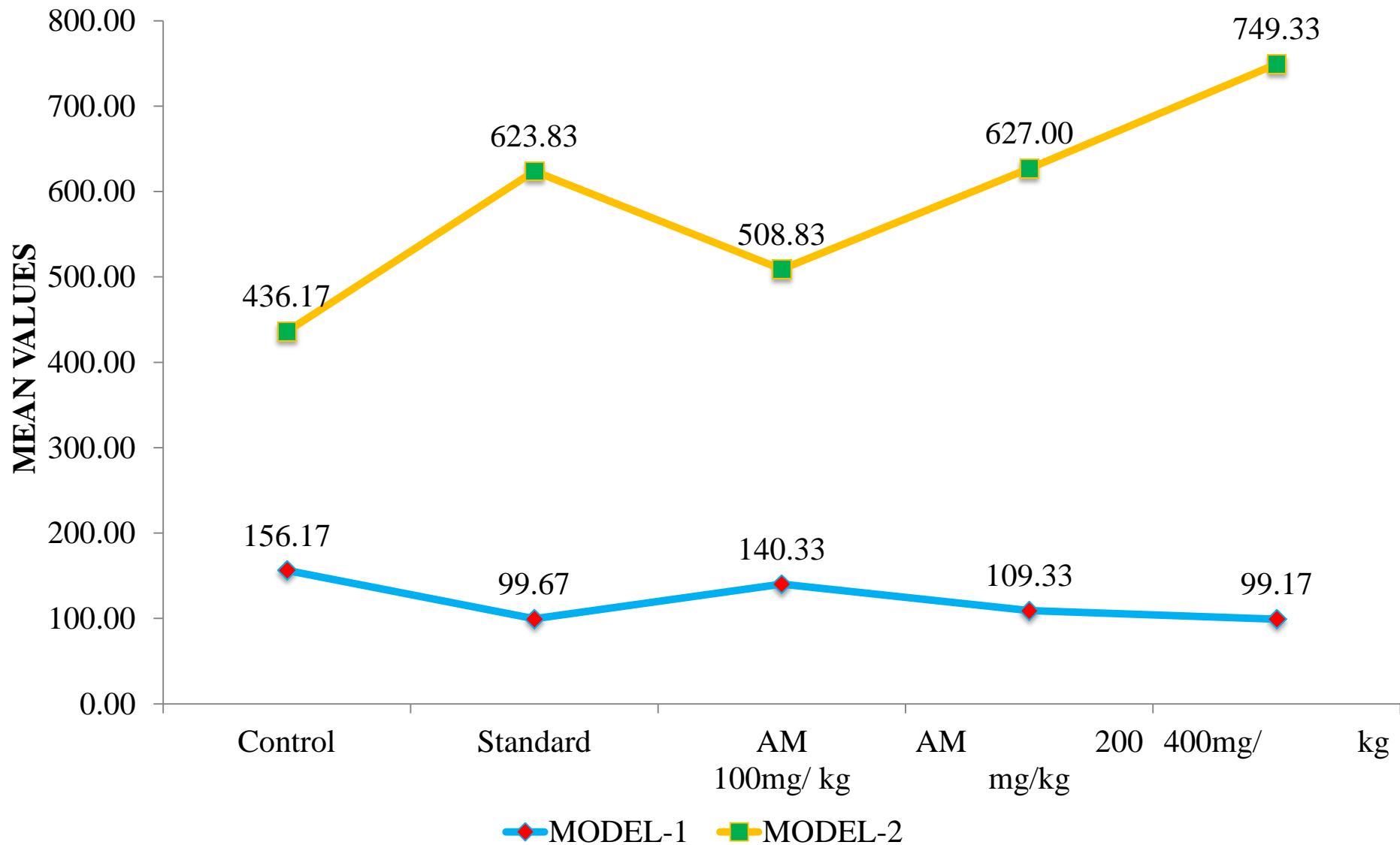
DISCUSSION

- In both actophotometer and tail suspension models AM has shown dose dependent significant increase in locomotor activity and decrease in the duration of immobility respectively.

- Various studies on AM have shown presence of phyto constituents like flavonoids, tannic acid, phenols, marmesinin, ascorbic acid, eugenol, skimmianine and saponin etc which may possess antidepressant properties.

- Alpha1 receptors in mediating antidepressant activity of agents which facilitate noradrenergic neurotransmission and it is attenuated by pre-treatment with alpha1 receptor blocker prazosin.

- Decreased dopamine neurotransmission is also plays role in depression pathology and some studies have demonstrated that blockade of dopamine receptor by haloperidol increased duration of immobility.

- Some studies have shown GABA$_B$ receptor agonist like baclofen is reported to exacerbate depression-like behaviour in animal model of depression and GABA$_B$ receptor antagonists have shown significant antidepressant results on forced swimming model by blocking GABA$_B$ receptors

- In our study methanol leaf extract of *Aegle marmelos* showed significant antidepressant activities probably by modifying monoamines level at post synaptic sites.

CONCLUSION

- Methanol extract of aegle marmelos showed significant antidepressant activity in both models compared to control and standard drug.

- Probably by modifying the monoamine levels in the synaptic sites.

- Hence *Aegle marmelos* may become potential resource for natural anti psychotherapeutic agent against various depression related disorders with fewer side effects compared to current therapy.

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THANK YOU…