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**Research**

# Evaluation of Antidepressant Activity of the Methanolic Extract of Boophone Disticha

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## Abstract

To evaluate the *in vivo* antidepressant activity of methanolic extract of *Boophone Disticha* leaves (MEBD) in Swiss albino mice. Methanolic extract of *Boophone Disticha* (MEBD) leaves was prepared by a continuous method using Soxhlet apparatus. The extract was subjected to phytochemical screening followed by acute oral toxicity studies in mice. MEBD in the doses of 100 and 200 mg/kg body weight was administered to test groups 1 and 2 respectively. Imipramine hydrochloride 15mg/kg body weight was administered to Standard group by oral route. Test group 3 received 100mg/kg (p.o) of MEBD + 10mg/kg (p.o) of Imipramine. Control group received Normal saline 10ml/kg body weight. Antidepressant activity was identified by using modified Forced Swimming Test (FST) and Tail Suspension Test (TST). Period of immobility was observed in both the models which was indicative of anti depressant activity. Standard statistical methods were used to evaluate the results. The results showed significant dose dependent antidepressant effect of MEBD in Swiss albino mice for both the models in all the test groups (Test group I, II and III). MEBD possess significant antidepressant activity. However, further investigations are required to determine its active constituents and molecular level of target mechanism of the extract for further use in humans.

**Keywords:** Antidepressant, MEBD, Forced Swimming test and Tail suspension test.

## INTRODUCTION

Archaeological evidence indicates that the use of medicinal plants dates back to the Paleolithic age,

approximately 60,000 years ago. Written evidence of herbal remedies dates back over 5,000 years, to the Sumerians, who compiled lists of plants. A number of ancient cultures wrote about plants and their medical uses in books called Herbals. In ancient Egypt, herbs are mentioned in Egyptian medical papyri, depicted in tomb illustrations, or on rare occasions found in medical jars containing trace amounts of herbs.1

Among the oldest, lengthiest, and most important medical papyri of ancient Egypt, the Ebers Papyrus dates from about 1550 BC, and covers more than 700 drugs, mainly of plant origin. The earliest known Greek herbals come from Theophrastus of Eresos who in the 4th c. B.C. wrote in Greek Historia Plantarum, from Diocles of Carystus who wrote during the 3rd century B.C, and from Krateuas who wrote in the 1st century B.C.

Herbs also commonly featured in the medicine of ancient India, where the principal treatment for diseases was diet. De Materia Medica, originally written in Greek by Pedanius Dioscorides (c. 40 – 90 AD) of Anazarbus, Cilicia, a Greek physician, pharmacologist and botanist, is a particularly important example of herbal writing; it dominated for some 1500 years until the 1600s.

Herbal Medicine is an interdisciplinary branch between Herbal Medicine and Ayurveda and it covers all the fields of Herbal Medicine related to Botany, Medicinal Plant Research, Pharmacognosy, Phytochemistry, Phytotherapy, botanical medicines, Ayurveda and Natural chemistry, Agriculture Science, Unani Medicine, Biotechnology and Biochemistry.

**Modern herbal medicine2**

The World Health Organization (WHO) estimates that 80 percent of the population of some Asian and African countries presently use herbal medicine for some aspect of primary health care. Pharmaceuticals are prohibitively expensive for most of the world's population, half of whom lived on less than $2 U.S. per day in 2002. In comparison, herbal medicines can be grown from seed or gathered from nature for little or no cost.

According to the World Health Organization, approximately 25% of modern drugs used in the United States have been derived from plants. At least 7,000 medical compounds in the modern pharmacopoeia are derived from plants. Among the 120 active compounds currently isolated from the higher plants and widely used in modern medicine today, 80% show a positive correlation between their modern therapeutic use and the traditional use of the plants from which they are derived.

**Indian system of medicine**

- Siddha
- Ayurvedha
- Unani
- Homeopathy

**Siddha Medicine**

Siddha medicine of traditional medicine originating in ancient Tamilakam (Tamil Nadu) in South India and Sri Lanka. Traditionally, it is taught that the siddhars laid the foundation for this system of medication. Siddhars were spiritual adepts who possessed the ashta siddhis, or the eight supernatural powers. Agastyar is considered the first siddha and the guru of all siddhars; the siddha system is believed to have been handed over to him by Murugan, son of Shiva and Parvati. Siddha is focused on "Ashtamahasiddhi," the eight supernatural power.

Concept of Disease and Cause It is assumed that when the normal equilibrium of the three humors — Vaadham, Pittham and Kapam — is disturbed, disease is caused. The factors assumed to affect this equilibrium are environment, climatic conditions, diet, physical activities, and stress.

**Diagnosis**

V arnam(colour)
Kural (voice)
Kan (eyes)
Thodal (touch)
Malam (stool)
Neer (urine)
Naadi (pulse).

**Ayurvedha Medicine**

The main classical Ayurveda texts begin with accounts of the transmission of medical knowledge from the Gods to sages, and then to human physicians.In Sushruta Samhita (Sushruta's Compendium), Sushrutawrote that

Dhanvantari, Hindu god of Ayurveda, incarnated himself as a king of Varanasi and taught medicine to a group of physicians, including Sushruta. Ayurveda therapies have varied and evolved over more than two millennia.

**Eight components in Ayurvedha**
Kayacikitsa
Kaumara
Salyatantra
Salakyatantra
Bhutavidya
Agadatantra
Rasayanatantra
Vajikaranatantra

**Diagnosis**
Ayurveda has eight ways to diagnose illness,
Nadi (pulse)
Mootra (urine)
Mala (stool)
Jihva (tongue)
Shabda (speech)
Sparsha (touch)
Druk (vision)
Aakruti (appearance)

**Treatment and Prevention**

Two of the eight branches of classical Ayurveda deal with surgery but contemporary Ayurveda tends to stress attaining vitality by building a healthy metabolic system and maintaining good digestion and excretion. Ayurveda also focuses on exercise, yoga, and meditation. Ayurveda follows the concept of Dinacharya, which says that natural cycles (waking, sleeping, working, meditation etc.) are important for health. Hygiene, including regular bathing, cleaning of teeth, skin care, and eye washing, is also a central practice.

**Unani Medicine**

"Unani" or "Yunani medicine" is the term for Perso-Arabic traditional medicine as practiced in Mughal India and in Muslim culture in South Asia and modern day Central Asia. The unani medicine is considered to be a product of pseudoscience by several skeptics. The term means "Greek", as the Perso-Arabic system of medicine was based on the teachings of the Greek physicians Hippocrates and Galen.
The Hellenistic origin of Unani medicine is still visible in its being based on the classical four humours.
Phlegm (Balgham)
Blood (Dam)
Yellow bile (Ṣafra)
Black bile (Sauda)
Diagnosis and Treatment
According to Unani medicine, management of any disease depends upon the diagnosis of disease. In the diagnosis, clinical features such as signs, symptoms, laboratory features and mizaj (temperament) are important. Qualitatively derangement of the normal equilibrium of akhlat (humors) of body which constitute the tissues and organs.

**Homeopathy**

Homeopathy is a system of alternative medicine created in 1796 by Samuel Hahnemann, based on his doctrine of like cures like, a claim that a substance that causes the symptoms of a disease in healthy people would cure similar symptoms in sick people. Homeopathy is a pseudoscience – a belief that is incorrectly presented as scientific.

Homeopathic preparations are not effective for treating any condition. The preparations are manufactured using a process of homeopathic dilution, in which a chosen substance is repeatedly diluted in alcohol or distilled water.

There have been four large scale assessments of homeopathy by national or international bodies, the Australian National Health and Medical Research Council; the United Kingdom's House of Commons Science and

Technology Committee.

Homeopathy uses animal, plant, mineral, and synthetic substances in its preparations, generally referring to them using Latin or faux-Latin names. Examples include arsenicum album (arsenic oxide), natrummuriaticum (sodium chloride or table salt), Lachesismuta (the venom of the bushmaster snake), opium, and thyroidinum (thyroid hormone).

## MATERIALS AND METHODS

The designing of methodology involves a series of steps taken in a systematic way in order to achieve the set goal(s) under the prescribed guidelines and recommendations. It includes in it all the steps from field trip to the observation including selection and collection of the medicinal plant, selection of dose value, standardization of protocol, usage of instruments, preparation of reagents, selection of specific solvents for extraction, formation of protocols and final execution of the standardized protocol. All this requires good build of mind and a good and soft technical hand to handle the materials and procedure in a true scientific manner.

**Drugs and Chemicals**

Drugs and Chemicals used in this study were of analytical grade and of highest purity procured from standard commercial sources in India.

**Table 1: Drugs and Chemicals**

| *S.No* | *Materials* | *Company Name* |
|---|---|---|
| 1. | Imipramine | Procured from Intas pharma |
| 2 | Methanol | Ecoline, Merck Ltd., India. |
| 3 | Normal saline | Ecoline, Merck Ltd., India. |

**Preliminary Phytochemical Screening**

Preliminary phytochemical screening of the plant extract was carried out for the analysis of Alkaloids, Carbohydrates, Tannins, Saponins, Steroids, Phenols, Flavonoids .as per the standard methods[40].

**Detection of Alkaloids:** Extracts were dissolved individually in dilute Hydrochloric acid and filtered.

**Mayer's Test:** Filtrates were treated with Mayer's reagent (Potassium Mercuric Iodide).Formation of a yellow coloured precipitate indicates the presence of alkaloids.

**Wagner's Test:** Filtrates were treated with Wagner's reagent (Iodine in Potassium Iodide). Formation of brown/reddish precipitate indicates the presence of alkaloids.

**Dragendroff's Test:** Filtrates were treated with Dragendroff's reagent (solution of Potassium Bismuth Iodide). Formation of red precipitate indicates the presence of alkaloids.

**Hager's Test:** Filtrates were treated with Hager's reagent (saturated picric acid solution).Presence of alkaloids confirmed by the formation of yellow coloured precipitate.

**Detection of Carbohydrates:** Extracts were dissolved individually in 5ml distilled water and filtered. The filtrates were used to test for the presence of carbohydrates.

**Molisch's Test:** Filtrates were treated with 2 drops of alcoholic α-naphthol solution in a test tube. Formation of the violet ring at the junction indicates the presence of Carbohydrates.

**Benedict's Test:** Filtrates were treated with Benedict's reagent and heated gently. Orange red precipitate indicates the presence of reducing sugars.

**Fehling's Test:** Filtrates were hydrolysed with dil. HCl, neutralized with alkali and heated with Fehling's A&B solutions. Formation of red precipitate indicates the presence of reducing sugars.

**Detection of saponins**

**Froth Test:** Extracts were diluted with distilled water to 20ml and this was shaken in a graduated cylinder for15 minutes. Formation of 1cm layer off a am indicates the presence of saponins.

**FoamTest:**0.5gm of extract was shaken with 2ml of water. If foam produced persists forten minutes it indicates the presence of saponins.

**Detection of steroids.**
**Salkowski's Test:** Extracts were treated with chloroform and filtered. The filtrates were treated with few drops of Conc. Sulphuric acid, shaken and allowed to stand. Appearance of golden yellow colour indicates the presence of triterpenes.

**Libermann Burchard's test:** Extracts were treated with chloroform and filtered. The filtrates were treated with few drops of acetic anhydride, boiled and cooled. Conc. Sulphuric acid was added. Formation of brown ring at the junction indicates the presence of phytosterols.

**Detection of Phenols**
**Ferric Chloride Test:** Extracts were treated with 3-4 drops of ferric chloride solution. Formation of bluish black colour indicates the presence of phenols.

**Detection of Tannins**
**Gelatin Test:** To the extract,1 %gelatin solution containing sodium chloride was added. Formation of white precipitate indicates the presence of tannins.

**Detection of Flavonoids**
**Alkaline Reagent Test:** Extracts were treated with few drops of sodium hydroxide solution. Formation of intense yellow colour, which becomes colourless on addition of dilute acid, indicates the presence of flavonoids.

**Leadacetate Test:** Extracts were treated with few drops of lead acetate solution. Formation of yellow colour precipitate indicates the presence of flavonoids.

**Experimental animals**
**Animals**

Swiss albino mice weighing 25-30g, of either sex were procured from the central animal facility of the Institute and maintained under the standard conditions: room temperature (25±3) °C, humidity 45%–55%, 12 /12hr light/dark cycle. They were fed with commercially available mouse pellet diet and water was allowed ad libitum.

**Grouping**
Animals were randomly divided into 5 groups of 6 each and received drugs as follows:
Group 1: Control group is treated with normal saline (10ml/kg)
Group 2: Standard group treated with drug Imipramine (15mg/kg p.o)
Group 3: Test group-1- MEBD (100mg/kg p.o)
Group 4: Test group -2- MEBD (200mg/kg p.o)
Group 5: -Test group-3- MEBD **(**100mg/kg p.o) +Imipramine (10mg/kg p.o)

**Plant materials and preparation of drug solutio**
**Preparation of plant extracts**
**Preparation of Methanolic Extract**

*Boophone Disticha* leaves were collected from Local Market. Fresh leaves of *Boophone Disticha* were collected and washed under tap water. The leaves extract used was prepared by taking 20gms of finely cut leaves into 250ml beaker containing 200ml of methanol. The contents were mixed well and then the mixture was boiled up to 50-600C for 4-5hrs. The leaves were subjected to wash with 70% of Methanol and made into coarse powder after a shade dry for 1 week. About 500grams of this powder was subjected to Soxhlet extraction for 12 h using Methanol as a solvent under suitable temperature. The extract was further concentrated using vacuum extractor for complete removal of the Methanol (absolute, e"99.5%). The concentrated Methanolic extract of *Boophone Disticha* leaves (MEBD) was used to evaluate the antidepressant activity. Stock solution was freshly prepared by using solvent as Normal saline before dosing from which the different doses were administered by selecting the appropriate

concentration. Before starting the actual experiment phytochemical screening of the methanolic extract and acute oral toxicity study was carried out.

**Forced swim test**

All the groups of animals were subjected to forced swim test after administering the respective drug solutions. On day 0, in training session, mice were forced to swim individually in a vertical Plexiglas cylinder (height: 40 cm; diameter: 18 cm) containing fresh water up to 15 cm maintained at 25°C for 15 minutes and the animals were observed for 6 minutes. In this test, after a brief spell of vigorous activity, animals show a posture of immobility which was characterized by floating motionless in the water making only those movements necessary to keep the head above the water. This immobility reflects the state of depression. Each mouse was subjected to this procedure 24h prior and 1h after administration of respective drugs for 5 minutes in the test session, and the duration of immobility during last 4 minutes was recorded. Actual test recordings were done on 1st, 7th and 14th day of treatment. After recording of mobility immobility time, the each mouse were removed, wiped with dry cloth and allowed to dry before being returned to their home cages.

**Tail suspension test**

All the groups of animals were subjected to this test by suspending them on a string held by a metal stand, by an adhesive tape placed 1 cm from the tip of the tail and the string was 58 cm above the table top. The duration of mobility immobility of the mice was recorded for a period of last 4 minutes during a period of 5 minutes observation. Mice were considered immobile when

They hang passively and completely motionless. During the experiment, each animal under test was both acoustically and visually isolated from other animals. Mice were considered immobile when they hang passively and completely motionless. Readings were taken on 1st, 7th and 14th day of treatment.

## STATISTICAL ANALYSIS

Statistical Analysis The results were computed using GRAPH PRISM PAD version 7 software, one way ANOVA test followed by Post-hoc Tukey's multiple comparison tests were applied for analysis. Observations were expressed as mean ±SD/SEM. The differences between means were considered to be significant at $p<0.05$(95% confidence individuals).

## RESULTS

**Phytochemical screening test**

The freshly prepared extract of the leaves of *Boophone Disticha* was subjected to phytochemical screening tests for the detection of various active constituents. The extract showed the presence of alkaloids, tannins, steroids, phenolic and flavonoids, carbohydrates, and glycosides in crude extract of *Boophone Disticha* leaves as depicted in Table 1.

**Table 2: Result of chemical group tests of the Methanolic extract of *Boophone Disticha* leaves.**

| Chemical Constituents | Results |
|---|---|
| Carbohydrates | ++ |
| Tannins | ++ |
| Flavonoid | ++ |
| Saponin | - |
| Phenols | ++ |
| Steroids | + |
| Alkaloids | +++ |
| Glycosides | +++ |

*ME- Methanolic extract; (+): Present; (-): Absent; (+++); Reaction intensity is high; (++): Reaction intensity is medium; (+): Reaction intensity is normal;*

**Table 3: Shows Acute Toxicity Studies on Methanolic Extract of *Boophone Disticha* leaves**

| Group | Dose (mg/kg) | No. of Animals | Dose difference a | Mortality b |
|---|---|---|---|---|
| 1 | 50 | 6 | - | No |

| | | | | |
|---|---|---|---|---|
| 2 | 100 | 6 | 50 | No |
| 3 | 500 | 6 | 400 | No |
| 4 | 1000 | 6 | 500 | No |
| 5 | 1500 | 6 | 500 | No |
| 6 | 2000 | 6 | 500 | No |

**Acute Oral Toxicity Study**

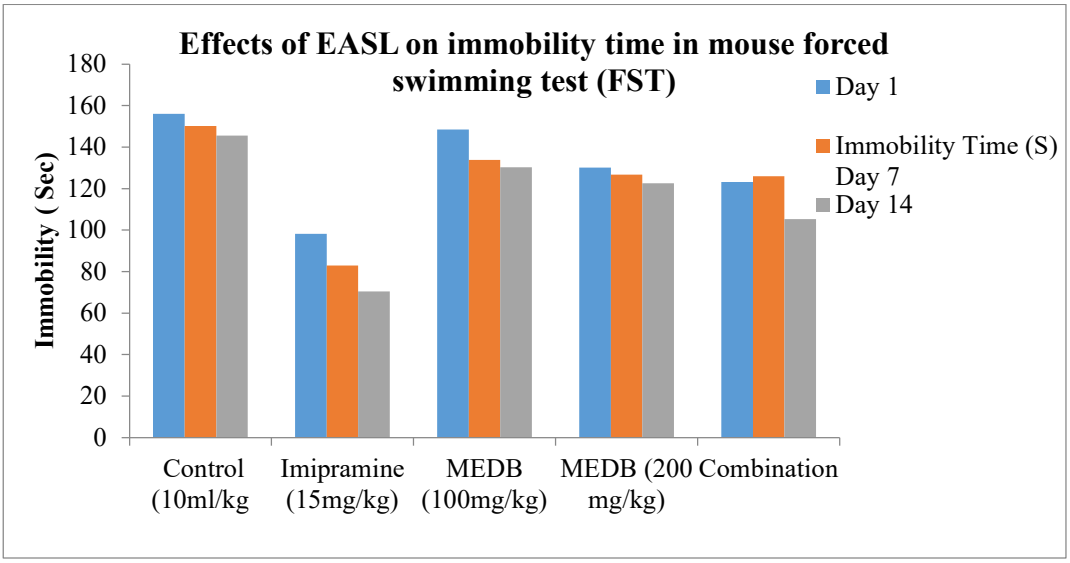
The acute toxicity study aims in establishing the therapeutic index, i.e. the ratio between the pharmacologically effective dose and lethal dose on the same strain and species. The extract of *Boophone Disticha* was safe up to the dose of 2000mg/kg (p.o) body weight. Behavior of the animals was closely observed for the first 3 h then at an interval of every 4 h during the next 48h.

The extract did not cause mortality in the mice during 48h observation but some behavioral changes were noted. There was no significant difference in food and water intake among the animal groups studied. Then the results of the LD50 study performed on mice were expressed using Karber's method. The results obtained were expressed in the table no. 2. From the table no. 2, it can be concluded that there is no mortality and toxicity symptoms for the Methanolic extract. So the dose was optimized up to 2000mg/kg11. (Table 2). LD50 = higher dose -Σ (a x b) /n, n = No. of animals in each group.

**Table 4: Effects of EASL on immobility time in mouse forced swimming test (FST)**

| Group no. | Treatment | Day 1 | Immobility Time (S) Day 7 | Day 14 |
|---|---|---|---|---|
| 1 | Vehicle Control (10ml/kg | 156.1±1.21 | 150.2±0.15 | 145.6±5.86 |
| 2 | Imipramine (15mg/kg) | 98.2± 5.1*** | 83±4.53*** | 70.42±68*** |
| 3 | MEBD (100mg/kg) | 148.5±2.86ns | 133.9±5.36*** | 130.3±5.53*** |
| 4 | MEBD (200 mg/kg) | 130.1±1.07*** | 126.7±0.92** | 122.5±0.62** |
| 5 | MEBD +Imipramine (100mg/kg + 10mg/kg) | 123.2±5.75** | 125.99±6.14** | 105.26±1.53** |

*Values are expressed as mean ± SEM. Comparison between control v/s all the other groups. Statistical test done by one-way ANOVA followed by Post-hoc Tukey's multiple comparison test, *p<0.05, **p<0.01; *** p<0.001; ****p<0.0001.*




*Results are expressed as mean ± SEM (n=6). Data was analyzed by one way analysis of variance (ANOVA) followed by Post-hoc Tukey's multiple comparison test, *p<0.05, **p<0.01; *** p<0.001; ****p<0.0001.*

**Fig 1: Effect of EASL on immobility in the FST using mice**

**Table 5: Effects of MEMP on immobility time in mouse Tail suspension test (TST)**

| Group no. | Treatment | Day 1 | Immobility Time (S) Day 7 | Day 14 |
|---|---|---|---|---|
| 1 | Vehicle Control (10ml/kg | 255±14.82 | 261.56±3.12 | 254.2±1.81 |

| | | | | |
|---|---|---|---|---|
| 2 | Imipramine (15mg/kg) | 115.1±3.598*** | 101.5±2.26*** | 100.1±3.155 |
| 3 | MEBD (100mg/kg) | 231.4±1.231** | 233.2±1.561* | 215.3 ±2.852*** |
| 4 | MEBD (200 mg/kg) | 205.5±1.453*** | 192.1±2.953*** | 175.2± 1.621*** |
| 5 | MEBD +Imipramine (100mg/kg + 10mg/kg) | 134.3±2.862*** | 122.5±1.986*** | 112.1±3.562*** |

*Values are expressed as mean ± SEM. Comparison between control v/s all the other groups. Statistical test done by one-way ANOVA followed by Post-hoc Tukey's multiple comparison test, *p<0.05, **p<0.01; *** p<0.001; ****p<0.0001.*

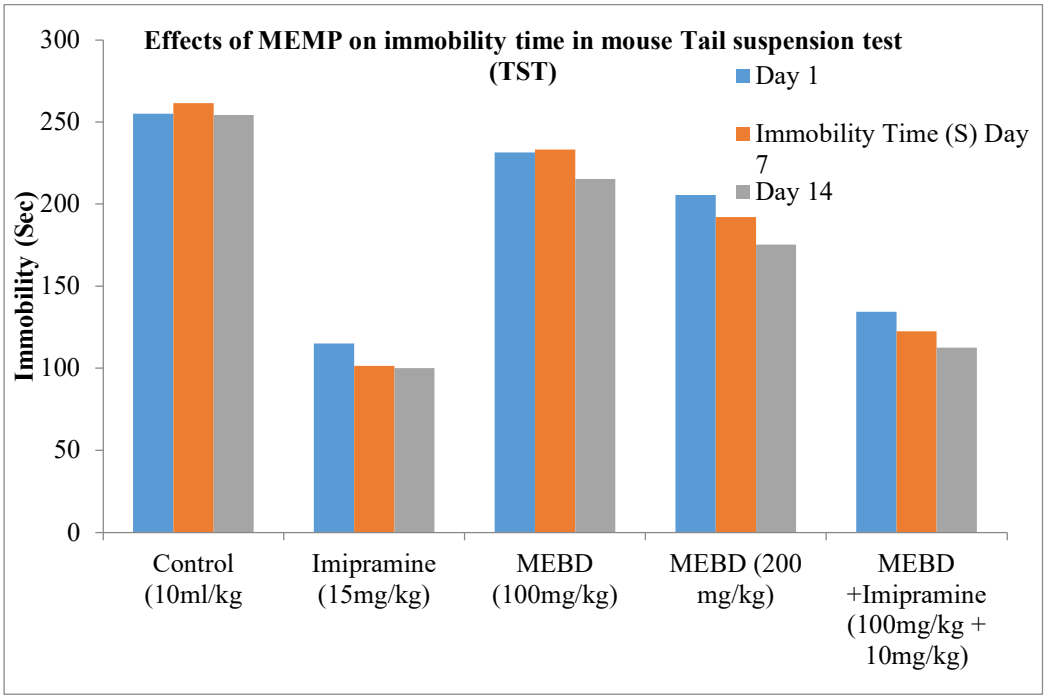



**Fig 2: Effect of EASL on immobility in the TST using mice**

Results are expressed as mean ± SEM (n=6). Data was analysed by one way analysis of variance (ANOVA) followed by Post-hoc Tukey's multiple comparison test, *p<0.05, **p<0.01; *** p<0.001; ****p<0.0001.

LD50 = 2000 – 0
= 2000 mg / kg
$ED_{50} = LD_{50}/ 10$
= 2000 / 10
= 200 mg / kg.

**Forced swim test**

The results of acute model of FST with mice are displayed in Table-3 & Graph-1. In this test, animals of all the test groups showed significant results. The MEMP extract (100 & 200mg/ kg body weight) treated groups exhibited significant delay in the onset of immobility and also significantly reduced time of immobility in the forced swimming test after 14 day of treatment. Post-hoc Tukey's multiple comparison tests analysis demonstrated that the test treatment significantly reduced the immobility time in comparison to the control group (p<0.0001). Combination of MEMP extract (100mg/kg b wt) and Imipramine in the reduced dose (10mg/kg b wt.) i.e. Test group-3 showed significantly reduced immobility and increase in the normal behavior of mice in water filled apparatus and also exhibited antidepressant activity comparable to the standard drug Imipramine (10mg/kg b wt.) i.e. the standard group. On day-1 of the test the immobility time was 156.1, 98.2, 148.5 seconds in test groups 1, 2 and 3. The results were statistically significant in test groups 2 and 3 when compared to control in which the immobility time was 156.1 seconds. However with subsequent drug administration the immobility time was significantly reduced in all test groups to 133.9, 126.7 and 125.99 seconds (test groups 1, 2 and 3 respectively) when compared to control group which was 150.2 seconds on day 7 of the test. On day 14 also reduction in immobility

time was significant in all test groups at 130.3, 122.5 and 105.26 seconds (test groups 1, 2 and 3 respectively) when compared to the control group which was 145.6 seconds. However, the results of the standard drugs were significantly better on all the test days at 98.2, 83 and 70.42 seconds on day 1, 7 and 14 respectively.

**Tail suspension test**

The results of the antidepressant effect of Methanolic extract of *Boophone Disticha* are presented in Table-4 and figure-2.

The extract showed slight reduction in immobility on 1 day treatment, but significantly reduced the immobility time after 7 and 14 days of treatment. Combined group showed almost nearly same significant reduction in immobility time comparable to standard Imipramine. On day 1 of the test the immobility time in test groups 1, 2 and 3 was 231.4, 205.5 and 134.3 seconds respectively which was statistically significant when compared to the control group in which the immobility time was 255seconds. On day 7 the of the test the immobility time in test groups 1, 2 and 3 was 233.2, 192.1 and 122.5 seconds respectively which was statistically significant when compared to the control group in which the immobility time was 261.56 seconds. Similarly on day 14 of the test the immobility time in test groups 1, 2 and 3 was 215.3, 175.2 and 112.1 seconds respectively which was statistically significant when compared to the control group in which the immobility time was 254.2 seconds. The standard drug was far superior in reducing the immobility time on all days of the test at 115.1, 101.5 and 100.1 seconds respectively on days 1, 7 and 14 of the test.

## DISCUSSION

The present study revealed the significant anti-depressant effect of methanolic extract of *Boophone Disticha* leaves in experimentally induced depression by Forced swim test and Tail suspension test models. The methanolic extract of *Boophone Disticha* leaves significantly decreased the immobility time in dose dependent manner which is an indicator of antidepressant activity. *Boophone Disticha* is known to contain natural phytonutrients such as alkaloids, Glycosides, Steroids, flavonoids, Amino acids which may be responsible for improving the vital neurotransmitters involved in memorization, information and processing that may be helpful in depression. The action of triterpinoids and saponins may have resulted in the enhancement of nerve impulse transmission. Literature review of the plant reveals that *Boophone Disticha* also contains Flavonoids & Tannin. Different types of neuroactive steroids were found to be ligands for the GABA receptors in the central nervous system; which indicates that they act as a benzodiazepine like molecules.

The anti-depressant effect may be attributed to the active compounds in the extract that act on GABA/benzodiazepine receptor complex as well as by stimulating glucocorticoid production and its release in the adrenal cortex.

MEBD extract reduced the immobility period during the forced swimming and tail suspension test in comparison with control and exhibited a dose dependent antidepressant activity. The characteristic behavior evaluated in these test, termed immobility, has been considered to reflect behavioral despair similar to that seen in the human depression, and hence any reduction in this parameter reflects antidepressant activity. There is a significant correlation between the clinical efficacy of antidepressant drugs and their potency in FST which was not found in any other model. Interestingly, our data indicate that higher doses of plant extracts were more effective than smaller doses both in forced swim test and tail suspension tests.

The major inhibitory neurotransmitter in central nervous system is Gamma amino butyric acid (GABA). Different type of antidepressants, muscle relaxants, sedative- hypnotic drugs exhibit their action through GABA-ergic inhibition in the CNS that leads to either decrease in the firing rates of critical neurons in the brain or direct activation of GABA receptors by the extracts15. This result indicates the significantly decreased immobility period in FST and TST by EASL. A probable mechanism being our plant extracts acting through GABAergic and/or glutamatergic transmission, cytokine or steroidal alterations cannot be ruled out.

Though the MEBD extract have a modest effect when compared to standard it can serve as an add-on drug to current regimens or may be used along with current regimens in lower dose. The reduction in dose of these Standard drugs is always a welcome change and may help in reducing the adverse effect profile which becomes obvious at higher doses. Further isolation and identification of the bioactive ingredient responsible for anti depressant activity is necessary.

## CONCLUSION

The present study has showed antidepressant activity of MEBD in all classic models such as forced swimming test (FST) and tail suspension test (TST) comparable to the standard drug Imipramine hydrochloride. It was protected the neuron from the neuronal damage and improved the cognitive behavior. However, PF centrally exerts an antidepressant-like effect in the FST by a mechanism involving inhibition of serotonin reuptake, inhibition of MAO activity and evaluated the level of acetylcholine, melatonin and noradrenalin in the brain. Given that these targets have been increasingly reported to be involved in the Pathophysiology of depression and on the antidepressant efficacy. Thus, poly herbal extract possesses antidepressant action demonstrated by modulation of serotonergic pathway, MAO receptors, acetylcholine, noradrenalin and melatonin in rats. However, further studies are needed to elicit its exact mechanism of action and to identify the active ingredient as a potent and efficacious antidepressant agent.

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