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PHYTOPHARMACOLOGICAL EVALUATION OF *CORDIA OBLIQUA* LEAVES FOR ITS ANTIDEPRESSANT POTENTIAL

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Abstract

Introduction: The traditional medicinal system of India, Ayurveda, has mentioned *Cordia Obliqua* as a potential treatment for various ailments. In the current research, the extracts of *Cordia Obliqua* was examined to evaluate their antidepressant potential.

Materials and methods: Here, green leaves of *Cordia Obliqua* were used to prepare chloroform, ethanol, and aqueous extracts (referred to as CdCe, CdEe, and CdAe respectively). The research focused on investigating the antidepressant effects of these extracts using behavioral models in experimental animals. Additionally, locomotor activity was assessed as part of the evaluation process.

Results: Immobility time was reduced with CdEe *Cordia Obliqua* rFST & mTST when at 200 mg/kg and 400 mg/kg body weight. The CdAe showed reduction in immobility time in the repeated rFST) at 400 mg/kg, while in the mTST, significant effects were observed at 200 and 400 mg/kg. Regarding the chloroform extract, it only exhibited a significant reduction in immobility time in the modified Tail Suspension Test (mTST) at a low dose of 200 mg/kg. However, no noticeable change in motor dysfunction was observed with CCl_4 and aqueous extracts at doses of 200 and 400 mg/kg. It is worth noting that the chloroform extract (CdCe) did lead to a significant decrease in locomotor activity at the same dosage level. Taken together, these findings suggest that extracts obtained from *Cordia Obliqua* leaves may possess antidepressant properties.

Keywords: *Cordia Obliqua*; Antidepressant; motor dysfunction; Open field test; Flavonoids.

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1.0 Introduction:

The human central nervous system (CNS) is an intricate and highly intricate framework comprised of over 12 billion nerve cells. Along with the endocrine system, have role for coordinating and regulating the activities of all the organs[1]. Affective disorders encompass a spectrum ranging from major depression to mania, both of which involve abnormal alterations in mood states. Major depression is characterized by various symptoms including feelings of sadness, loss of interest and pleasure, decreased energy levels, a sense of worthlessness, psychomotor retardation or agitation, changes in appetite or sleep patterns, and thoughts of self-harm or suicide[2].

According to WHO in 2008, depression is highly prevalent condition worldwide[3]. This disorder is known for its clinical and biological heterogeneity, presenting in various forms. Depression ranks among the most common and costly psychiatric disorders globally, with approximately 10-30% of women and 7-15% of men experiencing depressive episodes during their lifetime. Additionally, the WHO has identified depression as the fourth leading cause of disability worldwide. Neuropsychiatric disorder like depression increase global burden of diseases, accounting for approximately 14% of the overall burden. This can be primarily attributed to the chronic and disabling nature of depression and its impact on individuals' well-being[4].

Depression is a significant predictor of both physical and social impairment. Mental disorders were responsible for an estimated 40,000 deaths according to WHO in 2005[5]. Although depression is commonly observed among all age types. To achieve optimal remission, it is crucial to implement proactive and sustained antidepressant treatment. Despite the improved safety profiles of newer generation drugs like fluoxetine compared to older drugs like imipramine, their efficacy advantages are limited[6].

Moreover, it is crucial to address the adverse effects that can hinder patient compliance and diminish the effectiveness of the medication. Interestingly, a similar viewpoint was expressed by Bhattacharya et al. in the late 1990s. These authors emphasized the importance of an ideal antidepressant that not only exhibits enhanced efficacy and cost-effectiveness but also provides a rapid onset of action.[7,8]

Herbal medicines are recognized for their significant contributions to healthcare programs, including depression. In India, Ayurveda, a traditional medicinal system, places great emphasis on the pharmacological properties of numerous plants. Cordia Obliqua, a medium-sized tree belonging to the Boraginaceae family, is notable for its medicinal effects, such as astringent, anthelmintic, diuretic, demulcent, and expectorant properties.[9] Different parts of this plant are utilized medicinally for conditions such as chest ailments, bronchitis, and urinary passage issues (fruit). The kernels are externally applied to treat ringworm infections, while the bark decoction is used to address dyspepsia and fever.

One noteworthy aspect of Cordia Obliqua is its flavonoid content[10]. Flavonoids have mood improvement, protection against deficits, and addressing central nervous system disorders, all of which play a significant role in stress-induced depression[11-12]. Phytochemical investigations revealed the presence of flavonol glycosides, in study plant. The primary objective of this study was to investigate the impacts of crude extracts derived from the leaves of *Cordia Obliqua* on animal models[19-44].

2.0 Material and Method

2.1Plant Material:

Leaves of *Cordia Obliqua* were gathered from the surrounding locality. The leaves

underwent taxonomic identification and were verified by a senior botanist to ensure their authenticity. A voucher specimen has been appropriately stored within the department for future reference. Leaves were dried , powdered and subjected for Soxhlet extraction.

2.2 Experimental Animals

Healthy experimental animals were procured from an authorized vendor approved CPCSEA were maintained under suitable conditions with a regular 12-hour cycle of light and darkness. The experimental procedures were conducted in accordance with IAEC and CPCSEA.

2.3 Acute Toxicity study

An acute oral toxicity study was conducted using OECD guidelines-425. Female adult rats (Charles Foster; n = 5) were selected for the study and subjected to an overnight fast. The test substance was administered orally using the up-and-down procedure. Each rat was closely observed for a continuous period of 48 hours to monitor any potential behavioral and neurological changes, as well as to identify any signs or symptoms of mortality or toxic effects.[13].

2.4. Preliminary phytochemical Analysis

A pharmacognostic approach was employed to screen the leaf extract of *Cordia Obliqua* for the presence of active phytoconstituents[14].

3.0 Experimental Design

For the experimental protocol, Wistar rats of both genders with weights ranging from 150g to 200g were employed.

3.1 Rat forced swim test (rFST)[15]:

Each rat was placed in an acrylic cylinder measuring 42×14 cm, filled with water up to a height of 20 cm at a temperature of 25±2°C. Rats were forced to swim for 15-minute during which the duration of immobility was carefully observed and recorded.

3.2 Mice tail suspension test (mTST)[16-17]

The mice were positioned in a manner where they were suspended by their tails from a horizontal bar, approximately 50 cm above the floor. The adhesive tape was applied at a distance of 1 cm from the tip of tail.

3.3 Locomotor activity[18]:

The impact of central nervous system (CNS) drugs on locomotor activities in both humans and animals is well-known. Locomotor activity serves as an indicator of wakefulness and mental alertness (activity level). To evaluate the potential effects on locomotor activity, animals were treated with all extracts at doses of 200 and 400mg/kg. Rats were individually placed in a square arena within the actophotometer for a duration of 10 min & activity was recorded.[17].

4. Result and Discussion:

In the rFST, the acute administration of extract gave dose-dependent and statistically significant reduction in the duration of immobility, comparable to the imipramine (15mg/kg). The effect of 200mg/kg (CdEe-2) was significant compared to the vehicle-treated group but did not surpass the effect of 15mg/kg imipramine-treated animals. However, in the case of CdAe-treated animals, at 400mg/kg (CdAe-2), there was a significant reduction in the duration of immobility. On the other hand, the acute effect of CdCe formulations at 200 and 400mg/kg in the rFST was not significant compared to the vehicle-treated group. Indicating CdCe extract may not have an antidepressant effect.

Typically, animals immediately exhibit escape-oriented behavior followed by a progressive increase in immobility duration. Our observations revealed that acute administration of the test formulations resulted in a significant dose-dependent reduction in immobility duration compared to the vehicle-treated animals.

Moreover, the effect of extracts in the mTST was similar to that achieved by

orally administering imipramine. The effects of 200 mg/kg (CdEe-1) and 400 mg/kg (CdEe-2) were statistically significant. This indicates that the higher dose had a better effect than the lower dose of CdEe test formulations in the mTST.

After acute treatment with CdAe test formulations demonstrated a significant dose-dependent reduction in immobility duration. In the case of CdCe-treated animals, 200 mg/kg significantly reduced immobility duration compared to the vehicle-treated animals, whereas treatment with the high dose (400 mg/kg) may lead to decreased activity in the mTST.

Therefore, the ethanol, aqueous, and chloroform extracts of *Cordia Obliqua* may potentially engage one of the mechanisms employed by established agents. Acute oral administrations of CdEe and CdAe test formulations did not elicit any significant impact on locomotor activity in the open field tests. However, in the case of CdCe-treated animals, a dose-dependent effect was observed after acute treatment. Notably, there was a noteworthy reduction in locomotor activity at doses of 200 and 400 mg/kg compared to the vehicle-treated animals.

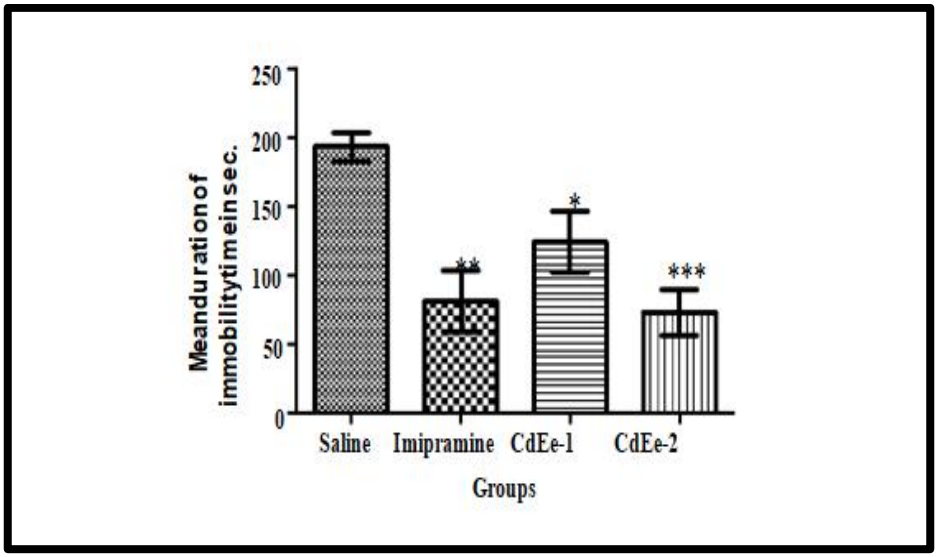

Fig 1: Comparative profile of immobility parameter in rFST after treatment of ethanol extract of *Cordia obliqua*

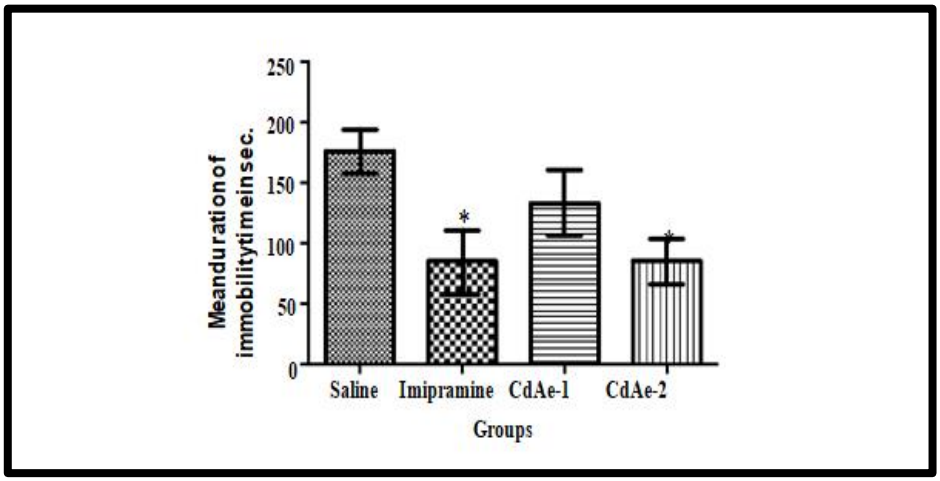

Fig 2: Comparative profile of immobility parameter in rFST after treatment of aqueous extract of *Cordia obliqua*

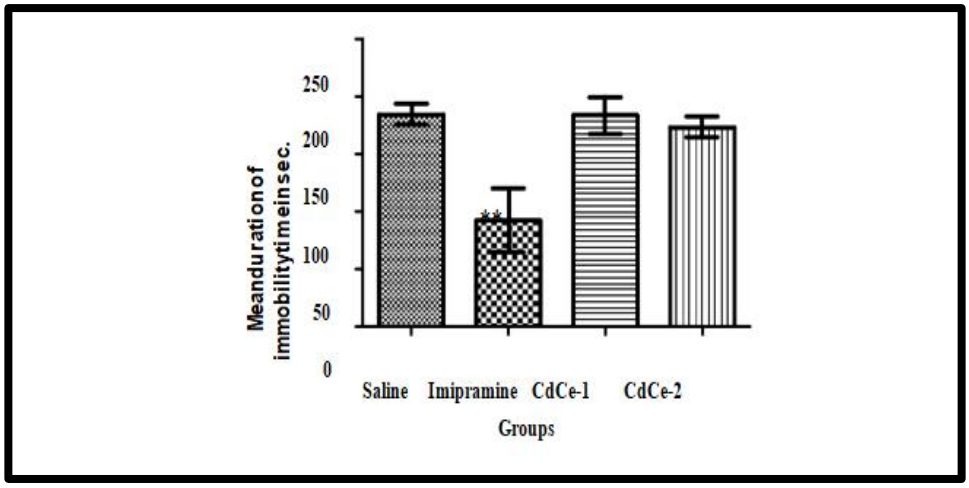

Fig 3: Comparative profile of immobility parameter in rFST after treatment of chloroform extract of *Cordia oblique*

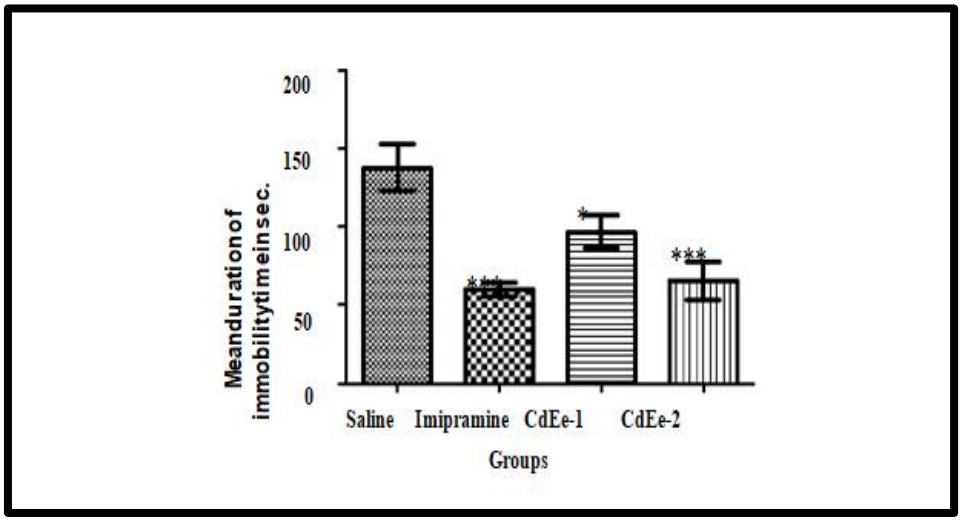

Fig 4: mTST after treatment if 200 and 400mg/kg of ethanol extract of *Cordia obliqua*

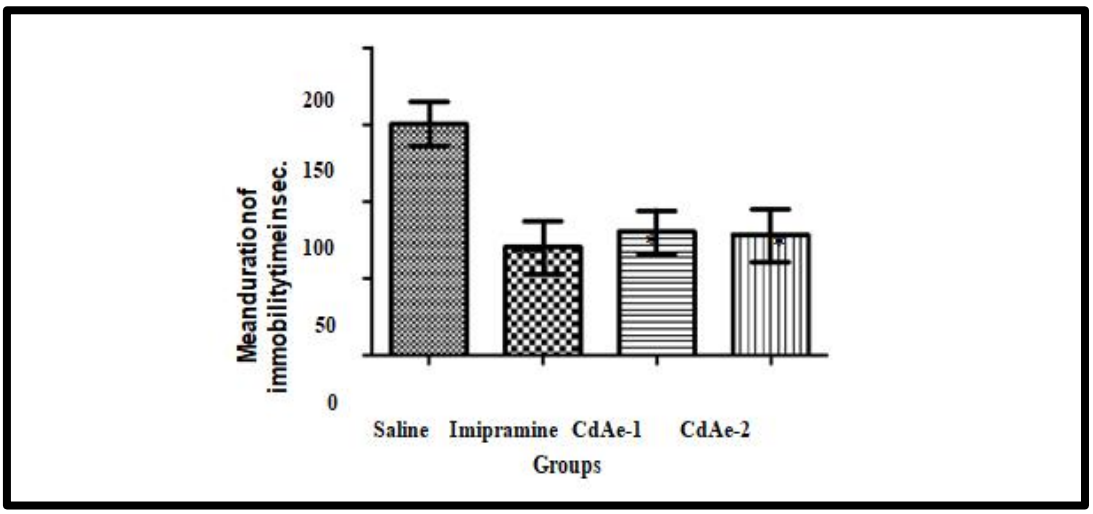

Fig 5: Comparative profile of immobility parameter in rTST after treatment of aqueous extract of *Cordia obliqua*

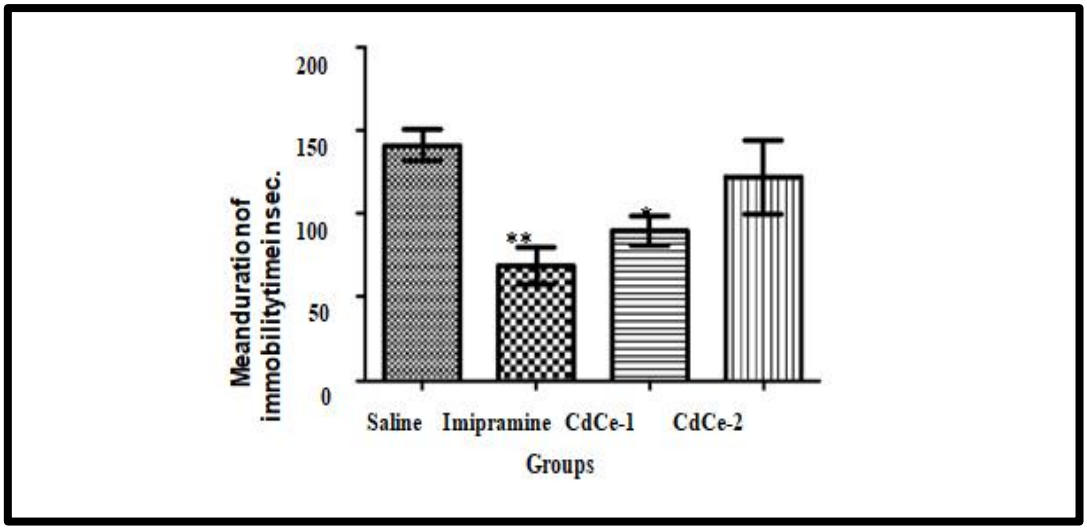

Fig 6: Comparative profile of immobility parameter in rTST after treatment of chloroform extract of *Cordia obliqua*

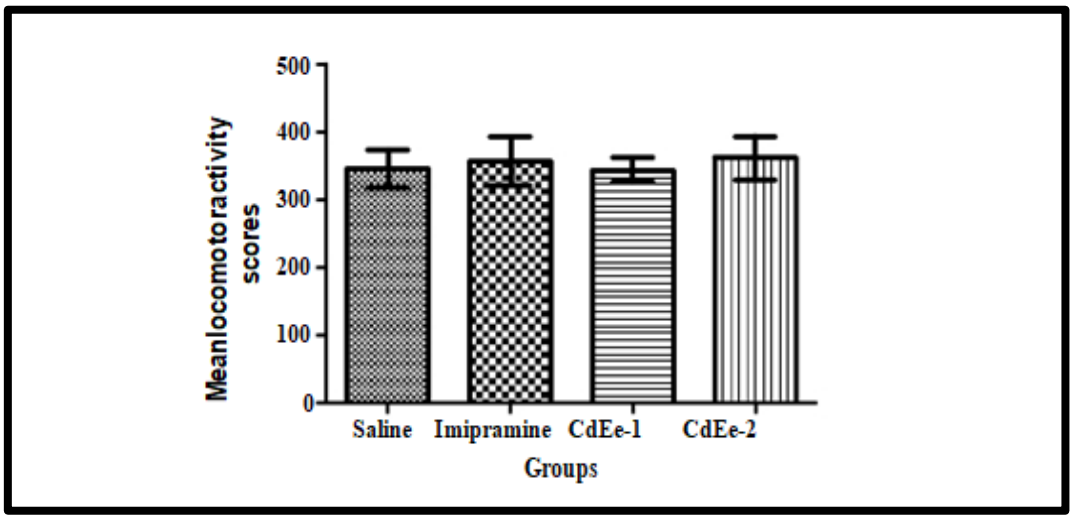

Fig 7: Comparative profile of changes in locomotor activity in rats after treatment of ethanol extract of *Cordia obliqua*

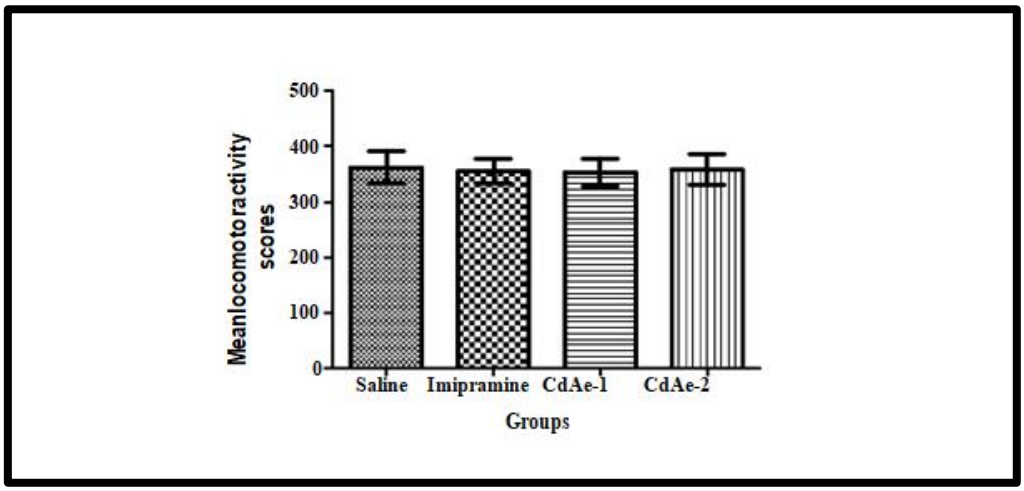

Fig 8: Comparative profile of changes in locomotor activity in rats after treatment of aqueous extract of *Cordia obliqua*

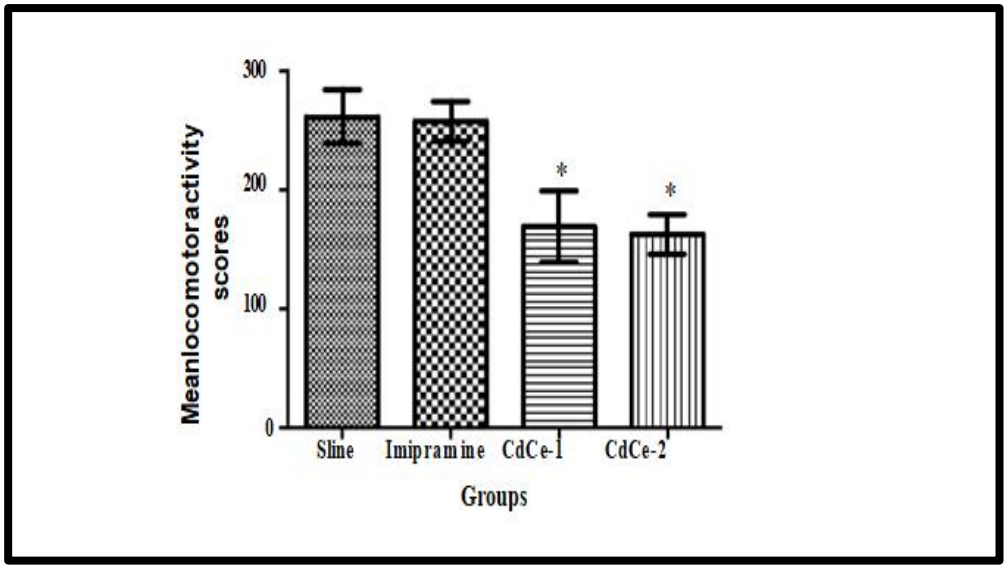

Fig 9: Comparative profile of changes in locomotor activity in rats after treatment of chloroform extract of *Cordia obliqua*

5. Conclusion:

Further investigation is needed to identify the specific bioactive compounds possesing antidepressant potential in *Cordia Obliqua* leaves. The presence of phytochemicals in the leaves indicates the potential for antidepressant activity.

6. References

1. Barar FSK. Essentials of Pharmacotherapeutics, 4th ed; S.Chand Publications, New Delhi.2006:62.
2. Tripathi KD. Essentials of Medical Pharmacology, 6th ed; Jaypee Publications, New Delhi.2008:423-438.
3. Newnham EA, Hooke GR, Page AC. Monitoring treatment response and outcomes using the World Health Organization's Wellbeing Index in psychiatric care. J Affect Disord. 2010; 122:133-8. doi: 10.1016/j.jad.2009.06.005.
4. Malberg JE, Blendy JA. Antidepressant action: to the nucleus and beyond. Trends Pharmacol. Sci. 2005; 26:631-638.
5. World Health Organization, the world health report 2001: Mental Health: new understanding, new hope. 2001, Geneva.
6. Martin P, Patel V, Saxena S, Maj M, Maselko J, Phillips MR, Rahman A. No health without mental health. Global Mental Health Lancet 2007;370:859-77.
7. Millan MJ. The role of monoamines in the actions of established and "Novel" antidepressant agents: a critical review.European Journal of Pharmacology 2004; 500:371-384.
8. Bhattacharya SK, Satyam KS, Ramanathan M. Experimental methods for evaluation of psychotropic agents in rodents: II- Antidepressants. Indian Journal of Experimental Biology 1999; 37:117-23.
9. Anjura J, Parabia M, Bhatt G, Kumar R. Nature heals, A glossary of selected indigenous medicinal plants of India 2nd ed. Sristi innovation Publication, Ahemadabad, 2002.
10. Kuppast IJ, Nayak PV. Wound healing activity of Cordia oblique forst. f. Fruits. Natural Product Radiance 2006; 5:99-102.

11. Caccia, Silvio. Antidepressant-Like Components of Hypericum perforatum extracts: An Overview of Their Pharmacokinetics and Metabolism. Current Drug Metabolism 2005; 6:531-543.
12. Sakakibara H, Ishida K, Grundmann O, Nkajima JI, Seo S, Butterweek V. Antidepressant effect of extract from *Ginkgo giloba* leaves in behavioral models. Biological & pharmaceutical bulletin 2006;29 (8) :1767-1770
13. OECD. (2006). Guideline for the testing of chemicals 425. Acute oral toxicity-UDP Limit test and Assessment No. 23.
14. Kokate, C.K. 1996, Practical Pharmacognosy. Delhi, Vallabh Prakashan.
15. Porsolt DR, Pichon LM, Jalpre M. Depression: a model sensitive to antidepressant treatments. Nature 1997; 266:730-734.
16. Steru L, Chermat R, Thierry B, Simon P. The tail suspension test: A New method for screening antidepressant in mice. Psychopharmacology 1985; 85:367-370.
17. Mahesh R, Sharma P, Gautam BK, Bhatt S, Pandey DK. Antidepressant-like activity of cannabinoid type-1 receptor antagonist, rimonabant. : Behavioral investigation in animal model depression. International Journal of Pharmacy and Biosciences 2010; 1:1-13.
18. Kulkarni SK, Hand Book of Experimental Pharmacology 3rd ed. Vallabh Publications.Delhi.2005:192.
19. Devhare, L. D., Ghugare, A. P., & Hatwar, B. P. (2015). Method development for determination of water content from various materials by spectrophotometry and it's validation. International journal of drug delivery, 7(4), 233-240.
20. Devhare, L. D., & Kore, P. K. (2016). A recent review on bioavailability and solubility enhancement of poorly soluble drugs by physical and chemical modifications. Research chronicle in health sciences, 2(5), 299-308.
21. Tonde, T. U., Kasliwal, R. H., & Devhare, L. D. (2016). Quantitative Estimation of Bacoside A in Polyherbal Memory Enhancer Syrup for Memory Boosting Activity Using HPTLC Method. Research Chronicle in Health Sciences, 2(6), 315-320.
22. Ghugare, A. P., Devhare, L. D., & Hatwar, B. P. (2016) Development and validation of analytical methods for the simultaneous estimation of Nimorazole and Ofloxacin in tablet dosage form. 8(3), 96-98.
23. Salpe, H. G., Devhare, L. D., Ghugare, A. P., & Singh, N. (2016). Formulation and evaluation of hpmc coated diltiazem hcl tablet and its comparison with other marketed preparation. Research chronicle in health sciences. 3(1), 11-17
24. Makhani, A. A., & Devhare, L. D. (2017). Development and validation of vierordt's spectrophotometric method for simultaneous estimation of Drotaverine and Nimesulide combination. Research chronicle in health sciences, 3(2), 22-28.
25. Makhani, A. A., & Devhare, L. D. (2017). Development and Validation of Analytical Methods for Drotaverine and Nimesulide Combination. Research Chronicle in Health Sciences, 3(3), 40-44.
26. Katole, G., & Devhare, L. D. (2020). Recent insight into some emerging natural resources with remarkable hepato protective potentials. International journal of pharmaceutical science and research, 5(1), 41-47.
27. Uplanchiwar, V. P., Raut, S. Y., & Devhare, L. D. (2021). Pharmacological assessment of

antiulcer activity of gloriosa superba linn tubers in experimentally induced gastric ulcers. Journal of medical pharmaceutical and allied science, 10(3), 2852-2856.

28. Devhare, L. D., & Gokhale, N. (2021). Acid neutralizing capacity and antimicrobial potential of selected solvent extract from various indigenous plants. Journal of Advanced Scientific Research, 12(04), 175-179.
29. Devhare, L. D., & Gokhale, N. (2022). Antioxidant and Antiulcer property of different solvent extracts of Cassia tora Linn. Research Journal of Pharmacy and Technology, 15(3), 1109-1113.
30. Devhare, L. D., & Gokhale, N. (2023). In silico anti-ulcerative activity evaluation of some bioactive compound from Cassia tora and Butea monosperma through moleculer docking approach. International journal of pharmaceutical sciences and research, 14(2), 1000-1008.
31. Devhare, L. D., & Gokhale, N. (2023). A brief review on: phytochemical and antiulcer properties of plants (fabaceae family) used by tribal people of gadchiroli maharashtra. International journal of pharmaceutical sciences and research, 14(4), 1572-1593.
32. Nikam N, R., Vaishnavi, A., & Devhare, L. D. (2023). Parenteral drug delivery approach: an overview. Journal of xidian university, 17(1), 386-400.
33. Shende, S. M., Bhandare, P., & Devhare, L. D. (2023). In-vitro: micropropagation of mint and investigate the antibacterial activity of mint extract. Eur. Chem. Bull, 12(5), 780-784.
34. Devhare, L. D., Bodhankar, S. S., Warambhe, P., Uppalwar, S. V., Uchibagle, S., & Shende, S. M. (2023). Important role of food and nutritional security during Covid-19: A survey. European Chemical Bulletin. 12(5), 1363-1374.
35. Pathak, N. R., Devhare, L. D., Sawarkar, K. R., Dubey, M., Trivedi, V., Thakre, A. R., & Thakare, V. M. (2023). Aclinial reveiew on pharmacological evaluation of Thiazolidine and Isatin in the new millenium as magic moieties. European Chemical Bulletin. 12(5), 3410-3417.
36. Singh, S., Minj, K. H., Devhare, L. D., Uppalwar, S. V., Anand, S., Suman, A., & Devhare, D. L. (2023). An update on morphology, mechanism, lethality, and management of dhatura poisoning. European Chemical Bulletin. 12(5), 3418-3426.
37. Suruse, P. B., Jadhav, B. A., Barde, L. G., Devhare, L. D., Singh, S., Minj, K. H., & Suman, A. (2023). Exploring the potential of Aerva Lanata extract in a herbal ointment for fungal infection treatment. Journal of Survey in Fisheries Sciences. 10(1), 1922-1932.
38. Shende, S. M., Meshram, B., Karemore, H., & Devhare, L. D. (2023). Development And Characterization of Glycerogelatin Suppositories For Enhanced Efficacy. European Journal of Pharmaceutical and Medical Research. 10(6), 522-528.
39. Thakare, V. M., Umare, S. A., & Devhare, L. D. (2023). Separation and purification of carboxymethyl cellulose from Spinacia Oleracea for use in pharmaceutical dosage form. European Chemical Bulletin. 12(5), 4062-4080.
40. Suruse, P. B., Deshmukh, A. P., Barde, L. G., Devhare, L. D., Maurya, V. K., Deva, V., & Priya, N. S. (2023). Rimegepant embedded fast dissolving films: A novel approach for enhanced migraine relief. Journal of Survey in Fisheries Sciences, 10(1) 2071-2084.
41. Prasad, M., Suman, A., Srivastava, S., Khosla, G., Deshmukh, A., Devhare,

L. D., & Meshram, S. S. Butea monosperma stem bark extract partially reverses high fat diet-induced obesity in rats. European Chemical Bulletin. 12(5), 4267 – 4273.

42. Shukla, M., Tiware, S. A., Desai, S. R., Kumbhar, S. T., Khan, M. S., Mavai, Y., & Devhare, L. D. (2023). Pharmacological Evaluation of Gloriosa Superba Linn Flower Extract For Antiulcer Activity. Journal of Survey in Fisheries Sciences. 10(2) 463-470.
43. Polireddy, P., Malviya, V., & Devhare, L. D. (2023). Assessment of Hepatoprotective Potential of Ecbolium Linneanum Extract on Experimental Animals. Journal of Coastal Life Medicine. 2(11) 884-890
44. Devhare, L. D., Hiradeve, S. M., & Bobade, T. (2017). Method Development & Validation For Determination of Water Content. LAP LAMBERT Academic Publishing.