Review Article

THE USE OF PLANT EXTRACT IN A MOUSE MODEL OF DEPRESSION: A REVIEW

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ABSTRACT

Depression is a mood disorder which is among the most dominant forms of psychiatric disorders and a major cause for morbidity and mortality. Since, many synthetic drugs are being used as anti-depressant, but due to adverse effects it leads to patient non-compliance. Thus, there is a need to search for plants oriented anti-depressant drugs and also develop a suitable animal model to clearly elucidate its effects. A number of medicinal plants have shown anti-depressant activities. This review attention is towards plant extract and its use in best animal model which will certainly highlights their influence on the development of novel therapeutic drugs.

Key words: Plant extract, depression, animal model, herbal medicine.

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INTRODUCTION

Depression is the most common disorders of mood rather than disturbances of thought or cognition; it may range from a very slight condition, bordering on normality, to severe depression accompanied by hallucinations and delusions. Worldwide, depression is a major cause of disability and premature death. In addition to the noteworthy suicide risk, depressed individuals are more likely to die from other causes, such as heart disease or cancer. There are two distinct types of depressive syndrome, namely *unipolar depression*, in which the mood swings are constantly in the same direction, and *bipolar affective disorder*, in which depression alternates with mania. The monoamine theory in 1965, recommends that depression results from functionally deficient monoaminergic (noradrenalin and/or 5hydroxytryptamine) transmission in the central nervous system[1]

According to the WHO report, approximately 450 million people suffer from a mental or behavioral disorder and only a small minority of the patient receives the basic treatment [2]. This mounts to 12.3% of the global burden of disease, and will rise to 15% by 2020[3]. Presently, out of a population of some 152 million the estimated number of mentally disturbed people in Pakistan is more than 14 million. According to World Health Organization statistics, about 46% to 66% of women and 15% to 25% of men in Pakistan, suffer from depression and anxiety (WHO, 2005).

Ambiguity about the biochemical pathogenesis of depression raises the opportunity of finding new antidepressants acting on other (non-amine-related) targets. Many different approaches have been taken, and several compounds are in development [4].

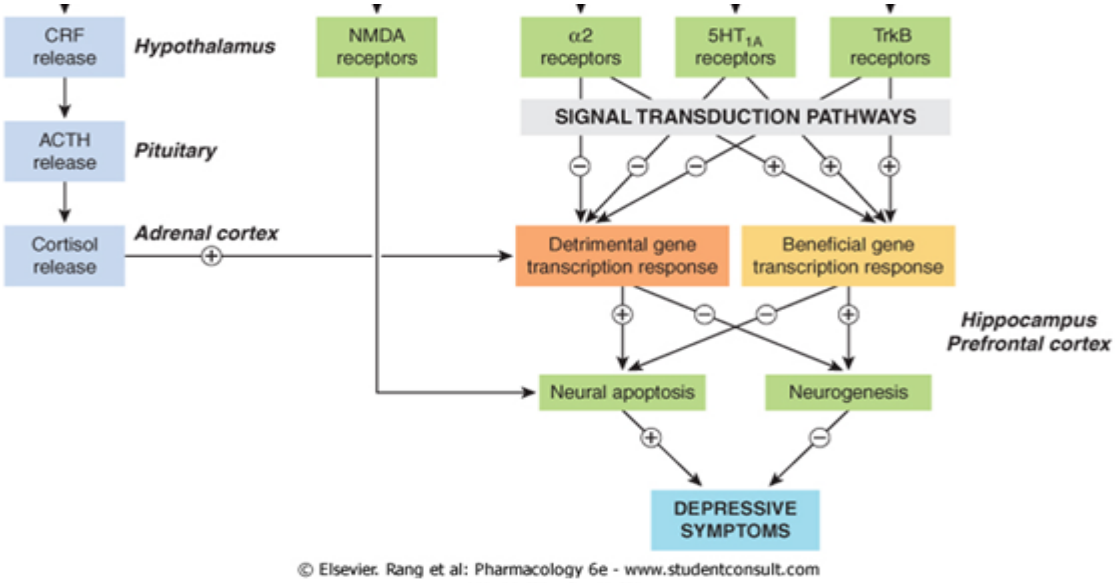

Figure: 1 Mechanisms supposed to be involved in the pathophysiology of depression [1]

They include antagonists of neuropeptides- including CRH and substance P-as well as compounds active on NMDA, acetylcholine and histamine receptors, and compounds that act on the signal transduction pathways responsible for neurogenesis, neural plasticity and apoptosis [1]. Antidepressant drugs such as, selective serotonin reuptake inhibitors (SSRI) are used to treat depression showing various side effect i-e nausea, anxiety, drowsiness, insomnia, sexual dysfunction, serotonin syndrome and thus, the search for a new antidepressant herb with less side effects is deemed important[5][6].In the search for new therapeutic products for the treatment of neurological disorders, medicinal plant research, worldwide, has progressed constantly, demonstrating the pharmacological effectiveness of different plant species in a variety of animal models[7].

Although synthetic drugs have been commonly used for the treatment of various psychological disorders in developed countries, herbal medicines still remain the widespread choice in the developing countries due to their ease of availability, lesser side effects and lower cost. According to world health organization (WHO), it has been estimated that about 75% of the world's population depend entirely on traditional medicines for the treatment of various diseases. Moreover, it has been estimated that approximately 70,000 plant species are used in traditional herbal medicines worldwide [8]. The plants reported for anti-depressant activity include *Ginko biloba* Linn, *Magnola officinlis* Rehdher & E.H.Wilson, *Mimosa pudica* Linn, *Curcuma long* Linn, *Mimosa pudica* Linn, *Ociumum sanctum* Linn, *Withania somnifera* Dunual, *Hypericum perforatum* Linn, *Piper methyticum* Forst, *Siphocampylus verticillatus* (Cham.) G.Don, *Perilla frustescens* (Linn.) Britton, *Rhizoma acori tatarinowii, Areca catechu* Linn, *Bacopa monnieri*

(Linn.) Penn, *Centella asiatica* (Linn.) Urbab, *Clitoria ternatea* Linn, *Cimicifuga racemosa* (Linn.), *Circuma longa* Linn, Evening primrose (Oenothera spp.) oil [9].

Mouse as a model for depression

Major advantages of using mouse as a model, is their remarkable similarity to human in genetics, anatomy and physiology. More than 95% of the mouse genome is similar to human beings, making mouse genetic research specifically appropriate to human disease. Other advantages of selecting mice as a model are, cost-effectiveness, small dose in relation to body weight, easy to handle and an accelerated breeding time, these points will definitely make the research easily manageable for the researcher. In addition, animal models of depression are crucial for identifying novel therapies for depression [10].

Behavioral tests for depression in mice

Tail suspension test (TST)

The Tail suspension test commonly used as behavioral model for screening antidepressant activity in mice [11]. The animals will be hung by the tail on a plastic string 75 cm above the surface with the help of an adhesive tape. The duration of immobility was observed for a period of 8 minutes. Mice will be considered to be immobile when they ceased struggling and remained floating motionless in water, making only those movements necessary to keep their head above water. After the swimming session, mice will be dried by a towel and returned to their housing conditions [9][12].

Forced swim test (TST)

The most frequently used behavioral model for screening antidepressant effect in rodents [13]. All mice were individually forced to swim in open glass chamber (25 ×15 × 25cm) containing fresh water to a height of 15 cm maintained at 26°±1°C. Each animal will show enthusiastic movement during initial 2 min period of the test. The duration of immobility will be manually recorded during the next 4 min of the total 6 min testing period. Mice will mbe considered to be immobile when they ceased struggling and remained floating motionless in water, making only those movements necessary to keep their head above water. Following swimming session, mice will be towel dried and returned to their housing conditions [9][12].

Light-dark test (LDT)

The apparatus consisted of a Plexiglas box with two compartments (20 cm×20 cm each), one of which will be illuminated with a white light while the other remained dark. Each animal will be placed at the center of the illuminated compartment, facing one of the dark areas. The time spent in illuminated and dark places, as well as the number of entries in each space, will be recorded for 5 minutes [14].

Open field test (OFD)

This test utilizes behavioral changes in rodents exposed to novel environments and is used to confirm that the observed antidepressant effect is not due to stimulation of general motor activity. The following parameters will be observed for 5 min10: activity in the center (number of central squares crossed), spontaneous ambulation (number of squares crossed at periphery) and rearing (No. of times the animal stands on the rear paws) [15].

DISCUSSION

Medicinal plants have played a significant role in human health care since the prehistoric times. Herbal medicines are getting more popularity because allopathic medicines have a lot of side effects. South Asian population is using traditional system of medicines to treat a number of diseases.

The available drugs for the treatment of depression, has shown numbers of relapses, side effects, and drug interactions. Like, Tricyclic antidepressants causes dry mouth, sour or metallic taste, epigastric distress, constipation, dizziness, tachycardia, palpitations, blurred vision and urinary retention. Cardiovascular effects include orthostatic hypotension, sinus tachycardia, and variable prolongation of cardiac conduction times with the potential for arrhythmias, particularly with overdoses [16][17]. Due to mention drawbacks of the available antidepressant drugs, attempts are proceeding to explore plants with antidepressant activity. Some important medicinal plants extracts reported as anti-depressant are: *Agapanthus campanulatus, Akebiae fructus, Albizzia julibrissin, Ginko biloba Linn. Allium cepa, Asparagus* and *Artemisia absinthium* [18]. Appropriate animal model is crucial for an activity to be fruitful. Most of the studies reported for evaluation of plants antidepressant activities confirm that mouse is the best animal model. However, more clinical studies are required for the plants showing anti-depressant activities in animal studies, so that depression can be treated effectively by using plants-based formulation. Medicinal plants are widely available in Pakistan and other countries. The widespread variety makes them attractive candidates for further research.

CONCLUSION

Thus, there is a need to conduct more research to explore the full potential of the alternative herbal medicine by using mouse as animal model to confirm its activity.

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