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# "Madhuca longifolia in Stress, Anxiety and Epilepsy Management: A Neuropharmacological Perspective"

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**ABSTRACT**
Stress and anxiety disorders are prevalent mental health concerns globally, warranting effective treatment modalities. The exploration of natural remedies has garnered significant attention in recent years. Madhuca longifolia, commonly known as Mahua, is a medicinal plant with a rich history in traditional medicine systems for its potential neuropharmacological benefits. This review aims to explore the multifaceted effects of Madhuca longifolia in managing oxidative stress, anxiety, and epilepsy from a neuropharmacological viewpoint. The plant's bioactive compounds, such as flavonoids, saponins, and polyphenols, exhibit significant antioxidant properties that contribute to mitigating oxidative stress-related neuronal damage. Additionally, Madhuca longifolia demonstrates anxiolytic effects through modulation of neurotransmitter systems, particularly GABAergic and serotonergic pathways, highlighting its potential in alleviating anxiety-related disorders. Furthermore, its antiepileptic properties, attributed to various mechanisms including ion channel modulation and inhibition of excitotoxicity, suggest promise as an adjunctive therapy for epilepsy management. This paper synthesizes existing literature on the neuropharmacological properties, mechanisms of action, and potential effects of Madhuca longifolia in mitigating stress and anxiety. Additionally, it discusses its implications for future research and clinical applications. This comprehensive review synthesizes current scientific evidence and provides insights into the neuropharmacological mechanisms underlying the therapeutic potential of Madhuca longifolia in oxidative stress, anxiety, and epilepsy management, emphasizing its significance in the development of novel therapeutic interventions for neurological disorders.

**KEYWORDS: -** Madhuca longifolia, Oxidative stress, Anxiety, Epileptic, Neuropharmacological

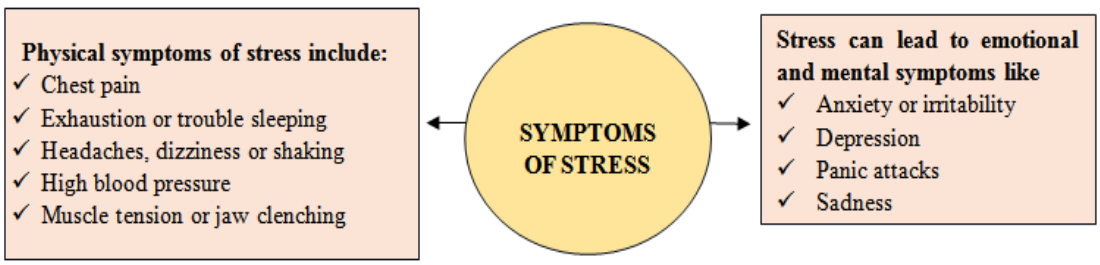
## I. INTRODUCTIONTO STRESS, ANXIETY AND EPILEPSY

### STRESS

Depression is a significant emotional condition, with a lifetime frequency of up to 21% in certain affluent nations' general populations[1].Stress is the body's reaction to a specific requirement. When anxious or furious, it can happen as a result of situations that make you frustrated. Because biological systems are constantly changing and compensating for both internal and external stimuli, stress induces a distinctive biological effect that is a major contributor to the breakdown of homeostatic functional balance.[2]

Prolonged stress exposure and stressful life events can cause major depression to develop[3].

### SYMPTOMS



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Chronic stress exposure may cause the brain to alter structurally and functionally, including causing neural damage, in addition to causing behavior resembling depression[3]. The pathophysiology of various infections from mental illnesses (such as tension, immunosuppression, and depression) and endocrine disorders (such as diabetes mellitus, cognitive dysfunctions, male sexual dysfunctions, peptic ulcers, hypertension, and ulcerative colitis) has been linked to stress[4]. Stress has become a normal part of life in this modern world. Stress must be closely monitored since it interferes with day-to-day functioning. When a person is under a lot of stress, their endurance is compromised and their homeostatic system becomes scarce[5].

The HPA (hypothalamic-pituitary-adrenal) axis is negatively regulated by the hippocampal region[6] as well as having a high threshold for stress[7]. Chronic stress suppresses cell proliferation in the hippocampal sub-granular zone and leads to activation of the HPA axis[7][8]. Chronic chemical antidepressant therapy, on the other hand, promotes cell division or even increases the survival of the immature neurons in the SGZ[9]. Furthermore, SGZ neurogenesis is necessary for the behavioral effects of some antidepressants[10]. Certain antidepressants can reverse the decrease in adult hippocampal cell proliferation induced by inescapable stress[11]. These results imply that the pathophysiology of depression involves neurogenesis and newly formed neuronal cells in the adult hippocampus, which may also be the target of depression-treating medications[9,12].

## ANXIETY

### ANXIETY AND DEPRESSION'S PREVALENCE AND DIAGNOSIS

Anxiety and depression are complex heterogeneous psychiatric disorders and leading causes of disability worldwide[13][14]. Changes in thinking, feeling, and behavior are signs of anxiety disorders[15]. Anxiety disorders affect 4–6% of people worldwide, and symptoms include elevated heart rate, high blood pressure, sweating, exhaustion, uncomfortable feelings, tension, irritability, and restlessness[16][17]. These symptoms have a detrimental effect on the individual, their families, and society at large. Without treatment, patients would eventually experience depression and occasionally consider taking their own lives[18]. By 2020, depression—which ranked as the fourth leading cause of disease burden globally in 1990—is predicted to rise to the second rank[19]. Major depressive disorder is present in community samples at a frequency of 2 to 3% in men and 5 to 9% in women[20]. Depression symptoms include having a low, melancholy, or depressed mood and/or losing interest in or enjoying once-enjoyable activities[21].

### THE NEUROBIOLOGY OF DEPRESSION AND ANXIETY

Effective treatment requires an understanding of the neurobiology of these conditions. Knowledge of neurobiology could lead to significant improvements in the comprehension of the neural mechanism of drugs as well as the prediction of potential patient responses to anxiolytic and antidepressant drugs[22]. One of the main pathways of the limbic systems, according to him, that links the cingulate gyrus, hippocampus, hypothalamus, and nuclei thalamus around the brainstem is the "system of emotion"[23]. suggested anatomical circuits between the amygdala and medial prefrontal cortex (MPC) in the framework of a model wherein the disinhibition of limbic transmission across the amygdala is caused by dysfunctional MPC. The disruption of neural chemistry, brain, hormone, immune, and autonomic systems are significant changes in the homoeostatic mechanisms that can lead to depression and anxiety [24]. A brain's structural alterations, disruption of neural networks and plasticity, impairment of neural function, and chemical imbalances could all be caused by changes in neuronal processes[25].

## EPILEPSY

One of the most prevalent and dangerous brain disorders is epilepsy[26][27]. The prevalence of epilepsy is about 1% of the population, and about one-third of patients have refractory epilepsy, which means that the right antiepileptic medication is not effective in controlling their seizures. About 75% of cases of epilepsy start in childhood, indicating the developing brain's propensity for seizures[28][29]. The term "epilepsy syndrome" describes a collection of clinical traits that share similarities in seizure types, age at onset, ECG findings, triggering factors, genetics, natural history, prognosis, and drug response. "A state produced by an abnormal excessive neuronal discharge within the central nervous system" is the definition of an epileptic seizure in terms of mechanism[30]. A paroxysmal change in brain

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activity known as a seizure is brought on by an excessive and heightened synchronous discharge of neurons. Epileptic seizure is actually used to distinguish a seizure caused by abnormal neuronal firing from a non-epileptic event, such as psychogenic seizures [31].Seizures in the elderly may have a variety of causes, such as head trauma, neurodegenerative diseases, ischemic and hemorrhagic strokes, tumors, and metabolic disorders and CNS infections[32].The primary cause of the heightened neuronal activity during a seizure is an abrupt imbalance between the brain's excitatory and inhibitory neurotransmitters, glutamate and γ-aminobutyric acid (GABA), respectively, and opioid receptor function[33].

**MADHUCA LONGIFOLIA**

According to estimates from the World Health Organization (WHO), 80% of people in developing nations get their primary medical care from traditional medicines, which are primarily plant-based drugs. In addition, a minimum of 25% of medications in the current pharmacopoeia are still derived from plants, and many more are synthetic equivalents based on plant-derived prototype compounds[34].

**BOTANICAL DESCRIPTION**

Madhuca longifolia, also known as mahua in India, is a member of the Sapotaceae family[35][36]. Grown in the subtropical region of the Indo-Pakistan subcontinent, it holds great economic significance. Called also the Indian butter tree, the name Madhuca comes from the word "Madhu," which means honey[37][38].Madhuca longifolia, sometimes known as butter nut or mahua tree (Mahukah, Irippa, Erappe, Mohva, Mohua, Madhukah, and Mohua), is a member of the Saporite family[39]. In the nations of South Asia, it is extensively available. This tree, also referred to as Mahua, bears fruits and edible flowers that are highly beneficial[40]. The tree's broad uses for its seeds, lumber, fruits, and flowers make it significant economically[41]. Mahua is a medium to large sized deciduous tree distributed in Nepal, Andhra Pradesh, Gujarat, Madhya Pradesh, Bihar, Uttar Pradesh, India and Odisha, Chhattisgarh, Jharkhand, Sri Lanka[42][43][44].

A dense, rounded, spreading, deciduous tree that grows to a height of 10 to 15 meters. Bark: When cut, it releases a white, milky sap and has a rough, brown color. It is also slightly cracked and fissured, with red inner bark. The elliptic leaves measure 15-25 cm by 8-15 cm, with a pointed tip, an angled base, a thick texture and hairy underneath. There are approximately 12 pairs of strong nerves, oblique tertiary nerves, and an entire, sometimes wavy, margin. Reddish stalk, 2-4 cm in length. White, 2 cm long, pointed, sweat-scented, fleshy flowers that grow in bunches at the tips of the branches. Fruits: 2-4 cm in diameter, ovoid, fleshy, greenish, with 1-4 seeds. Brown, shiny, elongated seeds that are 2 cm long[45][46].

Leaves: elliptic, basally cuneate, short acuminate, coriaceous. Many flowers that hang on pedicels near the tips of branches. Richly covered in rusty tomentum, the calyx is coriaceous. Yellow-white, fleshy tube-shaped corolla. A hispid anther with stiff hairs at the back, and stamens 20–30, Ovoid, fleshy, green berries with four to six seeds. March–April brings flowers, and April–May brings fruits[47]. Big, shade-loving mahua trees can be found throughout much of central India, in both wild and farmed environments. Principal constituents include vitamin A and C, ethylcinnamate, histidine, glutamic acid, and arbinose; flavones; chalcones—mallotus AB; tannins; cardenolide; srottlerin, isorottlerin; tannic acid; gum; and volatile oil [48][49]. Madhuca longifolia is reported by various scientist that it contain sapogenins, triterpenoids, steroids, saponins, flavonoids,tannin and glycosides[50][51][52][53]. The nutritional contents of Madhuca flower are 54.24% total inverts, 50.62% Reducing sugar, 3.43% Cane sugar, 54.06% total sugar, 19.8% Moisture, 6.37% Protein, 0.5% Fat, 4.36% ash, 8% calcium and 2% phosphorous[54]. The entire mahua seed has the following contents: 50–61% oil, 16.9% protein, 3.2% fiber, 22% carbohydrates, 3.4% ash, 2.5 % saponins, and 0.5% tannins. The primary ingredient, oil, is three times more abundant than protein. The de-oiled seed cake's composition is as follows: 30% protein, 1% oil, 8.6% fiber, 42.8% carbs, 6% ash, 9.8% saponins, and 1% tannins[55] . Due to their tannin content, leaves can be used to stop bleeding or secretion. For rheumatoid arthritis, an internal decoction of leaves or bark can be given. Skin soothing effects are aided by the flower and young leaf decoction. When treating bronchitis or inflamed testicles, Madhuca leaves work well. Relief can be obtained by applying a bandage to the injured areas, warming leaves coated in sesame oil, and warming them over a flame[56][57].Every component of mahua has a number of therapeutic benefits. cooling effects of fruit, aphrodisiac, tonic, and antiulcerative qualities. Entire leaf:

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antirheumatic, emollient, and anthelmintic. The properties of seeds include hepatoprotective, diuretic, refrigerant, liquor, and antihelmintic effects on milk production. Antivenom for bark toxin poisoning, stomach aches, and snakebite[58].Anxiety-related disorders such as generalized anxiety, panic, obsessive-compulsive disorder, phobias or post-traumatic stress are the most common mental illness and major cause of disability in the world[59]. The plant Madhuca longifolia exhibited notable suppression of superoxide release from polymorphonuclear cells as well as neutrophil production of hypochlorous acid[60]. It is employed for its antibacterial, anti-implantation, antispasmodic, oxytocic, uterotonic, antitumor, progestational, antagonistic, and wound-healing properties[61]. Mahua oil has also been used as a laxative and to treat rheumatism, headaches, and skin diseases. Astringent and applied as a lotion, the plant's fruits are used to treat acute and chronic tonsillitis, pharyngitis, and chronic ulcers[62]. Madhuca longifolia parts are used as astringents, emollients, stimulants, and demulcents. The plant's bark is used for diabetes mellitus, swelling, fractures, itching, and snake bites[62]. A significant portion of the British and Indian pharmacopoeias, among others, contain information about medicinal plants. Traditional medicines are made from these plants. But after receiving scientific approval, a lot of these traditional remedies could be turned into drugs[63].

**Table.1 -PHYTOCHEMISTRY OF MADHUCA LONGIFOLIA** [76]

| | |
|---|---|
| **Flower** | Vitamins A and C[64][65]. |
| **Seeds** | Myricetin, palmitic and stearic acids, α-alanine, quercetin, aspartic acid. |
| **Fruits** | α- and β- amyrin acetates [66][67]. |
| **Bark** | ethyl cinnamate, sesquiterpenes alcohol, α-terpineol, 3β-monocarpic ester of erythrodiol and 3β- capryloxy oleanolic acid. α- and β- amyrin acetates. |
| **Leaves** | Myricetin and its 3- O-arabinoside, quercetin and its 3-galactoside, sitosterol, quercetin |
| **Nut shell** | quercetin and dihyroquercetin, β-sitosterol and its 3β-D-glucoside. |

## NEURO-PHARMACOLOGICAL ACTION OF MADHUCA LONGIFOLIA

### ANTI-STRESS ACTIVITY

In a number of experimental models, the anti-stress properties of ethanolic extracts from the bark of Madhuca longifolia var. latifolia were assessed.According to the study's findings, the bark's ethanol extract has remarkable anti-stress properties.To determine the level of stress in anoxia, the onset of convulsion time was used as a parameter. The extract (200 mg/kg orally) administered group experienced an increase in the onset of convulsion time on days 7, 14, and 21, indicating that the extract has anti-stress properties.On day 14, the extract (100 mg/kg orally) subjected group experienced a slight increase in the onset of convulsion time. However, on the 7th, 14th, and 21st day, the standard used—ashwagandha extract at a dose of 100 mg/kg po—showed a notable anti-stress effect.release of corticosteroids and catecholamines as a result of the hypothalamo-hypophyseal axis (HPA) response due to higher blood urea nitrogen and glucose levels.In humans, stress activates the adreno-medullary system.

Subsequently, adrenaline triggers the activation of $\beta_2$ receptors in the pituitary gland, leading to an increased secretion of cortisol. Extracts of Madhuca longifolia var. latifolia (100 and 200 mg/kg orally) reduced the elevated levels of serum biochemical parameters, including blood urea nitrogen, cortisol, cholesterol, and glucose, in the immobilization stress model, indicating the plant's anti-stress activity[68].

The extract of Madhuca longifolia var. latifolia has been shown in studies to possess antimicrobial, anti-estrogenic, anti-progestational, anxiolytic, antioxidant, cardioprotective, and wound-healing properties. Nevertheless, no pharmacological evidence supports the effectiveness of M. longifolia extract as a stress reliever. BecauseM. longifolia bark contains flavonoids and saponins, it has been reported to have strong antioxidant activity[69]Remarkable antistress properties of antioxidants are well known[70].

As a result, research was studied to determine whether or not the ethanolic bark extract of M. longifolia has the ability to elevate anxiety[71].

### OXIDATIVE STRESS

There was also a decrease in SOD, Catalase, and GST in the plasma antioxidant of rats given DFC and Gpx with an increase in TBARS

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2141-2149 www.ijprajournal.com ISSN: 2249-7781

levels.The protracted effects of oxidative stress are what cause the change in the levels of the antioxidant enzymes SOD and CAT. Free radical-induced cellular damage can be avoided with the help of SOD and CAT. Scavenging free radicals is how antioxidant enzymes contribute to the first line of defense. Dismutase superoxide anion, free radicals, and SOD will all be converted to hydrogen peroxidase, which CAT may then turn into water. Lipid peroxidation and inflammation will not affect the tissues thanks to this method[72].When CAT activity is decreased, hydrogen peroxidase levels rise, which can lead to pathological kidney damage[73].Oxidative stress is indicated by a decrease in antioxidant levels, whereas in a healthy state, antioxidant enzymes will scavenge reactive oxygen species and nitrogen species. The adjustments brought on by DFC were able to be normalized by ALEML and SLY. Rats given ALEML alone demonstrated normal levels of antioxidants, indicating that it has no harmful effects. According to a study, giving Madhuca longifolia bark extract in an ethanolic extract form for five days may have an impact on antioxidant assay levels in response to $CCl_3$-induced toxicity[74].

**ANXIOLYTIC ACTIVITY**

The closed field test, which employed a hydro-alcoholic extract of M. longifolia leaves to assess the anxiolytic activity, demonstrates a significant reduction in the number of rearing, assisted rearing, and squares traveled in comparison to the control group following the administration of the hydro-alcoholic extract of M. longifolia leaves (100 mg/kg) or diazepam (1 mg/kg) standard[72].

**ANTI-CONVULSANT ACTIVITY/ANTI-EPILEPTIC ACTIVITY**

The anticonvulsant properties of M. longifolia fruit seeds were investigated using extracts at 200 mg/kg. In contrast to the standard medication phenytoin, which exhibits abolished tonic hind leg extension, the studies demonstrate that the extracts protect the animals from seizures and significantly shorten the duration of tonic hind leg extension. Animals given the standard medication phenytoin showed 100% protection against seizures, but different fruit and seed extracts of M. longifolia showed 95.65% and 95.65% protection, respectively[73].

Anticonvulsant effect of Madhuca has also been investigated. It is observed that at a dose of 400 mg/kg there is prolongation the onset of a seizure and also decrease in the seizure duration. It suggests that it may posses an active constituent entity having anticonvulsant nature which may help in the treatment or management of absence seizures. The in-vivo study proves the anti-convulsant potential of Madhuca and thus supports its traditional use as an anti-epileptic agent[74][75].

## II. CONCLUSION

"In summary, this comprehensive review highlights the promising neuropharmacological potential of Madhuca longifolia in mitigating oxidative stress, alleviating anxiety, and managing epilepsy. The array of bioactive compounds present in Madhuca longifolia exhibits neuroprotective, anxiolytic, and antiepileptic properties, as evidenced by various preclinical and clinical studies discussed herein. However, further investigations, including rigorous clinical trials, mechanistic studies, and standardized formulations, are imperative to elucidate its precise therapeutic mechanisms, optimize dosages, and ensure safety for potential clinical applications. None the less, the multifaceted neuropharmacological effects of Madhuca longifolia underscore its promising role as a natural therapeutic agent in combating neurological disorders, having the way for future research and development in this promising field of herbal medicine."

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The authors declares that there are no conflict of interest regarding the publication of this manuscript.

**Ethical approval**
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**List of abbreviation**

HPA- Hypothalamic-pituitary-adrenal
SGZ- Sub-granular zone
LPO- Lipid peroxidation
MPC- Medial prefrontal cortex
ECG- Electrocardiogram
CNS-Central Nervous System
GABA - glutamate and γ-aminobutyric acid
WHO -World Health Organization
SOD- superoxide dismutase
DFC - Diclofenac
TBARS- Thiobarbituric acid reactive substances
CAT- Catalase
SLY- Silymarin
ALEML- aqueous leaves extract of Madhuca longifolia
GSH- reduced glutathione
Gpx- glutathione peroxidase
GST- glutathione-S-transferase

## REFERENCES

[1]. Wong, M.L., Licinio, J., 2001. Research and treatment approaches to depression. Nat Rev Neurosci 2(5), 343-351.
[2]. Chrousos, G.P. 2009. Stress and disorder of the stress system. Nature Reviews Endochrinology 5(3): 74–81.
[3]. Pittenger, C., Duman, R.S., 2008. Stress, depression, and neuroplasticity: a convergence of mechanisms. Neuropsychopharmacology 33(1), 88-109.
[4]. Bhattacharya, S.K. & Muruganandam, A.V. 2003. Adaptogenic activity of Withania somnifera: an experimental study using a rat model of chronic stress. Pharmacology, Biochemistry and Behavior 75: 547–555.
[5]. Desai, S.K. & Desai, S.M. 2011. Antistress activity of Boerhaavia diffusa root extract and a polyherbal formulation containing Boerhaavia diffusa using cold restraint stress models. International Journal of Pharmacy and Pharmaceutical Sciences 3(1): 130–132.
[6]. Harvey, B.H., Brand, L., Jeeva, Z., Stein, D.J., 2006. Cortical/hippocampal monoamines, HPA-axis changes and aversive behavior following stress and restress in an animal model of post-traumatic stress disorder. Physiol Behav 87(5), 881-890.
[7]. Jankord, R., Herman, J.P., 2008. Limbic regulation of hypothalamo-pituitary adrenocortical function during acute and chronic stress. Ann N Y Acad Sci 1148, 64- 73.
[8]. Mirescu, C., Gould, E., 2006. Stress and adult neurogenesis. Hippocampus 16(3), 233- 238.
[9]. Schloesser, R.J., Manji, H.K., Martinowich, K., 2009. Suppression of adult neurogenesis leads to an increased hypothalamo-pituitary-adrenal axis response. Neuroreport 20(6), 553-557.
[10]. Malberg, J.E., Schechter, L.E., 2005. Increasing hippocampal neurogenesis: a novel 21 mechanism for antidepressant drugs. Curr Pharm Des 11(2), 145-155. Mirescu, C., Gould, E., 2006. Stress and adult neurogenesis. Hippocampus 16(3), 233- 238.
[11]. Santarelli, L., Saxe, M., Gross, C., Surget, A., Battaglia, F., Dulawa, S., Weisstaub, N., Lee, J., Duman, R., Arancio, O., Belzung, C., Hen, R., 2003. Requirement of hippocampal neurogenesis for the behavioral effects of antidepressants. Science 301(5634), 805-809.
[12]. P. Kalra, R. Karwasra, T.C. Nag, Y.K. Gupta, S. Singh, Protective effect of Emblica officinalis fruit extract on cisplatin-induced nephrotoxicity in female rats, Bull. Fac. Pharm. Cairo Univ. (2017).
[13]. Fajemiroye J.O., Galdino P.M., Florentino I.F. et al. Plurality of anxiety and depression alteration mechanism by oleanolic acid. J. Psychopharmacol. (2014) 28 923–934.
[14]. Experimental models of anxiety for drug discovery and brain research.
[15]. Seligman M.E.P., Walker E.F., Rosenhan D.L. Abnormal psychology. W.W. Norton & Company, New York, 2001.
[16]. Smith M. Anxiety Attacks and Disorders: Guide to the Signs, Symptoms, and Treatment Options. In: Help Guide website. 2008. [Online] 2009. www.helpguide.org/mental/anxiety_types _ symptoms_treatment.htm (accessed 3 March 2009).
[17]. Mauro V.M., Murray B.S. Quality of life in individuals with anxiety disorders. Am. J. Psychiatry (2000) 157 669–682.
[18]. CMU Institute. Treating depression and anxiety in primary care. Prim Care

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2141-2149 www.ijprajournal.com ISSN: 2249-7781

Companion J. Clin. Psychiatry. (2008) 10 145–152.

[19]. Lopez A.D., Murray C.J. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990–2020 and projected to 2020. Harvard University Press, Boston, MA, 1996.

[20]. Diagnostic and statistical manual of mental disorders, 4th edn, Text Revision DSM-IV-TR, American Psychiatric Association, USA, 2000.

[21]. Nestler E.J., Barrot M., DiLeone R.J., Eisch A.J., Gold S.J., Monteggia L.M. Neurobiology of depression. Neuron (2002) 34 13–25.

[22]. Duman R.S., Monteggia L.M. A neurotrophic model for stress-related mood disorders. Biol. Psychiatr. (2006) 59 1116–1127.

[23]. Palazidou E. The neurobiology of depression. Br. Med. Bull. (2012) 101 127–145.

[24]. McEwen B.S., Gianaros P.J. Central role of the brain in stress and adaptation: links to socioeconomic status, health, and disease. Ann. N. Y. Acad. Sci. (2010) 1186 190–222.

[25]. Castren E. Is mood chemistry Nat. Rev. Neurosci. (2005) 6 241–246.

[26]. Beghi E. The epidemiology of epilepsy. Neuroepidemiology. 2020 Dec 18;54(2):185-91.

[27]. Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson JL. Harrison's Principle of Internal Medicine. New York: McGraw-Hill; 2005.

[28]. Stafstrom, C.E., Carmant, L., 2015. Seizures and epilepsy: an overview for neuroscientists. Cold Spring Harb. Perspect. Med. 5, a022426.

[29]. Dipiro JT, Talbert RT, Yee GC, Matzke GR, Wells BG, Posey LM. Pharmacotherapy- A pathophysiologic Approach. New York: McGraw-Hill; 2002.

[30]. Penfield, W., Erickson, T.C., 1941. Epilepsy and cerebral localization: A study of the mechanism, treatment and prevention of epileptic seizures. Springfield, Ill: C.C. Thomas.

[31]. Shorvon, S.D., Andermann, F., Guerrini, R., 2011. The causes of epilepsy: Common and uncommon causes in adults and children. Cambridge University Press 1212.

[32]. Patel S, Patel S, Patel V. Investigation into the mechanism of action of Madhuca longifolia for its anti-epileptic activity. methods. 2011;10(11).

[33]. Rang HP, Dale MM, Ritter JM, Moore PK. Pharmacology. New Delhi: Reed Elsevier India Pvt Ltd; 2006

[34]. VD Rangari. Pharmacognosy and Phytochemistry Part-II, Ist ed. Nishad Deshmukh Carrior Publication, India, 2008; pp.170.

[35]. Dahake AP, Chakma CS, Chakma RC and Bagherwal P: Antihyperglycemic activity of methanolic extract of Madhuca longifolia bark. Diabetol Croat 2010; 39: 3-8.

[36]. Khare P, Kishore K, Sharma DK. Investigation of Memory Enhancing Activity of Madhuca longifolia Leaf Extract against Colchicine: An Experimental Study and Biochemical Alterations in Mice. INDIAN JOURNAL OF PHARMACEUTICAL EDUCATION AND RESEARCH. 2022 Apr 1;56(2):S303-11.

[37]. Sinha J, Singh V, Singh J, Rai AK. Phytochemistry, ethnomedical uses and future prospects of Mahua (Madhuca longifolia) as a food: a review. J Nutr Food Sci. 2017;7(573):2.

[38]. Annalakshmi R, Uma R, Chandran GS, Sahayam CS, Charles A, Evaluation of physicochemical constants and phytochemical analysis of Madhuca longifolia. Int J Nat Prod Res, 2012, 1(3):64-6

[39]. Banerji R, Mitra R. Mahua (Madhuca species): Uses and potential in India. Appl Bot Abstract 1996; 16: 260-277.

[40]. K.N. Akshatha, S.M. Murthy, N. Lakshmidevi. Ethnomedical uses of Madhuca longifolia – A review. International Journal of Life Science and Pharma Research. 3 (1) (2013) 44-53.

[41]. Ramadan MF, Moersel J-T (2006) Mowrah butter: nature's novel fat. Inform 17:124–126.

[42]. Roy SP, Kumar KS, Manharlal PN, Muralikrishna KS. EVALUATION OF MOOD ELEVATING ACTIVITY OF MADHUCA LONGIFOLIA VAR.

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2141-2149 www.ijprajournal.com ISSN: 2249-7781

LATIFOLIA BARK BY IN VIVO METHODS.

[43]. Ramar Perumal Samya, Maung Maung Thwina, Ponnampalam Gopalakrishnakone Savarimuthu Ignacimuthu Ethnobotanical Survey Of Folk Plants For The Treatment Of Snakebites In Southern Part Of Tamilnadu, India Journal of Ethnopharmacology , 2008 ;115: 302–312.

[44]. Sunita M, Sarojini P. Madhuca lonigfolia (Sapotaceae): A review of its traditional uses and nutritional properties. International Journal of Humanities and Social Science Invention. 2013 May;2(5):30-6.

[45]. Xu, Y., Wang, C., Klabnik, J. & O'Donnell J.M. 2014. Novel therapeutic targets in depression and anxiety: antioxidants as a candidate treatment. Current Neuropharmacology 12(2):108–119. doi: 10.2174/1570159X11666131120- 231448.

[46]. Patil JK, Patel MR, Sayyed HY, Patel AA, Pokal DM, Suryawanshi HP, et al, Pharmacognostic and phytochemical investigation of Bauhinia variegata (linn.) benth stem bark. Pharma. Sci. Monitor, 2012, 3:1-12

[47]. Chatterjee Asima and Pakrashi Satyesh Chandra. "The Treatise on Indian medicinal plants" Vol-4 reprint 2000, 56-58.

[48]. Ray SD, Mumaw VR, Raje RR, Fariss MW. Protection of AAPinduced hepatocellular apoptosis and necrosis by cholesteryl hemisuccinate pretreatment. J. Pharmacol. Experiment. Therapeutics, 1996; 279:1470-1483.

[49]. Kumar KP, Vidyasagar G, Ramakrishna D, Reddy IM, Gupta VSSS and Raidu Ch.S: Screening of Madhuca indica for antidiabetic activity in streptozotocin and streptozotocin-nicotinamide induced diabetic rats. Int J Pharmtech Res 2011; 3: 1073-7.

[50]. Ekka A, Ekka NS. Madhuca longifolia var. latifolia: An Important Medicinal Plant used by tribes of North–East part of Chhattisgarh. Online International Interdisciplinary Research Journal. 2014;4:227-31.

[51]. K Pavan Kumar, G Vidyasagar, D Ramakrishna, I Madhusudhana Reddy, VSSS Gupta Atyam and Ch Sarva Raidu Screening of Madhuca indica for Antidiabetic Activity in Streptozotocin and Streptozotocin – Nicotinamide induced Diabetic Rats, International Journal of PharmTech Research Vol. 3, No.2, pp 1073-1077, April June 2011.

[52]. Yoshikawa K, Tanaka M, Arihara S, Chandra BP, Roy SK, Matsumura E, Katayama S (2000) New oleanene trirerpenoid saponins from Madhuca longifolia. J Nat Prod 63:1679–1681

[53]. Yosioka I, Inada A, Kitagawa I (1974) Soil bacterial hydrolysis leading to genuine aglycone-VIII structures of a genuine sapogenol protobassic acid and a prosapogenol of seed kernels of Madhuca longifolia L. Tetrahedron 30:707–714.

[54]. Madhuca Lonigfolia (Sapotaceae): A Review of Its Traditional Uses and Nutritional Properties, Mishra Sunita & Padhan Sarojini. International Journal of Humanities and Social Science Invention. 2013; 2(5):30- 36.

[55]. Singh A, Singh IS (1991) Chemical evaluation of mahua (Madhuca indica) seed. Food Chem 40:221–228.

[56]. Kazuko Yoshikawa, Masami Tanaka, ShigenobuArihara, Bikas Chandra Pal, Subodh Kumar Roy, Eiko Matsumura, Satoshi Katayama.New oleanane triterpenoid saponins from Madhuca longifolia.J. Nat. Prod. 63 (12): 1679-1681, (2000).

[57]. http://www.herbalcureindia.com/herbs/madhuka longifolia.htm

[58]. Kumar SR, Sarma K, Rao CP, Jyothi Ch VS, Kumar R, Evaluation of anthelminthic activity of leaves of Madhuca longifolia. International Journal of Pharmacology & Toxicology, 2014, 4:99-104.

[59]. CK Kokate; AP Purohit; SB Gokhale. Pharmacognosy, 13 th ed., Nirali Prakashan, Pune, India, 1999; pp. 212

[60]. Pawar RS, Bhutani KK (2004) Madhucosides A and B, protobassic acid glycosides from Madhuca indica with inhibitory activity on free radical release from phagocytes. J Nat Prod 67:668–671.

[61]. Yadav, P., Singh, D., Mallik, A. & Nayak, S. 2012. Madhuca longifolia (Sapotaceae), a review of its traditional uses, phytochemistry and pharmacology. International Journal of Biomedical Raeserch 3(7): 291–305.

[62]. KR Kirtikar; BD Basu .Indian medicinal plants, Ist ed, Sudhindra Nath Basu, Allahabad, India, 1918; pp.747.
[63]. CC Barua; A Talukdar; SA Begum; P Borah; M Lahkar; Indian journal of pharmacology, 2012, 44(1), 63-67.
[64]. Fowler GJ, Behram GDE, Bhate SN, Hasan KH, Mehdihassan H, Inuganti NN. Biochemistry of Mahua flower. J Indian Inst Sci 1920; 3: 81.
[65]. Awasthi YC, Mitra CR. Madhuca butyracea. Constituents of the fruit pulp and the bark. Phytochemistry 1968; 7(4): 637-640.
[66]. Bhatnagar SC, Awasthi YC, Mitra CR. Steroidal and other constituents of Madhuca latifolia leaves. Phytochemistry 1972; 11(4): 1533.
[67]. Bhatnagar SC, Awasthi YC, Mitra CR. Constituents of Madhuca longifolia leaves. Phytochemistry 1972; 11(1): 465-467.
[68]. Nimbkar, S.R., Patki, V.P. & Patki, M.P. 2001. Pharmacological evaluation of anti-stress and androgenic activity of polyherbal formulation AP–3000 containing Panax ginseng. Indian Drugs 38(1): 27–31.
[69]. Jha, D. & Mazumder, P.M. 2018. Biological, chemical and pharmacological aspects of Madhuca longifolia. Asian Pacific Journal of Tropical Medicine 11(1): 9–14.
[70]. Xu, Y., Wang, C., Klabnik, J. & O'Donnell J.M. 2014. Novel therapeutic targets in depression and anxiety: antioxidants as a candidate treatment. Current Neuropharmacology 12(2):108–119. doi: 10.2174/1570159X11666131120- 231448.
[71]. Umukoro, S. & Aladeokin, A.C. 2010. Evaluation of the antistress and anticonvulsant activities of leaf extract of Alchornea cordifolia in mice. Journal of Ethnopharmacology 127(3):768–770.
[72]. Harpreet Singh and Munish Mani. Evaluation of anxiolytic activity of hydro-alcoholic extract of Madhuca longifolia leaves. J. Nat. Prod. Plant Resources. 2014; 4 (1):19-22.
[73]. Mahendar Boddupally, Asish Bhaumik, Chaitanya Reddy G.V, Prasenjit Das and Shibu Das. The Biomolecules present in the fruit-seeds of Madhuca longifolia (L) act as potential anticonvulsant agents against mes induced rats. International Journal of Current Medical and Pharmaceutical Research. 2015; 1(7): 96-98
[74]. Patel S, Patel S, Patel V. Investigation into the mechanism of action of Madhuca longifolia for its anti-epileptic activity. Phcog Commn 2011; 1(2): 18-22.
[75]. Inganakal TS, Ahmed ML, Swamy P. Neuropharmcological potential of methanolic extract and a triterpene isolated from Madhuca longifolia L leaves in mice. Indian J Exp Biol 2012; 50(12): 862.
[76]. Chavan GM, Vasaikar RS, Patil JK, Hamid HS, Akash J, Jain VH. Study of CNS Depressant activity of Ethanolic extract of Madhuca longifolia Flower. Research Journal of Pharmacology and Pharmacodynamics. 2019;11(4):127-31.