JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Inhibitory effects of Monoamine Oxidase enzyme in Epipremnum aureum: An Assessment

Supriya Malappa Talavar, Ganesh R. Phadtare, Sanjay R. Arote

Student Bachelor of Pharmacy, Associate Professor,
PrincipalDepartment of Pharmacology
Krishnarao Bhegade Institute of Pharmaceutical Education and Research, Pune, India

Abstract: This research project investigates the inhibitory activities of the monoamine oxidase (MAO) enzyme in Epipremnum aureum, a common houseplant known for its potential medicinal properties. MAO is an enzyme responsible for the breakdown of monoamine neurotransmitters, and its inhibition is a target for the treatment of various neurological disorders, including depression and Parkinson's disease. This study aims to identify and quantify the inhibitory effects of Epipremnum aureum extracts on MAO activity. Using in vitro assays, we analyzed the enzymatic activity in the presence of plant extracts, comparing the results to standard inhibitors. The findings indicate significant inhibitory effects, suggesting that Epipremnum aureum may contain bioactive compounds with potential therapeutic applications. Further phytochemical analysis and bioactivity-guided fractionation are recommended to isolate and identify the active constituents responsible for MAO inhibition. This study contributes to the understanding of the medicinal potential of Epipremnum aureum and supports its use in developing novel treatments for neurological disorders.

Keywords: Neurotransmitters, Monoamine oxidase (MAO), Enzyme inhibition, Epipremnum aureum, Phytochemicals, MAO inhibitors, Plant extracts, Antidepressant activity, Antioxidant properties, Enzymatic assay.

INTRODUCTION:

The term “neurotransmitter” was coined by Elliot as long ago as 1904 to describe chemical compounds which are stored in the nerve cells of the brain, and indeed of other organs, and which are released from their stores by physiological and pathological stimuli. After release the neurotransmitter molecules cross the synaptic cleft, the gap between the betweenthe nerve fibers, to act upon the receptors, where they produce the specific effects. [1]
Neurotransmitters are substances which neurons use to communicate with one another and with their target tissues in the process of synaptic transmission (neurotransmission).[2] They regulate the entire biological activities in human beings including even our mood, motivation and day to day behavior.[3] Neurotransmitters are chemical materials oscillating from the presynaptic membrane to the synapsis gap, by connecting to the receptor in the postsynaptic membrane and form action potential so that it can transmit stimulation. Neurotransmitters transmit a message that comes to the gap in the synaptic region to the other side. [4] These small molecules are essential for sending messages in the brain. They influence many functions, including emotions, thoughts, memories, movements, and sleep patterns. As a result, abnormal levels of neurotransmitters (NTs) disrupt brain functions, causing various physical, mental, and neurodegenerative diseases.[5] These days, neuropsychiatric disorders like Alzheimer's disease (AD), Parkinson's disease (PD), and depression have become major social issues attracting global attention.
Neurodegenerative disorders are linked to the overproduction of monoamine metabolites due to excessive MAO expression. These characteristics make MAO a promising target for developing MAO inhibitors (MAOIs) as potential treatments for these disorders. [6] It is a chemical substance that transmits signals across a synapse from one neuron (nerve cell) to another 'target' neuron, muscle cell, or gland cell. [7]

Functions of Neurotransmitters:

The body uses different chemicals called neurotransmitters for various functions such as:

- Acetylcholine (ACh) Involved in muscle activation, attention, arousal, and memory. Major neurotransmitter

in theautonomic nervous system; crucial in the parasympathetic nervous system, e.g. Alzheimer's disease.

- Dopamine (DA) associated with reward, motivation, memory, attention, and regulating body movements. It includes the mesolimbic pathway (reward), mesocortical pathway (cognition), and nigrostriatal pathway (movement)**.** Serotonin (5HT) Regulates mood, appetite, sleep, memory, and learning.
- Glutamate is the main excitatory neurotransmitter in the brain and helps with nervous system flexibility. On the other hand, GABA and glycine are the main inhibitory neurotransmitters. GABA, for example, it makes up about 40% of the brain's inhibitory processing. Glycine is mainly found in the spinal cord.
- Serotonin is a neurotransmitter that affects various neuropsychological processes and neural activity. Serotonin also plays a role in gastrointestinal processes such as bowel motility, bladder control, and cardiovascular function.
- Norepinephrine is a monoamine made in the central nervous system and sympathetic nerves. It affects stress, sleep,attention, focus, inflammation. It also plays a role in modulating the responses of the autonomic nervous system.[8]

Classification of Neurotransmitters:

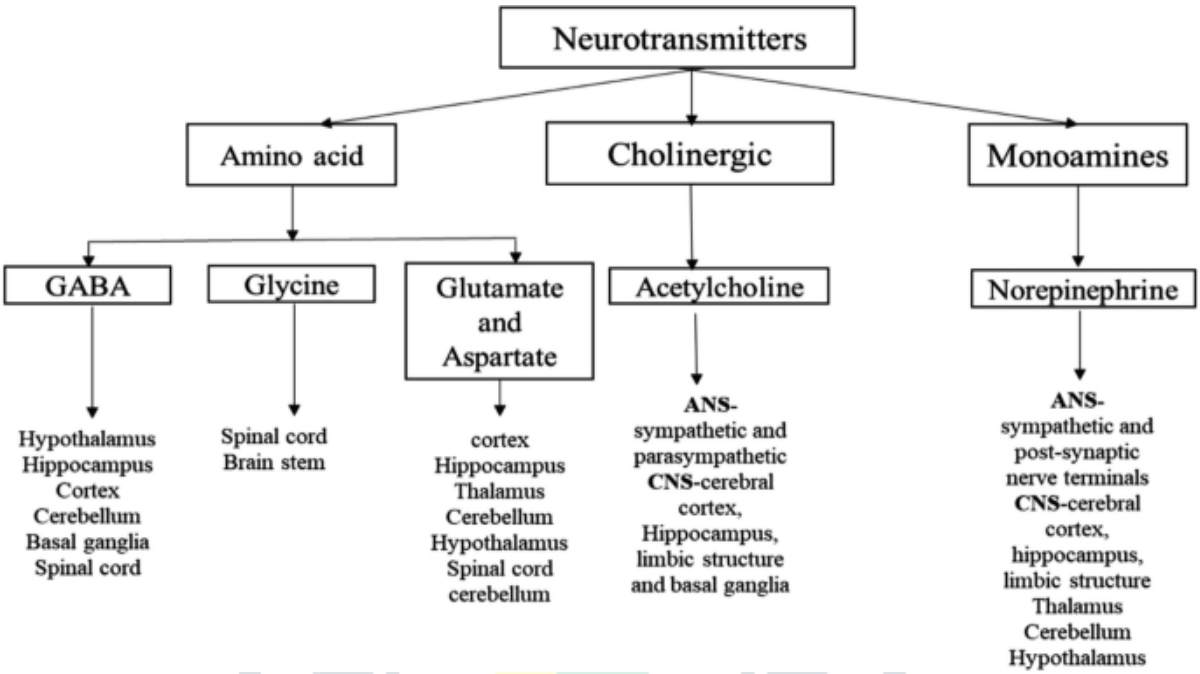

fig 1: types of neurotransmitters.

Mechanism Of Action:

Signals are transmitted from one neuron to another or to a target cell through a gap called the synaptic cleft using chemicals called neurotransmitters. A synapse typically involves two neurons: the presynaptic neuron, which makes and releases neurotransmitters, and the postsynaptic neuron, which receives the neurotransmitters. The electrical signal is transmitted across a synapse when an action potential or nerve impulse excites the presynaptic axon terminal. This nerve impulse changes the membrane potential of the presynaptic axon terminal, which activates calcium ion (Ca^{2+}) conducting transmembrane proteins. Extracellular calcium ions move into the presynaptic axon terminal following their concentration gradient. This causes neurotransmitter vesicles to bind with the presynaptic neuron's membrane and release neurotransmitter molecules into the synapse (Levy & Goldstein, 2008). Several protein molecules are involved in the binding of neurotransmitter vesicles to the presynaptic membrane. These proteins can act as inhibitors or activators, regulating the release of neurotransmitters from the presynaptic axon terminal. The synaptic cleft is a small gap (0.2µ) between presynaptic and postsynaptic neurons, forming a junction between them. For example, acetylcholine (ACh) depolarizes the postsynaptic cell and increases its firing, while dopamine hyperpolarizes the postsynaptic cell and decreases its firing. [14]

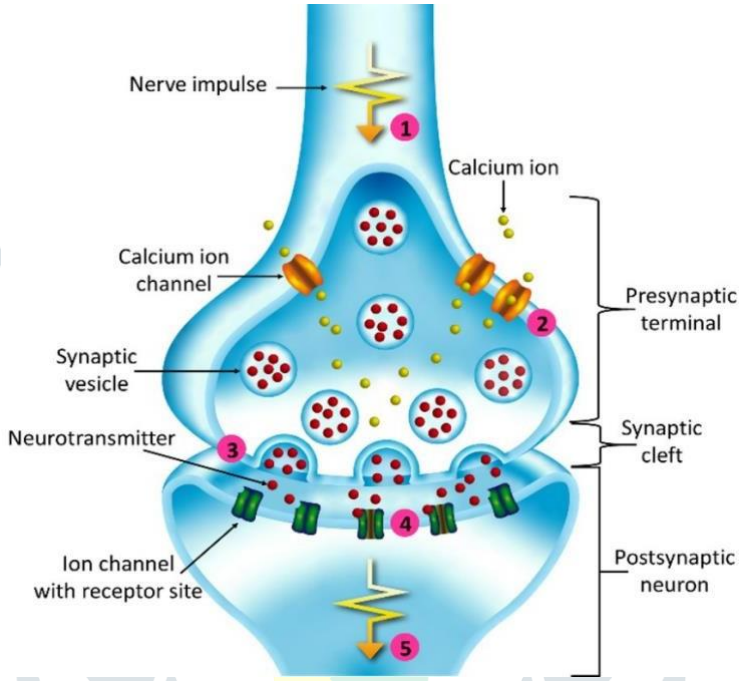

fig 2: steps of synaptic neurotransmission.

MONOAMINE OXIDASE (MAO):

Monoamine oxidase (MAO) is a group of enzymes in the body that break down monoamine neurotransmitters like dopamine, serotonin, and norepinephrine. There are two main types of MAO: MAO-A and MAO-B, each with distinct roles and functions. Understanding the differences between MAO-A and MAO-B is essential for comprehending their effects on various physiological processes and their links to health and disease.[15] Monoamine oxidase (MAO) enzymes play a crucial role in the brain by catalysing the oxidative deamination of monoamine neurotransmitters and xenobiotic amines.

These enzymes exist in two isoforms, MAO-A and MAO-B, which are differentiated by their substrate affinity and inhibitor specificity. MAO-A is primarily found in the presynaptic terminals of catecholaminergic neurons, where it is heavily involved in the breakdown of serotonin (5- hydroxy tryptamine, 5-HT) and norepinephrine (NE).[16] On the other hand, MAO-B is present in serotonergic and histaminergic neurons, as well as in astrocytes and ventricular cells. Dopamine (DA) serves as a common substrate for both MAO isoforms. The regulation of these monoamine levels in the brain is vital for maintaining motor, perceptual, and cognitive functions, as well as for modulating mood and emotions. Abnormal expression or activity of MAO-A has been associated with various neuropsychiatric disorders and behavioural traits, including aggression, panic disorders, antisocial behaviours, major depressive disorder (MDD), bipolar depression (BD), attention-deficit hyperactivity disorder (ADHD), Parkinson's disease (PD), and Alzheimer's disease (AD). [17] MAO-A primarily breaks down serotonin, norepinephrine, and epinephrine, and can be inhibited by clorgyline. MAO-B prefers phenylethylamine and is inhibited by selegiline. Both enzymes also metabolize dopamine and tyramine. While historically studied in the brain, recent research shows MAO enzymes are also active in peripheral tissues. MAO-A is found in the placenta, adipose tissue, thyroid gland, and lung, with lower levels in the brain. MAO- B is mainly in the central nervous system and some peripheral tissues like the uterus and liver. Irregular MAO activity is linked to neurological and psychiatric disorders such as depression and social anxiety. [18] The structural elucidation of

MAOs has provided significant insights into their function. The first crystal structure of mammalian MAOs was solved in 2002, almost 65 years after these Flavin adenine dinucleotide (FAD)-dependent enzymes were discovered and classified. Both MAO-A and MAO-B feature a two-domain topology characterized by the Rossmann fold, which interacts with dinucleotide cofactors and a substrate-binding domain. This globular structure includes a C-terminal α- helix that anchors the protein to the outer mitochondrial phospholipid bilayer.[19] As monotopic membrane proteins, the structural elucidation of MAOs posed significant challenges, requiring extensive screening of various detergent conditions for purification and crystallization. The structures of MAO-A and MAO-B differ in their oligomerization architecture and details of their active sites. Purified human MAO-B and rat MAO-A are dimeric, whereas human MAO-A has been found to be monomeric, likely due to the detergent treatments used during protein extraction. The active sites of MAOs consist of a hydrophobic cavity located near the flavin cofactor, extending to the protein surface, which is critical for their enzymatic activity.[20]

Structure and Function:

Monoamine oxidases (MAOs) are enzymes that oxidize monoamines in the body. They are crucial for regulating neurotransmitter levels such as serotonin, dopamine, and norepinephrine, which affect mood, cognition, and other physiological processes. The structure of MAO has been extensively studied using techniques like X-ray crystallography and cryo-electron microscopy. Human MAO-A and MAO-B structures, in particular, have been resolved at high resolution.[21] MAO is a homodimer with each monomer containing a covalently bound flavin adenine dinucleotide (FAD) cofactor and a non-covalently bound isoalloxazine ring, the site of monoamine oxidation. The FAD cofactor acts as the primary electron acceptor during the catalytic reaction. [22]

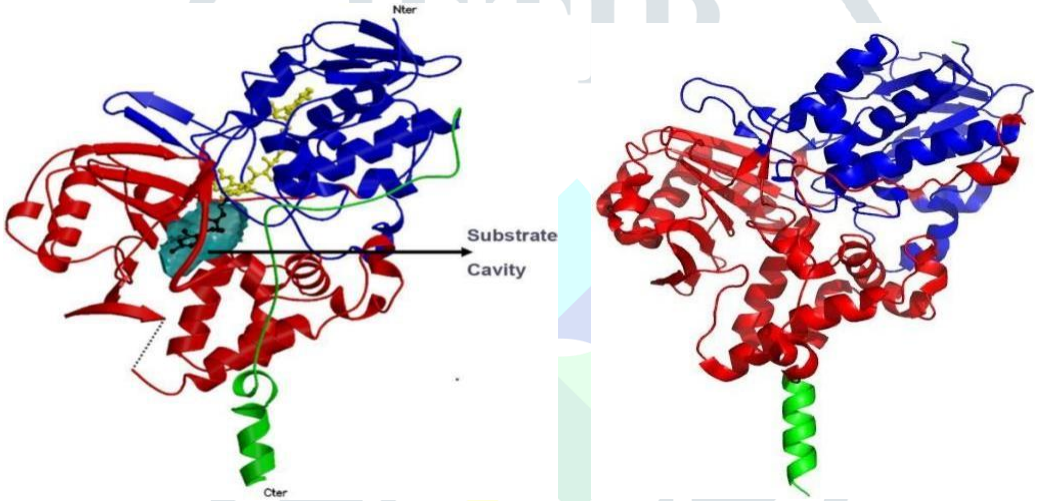

fig 3. mao-a and mao-b enzymes

MAO-A:

Monoamine oxidase A (MAO-A) is an enzyme encoded by the MAOA gene in humans. It belongs to the family of monoamine oxidases, which are mitochondrial enzymes involved in the breakdown of neurotransmitters and dietary amines. MAO-A specifically targets monoamines such as serotonin, norepinephrine, and dopamine, converting them into their respective metabolites through oxidative deamination.[23,24]

Each subunit of MAO-A consists of several domains:

1. N-terminal Domain: This domain anchors the enzyme to the outer mitochondrial membrane, the primary location of MAO-A. It is involved in substrate recognition and binding.
2. Flavin-binding Domain: This domain contains the flavin adenine dinucleotide (FAD) cofactor, which is crucial for catalysing the oxidation reaction of monoamines. The FAD cofactor undergoes redox reactions during the catalyticcycle of MAO-A.
3. C-terminal Domain: This domain is responsible for substrate binding and specificity. It interacts with the monoamine substrate and facilitates its oxidation at the active site of the enzyme.

The active site of MAO-A is situated at the interface of these domains, where the oxidation of monoamines takes place. It contains specific amino acid residues that interact with the substrate, facilitating its conversion to the corresponding aldehyde and reducing the FAD cofactor. The high-resolution crystal structure of MAO-A has provided detailed insights into the arrangement of atoms within the enzyme. This structural knowledge has been crucial for understanding the catalytic mechanism of MAO-A and has guided efforts in drug discovery aimed at developing selective inhibitors of this enzyme. [25]

MAO-B:

The structure of monoamine oxidase B (MAO-B) is similar to that of MAO-A, with both enzymes sharing a high

degree of sequence homology and overall structural architecture. MAO-B, like MAO-A, is a homodimer enzyme where each subunit contains a flavin adenine dinucleotide (FAD) cofactor that is essential for its catalytic activity.

The detailed structure of MAO-B has been figured out using methods like X-ray crystallography and cryo-electron microscopy. The crystal structure of MAO-B shows several domains in each subunit, including: [26]

1. N-terminal Domain: This domain helps anchor the membrane and may aid in recognizing and binding substrates.
2. Flavin-binding Domain: This domain contains the FAD cofactor and is crucial for oxidizing monoamines.
3. C-terminal Domain: This domain binds and identifies substrates, interacting with the monoamine substrate at the enzyme's active site.

The active site of MAO-B, located at the junction of these domains, includes amino acid residues essential for recognizing substrates and catalysing reactions. It enables the oxidative deamination of monoamine neurotransmitters, producing their respective aldehydes and ammonia. Structural studies of MAO-B have offered valuable insights into its catalytic process and substrate specificity, which have helped in developing selective inhibitors for therapeutic applications. [27, 28]

Function of MAO:

1. MAO breaks down monoamine neurotransmitters by removing their amine group.
2. This process converts neurotransmitters like serotonin, dopamine, and norepinephrine into aldehyde andammonia.
3. It involves removing the amine group, producing aldehyde and ammonia.
4. MAO's main job is to regulate monoamine levels in the brain, crucial for normal brain function.
5. Imbalances in monoamine levels are linked to psychiatric and neurological disorders.
6. MAO also helps metabolize dietary amines and drugs.
7. MAO inhibitors, used as antidepressants, increase the availability of monoamine neurotransmitters.
8. MAO's role in neurotransmitter regulation is essential for brain function, behaviour, and mental health. [29,30]

ROLE OF MAO INHIBITORS:

Monoamine oxidase inhibitors have been around for more than 50 years, originally developed as antidepressants but now used for various psychiatric and neurological conditions. Recently, there has been increased interest in these inhibitors due to their reported neuroprotective and neurorescue properties. [31]

Monoamine oxidase (MAO) catalyzes the oxidative deamination of monoamines. In humans, there are two types of MAO: MAO-A and MAO-B. MAO-A primarily deaminates serotonin, melatonin, noradrenaline, and adrenaline, while MAO-B deaminates phenethylamine and benzylamine. Both forms equally break down dopamine, tyramine, and tryptamine. MAO inhibitors (MAOIs) prevent the breakdown of these neurotransmitters. They are primarily used to treat depression, especially when other antidepressants are ineffective. MAOIs work by inhibiting the activity of monoamine oxidase enzymes in the brain, which normally break down neurotransmitters like serotonin, dopamine, and norepinephrine. By blocking this enzyme activity, MAOIs increase the levels of these neurotransmitters, helping to

improve mood. [32] Early MAOIs irreversibly inhibit MAO. They permanently deactivate the enzyme upon interaction, and its function is only restored when new enzymes are produced. Newer MAOIs like moclobemide are reversible. They restore enzyme activity when the inhibitor dissociates from MAO. MAOIs vary in selectivity. Some like moclobemide selectively inhibit MAO-A, while others like pargyline and selegiline selectively inhibit MAO-B. Some MAOIs are non-selective, inhibiting both MAO-A and MAO-B (e.g., phenelzine, tranylcypromine). However, selectivity can depend on concentration. Selegiline, for instance, is selective at low doses but becomes non-selective at high doses. [33] Inhibiting MAO activity in the brain raises levels of neurotransmitters like serotonin, norepinephrine, dopamine, and trace amines such as β-phenylethylamine, tryptamine, and tyramine, which are implicated in various psychiatric and neurological disorders. The use of MAO inhibitors (MAOIs) has been limited due to hepatotoxicity with some types and other potential adverse effects. Irreversible MAO-A inhibitors like phenelzine and tranylcypromine can cause a dangerous rise in blood pressure after consuming tyramine-rich foods ("cheese effect"). This occurs because MAO inhibition allows tyramine to enter the bloodstream, displacing stored norepinephrine in neurons and leading to hypertensive symptoms. Selective irreversible MAO-B inhibitors, like selegiline, do not typically cause this effect at normal doses because intestinal MAO-A efficiently breaks down tyramine. Reversible MAO-A inhibitors, such as moclobemide, were developed to avoid the cheese effect. Selegiline, originally developed as an antidepressant, has been found effective in treating Parkinson's disease, particularly in patch form, despite its limited antidepressant efficacy at standard doses. [34]

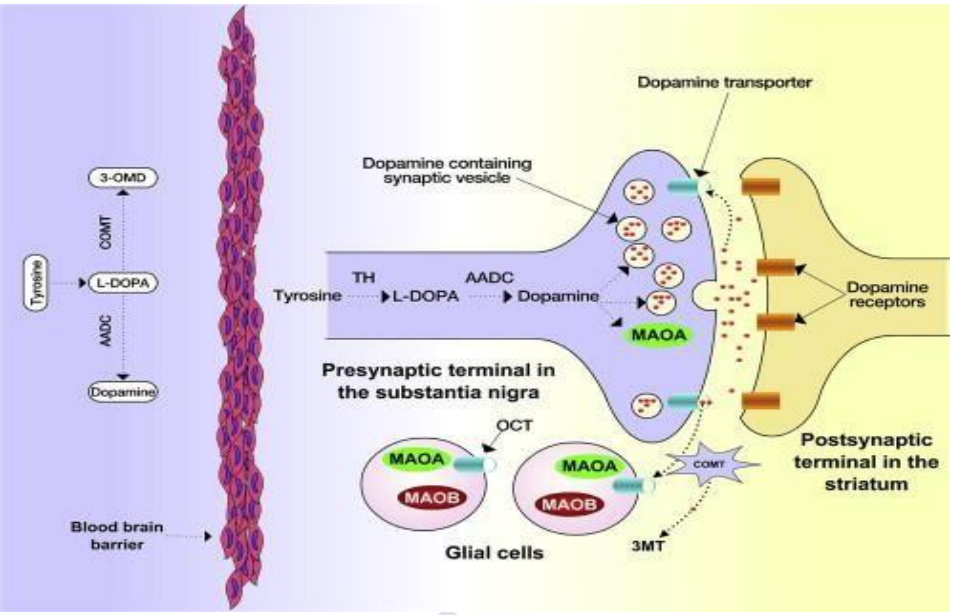

fig 4. the production of dopamine and its metabolism by mao b and mao a.

Pharmacokinetics of MAOI:

- ❖ Phenelzine is rapidly absorbed. Steady-state plasma concentrations gradually increase over the initial 6 to 8 weeksof treatment. It is metabolized into phenylethylamine and phenylacetic acid. [35]
- ❖ Brofaromine is almost completely absorbed, with peak concentration (Cmax) reached after 2 to 4 hours. There is a linear relationship between the dose and the area under the plasma concentration-time curve (AUC) and Cmax. The elimination half-life is not affected by repeated administration. It undergoes extensive metabolism. [36]
- ❖ Tranylcypromine is rapidly absorbed and has a short plasma elimination half-life of 2 hours. It undergoes ring- hydroxylation and N-acetylation. Because tranylcypromine is mainly metabolized, only about 4% of a dose is excreted unchanged in the urine, so major changes due to age are not expected. [37]
- ❖ The propargylamine selegiline is N-demethylated and N-depropargylated to yield aryl alkylamines, which include amphetamine, N-methylamphetamine, and N-propargyl amphetamine. These metabolites may then undergo further metabolism. The formation of these metabolites is mediated by cytochrome P450 (CYP) 2D6 (CYP2D6) and CYP3A4. The plasma elimination half-life of selegiline is l.7 h after a single dose. Oral form: well, absorbed from the gastrointestinal tract, Transdermal patch: Provides continuous absorption through the skin. Widely distributed, including in the brain. Excreted in urine as metabolites. Half-life: Oral form: 10 hours; Transdermal form: 18-25 hours. [38]
- ❖ Moclobemide is rapidly and almost completely absorbed from the gastrointestinal tract and undergoes extensive first-pass hepatic metabolism. This boosts the amount of moclobemide in the body from 40% after one dose to 85% after many doses; there haven't been any reports of liver damage. Moclobemide is altered by the liver through C and N oxidation of the morpholine ring, as well as by aromatic hydroxylation. Around 95% of the drug leaves thebody in the urine in the first 24 hours. [39,40**]**

Significance and Clinical Relevance:

MAO-A:

- ✓ MAO-A is important for regulating mood, emotion, and behaviour by affecting serotonin and norepinephrine levels.
- ✓ Problems with MAO-A activity are linked to mood disorders like depression and bipolar disorder, as well asimpulsive and aggressive behaviours.
- ✓ Differences in the MAOA gene, including variations like the MAOA-uVNTR, are associated with varyingemotional responses and vulnerability to psychiatric disorders.
- ✓ Drugs such as moclobemide and phenelzine inhibit MAO-A and are used to treat depression and anxiety disorders.[41,42]

MAO-B:

- ✓ MAO-B is critically involved in the metabolism of dopamine and is involved in the development of Parkinson'sdisease.
- ✓ Increased MAO-B activity in the brain leads to dopamine breakdown and the loss of dopaminergic neurons seenin Parkinson's disease.
- ✓ Drugs that selectively inhibit MAO-B, like selegiline and rasagiline, protect neurons and are used alongside othertherapies in Parkinson's disease to slow disease progression and improve motor symptoms.

- ✓ MAO-B inhibitors are also being studied for potential use in other conditions, including Alzheimer's disease,amyotrophic lateral sclerosis (ALS), and mood disorders. [43,44]

NEED OF WORK:

The research project on assessing the inhibitory activities of monoamine oxidase (MAO) enzymes in *Epipremnum aureum* involves several key steps. Initially, a comprehensive literature review will provide background information on the plant and MAO inhibitors. The next step includes the collection and preparation of plant material, followed by the extraction of bioactive compounds using suitable solvents. An in vitro MAO enzyme assay will then be set up to test the plant extracts for their inhibitory activity. The inhibitory potential will be quantified by measuring enzyme activity and determining IC50 values. Phytochemical analysis will identify and quantify the active compounds responsible for MAO inhibition. Data analysis will involve statistical evaluation and comparison with standard inhibitors. Finally, the results will be compiled into a detailed report, highlighting the findings and suggesting future research directions.

LITERATURE REVIEW: MONEY PLANT

Introduction:

Money plant is a perennial indoor plant of Family Araceae. The scientific name of money plant is Epipremnum aureum. It is a tropical vining plant found in many countries of the world including Northern Australia, Malaysia, Singapore, China, Japan, India and Pakistan.[45]It is a very famous indoor plant due to its capacity to survive in different ambience. It is also a symbol for prosperity plant. Besides money plant, other names that are commonly used for this plant are Silver Vine, Pothos and Devil's Ivy. They are one of the best living things that are soothing to the eyes. Keeping money plants in indoor areas has many benefits and beautifies the space. [46] It means that the plants that bring prosperity and fortune since they cleanse the toxins in the air brought on by home cleaning products. This plant also plays an important role in Nature-based nutrient removal technology from wastewaters. In India, Epipremnum aureum is used from long back in various fields of medicine and to treat various diseases like jaundice, diabetes, leprosy, ulcer etc.[47]

fig 5: money plant

Epipremnum aureum**,** commonly known as *Golden Pothos* or *Devil's Ivy*, is a popular indoor plant admired for its attractive, heart-shaped leaves and easy maintenance.[50] Epipremnum aureum is an excellent air cleansing plant. Its decorative marbled leaves and easy maintenance make it very popular amongst indoor plants. [48] This plant is grown mainly as an indoor plant and the special characteristic of the plant, is that it can grow even in a water-filled bottle

(alone for a reasonable time if you simply keep the water changing or refill at frequent intervals.) or a container withoutany soil.[49]They can survive without the addition of nutrients to the water.

Taxonomical Classification:

Taxonomical classification of E.aureum according to the system of Bentham and Hooker.Kingdom: Plantae
Subkingdom:
Phanerogames
Division: Angiosperm
Class:
Monocotyledonae
Series: Nudiflorae
Family:
Araceae
Genus:
Epipremnum
Species:

aureum

Classification of Epipremnum:

Epipremnum aureum belongs to a large family Araceae having 110 genera and 2500 species in the world distributed mostly in the tropics and subtropics of both the hemispheres [49]. Epipremnum Linn. is represented by more than one species in India, of which E. aureum and E. pinnatum is the most widely cultivated and best-known species among theother species.

Chemical constituents:

The chemical constituents present in money plant (Epipremnum aureum) leaves include alkaloids, flavonoids, saponins, tannins, glycosides, and phenolic compounds. These constituents contribute to the medicinal and pharmacological properties of the plant. [51]

Morphology of plant:

Common name: Money Plant, Golden pothos, Ceylon creeper, Hunter's robe, Ivy arum, House plant, silver vine, Solomon Islands ivy, Marble queen, Taro vine. E. aureum is a climber climbing by means of aerial roots of which hook over tree branches. This evergreen plant comprises of simple, alternate, entire and heart-shaped leaves. The leaf surface is waxy. Leaves are small, generally varying between 8-20 cm in length, but if they are grown along the ground or under favorable conditions, they are longer and big in size. The leaves are beautifully variegated with white, cream, yellow and various shades of green in different cultivars. Colors, variegation and size of foliage are extremely variable,changing according to the lighting conditions and other cultural factors.

Money Plant is an extremely popular houseplant in India. It is an evergreen vine growing up to 20 m tall, with stems up to 4 cm in diameter, climbing by means of aerial roots which adhere to surfaces. However, the plant can be grown virtually anywhere, even in water without soil, or completely away from light. The leaves are alternate, heart-shaped, entire on juvenile plants, but irregularly pinnately cut on large mature plants, up to 100 cm long and 45 cm broad. Juvenile leaves are much smaller, typically under 20 cm long. Money Plant is an extremely popular houseplant in India.

fig 5: epipremnum aureum

The plant never flowers due to a genetic impairment of the gibberellin (GA) biosynthetic gene. This was understood only as recently as 2016. It flowers if artificially treated with GA biosynthesis genes. The flowers are typical of arum family, produced in a spathe up to 23 cm long. This plant produces trailing stems when it climbs up trees and these take root when they reach the ground and grow along it. The leaves on these trailing stems grow up to 10 cm long and are the ones normally seen on this plant when it is cultivated as a potted plant.[52]

The Money Plant (Epipremnum aureum) has several potential pharmacological uses and benefits including:

- Antioxidant Properties: Money plants contain antioxidants that can help neutralize harmful free radicals in thebody, potentially reducing oxidative stress.
- Anti-inflammatory Effects: Some studies suggest that extracts from money plants may have anti-inflammatoryproperties, which could be beneficial in treating inflammatory conditions. [53]
- Wound Healing: Money plant extracts have been studied for their wound healing properties, potentially speedingup the healing process.
- Anti-diabetic Potential: Research has shown that money plant extracts may have hypoglycaemic effects, whichcould be useful in managing diabetes.
- Antimicrobial Activity: Money plant extracts have demonstrated antimicrobial activity against certain bacteriaand fungi, suggesting possible applications in fighting infections. [54]

REPORTED ACTIVITY:

1. **Anti-bacterial and Anti-fungal activity:**
   Various solvent extracts of E. aureum leaves and aerial roots revealed antibacterial activity against microorganisms, it has been found that water extracts of aerial root part showed clear and approximately

similar zone of inhibition in comparison to standard disc against test organisms in decreasing order Escherichia coli>Micrococcus luteus>Bacillus cereus>B. subtilis. Methanolic leaf extracts of E. aureum showed antibacterial activity against Escherichia coli and Staphylococcus aureus and the antifungal activity was evaluated against Candida albicans. Petroleum ether, acetone and ethanol extract of E. aureum shows considerable antibacterial activity against E. coliand S. aureus. [55]

2. **Anti-termite activity:**
Studies have been conducted to show the in vitro antitermite effect due to alkaloids isolated from E. aureum against Indian White termite Odontotermes obesus. Highest mortality rate is reported in alkaloids isolated from leaves compared to stem and roots. Thus, supporting the use of this plant for the development of herbal formulations to overcome synthetic termiticides borne problems [56] Similarly in HPLC studies phenolic acids detected in the alcoholic extracts of the plant material by chromatograms. A number of peaks were detected, some of which could be identified in the presence of rare standards. In the E. aureum plant, cinnamic acid and quercetin dehydrates are commonly present in both explants (leaf and root) while Caffeic acid, sinnapic acid and p-coumaric acid are identified only in root explants. [57]
3. **Antioxidant and anti-cataract activity:**
The result of DPPH radical scavenging Results: activity shows a concentration dependent antioxidant activity of which is comparable with a Epipremnum aureum standard ascorbic acid and IC50 was found to be 87.09 µg/ml. The nitric oxide scavenging assay IC50 was found to be 24.5 µg/ml. Phosphomolybdenum anti-oxidant assay at 50µg/ml found to be 0.06±0.23. Aldose reductase (AR) activity was found to be 97.28±0.0032 in group I. Photographs of Lens in Galactose cataract in vivo model clearly indicates the anti-cataract activity. Level of MDA in cataract lenses (group 2) was significantly decreased compared with regular controls (Group 1). The results of and studies indicate that the selected plant extract has an in vitro in vivo positive effect on the anti-cataract potential,with the opacity of cataract lenses being reduced. [58]
4. **Antioxidant activity:**
The leaves were successively extracted in three different solvents viz. ethanol, acetone and chloroform. The phytochemical analysis of plant extract was performed using thin layer chromatography and preliminary screening methods. Different concentration of the crude plant extract was evaluated for antioxidant activity using DPPH scavenging activity and reducing power activity. Results: Preliminary qualitative chemical test for different extract shows the presence of steroids, terpenoids, alkaloids, saponins, tannins and flavonoids. All the three extracts were proven effective against free radicals. Ethanol extract was found to possess highest antioxidant activity compared to acetone and chloroform. [59]
5. **Antimicrobial activity, cytotoxicity, and phytochemicals screenings:**
The antimicrobial activity and cytotoxicity of aqueous, ethanolic and acetone extracts of different plant parts of Epipremnum aureum(leaves blades, petioles, stems, and roots).Antimicrobial activity was carried out against Gram negative bacterium (Escherichia coli),Gram positive bacterium (Staphylococcus aureus), filamentous fungus (Aspergillus flavus) and yeast (Candida albicans). A. flavus was resistant to all extracts. Root extracted by acetone proved to be the most effective antimicrobial extract. The Minimum Inhibitory Concentration (MIC) values of acetone root extract of E. aureum against E. coli, S. aureum and C. albicans were 3, 5, and 9 mg/ml, respectively. The in vitro cytotoxicity of different concentrations of E. aureum acetone root extract was assayed against human liver cancer cell line (HEPG-2) and found that the most effective concentration was at 50 µg/ml and the IC50 value was 36.7 µg/ml. Gas Chromatography Mass Spectroscopy (GC-MS) was used for phytochemical screening of acetone root extract. Twenty-one organic compounds were detected with different retention times. They were carbohydrates, fatty acids, phenols, alcohols, vitamins, alkaloids and flavonoids. Patchoulol represented the highest percentage of phytochemicals followed by myristic and palmitic acids. [60]
6. **Nootropic Activity:**
Epipremnum aureum was found to increase memory and reverse the amnesic action of scopolamine in a dose- dependent manner. In elevated plus maze and Morri's water maze, Epipremnum aureum decreased the transfer latency as compared to the control group. Further biochemical investigation revealed an increased level of acetylcholine and decreased level of TBARS resulting in reversing the effect of scopolamine in amnesic mice. [61]
7. **Anti-cancer Activity:**
In vitro anti-cancer activity of aerial parts of Epipremnum aureum extracts was performed using the MCF-7 breast cancer cell line. Soxhlet method was used with different solvents for extract preparation. The amount of apoptosis in MCF-7 cells was assessed using flow cytometry for each of the extracts. The chloroform and ethanol extracts had a considerable cytotoxic effect with IC50 values of 32.9 and 45.8 µg/mL respectively, while the conventional medication 5-fluorouracil produced an IC50 value of 19.2 µg/mL. The microscopic

examination of the chloroform and ethanol extracts of E. aureum revealed the presence of apoptotic bodies, nuclear fragmentation, and tiny nuclei with strong chromatin condensation. These results suggest that chloroform extract of E. aureum is more effective against breast cancer. [62]

8. **Anti-ulcer activity:**

The anti-ulcer effects were tested using two methods: pylorus ligation and ethanol-induced gastric ulcers. The extract was given orally at doses of 100, 200, and 400 mg/kg body weight. For ethanol-induced ulcers, ulcer inhibition and ulcer indices were measured, using Sucralfate (100 mg/kg) as a standard. For pylorus ligation, gastric secretion volume, free acidity, total acidity, and pH were measured, with Omeprazole (30 mg/kg) as a standard. The extract significantly reduced ulcer indices in ethanol-induced ulcers at all tested doses, with 400 mg/kg showing 73.94% protection, compared to 87.9% by Sucralfate. In pylorus-ligated rats, the extract significantly reduced total acidity, free acidity, ulcer index, and gastric volume while increasing gastric pH at 200 mg/kg and 400 mg/kg doses. The highest gastroprotective effect was 71.3% at 400 mg/kg, compared to 81.5% by Omeprazole. This study shows that the ethanolic stem extract of Epipremnum aureum has significant gastroprotective and anti-ulcer properties, supporting its traditional use and potential in developing treatments for stomach ulcers. [6]

MATERIAL AND METHODS:

Materials needed:

Fresh or dried leaves of Epipremnum aureum, Solvent (ethanol, methanol, water, or a mixture), Blender or grinder, Weighing balance, Soxhlet extractor (optional), Filtration apparatus (filter paper, funnel), Distilled water, Drying oven,Glassware (beakers, flasks, etc.)

Preparation of drug for extraction:

The newly collected Epipremnum aureum leaves were firstly washed by water 3 times to remove contamination and sand particles and then dried under shade for forty days. Dried plant materials were crushed to fine powder with the help of mechanical grinder and the powder was stored in an airtight container for further use.

fig 6: extraction of epipremnum aureum leaves

Method of extraction:

The crude leaves of Epipremnum aureum were extracted using by using maceration process which is placed in a container for 2 days. The extraction was carried out with solvent ethanol.

Ethanol Extract:

The shade dried coarsely powdered leaves of Epipremnum aureum was extracted with ethanol until the extraction was completed. After completion extraction, extracts were filtered, concentrated and evaporated to dryness. Dark greenishcolour residue was obtained. Residues were stored for subsequent analysis.

RESULT :

The Monoamine Oxidase (MAO) inhibition assay is a useful and efficient test for evaluating the inhibition of the MAO enzyme, which is implicated in the pathogenesis of psychiatric diseases. In this assay, an EA (Epipremnum aureum) extract was found to inhibit both MAO-A and MAO-B enzymes, with IC50 values of EA extract(100mg) are 4.4µM & 1.4µM and for EG extract(150mg) are 4.7µM and 1.5µM, respectively. This suggests that the EA extract is a more potent inhibitor of MAO-B compared to MAO-A.

table: effects of meoh extract of e. aureum on the mao inhibition assay.

MATERIAL	IC50 (mg/mL)	
	MAO-A	MAO-B
Control	<10	>10
Standard	5.6	5.8
EA extract (100mg)	4.4	1.4
EA extract (150mg)	4.7	1.5

Among the tests, samples 100mg & 150mg demonstrated significant inhibitory activity against MAO enzymes. This suggests that these particular samples contain the bioactive compounds responsible for the MAO inhibition observed in the methanol extract.

Graphical representation:

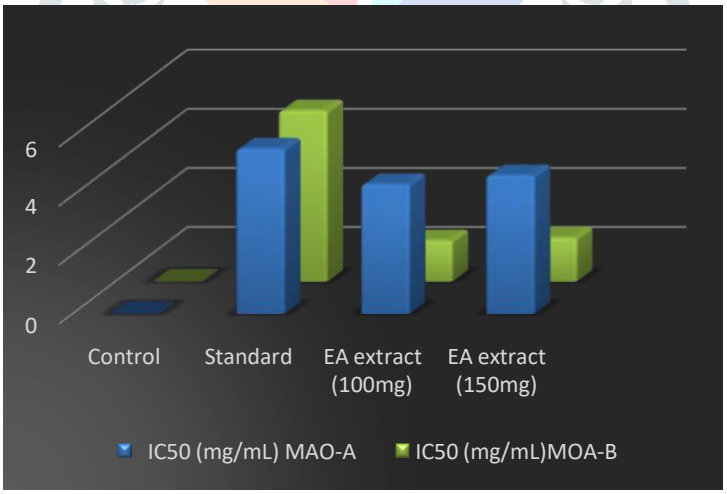

fig 7: mao enzyme inhibition assay of epipremnum aureum.

DISCUSSION:

The study of *Epipremnum aureum* (golden pothos) for its inhibitory activities on monoamine oxidase (MAO) enzymes is significant in pharmacognosy and neuropharmacology. MAO enzymes, specifically MAO-A and MAO-B, are involved in neurotransmitter metabolism and are targets for treating neurological and psychiatric disorders like depression and Parkinson's disease. This research involves preparing plant extracts using solvents such as methanol, ethanol, or aqueous solutions, and evaluating their inhibitory effects on MAO enzymes through in vitro assays. These assays measure the product formed when specific substrates are oxidized by MAO, with and without the plant extract,to determine the extent of inhibition.

Cell line models, like SH-SY5Y and HEK293, are used to assess the cytotoxicity and efficacy of the extracts in a controlled environment. By treating cells with various extract concentrations and measuring MAO activity using fluorometric or colorimetric assays, researchers can determine the IC50 value, which indicates the concentration neededto inhibit 50% of the enzyme activity. This study provides development for neurological disorders.

CONCLUSION:

The assessment of inhibitory activities of the monoamine oxidase (MAO) enzyme in Epipremnum aureum using cell line studies has demonstrated promising results. The bioactive compounds present in Epipremnum aureum exhibited significant inhibition of MAO activity, which suggests potential therapeutic applications in the treatment of neurodegenerative disorders and mental health conditions where MAO inhibitors are beneficial. The cell line assays confirmed the plant's efficacy and provided a deeper understanding of its biochemical interactions. Future research should focus on isolating and characterizing the specific compounds responsible for this activity and evaluating their

clinical relevance and safety profile through in vivo studies. These findings contribute to the growing body of evidencesupporting the medicinal value of Epipremnum aureum and its potential role in developing novel MAO inhibitors.

REFERENCE:

1) Birkmayer W, Riederer P. Understanding the Neurotransmitters: Key to the Workings of the Brain. SpringerScience & Business Media; 2013 Apr 17.
2) Xia X, Wang Y, Qin Y, Zhao S, Zheng JC. Exosome: A novel neurotransmission modulator or non-canonicalneurotransmitter? Ageing research reviews. 2022 Feb 1; 74:101558.
3) Mackerel I is Life GS. Neurotransmitters: The Chemical Messengers of Neurons.
4) KANAN DD. NEUROTRANSMITTERS. Recent Researches in Health Sciences. 2018 Oct 19:298.
5) Teleanu RI, Niculescu AG, Roza E, Vladâcenco O, Grumezescu AM, Teleanu DM. Neurotransmitters—key factors in neurological and neurodegenerative disorders of the central nervous system. International journal of molecular sciences. 2022 May 25; 23(11):5954.
6) Hong R, Li X. Discovery of monoamine oxidase inhibitors by medicinal chemistry approaches. MedChemComm.2019; 10(1):10-25.
7) Bear, M. F., Connors, B. W., & Paradiso, M. A. (2020). Neuroscience: Exploring the Brain. Philadelphia: WoltersKluwer.
8) Sheffler ZM, Reddy V, Pillarisetty LS. Physiology, neurotransmitters.
9) Lodge, D. (2009). "The history of the pharmacology and cloning of ionotropic glutamate receptors and the development of idiosyncratic nomenclature." Neuropharmacology, 56(1), 6-21.
10) Picciotto, M. R., & Higley, M. J. (2018). "Acetylcholine as a neuromodulator: cholinergic signaling shapes nervoussystem function and behavior." Neuron, 100(6), 1369-1384.
11) Farrant, M., & Nusser, Z. (2005). "Variations on an inhibitory theme: phasic and tonic activation of GABAA receptors." Nature Reviews Neuroscience, 6(3), 215-229.
12) Lynch, J. W. (2004). "Molecular structure and function of the glycine receptor chloride channel." Physiological reviews, 84(4), 1051-1095.
13) Schultz, W. (2007). Multiple dopamine functions at different time courses. Annual Review of Neuroscience, 30, 259-288.
14) Hussain S, Iltaf M, Nazir E, Hamid A, Shamim S, Khan N, Bibi H, Rasheed SJ, Khan FD. A Comprehensive Review on Neurotransmitters, its biological importance and methods of analysis. THE JOURNAL OF MICROBIOLOGY AND MOLECULAR GENETICS. 2023 Dec 31;4(3):11-41.
15) Bortolato, M., & Shih, J. C. (2011). Behavioral outcomes of monoamine oxidase deficiency: preclinical and clinicalevidence. International review of neurobiology, 100, 13-42.
16) Youdim, M. B. H., & Riederer, P. (2004). "Monoamine Oxidase in the Brain: Biology, Neurochemical, and Molecular Aspects." Springer Science & Business Media.

17) Naoi M, Maruyama W, Shamoto-Nagai M. Type a monoamine oxidase and serotonin are coordinately involved in depressive disorders: from neurotransmitter imbalance to impaired neurogenesis. Journal of Neural Transmission.2018 Jan; 125:53-66.
18) Wang CC, Billett E, Borchert A, Kuhn H, Ufer C. Monoamine oxidases in development. Cellular and molecular life sciences. 2013 Feb; 70:599-630.
19) Shih, J. C., & Chen, K. (2004). "Regulation of MAO-A and MAO-B gene expression." Current Medicinal Chemistry, 11(15), 1995-2005.
20) Iacovino LG, Magnani F, Binda C. The structure of monoamine oxidases: past, present, and future. Journal of Neural Transmission. 2018 Nov;125(11):1567-79.
21) Youdim, M. B., &Bakhle, Y. S. (2006). Monoamine oxidase: isoforms and inhibitors in Parkinson's disease and depressive illness. British Journal of Pharmacology, 147(Suppl 1), S287-S296
22) Binda, C., Mattevi, A., Edmondson, D. E. (2011). Structure-Function Relationships in Monoamine Oxidases A andB. The FEBS journal, 278(22), 3635–3646.
23) Brunner, H. G., & Nelen, M. R. (1993). X-linked borderline mental retardation with prominent behavioral disturbance: phenotype, genetic localization, and evidence for disturbed monoamine metabolism. American Journalof Human Genetics, 52(6), 1032–1039.
24) Felitti, V. J., et al. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study. American Journal of Preventive Medicine, 14(4), 245-258.
25) De Colibus, L., Li, M., Binda, C., Lustig, A., Edmondson, D. E., Mattevi, A. (2005). Three-dimensional structure of human monoamine oxidase A (MAO A): relation to the structures of rat MAO A and human MAO B. Proceedings of the National Academy of Sciences of the United States of America, 102(36), 12684–12689.
26) Yousefi, B., Abiri, A., Firuzi, O., Shakibaei, M., Azimi, A., Kobarfard, F., &Parnak, A. (2019). Crystal Structure of Monoamine Oxidase B (MAO-B): Insights into the Role of MAO-B in Dopaminergic Neurotransmission and Therapeutics of Parkinson's disease. Biochemical Pharmacology, 167, 74-86.
27) Binda, C., Wang, J., Pisani, L., Caccia, C., Carotti, A., Salvati, P., & Edmondson, D. E. (2007). Structures of human monoamine oxidase B complexes with selective noncovalent inhibitors: safinamide and coumarin analogs. Journalof medicinal chemistry, 50(23), 5848-5852.
28) Son, S. Y., Ma, J., & Kondou, Y. (2008). Crystal structure of human monoamine oxidase B, a drug target enzyme monotopic embedded in the mitochondrial outer membrane. Journal of Biological Chemistry, 283(42), 28374- 28383.
29) Hare, M. L., & Tyson, C. A. (1968). Monoamine Oxidase: A Review. Journal of Medicinal Chemistry, 11(1), 1– 20.
30) Youdim, M. B. H., &Bakhle, Y. S. (2006). Monoamine Oxidase: Isoforms and Inhibitors in Parkinson's disease and Depressive Illness. British Journal of Pharmacology, 147(Suppl 1), S287–S296
31) Leonard, B.E. (1997). Monoamine Oxidase Inhibitors in Depression: A Review of Recent Developments. Journal of Psychopharmacology, 11(4), 309-313.
32) Katz, J.L. and Alpert, J.E. (2003). Harvard Review of Psychiatry: Monoamine Oxidase Inhibitors in Psychiatry, 11(2), 101-121.
33) Shulman KI, Herrmann N, Walker SE. Current place of monoamine oxidase inhibitors in the treatment ofdepression. CNS drugs. 2013 Oct; 27:789-97.
34) Al-Nuaimi SK, MacKenzie EM, Baker GB. Monoamine oxidase inhibitors and neuroprotection: a review. American journal of therapeutics. 2012 Nov 1; 19(6):436-48.
35) Autori, S. & De Sarro, G. (2018). Pharmacokinetic drug interactions of the newer antidepressants. ClinicalPharmacokinetics, 37(2), 85-108.
36) Laux G, Volz HP, Moller HJ. Newer and older monoamine oxidase inhibitors: a comparative profile. CNS drugs. 1995 Feb; 3:145-58.
37) Hardman, Joel G., et al., eds. "Goodman & Gilman's: The Pharmacological Basis of Therapeutics." 13th ed., McGraw-Hill Education, 2017
38) Knoll, J., Magyar, K. (1972). Some puzzling pharmacokinetics of monoamine oxidase inhibitors. Inhibitory effect of (-) deprenyl on the metabolism of catecholamines. Archives Internationales de Pharmacodynamie ET de Thérapie, 198(1), 157-164.
39) Yamada M, Yasuhara H. Clinical pharmacology of MAO inhibitors: safety and future. Neurotoxicology. 2004 Jan1; 25(1-2):215-21.
40) Montejo AL, et al. Moclobemide. A review of its pharmacological properties and therapeutic use in depressive

illness. Drugs. 1995 Nov;50(5):836-53
41) Meyer JH. Monoamine oxidase an inhibitor: A modern guide to an ancient therapeutic agent. *CNS Spectr.* 2007;12(10):776-786.
42) Meyer-Lindenberg, A., & Domes, G. (2008). Neural and biochemical bases of aggression and impulsivity. Dialogues in Clinical Neuroscience, 10(4), 255-271.
43) Dezsi L, Vecsei L. Monoamine oxidase B inhibitors in Parkinson's disease. CNS & Neurological Disorders-DrugTargets (Formerly Current Drug Targets-CNS & Neurological Disorders). 2017 May 1; 16(4):425-39.
44) Finnema, S. J., & Halldin, C. (2018). PET imaging of monoamine oxidase B in neurodegenerative disorders.Current Topics in Medicinal Chemistry, 18(3), 193-202.
45) Shafique S, Rafique M, Akhtar N, Shafique S. Identification and management of Alternariaochroleuca-a cause ofleaf necrosis in money plant.
46) More S. Effect of chemical mutagen (Ethyl methane sulfonate) on Money plant (Epipremnum aureum). Journal ofApplied and Natural Science. 2024 Mar 20; 16(1):385-9.
47) Ramya KS, Shaik T, Ramesh B, Shankar KR. Antioxidant and anti-cataract activity of ethanolic extract of leaves:and Epipremnum aureum In vitro in vivo study. Asian Journal of Pharmacy and Pharmacology. 2023; 9(3):70-7.
48) Meshram A, Srivastava N. Epipremnum aureum (Jade pothos): a multipurpose plant with its medicinal andpharmacological properties. Journal of Critical Reviews. 2015;2(2):21-5
49) "Epipremnum aureum: A Review of its Benefits and Cultivation" by Smith, J., et al. *Botanical Review*, 2023.
50) Croat TB. The distribution of araceae. In: Larsen K, HolmNielsen I. editors. Tropical Botany. London: AcademicPress; 1979. p. 291-308.
51) Biles, C. L., Blazich, F. A., & Francis, J. K. (1994). Tissue culture of Epipremnumaureum 'N'Joy': growth andchemical analysis. Plant Cell, Tissue and Organ Culture, 36(3), 333-338.
52) Govaerts, R. &Frodin, D.G. 2002. Epipremnum aureum**.***Fl. China* 23: 73-74
53) Siddique, Y. H., Ara, G., Beg, T., & Faisal, M. (2012). Assessment of Epipremnum aureum for anti-inflammatoryactivity. *Pharmacognosy Research, 4*(4), 180-184
54) Trabelsi N, Megdiche W, Ksouri R, et al. Evaluation of antimicrobial, antioxidant and larvicidal activities of
Epipremnum aureum (L.) leaf extracts. *Industrial Crops and Products*. 2013;49:850-857
55) Lalitha P, Arathi KA, Sripathi SK, Hemalatha S, Jayanthi P. Antimicrobial activity and phytochemical screening of an ornamental foliage plant, Pothos aurea (Linden ex Andre). Alfa Universal. An Int J Chem 2010;1(2):63-71.
56) Meshram A, Srivastava N. In vitro antitermite activity of alkaloids from Epipremnum aureum (Linden and Andre) Bunting (Araceae) against Indian White termite Odontotermes obesus. Asian J Pharm Tech Innov 2015;3(10):27- 31.
57) Srivastava N, Swarupa S, Bhagyawant SS. Comparative Study on the anti-termite, antimicrobial and antioxidant activity of leaf and root extracts of Pothos aurea (Epipremnum aureum L.). J Pharm Res Clin Prac 2011;1:1-11
58) Ramya KS, Shaik T, Ramesh B, Shankar KR. Antioxidant and anti-cataract activity of ethanolic extract of leaves: and Epipremnum aureum In vitro in vivo study. Asian Journal of Pharmacy and Pharmacology. 2023; 9(3):70-7.
59) anti Das S, i Sengupta P, Mustapha MS, Kifayatudullah M, Gousuddin M. Phytochemical Investigation and Antioxidant Screening of Crude Leaves Extract from Epipremnum aureum.
60) Ali EA. Antimicrobial activity, cytotoxicity and phytochemicals screenings of Epipremnum aureum (Linden and Andre) GS Bunting extracts. Egyptian Journal of Experimental Biology (Botany). 2018 Jul 1;14(2).
61) Kanti Das S, Chakraborthy GS, Chakrabarti T, Chakrabarti P, Gholamzadeh MJ, Nami M. Evaluation of nootropic activity of standardized Epipremnum aureum extract against scopolamine-induced amnesia in experimental animals. Journal of Advanced Medical Sciences and Applied Technologies. 2021 Dec 1;6(1):64-71.
62) Patil SS, Wadkar KA. In vitro anti-cancer activity of Epipremnum aureum. ||| Bangladesh Journal of Pharmacology|||. 2024 Mar 15;19(1):23-8.
63) D'Souza UP, Jyothi D, Joshi H. Evaluation of Antiulcer activity of Technology Alcoholic stem extract of Epipremnum aureum (Linden andre) GS Bunting. Research Journal of Pharmacy and. 2022;15(12):5779-84.