CENTRAL NERVOUS SYSTEM ACTIVITY OF ETHANOLIC EXTRACT OF *Canavalia maritima* LEAVES

Dissertation submitted to

The Tamil Nadu Dr. M.G.R. Medical University, Chennai-32

In partial fulfillment for the award of the degree of

MASTER OF PHARMACY

IN

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Submitted by

Reg.No. 26103098

Under the Guidance of

Mrs. M.SUDHA, M. Pharm

Asst. professor

DEPARTMENT OF PHARMACOLOGY

J.K.K. NATTRAJA COLLEGE OF PHARMACY

Komarapalayam – 638183

Tamilnadu.

MAY-2012

CERTIFICATES

EVALUATION CERTIFICATE

This is to certify that the dissertation work entitled **"central nervous system activity of ethanolic extract of *Canavalia maritima* leaves"** submitted by the student bearing **Reg. No:26103098** to "The Tamil Nadu Dr. M.G.R. Medical University", Chennai, in partial fulfillment for the award of **Master of Pharmacy** in **Pharmacology** was evaluated by us during the examination held on ……

Internal Examiner **External Examiner**

CERTIFICATE

This is to certify that the work embodied in this dissertation entitled **"Central Nervous System Activity of ethanolic extract of *Canavalia maritima* leaves"**, submitted to "The Tamil Nadu Dr. M.G.R. Medical University", Chennai, in partial fulfillment to the requirement for the award of degree of **Master of Pharmacy** in **Pharmacology**, is a bonafide research work carried out by **Mr. KRISHNA CHAITANYA. A, [Reg. No:26103098]**, during the academic year 2011-2012, under the guidance and supervision of **Mrs. SUDHA , M. Pharm.,** Assistant Professor and Head of Department of Pharmacology, J.K.K. Nattraja College of Pharmacy, Komarapalayam during the academic year 2011-2012.

Place: Komarapalayam
Date:

Dr. P. PERUMAL, M.Pharm., Ph.D., AIC.,
Professor& Principal,
J.K.K. Nattaraja College of Pharmacy.
Komarapalayam-638183.

CERTIFICATE

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Place: Komarapalayam
Date:

Mrs M.SUDHA, M.Pharm,
Assistant Professor,
Department of Pharmacology,
J.K.K. Nattraja College of Pharmacy
Komarapalayam-638 183.
Tamil Nadu.

DECLARATION CERTIFICATE

I here by declare that the dissertation work entitled **"Central Nervous System Activity of ethanolic extract of *Canavalia maritima* leaves"**, submitted to "The Tamil Nadu Dr. M.G.R. Medical University", Chennai, in partial fulfillment to the requirement for the award of degree of **Master of Pharmacy** in **Pharmacology**, is a bonafide research work carried out by me during the academic year 2011-2012, under the guidance and supervision of **Mrs. M.SUDHA, M. Pharm.,** Assistant Professor in the Department of Pharmacology, J.K.K. Nattraja College of Pharmacy, Komarapalayam Erode.

I further declare that, this work is original and this dissertation has not been submitted previously for the award of any other degree, or any other University. The information furnished in this dissertation is genuine to the best of my knowledge and belief.

Place: Komarapalayam

Date:

KRISHNA CHAITANYA.A

Reg. No. 26103098,

Department of Pharmacology,
J.K.K.Nattraja College of Pharmacy,
Komarapalayam- 638183
Tamilnadu.

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Mr. KRISHNA CHAITANYA.A

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1. INTRODUCTION

1.1 HERBAL MEDICINE

Herbal medicine also called botanical medicine or phytomedicine refers to using a plant's seeds, berries, root, leaves, bark or flowers for medicinal purposes. Herbalism has a long traditional of use outside of conventional medicine. It is becoming more main stream as improvement in analysis and quality control along with advance in clinical research show the value of herbal medicine in the treating and preventing disease.

Herbal Medicine is the use of whole plant preparations and is the oldest known form of medicine. It has been used for over 2,000 years and is still the major form of medicine for over 75% of the world's population. Our ancestors used trial and error to discover the most effective local plants for the treatment of illnesses. Advances in science have enabled a better understanding of the physiological effects of herbs on the human body and therefore their role in restoring health. Herbal medicines support the body's natural healing process and aim to treat the person as well as the disease. This means it can bring about a deep and lasting change.

During the course of history the cure of disease and the use of medicinal plant have been much influenced by religious practice and exercise of magical rites. An herbal remedy is one in which the main therapeutic activity depends on the plant or fungal metabolites. From a pharmacological viewpoint the study of herbal medicines differ little from that for hallopathic medicinal plant. In practice however, many herbal medicines have not been extensively studied either pharmacologically or phytochemically.

Herbal medicines are a major component in all indigenous people's traditional medicine and a common element in Ayurvedic, Homeopathic, Naturopathic, Traditional, Oriental, and Native American Indian medicine. Many drugs commonly used today are of herbal origin. Indeed, about 25 percent of the prescription drugs dispensed in the United States contain at least one active ingredient derived from plant material. Some are made from plant extracts; others are synthesized to mimic a natural plant compound. Major pharmaceutical companies are currently conducting extensive research on plant materials gathered from the rain forests and other places for their potential medicinal value. As a result

of modern isolation techniques and pharmacological testing procedures, new plant drugs usually find their road into the medicines as purified substances **(Sectoral study, 1996., Kokate *et al.*, 1997).**

1.2 INDIAN HERBAL MARKET

India can be a major player in the global market for herb based medicines. Exports of herbal materials and medicines can jump from just Rs. 456 crore now to Rs.10,000 crore by 2010 (Gupta and Chitme, 2000). Herbal medicines also find market as nutraceuticals (health foods), whose current market is estimated at about $ 80-250 billion in USA and also in Europe **(Kamboj, 2000).**

The criteria for the selection of plants for herbal drug research for various human ailments are as follows:

- Actual use of the medicinal plants in the countries of the region.
- Scientific literatures indicating therapeutic efficacy of the plants in certain diseases.
- Mention of the plants in early texts as having therapeutic effects.
- Use of medicinal plants for therapeutic purposes in countries outside the region.

To evaluate plants with possible therapeutic effects, the first World Congress of Clinical Pharmacology and Therapeutics was held in London in 1980. The traditional approach on herbal drug research consists of the following steps.

- Identification of the plant reportedly in use.
- Collection of the plant.
- Transport of the plant to the research laboratory.
- Storage of the plant.
- Preparation of the extracts.
- Toxicity studies of the plant extracts in animals.
- Evaluation of therapeutic efficacy of the extract in animal models.
- Identification of the extracts which is having more activities.
- Further fractionation of the active molecule.
- Structural elucidation of the bio-active molecule.
- Synthesis of bio-active molecule.

Today, phytomedicines are flooding the markets of advanced countries and the consumer world over have shown the preference for natural herbal based formulations. With the advent of automated high-throughput screening methods, the pharmaceutical industry in the West has demonstrated a renewed commitment to searching for new medicinal agents from higher plants. *Solanum torvum*(Telesphore et al.,2008), *Toona ciliate*(Malairajan et al., 2007), *Ocimum suave*(paul v. et.al.,2002), *Rhizopora mangle* L(Berenguer et.al.,2005), *Asparagus racemosus*(Sairam k et.al.,2002), *Ficus glomerata*(Rao, C V.et.al.,2008) are some of the plants reported to possess gastroprotective properties, containing flavonoids, triterpenoids, saponins and tannins and phenolic compounds as their important phytoconstituent.

1.3 TRADITIONAL HERBAL MEDICINES AND PUBLIC HEALTH CARE

Indian traditional medicine is based on various system including ayurveda, siddha and unani. These traditional system of Indian medicine have their uniqueness, but there is a common fundamental principle and practices.

According to the WHO, the definition of traditional medicine may be summarized as the sum of total of all the knowledge and practice, used in the diagnosis, prevention and elimination of physical, mental or social imbalance and relaying exclusivisely on practical experience and observation handed down from generation to generation, whether verbally or in writing. The medicinal plant play a major role and constitute the backbone of the traditional medicine. Indian material includes about 2000 drugs of natural orgin.

1.4 DIFFERENT TRADITIONAL SYSTEM AND FOLKLORE PRACTICES.

The traditional system of health care has its own particulars approach to health have undergone a major revival in the last twenty years. Every region has its history of traditional medicine. The medicine is traditional because it is deeply rooted in a specific socio-cultural context, which varies from one community to another. Each community has its own particular approach to health and disease even at the level of ethenopathogenic perception of disease and therapeutic behaviour.

Traditional use of herbal medicine is the basis and integral part of various culture for thousand of years. plant based drugs(natural drug) may be used directly or they may be

collected, dried and used as therapeutic agents(crude drug) or their chief active constituents are separated by various chemical process which are employed as medicines.

1.5 IMPORTANCE OF HERBAL

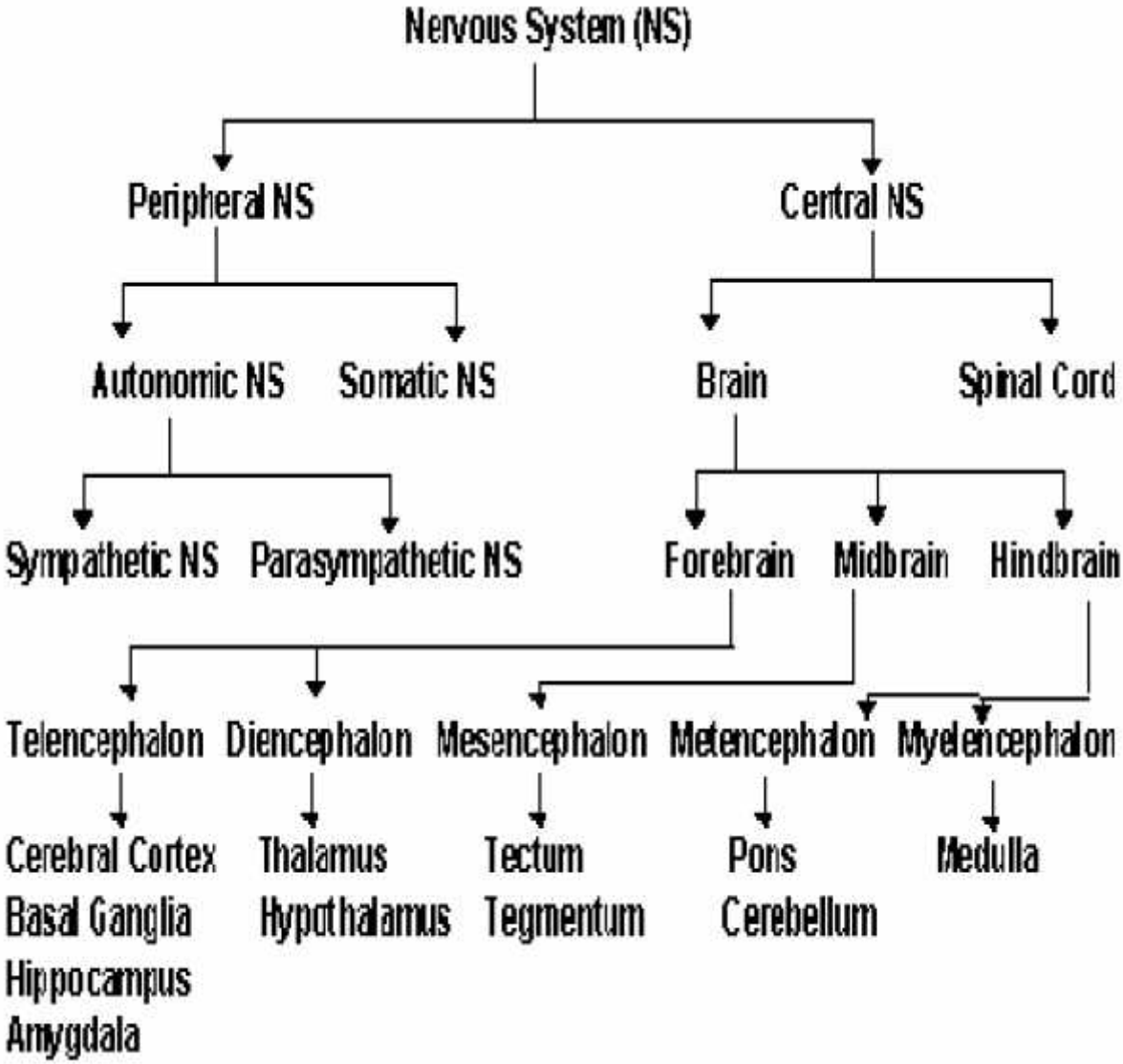
Herbs are staging a comeback and herbal 'renaissance' is happening all over the globe. The herbal products today symbolise safety in contrast to the synthetics drug that are regarded as unsafe to human and environment. Although herbs had been priced for their medicinal, flavouring and aromatic qualities for centuries, the synthetic products of the modern age surpassed their importance, for a while. However, the blind dependence on synthetics is over and people are returning to the naturals with hope of safety and security.

Our ancestors used trial and error to discover the most effective local plants for the treatment of illnesses. Advances in science have enabled a better understanding of the physiological effects of herbs on the human body and therefore their role in restoring health. Herbal medicines support the body's natural healing process, and aim to treat the person as well as the disease. This means it can bring about a deep and lasting change.

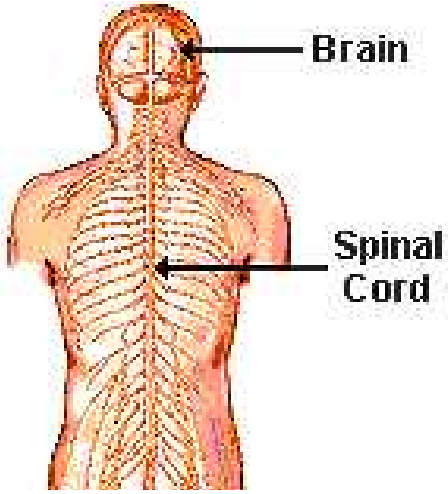
1.6 PROSPECTS OF HERBAL RESEARCH

There is a worldwide 'green revolution, (Mukherjee, P.K., 2002) which is reflected in the belief that herbal remedies are safer and less damaging to the human body than synthetic drugs. Furthermore, underlying this upsurge of interest in plants is the fact that many important drugs in use today were derived from plants or from starting molecules of plant origin.

Nervous system

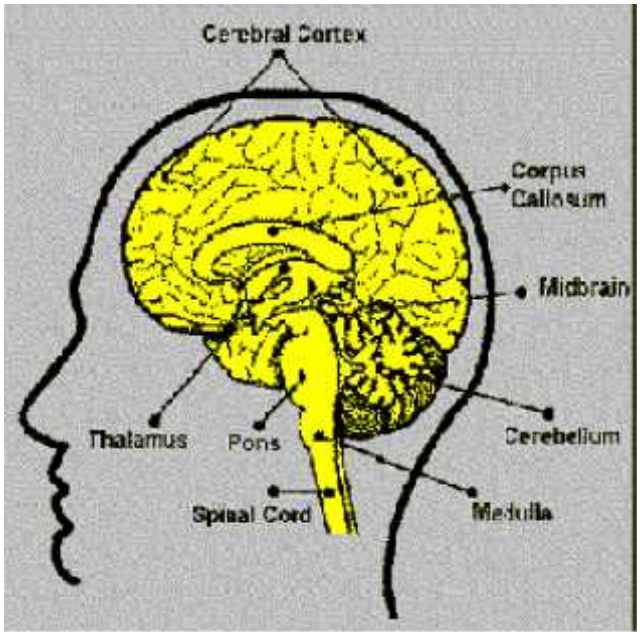


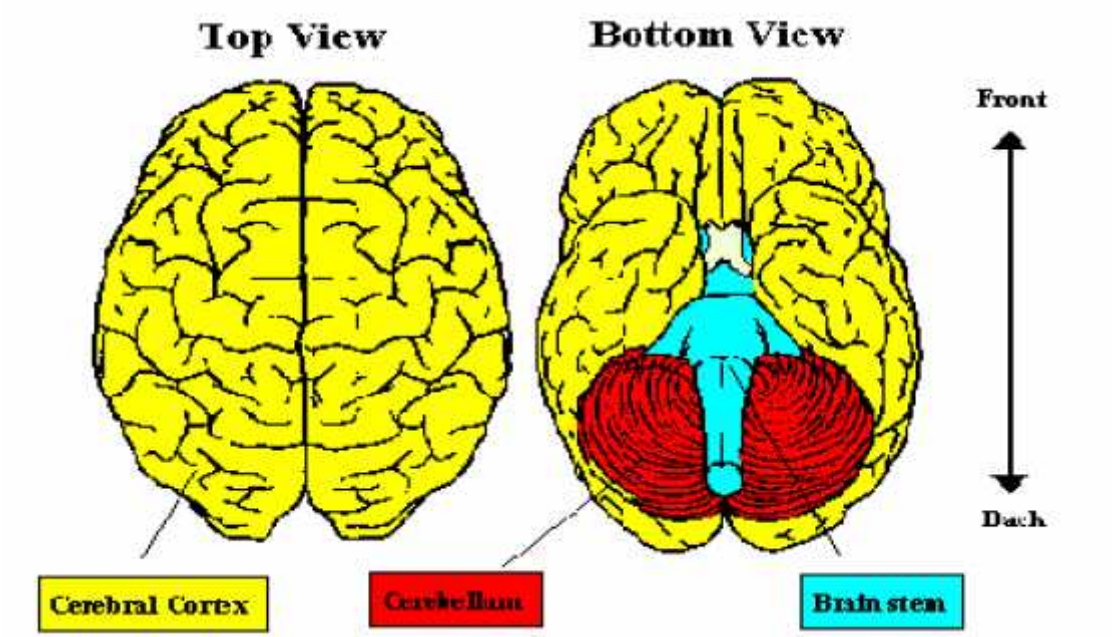
Central Nervous System:-

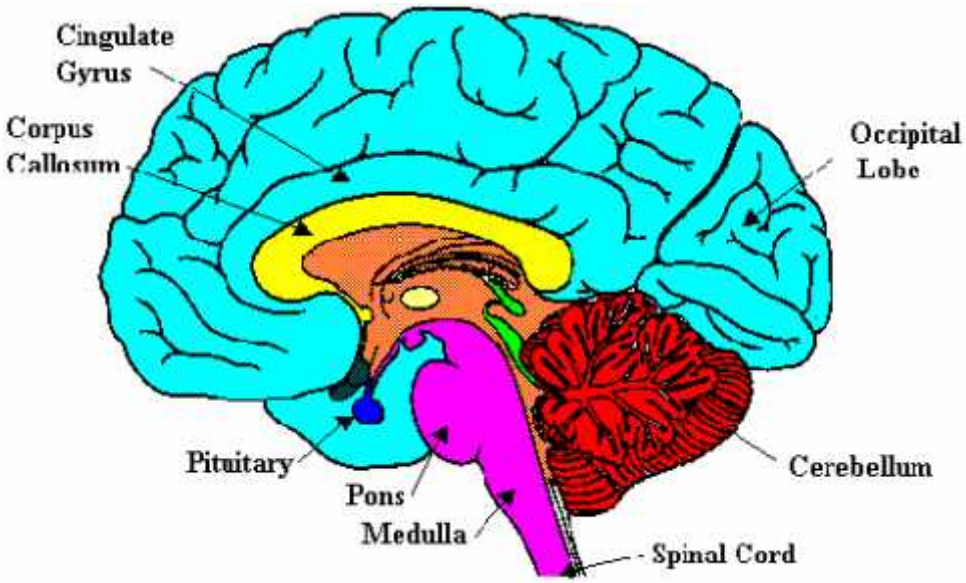


The central nervous system is divided into two major parts: the brain and the spinal cord. The average adult human brain weighs 1.3 to 1.4 kg. The brain contains nerve cells (neurons) and "support cells" called glia. The spinal cord is about 43 cm long in adult women and 45 cm long in adult men and weighs about 35-40 grams. The vertebral column, the collection of bones (back bone) that houses the spinal cord, is about 70 cm long. Therefore, the spinal cord is much shorter than the vertebral column.

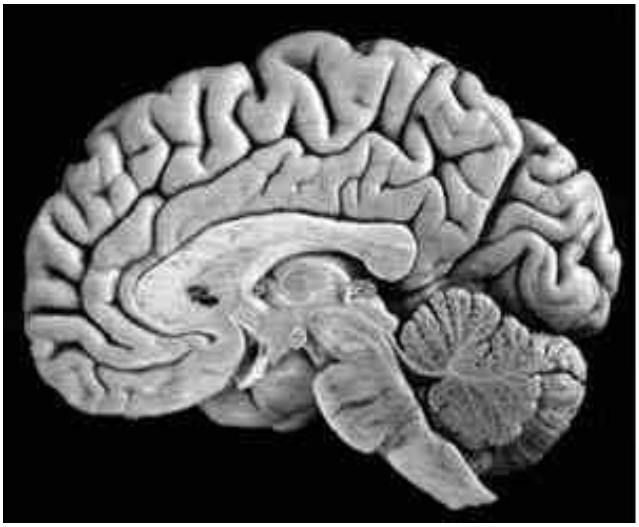
Brain

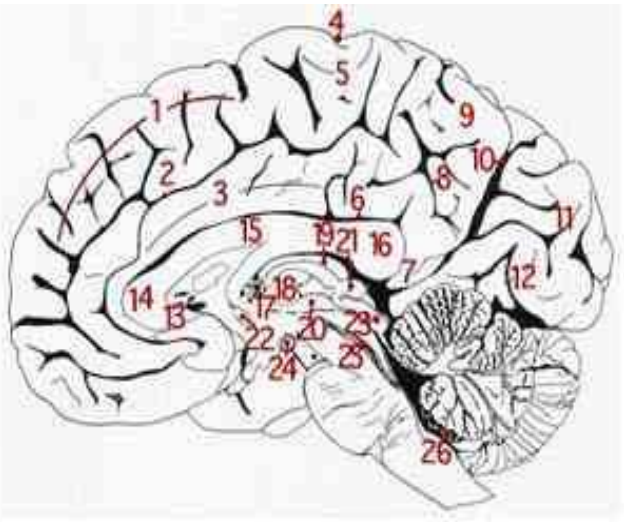




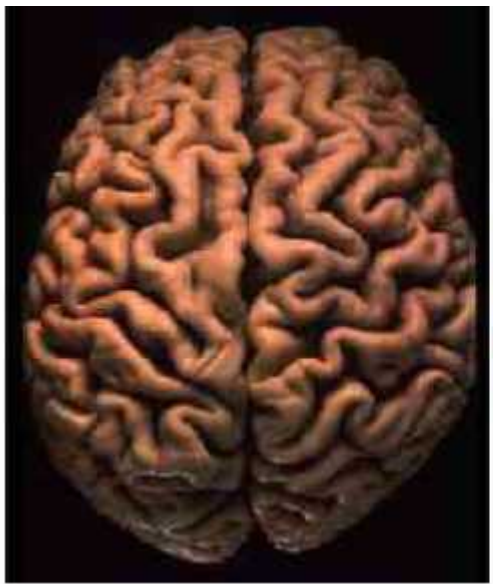


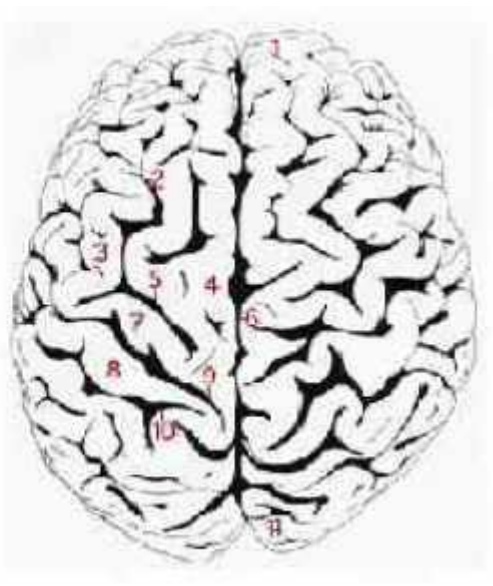
Saggital section





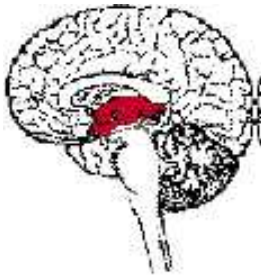
1. Medial frontal gyrus **2.**Cingulate sulcus **3.** Cingulate gyrus 4.Central sulcus **5.**Paracentral lobule **6.**Callosal sulcus **7.**Isthmus of cingulate gyrus **8.**Subparietal sulcus **9.**Precuneus **10.**Parieto-occipital sulcus **11.**Cuneus **12.**Calcarine sulcus or fissure **13.**Rostrum of corpus callosum **14.**Genu of corpus callosum **15.**Trunk of corpus callos **16.**Splenium of corpus callosum **17.**Choroid plexus in interventricular foramen **18.**Interthalamic adhesion **19.** Habenular trigone **20.**Hypothalamic sulcus **21.** Pineal body **22.**Anterior (rostral) commissure **23.**Tectum of midbrain **24.**Mamillary body **25.**Medial longitudinal fasciculus **26.** Choroid plexus of 4th ventricle



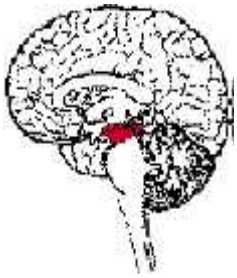


1. Frontal pole **2.**Superior frontal sulcus **3.**Middle frontal gyrus **4.**Superior frontal gyrus **5.**Precentral sulcus **6.**Longitudinal cerebral fissure **7** Precentral gyrus **8.**Postcentral gyrus **9.** Central sulcus **10.**Postcentral sulcus **11.** Occipital pole

Telencephelon



Diencephelon



Metencephelon

Mesencephelon

Myelencephelon

Cerebral Cortex

The word "cortex" comes from the Latin word for "bark" (of a tree). This is because the cortex is a sheet of tissue that makes up the outer layer of the brain. The thickness of the cerebral cortex varies from 2 to 6 mm. The right and left sides of the cerebral cortex are connected by a thick band of nerve fibers called the "corpus callosum." In higher mammals such as humans, the cerebral cortex looks like it has many bumps and grooves. A bump or bulge on the cortex is called a gyrus (the plural of the word gyrus is "gyri") and a groove is called a sulcus (the plural of the word sulcus is "sulci"). Lower mammals like rats and mice have very few gyri and sulci.

Functions: Thought, Voluntary movement, Language, Reasoning, Perception.

Cerebellum

The word "cerebellum" comes from the Latin word for "little brain." The cerebellum is located behind the brain stem. In some ways, the cerebellum is a bit like the cerebral cortex: the cerebellum is divided into hemispheres and has a cortex that surrounds these hemispheres.

Functions: Movement, Balance, Posture.

Hypothalamus

The hypothalamus is composed of several different areas and is located at the base of the brain. It is only the size of a pea (about 1/300 of the total brain weight), but it is responsible for some very important behaviours. One important function of the hypothalamus is the control of body temperature. The hypothalamus acts like a “thermostat" by sensing changes in body temperature and then sending out signals to adjust the temperature. For example, if you are too hot, the hypothalamus detects this and then sends out a signal to expand the capillaries in your skin. This causes blood to be cooled faster. The hypothalamus also controls the pituitary.

Functions: Body Temperature, Emotions, Hunger, Thirst, Circadian Rhythms.

Brain stem

The brain stem is a general term for the area of the brain between the thalamus and spinal cord. Structures within the brain stem include the medulla, Pons, tectum, reticular formation and tegmentum. Some of these areas are responsible for the most basic functions of life such as breathing, heart rate and blood pressure.

Functions: Breathing, Heart Rate, Blood Pressure

Thalamus

The thalamus receives sensory information and relays this information to the cerebral cortex. The cerebral cortex also sends information to the thalamus which then transmits this information to other areas of the brain and spinal cord.

Functions: Sensory Integration, Motor Integration

Limbic System

The limbic system (or the limbic areas) is a group of structures that includes the amygdala, the hippocampus, mammillary bodies and cingulate gyrus. These areas are important for controlling the emotional response to a given situation. The hippocampus is also important for memory.

Functions: Emotional Behaviour

Hippocampus

The hippocampus is one part of the limbic system that is important for memory and learning.

Functions: Learning, Memory.

Basal Ganglia

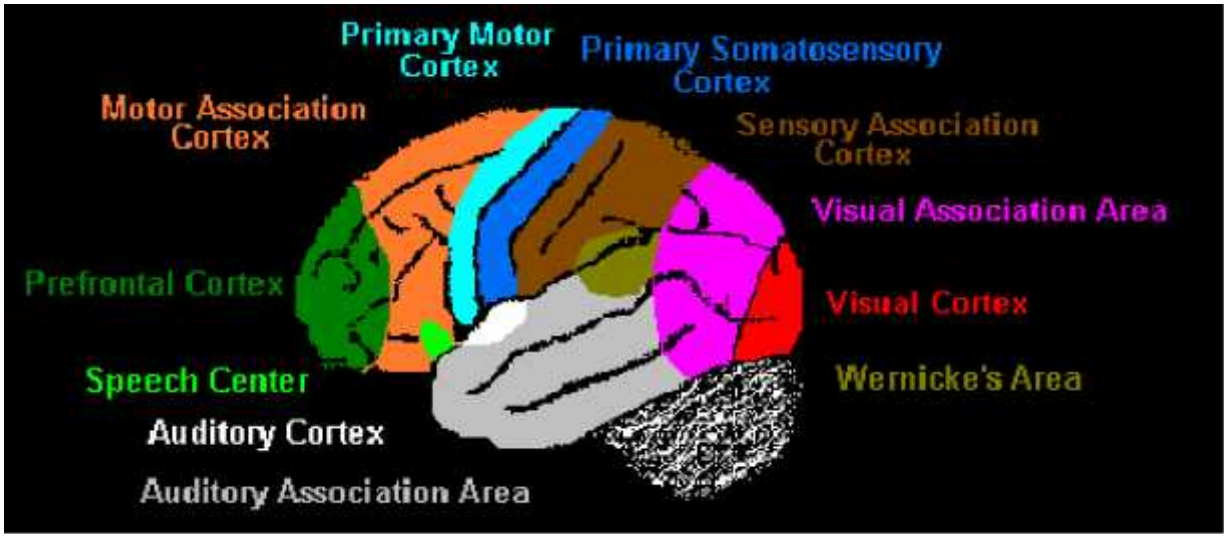
The basal ganglia are a group of structures, including the globus pallidus, caudate nucleus, subthalamic nucleus, putamen and substantia nigra that are important in coordinating movement.

Functions: Movement

Midbrain

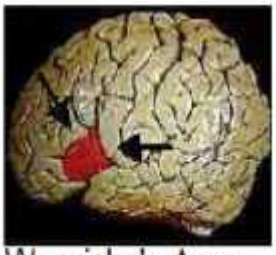
The midbrain includes structures such as the superior and inferior colliculi and red nucleus. There are several other areas also in the midbrain.

Functions: Vision, Audition, Eye Movement, Body Movement.



Cortical Area	Function
Prefrontal Cortex	Problem Solving, Emotion, Complex Thought
Motor Association Cortex	Coordination of complex movement
Primary Motor Cortex	Initiation of voluntary movement
Primary Somatosensory Cortex	Receives tactile information from the body
Sensory Association Area	Processing of multisensory information
Visual Association Area	Complex processing of visual information
Visual Cortex	Detection of simple visual stimuli
Wernicke's Area	Language comprehension
Auditory Association Area	Complex processing of auditory information
Auditory Cortex	Detection of sound quality (loudness, tone)
Speech Center (Broca's Area)	Speech production and articulation

Broca's Area



Wernicke's Area

Images courtesy of *Slice of Life*.

Hind brain:-

The **hindbrain** or **brain stem** consists of three parts. The first is the **medulla**, which is actually an extension of the spinal cord into the skull. Besides containing tracts up and down to and from the higher portions of the brain, the medulla also contains some of the essential nuclei that govern respiration and heart rate. The upper part of the medulla contains a pinky-sized complex of nuclei called the **reticular formation**. It is the regulatory system for sleep, waking, and alertness.

The second part is the **pons**, which means bridge in Latin. The pons sits in front of the medulla, and wraps around it to the back. It is primarily the pathways connecting the two halves of the next part, which is called the cerebellum.

The **cerebellum**, which means "little brain" in Latin, is in fact shaped like a small brain, and it is primarily responsible for coordinating involuntary movement. It is believed that, when you learn complex motor tasks, the details are recorded in the cerebellum.

Functions:-

The Medulla Oblongata

Helps control the body's autonomic functions (things you don't need to think about to perform) like respiration, digestion and heart rate. Also acts as a relay station for nerve signals going to/from the brain

- **The Pons**

Have roles in your level of arousal or consciousness and sleep. Relays sensory information to/from the brain. Also involved in controlling autonomic body functions.

- **The Cerebellum**

Mostly deals with movement. It regulates and coordinates movement, posture and balance. Also involved in learning movement.

Spinal cord:-

The **spinal cord** is a long, thin, tubular bundle of nervous tissue and support cells that extends from the brain (the medulla oblongata specifically). The brain and spinal cord together make up the central nervous system (CNS). The spinal cord begins at the occipital bone and extends down to the space between the first and second lumbar vertebrae; it does not extend the entire length of the vertebral column. It is around 45 cm (18 in) in men and around 43 cm (17 in) long in women. Also, the spinal cord has a varying width, ranging from 1/2 inch thick in the cervical and lumbar regions to 1/4 inch thick in the thoracic area. The enclosing bony vertebral column protects the relatively shorter spinal cord. The spinal cord functions primarily in the transmission of neural signals between the brain and the rest of the body but also contains neural circuits that can independently control numerous reflexes and central pattern generators. The spinal cord has three major functions: as a conduit for motor information, which travels down the spinal cord, as a conduit for sensory information in the reverse direction, and finally as a center for coordinating certain reflexes.

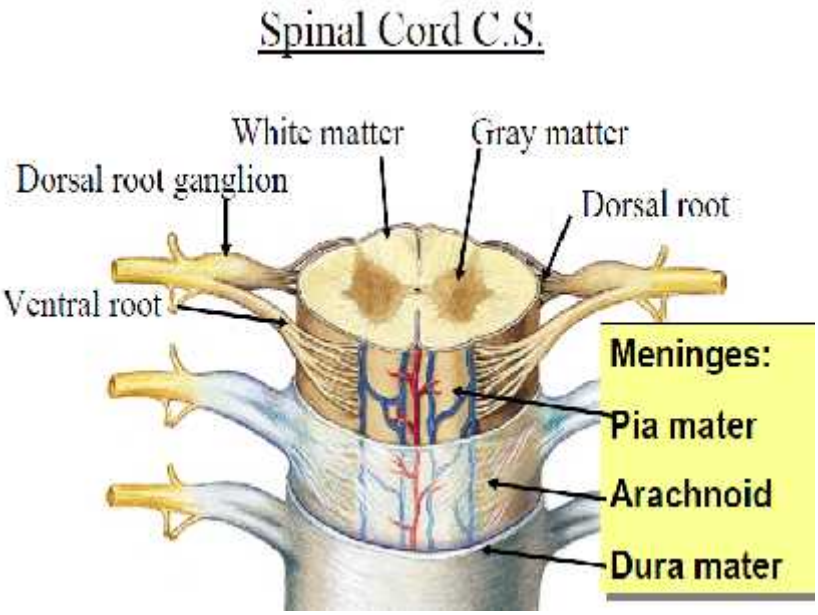
Structure:-

The spinal cord is the main pathway for information connecting the brain and peripheral nervous system. The length of the spinal cord is much shorter than the length of the bony spinal column. The human spinal cord extends from the foramen magnum and continues through to the conus medullaris near the second lumbar vertebra, terminating in a fibrous extension known as the filum terminale.

It is about 45 cm (18 in) long in men and around 43 cm (17 in) in women, ovoid-shaped, and is enlarged in the cervical and lumbar regions. The cervical enlargement, located from C3 to T2 spinal segments, is where sensory input comes from and motor output goes to the arms. The lumbar enlargement, located between L1 and S3 spinal segments, handles sensory input and motor output coming from and going to the legs.

The spinal cord is protected by three layers of tissue, called spinal meninges that surround the canal. The dura mater is the outermost layer, and it forms a tough protective coating. Between the dura mater and the surrounding bone of the vertebrae is a space called the epidural space. The epidural space is filled with adipose tissue, and it contains a network of blood vessels. The arachnoid mater is the middle protective layer. Its name comes from the fact that the tissue has a spider web-like appearance. The space between the arachnoid and the underlyng piamatter is called subarachnoid space. The subarachnoid space contains cerebrospinal fluid (CSF). The pia mater is the innermost protective layer. It is very delicate and it is tightly associated with the surface of the spinal cord. The cord is stabilized within the duramater by the connecting denticulate ligaments, which extend from the enveloping pia mater laterally between the dorsal and ventral roots. The dural sac ends at the vertebral level of the second sacral vertebra.

In cross-section, the peripheral region of the cord contains neuronal white matter tracts containing sensory and motor neurons. Internal to this peripheral region is the gray, butterfly-shaped central region made up of nerve cell bodies. This central region surrounds the central canal, which is an anatomic extension of the spaces in the brain known as the ventricles and, like the ventricles, contains cerebrospinal fluid. The spinal cord has a shape that is compressed dorso-ventrally, giving it an elliptical shape. The cord has grooves in the dorsal and ventral sides. The posterior median sulcus is the groove in the dorsal side, and the anterior median fissure is the groove in the ventral side.



CNS Neurotransmitters:-

Type	Neurotransmitter	Postsynaptic effect
	Acetylcholine	Excitatory
Amino acids	Gamma amino butyric acid GABA	Inhibitory
	Glycine	Inhibitory
	Glutamate	Excitatory
	Aspartate	Excitatory
Biogenic amines	Dopamine	Excitatory
	Noradrenaline	Excitatory
	Serotonin	Excitatory
	Histamine	Excitatory

Neuropeptide neurotransmitters	
Corticotrophin releasing hormone	Somatostatin
Corticotrophin (ACTH)	Bradykinin
Beta-endorphin	Vasopressin
Substance P	Angiotensin II
Neurotensin	

Neurotransmitter	Actions
Acetylcholine	Muscle activation, learning, and memory, arousal.
GABA	Inhibition
Glutamate	Excitation
Serotonin	Mood, anxiety, appetite, eating behaviour, sleep
Dopamine	Attention and executive functioning, motivated behaviours (reward- and pleasure-seeking), addictions, mood, movement, psychosis
Norepinephrine	Arousal, concentration, learning and memory, mood, stress response
Epinephrine (adrenaline)	Peripheral activation and arousal, fight or flight response

Overview of Transmitter Pharmacology in the Central Nervous System

TRANSMITTER	TRANSPORTER BLOCKER*	RECEPTOR SUBTYPE	AGONISTS	RECEPTOR-EFFECTOR COUPLING MOTIF (IR/GPCR)	SELECTIVE ANTAGONISTS
GABA	Guvacine, nipecotic acid	$GABA_A$	Muscimol	IR: classical fast inhibitory transmission via Cl^- channels	:bicuculline
		α, β, γ, δ, σ isoforms	Isoguvacine		Picrotoxin
			THIP		SR 95531
	(β-Alanine for glia)	$GABA_B$	Baclofen	IR: pre- and post-synaptic effects	2-hydroxy-*s*-Saclofen
			3Aminopropyl phosphinic acid		CGP35348
					CGP55845
		$GABA_C$		IR: slow, sustained responses *via* Cl^- channels	
Glycine	? Sarcosine	α and β subunits	β-Alanine; taurine	IR: classical fast inhibitory transmission *via* Cl^- channels (insensitive to bicuculline and picrotoxin)	Strychnine
Glutamate	—	AMPA	Quisqualate	IR: classical fast excitatory transmission *via* cation channels	NBQX
Aspartate	—	GLU 1-4	Kainate		CNQX
			AMPA		GYK153655
			KA	Domoic acid	CNQX
		GLU 5-7; KA 1,2	Kainate		LY294486
		NMDA	NMDA	IR: depolarization Mg^{2+}-gated slow excitatory transmission	MK801
		NMDA $1,2_{A-D}$	GLU, ASP		AP5
					Ketamine, PCP
		mGLU 1,5 (Group I mGluRs)	3,5-DHPG	GPCRs: modulatory; regulate ion channels, second messenger production, and protein phosphorylation *In vitro* coupling; Group I, G_q; Groups II and III, G_i	
		mGLU 2,3 (Group II mGluRs)	APDC		
			LY354740		
			mGLU 4,6,7,8 (Group III mGluRs)		L-AP4

Acetylcholine	—	Nicotinic		IR: classical fast excitatory transmission *via* cation channels	α-Bungarotoxin
		α2-4 and β2-4 isoforms			Me-Lycaconitine
		α 7			
		Muscarinic		GPCR: modulatory	M_1: Pirenzepine
		M_{1-4}		M_1, M_3: G_q, $\uparrow IP_3/Ca^{2+}$	M_2: Methoctramine
				M_2, M_4: G_i, $\downarrow$cAMP	M_3: Hexahydrosiladi-fenidol
					M_4: Tropicamide
Dopamine	Cocaine; mazindol; GBR12-395; nomifensine	D_{1-5}	D_1: SKF38393	GPCR: D_1 D_5: G_s coupled; $D_{2,3,4}$: G_i coupled	D_1: SCH23390
			D_2: Bromocriptine		D_2: Sulpiride, domperidone
			D_3: 7-OH-DPAT		
Norepinephrine	Desmethylimipramine; mazindol, cocaine	α_{1A-D}	α_{1A}: NE > EPI	GCPR: $G_{q/11}$ coupled	WB4101
		α_{2A-C}	α_{2A}: Oxymetazoline	GCPR: $G_{i/o}$ coupled	α_{2A-C}: Yohimbine
					α_{2B}, α_{2C}: Prazosin
		β_{1-3}	β_1: EPI = NE	GPCR: G_s coupled	β_1: Atenolol
			β_2: EPI >> NE		β_2: Butoxamine
			β_3: NE > EPI	GPCR: G_s/$G_{i/o}$ coupled	β_3: BRL 37344
Serotonin	Clomipramine; sertraline; fluoxetine	5-HT_{1A-F}	5-HT_{1A}: 8-OH-DPAT	GPCR: $G_{i/o}$ coupled	5-HT_{1A}: WAY101135
			5-HT_{1B}: CP93129		5-HT_{1D} GR127935
			5-HT_{1D}: LY694247		
		5-HT_{2A-C}	α-Me-5-HT, DOB	GPCR: $G_{q/11}$ coupled	LY53857; ritanserin; mesulergine; ketanserin
		5-HT_3	2-Me-5-HT; m-CPG	IR: classical fast excitatory transmission *via* cation channels	Tropisteron: ondansetron; granisetron
		5-HT_{4-7}	5-HT_4: BIMU8; RS67506; renzapride	GPCR: 5-$HT_{4,6,7}$, G_s coupled 5-HT_5, G_s coupled?	5-HT_4: GR113808; SB204070
Histamine	—	H_1	2-Pyridylethylamine	GPCR: $G_{q/11}$ coupled	Mepyramine
			2-Me-histamine		
		H_2	Methylhistamine; dimaprit, impromadine	GPCR: G_s coupled	Ranitidine, famotidine, cimetidine
		H_3	H_3: R-α-Me-histamine	GPCR: $G_{i/o}$?	H_3: Thioperamide
				Autoreceptor function: inhibits transmitter release	
		H_4	Imetit, clobenpropit	GPCR: G_q, G_i?	JNJ777120
Vasopressin	—	$V_{1A,B}$	—	GPCR: $G_{q/11}$ coupled; modulatory; regulates ion channels, second messenger production, and protein phosphorylation	$V1_A$: SR 49059
		V_2	DDAVP	GPCR: G_s coupled	$d(CH_2)_5[dIle^2Ile^4]AVP$
Oxytocin	—		$[Thr^4,Gly^7]OT$	GPCR: $G_{q/11}$ coupled	$d(CH_2)_5[Tyr(Me)^2, Thr^4, Orn^8]OT_{1-8}$

Tachykinins	—	NK_1 (SP > NKA > NKB)	Substance P Me ester	GPCR: $G_{q/11}$ coupled; modulatory; regulates ion channels, second messenger production, and protein phosphorylation	SR140333
					LY303870
					CP99994
			NK_2 (NKA > NKB > SP)	β-[Ala^8]NKA_{4-10}	GR94800
		GR159897			
		NK_3 (NKB > NKA > SP)		GR138676	SR142802
			SR223412		
			[Pro^7]NKB		
CCK	—	CCK_A	CCK8 >> gastrin 5 = CCK4	GPCR: $G_{q/11}$ and G_s coupled	Devazepide; lorglumide
		CCK_B	CCK8 > gastrin 5 = CCK4	GPCR: $G_{q/11}$ coupled	CI988; L365260; YM022
NPY	—	Y_1	[Pro^{34}]NPY	GPCR: $G_{i/o}$ coupled	—
		Y_2	NPY_{13-36}; NPY_{18-36}		
		Y_{4-6}	NPY_{13-36}; NPY_{18-36}		
Neurotensin	—	NTS1	—	GPCR: $G_{q/11}$ coupled	SR48692
		NTS2			
Opioid peptides	—	u (β-endorphin)	DAMGO, sufentanil; DALDA	GPCR: $G_{i/o}$ coupled	CTAP; CTOP; β-FNA
		δ (Met^5-Enk)	DPDPE; DSBULET; SNC-80		Naltrindole; DALCE; ICI174864; SB205588
		κ (Dyn A)	U69593; CI977; ICI74864		Nor-binaltorphimine; 7-[3-(1-piperidinyl) propanamido] morphan
Somatostatin	—	sst_{1A-C}	SRIF1A; seglitide	GPCR: $G_{i/o}$ coupled	—

		$sst_{2A,B}$	Octreotide; seglitide, BIM23027		Cyanamid 154806
		$sst_{3,4}$	BIM23052, NNC269100		
		sst_5	L362855		BIM23056
Purines	—	P1 ($A_{1,2a,2b,3}$)	A_1: N6-cyclopentyladenosine	GPCR: $G_{i/o}$ coupled	8-Cyclopentyl theophylline; DPCPX
			A_{2a}: CGS21680; APEC; HENECA	GPCR: G_s coupled	CO66713; SCH58261; ZM241385
		P2X	α,β-methylene ATP	IR: transductive effects not yet determined	Suramin (nonselective)
		P2Y	ADP β F	GPCR: $G_{i/o}$ and $G_{q/11}$ coupled	Suramin

CNS Depression:-

The causes of depression are not entirely understood, but are thought to be multi-factorial. Studies indicate that depression is, at least in part, an inherited condition involving abnormalities in neurotransmitter functioning. Although inheritance is an important factor in major depression, it does not account for all cases of depression, implying that environmental factors may either play an important causal role or exacerbate underlying genetic vulnerabilities. Some of the common causes of depression which have been identified include the following:

1. Genetics:-Research indicates that depression is, at least in part, inherited. Thus far, however, no studies have isolated the specific genes responsible for depression.

2. Brain Chemistry Imbalance: - Depression is believed to be caused by an imbalance in the neurotransmitters which are involved in mood regulation. Neurotransmitters are chemical substances which help different areas of the brain communicate with each other. When certain neurotransmitters are in short supply, this may lead to the symptoms we recognize as clinical depression.

3. Circadian Rhythm Disturbance: - One type of depression, called seasonal affective disorder, is believed to be caused a disturbance in the normal circadian rhythm of the body. Light entering the eye influences this rhythm, and, during the shorter days of winter, when people may spend limited time outdoors, this rhythm may become disrupted.

4. Poor Nutrition: - A poor diet can contribute to depression in several ways. A variety of vitamin and mineral deficiencies are known to cause symptoms of depression. Researchers have also found that diets either low in omega-3 fatty acids or with an imbalanced ratio of omega-6 to omega-3 are associated with increased rates of depression. In addition, diets high in sugar have been associated with depression.

5. Medical Illnesses: - Illness is related to depression in two ways. The stress of having a chronic illness may trigger an episode of major depression. In addition, certain illnesses -- for example, thyroid disorders, Addison's disease and liver disease -- can cause depression symptoms.

6. Drugs, Both Legal and Illegal: - Several prescription drugs have been reported to cause symptoms of depression. In addition, a variety of drugs of abuse have been associated with depression symptoms.

7. Female Sex Hormones: - It has been widely documented that women suffer from major depression about twice as often as men. Because the incidence of depressive disorders peaks during women's reproductive years, it is believed that hormonal risk factors may be to blame. Women are especially prone to depressive disorders during times when their hormones are in flux, such as around the time of their menstrual period, childbirth and perimenopause. In addition, a woman's depression risk declines after she goes through menopause.

8. Grief and Loss: - Although grief is a normal response to death and loss, the extreme stress associated with grief can trigger an episode of major depression.

9. Stressful Life Events: - Stressful life events, which overwhelm a person's ability to cope, may be a cause of depression. Scientists have theorized that the high levels of the hormone cortisol, which are secreted during periods of stress, may somehow induce depression by affecting the neurotransmitter serotonin.

Depression due to neurotransmitters:-

Depression is believed to occur when there are imbalances in the brain of mood-regulating chemicals called neurotransmitters. Neurotransmitters are chemical messengers that help nerve cells communicate with each other when they are in short supply, problems may occur. There are three basic molecules, known chemically as monoamines, which are thought to play a role in mood regulation: **norepinephrine, serotonin and dopamine**.

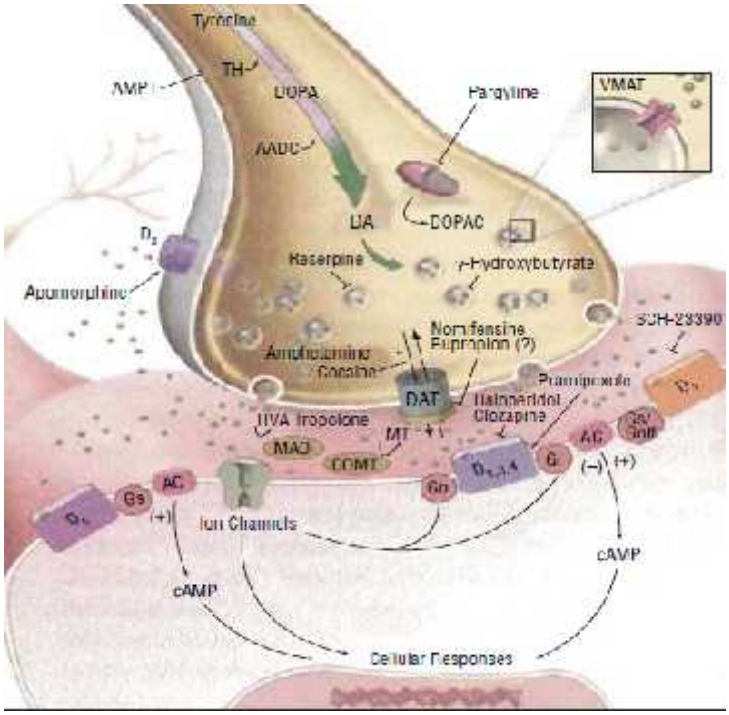
Motivation, psychomotor speed, concentration, and the ability to experience pleasure are all linked in that (1) they are regulated in part by dopamine containing circuits in the central nervous system and (2) impairment of these functions are prominent features of depression. Despite this theoretical underpinning, research on the role of dopamine in depression has been largely overshadowed by research on norepinephrine and serotonin containing circuits. Recent findings clearly warrant scrutiny of the role of dopamine in the pathophysiology of depression and, moreover, whether there exists a "dopaminergic dysfunction" subtype, characterized by a poor response to antidepressants that act primarily on serotonin or noradrenaline neurons.

Role of Dopamine in CNS depression:- The dopamine is the important neurotransmitter that plays a major in depression, psychosis, anxiety, addictions, mood, movement, attention and executive functioning, motivated behaviours (reward- and pleasure-seeking).

DOPAMINE SYNTHESIS & SIGNALING:-

Dopamine is synthesized in the cytoplasm of presynaptic neurons from the amino acids phenylalanine and tyrosine. Dopamine is biosynthesized in the body (mainly by nervous tissue and the medulla of the adrenal glands) first by the hydroxylation of the amino acid L-tyrosine to L-DOPA via the enzyme tyrosine 3-monooxygenase, also known as tyrosine hydroxylase, and then by the decarboxylation of L-DOPA by aromatic L-amino acid decarboxylase (which is often referred to as dopa decarboxylase). In some neurons, dopamine is further processed into norepinephrine by dopamine beta-hydroxylase.

In neurons, dopamine is packaged after synthesis into vesicles, which are then released into the synapse in response to a presynaptic action potential.



Dopaminergic synaptic signaling. Szabo et al (2004).5 AADC indicates aromatic acid decarboxylase; AMPT,-methylparatyrosine; AC, adenylyl cyclase; cAMP, cyclic adenosine monophosphate; COMT, catechol-*O*-methyltransferase; D1-D5, dopamine receptors 1 through 5; DA, dopamine; DAT, dopamine transporter; DOPA, 3,4-dihydroxyphenylalanine; DOPAC, dihydroxyphenylacetic acid; Gi, Go, and Gs, protein subunits; HVA, homovanillic acid; MAO, monoamine oxidase; MT, 3 methoxytyramine; TH, tyrosine hydroxylase; and VMAT, vesicular monoamine transporter.

Dopamine exerts its effects on the postsynaptic neuron through its interaction with 1 of 5 subtypes of dopamine receptors, divided into 2 groups:-

D1 family comprising the D1 and D5 subtypes receptors &

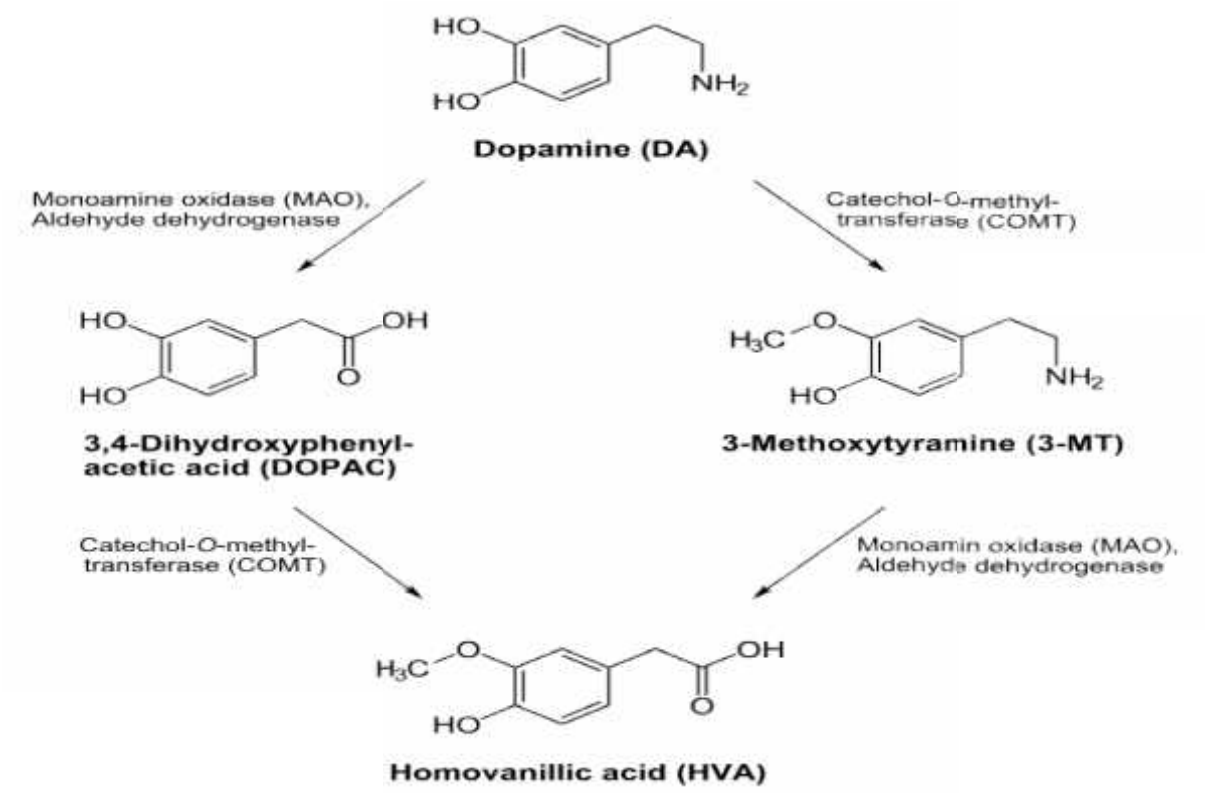
D2 family comprising the D2, D3, and D4 subtypes receptors.

The structure of all of the receptor subtypes conforms to the structural model for a G-protein coupled receptor with 7 membrane-spanning alpha-helices and an extracellular amino terminal. Each receptor subtype has a characteristic anatomical distribution with the D1 and D2 subtypes present in significantly greater amounts than the others. On binding an agonist, D1 and D5 receptors activate the adenylate cyclase second messenger system, elevating intracellular cyclic adenosine monophosphate concentrations. Cyclic adenosine monophosphate increases protein kinase A activity with resulting changes in activity levels of enzymes or other proteins within the cell.

D1 receptors may also activate other second messenger pathways, perhaps contributing to intracellular cross-talk between D1 and D2 receptors.13 The D2 family of receptors, when stimulated, all reduce adenylate cyclise activity. Somatodendritic and presynaptic D2 receptors also function as autoreceptors with activation of somatodendriticD2 receptors resulting in reduced DA cell firing and activation of presynaptic D2 receptors reducing the amount of DA released per action potential.

In the basal ganglia, DA is cleared from the extracellular space primarily by presynaptic nerve terminal uptake mediated by the dopamine transporter (DAT). The prefrontal cortex in man and nonhuman primates represents something of an anomaly in that there is an absence of DAT on DA nerve terminals. Consequently, the DA signal is terminated by DA uptake into NE terminals by the norepinephrine transporter (NET). Postsynaptically, dopamine is inactivated by catechol-o-methyl transferase (COMT).

Both the A and B forms of monoamine oxidase (MAO-A and MAO-B) can metabolize DA, which, along with COMT, serially catabolises DA to produce the intermediate breakdown products dihydrophenylacetic acid and 3-methoxytyramine before forming the final excretion product, homovanillic acid (HVA).



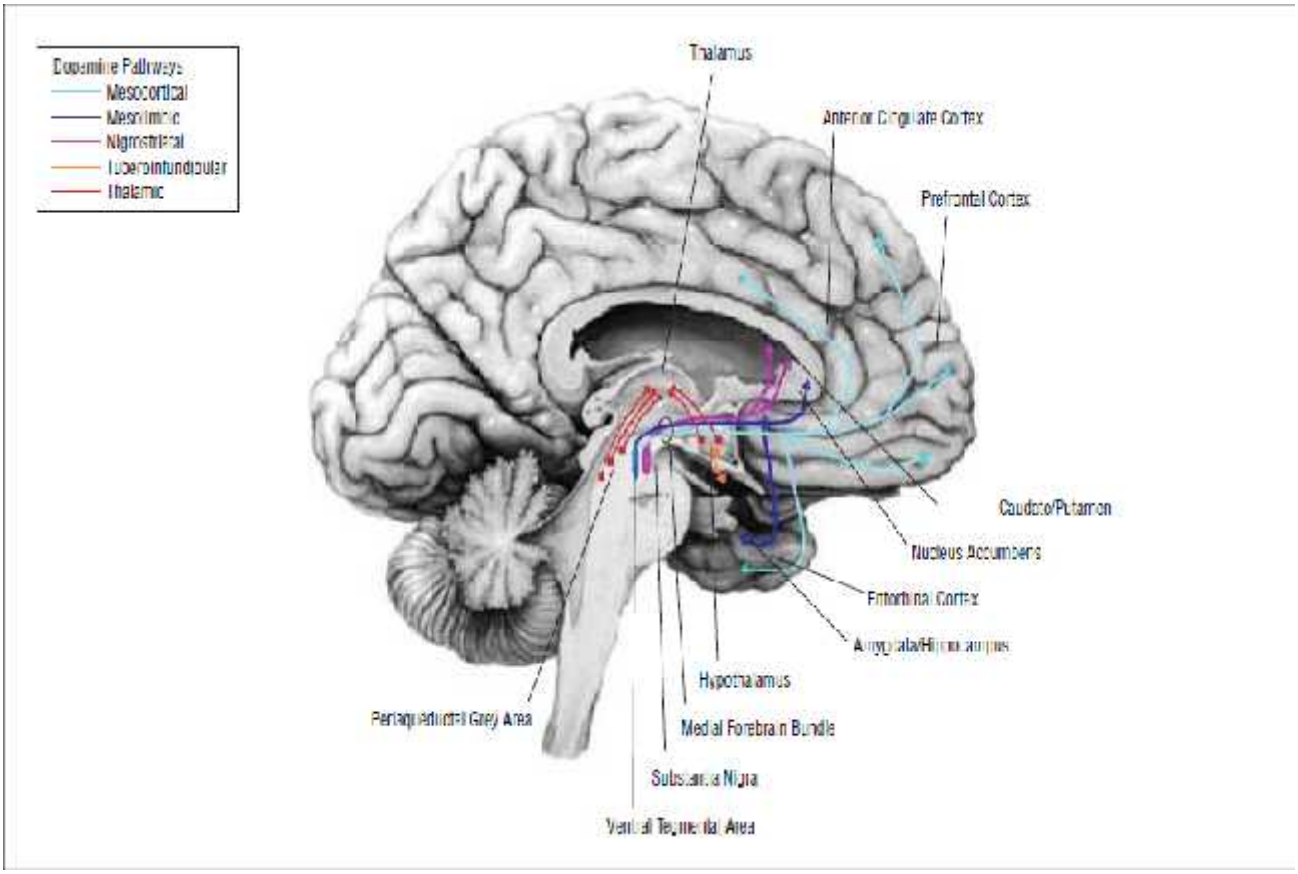
Dopamine signaling occurs in 2 forms. Phasic DA release results from burst firing of VTA neurons and is thought to occur in response to behaviourally salient stimuli, such as those that may predict reward. This phasic DA release activates postsynaptic D2 receptors and is terminated via reuptake by DAT. Tonic dopamine release arises from slow, irregular activity of the VTA, resulting in low concentrations of extracellular DA that act at presynaptic DA receptors to inhibit phasic DA neuron firing, and is subject to metabolism by COMT. There is considerable evidence that the DA system is dynamic, with up- and down-regulation of D2 receptors and DAT based in part on DA availability. Reserpine, which depletes DA, induces a significant decrease in DAT density and reduces

DA uptake. Similarly, amantadine, which in part acts to induce DA release, increases DAT density.

D1 receptor density appears to be less responsive to changes in DA availability. Although beyond the scope of this review, it should be noted that there is substantial evidence that DA signaling in the dorsal and ventral striatum serves in a gating capacity for glutamatergic inputs from the hippocampus, basolateral amygdala, thalamus, and prefrontal cortex. Dopamine performs a similar gating function over the ability of the prefrontal cortex to regulate basolateral amygdala output.

DOPAMINERGIC PATHWAYS IN THE CENTRAL NERVOUS SYSTEM

Most DA-producing neurons in the brain are located in brainstem nuclei: the retro-rubro field (A8), substantia nigra pars compacta (A9), and the ventral tegmental area (VTA) (A10). Projection pathways of the axons arising from these cell bodies follow 1 of 3 specific paths (with some overlap) via the medial forebrain bundle to innervate specific cortical and subcortical structures, unlike the more diffuse innervation patterns of serotonergic and noradrenergic cells. The nigrostriatal pathway projects from the substantia nigra pars compacta to the dorsal striatum (caudate and putamen) and has a prominent role in the motor planning and execution of movement, although it clearly also plays an important role in non motor functions, such as cognition.



The mesocortical pathway arises from the VTA and projects to the frontal and temporal cortices, particularly the anterior cingulate, entorhinal, and prefrontal cortices. This pathway is believed to be important for concentration and executive functions such as working memory.

The mesolimbic pathway also arises in the VTA but projects to the ventral striatum (including the nucleus accumbens), bed nucleus of the stria terminalis, hippocampus, amygdala, and septum. It is particularly important for motivation, the experience of pleasure, and reward. Aspects of anterior pituitary function are also under dopaminergic control.

The tuberoinfundibular pathway arises from the arcuate nucleus of the hypothalamus (A12) and projects to the median eminence of the hypothalamus, where DA released into the portal vessels acts to inhibit the secretion of prolactin from the anterior

pituitary. This pathway is also involved in dopaminergic regulation of growth hormone release from the anterior pituitary.

The incertohypothalamic pathway originates from cell bodies in the medial portion of the zona incerta (A13) and innervates amygdaloid and hypothalamic nuclei involved in sexual behavior. Recently, significant dopaminergic innervation of the thalamus has been demonstrated in primates, although it is largely absent in rodents. Unlike the other dopaminergic pathways, this "thalamic dopamine system" arises from multiple sites, including the periaqueductal gray matter, the ventral mesencephalon, hypothalamic nuclei, and the lateral parabrachial nucleus. This DA pathway may contribute to the gating of information transferred through the thalamus to the neocortex, striatum, and amygdala.

Dysfunction of dopaminergic system & major role in depression:-

The fluctuations in the functions of dopaminergic system can play a major role in altering the depression, psychosis, anxiety, addictions, mood, movement, attention and executive functioning, motivated behaviours (reward- and pleasure-seeking).

Research information on role of dopamine in depression:-

Dopamine neurons have long been known to be critical to a wide variety of pleasurable experiences and reward. Severity of major depressive disorder has been found to correlate highly with the magnitude of reward experienced after oral d-amphetamine, which increases DA availability by a variety of mechanisms. One explanation for these findings is that in severe depression, there is a reduction in DA release, resulting in compensatory mechanisms, such as up-regulation of postsynaptic DA receptors and decreased DAT density, which taken together would increase DA signal transduction resulting from amphetamine- induced DA release into the synapse. The markedly greater

behavioural response to the rewarding effects of the psychostimulant and altered brain activation of the ventrolateral prefrontal cortex, orbitofrontal cortex, caudate, and putamen. These findings further implicate DA circuit dysfunction in major depression.

Relatively few studies have examined DA system alterations in depression with neuroimaging methods. Published studies have focused largely onD2 receptor or DAT occupancy. Interpreting results of earlier studies using 2βcarboxymethoxy-3β-(4-iodophenyl)tropane(123I-β-CIT) to image the DAT are problematic in that the binding profile for this ligand is not specific for this monoamine transporter, although in the striatum, the vast majority of binding is indeed to the DAT. Few studies of DAT binding or uptake have been performed with more specific ligands. Results of neuroimaging studies of D2 receptor binding in major depressive disorder have been inconsistent. Lots of research to be performed in present and future to know the complete role of dopamine in depression.

SCREENING OF CNS DEPRESSION ACTIVITY:-

- **SCREENING MODELS OF ANTIPSYCHOTIC DRUGS**:-

1. Catalepsy test in rodents

2. Pole climbing avoidance in rats

3. Foot shock induced aggression

4. Inhibition of amphetamine stereotype in rats

5. Inhibition of amphetamine climbing in rats

6. Inhibition of apomorphine stereotype in rats

7. Yawing and penile erection syndrome in rats

8. Active avoidance test

8.1 Shuttle box avoidance (two way shuttle box) test

8.2 Jumping avoidance (one way shuttle box) test

8.3 Runway avoidance test

8.4 Jumping avoidance test

9. Passive avoidance test

9.1 Step down test

9.2 Step through test

9.3 Up hill avoidance tet

9.4 Two compartment test

9.5 Scopolamine induced amnesia test

10. Conditional avoidance response test in rats

- **SCREENING MODELS OF ANXIOLYTIC DRUGS:-**

1. **Light dark model (anti anxiety test)**
2. **Elevated plus maze test**
3. **Water maze test**
4. **Y maze test**
5. **Staircase test**
6. **Forced swimming test**
7. **Open field test**
8. **Isolation induced aggression**
9. **Hole board test**
10. **Resident intruder aggression test**

11. Foot shock induced aggression

12. Isolation induced aggression

13. Water competition test

- **SCREENING MODELS OF MYORELAXANT DRUGS:-**

1. **Traction test**
2. **Rotarod test**
3. **Chimney test**
4. **Grip strength**
5. **Inclined plane test**

- **SCREENING MODELS OF SEDATIVE DRUGS:-**

1. **Potentiation of hexobarbital sleeping time**
2. **Potentiation of Pentobarbitone sleeping time**
3. **Experimental insomnia in rats**
4. **EEG registration of conscious rat**
5. **Automated rat sleep analysis system**

Drug profile:-

Haloperidol:- It is a typical antipsychotic drug in butyrophenone class of antipsychotic drugs.

MOA: - Haloperidol is first-generation Neuroleptics that bind non selectively to a broad range of receptors. It can bind to dopamine D1 and D2, 5-HT2, histamine H1 and α2 adrenergic receptors in the brain. The efficacy of neuroleptics is thought to be due to antagonism of dopamine receptors in the mesolimbic and mesofrontal systems. Haloperidol

blocks postsynaptic dopamine D_1 and D_2 receptors in the mesolimbic system. It produces calmness and reduces aggressiveness with disappearance of hallucinations and delusions.

Diazepam:- It belongs to benzodiazepam class commonly used for for treating anxiety, insomnia, seizures including status epilepticus, muscle spasms, restless legs syndrome, alcohol withdrawal, benzodiazepine withdrawal and Ménière's disease.

MOA: - it binds to a specific subunit on the $GABA_A$ receptor at a site that is distinct from the binding site of the endogenous GABA molecule. The $GABA_A$ receptor is an inhibitory channel which, when activated, decreases neuronal activity.

Pentobarbitone: - It is a short-acting barbiturate commonly used as hypnotic & sedative drug.

MOA: - GABA is the principal inhibitory neurotransmitter in the mammalian central nervous system (CNS). Barbiturates bind to the $GABA_A$ receptor at the alpha subunit, which are binding sites distinct from GABA itself and also distinct from the benzodiazepine binding site. In addition to this GABA-ergic effect, barbiturates also block the AMPA receptor, a subtype of glutamate receptor. Glutamate is the principal excitatory neurotransmitter in the mammalian CNS. Taken together, the findings that barbiturates potentiate inhibitory $GABA_A$ receptors and inhibit excitatory AMPA receptors can explain the CNS-depressant effects of these agents.

2. LITERATURE REVIEW

4.1 DESCRIPTION OF THE PLANT:-

Fig.5.1. ***Plant image of*** **Canavalia** ***maritima (Abul.)***

- **Botanical information:**

Canavalia *maritima (Aubl*.)

Family **:** Fabaceae

Synonyms **:** *Canavalia lineate auct*

Canavalia. rosea (SW.)DC. - Baybean

Canavalia obtusifolia DC.

Canavalia thours.

Vernacular Names

English	:	Seaside sword bean, beach bean
Tamil	:	Kaathuthambattan

Taxonomical classification

Kingdom	:	Plantae – Plants
Subkingdom	:	Tracheobionta – Vascular plants
Super division	:	Spermatophyta – seed plants
Division	:	Magnoliophyta – Flowering plants
Class	:	Magnoliopsida - Dicotyledons
Subclass	:	Rosidae
Order	:	Fabales
Family	:	Fabaceae– Pea family
Genus	:	Canavalia adans.- jackbean
Species	:	*Canavalia maritima*

Description:

Coastal Jack-bean is a trailing, herbaceous vine that forms mats of foliage. Stems reach a length of more than 6 m (20 ft) and 2.5 cm (0.98 in) in thickness. Each compound leaf is made up of three leaflets 5.1–7.6 cm (2.0–3.0 in) in diameter, which will fold when exposed to hot sunlight. The flowers are purplish pink and 5.1 cm (2.0 in) long. The flat pods are 10.2–15.2 cm (4.0–6.0 in) long and become prominently ridged as they mature. The buoyancy of the seeds allows them to be distributed by ocean currents. The plant seems to contain L-Betonicine.

Habitat:

C. maritima inhabits upper beaches, cliffs, and dunes throughout the world's coastal tropics. It is highly salt-tolerated and prefers sandy soils.

Propagation: By seeds

Parts used : Leaves and beans

Chemical constituents:

Catalase, amylase, invertase, lipase, tannase and glucosidase. Canarosine a guanidine alkaloid. β–sitosterol, stigmasterol, daucosterol, epi-inositol 6-o methyl ether and rutin. L-betonicine, canavanine, trigonelline are the active principle. It also contain glycoside moiety like saponin, flavonoids.

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Uses

This is a good pioneer plant for coastal revegetation used as folkloric, paste of leaves used for boils. It is mild psychoactive when smoked. It is used in tobacco smoking. Plant decoction is used to treat tuberculosis. The fresh and dried flowers were used as a garnish and for flavoring. Leaf powder is smoked as substitute for marijuana. The leaves help to relieve pain and promote healing of burns. Powdered leaves are used for cuts, wounds, ulcers, and swellings. An infusion of the Root is good for cold, rheumatism, leprosy, aches and pain.

4.2 Collection of Plant:-

Plant was collected from Chudaloor seashore, Tamilnadu and authenticated by Dr.G.V.S Murthy Scientist & Head of office, Botanical Survey of India, Coimbatore, Tamilnadu. The fresh leaves of the plant were separated from adulterants, shade dried, broken into small pieces and powdered coarsely.

SCIENTIFIC REVIEW:-

Senthil kumar et al.,(2010) Has evaluated the antibacterial activity and preliminary phytochemical analysis of leaf extract of *Canavalia rosea* using nine solvents. The preliminary phytochemical screening revealed the presence of tannins, phlobatannins, saponin, flavonoids, alkaloid, cardiac glycoside and phenolics. Presence of bioactive constituents is associated with the anti microbial activity of the plant. Minimum inhibition concentration and maximum bactericidal concentration on selective organisms that were found susceptible in agar diffusion assay.

Rutt Suttisri et al., (2008) A new acyclic guanidine alkaloid, canarosine (1), together with five known compounds, b-sitosterol (2), stigmasterol (3), daucosterol (4), epi-inositol 6-O-methyl ether (5), and rutin (6), were isolated from the aerial parts of Canavalia rosea. Their structures were established on the basis of their spectroscopic data. In the radioligand receptor binding assay, canarosine (1), at a concentration of 100mg/ml, caused 91% inhibition of the dopamine D1 receptor binding with an IC50 value of 39.4 ^ 5.8mM.

Jain BG et al., (2010). Evaluated the effect of aqueous ethanolic extract of *Tinospora Cordifolia* for its putative antipsychotic activity using amphetamine challenged mice model. Haloperidol (1 mg/kg i.p.) was administered acutely to mice as standard drug. Control animals received vehicle (10% DMSO). The in vivo receptor binding studies were carried out to correlate the antipsychotic activity of the extract with its capacity to bind to the DAD2 receptor. The results in SLA showed that the hydro alcoholic extract of the stems of *Tinospora cordifolia* at a dose level of 250 mg/kg and 500 mg/kg showed no significant antipsychotic activity in amphetamine induced hyperactivity in mice when compared to standard. Extract alone treated group at a dos level of 250 mg/kg and 500 mg/kg showed a decreased in locomotor activity when compared to the control. The plant extract increased the DAD2 receptor binding in a dose dependent manner in treated mice compared to the control group.

Rajesh J Oswal et al.,(2011) determined the antipsychotic ethanolic extract of activity of dried fruits of Catunargaom spinosa (Thumb.) in rats by **Compulsive behavior test.** Where Amphetamine is used to produce psychosis and Haloperidol is used as standard drug to block psychosis and decrease dopamine levels. The ethanolic extract of Fruits of *Catunargaom spinosa (Thunb.)* 400mg*/kg* protected some of the animals against the psychosis induced by amphetamine and lowers the rate of Sniffing, Licking, and Rearing. The result showed that ethanol extract of *Catunargaom spinosa (Thunb)*, possess antipsychotic activity in mice in over secretion of dopamine in Mesolimbic pathway causes psychosis to occur after administration of Amphetamine.

C.A.Suresh kumar, et al., (2010) has investigated the Psychopharmacological studies on different extracts (ethanolic, chloroform & aqueous) of stem of Saccharum spontaneum on antipsychotic and spontaneous locomotor activity. The locomotor activity of normal rat animal shows the C.N.S. depressant activity (6.53%). The ethanol extract shows the 10 times (62.0%) more activity while other extracts like Aqueous extract (21.9%) shows the 4 times more activity and chloroform extract shows the 2 times (10.0%) more C.N.S. depressant activity than the control. The aqueous & ethanolic extract of *Saccharum spontaneum* delays the latency to climb the pole to (5±0.96), (4±0.76) which compared to the control groups of rats (3±0.57). The above extracts show the antipsychotic activity but are less when compared with standard drug of chlorpromazine. The overall results show that Ethanol and Aqueous extract of *Saccharum spontaneum* must have a significant C.N.S. depressant activity than chloroform and aqueous extracts when compared to control.

J. Srikanth et al., studied the CNS Activity of the Methanol Extracts of *Sapindus emarginatus* Vahl in Experimental Animal Models. The metholic extract at 50mg/kg, 100mg/kg, 200mg/kg influenced the general behavioral profiles, as evidenced in the spontaneous activity, righting reflex, pinna reflex, grip strength and pain responses. Reduction of awareness and depressant action may be due to the action of the extract on

CNS. Reduction of pinna reflex may be due to blocking synapses of the afferent pathway. Different doses of methanol extract of *S. emarginatus* have produced a significant increase in the hypnotic effect induced by the Phenobarbitone, in a dose dependent manner, thus suggesting a profile sedative activity. The myorelaxant effect was observed only with the higher dose of methanol extract of *S. emarginatus* which resulted in an increase in the number of falls and a decrease in the time on the bar as detected by the rotarod test. The extract showed significant reduction in exploratory behavior in Y maze test & Head dip test showing its anxiolytic activity. The antipsychotic activity is evaluated by cocaine induced stereotype behavior in rats. Administration of cocaine to rats, which releases both dopamine and noradrenalin, causes a cessation of normal 'ratty' behavior and the appearance of repeated 'stereotyped' behavior unrelated to external stimuli. These effects are prevented by dopamine antagonists and by destruction of dopamine-containing cell bodies in the midbrain, but not by drugs that inhibit the noradrenergic system. The methanol extracts of *S. emarginatus* produced a partial reduction in the hyperactivity produced by cocaine. A number of scientific reports indicated that triterpenoids produced CNS depressant action. Therefore the presence of these active constituents in the methanol extract of *S. emarginatus* may be responsible for the CNS activity.

K. Umasankar et al., (2010) evaluated the CNS Activity of Ethanol Extract of *Wedelia chinensis* in Experimental Animals. The CNS effects were evaluated by general behaviour, exploratory behaviour, muscle relaxant activity and Phenobarbitone sodium–induced sleeping time using standard procedures in experimental animal models. The Phytochemical screening revealed the presence of tannins, terpenoids, flavonoids, steroids and reducing sugars. The results revealed that the ethanol extract at 200 and 300 mg/kg caused a significant reduction in the spontaneous activity (general behavioural profile), exploratory behavioural pattern (Y–maze and head dip test), muscle relaxant activity (rotarod and traction tests), and significantly potentiated Phenobarbitone sodium–induced sleeping time. The results conclude that the extract exhibit CNS depressant activity in tested animal models.

Ramanathan Sambath Kumar, et al., (2008) investigated CNS activity of the methanol extracts of Careya arborea in experimental animal model. General behaviour, exploratory behaviour, muscle relaxant activity and Phenobarbitone sodium–induced sleeping time were studied. The results revealed that the methanol extract of barks of *Careya arborea* at 100 and 200 mg/kg caused a significant reduction in the spontaneous activity (general behavioural profile), remarkable decrease in exploratory behavioural pattern (Y–maze and head dip test), a reduction in muscle relaxant activity (rotarod and traction tests), and also significantly potentiated Phenobarbitone sodium–induced sleeping time. The results suggest that methanol extract of *Careya arborea* exhibit CNS depressant activity in tested animal models.

Salahdeen H.M et al., (2006) evaluated the Neuropharmacological Effects of Aqueous Leaf Extract of *Bryophyllum Pinnatum* in Mice. Effects of aqueous leaf extracts of bryophyllum pinnatum (AEBP) dosages (50,100 and 200 mg/kg) was found to produce a profound decrease in exploratory activity in a dose-dependent manner. It also showed a marked sedative effect as evidenced by a significant reduction in gross behaviour and potentiation of pentobarbitone-induced sleeping time. It delayed onset in strychnine-and picrotoxin-induced convulsion (seizures) respectively with the protective effect being significantly higher in picrotoxin- than strychnine-induced convulsion. It also decreases the rate of picrotoxin-induced mortality in mice with LD50 of 641mg/kg. The totality of these effects showed that the extract possesses depressant action on the central nervous system.

Abiodun O. Ayoka et al., (2005) evaluated the effects of air-dried *Spondias mombin* leaves extracted with aqueous, methanol and ethanol solvents on Sedative, antiepileptic and antipsychotic effects in mice and rats. . All residues from different extractions were dissolved in normal saline and administered intraperitoneally (i.p.). The methanolic and ethanolic extracts (12.5–100 mg/kg i.p.) prolonged the hexobarbital-induced sleeping time and reduced the NIR in both mice and rat in a dose-dependent manner. The aqueous extract prolonged the hexobarbital-induced sleeping time and reduced (NIR) at doses of

50 and 100 mg/kg. Phenolic compounds were present in the ethanolic and methanolic extracts, which exhibited anticonvulsant properties in the picrotoxin-induced convulsions model. The extracts decreased the amphetamine/apomorphine-induced stereotyped behavior, which suggest that these extracts possess antidopaminergic activity. These results suggest that the leaves extracts of *Spondias mombin* possess sedative and antidopaminergic effects.

Sanjita Das, D et al., (2008) evaluated the CNS Depressant Activity of Different Plant parts of *Nyctanthes arbortristis* Linn. The CNS depressant activity was evaluated by observing the prolongation of sleeping time induced by pentobarbital sodium in mice and to explore the possible mechanism behind this activity by determining their effect on brain monoamine neurotransmitters like dopamine and serotonin. The leaves, flowers, seeds and barks (600 mg/kg) showed significant and dose-dependent prolongation of onset and duration of sleep and so found to cause decrease dopamine and increase serotonin level. These results concluded that the CNS depressant activity of the ethanol extracts of seeds, leaves and flowers may be due to the decrease in dopamine and increase in serotonin level.

VJ Galani and BG Patel (2009) studied the Central Nervous System Activity of Argyreia Speciosa Roots in Mice. They studied the action of the n-hexane (n-HF), chloroform (CF), ethyl acetate (EAF) and water (WF) fractions of hydroalcoholic extract of roots of *Argyreia speciosa* on the central nervous system. All the fractions (100, 200 and 500 mg/kg, p.o.) were evaluated for neuropharmacological activity using spontaneous motor activity and pentobarbital-induced sleeping time in mice. Chlorpromazine was used as a positive control. Central nervous system depressant activity was observed with all the fractions as indicated by the results in which they reduced spontaneous motor activity and potentiated pentobarbital induced hypnosis in mice. These results suggest that the active principles present in the root of *Argyreia speciosa* may responsible for central nervous depressant activity.

Silvia R.Etcheverry et al., (2003) conducted the pharmacological studies and Phytochemical screening of Erythrina crista-galli extracts. The aqueous and organic extracts of the leaves were tested by the Hippocratic Screening test, Spontaneous Locomotor activity, potentiation of pentobarbitone sleeping time test. Two extract in all the tests showed a significant CNS depression.

SINGH**, G. K. AND KUMAR, V.** has evaluated the Neuropharmacological Screening & Lack of Antidepressant activity of Standardized extract of Fumaria indica withstandardized 50% ethanolic extract of Fumaria indica (FI) containing 0.45% fumaric acid and 0.35% dimethyl fumarate w/w, was used in this study. Five groups of rats and mice of either sex, each group comprising of six animals, were used (i.e. control, respective standard drug, and 100 mg/kg, 200 mg/kg and 400 mg/kg doses of FI, p.o.). Potentiation of pentobarbital induced sleeping time, locomotor activity, effect on muscle grip performance of mice, maximal electroshock seizures (MES) in rats and pentylenetetrazole (PTZ) induced convulsions in mice were used as behavioural models to evaluate general effects of the FI on central nervous system. Further, antidepressant activity of the extract was also evaluated using validated models of depression in rodents viz. behavioural despair test, learned helplessness test, tail suspension test, reserpine induced hypothermia, 5-Hydroxytryptophan (5-HTP) induced head twitches in mice and L-dopa induced hyperactivity and aggressive behaviour in mice. The animals treated with FI showed significant and dose dependent increase in pentobarbital-induced sleeping time and marked decrease in onset of sleeping time in rats. FI and diazepam have shown significant decrease in locomotor activity. FI did not show any muscle relaxant effect in the rota-rod test in mice while diazepam has shown significant muscle relaxant effect. FI, phenobarbitone and diazepam showed significant anticonvulsant activity in MES in rats and PTZ induced convulsions in mice respectively. However, no antidepressant activity was observed with FI in any of above six validatedmodels of depression. It may be concluded that FI has significant central nervous system depressant activity and lacking antidepressant activity in rodents.

Maribel Herrera-Ruiz et al., (2006) worked on Antidepressant and anxiolytic effects of hydroalcoholic extract from Salvia elegans In this work, the antidepressant and anxiolytic like effects of hydroalcoholic (60%) extract of Salvia elegans (leaves and flowers) were evaluated in mice. The extract, administered orally, was able to increase the percentage of time spent and the percentage of arm entries in the open arms of the elevated plus-maze, as well as to increase the time spent by mice in the illuminated side of the light–dark test, and to decrease the immobility time of mice subjected to the forced swimming test. The same extract was not able to modify the spontaneous locomotor activity measured in the open field test. These results provide support for the potential antidepressant and anxiolytic activity of Salvia elegans.

Urmilesh Jha et al., (2011) evaluated the CNS activity of methanol extract of *Parthenium hysterophorus L*. In experimental animals. The present study was carried out to evaluate the effect of methanol extract of parthenium hysterophorus l (PH) on psychological behavior of animals. The PH was administered orally in Swiss albino mice and the CNS effects were evaluated by general behavior, exploratory behavior, and phenobarbitone sodium induced sleeping time using standard procedures in experimental animal models.The results revealed that PH at 2.5 and 5 mg/kg caused a significant reduction in the spontaneous activity (general behavioural profile), exploratory behavioural pattern (Y maze and head dip test and significantly potentiated Phenobarbitone sodium–induced sleeping time.The results conclude that the extract exhibit CNS depressant activity in tested animal models.

AHMAD BILAL et al., (2005) conducted the pharmacological activities on Ethanol extract of seed of Cassia sophera, Linn. var. purpurea, Roxb. in rats. Eddy's hot plate and Analgesiometer tests were used to asses antinociceptive activity of Cassia sophera.
Pentobarbitone narcosis potentiation test was used to evaluate hypnotic and sedative effect, while anticonvulsant activity was evaluated by Maximum electroshock-induced seizure test and Pentylenetetrazol induced seizure test. Test drug (440 mg/kg) produced significant analgesia, potentiated the pentobarbitone induced sleeping time and exhibited

anticonvulsant effect against hind limb tonic extension phase of maximum electroshock induced seizure test and seizures induced by pentylenetetrazol.

S. V. Joshi et al., (2011) evaluated the aqueous extract of *Ocimum sanctum* in experimentally induced Parkinsonism using haloperidol induced catalepsy in rat and muscle rigidity in mice effects of aq. extract of Ocimum sanctum (OSEaq) were studied. Haloperidol was administered to induce either short term model (0.5mg/kg i.p) or long term model (4mg/kg s.c.) to observe changes in catalepsy and muscle rigidity as measured using rota-rod test and chimney test. Out of 100mg, 200mg, 300mg and 600mg/kg p.o, doses of O. sanctum, 300mg/kg dose showed maximum shortening of onset and duration of catalepsy as compared with other dose levels in short term and long term model. Pretreatment with OSEaq (300mg and 450mg/kg p.o.) significantly reduces initial decrease in activity in rota rod and significantly improves performance of mice in chimney test as compared with control in short term and long term models. In conclusion, OSEaq in the dose 300mg/kg i.p. shows anticataleptic action in rats as well as in the dose 300 and 450mg/kg i.p. improves the performance of mice in rota-rod and chimney test indicating reduction of muscle rigidity. Active constituent-linalool, modulation of central neurotransmission might be responsible for the antiparkinsonian activity exhibited by OSEaq.

K. S. Reddy et al., (2012) conducted Psychopharmacological Studies of Hydro Alcoholic Extract of Whole Plant of Marsilea quadrifolia. The hydro alcoholic extract of the entire plant *Marsilea quadrifolia* (HEMQ) was evaluated for different psychopharmacological actions such as behaviour, exploratory behaviour, muscle relaxant activity and phenobarbitone induced sleeping time. The extract was found to cause reduction in spontaneous activity, decrease in exploratory behavioural pattern by swimming and pole climbing test., reduction in the muscle relaxant by traction test. In addition, the extract significantly potentiated the phenobarbitone-induced sleeping time. Preliminary tests indicate that the hydro alcoholic extract of *Marsilea quadrifolia* in doses of 200-400 mg/kg has significant psychopharmacological activity.

De Almeida ER et al.,(2010) investigated the Anxiolytic and anticonvulsant effects of dioclenol flavonoid isolated from stem bark of *dioclea grandiflora* on mice. Groups of mice treated by the intraperitoneal (i.p.) route with doses of 15, 30, and 60 mg/kg (i.p.) of the fraction and Dioclenol with a dose of 10 mg / kg showed significant action in the Elevated Plus maze (EPM) (time spent in open arms and time in spent in the closed arms). The Hole-board Test also showed a significant increase in the time spent in the Head-dip and Marble-Burying Tests. The same treatment increased the duration of the sleeping time induced by Sodium Pentobarbital, and showed a significant increase in protection against Pentylenotetrazole induced convulsion. These results indicate an anxiolytic-like and anticonvulsant-like effect of the fraction of stem bark of Dg and Dioclenol in mice. The phytochemical analysis suggests that the alcoholic fraction has higher concentration of flavonoid active (Dioclenol) and deserves further analysis. The studies conducted with the *Dioclea grandiflora*, can contribute, in the long term, in the field of its action in the CNS this flavonoid

Boadie W. Dunlop, et al.,(2011) has performed an research oriented clinical studies in human depressed subjects using sophisticated methods like neuroimaging, radioligand detection etc to determine the role of dopamine in depression.

3. AIM AND OBJECTIVE

Medicinal plants have been in India for centuries as a therapeutic source for treating wide variety of ailments and have been found to be of immense global importance. It is estimated by World Health Organization that, 80% of the world population must rely on traditional medicines for health care: these traditional medicines are mainly plant based. Most of the studies demonstrate the importance of natural products in drug discovery. The use of phytoconstituents as drug therapy to treat major ailments has proved to be clinically effective and less relatively toxic than the existing drugs. The selection of plant was made on the basis of its availability, therapeutic value and degree of research work which is not done.

Depression occurs due to different reasons but majorly the depression occurs due to brain chemistry imbalance. This is the reason for imbalance of neurotransmitters in brain. This imbalance in neurotransmitters causes depression. In the CNS system the depression is due to mainly three types of monoaminogenic neurotransmitters norepinephrine, serotonin and dopamine. The unavailability of these neurotransmitters causes depression. Depression is beneficial in diagnosing psychosis, anxiety, sedation and to produce reduced psychomotor activity etc. Many drugs are available in market which acts on these neurotransmitters receptors, but clinical evaluation of these drugs has shown incidence of relapse, side effects, and drug interaction. This has been the rationale for the development of new drugs and search for novel molecules has been extended to herbal drugs that offer better activity with less side effects & interaction.

The motive of my present study is to reveal & show the presence of phytoconstituents in extract of Canavalia maritima that are responsible in producing depression.

OBJECTIVES OF THE STUDY

The objectives of the present study are-

- Exploring the traditional medicines with proper chemical and pharmacological profiles.
- Extraction of *Canavalia maritima* leaf by different solvents.
- To conduct systematic phytochemical investigation of *Canavalia maritima*.
- To perform the acute oral toxicological studies.
- To evaluate the antipsychotic activity in rats.
- To evaluate the anxiolytic activity in mice.
- To evaluate the sedative activity in mice.
- To evaluate the spontaneous locomotor activity in mice.
- To evaluate the muscle rigidity activity in mice.

4. PLAN OF WORK

PHYTOCHEMICAL STUDIES:

1. Collection of plant (Canavalia *maritima*) leaves and shade dried.
2. Extraction of *Canavalia maritima* leaf powder using ethanol in soxhlet apparatus for 72 hrs.
3. Phytochemical investigation of ethanolic extract of *Canavalia maritima* leaf.

EVALUATION OF ACUTE ORAL TOXICITY STUDIES

PHARMACOLOGICAL STUDIES

1. Evaluation of antipsychotic activity of *Canavalia maritima* by

- Haloperidol induced catalepsy test.

2. Evaluation of anxiolytic activity of *Canavalia maritima* by

- Forced swim test.

3. Evaluation of sedative activity of *Canavalia maritima* by

- Potentiation of Pentobarbitone sleeping time.

4. Evaluation of muscle relaxant activity of *Canavalia maritima* by

- Muscle grip strength activity by Rotarod method.

5. Evaluation of spontaneous locomotor activity of *Canavalia maritima* by

- Locomotion activity by Actophotometer method.

5. MATERIALS AND METHODS

5.1. PHYTOCHEMICAL STUDIES

5.1.1 EXTRACTION OF PLANT MATERIAL

- **Ethanolic extraction:**

About 300 gm of air dried powdered material was taken in 1000ml soxhlet apparatus and extracted with petroleum ether for 18 hours till the solvent became colourless. At the end of the extraction process the marc was taken out and it was dried. After drying, the powdered marc was weighed & again packed and extracted with ethanol for another 72 hours till it became colourless. After that extract was concentrated by distillation. The final solution was evaporated, to obtain a syrupy greenish mass.

5.1.2. PRELIMINARY PHYTOCHEMICAL ANALYSIS

The plant may be subjected to preliminary Phytochemical screening for detection of various bioactive chemical constituents. The important steps involved in the Phytochemical screening of a plant include extraction of constituents using suitable solvents followed by screening with various chemical tests.

In the process of phytochemical screening, the crude extracts or isolated constituents are subjected to qualitative and quantitative chemical analysis. Qualitative chemical analysis includes the determination of nature of the constituents in an extract or its fractions which lead to the isolation of the active lead compound. Quantitative

chemical analysis includes the determination of the purity of isolated substances or group of substances in a mixture by finger printing and different analytical techniques.

Qualitative tests:-

A) Test for carbohydrates;

1. Molisch Test:

It consists of treating the compounds of α-naphthol and concentrated sulphuric acid along the sides of the test tube. Purple colour or reddish violet colour at the junction between two liquids.

2. Fehling's Test:

Equal quantity of Fehling's solution A and B is added. Heat gently, brick red precipitate is obtained.

3. Benedict's test:

To the 5ml of Benedict's reagent, add 8 drops of solution under examination. Mix well, boiling the mixture vigorously for two minutes and then cool. Red precipitate is obtained.

4. Barfoed's test:

To the 5ml of the Barfoed's solution add 0.5ml of solution under examination, heat to boiling, formation of red precipitate of copper oxide is obtained.

B) Test for Alkaloids

1. **Dragendroff's Test:**

To the extract, add 1ml of Dragendroff's reagent Orange red precipitate is produced.

2. **Wagner's test:**

To the extract add Wagner reagent. Reddish brown precipitate is produced.

3. **Mayer's Test:**

To the extract add 1ml or 2ml of Mayer's reagent. Dull white precipitate is produced.

4. **Hager's Test:**

To the extract add 3ml of Hager's reagent, yellow precipitate is produced.

C) Test for Steroids and Sterols

1. **Liebermann Burchard test:**

Dissolve the test sample in 2ml of chloroform in a dry test tube. Now add 10 drops of acetic anhydride and 2 drops of concentrated sulphuric acid. The solution becomes red, then blue and finally bluish green in colour.

2. **Salkowski test:**

Dissolve the sample of test solution in chloroform and add equal volume of conc. sulphuric acid. Bluish red cherry red and purple color is noted in chloroform layer, whereas acid assumes marked green fluorescence.

D) Test for Glycosides

1. **Legal's test:** Sample is dissolved in pyridine; sodium nitroprusside solution is added to it and made alkaline. Pink red colour is produced.

2. **Baljet test:**

To the drug sample, sodium picrate solution is added. Yellow to orange colour is produced.

3. **Borntrager test:**

Add a few ml of dilute sulphuric acid to the test solution. Boil, filter and extract the filtrate with ether or chloroform. Then organic layer is separated to which ammonia is added, pink, red or violet colour is produced in organic layer.

4. **Killer Killani test:**

Sample is dissolved in acetic acid containing trace of ferric chloride and transferred to the surface of concentrated sulphuric acid. At the junction of liquid reddish brown color is produced which gradually becomes blue.

E) Test for Saponins

Foam test:

About 1ml of alcoholic sample is diluted separately with distilled water to 20ml, and shaken in graduated cylinder for 15 minutes.1 cm layer of foam indicates the presence of saponins.

F) Test for Flavonoids

Shinoda test:

To the sample, magnesium turnings and then concentrated hydrochloric acid is added. Red colour is produced.

Lead acetate test:

The extracts were treated with few drops of lead acetate solution, formation of yellow precipitate indicates the presence of flavonoids.

Alkaline reagent test:

The extracts were treated with few drops of sodium hydroxide separately. Formation of intense yellow color, which becomes colorless on addition of few drops of dilute acid, indicates the presence of flavonoids

G) Test for Triterpenoid:

In the test tube, 2 or 3 granules of tin was added, and dissolved in a 2ml of thionyl chloride solution and test solution is added. Pink colour is produced which indicates the presence of triterpenoids.

H) Test for Protein and Amino acid

1**. Biuret test:**

Add 1 ml of 40% sodium hydroxide and 2 drops of 1% copper sulphate to the extract, a violet colour indicates the presence of proteins.

2. **Ninhydrin test:**

Add 2 drops of freshly prepared 0.2% ninhydrin reagent to the extract and heat. A blue colour develops indicating the presence of proteins, peptides or amino acids.

3. **Xanthoprotein test:**

To the extract, add 20% of sodium hydroxide or ammonia. Orange colour indicates presence of aromatic amino acid. **(Evans W.C 1996, Kandelwal, 2004.)**

5.2 ACUTE ORAL TOXICITY STUDIES

Animals:-

Swiss albino mice of female sex weighing 20-25gms were used for the study. The animals were were housed in polypropylene cages. The animals were maintained under standard laboratory conditions ($25^0 \pm 2^0$C; 12hr light and dark cycle). The animals were fed with standard diet and water *ad libitum*. Ethical clearance (for handling of animals and the procedures used in study) was obtained from the Institutional Animal Ethical Committee before performing the study on animals.

Acute toxicity Test:

Acute oral toxicity study for methanol extract of Canavalia *maritima* leaves was carried out as per OECD guideline 425 (Up and Down procedure). The test procedure minimizes the number of animals required to estimate the acute oral toxicity. The test allows the observation of signs of toxicity and can also be used to identify chemicals that are likely to have low toxicity.

Animals were fasted (food but not water was with held overnight) prior to dosing. The fasted body weight of each animal was determined and the dose was calculated according to the body weight.

5.3 PHARMACOLOGICAL EVALUATION

Animal study:

Male albino-Wistar rats weighing 200-250g, Swiss albino mice weighing 20-25g were used in the present study.

Housing and feeding condition:

All the rats were kept at room temperature (22±30°C) in the animal house. All the animals were housed and treated as per the internationally accepted ethical guidelines for the care of laboratory animals. Prior to the experiments, rats were fed with standard food and were acclimatized to standard laboratory conditions of temperature (22±30°) and maintained an 12:12 hr light: dark cycle. They were provided with regular rat chow and distilled water *ad libitum.* All the experimental procedures were performed on animal after approval from the ethics committee and in accordance with the recommendations for the proper care and use of laboratory animals.

Extract:

Ethanolic extract of *Canavalia maritima* leaf

Standard drug used:

Haloperidol (1mg/kg)

Diazepam (2mg/kg & 5mg/kg)

Pentobarbitone (40mg/kg)

5.3.1 Evaluation of Antipsychotic activity:

The antipsychotic potential of ethanolic extract of *Canavalia maritima* leaf was investigated by Haloperidol induced catalepsy in experimental Wistar rats because Conditioned avoidance response (CAR) behaviour and catalepsy (CAT) are the standard preclinical tests used to predict antipsychotic activity and motor side-effect liability respectively.

HALOPERIDOL INDUCED CATALEPSY TEST:-

Catalepsy is defined as a failure to correct an externally imposed, unusual posture over a prolonged period of time. Neuroleptics which have an inhibitory action on the nigrostriatal dopamine system induce catalepsy. This model is used to elucidate the possible mechanism of action of the ethanolic extract of *Canavalia maritima.* The respective standard drug (Haloperidol 1mg/kg) is used for this experimental model.

Experimental Design:

Experimental rats were divided into five groups each groups comprising of six animals. The treatment group is designated as follows.

Experimental design

Group(n=6)	**Treatment**
Group I	Normal Control rats.
Group II	Rats treated with C .*maritima* Ext.(400mg /kg)
Group II	Rats treated with C. *maritima* Ext.(800mg /kg)
Group IV	Rats treated with standard drugs

EXPERIMENTAL PROCEDURE

Male albino-Wistar rats were divided in to four groups as mentioned above of six animals per group weighing between 200-250g are used.

Group I - normal control (0.5% CMC solution)

Group II - received 400mg/kg, p.o ethanolic extract of *Canavalia maritima* leaf.

Group III - received 800mg/kg, p.o ethanolic extract of *Canavalia maritima* leaf.

Group IV - received 1 mg/kg, i.p haloperidol as standard.

The test and standard treated animals are measured for catalepsy as follow:-

Scoring for catalepsy:-

The following scoring system was used:

- 0 – rat moved normally when placed on the table;
- 0.5 – rat moved only when touched or pushed;
- 0.5 - rat placed on the table with front paws set alternately on a 3 cm high wooden block, failed to correct the posture. Time (in sec.) taken to correct the posture (2 min. was considered as cut off time) was multiplied by the score for each paw;
- 1.0 - rat failed to correct posture when front paws are placed on a 9 cm high wooden block, Time (in sec.) taken to correct the posture (2 min. was considered as cut off time) was multiplied by the score for each paw.

Formula to calculate catalepsy score: -

Total Score =0.5 + (0.5 x Time in sec. of front right paw on 3 cm high wooden block) + (0.5 x Time in sec. of front left paw on 3 cm high wooden block) + (1 x Time in sec. of front right paw on 9 cm high wooden block) + (1 x Time in sec. of front left paw on 9 cm high wooden block).

For example, rat move only when touched or pushed then score 0.5. Then rat placed on the table with front right paw set on a 3 cm high wooden block, fails to correct the posture in specific time (in sec.) say 100 sec. (2 min. was considered as cut off time), the score 0.5 multiplied by the time taken to correct the posture, the score become 0.5 x 100 = 50. Similarly with left paw, taking time 90sec to correct the posture, score become 0.5 x 90=45. In case of right paw placed on 9 cm high wooden box, taking time of 60 sec to correct the posture, the score will be 1 x 60 = 60. Similarly with left paw, taking time 80 sec to correct posture, score will be 1 x 80 = 80.

Total score in the above example will be 0.5+50+45+60+80=235.5

Thus, according to the formula, for a single rat, the maximum possible cumulative score of catalepsy was 360.5. The catalepsy score at the given time interval was plotted against time and following observations were noted.

1. **Onset of overall catalepsy** was the time at which animals started showing the catalepsy.

2. **Duration of overall catalepsy** was total duration of catalepsy produced.

3. **Onset of maximum catalepsy** was the time at which animals started to show maximum score of catalepsy i.e. above 335

4. **Duration of maximum catalepsy** was the duration of catalepsy at which the score was nearer to the maximum score i.e. above 335.

All the rats are measured for their catalepsy score for every 0.5hr, 1hr, 2hr, 3hr and the mean values of each group is calculated.

5.3.2 EVALUATION OF ANXIOLYTIC ACTIVITY:-

The anxiolytic activity of ethanolic extract of Canavalia *maritima* was evaluated by **Forced swim test.**

FORCED SWIM TEST (FST):-

The FST is the most widely used pharmacological in vivo model for assessing antidepressant activity. The mice were forced to swim in restricted space from which they cannot escape are induced to a characteristic behavior of immobility. This behavior reflects a state of depression which can be increased or reduced by test and standard drug (diazepam 2mg/kg).

Experimental Design:

Experimental rats were divided into five groups each groups comprising of six animals. The treatment group is designated as follows.

Experimental design

Group(n=6)	Treatment
Group I	Normal Control mice.
Group II	Mice treated with C. *maritima* Ext(400mg /kg)
Group III	Mice treated with C. *maritima* Ext(800mg /kg)
Group IV	Mice treated with standard drugs

EXPERIMENTAL PROCEDURE

Swiss albino mice were divided in to four groups as mentioned above of six animals per group weighing between 20-25g are used.

Group I - normal control (0.5% CMC solution)

Group II - received 400mg/kg, p.o ethanolic extract of *Canavalia maritima* leaf.

Group III - received 800mg/kg, p.o ethanolic extract of *Canavalia maritima* leaf.

Group IV - received 2 mg/kg, i.p diazepam as standard.

The apparatus consisted of a clear plexiglass cylinder (20 cm high×12 cm diameter) filled to a 15 cm depth with water (24±1 ◦C). When rats are placed in the cylinders for the first time they are initially highly active, vigorously swimming in circles, trying to climb the wall or diving to the bottom. After 2–3 min activity begins to

subside and to be interspersed with phases of immobility or floating of increasing length. After 5–6 min immobility reaches a plateau where the rats remain immobile for approximately 80% of the time. After 15 min in the water the rats are removed and allowed to dry in a heated enclosure (32 °C) before being returned to their home cages. They are again placed in the cylinder 24 h later and the total duration of immobility is measured during a 5 min test. Floating behaviour during this 5 min period has been found to be reproducible in different groups of mice. An animal is judged to be immobile whenever it remains floating passively in the water in a slightly hunched but upright position, its nose just above the surface. Test drugs or standard are administered 30 min prior to testing .It was suggested that the immobility reflected a state of lowered mood in which the animals had given up hope of finding an exit and had resigned themselves to the experimental situation.

The immobility of each group is observed before and after the administration of drugs and their mean values are calculated for every group.

5.3.3 EVALUATION OF SEDATIVE ACTIVITY:-

The sedative & hypnotic activity of ethanolic extract of Canavalia *maritima* was evaluated by Potentiation of Phenobarbitone sleeping time.

POTENTIATION OF PENTOBARBITONE SLEEPING TIME:-

The induction or Potentiation of Pentobarbitone sleeping time is the most widely used in vivo model in assessing the hypnotic & sedative activity. This test is

used to evaluate CNS active or depression properties of several drugs such as hypnotics, sedatives, tranquilizers & also antidepressants at high doses. Mice are used in this test since metabolic elimination of pentobarbital is rapid in this species.

Experimental Design:

Experimental mice were divided into five groups each groups comprising of six animals. The treatment group is designated as follows.

Experimental design

Group(n=6)	**Treatment**
Group I	Normal Control mice.
Group II	Mice treated with C. *maritima* Ext. (400mg /kg)
Group II	Mice treated with C. *maritima* Ext. (800mg /kg)

** All groups receive pentobarbital i.p, (40mg/kg) 30 min after administering the control & test compounds.

EXPERIMENTAL PROCEDURE

Swiss albino mice were divided in to four groups as mentioned above of six animals per group weighing 25gs are used.

Group I - normal control (0.5% CMC solution)

Group II - received 400mg/kg, p.o ethanolic extract of *Canavalia maritima* leaf.

Group III - received 800mg/kg, p.o ethanolic extract of *Canavalia maritima* leaf.

The selected mice are dosed with control, test and standard compounds as mentioned above. Thirty min later, all the groups were administered with pentobarbital sodium i.p, (40mg/kg). The animals are placed on their back on warmed pad or on dry warm cotton. The duration of loss of righting reflex was noted and duration of sleep was measured as the time interval between loss and regain of righting reflux.

5.3.4 EVALUATION OF MUSCLE RELAXANT ACTIVITY:-

The muscle relaxant activity of ethanolic extract of Canavalia *maritima* is evaluated by **ROTAROD METHOD**.

Rotarod test:-

The test is used to evaluate the activity of drugs interfering with motor coordination. The skeletal muscle relaxation induced by test compounds can be evaluated by testing the ability of a mice or rat to remain on revolving rod.

Experimental Design:

Experimental mice were divided into five groups each groups comprising of six animals. The treatment group is designated as follows.

Experimental design

Group(n=6)	Treatment
Group I	Normal Control mice.
Group II	Mice treated with C. *maritima* Ext. (400mg /kg)
Group III	Mice treated with C. *maritima* Ext. (800mg /kg)
Group IV	Mice treated with standard drugs

EXPERIMENTAL PROCEDURE

Swiss albino mice were divided in to four groups as mentioned above of six animals per group weighing 20-25g are used.

Group I - normal control (0.5% CMC solution)

Group II - received 400mg/kg, p.o ethanolic extract of *Canavalia maritima* leaf.

Group III - received 800mg/kg, p.o ethanolic extract of *Canavalia maritima* leaf.

Group IV – received 2 mg/kg, i.p diazepam as standard.

The apparatus consists of a horizontal metal rod coated with rubber with 3cm diameter attached to a motor with a speed adjusted to 5 rotations per minute. The rod is 75 cm long, divided in to 6 partitions by plastic discs. This helps in testing all the 6 mice at a time. The rod is 50 cm height above the table top to avoid jumping of animals from roller. The plates below the roller ceases immediately when animal falls on them showing the time that animal managed on moving roller.

The animals of suitable weight are taken and are placed on rod rotating at 5 rpm. The mice capable of remaining on the top for 3 min or more, in three successive trails were selected for the study. The control, test & standard groups are dosed as mentioned above and 30 min later they are again placed on Rotarod for 5 min test. The number of falling & fall off time from the roller are noted.

5.3.5 EVALUATION OF SPONTANEOUS LOCOMOTOR ACTIVITY:-

The spontaneous locomotor activity of ethanolic extract of Canavalia *maritima* is evaluated using the Actophotometer method. The locomotor activity is the index of wakefulness of mental activity.

Actophotometer method:-

Most of the CNS drugs influence the locomotor activity in animals & man. The CNS depressants reduce the locomotor activity while stimulants increase the activity. The locomotor activity can be measured easily by using the Actophotometer method.

The Actophotometer operates on photoelectric cells which are connected in circuit with a counter. When the beam of light falling on photocell is cut off by the animal, count is recorded. An Actophotometer could have either circular or square arena in which the animals moves. The animals are allowed to move freely in the activity cage before and after administration of drugs. The locomotor activity scores are recorded and displayed digitally on screen.

Experimental Design:

Experimental rats were divided into five groups each groups comprising of six animals. The treatment group is designated as follows:

Experimental design

Group(n=6)	Treatment
Group I	Normal Control rats.
Group II	Rats treated with C. *maritima* Ext. (400mg /kg)
Group II	Rats treated with C .*maritima* Ext. (800mg /kg)
Group IV	Rats treated with standard drugs

EXPERIMENTAL PROCEDURE

Male albino-Wistar rats were divided in to four groups as mentioned above of six animals per group weighing between 200-250g are used.

Group I - normal control (0.5% CMC solution)

Group II - received 400mg/kg, p.o ethanolic extract of *Canavalia maritima* leaf.

Group III - received 800mg/kg, p.o ethanolic extract of *Canavalia maritima* leaf.

Group IV - received 5 mg/kg, i.p diazepam as standard.

Turn on the equipment and check whether all the photocells are working for accurate recording. Place invidually each rat in the activity cage for 10 min. Note the basal activity score of all the animals. The animals were administered orally and

after 30 mins retest is performed to each rat for activity scores for 10 mins. Note the difference in the activity before and after administration of plant extracts.

Calculated the percent change

$$\text{in motor activity by following formula} = \frac{\text{Before treatment- after treatment}}{\text{Before treatment}} \times 100$$

6. RESULTS AND DISCUSSION

The present study shows that the ethanolic extract of *Canavalia maritima* leaves shows Central Nervous System depression activity in experimental animal models. The present study was done on some disorders that are caused due to CNS depression. They are

- Antipsychotic activity by Haloperidol induced catalepsy test.
- Anxiolytic activity by Forced swim test.
- Sedative & Hypnotic activity by Potentiation of Pentobarbitone sleeping time.
- Muscle relaxant activity by Rotarod method.
- Spontaneous locomotor activity by Actophotometer method.

6.1 PRELIMINARY PHYTOCHEMICAL ANALYSIS

Percentage yield and physical appearance of different extracts

S. No.	Extract	Colour	Yield (%w/w)
1	Pet ether (*C. maritima*)	Greenish Black	4.01
2	Ethanol (*C. maritima*)	Greenish	5.23

Table showing qualitative chemical tests of leaf extracts of *Canavalia maritima*:

Phytoconstituents	**Extract**	
	Petroleum ether	**Ethanol**
Carbohydrates	+	+
Glycosides	-	-
Alkaloids	-	+
Phytosteroids	-	-
Flavonoids	-	+
Protein and amino acids	-	-
Saponins	+	+
Phenols & tannins	-	+
Terpenoids	-	+

+ = Present, - = Absent

The percentage yield of the extract obtained from the powdered leaves of *Canavalia maritima* using successive extraction procedure with solvents of increasing polarity is shown in Table:7 the percentage yield of extract obtained.

The preliminary Phytochemical screening of the extract of *Canavalia maritima* leaves showed the presence of carbohydrates, alkaloids, sterols, flavonoids, saponins, tannins and phenolic compounds. The various phytoconstituents present in the extract is shown in the Table 8.

The phytoconstituents like flavonoids, tannins, terpenoids, phenols, tannins, saponins, alkaloids and sterols have been reported to cause Psychopharmacological actions. The alkaloids such as canarosine a guanidine alkaloid acts as dopamine inhibitor at D_1 receptors. **[Rutt Suttisri et al., (oct 2008)].**

It is suggested that these compounds will be able to produce Psycopharmacological changes. They may act on the inhibitory receptors present in the Central Nervous System Activity such as GABAergic receptors, Dopamine receptors. **[C.A. Suresh Kumar et al., (Jan 2010)]**

Similarly, the ethanol extract of *Canavalia mairtima* leaf, showed the presence flavonoids and their alkaloids, phenols and tannins, triterpenoids and saponins. These phytoconstituents present in the extract could be the possible agents involved in producing the depression in Central Nervous System. This depression produced may be useful in treating the Psychosis, Anxiety and also to produce Sedation, Myorelaxant nature & reduced psychomotor activities. Flavonoids are also capable of scavenging the free radicals. Phenols and Phenolic compounds have potent antioxidant properties **(Berenguer et.al., 2005),**

6.2 PHARMACOLOGICAL STUDIES

6.2.1 ACUTE ORAL TOXICITY STUDIES:-

The acute oral toxicity of the ethanolic extract of *Canavalia maritima* was carried out as per OECD 425-guideline. The acute toxicity studies revealed that LD50>2000mg/kg for the extract.

Acute oral Toxicity study (425) observations.

RESPIRATORY BLOCKAGE IN NOSTRIL	
Dyspnoea	Nil
Apnoea	Nil
Tachypnea	Nil
Nostril discharge	Nil
MOTOR ACTIVITIES	
Locomotion	Normal

Somnolence	Nil
Loss of righting reflex	Nil
Anaesthesia	Nil
Ataxia	Nil
Toe walking	Nil
Prostration	Nil
Fasciculation	Nil
Tremor	Nil
CONVULSION (INVOLUNTRAY CONTRACTION)	
Clonic/tonic/tonic-clonic convulsion	Nil
Asphyxial convulsion	Nil

Opistotones (titanic spasm)	Nil

REFLEXES	
Corneal	Normal
Eyelid closure	Normal
Righting	Normal
Light	Normal
Auditory and sensory	Normal
OCULAR SIGNS	
Lacrimation	Nil
Miosis	Nil

Mydriasis	Nil
Ptosis	Nil
Chromodacryorrhea	
Iritis	Nil
Conjunctivitis	Nil
SALIVATION	
Saliva secretion	Nil
PILOERECTION	
Contraction of erectile tissue	Nil
ANALGESIA	
Decrease in reaction to induced pain	Nil
MUSCLE TONE	
Hypo or hypertonia	Nil

GIT SIGN	
Solid dried / watery stool	Nil
Emesis	Nil
Red urine	Nil
SKIN	
Oedema	Nil
Erythema	Nil

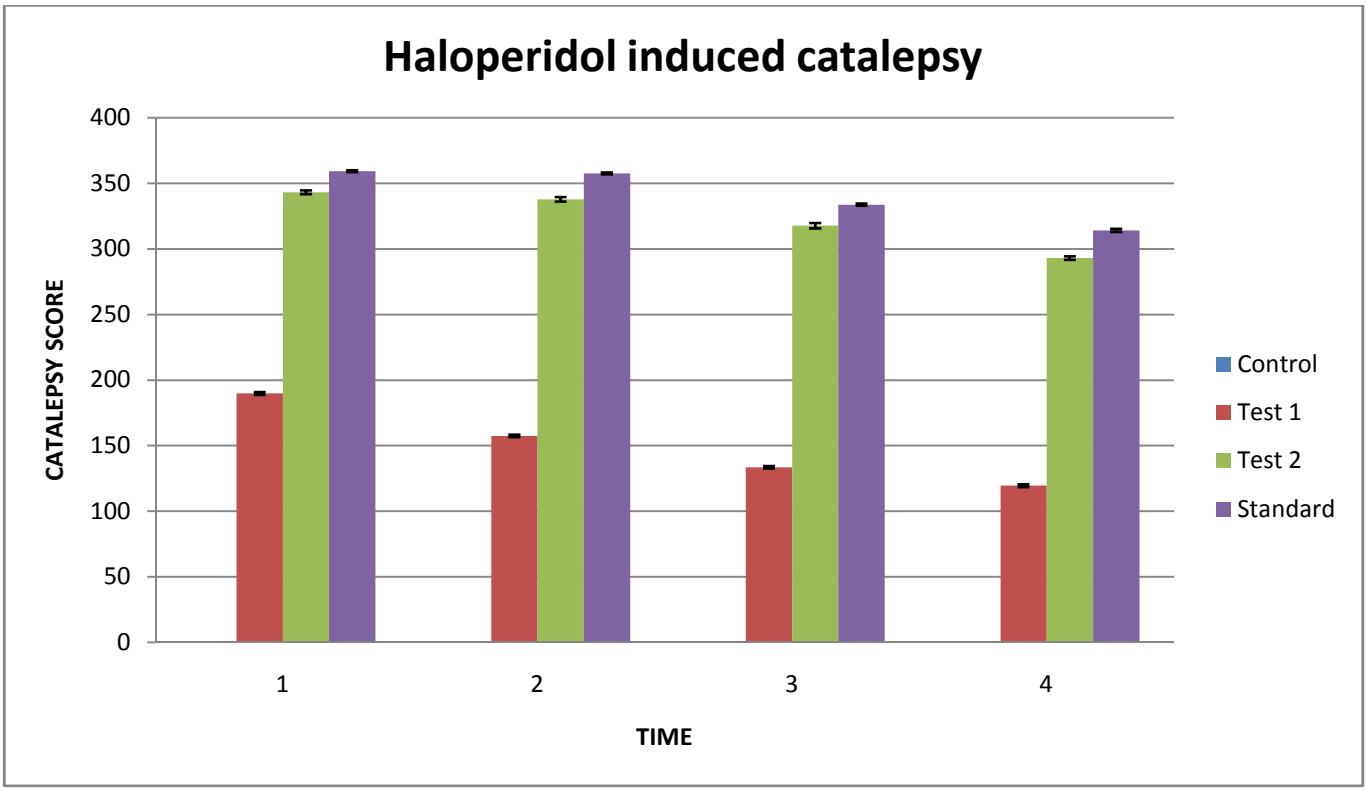
6.2.3. ANTIPSYCHOTIC ACTIVITY:-

HALOPERIDOL INDUCED CATALEPSY TEST

S.No	Group	Dose	Degree of catatonia(score)			
			0.5hr	1hr	2hr	3hr
1	Control	0.5% CMC	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
2	Test $_1$	Ext 400mg/kg	189.8±1.4**	157.5±1.5**	133.5±2.8**	119.5±2.3**
3	Test $_2$	Ext 800mg/kg	343.2±1.4**	337.7±1.7**	317.7±2.0**	293±1.3**
4	Standard	1 mg/kg	359.2±0.61**	357.5±0.77**	333.7±0.83**	314±1.2**

All values are expressed as mean ± S.E.M.; (n=6) animals in each group. **P<0.01.

GRAPHICAL REPRESENTATION



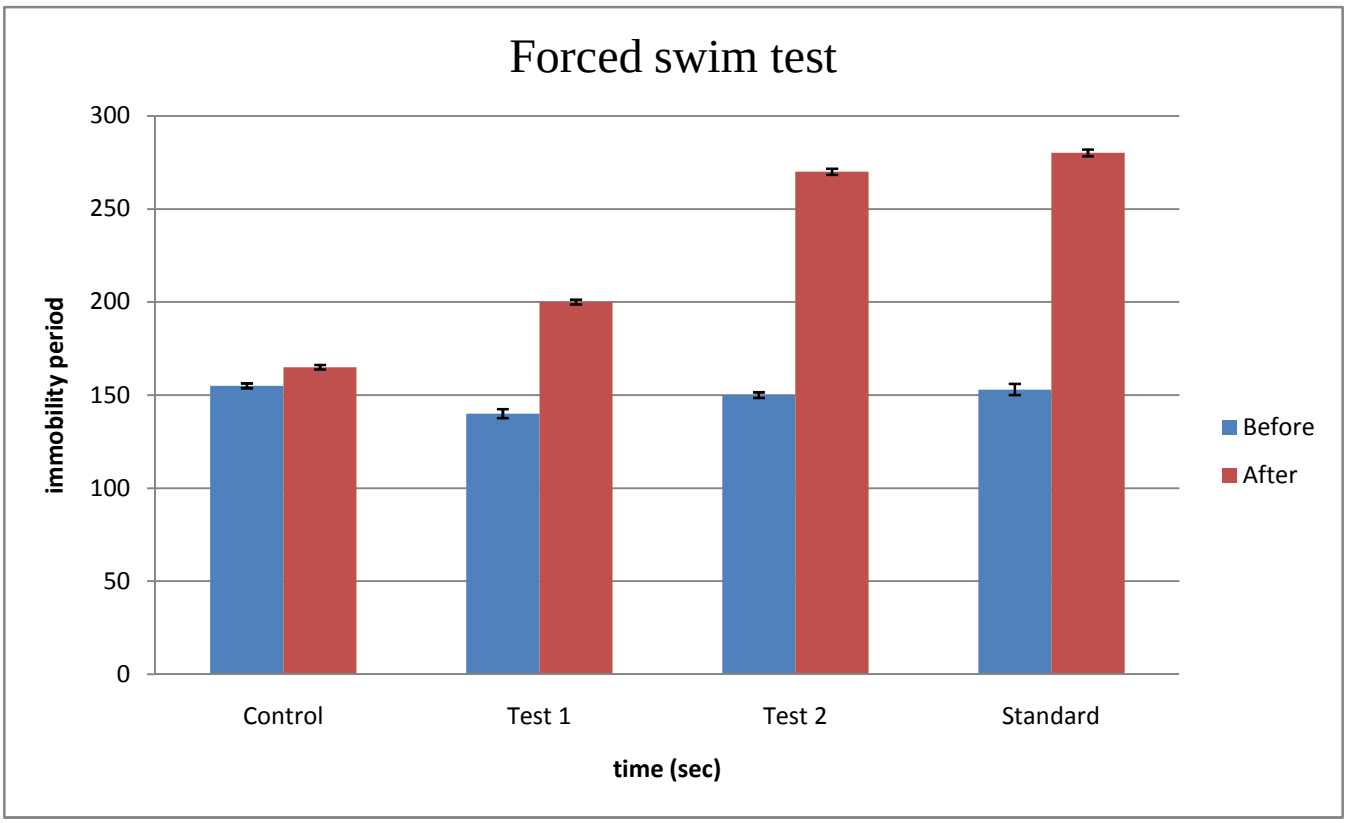
6.2.3. ANXIOLYTIC ACTIVITY:-

FORCED SWIM TEST

S.No	Group	Dose	Immobility(sec)		% increase in immobility
			Before	After	
1	Control	0.5% CMC	155±1.3**	165±1.2**	6.45%
2	Test $_1$	Ext 400mg/kg	140±2.4**	200±1.3**	42.8%
3	Test $_2$	Ext 800mg/kg	150±1.5**	270±1.6**	80%
4	Standard	2 mg/kg	153±3.0**	280.2±1.8**	83.1%

All values are expressed as mean ± S.E.M.; (n=6) animals in each group. **P<0.01.

GRAPHICAL REPRESENTATION



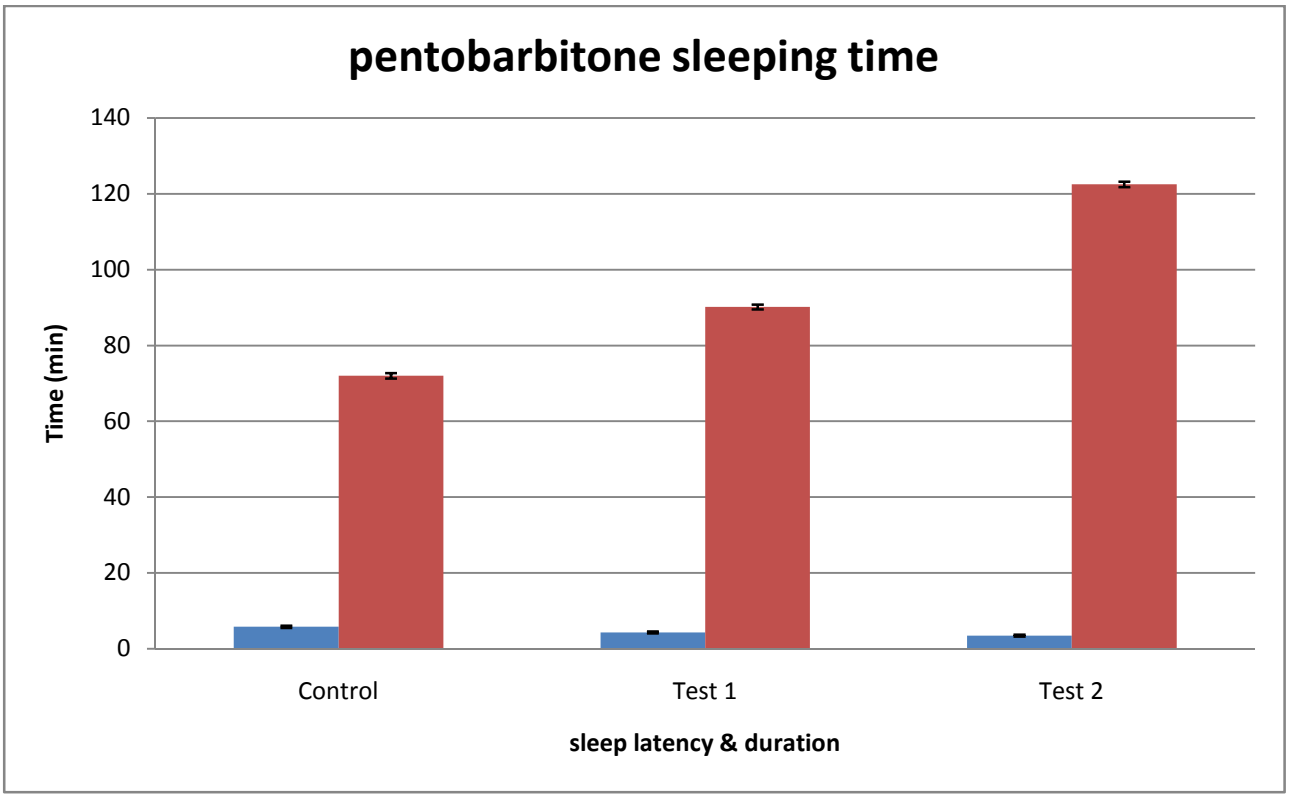
6.2.4. HYPNOTIC & SEDATIVE ACTIVITY:-

POTENTIATION OF PENTOBARBITONE SLEEPING TIME

S.No	Group	Dose	Sleep latency (min)	Duration of sleep (min)
1	Control	0.5% CMC	5.83±0.30**	72±0.73**
2	Test $_1$	Ext 400mg/kg	4.33±0.21**	90.16±0.65**
3	Test $_2$	Ext 800mg/kg	3.5±0.22**	122.5±0.71**

All values are expressed as mean ± S.E.M.; (n=6) animals in each group. **P<0.01.

GRAPHICAL REPRESENTATION



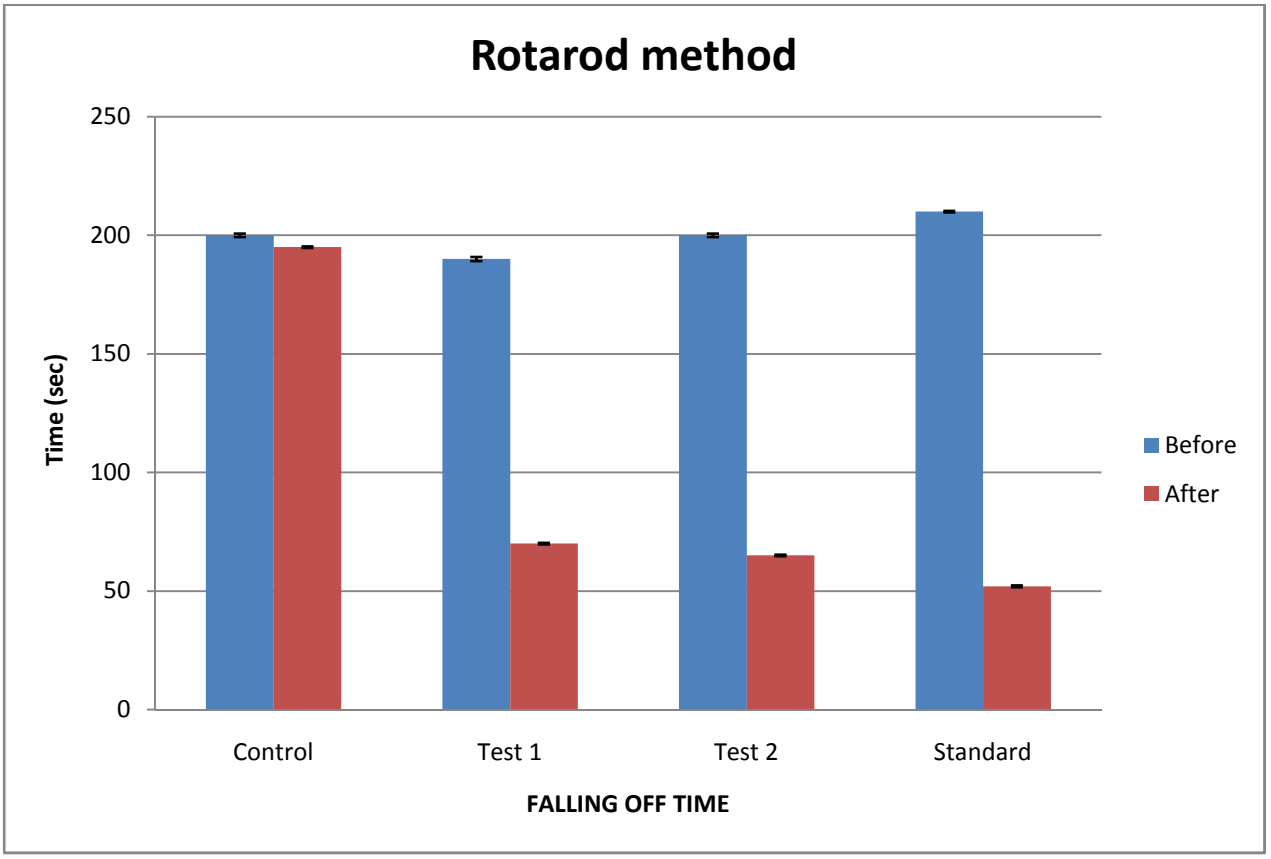
6.2.5. MUSCLE RELAXANT ACTIVITY:-

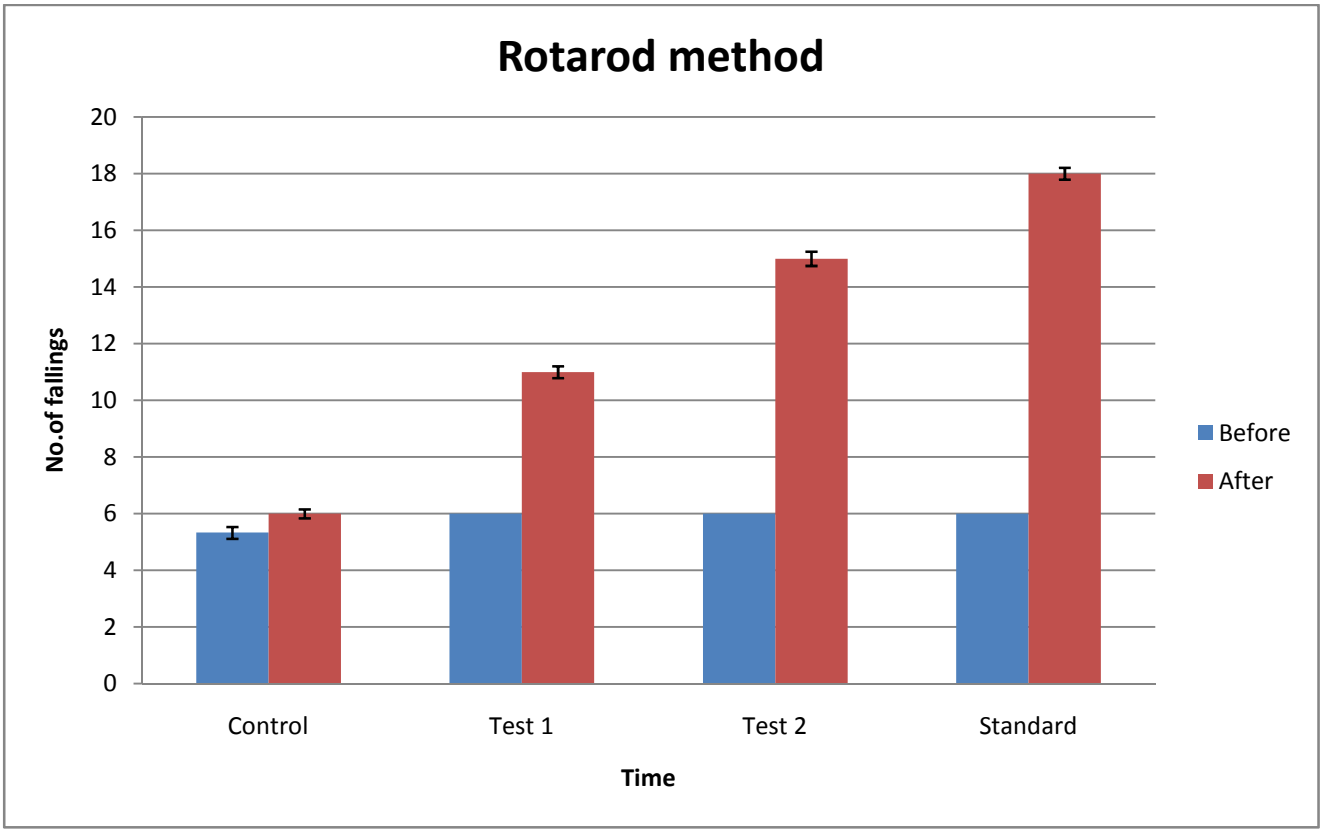
ROTAROD METHOD

S.No	Group	Dose	Falling off time (sec)		No of fallings	
			Before	After	Before	After
1	Control	0.5% CMC	200±0.73**	195±0.33**	5.33±0.21**	6±0.16**
2	Test $_1$	Ext 400mg/kg	190±0.89**	70±0.30**	6±0.00	11±0.21**
3	Test $_2$	Ext 800mg/kg	200±0.73**	65±0.33**	6±0.00	15±0.25**
4	Standard	2 mg/kg	210±0.36**	52±0.36**	6±0.00	18±0.21**

All values are expressed as mean ± S.E.M.; (n=6) animals in each group. **P<0.01.

GRAPHICAL REPRESENTATION




Rotarod method
20
18
16
14
12
10
8
6
4
2
0
No.of fallings
Control
Test 1
Test 2
Standard
Time
Before
After

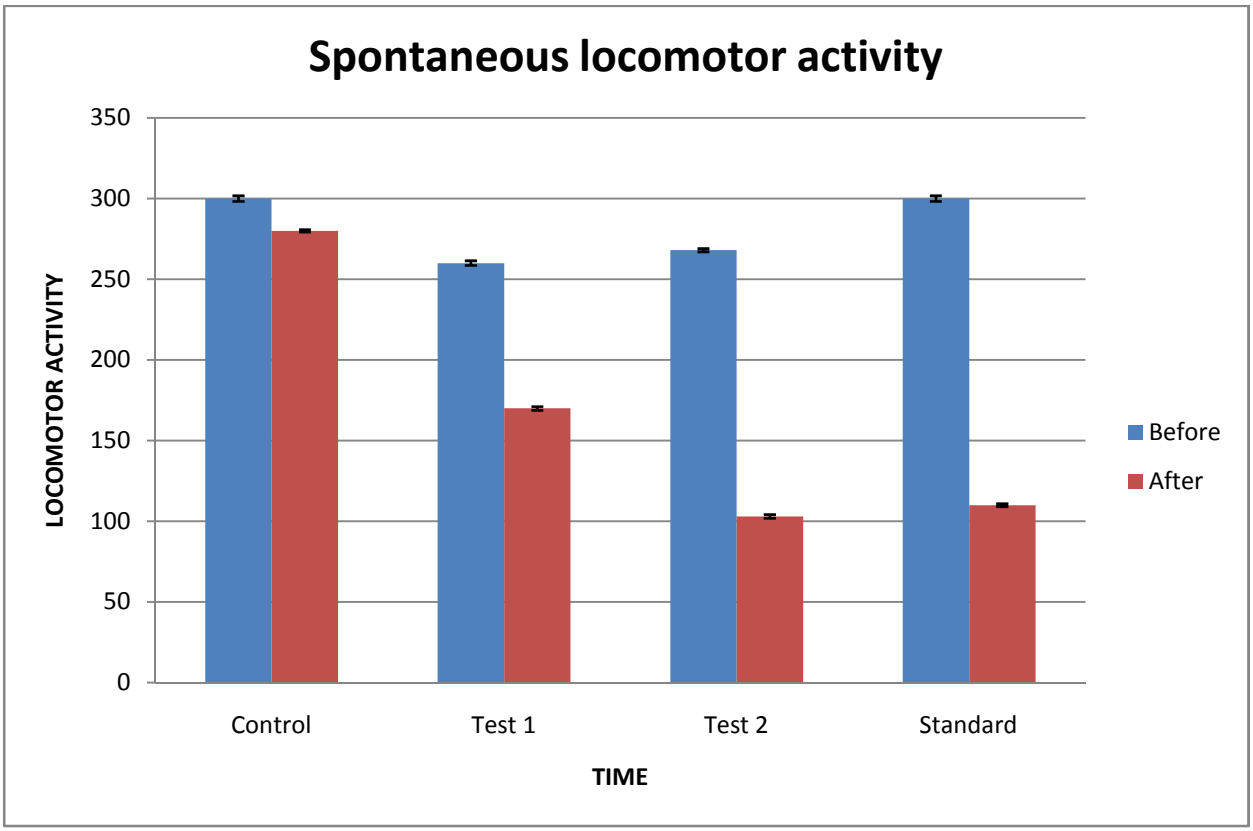
6.2.6. SPONTANEOUS LOCOMOTOR ACTIVITY:-

ACTOPHOTOMETER METHOD

S.No	Group	Dose	Locomotor activity score (10 min)		% decrease in activity
			Before	After	
1	Control	0.5% CMC	300±1.7**	280±0.85**	6.66%
2	Test $_1$	Ext 400mg/kg	260±1.46*	170±1.15*	34.61%
3	Test $_2$	Ext 800mg/kg	268±0.98**	103±1.13*	61.5%
4	Standard	2 mg/kg	300±1.71*	110±0.89**	63.33%

All values are expressed as mean ± S.E.M.; (n=6) animals in each group. **P<0.01, *P<0.1

GRAPHICAL REPRESENTATION



Discussion:-

The present study involves the evaluation of Central Nervous System activity of ethanolic extract of Canavalia *maritima* on behavioral studies such as Potentiation of Phenobarbitone Sleeping time, Actophotometer activity test, Rotarod Test, Forced Swim Test, Haloperidol induced catalepsy test in mice and rats was performed. These screening models are classic models for evaluating Central Nervous System actions providing information about Hypnotic & Sedative activity, Spontaneous Locomotor activity or Psychomotor activity, Myorelaxant activity, Anxiolytic activity and Antipsychotic activity.

The present study showed the effect of ethanolic extracts of Canavalia *maritima* on Antipsychotic activity was evaluated by Haloperidol induced catalepsy test in rat. The catalepsy score is the parameter measured. The results showed that the mean catalepsy score produced in $test_1$ group (400mg/kg) is 189.8±1.4**, 157.5±1.5**, 133.5±2.8**, 119.5±2.3** showed less catalepsy while $test_2$ group (800mg/kg) produced significant catalepsy 343.2±1.4**, 337.7±1.7**, 317.7±2.0**, 293±1.3**compared to standard group (haloperidol 1mg/kg) 359.2±0.61**, 357.5±0.77**, 333.7±0.83**, 314±1.2**at 0.5, 1,2, 3hrs of time. The maximum catalepsy score & catalepsy was observed for 1 hr after administration of extract in $test_2$ group(800mg/kg). The results show that the $test_1$, $test_2$ concentrations of ethanolic extract of Canavalia *maritima* produced a dose dependent catalepsy in experimental rats.

The Anxiolytic effect of ethanolic extracts of Canavalia *maritima* on was evaluated by Forced Swim Test in mice. The immobility period of mice in water is the parameter measured. The results show that $test_1$ group (400mg/kg) produced less immobility period while $test_2$ group (800mg/kg) showed a significant immobility time compared to standard group (diazepam 2 mg/kg). The % increase of immobility time in $test_1$, $test_2$ & standard groups are 42.8%, 80%, 83.1%. These results suggests that the $test_1$, $test_2$ group (400

&800 mg/kg) concentrations of ethanolic extract of Canavalia *maritima* produced a dose dependent prolongation of immobility period in mice.

The effect of ethanolic extracts of Canavalia *maritima* on Sedative activity was evaluated by Potentiation of Pentobarbitone Sleeping time. The sleeping latency & sleep duration are the parameters evaluated. The results showed that $test_1$ group (400mg/kg) & $test_2$ group produced sleep latency in 4.33 min and 3.5 min while the control group produced sleep latency in 5.83 min. Similarly the $test_1$ & $test_2$ concentrations prolonged the duration of sleep (min) in both the test group mice 90.16±0.65**, 122.5±0.71** than control group 72±0.73**. This showed that ethanolic extracts of C .*maritima* produced a dose dependent sedation in experimental mice.

The effect of ethanolic extracts of Canavalia *maritima* on Myorelaxant activity was evaluated by Rotarod method. The falling off time and number of fallings were the parameters evaluated. There is a decrease in falling off time in test1 group (400mg/kg) 70±0.30**, $test_2$ group (800mg/kg) 65±0.33** & standard group (diazepam 5mg/kg) 52±0.36**, before and after administration of extract and standard compounds. Similarly there is an increase in number of fallings in test1 group (400mg/kg) 11±0.21**, $test_2$ group (800mg/kg) 15±0.25** & standard group 18±0.21**, before and after the administration of extract and standard compounds. These results showed that ethanolic extract of C. *maritima* produced a gradual increase in no of falling & gradual decrease in falling off time in experimental test mice compared to standard while control group showed no significant variation.

The Psychomotor activity of ethanolic extracts of Canavalia *maritima* was studied using the Actophotometer activity cage. The locomotor activity score is taken as parameter for evaluation. The activity score was reduced in $test_1$ 260±1.46* to170±1.15*,

$test_2$ 268±0.98** to 103±1.13* and standard groups 300±1.71* to 110±0.89**. The $test_1$ concentration produced moderate %decrease in activity 34.61% while the $test_2$ produced very significant %decrease in activity 61.5% when compared to standard group 63.33% in experimental rats after administering the test & standard group compounds. Thus C. *martima* produced a dose dependent decrease in locomotor activity in rats.

7. SUMMARY AND CONCLUSION

The present study shade dried leaves of *Canavalia maritima* belonging to family Fabaceae having medicinally important active constituent is reviewed, with special emphasis on the biological activities. It has been studied to report on preliminary Phytochemical and pharmacological activities.

The preliminary Phytochemical screening of the extract of *Canavalia maritima* leaves showed the presence of carbohydrates, glycosides, sterols, flavonoids, saponins, tannins, terpenoids and phenolic compounds. The alkaloids, tannins, terpenoids and glycosides are present in the extract which may possibly responsible for the psychopharmacological depression action Canavalia *maritima*.

For evaluating the Antipsychotic activity haloperidol induced catalepsy was used. The ethanolic extracts of Canavalia *maritima* (400mg/kg & 800mg/kg) produced dose dependent catalepsy in rats compared to standard drug (haloperidol). The inhibition of dopamine at its receptors is one of the reasons for producing the antipsychotic activity. The alkaloids such as canarosine a guanidine alkaloid may be responsible for inhibiting the dopaminergic transmission at its receptors. Along with alkaloids other phytochemical constituents such as tannins, terpenoids and glycosides present in the extract which may be possibly responsible for the Antipsychotic action of Canavalia *maritima*. Further studies to be done to confirm the antipsychotic activity with varying dose level and with varying chronic & acute models may suggest the exact mode of action.

The Anxiolytic activity is evaluated by Forced Swim Test. The immobility period of mice in water is considered in this experiment. The ethanolic extracts of Canavalia *maritima* (400mg/kg & 800mg/kg) produced dose dependent prolongation of immobility

period in $test_1$ & $test_2$ group mice compared to standard group. The present study demonstrates that ethanolic extracts of C. *maritima* (400 &800mg/kg) has anxiolytic activity. This action of C. *maritima* is functionally similar to benzodiazepines which are widely used as anxiolytic. The benzodiazepines act through GABA receptors. The mechanism of anxiolytic activity of C. *maritima* extract may involve an action in GABAergic transmission; however further studies are needed to ascertain this.

Earlier reports on the chemical constituents of plants and their pharmacology suggest that plant containing flavonoids, tannins, saponins possess activity against the CNS disorders. The phytochemical investigations of C. *maritima* show that ethanolic extract contains the flavonoids, tannins, saponins, and terpenoids. It is assured that anxiolytic activity may be produced due to binding of any of these phytochemical constituents with $GABA_A$-BZDs complex.

The Sedative activity was studied by Potentiation of Pentobarbitone sleeping time. The sleep latency and sleep duration are the parameters evaluated. The ethanolic extract concentrations (400 & 800 mg/kg) produced sleep latency in lesser time in $test_1$ & $test_2$ groups than control group. They also increased the sleep duration in two test group than the control group. The ethanolic extract of C. *maritima* produced a dose dependent sedation in mice suggesting a profile sedative activity. The sedative effect recorded in this study may be related to an interaction with benzodiazepines and related compounds that bind to receptors in the CNS and have already been identified in certain plant extracts.

The Myorelaxant activity was performed using the Rotarod method. The falling off time and no of fallings are given criteria as parameters. The ethanolic extract concentrations (400 & 800 mg/kg) increased the no of fallings and decreased the falling off time in rats of both the test groups when compared to standard groups after the administration

of test & standard compounds. This shows that C. *maritima* extract produced a significant dose dependent Myorelaxant activity.

The exploratory behaviour is studied by Spontaneous Locomotor Activity of rats in Actophotometer activity cage. The ethanolic extract concentrations (400 & 800 mg/kg) produced reduced exploratory behaviour in both the test groups compared to standard groups. The $test_2$ concentration 800mg/kg produced a very significant reduction in locomotor activity than standard. This suggests that ethanolic extract of C. *maritima* produced reduction in locomotor activity showing depression activity.

It has been reported that C. *maritima* contains tannins, alkaloids, flavonoids triterpenoids & saponins. A number of scientific reports indicated that these phytochemical constituents produce CNS depressant action. Therefore the presence of these active constituents in the ethanolic extract of C. *maritima* may be responsible for the CNS activity. Since the pharmacological profiles of the present investigation of the ethanolic extract of *C. maritima* was similar to that of dopamine it is also possible that they might interact with dopamine receptor.

However, further investigation is underway to determine the exact phytoconstituents that are responsible for CNS depressant activity of ethanolic extract of *C.maritima* and the receptors involved for the execution of the activity.

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