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Neutraceutical Approach of Prunus Armeniaca in Managing Risk of Epilepsy Neurological Disorder

Prof. Ummeroman Mazharuddin Shaikh[1], Ms. Usha Gubdappa Habul[2], Ms. Janvi Hariom Rathod[3], Mr. Tejas Rajkumar Chopade[4], Ms Sakshi Nanasaheb doke[5], Mr. Pawan Ratan magare[6], Mr. Kalpesh Jadhav[7]

[1,2,3,4,5,6,7]SCT College

ABSTRACT

The present investigation has been undertaken to study the anticonvulsant activity of Ethanolic extract of Prunus Armeniaca fruit. The plant Prunus Armeniaca (Apricot)of family Rosaceae is an Ayurvedic herb which is known for its significant medical properties. Experiments were conducted following standard procedures. The Ethanolic extract of Prunus Armeniaca were evaluated for anticonvulsant properties. The anticonvulsant activity of Prunus Armeniaca was evaluated using pentylenetetrazol induced convulsion models. Diazepam was used as standard for PTZ. Extracts treated groups showed higher anticonvulsant activities. The result may be attributed to the chemical constituents such as isoflavonoids present in it which may be due to their individual or cumulative effect that enhanced anticonvulsant activity and provided scientific evidence to the ethnomedicinal features of Prunus Armeniaca. These findings could justify the inclusion of this plant in the management of epilepsy.

Keywords: Prunus Armeniaca, anticonvulsant, chemical constituents.

INTRODUCTION

Epilepsy is one of the World' s oldest recognized conditions, with written records dating back to 4000 BCE. It is a widespread non- contagious common medical condition characterized by multiple or complex neurological causes and has variable prognosis. Epilepsy is also known as gontopathy and was first recognized in 1997. Near about 50 new cases per 100,000 population arise per day. In which about one third of patients have refractory epilepsy. Approx. 75 percent of epilepsy begins during childhood reflecting the heightened susceptibility of the developing brain to seizures. In many CNS disorders epileptic seizures may occur as in simple or complex range. Epilepsy syndrome refers to a group of chemical characteristics that consistently occur together, with similar seizure types, age of onset, EEG findings, triggering factors, genetics, natural history, prognosis, and response to antiepileptic drugs. [1]

International League Against Epilepsy [ILAE] defines epilepsy as short-lived reoccurring episodes of seizures which shows abnormal, excessive neuronal activity. Seizures are caused by sudden alteration of neurological function caused by excessive and synchronous discharge of neurons in the brain. Different parts of the brain can be the sites of such discharges. Seizures can vary from the briefest lapses of attention or muscles jerks to severe and prolonged convulsions. Seizures can also vary in frequency, from less than one per year to several per day.

One seizure does not signify epilepsy (up to 10% of people worldwide have one seizure during their lifetime) It is said to be having epilepsy after two or more unprovoked seizures. Characteristics of seizures vary and depend on where in the brain the disturbance first starts, and how far it spreads. Temporary symptoms occur, such as loss of awareness and disturbances of movements, sensation (including vision, hearing, taste), mood or other cognitive functions. [2]

1.1 BACKGROUND OF THE STUDY

Epilepsy is a chronic disorder of the brain that affects people worldwide. As per WHO, epilepsy is characterized by recurrent seizures, which are brief episodes of involuntary movement that may involve a part of the body (partial) or the entire body (generalized), and are sometimes accompanied by loss of consciousness and control of bowel or bladder function.[1]

Epilepsy was one of the first brain disorders to be described. It was mentioned in ancient Babylon more than 3,000 years ago. The strange behavior caused by some seizures has contributed through the ages to many superstitions and prejudices. From Greek word attack, the word epilepsy is derived. In earlier times, People once thought that those with epilepsy were being visited by demons or gods. However, in 400 B.C., the early physician Hippocrates suggested that epilepsy was a disorder of the brain, and we now know that he was right. [2]

Epilepsy is a major neurological disorder and up to 5% of the world population develops epilepsy in their lifetime. The current therapy of epilepsy with modern antiepileptic drugs is associated with side effects, dose-related and chronic toxicity as well as teratogenic effects and approximately 30% of the patients continue to have seizures with current antiepileptic drug therapy.

Traditional systems of medicines are popular in developing countries and up to 80% of the population relies on traditional medicines/ folk remedies for their primary health care need. Hence, there is a need to discover an alternative agent from natural sources.

Prunus Armeniaca used as a herbal medicine and is well known for its traditional uses such as expectorants, diuretics, laxative etc. Various studies shows that the active principle diterpene alkaloids having a crucial role in treatment of epilepsy.

Prunus Armeniaca is rich in flavonoids. Since Prunus Armeniaca have not been studied for its antiepileptic activity, the present study was aimed to evaluate the antiepileptic activity of Ethanolic extract of Prunus Armeniaca.

1.2 STATEMENT OF THE PROBLEM

More than 2 million people in the United States have experienced an unprovoked seizure or been diagnosed with epilepsy. For about 80 percent of those diagnosed with epilepsy, seizures can be controlled with modern medicines and surgical techniques. However, about 25 to 30 % of people with epilepsy will continue to suffer from seizures with the current available treatment. Doctors call this situation intractable epilepsy. Having a seizure does not necessarily mean that a person has epilepsy. Only when a person has had two or more seizures is he or she considered to have epilepsy. [2]

Approximately 50 million people currently live with epilepsy worldwide. An estimate shows that people suffering from epilepsy (i.e. continuing seizures or with the need for treatment) at a given time is between 4 and 10 per 1000 people. However, some studies shows that the proportion is much higher in low- and middle-income countries, between 7 and 14 per 1000 people.

Globally, each year epilepsy was diagnosed on estimating 2.4 million people. In high-income countries, annual new cases are between 30 and 50 per 100 000 people in the general population. This figure can be up to two times higher in low- and middle-income countries.

Various factors such as higher incidence of road traffic injuries, birth-related injuries, variations in medical infrastructure, availability of preventative health programs and awareness among people can be the reason for these. Close to 80% of people with epilepsy live in low- and middle-income countries.[1]

It is estimated that there are more than 10 million persons with epilepsy in India. Its prevalence is about 1% in our population. The prevalence is higher in the rural (1.9%) compared to urban population (0.6%). In the Bangalore Urban Rural Neuro-epidemiological Survey (BURNS), estimated that a prevalence rate of 8.8/1000 population was observed, with the rate in rural communities (11.9) being twice that of urban areas (5.7).[4]

Epilepsy accounts for 0.6%, of the global burden of disease, a time-based measure that combines years of life lost due to premature mortality and time lived in less than full health. In terms of health care needs, premature death and lost work productivity, epilepsy has significant economic implications.

An Indian study conducted in 1998 calculated that the cost per patient of epilepsy treatment was as high as 88.2% of the country's per capita Gross National Product (GNP), and epilepsy-related costs, which included medical costs, travel, and lost work time, exceeded $2.6 billion/year (2013 USD). [1]

Estimates suggest that available medication controls the seizures in only 50% of patients or decreases the incidence in only 75% of patients. The search for agents with anticonvulsant activity with more selectivity and lower toxicity continues to be an area of investigation in future. [4]

1.3 PURPOSE OF STUDY

The current therapy of epilepsy with modern antiepileptic drugs (AEDs) is associated with side effects, dose-related and chronic toxicity, as well as teratogenic effects, and approximately 30% of the patients continue to have seizures with current antiepileptic drugs therapy. The discovery of novel antiepileptic drugs relies upon the preclinical employment of animal models to establish efficacy and safety prior to the introduction of the AEDs in human volunteers. Natural products from folk remedies have contributed significantly in the discovery of modern drugs and can be an alternative source for the discovery of AEDs with novel structures and better safety and efficacy profiles. For the detection of antiepileptic activity, several plants are used for the treatment of epilepsy in different systems of traditional medicine and these plants have shown activity when tested in modern bioassays and many such plants are yet to be scientifically investigated. Medicinal plants used for the therapy of epilepsy in traditional medicine have been

shown to possess promising anticonvulsant activities in animal models of anticonvulsant screening. [8]

Various studies shows that the active principle isoflavonoids having a crucial role in treatment of epilepsy. Prunus Armeniaca is rich in isoflavonoids. The purpose of the study is to evaluate the antiepileptic activity of Ethanolic extract of Prunus Armeniaca.

1.4 AIM AND OBJECTIVES

AIM

The aim of the present study is "Antiepileptic effect of Prunus Armeniaca in Pentalyntetrazol induced seizures in mice."

OBJECTIVES

- There are some objectives to achieve the aim
- Collection and authentication of plant material.
- Extraction of flavonoids with suitable solvents.
- Identification of safe dose regimen of flavonoids rich extract.
- Pharmacological screening of herbal drug for its anti-epileptic effect on mice.

1.5 PLAN OF WOEK

PHASE 1

- Literature survey
- Selection of plant: selection of plants was based on the extensive literature review of traditional system of medicine and scientific research work

PHASE 2

- Procurement of chemicals
- Collection of leaves of Punica granatum and preliminary investigation
- Extraction and isolation of flavonoids.

PHASE 3

- Selection of doses of flavonoids based on acute oral toxicity test as per Organization for Economic Co-operation and Development (OECD) guidelines
- Pharmacological screening of anti-anxiety effect of flavonoids on mice
- Obtaining experimental data, obtained data will be subjected to statistical analysis

2. LITERATURE REVIEW

2.1 EPILEPSY

Epilepsy is a chronic CNS disorder characterized by brief episodes of seizures and excessive EEG discharge. It is usually associated with loss of consciousness, violent spasmodic contractions of skeletal muscles (convulsions) and autonomic hyperactivity.[9] Epilepsy is one of the most common neurological disorders. Worldwide, the prevalence is estimated to be 0.5- 1%, and there is a life time incidence of 1-3%. It has important medical, social and psychological consequences. Epilepsy is a heterogeneous symptom complex, a chronic disorder characterized by recurrent seizures. Seizures resulting from abnormal discharge of cerebral neurons and are finite episodes of brain dysfunction. It is estimated that in India (with population more than 1 billion), there will be 6- 10 million people with epilepsy, accounting for nearly 1/5 of global burden. The current treatment of epilepsy with modern antiepileptic agents is associated with side effects, dose-related and chronic toxicity, as well as teratogenic effects, and approximately 30% of the patients continue to have seizures with current antiepileptic drugs therapy. Therefore, there is a great need for the development of cheap, effective and safe anticonvulsant agents from plants and other sources.[10]

Epilepsy is one of the World’ s oldest recognized conditions, with written records dating back to 4000 BCE. It is a widespread non- contagious common medical condition characterized by multiple or complex neurological causes and has variable prognosis. Epilepsy is also known as gontopathy and was first recognized in 1997. Near about 50 new cases per 100,000 population arise per day. In which about one third of patients have refractory epilepsy. Approx. 75 percent of epilepsy begins during childhood reflecting the heightened susceptibility of the developing brain to seizures. In many CNS disorders epileptic seizures may occur as in simple or complex range. Epilepsy syndrome refers to a group of chemical characteristics that consistently occur together, with similar seizure types, age of onset, EEG findings, triggering factors, genetics, natural history, prognosis, and response to antiepileptic drugs. [1]

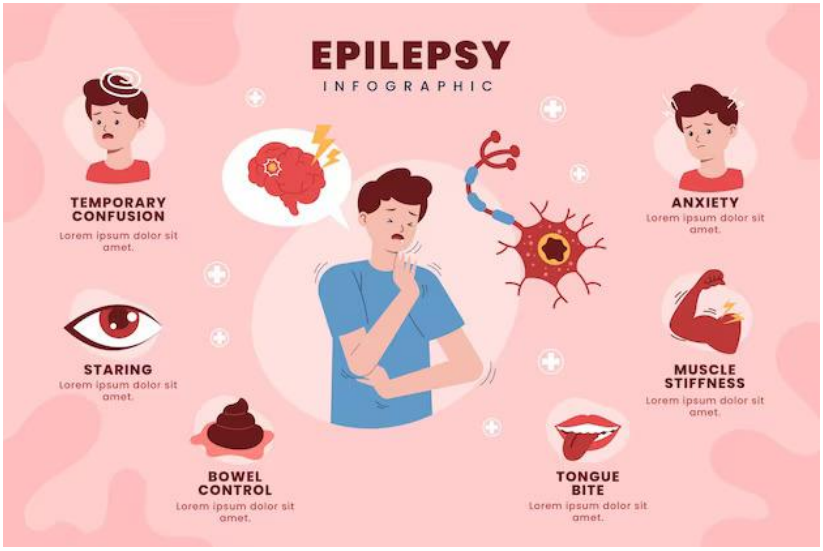


Fig.1. introduction to epilepsy

2.2 CLASSIFICATION OF EPILEPSY

FOCAL	GENERALIZE	UNKNOWN
•**MOTOR ON SET** •AUTOMETISM •ATONIC •CLONIC •EPILEPTIC SPASM •HYPERKINETIC •MYOCLONIC •TONIC •**NON MOTOR ON SET** •AUTONOMIC •BEHAVIOR ARREST •COGNETIVE •EMOTIONAL SENSORY	•**MOTOR** •TONIC CLONIC •CLONIC •TONIC •MYOCLONIC •MYOCLONIC TONIC CLONIC •MYOCLONIC ATONIC •ATONIC •EPILEPTIC SPASM •**NON MOTOR** •TYPICAL •ATYPICAL •MYOCLONIC •EYELID MYOCLONIA	•**MOTOR** •TONIC CLONIC •EPILEPTIC SPASM •**NON MOTOR** •BEHAVIOR ARREST •**UNCLASSIFIED**

[4]

Fig. 2. Classification of epilepsy

Focal Seizures

They are also known as partial seizures. They have a unilateral localized origin in brain, but may spread to small or large area, or to the whole brain.

- Atonic: Unique type of seizures leading to sudden loss of muscle tone
- Clonic: Type of seizure which leads to repetitive, rhythmic muscle contraction
- Epileptic Spasm: seizures characterized by repetitive twitching, posture changes, etc
- Simple partial seizures: Depends on the location within the cortex of the seizures,20-60 seconds in length, and person remain conscious

- Complex partial seizures: Unconscious for 30 sec to 2 min and is often associated with lap smacking hand wringing, or another purpose less movement

Generalized seizures

This type of seizure affects both hemispheres of the brain simultaneously leading to a range of symptoms

- Tonic-Clonic: It involves loss of consciousness, sustain muscle contraction followed by periods of relaxation, and lasts 1-2 min
- Absence seizures: It involves abrupt loss of consciousness with starting and loss of activity for less than 30 min
- Myoclonic seizures: It involves shock-like muscle contraction which may or may not be specific to one extremity and is very brief
- Atonic seizures: It involves brief loss of consciousness with relaxation of all muscles

Unknown seizures

They are characterized by and unclear or uncertain seizure

- Behavioural arrest: It involves sudden interruption in person's activity featuring sudden blank stare, unresponsiveness and no memory [5][6]

2.3 CAUSES

- Changes in blood glucose concentration
- Plasma pH
- Total osmotic pressure and electrolytes composition of extra cellular fluids
- Fatigue
- Emotional stress
- Nutritional deficiency [4]
- Genetic Factors
- Head Injury
- Prenatal Injury and Developmental Problems

2.4 SYMPTOMS

- a convulsion with no temperature (no fever)
- Confused memory or short spells of blackout
- intermittent fainting spells, during which loss of bowel or bladder control, followed by extreme tiredness
- for a short period, the person is unresponsive to instructions or questions
- the person becomes stiff, suddenly, for no apparent reason
- the person suddenly falls
- the person shows sudden bouts of blinking without apparent stimuli
- sudden bouts of chewing, without any apparent reason
- for a short time, the person seems dazed and unable to communicate
- repetitive movements that seem inappropriate
- the person becomes fearful for no apparent reason; they may even panic or become angry
- peculiar changes in senses, such as smell, touch, and sound
- the arms, legs, or body jerk, in babies these will appear as a cluster of rapid jerking movements

The following conditions need to be eliminated as they may appear as similar symptoms and are sometimes misdiagnosed as epilepsy:

- high fever with epilepsy-like symptoms
- fainting
- narcolepsy - recurring episodes of sleep during the day
- cataplexy - periods of extreme weakness
- sleep disorders
- nightmares
- panic attacks
- fugue states - rare psychiatric disorder
- psychogenic seizures [13]

2.5 SYNDROMES

Cases of epilepsy may be arranged into epilepsy syndromes on the basis of specific features that are present. These features include, the seizure types, EEG findings, the age that seizure begins. Identifying an epilepsy syndrome is useful as it helps determine the underlying causes as well as what anti-seizure medication should be tried.

Since the onset of seizures is commonly early, the ability to categorize a case of epilepsy into a specific syndrome occurs more often with children. Less serious examples are benign Rolandic epilepsy (2.8 per 100,000), childhood absence epilepsy (0.8 per 100,000) and juvenile myoclonic epilepsy (0.7 per 100,000). Severe syndromes with diffuse brain dysfunction caused, at least partly, by some aspect of epilepsy, are also commonly known as epileptic encephalopathies. These are associated with frequent seizures that are resistant to treatment and severe cognitive dysfunction, for instance Lennox–Gastaut syndrome and West syndrome. Genetics is believed to play an important role in epilepsies by a number of mechanisms. Simple and complex modes of inheritance have been identified for some of them. However, extensive screening has failed to identify many single gene variants of large effect.

Syndromes in which causes are not clearly identified are difficult to match with categories of the current classification of epilepsy. Categorization for these cases was made somewhat arbitrarily. In case of 2011 classification (idiopathic category) includes syndromes in which the general clinical features and/or age specificity strongly point towards a genetic cause. Some childhood epilepsy syndromes are included in the unknown cause category in which the cause is presumed genetic, for instance benign Rolandic epilepsy. Others are included in symptomatic in some cases despite a presumed genetic cause, for example Lennox-Gastaut syndrome. Clinical syndromes in which epilepsy is not the main feature (e.g. Angelman syndrome) were categorized symptomatic but it was argued to include these within the category idiopathic. Classification of epilepsies and particularly of epilepsy syndromes will change with advances in research.[14]

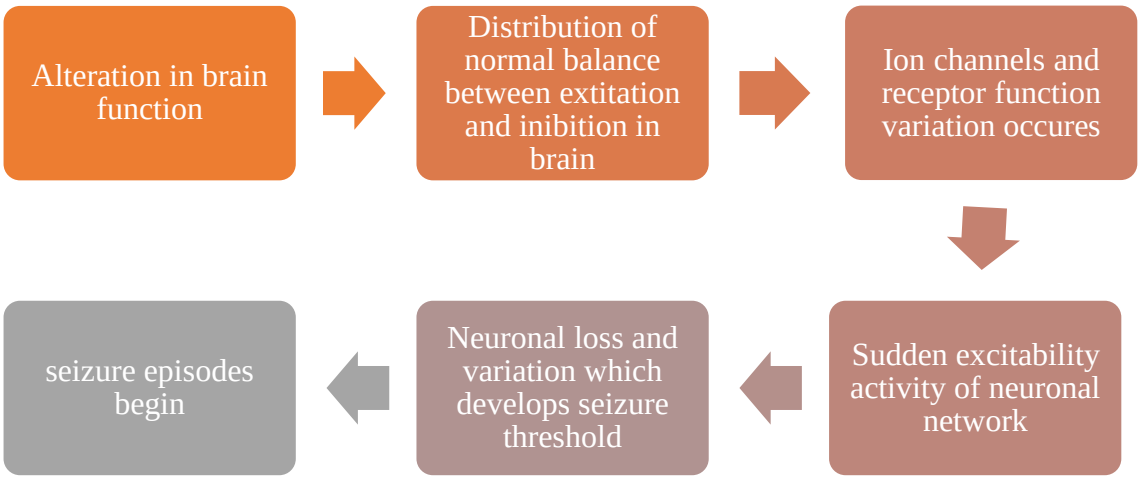
2.6 PATHOPHYSIOLOGY OF EPILEPSY

Action potential is the basic mechanism of neuronal excitability. Action potential is a hyperexcitable state can result from increased excitatory synaptic neurotransmission, decreased inhibitory neurotransmission, an alteration in voltage-gated ion channels, or an alteration of intra- or extra-cellular ion concentrations in favor of membrane depolarization. Membrane potential can vary with activation of ligand-gated channels, whose conductance is affected by binding to neurotransmitters; or with activation of voltage-gated channels, whose conductance is affected by changes in transmembrane potential; or with changes in intracellular ion compartmentalization.

The major neurotransmitters in the brain are glutamate, gamma-amino-butyric acid (GABA), acetylcholine (ACh), norepinephrine, dopamine, serotonin, and histamine. The major excitatory neurotransmitter is the amino acid glutamate. All ionotropic glutamate receptors are permeable to Na+ and K+, and it is the influx of Na+ and outflow of K+ through these channels that contribute to membrane depolarization and generation of the action potential. The NMDA receptor also has a Calcium channel and in resting state, calcium channel is blocked by Magnesium ions, but under conditions of local membrane depolarization, Mg++ is displaced and the channel becomes permeable to Ca++. Influx of Ca++ tends to further depolarize the cell, and is thought also to contribute to Ca++ mediated neuronal injury under conditions of excessive neuronal activation (such as status epilepticus and ischemia), potentially leading to cell death, a process termed excitotoxicity.

The major inhibitory neurotransmitter, GABA, interacts with 2 major subtypes of receptor: GABAA and GABAB receptors. GABAA receptors are found postsynaptically, while GABAB receptors are found presynaptically, and can thereby modulate synaptic release. GABAA receptors are permeable to Cl- ions in adult brain and action potential is inhibited by upon activation Cl- influx hyperpolarizes the membrane. Therefore, substances which are GABAA receptor agonists, such as barbiturates and benzodiazepines, are well known to suppress seizure activity. Rather than Cl- channels, GABAB receptors are associated with second messenger systems, and due to their presynaptic location, attenuation of transmitter release occurs. The second messenger systems often result in opening of K+ channels, leading to a hyperpolarizing current.

Certain GABAB agonists, such as baclofen, have been reported to exacerbate hyperexcitability and seizures. [15]



[7]

Fig. 3. Pathophysiology of epilepsy

2.7 DIAGNOSIS

The history and neurologic examination are the cornerstones of the diagnosis of seizures and epilepsy, whereas laboratory evaluations serve as adjunctive tests. The neurological examination assesses focal signs that might implicate or localize cerebral pathology.

Various diagnostic methods/ tests are as follows: -

- EEG (Electroencephalogram)
- Video EEG (LTM): Video- Electroencephalogram long term - monitoring

- CT head
- MRI Brain
- PET scan
- Laboratory test
- Blood glucose
  - Toxicology screen
  - FBC
  - Electrolyte panel
- Genetic testing

Misdiagnosis of epilepsy is a huge medical problem with a significant impact on the patient. Patients with epileptic seizures may be mis diagnosed as migraine, encephalitis, or other paroxysmal non - epileptic events. They are likely to be mismanaged with treatments that cannot help them and also deprived of specific therapies

People with epilepsy tend to have more physical problems as well as higher rates of psychological conditions, including anxiety and depression. The risk of premature death in people with epilepsy Is up to three times higher than in the general population. Patients diagnosed with epilepsy are influenced by various lifestyle managements such as seizure control, ADR monitoring, Mood balance, Access to education, etc. Seizures can be controlled. up to 70 % of people living with epilepsy could become seizure free with appropriate use of antiseizure medicines. conventional medicines are apparently used for treating seizures. To make up for ADRs caused by allopathic conventional medicines, Herbal medicines are now a new approach. combination of allopathic and herbal can be a more effective way.

To raise awareness about epilepsy ILAE and IBE celebrates 2 Nd Monday of February each year as INTERNATIONAL EPILEPSY DAY. WHO produced the first global report in 2019 on epilepsy entitled as, Epilepsy: A Public health imperative, highlighting the evidence on the burden of epilepsy and the public health response required at global, regional and national levels.[3]

2.8 CONVENTIONAL DRUGS USED IN EPILEPSY

The allopathic approach to managing epilepsy focuses on using conventional medical treatments, primarily medications, to control seizures and improve the quality of life for individuals with this neurological disorder.

It is a comprehensive strategy that involves accurate diagnosis, the use of anti-epileptic medications as the primary treatment, lifestyle modifications, and the consideration of surgical or dietary interventions when necessary. It emphasizes ongoing monitoring and adjustments to provide the best possible seizure control and quality of life for individuals with epilepsy**.** It's important to note that the specific approach and treatment plan will be highly individualized based on the specific type of epilepsy, the patient's individual needs, and the expertise of the healthcare professionals involved. If you or someone you know has epilepsy, it is crucial to consult with a neurologist for proper diagnosis and management

CLASS	***DRUGS***
Barbiturates	Phenobarbitone
Deoxybarbiturates	Primidone
Hydantoin	Phenytoin , Fosphenytoin

Iminostilbene	Carbamazepine, Oxcarbazepine , Eslicarbazepine
Succinamide	Ethosuximide
Aliphatic Carboxylic Acid	Valproate , Divalproex
Benzodiazepines	Clonazepam , Diazepam , Lorazepam , Clobazepam
Phenyltriazine	Lamotrigine
Cyclic GABA receptor	Gabapentin , Pregabalin
New Drugs	Topiramate , Levetiracetam , Zonisamide , Vigabatrin , Tiagabine , Lacosamide
Azoles	Acetazolamide

Table. No 1

2.9 MECHANISM OF ACTION OF ANTIEPILEPTIC DRUG

- *PROLONGATION OF SODIUM CHANNEL INACTIVATION*

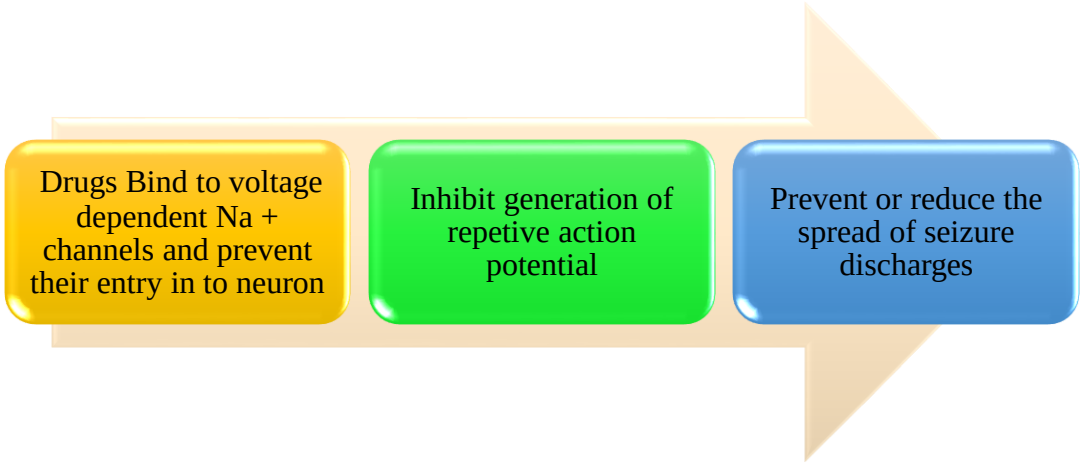


Fig. 4.1

Sodium channels are crucial for the generation and propagation of action potential in neurons. During an action potential, sodium channels open, allowing sodium ions to flow in. As the membrane depolarizes, the channels eventually inactivate, closing and preventing sodium influx. Drugs like Phenytoin, Fosphenytoin, Carbamazepine, Sodium Valproate, Lamotrigine, Topiramide , Zonisamide bind to voltage dependent sodium channels and stabilize neuronal membrane either by blocking sodium channels or modulating the inactivation of sodium channels .This inhibits repetitive action potentials and therefore , prevent or reduce the spread of seizure discharges .

- ***FACILITATION OF GABA MEDIATED Cl CHANNEL OPENING***

GABA [gamma- aminobutyric acid] is an inhibitory neurotransmitter that plays a crucial role in regulating neuronal excitability . GABA receptors are of mainly 2 types :- GABA_A and GABA_B Receptors. Drugs like Barbiturates and Benzodiazepines bind to GABA_A receptor ehich facilitate the

flow of chloride ions into neuron , leading to hyperpolarization and reduced excitability .Drugs like tiagabine and vigabatrin block GABA reuptake , increasing the amount of GABA for synaptic transmission.

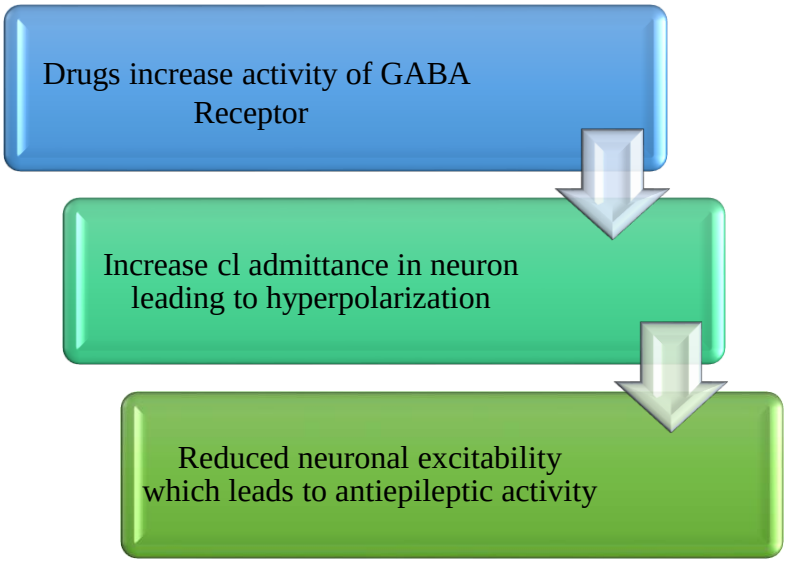


Fig. 4.2

- ***INHIBITION OF T TYPE Ca +2 CURRENT***



Fig. 4.3

T [transient] current is low threshold Ca+2 current. T- type Ca+2 channels are overactive, contributing to excessive neuronal excitability and seizure activity. This generates absence seizures. Drugs like ethosuximide, valproate sodium, trimethadione inhibit T- type Ca+2 channels, reducing neuronal excitability.

- ***DECREASE IN EXCITATORY NEUROTRANSMISSION***

Excitatory Neurotransmission is the process by which neurons transmit signals to each other, leading to an increase in neuronal activity. Glutamate and aspartate act as major excitatory amino acid in the brain. Ionotropic NMDA receptor stimulates glutamate. Drugs like Felbamate acts by inactivating NMDA receptor. This reduces frequency of seizures.[8]

2.10 ANTIEPILEPSY ACTIVITY

Avanthi E et al., (2016) evaluated the antiepileptic activity of clove oil by MES model in mice. A total of thirty mice were taken, they were given an electroconvulsive shock. Thirty mice were divided into five groups of six animals each, the control group received distilled water 5ml/kg i.p. standard received Inj. Sodium valproate 200 mg/kg i.p. another group received Sesame oil – 10ml/kg i.p(control), test groups received Clove oil- 0.075 ml/kg i.p. Clove oil-0.1ml/kg
i.p respectively. All the injections were given 30 minutes before the test. The results showed Clove oil produced significant antiepileptic effect at all the doses. [17]

K Sandeep Kumar et al., (2015) evaluated the antiepileptic activity of ethanolic extract of Biophytum sensitivum in animal models. The anticonvulsant activity was assessed using MES and PTZ using albino mice. The extract reduced the duration of tonic hind limb extension and delayed the onset of tonic clonic convulsion. The result showed that the ethanolic extract of the plant beneficial in both tonic clonic and absence seizures.[10]

Nirmala D (2015) performed a study which involves in detecting anticonvulsant activity from Annacyclus pyrethrum roots by using maximal electroshock seizure (MES) in a dose-dependent way. MES-induced tonic seizures can be prevented either by drugs that inhibit voltage dependent Na+ channels, such as phenytoin, valproate and lamotrigine or by drugs that block glutamatergic excitation mediated by the NMDA receptor such as felbamate. The study showed that ethanolic extract from roots of A. pyrethrum can inhibit voltage dependent Na+ channels as phenytoin in MES induced tonic seizures.[18]

Gummalla Pitchaiahet al., (2015) evaluated the anticonvulsant activity of methanolic extract of Allium cepa (Onion) bulbs in Swiss albino mice. The anticonvulsant effect was assessed using maximal electroshock (MES) and Isoniazid (INH) induced seizure models. Methanolic extract (200 and 400 mg/kg) showed significant reduction in the duration of hind limb extensor phase in electroshock convulsions; protected the mice against the Isoniazid induced convulsions. The results showed significant improvement in brain GABA levels after Allium cepa treatment. [19]

Santilna K S et al., (2014) studied the anticonvulsant activity study of Artemisia nilagirica. The leaves part of the plant was dried, powdered and subjected to maceration using diethyl ether, chloroform and ethanol. The results showed that the alkaloids, flavonoids and terpenoids were identified to be present in all three solvents extracts. The result obtained suggests that the ethanolic and chloroform extracts of Artemisia nilagirica may be beneficial in the treatment of epilepsy. [20]

Ravindra C Sutar et al., (2014) evaluated the anticonvulsant activity of leaf extract of Holoptelea integrifolia. The petroleum ether and methanolic extract of the leaves was evaluated using Pentylenetetrazol (PTZ) induced convulsions in mice and maximal electro shock (MES) induced Convulsions and lithium-pilocarpine induced status epilepticus in rats. The petroleum ether extract and methanolic extract delayed onset of PTZ- induced convulsions and also prolonged the onset of tonic convulsions in mice. Both the extracts failed to protect the rats from MES induced convulsions. The extracts also protected rats against seizures induced by lithium-pilocarpine. The results indicate that petroleum ether and methanol extracts contained such phytochemical compounds which are active in case of Pentylenetetrazol (PTZ) and lithium pilocarpine induced status epilepticus, which support the ethnomedicinal application of the plant as an anticonvulsant agent. [21]

DilnawazPathanet al., (2014) evaluated the anticonvulsant effect of ethanolic extract of roots of Picrorhiza kurroa on electrically and chemically induced seizures. The extract was studied for its anticonvulsant effect on maximal electroshock-induced seizures and pentylenetetrazol, picrotoxin induced

seizures in mice. It has been observed in the present study that extract (100 mg/kg) showed significant increase in latency to clonic convulsions and reduced mortality. The results shows that Picrorhiza kurroa possess anticonvulsant activity against Pentylenetetrazol, Maximal electroshock and Picrotoxin induced convulsions in mice.[22]

Ganapathi G. Varmaet al., (2014) performed the evaluation of antiepileptic activity of methanolic leaves extract of Tragia involucrata in mice. In vivo screening models like maximal electroshock-induced convulsion (MES), pentylenetetrazol (PTZ) and picrotoxin (PTX) induced models are used to evaluate the antiepileptic effects of the extracts. In the MES induced convulsion, methanolic extract (800 mg/kg), showed high significant inhibition on tonic hind limb extension and decrease in duration of stupor period. In PTZ and PTX induced model extract (400 mg/kg and 800 mg/kg) showed delay on the onset of convulsions, decreased duration of convulsion and reduced mortality significantly. The results showed that Tragia involucrata possesses dose dependent antiepileptic activity.[23]

Mehrdad Modaresi et al., (2014) studied the antiepileptic activity of hydroalcoholic extract of Ocimum basilicum in mice. The experimental groups comprised control, sham, and four treatment groups receiving the extract at 100, 250, 300, and 350 mg/kg doses 65 minutes before PTZ injection. The obtained results of using different doses of the extract indicated that the mice receiving the extract at 100 and 250 mg/kg doses exhibited the highest and lowest frequency of myoclonic twitches, respectively.[24]

Chinchawade A B et al., (2013) observed the anticonvulsant activity of chloroform extract of bark & root of Erythrina variegate. The pentylenetetrazol (PTZ) and the maximal electroshock seizure (MES) models were used for assessing the anticonvulsant effects of the chloroform extract in mice and rats. The extract produced significant protection against PTZ-induced and MES-induced convulsions in rat. The results obtained from this study indicate that the chloroform root and bark extract of Erythrina variegate may be beneficial in both absence and tonic clonic seizures. [25]

Abubakar K et al., (2013) evaluated the anticonvulsant effect of methanolic extract of Evolvulus alsinoides in mice using pentylenetetrazol (PTZ) and the maximal electroshock seizure (MES) model. The extract significantly increased the latency of PTZ induced seizure. In the MES test a dose dependent decrease in the duration of seizure was also observed. These findings suggest that the methanol extract of the plant contains bioactive principles that may be beneficial in the treatment of epilepsy. [26]

Ashish P Anovadiya et al., (2013) performed the antiepileptic and memory retention activity of Curcumin perse and in combination with antiepileptic drugs. In this study, antiepileptic activity of curcumin and its combination with phenytoin and sodium valproate were studied in chronic model (14 days) of Maximal Electroshock Seizure (MES) and Pentylenetetrazol (PTZ) induced seizure respectively. Curcumin (100 mg/kg) reduced clonic phase and significantly inhibited PTZ induced seizure. Addition of curcumin to sub therapeutic dose of sodium valproate showed synergistic effect. Curcumin found to be effective in absence seizure alone and as add on with sodium valproate. [27]

Prabhat Singh et al., (2012) studied antiepileptic activity of aqueous extract of fruits of Tricosanthes dioica. The antiepileptic efficacy of aqueous extract was evaluated by hand limb extension induced by MES and PTZ induced seizures in mice models. The aqueous extract was showed significant antiepileptic activity in both models and it was found to be due to activity against generalized tonic-clonic and cortical focal seizures. [28]

Vikas Saroch et al., (2012) evaluated the anticonvulsant Activity of Apasmarari rasa. Apasmarari rasa was subjected to assess the LD 50 and Anti-convulsant activity on Male Albino rats was by means of MES (Maximal Electro convulsing Shock) Method. A supramaximal strength was 150mA in rats for 0.2 seconds

and stimulus was applied via ear clip electrodes. The animal dose of Phenytoin (7.2mg/kg), Smritisagar rasa (18mg/kg) and Apasmarari rasa (5.4mg/ kg) was given orally to different groups. The animals were observed for a period of 180 minutes after being subjected to electro convulsions. Both standard drugs also shown good results when it comes to HLE (hind limb extension), butother factors such as time duration of flexion, tonus, clonus, recovery time amongst others in test drug group (Apasmarari rasa) showed significantly better results. [29]

Vipin K Garget al., (2011) evaluated the anticonvulsant activity of ethanolic extract of Cynodon dactylon. The anticonvulsant activity was studied using maximal electroshock (MES) and Pentylenetetrazol (PTZ) induced convulsions in mice. The extract suppressed hind limb tonic extensions (HLTE) induced by MES and also exhibited protector effect in PTZ-induced seizures. The results showed that the ethanolic extract of Cynodon dactylon has anticonvulsant effect in the both models suggesting their possible depressant action in the central nervous system. [30]

Shyamjith Manikkoth et al., (2011) performed Phyllanthus amarus on maximal electroshock-induced seizures (MES) and pentylenetetrazole (PTZ) induced seizures. The aqueous and ethanolic extracts of the leaves and stems of P. amarus significantly abolished the hind limb extension induced by MES. The same dose also significantly protected the animals from PTZ induced tonic convulsions. [31]

Harish Babu B et al., (2010) performed anticonvulsant activity of the methanolic extract of Martynia annua on Maximal Electroshock(MES) and Pentylenetetrazole (PTZ) induced seizures models in albino wistar rats. These studies showed, the mean duration of extensor phase of test group reduced to significant level as compared to control group. In Pentylenetetrazol induced seizure test, onset of myoclonic spasm and clonic convulsion was delayed in the test group. The study concluded Martynia annua possesses an anticonvulsant effect which results from the potentiation of the activity of GABA. [32]

2.11 PRUNUS ARMENIACA:

S. GUPTA, M. CHHAJED, S. AROR et al

Herbs are one of the most important sources of medicines for humans for confronting diseases and disorders. Even after several developments in the field of allopathic system of medicine, untoward reactions could not be prevented from being an integral part of modern medicines. Plants are one of the major sources of drug discovery in modern as well as traditional system of medicines worldwide. More than 70 % of marketed drugs are either natural or semisynthetic materials derived from plants. Most literature on complementary alternative medicine worldwide either report the structure of phytoconstituents present in medicinal plants or demonstrate a mechanistic basis for the pharmacological activities possessed by them. Medicinal and therapeutic impact of apricot has not been explored so far. In this review, an attempt has been made highlight the medicinal impact of apricot and its kernel for the treatment of alimentary disorders by summarizing published literature reports till date. Apricot exhibited diversified effects on liver regeneration to myocardial ischemia reperfusion. [33]

Omar Alajil, Vidya R. Sagar, Charanjit Kaur, Shalini Gaur Rudra, R. R. Sharma, Rajeev Kaushik, Mahendra K. Verma, Maharishi Tomar, Manoj Kumar and Mohamed Mekhemar et.al

Apricot (Prunus Armeniaca L.) is a nutritious fruit, rich in bioactive compounds, known for their health benefits. The present study attempts to evaluate nutritional (sugars, organic acids, minerals) and nutraceutical traits (total phenolics, flavonoids, carotenoids, antioxidant activity) six commercial apricot genotypes grown in India. Antioxidant activity was determined using three in-vitro assays, namely CUPRAC (cupric reducing antioxidant capacity), FRAP (ferric reducing antioxidant power) and DPPH (1,1-diphenyl-2-picryl-hydrazyl). Significant ($p < 0.05$) differences were observed in the genotypes

concerning nutritional and nutraceutical traits. Sucrose accounted for more than 60% of total sugars in most genotypes, followed by glucose and fructose. Citric acid accounted for more than 50% of the total organic acids present, followed by malic and succinic acids. Apricot is a good source of potassium (1430.07 to 2202.69 mg/100 g dwb) and iron (2.69 to 6.97 mg/100 g dwb) owing to its mineral composition. Total carotenoids content ranged from 0.44 to 3.55 mg/100 g, with β-carotene accounting for 33–84% of the total content. The results strongly suggest that genotypes 'CITH-A-1' and 'CITH-A-2', which have high dry matter and carotenoids content, are well suited for drying. 'Roxana' and 'CITH-A-3' are great for fresh consumption, while 'Shakarpara' and 'Gold Cot' are excellent for juice processing. [34]

GRACA MIGUEL, SUSANA DANDLEN, ALCINDA NEVES AND DULCE ANTUNES CDCTPV, Universidade do Algarve, Campus de Gambelas, 8005-139 Faro, Portugal maneves@ualg.pt

Several epidemiological studies have revealed that natural antioxidants are important in health maintenance and the prevention of chronic and degenerative diseases. Special attention has been given to flavonoids since many studies have revealed a great cultivar of beneficial effects in diseases such as cardiovascular and cerebrovascular diseases, some forms of cancer and Parkinson's and Alzheimer's diseases. Several cultivars and accessions of apricots (Prunus Armeniaca L.) belonging to the germplasm collection of local apricot (Agronomic Experimental Centre of Tavira, CEAT, Algarve, Portugal) were studied for flavonoids' content and quality indices. Three main flavonoids could be detected in the samples. Quercetin-3-rutinoside, quercetin-3-galactoside and quercetin-3-glucoside. Quercetin-3-rutinoside was absent in 5 samples of apricot: Priana cultivar, and the accessions 13, 5, 9 and 12, nevertheless when present it constituted the most important in the remaining samples. [35]

Sahil Kalia, Vijay K. Bharti, Arup Giri, Bhuvnesh Kumar. Defense Institute of High-Altitude Research (DIHAR), DRDO, C/o- 56 APO, Leh-Ladakh (J and K), India. Defense Institute of Physiology and Allied Sciences (DIPAS), New Delhi, India

Extreme climatic conditions and hypobaric hypoxia at high altitude hinders the growth and productivity of chickens. The present study was carried out to examine the effect of aqueous extract of Prunus Armeniaca seeds on health, survivability, antioxidants, plasma biochemical parameters, and immune status of broiler chickens at high altitude. Phytochemical analysis of extract revealed the presence of high phenolics, flavonoids, and carotenoids contents. Before the in vivo study, in vitro efficacy evaluation indicated a significant protective effect of the extract in chicken peripheral blood lymphocytes. For in vivo study, experimental groups include control (fed the basal diet), and treatment T1, T2, T3, T4, T5, and T6 which received an aqueous extract of P. Armeniaca in drinking water at concentrations of 100, 150, 200, 300, 400, and 800 mg/kg body weight of chicken respectively, along with basal diet for 42 days. Body weight was significantly increased in all treatment groups as compared to control group and the highest body weight was recorded in T3 group. Higher profit was gained in treatment groups due to lesser mortality in chickens. Moreover, chicken in the treatment groups had significantly higher total antioxidant capacity, free radical scavenging activity, interleukin-2, total protein, albumin, globulin level and lower malondialdehyde, interleukin-6, glucose, cholesterol, triglyceride, ALT and AST level as compared to control group. Results suggest that, P. Armeniaca extract at 200 mg/kg body weight of chicken, exhibited the beneficial effect on growth performance and survivability rate of broilers and therefore, could be useful as phytogenic feed additive for broiler chickens at high altitude cold desert. [36]

AYSE DILEK OZSAHIN* and OKKES YILMAZ
Department of Biology, Faculty of Science, Firat University, 23169-Elazig, Turkey Fax: (90)(424)2330066; E-mail: molekuler@gmail.com

The aim of this study is to investigate the preventive effects of the Prunus Armeniaca L. c Kabaasi fruits extract on the lipid peroxidation (LPO) formation in the Fenton reagent environment and analyze the flavonoid, sugar and vitamin contents. The LPO level in the Fenton R group was significantly higher than the control group ($p < 0.0001$), but its level in the fruit extract group was lower than the Fenton R group ($p < 0.001$). In addition, the LPO level in the fruit extract group was significantly decreased when the fruit extract amount was gradually increased ($p < 0.0001$). It was determined that apricot extracts had scavenging effect on the DPPH radical depending on the fruit extract amount. The examined apricot varieties were found to contain β-sitosterol, α-tocopherol, stigmasterol, vitamin D, Vitamin K, ergosterol and polyphenols such as catechin, rutin, resveratrol and myricetin. The results confirm that the apricot fruit extracts decrease LPO level in the Fenton reagent environment and have scavenging effect on the DPPH depending on extract level. The examined apricot varieties are seemed to be good sources biologically active compounds such as lypophilic vitamins and phytosterols. [37]

Key Words: Apricot, Lipid peroxidation, α, α-Diphenyl-β, β-picrylhydrazyl, Flavonoids, Fruit sugars, Phytosterol

Yasaman Vahedi-Mazdabadia, Elahe Karimpour-Razkenarib Tahmineh Akbarzadehb, c, Hania Lotfianc, Mohammad Toushihd et.al

Apricot (Prunus armeniaca L.) is a fruit cultivated in various parts of the world. Both sweet and bitter kernels of apricot have been used for the treatment of different diseases such as loss of memory in Iranian traditional medicine (ITM). In the present study, the inhibitory activity of sweet and bitter extracts of apricot kernels towards cholinesterase (ChE) enzymes, both acetyl and butyrylcholinesterase was examined through Ellman's method. In addition, neuroprotectivity of aqueous extracts and amygdalin were investigated against H2O2-induced cell death in PC12 neurons. Among them, the best acetylcholinesterase (AChE) inhibitory activity ($IC50 = 134.93 \pm 2.88$ µg/mL) and neuroprotectivity (P-value < 0.0001) were obtained by the aqueous extract of bitter type. It was found that all extracts showed no butyrylcholinesterase (BChE) inhibitory activity. [38]

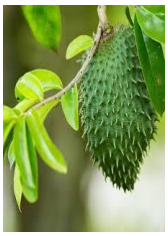
Keywords: Alzheimer's disease; Amygdalin; Cholinesterase inhibitors; Neuroprotectivity; P. armeniaca.

2.12 HERBAL DRUGS APPROACH

Advantages of herbal drugs over conventional drugs include a broad spectrum of antiepileptic, involving less adverse reactions, higher safety, and less drug -drug reactions. Natural drugs retain the natural and biological activities of their constituents. Natural drugs have limited or no non- toxic side effects. The paper reviewed the effects of active components of natural drugs on epilepsy including flavonoids, alkaloids, glycosides, coumarins, and terpenoids which demonstrated significant activity against epilepsy. Flavonoids resembles similar structure to benzodiazepine and shows on anti-epileptic role through the modulation of GABAA-Cl^- channel complex

Herbal medicines offer low toxicity and contains several effective monomers that shows specific pharmacological activities.

Some plants shows toxicity such as Datura stramonium, Ricinus communis and Securidaca longepedunculata. Their extract result 100% mortality in mice within 24 hours of administration.

Sr. no	Herbal plant	Family	Part of plant	Geographical source	Chemical Constituent	Mechanism of action	Citation
1.	Abelmoschus manihot (Linn.) 	Malvaceae	Roots, Leaves	China, India, Southeast, Pacific Islands	Isoquercitrin	Modulating the GABAA-Cl^- channel	Ukpo et al., (2011)
2.	Astragalus spp. 	Fabaceae	Roots	China, Mongolia, Eastern, Europe, Western Asia	Baicalin	Decreasing Bcl-2, GSH, SOD, IL- β, Bax, caspase-3, TNF-α, lipid peroxidation, nitrite	Zhang et al., (2012)
3.	Achillea millefolium L. 	Asteraceae	flowers, Leaves, Stems	Europe, Western Asia, North, America	Kaempferol	Inhibition of DNA topoisomerase I enzyme	Kheirabadi et al., (2008)
4.	Annona muricata 	Annonaceae	Leaves	Cameroon, Forest areas	Quercetin	Inhibition of NF-KB, Modulation of neurotransmitters, Antioxidant activity, Inhibition of excitatory amino acids, Activation of K^+ channels	Adeyemi et al., (2013)
5.	Annona senegalensis	Annonaceae	Leaves, Roots	Cameroon, Central Africa,	Quercetin	Modulate the activity of GABA, glutamate, and serotonin,	Ojewole et al., (2007)

				West Africa, South Africa		Reduce oxidative stress and inflammation, Inhibition of NF-kB, Modulation of ion channels	
6.	Bupleurum chinense 	Umbelliferae	Root	China, East Asia	Quercetin	Influencing inotropic GABA receptors	Wang et al., (2010)
7.	Bidens Pilosa 	Asteraceae	Leaves	Cameroon, Central America	Quercetin, Kaempferol, Isorhapontigenin, Luteolin, Apigenin	inhibition of voltage-gated Na^+ channels, Activation of GABA receptors, Inhibition of glutamate release, Antioxidant, Modulate AMPA and NMDA receptors	Tchamadeu et al., (2011)
8.	Bryophyllum pinnatum 	Crassulaceae	Leaves	Central Africa	Quercetin, Kaempferol, Rutin	Modulation of neurotransmitters, Antioxidant activity, Inhibition of excitatory amino acids, Activation of K^+ channels	Mirza et al. (2018)

9.	Citrus reticuata Blanco 	Rutaceae	Peel, Seeds	Southeast Asia	Nobiletin	Modulating expression of GABAA and GAD65; recovering Glu and GABA balance, Antiapoptotic	Huang et al. (2011)
10.	Curcuma longa L. 	Zingiberaceae	rhizome	India, Southeast Asia, China	Curcumin, Curzerene	Antioxidant, Inhibiting acetylcholinesterase and mediating monoaminergic regulation, Effecting GABAergic and opioid system	Agrawal et al., (2011)
11.	Crataegus pinnatifida Bunge 	Rosaceae	fruit	East Asia, China, Korea	Hesperidin	Blocking the effect of enhanced Ca^{2+}	Zhang et al., (2004)
12.	Chlorophora tinctoria (L.) 	Moraceae	leaf	Central and South America, Mexico, Costa Rica, Brazil	Morin hydrate	Modulating the concentration Na^{+}/K^{+}-ATP; antioxidant status	Okoye et al., (2013)
13.	Citrus aurantium (L.)	Rutaceae	Peel, flower	Southeast Asia, China, India	Naringin	Reducing GCD and mtorc1 activation	Carvalho-Freitas et al., (2006)

							
14.	Citrus sinensis 	Rutaceae	Leaves, Flowers, Barks, Roots	Humid tropical areas	Naringenin, Hesperidin, Sinensetin, Aurantiamide	Inhibition of P-glycoprotein, reduce neuroinflammation, Activation of cannabinoid receptors, Inhibition of oxidative stress	Ogunwande et al., (2011)
15.	Clerodendron thomsoniae 	Lamiaceae	Leaves, Roots	Cameroon, India	Apigenin	Inhibition of NMDA receptors, Activation of K^+ channels, Modulation of GABA receptors,	Nwawuo et al., (2013)
16.	Camellia sinensis (L.) 	Theaceae	Leaf	Asia, China, India, Japan, Sri Lanka	Epigallacatechin-3-gallate (EGCG), Catechin	Increasing impression of GABA, Ameliorating cognitive impairment and oxidative stress, Ameliorating cognitive impairment and oxidative stress, inhibiting TLR4, NF-$_k$B signaling pathway; antioxidant, inhibiting oxidative injury	Kapoor et al., (2009)

17.	Cotinus coggygria 	Anacardiaceae	Root, leaf	Southern Europe, Western Asia, North Africa	Fisetin	Increasing GABA level in brain, protecting endogenous enzyme level	Orhan et al., (2012)
18	Daniellia oliveri 	Fabaceae	Barks, roots	Angola, Cameroon, Sudan, West Africa, Central Africa	Quercetin, Kaempferol, Isorhapontigenin	Inhibition of voltage-gated calcium channels	Amos et al., (2012)
19.	Datura stramonium 	Solanaceae	Fruits, Leaves	Africa, Asia, America, Europe	Quercetin, Kaempferol	Anticholinergic activity, Modulation of GABA receptors, Inhibition of glutamate release,	Al-Snafi, (2016)
20.	Detarium microcarpum 	Fabaceae	Leaves, Barks, Roots	West Africa, Central Africa	Quercetin, Isoquercitrin, Kaempferol	Inhibition of voltage-gated Na^+ channels, Antioxidant, Inhibition of inflammatory pathways	Abdu-Aguye et al., (2001)
21.	Eclipta prostrata L. 	Asteraceae	Whole plant	Africa, Asia, Australia, Americas	Luteolin	Inhibiting oxidative stress	Singh et al., (2013)

22.	Euphorbia hirta 	Euphorbiaceae	Whole plant	Africa continent	Quercetin, Kaempferol, Rutin	Anti-inflammatory, Antioxidant, Neuroprotective activities	Chakraborty et al., (2010)
23.	Folium Sennae 	Fabaceae	Leaf	Africa, Arabia, India, China	Vitexin	Neuroprotective effects, Antioxidant, Inhibition of inflammatory pathways,	Zhang et al., (2012)
24.	Flacourtia indica 	Flacourtiaceae	Stem, Barks, Fruits, Leaves	Asia, Africa	Flacourtiaceae, Quercetin, Kaempferol,	Inhibition of voltage-gated Ca^{+} channels,	Hsieh et al., (1999) and Zhu et al., (2016)
25.	Gastrodia elata Blume 	Orchidaceae	Tuber	China, Japan, Korea, Southeast Asia	Gastrodin	Increasing CAT, GSH, SOD	Hsieh et al., (1999)

27.	Hymenocardia acida 	Phyllanthaceae	Leaves, Barks, Roots	Cameroon, Central Africa, West Africa	Quercetin, Kaempferol, Rutin	Inhibiting GABA transaminase, Modulating voltage-gated sodium channels, Scavenging free radicals	Iwalewa et al., (2008)
28.	Jatropha gossypiifolia 	Euphorbiaceae	Leaves, Roots	Cameroon, Central Africa, West Africa	Quercetin, Kaempferol, Isorhapontigenin	Enhancing GABAergic transmission, Inhibiting calcium channels, Modulating neuronal excitability	Ojewole et al., (2008)
29.	Khaya senegalensis 	Meliaceae	Leaves, Barks, Roots	Cameroon	Quercetin, Kaempferol, Naringenin	Inhibiting voltage-gated sodium channels, Enhancing GABAergic activity, Exhibiting antioxidant effects	N'Goue mo et al., (2006)
30	Matricaria chamomilla (L.) 	Asteraceae	Flower head	Europe, Asia	Apigenin	Curbing benzodiazepine agonist	Formby et al., (1987)

32.	Milk thistle 	Asteraceae	Seed	Europe, Asia, North Africa	Silibinin	Decreasing TNF-α, IL-1β, and IL-6, Decreasing Hif-1 α	Sonnenbichler et al., (1999)
33.	Mentha cordifolia 	Lamiaceae	Leaves	Cameroon	Luteolin, Apigenin, Rosmarinic acid	Modulating GABA receptors, Blocking calcium channels, Inhibiting neuronal excitability	Almeida et al., (2009)
34.	Nandina domestica thumb 	Berberidaceae	Root, Rhizome	China, Japan, Korea	Amentoflavone	Decreasing IL-1β, and TNF-α, inhibition of microglial activation and reactive proliferation of astrocytes, decreasing COX-2, NF-$_k$B p65,	Kim et al., (2009)
35.	Passiflora caerulea L. var. Hort 	Passifloraceae	Leaves, Barks	Cameroon, West Africa	chrysin	Myorelaxant action agonizing the benzodiazepine receptor	Dhawan et al., (2001)

37.	Prosopis Africana 	Fabaceae	Bark	Nigeria, Senegal, Guinea	Quercetin, Kaempferol, Isorhapontigenin	GABAergic transmission, Inhibiting glutamate release, Scavenging free radical	Adzu et al., (2003)
38.	Radix Astragali 	Fabaceae	Root	China, Mongolia, Korea	Baicalin	Increasing impression of GABA	Zhang et al., (2012)
39.	Radix puerariae lobatae 	Fabaceae	Root	China, Japan, Korea	Puerarin	Decreasing IL – 10, decreasing NF-$_k$B; antioxidant and antiapoptopic mechanism	Wang et al., (2010)
40.	Ricinus communis 	Euphorbiaceae	Leaves, Flowers	Central Africa, West Africa	Quercetin, Kaempferol, Isorhapontigenin	Inhibiting acetylcholinesterase, Modulating GABA receptors, Reducing inflammation	Adzu et al., (2007)
41.	Scutellaria baicalensis L.	Lamiaceae	Root	China, Japan, Russia	Wogonin	Enhancing expression of GABAA receptors	He et al., (2009

							
43.	Securidaca longipedunculata 	Polygalaceae	Barks, Roots, Leaves	Central Africa, West Africa	Quercetin, Kaempferol, Apigenin	Enhancing GABAergic transmission, Inhibiting voltage-gated sodium channels, Exhibiting antioxidant, Anti-inflammatory effects	Ngadjui et al., (1999)
44.	Senna singueana 	Fabaceae	Leaves, Flowers, Barks, Roots	Cameroon, Mali, Sudan, East and south Africa	Naringenin, Quercetin, Kaempferol	Modulating GABA receptors, Inhibiting glutamate release, Exhibiting antioxidant activity	Tchoumbougnang et al., (2009)
45.	Terminalia glaucescens 	Combretaceae	Leaves, Barks, Roots	Nigeria, Ghana, Senegal, Mali	Quercetin, Kaempferol, Rutin	Inhibiting voltage-gated sodium channels, Enhancing GABAergic transmission, Exhibiting antioxidant, Anti-inflammatory effects	N'gouemo et al., (2009)

46.	Terminalia mollis 	Combretaceae	Roots	Cameroon, Congo, Gabon, Guinea	Quercetin, Kaempferol, Rutin	Modulating GABA receptors, Inhibiting calcium channels, Exhibiting antioxidant activity, Reducing neuronal excitability	Ojewole et al., (2008)
47.	Terminalia emetica 	Combretaceae	Roots, Barks	Savanna belt, Open woodland in Africa	Quercetin, Kaempferol, Luteolin	enhancing GABAergic transmission, Inhibiting voltage-gated Na^+ channels, Exhibiting antioxidant, Anti-inflammatory effects	Mulaudzi et al., (2013)
48.	Vitellaria paradoxa 	Sapotaceae	Leaves, Barks	Cameroon, Brazil	Naringenin, Quercetin, Kaempferol	Modulating GABA receptors, Inhibiting glutamate release, Exhibiting antioxidant activity, Reducing neuronal excitability	ljeh et al., (2014)

[9]

Table No. 2

2.13 FLAVONOID USED AS ANTIEPILEPTIC AGENT

Flavonoids are phyto-nutrients found in almost all plant, vegetables along with Carotenoids which is responsible for colours in fruits, flowers, vegetables. Polyphenols constitute largest group of phytochemicals distributed amongst plant kingdom which covers flavonoids, Non-flavonoids and phenolic acids.

Flavonoids compounds are found as C_6-C_3-C_6 compounds (fifteen carbon skeleton). Flavonoids compounds usually occur in plants as glycosides in which one or more of phenolic hydroxyl groups are compound with sugar residues. Hydroxyl group are found in position 5 and 7 in ring A whereas hydroxyl or alkoxy groups found in ring B.

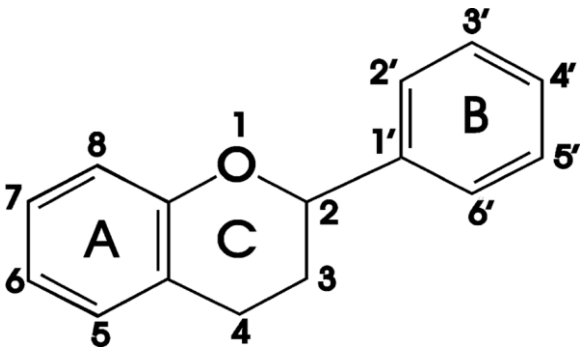
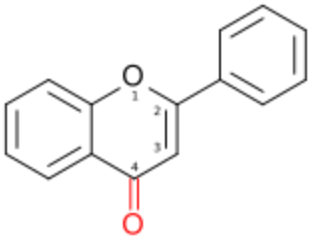
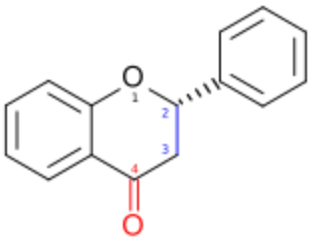


Fig. 5. Basic structure of flavonoid

Flavonoids consist of aromatic ring A, condensed to heterocyclic ring C attached to second aromatic ring B. this structure is also know as flavonoid diphenyl propane skeleton. Flavonoids divided into anthocyanins and anthoxanthins. Anthocyanins is the glycosides of anthocyanidin which is the most important class of water-soluble plant pigments responsible for various beautiful colours such as purple, blue and red to fruits, flowers and leaves. Anthoxanthins are white or yellowish or colourless compound and it includes flavanol, flavonol, isoflavones, flavanones.[10]

Following table gives classification of flavonoids:[10]

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Sr. no	Classification of flavonoids		
1.	Flavanol		Catechin Epicatechin Gallocatechin
2.	Flavonone		Naringenin Eriodyctiol Hesperitin Pinocembrin Prunin Naringin

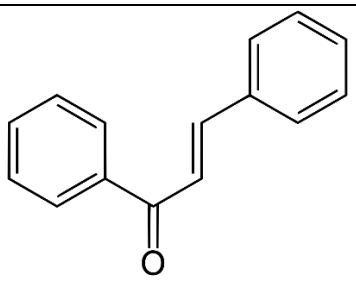
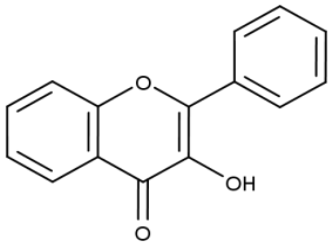
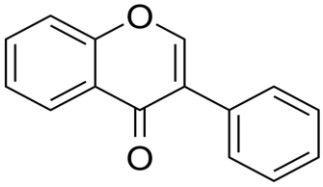
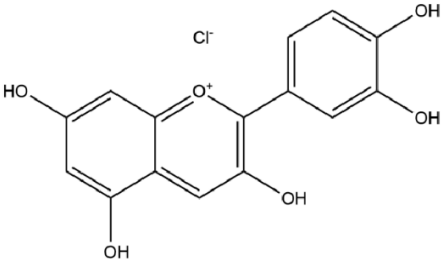
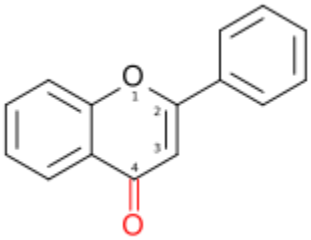
3.	Chalcone		Phloretin Arbutin Phlioridzin Chalconaringenin
4.	Flavonol		Kaempferol Quercetin Myricetin Rutin Robinin Morin
5.	Isoflavone		Biochanin A Formononetin Daidzein Genistein Glycitein Daidzin Genistin
6.	Anthocyanin		Cyanidin Delphinidin Pelargonidin Malvidin Petunidin Peonidin
7.	Flavone		Apigenin Baicalein Luteolin Diosmetin Tangeretin

Table. No. 3

1. Quercetin

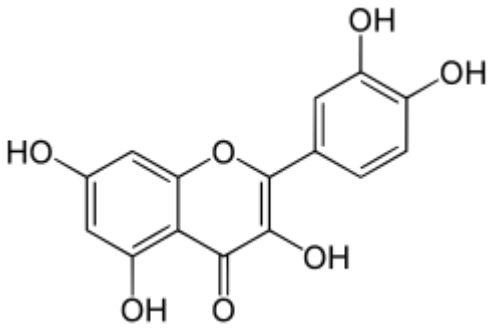


Fig. 6.1

Quercetin, a flavonol belonging to the flavonoid class of polyphenols, has been known by its name since 1857, which originates from the Latin term "quercetum," meaning oak forest. Typically, people consume around 25-50 milligrams of quercetin per day.

2. Isoquercetin

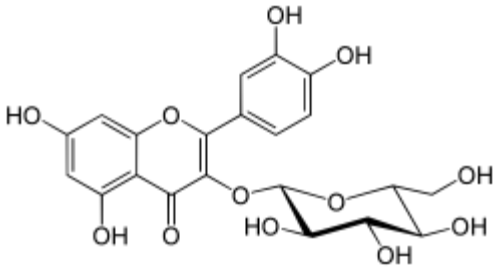


Fig. 6.2

Isoquercetin, also referred to as isoquercitrin or isotrifoliin, is a naturally occurring flavonoid compound that can be described as the 3-O-glucoside derivative of quercetin.

3. Baicalin

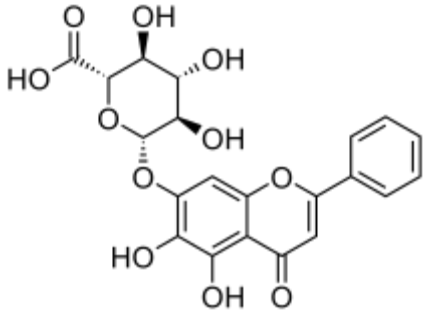


Fig. 6.3

Baicalin is classified as a flavonoid, specifically a flavone glycoside, and can be described as the glucuronic acid conjugate of baicalein.

4. Kaempferol

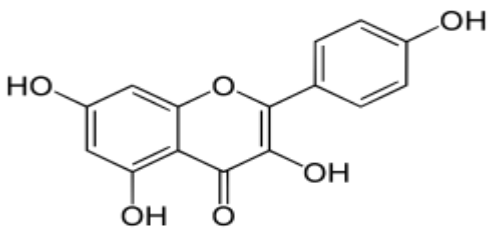


Fig. 6.4

Kaempferol, a naturally occurring flavonol, is a type of flavonoid compound. This yellow crystalline substance has a melting point range of 276–278 °C and exhibits limited solubility in water, while being highly soluble in hot ethanol, ethers, and dimethyl sulfoxide (DMSO). The compound is named in honor of Engelbert Kaempfer, a 17th-century German naturalist who made significant contributions to the field.

5. Isorhapontigenin

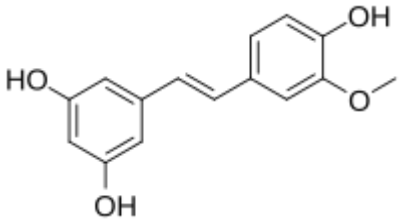


Fig. 6.5

Isorhapontigenin is a stilbenoid compound characterized by its tetrahydroxylated structure and methoxy group. This compound is an isomer of rhapontigenin and shares similarities with resveratrol. Isorhapontigenin can be found in various plant sources, including the Chinese herb Gnetum cleistostachyum, Gnetum parvifolium, and the seeds of the palm Aiphanes aculeata. Furthermore, a tetrameric form of isorhapontigenin, known as gnetuhainin R, has been isolated from the lianas of Gnetum hainanense. Additionally, isorhapontin, a glucoside derivative of isorhapontigenin, has also been identified.

6. Luteolin

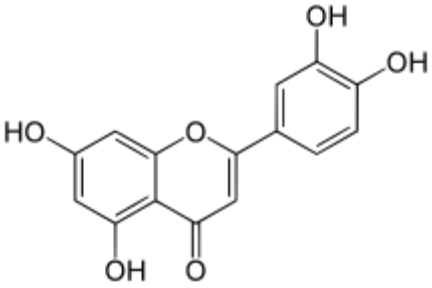


Fig. 6.6

Luteolin is a flavonoid compound that belongs to the flavone subclass, characterized by its distinctive yellow crystalline form. The isolation and naming of luteolin in its pure form date back to 1829, when French chemist Michel Eugène Chevreul first identified it.

7. Apigenin

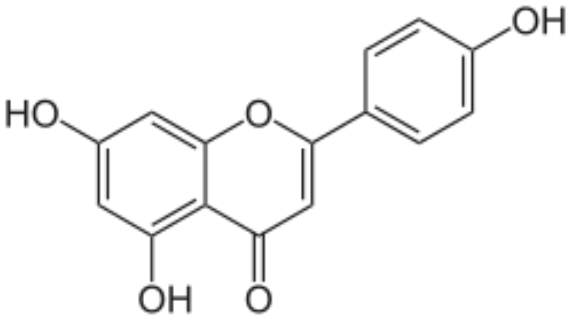


Fig. 6.7

Apigenin, a naturally occurring compound found in various plant species, is a flavone-class molecule that serves as the aglycone for several glycosides. This yellow crystalline substance has been utilized as a dye for wool, showcasing its vibrant color properties.

8. Rutin

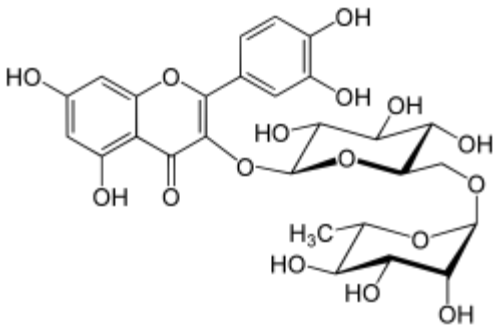


Fig. 6.8

Rutin, also known as rutoside or sophorin, is a glycoside formed by the combination of the flavonol quercetin and the disaccharide rutinose. This flavonoid glycoside is widely distributed in various plant species, including citrus fruits, and is composed of a quercetin molecule bonded to a rutinose disaccharide unit.

9. Nobiletin

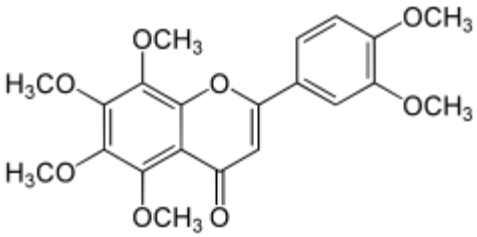


Fig. 6.9

Nobiletin is a flavonoid compound that can be extracted from the peels of citrus fruits, and is characterized as an O-methylated derivative of flavone.

10. Hesperidin

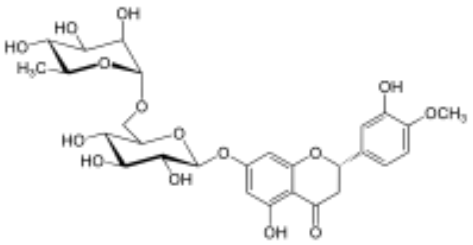


Fig. 6.10

Hesperidin is a type of flavanone glycoside that occurs naturally in citrus fruits, with hesperetin serving as its aglycone. The name "hesperidin" originates from the term "hesperidium," which refers to the fruit of citrus trees. French chemist M. Lebreton first extracted hesperidin from the inner white layer of citrus peels, known as the mesocarp or albedo, in 1828.

11. Morin

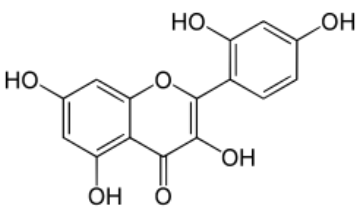


Fig. 6.11

Morin is a yellow-colored compound that can be extracted from various plant sources, including the Osage orange (Maclura pomifera), old fustic (Maclura tinctoria), and the leaves of the common guava (Psidium guajava). Notably, morin forms glycosides with certain sugars, such as arabinose and lyxose, resulting in compounds like morin-3-O-arabinoside and morin-3-O-lyxoside.

12. Naringin

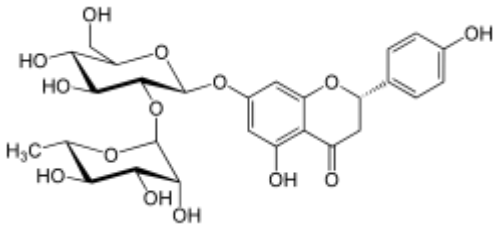


Fig. 6.12

Naringin is a flavanone glycoside formed by the combination of naringenin and the disaccharide neohesperidose. This compound features a core flavonoid structure with a rhamnose and glucose unit attached to the 7-carbon position of its aglycone, naringenin.

13. Sinensetin

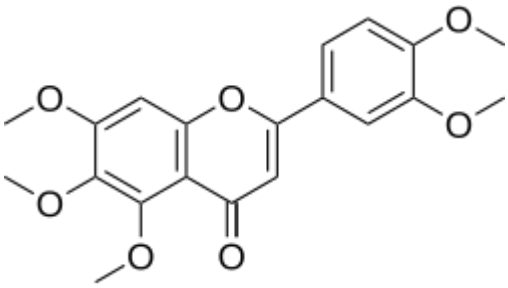


Fig. 6.13

Sinensetin is a flavone compound characterized by its O-methylated structure, and it has been identified in the plant Orthosiphon stamineus and also in the essential oil of oranges.

14. Catechin

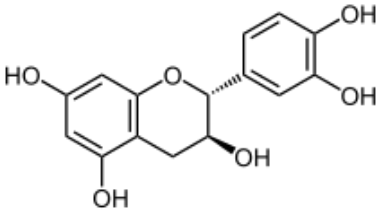


Fig. 6.14

Catechin is a flavan-3-ol compound, a type of secondary metabolite that plays a crucial role in plant antioxidant defenses. As a member of the flavonoid subgroup, catechin is classified as a polyphenol. The term "catechin" originates from the word "catechu," which refers to the tannin-rich extract derived from the Mimosa catechu plant, also known as Acacia catechu.

15. Fisetin

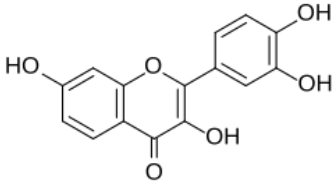


Fig. 6.15

Fisetin, a flavonol compound, is a member of the polyphenol family and is found in various plant species, where it functions as a yellow pigment. The chemical structure of fisetin was initially elucidated by Austrian chemist Josef Herzig in 1891.

16. Genistein

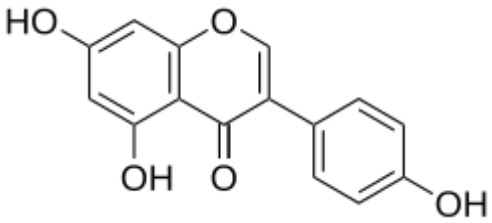
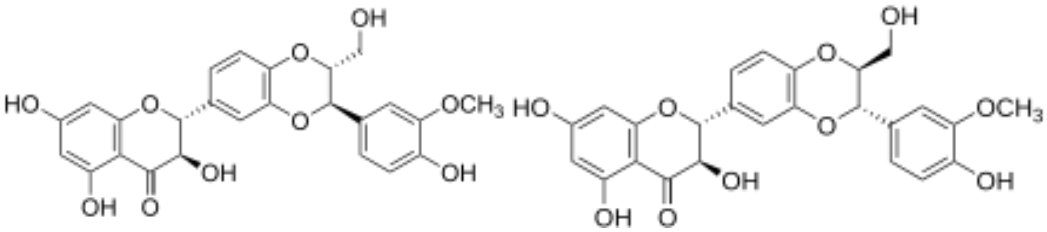


Fig. 6.16

Genistein, a naturally occurring compound with the chemical formula C15H10O5, falls under the category of isoflavones. Its origin dates back to 1899, when it was initially extracted from the plant Genista tinctoria, also known as dyer's broom, which is where it gets its name.

17. Silibinin



Silibinin A **Silibinin B**

Fig. 6.17

Silibinin, also referred to as silybin, is the primary active component of silymarin, a standardized extract derived from the milk thistle plant. Silymarin is a complex mixture of flavonolignans, including silibinin, isosilibinin, silychristin, and silidianin, among others. Notably, silibinin itself comprises two diastereomers, silybin A and silybin B, which are present in roughly equal proportions.

18. Amentoflavone

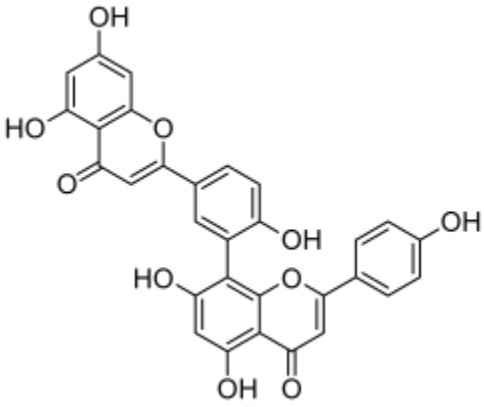


Fig. 6.18

Amentoflavone is a biflavonoid compound, specifically a dimer of apigenin, where two apigenin molecules are linked at the 8 and 3′ positions, forming a 3′,8″-biapigenin structure.

19. Chrysin

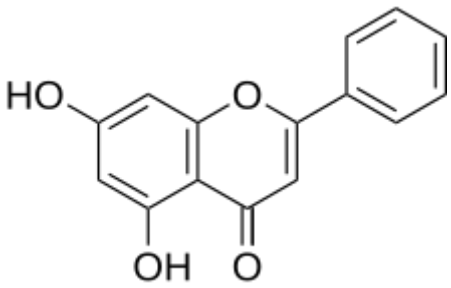


Fig. 6.19

Chrysin, a naturally occurring flavone also known as 5,7-dihydroxyflavone, has limited bioavailability and is quickly eliminated from the body.

20. Hispidulin

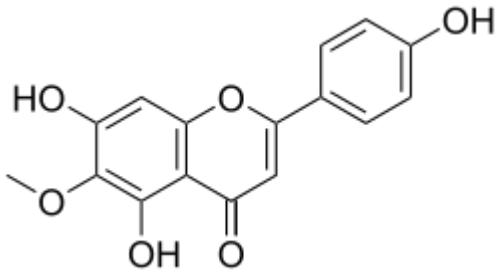


Fig. 6.20

Research has shown that hispidulin, a naturally occurring flavone compound, exhibits potential antiepileptic properties in animal models, including rats and gerbils.

21. Puerarin

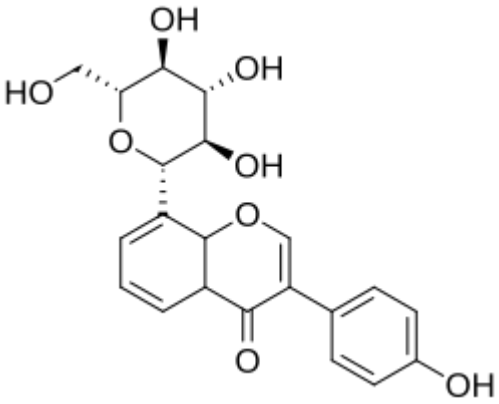


Fig. 6.21

Puerarin is isoflavones, notable for its presence in several plant species, including the root of the kudzu plant. This compound is specifically characterized as the 8-C-glucoside derivative of daidzein.

22. Wogonin

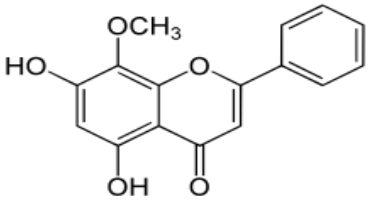


Fig. 6.22

Wogonin is a flavonoid compound characterized by its O-methylated structure, and it is notably found in the plant Scutellaria baicalensis. The glycosidic derivatives of wogonin are referred to as wogonosides.[11]

2.14 NOVEL DRUGS AND HERBAL DRUG APPROACHES FOR THE USE OF ISOFLAVONOIDS IN NEUTRACEUTICSLS

Isoflavonoids, particularly found in soy and other legumes, are a class of phytochemicals known for their health benefits. They are commonly categorized as phytoestrogens due to their structural similarity to estrogen. Here's an overview of novel and herbal drug approaches in the use of isoflavonoids as nutraceuticals:

Health Benefits

- Hormonal Balance: Isoflavonoids can help alleviate menopausal symptoms due to their estrogenic properties.
- Bone Health: They may support bone density and reduce the risk of osteoporosis.
- Cardiovascular Health: Isoflavonoids contribute to heart health by improving lipid profiles and reducing oxidative stress.
- Antioxidant Properties: They possess antioxidant effects that help combat free radicals.

Novel Drug Approaches

- Targeted Delivery Systems: Development of nanocarriers for enhanced bioavailability and targeted delivery of isoflavonoids.
- Combination Therapies: Using isoflavonoids in conjunction with other herbal extracts or pharmaceuticals to enhance therapeutic effects
- Bioenhancers: Research into compounds that can enhance the bioavailability of isoflavonoids, improving their efficacy.

Herbal Formulations

- Traditional Medicines: Incorporation of isoflavonoid-rich herbs like red clover and chickpeas in traditional remedies.
- Functional Foods: Development of foods fortified with isoflavonoids, such as soy milk or supplements.
- Tea and Extracts: Herbal teas and concentrated extracts that utilize isoflavonoid-rich plants.

Research and Development

- Ongoing studies are exploring the synergistic effects of isoflavonoids with other nutraceuticals.
- Clinical trials assessing the efficacy of isoflavonoids for various health conditions.

Isoflavonoids represent a promising area for nutraceutical development due to their diverse health benefits and potential for integration into novel therapeutic approaches. Continued research will further enhance our understanding and utilization of these compounds in health and wellness[12]

2.15 INTRODUCTION OF ISOFLAVONOIDS

Isoflavonoids are a subclass of flavonoids, which are polyphenolic compounds commonly found in various plants, particularly legumes, such as soybeans, chickpeas, and red clover. These compounds have gained significant attention due to their diverse biological activities and potential health benefits.

Chemical Structure

Isoflavonoids have a structure similar to that of estrogen, which allows them to exhibit phytoestrogenic activity. This characteristic enables them to bind to estrogen receptors in the body, potentially influencing hormonal balance.

Sources

The primary dietary sources of isoflavonoids include:

- Soy Products: Tofu, soy milk, and edamame are rich in isoflavones like genistein and daidzein.
- Legumes: Other beans and lentils also contain varying amounts of isoflavonoids.
- Herbs: Plants such as red clover are notable for their isoflavonoid content.

Health Benefits

Isoflavonoids are associated with several health benefits, including:

- Hormonal Regulation: They may help manage menopausal symptoms and support reproductive health.
- Bone Health: They play a role in maintaining bone density and preventing osteoporosis.
- Cardiovascular Protection: Isoflavonoids can improve lipid profiles and support heart health.
- Antioxidant Effects: Their ability to scavenge free radicals contributes to overall health and longevity.

Research and Applications

Ongoing research is exploring the therapeutic potential of isoflavonoids in various health conditions, including:

- Cancer prevention and treatment
- Metabolic disorders
- Cardiovascular diseases

In summary, isoflavonoids are important bioactive compounds with promising health benefits, making them a key focus in nutrition and pharmacology. Their incorporation into functional foods and supplements is an area of growing interest for enhancing public health.[13]

2.16 PHARMACOLOGICAL ACTION OF ISOFLAVONOIDS

Isoflavonoids are a class of phytoestrogens, primarily found in soybeans and other legumes. They exhibit various pharmacological actions, including:

Estrogenic Activity

- Isoflavonoids can mimic estrogen in the body, binding to estrogen receptors and potentially influencing reproductive health, menopause symptoms, and bone density.

Antioxidant Properties

- They possess strong antioxidant capabilities, helping to neutralize free radicals and reduce oxidative stress, which may protect against chronic diseases.

Cardiovascular Benefits

- Isoflavonoids may improve lipid profiles, lower blood pressure, and enhance endothelial function, contributing to cardiovascular health.

Anti-Inflammatory Effects

- These compounds can modulate inflammatory responses, potentially reducing the risk of inflammatory diseases.

Cancer Prevention

- Some studies suggest that isoflavonoids may have protective effects against certain types of cancer, particularly breast and prostate cancer, by inhibiting cancer cell growth and inducing apoptosis.

Bone Health

- Isoflavonoids may help in maintaining bone density and reducing the risk of osteoporosis, particularly in postmenopausal women.

Metabolic Effects

- They may improve insulin sensitivity and have a role in glucose metabolism, which can be beneficial for managing metabolic syndrome and diabetes.

Overall, isoflavonoids are associated with a range of health benefits, but further research is needed to fully understand their mechanisms and potential therapeutic applications. [14]

2.17 ISOFLAVONOIDS ARE USED AS AN ANTIEPILEPTIC

Isoflavonoids have been studied for their potential neuroprotective and anticonvulsant properties, although research is still emerging in this area. Here's a brief overview of their potential use as anti-epileptic agents: Antiepileptic Properties of Isoflavonoids

Mechanism of Action

- Isoflavonoids may modulate neurotransmitter systems, particularly by influencing GABAergic activity, which can help reduce neuronal excitability and seizures.

Neuroprotective Effects

- They possess antioxidant properties that may protect neurons from oxidative stress, a factor involved in seizure activity and neurodegeneration.

Anti-inflammatory Effects

- Isoflavonoids can reduce neuroinflammation, which may contribute to the pathophysiology of epilepsy.

Studies and Evidence

- Some animal studies have shown that specific isoflavonoids can reduce the frequency and severity of seizures, but clinical evidence in humans is limited.

Potential for Combination Therapy

- Isoflavonoids may enhance the efficacy of conventional antiepileptic drugs, although more research is needed to establish safe and effective dosages.

While isoflavonoids show promise as potential antiepileptic agents, further clinical studies are necessary to confirm their efficacy and safety in epilepsy treatment. Always consult healthcare professionals before considering any new treatment options.[7,15]

2.18 MECHANISM OF ACTION OF ISOFLAVONOID

Isoflavonoids may exhibit antiepileptic properties through several mechanisms of action. Here are the key mechanisms by which they may exert their effects:

Modulation of GABAergic Activity

- Isoflavonoids may enhance the activity of gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the brain. By increasing GABAergic transmission, they can help reduce neuronal excitability and the likelihood of seizure activity.

Calcium Channel Blockade

- Some isoflavonoids may inhibit voltage-gated calcium channels, reducing calcium influx into neurons. This can diminish neurotransmitter release and decrease excitatory synaptic transmission, thereby lowering the risk of seizures.

Antioxidant Activity

- Isoflavonoids possess significant antioxidant properties, which help protect neurons from oxidative stress. Oxidative stress can lead to neuronal damage and increased seizure susceptibility, so reducing it may help stabilize neuronal function.

Anti-inflammatory Effects

- By modulating inflammatory responses in the brain, isoflavonoids can reduce neuroinflammation, which is often associated with epilepsy. This can help protect against seizure-related damage and

improve overall neuronal health.

Influence on Neurotransmitter Release

- Isoflavonoids can affect the release of other neurotransmitters, such as glutamate, which is the main excitatory neurotransmitter. By balancing neurotransmitter levels, they can help prevent excessive excitatory signalling that leads to seizures.

Neuroprotective Effects

- Isoflavonoids may support neuronal survival and function, further contributing to their potential antiepileptic effects by preventing neuronal damage associated with chronic seizures.

While the exact mechanisms of action of isoflavonoids as antiepileptic agents are still being researched, their ability to modulate neurotransmission, reduce oxidative stress, and exert anti-inflammatory effects highlights their potential in managing epilepsy. Further studies, particularly in clinical settings, are needed to fully understand these mechanisms and their therapeutic implications[16]

2.19 PLANT PROFILE

Plant name : Prunus Armeniaca
Family : Rosaceae
Synonyms : Tibetan, Apricot, Qinghai, Shaanxi, Sichuan
Vernacular Names:
English : Apricot
Hindi : Khubanee, Jardalu
Kannada : Aprekat
Malayalam : Aprikkeatt
Sanskrit : Urumana
Tamil : Patami Palam
Telungu : Neredu Pandu [79]

2.20 HISTORY AND CULTIVATION

The apricot was originally domesticated in China but is now cultivated on every continent except Antarctica. Archaeological evidence shows that apricots were eaten in ancient Armenia, and they were first introduced to the New World in the early 18th century by Spanish missionaries in California. In 2019 the top five producers of apricots were Turkey, Uzbekistan, Iran, Italy, and Algeria. Apricots are propagated by budding on peach or apricot rootstocks, and peaches, plums, and apricots may be readily integrated. The tree succeeds in well-drained loamy soil, preferably light rather than heavy. Most varieties withstand winter cold as well as peaches, but the blossom buds, opening earlier than those of the peach, are frequently killed by late freezes. The trees are quite drought-resistant and under favorable growing conditions are long-lived, some living 100 years or longer. [78]

2.21 PLANT DESCRIPTION

Apricot is a small tree, 7-10 m tall with a trunk up to 40 cm in diameter and a dense spreading canopy.
The leaves are ovate, 5-9 cm long and 4-8 cm wide, with a rounded base, a pointed tip and a finely serrated margin.
The flowers are 2-4.5 cm in diameter, with five white to pinkish petals; they are produced singly or in pairs in early spring before the leaves.

The fruit is a drupe similar to a small peach, 1.5-2.5 cm diameter, from yellow to orange, often tinged red on the side. [79]

Table 4: Chemical composition of apricot (Prunus Armeniaca) in 100g dried weight basis (dwb) [80]

Constituent	Concentration/100 gm
Standard sugars (sucrose, fructose, glucose)	9.79 to 15.059g/100g
Organic acids (citric acid,malic acid, succinic acid and ascorbic acid)	0.40to 01.43g/100g
Total carotenoids	0.19- 2.93mg/100g
Mineral content	(Abundantly found potassium) 2202.69mg/100g
Total flavonoids (aglycon flavonoids - genistein, diadzein), and phenolic content	25.31-89.95mg/100g

Table. No 4

2.22 TRADITIONAL USE

Apricot fruits contain citric and tartaric acid, carotenoids and flavonoids. They are nutritious, cleansing and mildly laxative. They are a valuable addition to the diet working gently to improve overall health. The salted fruit is anti -inflammatory and antiseptic. It is used medicinally in Vietnam in the treatment of respiratory and digestive diseases. Antipyretic, antiseptic, emetic, ophthalmic. The flowers are tonic, promoting fecundity in women. The bark is astringent. The inner bark and/or the root are used for treating poisoning caused by eating bitter almond and apricot seeds (which contain hydrogen cyanide). Another report says that a decoction of the outer bark is used to neutralize the effects of hydrogen cyanide. The decoction is also used to soothe inflamed and irritated skin conditions. The seed is analgesic, anthelmintic, anti-asthmatic, antispasmodic, antitussive, demulcent, emollient, expectorant, pectoral, sedative and vulnerary. It is used in the treatment of asthma, coughs, acute or chronic bronchitis and constipation. The seed contains 'laetrile', a substance that has also been called vitamin B17. This has been claimed to have a positive effect in the treatment of cancer, but there does not at present seem to be much evidence to support this[K]. The pure substance is almost harmless, but on hydrolysis it yields hydrocyanic acid, a very rapidly acting poison - it should thus be treated with caution. [79]

PLANT OF PRUNUS ARMENIACA



Fig. 7. Plant of Prunus Armeniaca

DREID FORM OF FRUIT



Fig. 8. Dried form of fruit

3. METHODOLOGY

3.1 PLANT COLLECTION AND AUTHENTICATION

Prunus Armeniaca (Apricot) is nutraceutical plant product. Procured from local market Aurangabad Maharashtra.

3.2 LIST OF CHEMICALS

(extraction and isolation)

Ethanol, yellow paraffin wax

(Phytochemical Screening)

Concentrated HCL, concentrated sulfuric acid, magnesium turnings, lead acetate solution, ferric chloride solution, NaOH solution, zinc dust, molish reagent, potassium dichromate, tannic acid, hager's reagent, wager's reagent.

(Performing & evaluating anti-epileptic activity)

Diazepam Pentylene Tetrazole DMSO Dimethyl Sulfoxide Ethanol

3.3 LIST OF EQUIPMENT

Glass wares, Soxhlet apparatus, Heating mantal, Digital Weighing balance

3.4 EXTRACTION OF THE PLANT MATERIAL

Disease free plant material (fruits) of selected plant were inspected. The seeds were separated and the fruit parts were shade dried with occasional shifting for the remaining moisture content.

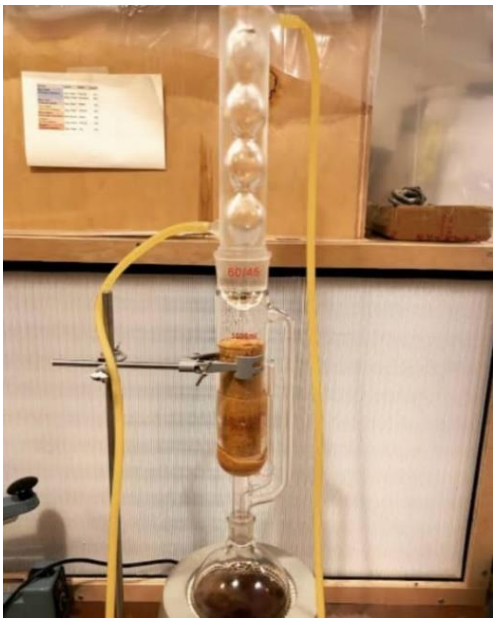


Fig. 9. Soxhlet apparatus

After drying at 37°C temperature dried plant material were powdered with the help of a grinder machine. Exposure to direct sunlight was avoided to prevent the loss of active compounds. Selected powdered plant material was subjected to Soxhlet extraction with ethanol (60-80°C) for 48 hours in the order is increasing polarity of solvents. [81]

3.5 PHARMACOLOGICAL STUDY

Preliminary phytochemical evaluation of the extract:

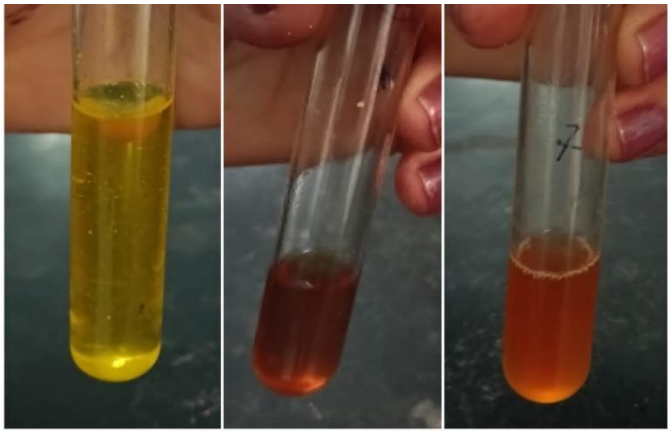
The concentrated solid form of extract was used for preliminary phytochemical screening. Extracts was dissolved in suitable form of solvents then used for the phytochemical screening. The following tests were carried out on the standardized herbal extract to detect various phytoconstituents present in them. [83]

Detection of Alkaloids:

About 50 mg of solvent-free extract was stirred with little quantity of dilute HCI and filtered. The filtrate was tested carefully with various alkaloid reagents as follows.

Sr. No	Test	Observation	Inference
1.	**Hager's test:** Drug solution + few drops of hager's reagent (Saturated aq. Solution of picric acid).	Formation of crystalline yellow precipitate.	Presence of alkaloid
2.	**Wagner's test:** Drug solution + few drops of wagner's reagent (dilute iodine solution).	Formation of reddish-brown precipitate.	Presence of alkaloid

3.	**Tannic acid test:** Drug solution + few drops of tannic acid solution.	Formation of buff coloured precipitate.	Presence of alkoloid

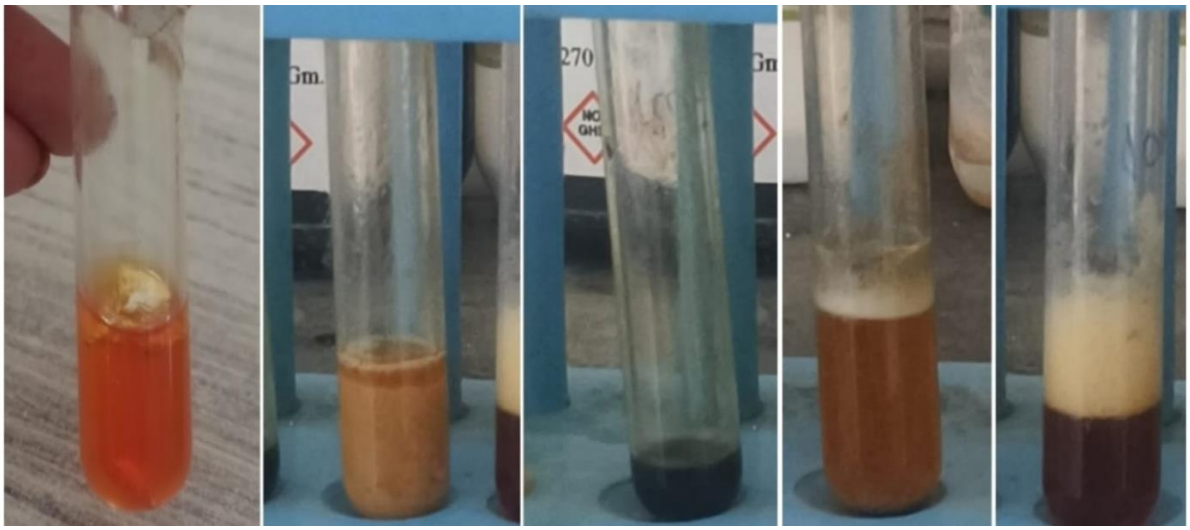


1. 2. 3.

Fig. 10. Test of alkaloid

Detection of flavonoid

Sr. No	Test	Observation	Inference
1.	**Shinoda test:** Test solution + (alcoholic extract of drug) + few magnesium turnings + concentrated HCl drop wise	Formation of pink colour/ orange colour/ Purple colour	Presence of flavonoid
2.	**Lead acetate test:** Test solution + lead acetate solution	Formation of Yellow coloured precipitate	Presence of flavonoid
3.	**Ferric chloride test:** Test solution + few drops of $FeCl_3$	Formation of blackish red colour	Presence of flavonoid
4.	**Alkaline reagent test:** Test solution + few drops of NaOH solution	Formation of yellow colour, colour disappear after the addition of acid	Presence of flavonoid
5.	**Zinc hydrochloride test ($Zn(HCl)^2$):** Test solution + mixture of zinc dust and conc. HCl	Formation of red or magenta colour	Presence of flavonoid



1 . 2. 3. 4. 5.

Fig. 11. Test for flavonoid

Detection of tannins and phenolic compound

About 50 mg of solvent-free extract was stirred with little quantity of dilute HCl and filtered. The filtrate was tested carefully with various alkaloid reagents as follow.

Sr. No	Test	Observation	Inference
1.	**Potassium dichromate test:** Filtrate + potassium dichromate	Formation of Red coloured precipitate	Presence of tannins



1.

Fig. 12. Test for tannins and phenolic compound

Detection of saponin

Sr. No	Test	Observation	Inference
1.	**Foam test:** a) 1 ml of solution of extract was diluted with distilled water to 20 ml & shaken in graduated cylinder for 15 minutes. b) 1 ml extract was treated with 1% lead acetate solution.	Development of stable foam white precipitate	Presence of saponin Presence of saponin



a) b)

Fig. 13. Test for saponins

Detection of carbohydrate

Sr. No	Test	Observation	Inference
1.	**Molisch's test:** Few ml of solution of extract is combined with molisch's reagent (α-naphthol dissolved in ethanol) + sulfuric acid on the side of the tube	Purple red ring at the interface	Presence of carbohydrate



1.

Fig. 14. Test for carbohydrate

3.5.1 EVALUATION OF ANTIANXIETY EFFECT OF PRUNUS ARMENIACA:

ROTA-ROD TEST:



Fig 11: Rota Rod

Principle: The length of time that a given animal stays on the rotating rod is a measure of their balance, Co-Ordination.

Procedure: Mice weighing 20 to 30 gm are grouped after 30 min of drug & extract dose administration Animal is placed on rotarod

ELEVATED PLUS MAZE TEST:

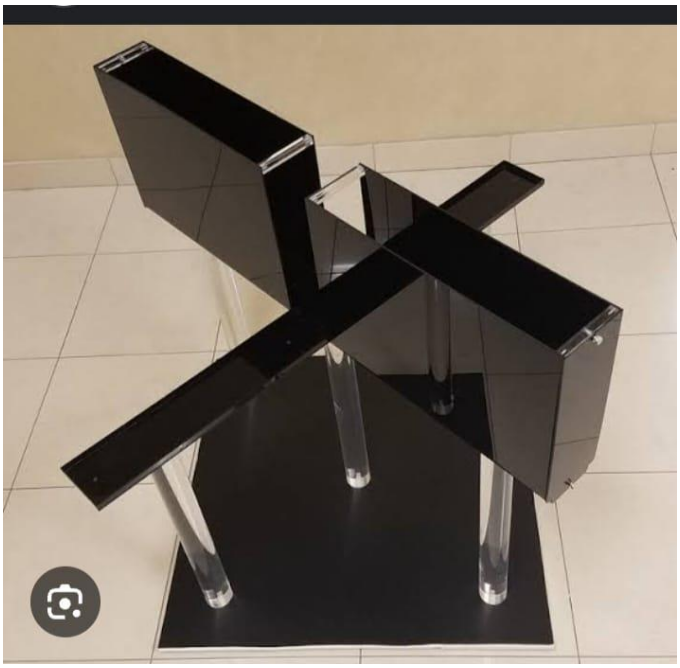


Fig 12: Elevated Plus Maze

Procedure: Mice weighing 20 to 30 gm are grouped and after 30 min of drug & extract dose administration Animal is placed on elevated plus maze test.

3.5.2 ANIMALS AND MANAGEMENT



Fig 13: Swiss Albino Mice

Healthy adult Swiss albino mice of either sex weighing 20-30 gm will be selected. The animals will be housed in large, spacious, hygienic cages during the course of experimental period. The animal house will be well maintained and the animals will have 12 ± 1 hour day and night schedule with a temperature [64-79°F] maintained at standard experimental condition. The animals will be fed with standard rodent pellet

feed and water ad libitum. The experimental procedure was approved by IAEC (Institutional animal ethical committee of KMCH, governed by CPCSEA, Government of India)

3.5.3 EVALUATION OF ANTIEPILEPTIC ACTIVITY OF PRUNUS ARMENIACA

Introduction

Pentylenetetrazol

Pentylenetetrazol (PTZ) is a GABA-A receptor antagonist. An intraperitoneal injection of PTZ into an animal induces an acute, severe seizure at a high dose, whereas sequential injections of a sub convulsive dose have been used for the development of chemical kindling, an epilepsy model. A single low-dose injection of PTZ induces a mild seizure without convulsion. However, repetitive low-dose injections of PTZ decrease the threshold to evoke a convulsive seizure. Finally, continuous low-dose administration of PTZ induces a severe tonic-clonic seizure. This method is simple and widely applicable to investigate the pathophysiology of epilepsy, which is defined as a chronic disease that involves repetitive seizures. This chemical kindling protocol causes repetitive seizures in animals. With this method, vulnerability to PTZ-mediated seizures or the degree of aggravation of epileptic seizures was estimated. These advantages have led to the use of this method for screening anti-epileptic drugs and epilepsy-related genes. In addition, this method has been used to investigate neuronal damage after epileptic seizures because the histological changes observed in the brains of epileptic patients also appear in the brains of chemical-kindled animals. Thus, this protocol is useful for conveniently producing animal models of epilepsy. [84]

Pentylenetetrazol [PTZ] model

Experimental design

Swiss Albino mice weighed around 20-30 gm were used for the study. Mice were divided into four groups of 5 animals each.

Table 10: Pentylenetetrazol Model

Model II: **Pentylenetetrazol Model**	
Group 1:	*Vehicle control* [Equivalent normal saline i.p]
Group 2:	*Standard* Diazepam (4 mg/Kg BW i.p)
Group 3:	*Prunus Armeniaca* low dose (100 mg/kg) i.p
Group 4:	*Prunus Armeniaca* high dose (200 mg/kg) i.p

Procedure

Animals in the control group [Group 1] will be administered equivalent volume of normal saline by i.p route. Animals in Group 2 will be administered standard drug Diazepam. In Groups 3 and 4 Prunus Armeniaca low dose and high dose will be administered by IP route in DMSO (Dimethyl Sulfoxide) solution respectively. Extract dose & standard dose will be given regularly for 07 days. On 8th day after 30 minutes of administration of above drugs, all the animals will be given Pentylenetetrazol [PTZ] and the various parameters will be recorded.

4. RESULT

4.1 EXTRACTIVE YIELD OF PRUNUS ARMENIACA

A. Percentage Yield

The crude powder of *Prunus Armeniaca* were extracted with ethanol using soxhlet apparatus after defatting with petroleum ether. The percentage yield of extract was found to be 20 % w/w.

B. Ethanolic fractionation yield of flavonoids is found to be 750 mg i.e., 3.75%.

4.2 PRELIMINARY PHYTOCHEMICAL EVALUATION OF EXTRACT

The ethanolic extract of Prunus Armeniaca was subjected to preliminary phytochemical screening shown in table. Which shows the presence of Flavonoids, Tannins, Alkaloids, Carbohydrate, Saponins.

Sr. No.	Phytochemicals	Inference
1	Alkaloid	+ve Present
2	Glycoside	+ve Present
3	Flavonoids	+ve Present
4	Tannins	+ve Present
5	Reducing sugars	+ve Present
6	Saponins	+ve Present
7	Terpenoids	+ve Present
8	Anthraquinones	-ve Absent
9	Cardiac glycosides	-ve Absent

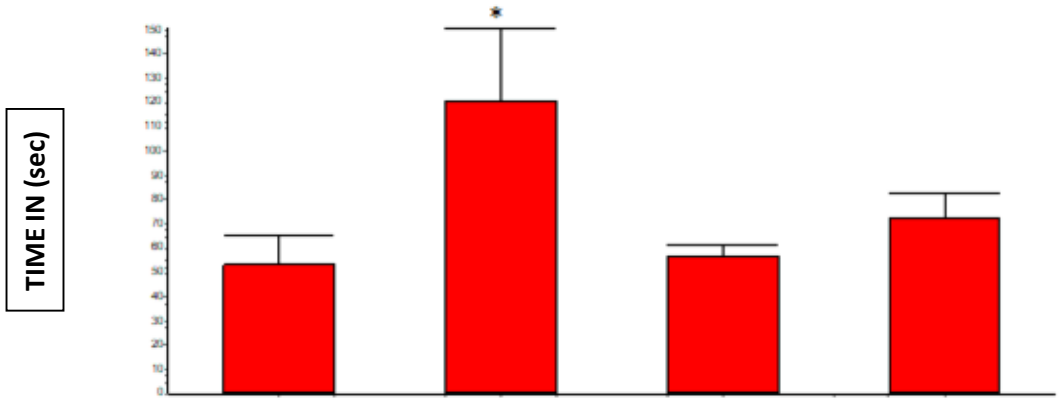
4.3 EVALUATION OF ANTIEPILEPTIC ACTIVITY

Table 16: Effect of Ethanolic extract of *Prunus Armeniaca* on phases of convulsions in PTZ induced seizures models

	Phases of convulsion in seconds					
Groups	**Myoclonic Jerks**	**Straub's Stail**	**Clonus**	**Tonic Extension**	**Death**	**Recovery**
Control	53.60 ±26.51	93.80 ±51.45	121.40 ±12.64	224 ±71.71	224 ±71.71	Mortality
Diazepam (4 mg/kg)	120.80 ±67.42*	135 ±42.39	220 ±56.12**	289 ±48	224 ±72.25**	Mortality

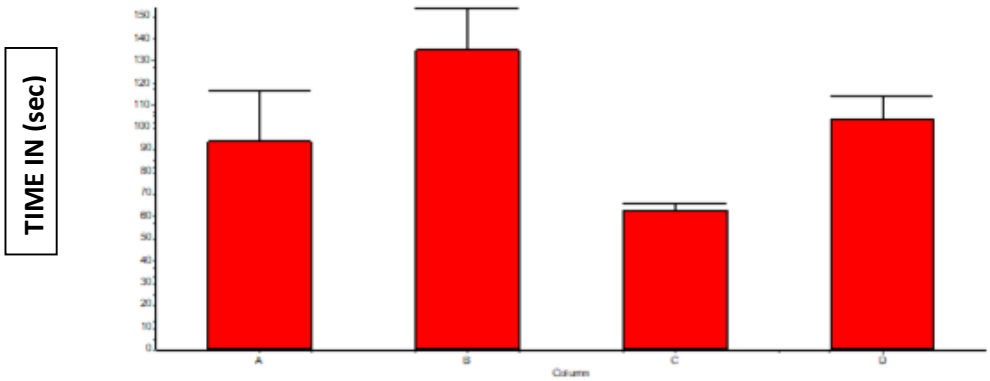
EEPA (100mg/kg)	57 ±10.23	63 ±6.70	124 ±53.08**	270 ±28.24	340 ±64.04*	Mortality
EEPA (200mg/kg)	72 ±22.50	104 ±23.03	277 ±23.87***	371 ±56**	595 ±8.66***	Recovery

Statistical comparison: One way ANOVA, followed by Dunett's multiple comparison test. Comparisons were maid with control group vs, all treated group, where ** and * represents statistical significance at P<0.01 and P<0.05 respectively.



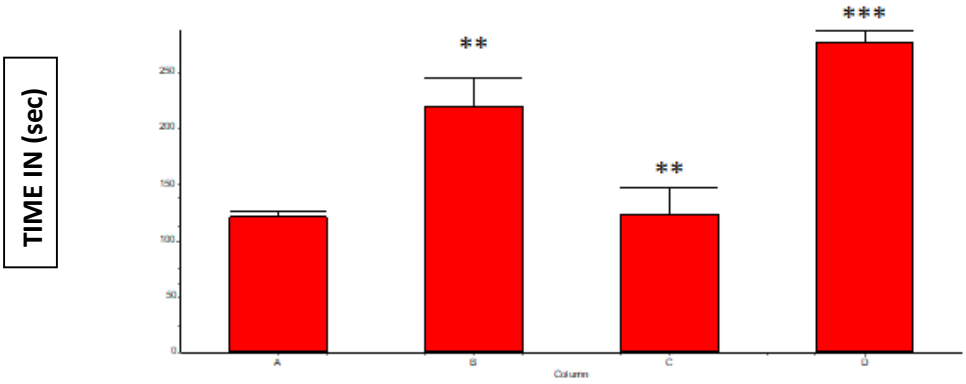
control standard extract dose 100 mg/kg extract dose 200 mg/kg

Histogram No: 1 EFFECT OF EEPA ON MYCLONIC JERKS PHASE OF CONVULSION



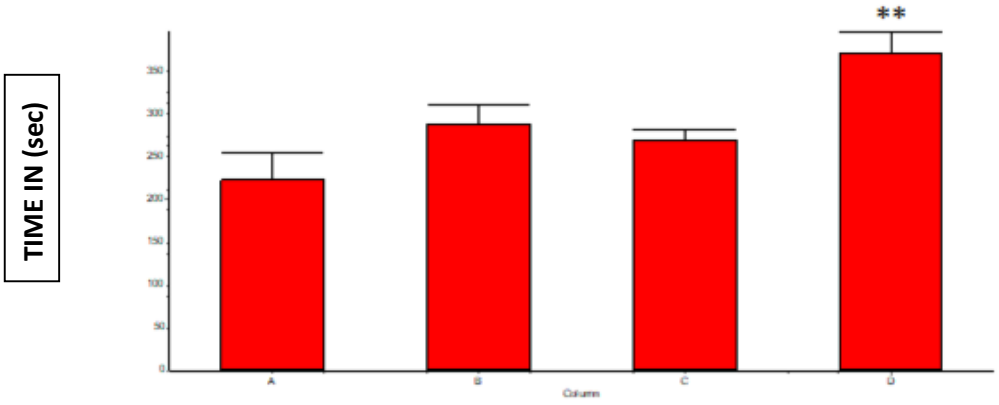
control standard extract dose 100 mg/kg extract dose 200 mg/kg

Histogram No: 2 EFFECT OF EEPA ON STRAUB'S TAIL PHASE OF CONVULSION



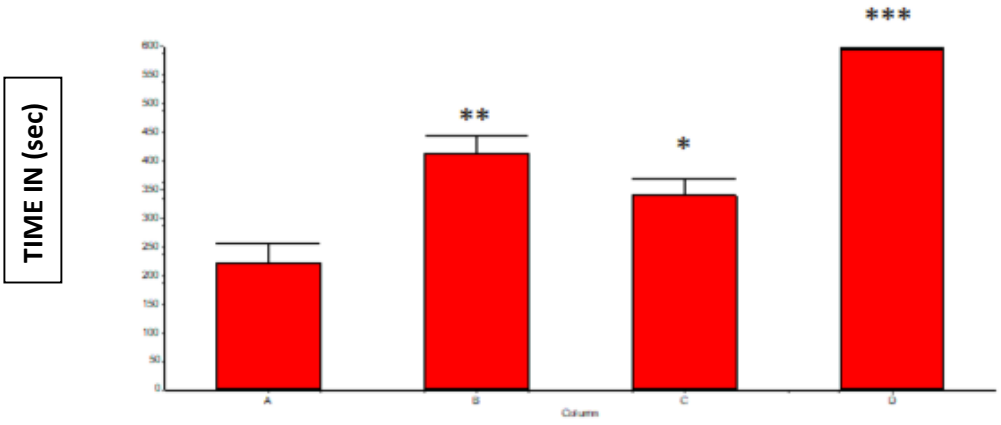
control standard extract dose 100 mg/kg extract dose 200 mg/kg

Histogram No: 3 EFFECT OF EEPA ON CLONUS PHASE OF CONVULSION



control standard extract dose 100 mg/kg extract dose 200 mg/kg

Histogram No: 4 EFFECT OF EEPA ON TONIC EXTENSION PHASE OF CONVULSION



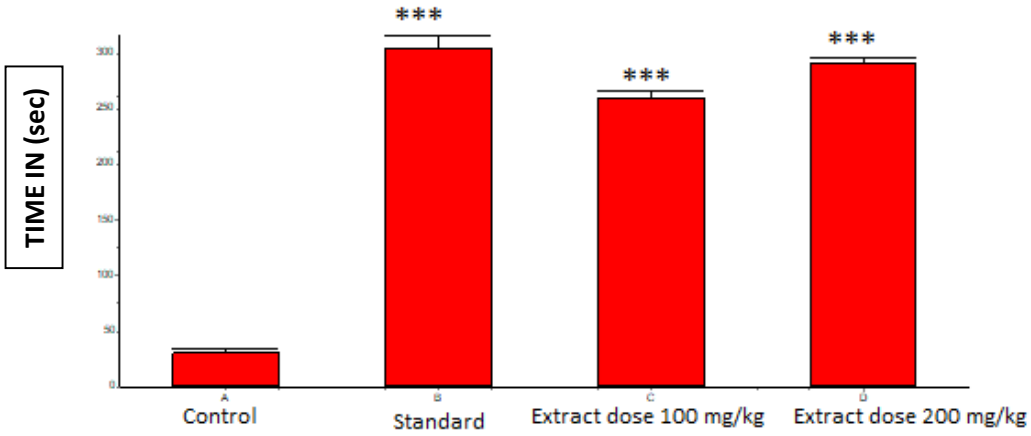
control standard extract dose 100 mg/kg extract dose 200 mg/kg

Histogram No 5: EFFECT OF EEPA DEATH ON PHASE OF CONVULSION

ANTI-ANXIETY EVALVUATION

RESULTS:

Histogram No: 6 Motor in-coordination by Rota Rod apparatus



Results are expressed as Mean ± SEM (n = 5). The data was analyzed using One-way ANOVA followed by *Tukey's* multiple comparison test

**P<0.01 vs negative control group

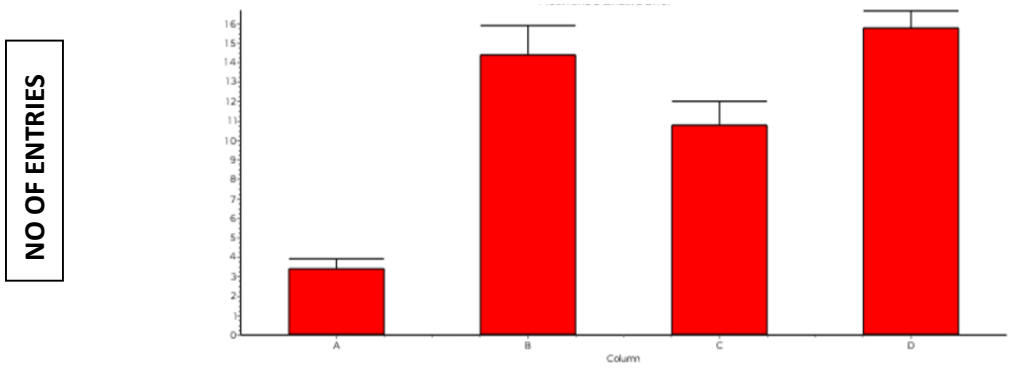
$P<0.01 vs negative control group

Group	Fall time
Control	30.6 ± 8.64
Diazepam	304.60 ±26.05***
EEPA (100mg/kg)	260.80 ±13.48***
EEPA (200mg/kg)	291 ±12.32***

Table 10.3 Effect of Diazepam and EEPA treatment on fall- of time in Rota rod Results are expressed as Mean ± SEM (n = 5). The data was analyzed using One-way ANOVA followed by *Tukey's* multiple comparison test **P<0.01 vs negative control group $P<0.01 vs negative control group.

Elevated plus maze

OPEN ARM ENTRIES



control standard extract dose 100 mg/kg extract dose 200 mg/kg

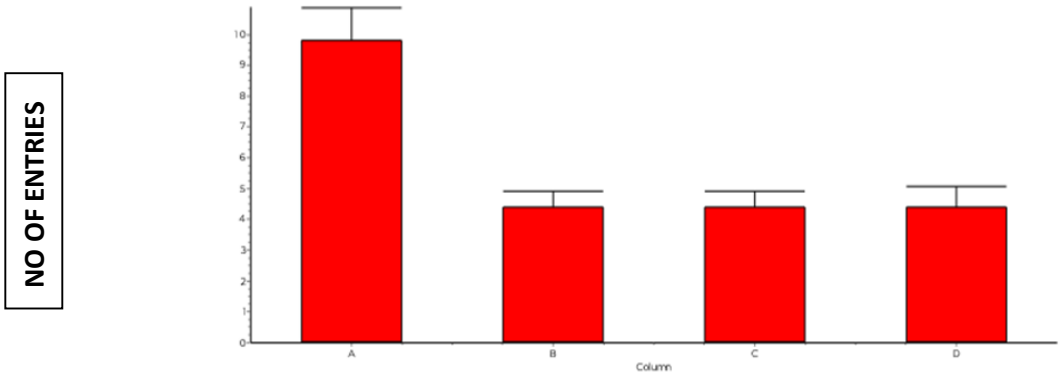
Histogram No: 7: Effect of diazepam and EEPA treatment on open arm entries

Results are expressed as Mean ± SEM (n = 5). The data was analyzed using One-way ANOVA followed by *Tukey's* multiple comparison test
*P<0.05 vs normal control group
# P<0.0001 vs negative control group
$P<0.001 vs negative control group

Group	No of entries
Control	30.6±8.64
Diazepam	304.60±26.02**
EEPA (100mg/kg)	260.80±13.48**
EEPA (200 mg/kg)	291±12.32**

Effect of diazepam and EEPA treatment on open arm entries
Results are expressed as Mean ± SEM (n = 5). The data was analyzed using One-way ANOVA followed by *Tukey's* multiple comparison test *P<0.05 vs normal control group # P<0.0001 vs negative control group $P<0.001 vs negative control group @ P<0.0001 vs negative control group

CLOSE ARM ENTRIES



control standard extract dose 100 mg/kg extract dose 200 mg/kg

Histogram No: 8. Effect of diazepam and EEPA treatment on CLOSE arm entries

Results are expressed as Mean ± SEM (n = 5). The data was analyzed using One-way ANOVA followed by *Tukey's* multiple comparison test
*P<0.05 vs normal control group
#P<0.05 vs negative control group
$P<0.01 vs negative control group

Group	No of entries
Control	9.8±3.38
Diazepam	4.4±1.14**
EEPA (100 mg/kg)	4.4±1.14**
EEPA (200 mg/kg)	4.4±1.57**

Results are expressed as Mean ± SEM (n = 5). The data was analyzed using One-way ANOVA followed by *Tukey's* multiple comparison test *P<0.05 vs normal control group

#P<0.05 vs negative control group
$P<0.01 vs negative control group

5. DISCUSSION

Epilepsy is a chronic disorder of the brain that affect people worldwide. Nearly about 50-80% of the patients with epilepsy are controlled with currently available antiepileptic drugs. But these drugs cannot able to control seizures effectively in about 10-20% of the patients. The treatment of epilepsy still remains inadequate even though new anticonvulsants are being developed. Furthermore the current therapy of epilepsy with modern antiepileptic drugs is associated with side effects, dose related and chronic toxicity as well as teratogenic effects.

Traditional systems of medicines are popular in developing countries and up to 80% of the population relies on traditional medicines/ folk remedies for their primary health care need. Hence, there is a need to discover an alternative agent from natural sources.

Prunus Armeniaca used as a herbal medicine and is well known for its traditional uses such as expectorants, diuretics, laxative etc. Various studies shows that the active principle flavonoids & isoflavonoids having a crucial role in treatment of epilepsy. Since Prunus Armeniaca have not been studied for its antiepileptic activity, the present study was aimed to evaluate the antiepileptic activity of ethanol extract of Prunus Armeniaca.

The pentylenetetrazol induced convulsion in animals represents petit mal type of epilepsy. The tonic extensor phase is selectively abolished by the drugs effective in generalized tonic clonic seizure. The result of the present study shows that the ethanolic extract of Prunus Armeniaca at doses 100 and 200 mg/kg significantly delayed the onset of HTLE and reduced the duration of HTLE. And also both doses completely abolished the phase of convulsion in PTZ induced convulsion models.

6. CONCLUSION

Epilepsy is a neurological disorder that affects a wide range of people throughout the world. Approximately 30% of the patients continue to have seizures with current antiepileptic drug therapy. Natural products from folk remedies have contributed significantly in the discovery of modern drugs and can be an alternative source for the discovery of antiepileptic drugs with novel structures and better safety and efficacy profiles.

The ethanolic extract of Prunus Armeniaca delayed the onset and reduced the duration of convulsion in PTZ induced convulsion models and can be used as an adjuvant therapy against cognitive deficit in convulsions. It can be concluded that the EEPA possesses good anticonvulsant activity. Further studies are needed to explore the mechanism as well as the active principle responsible for the anticonvulsant activity of Prunus Armeniaca.

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