IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Encyclopaedic Review Of Anti-Epileptic Activity Of Isoflavonoids As Herbal Approach

Pawan Ratan Magare[1], Omkar Vijay Jadhav[2], Usha Gundappa Habul[3], Kalpesh Sunil Jadhav[4], Tejas Rajkumar Chopde[5], Sakshi Nanasaheb Doke[6], Janvi Hariom Rathod[7], Prof. Umme Ruman S[8]

➢ ABSTRACT

One of the most prevalent and incapacitating neurological disorders is epilepsy. With the intention of offering herbal remedies for epilepsy, this article examines the clinical features of seizures and epilepsy. It defines seizures and epilepsy, discusses diagnostic techniques, classifies them, and discusses the usage of flavonoids. We have suggested using flavonoid-containing natural sources as neutraceuticals for epilepsy.

Keywords: Natural flavonoids, Epilepsy, Herbal sources, Neutraceuticals.

➢ 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]

➢ 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]

➢ 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]

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

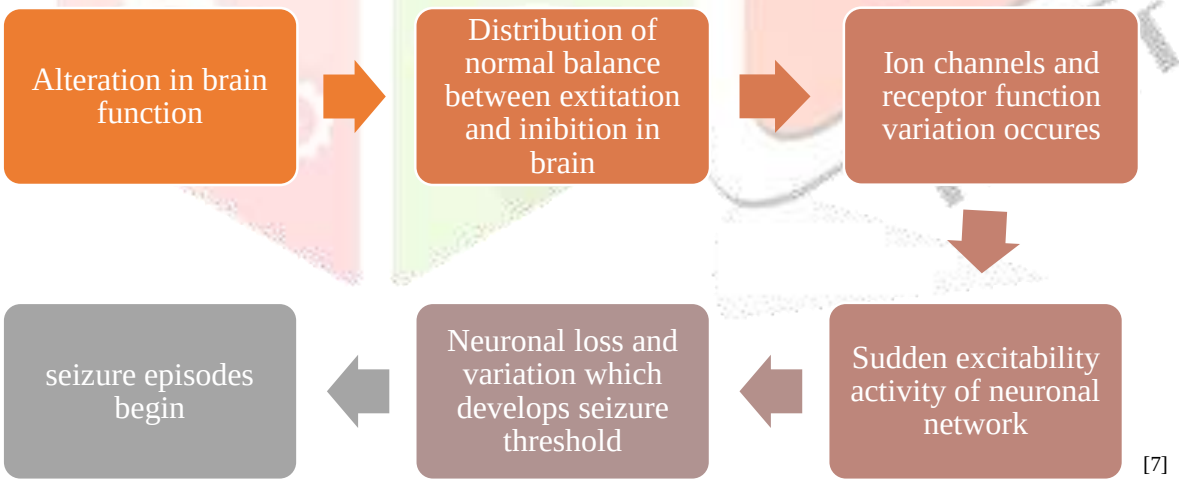
- Tonic-Clonic: It involves loss of consciousness, sustain muscle contraction followed by periods of relaxation, and lasts 1-2 min
- Absence seizures: It involves abrupt loss of consciousness with starting and loss of activity for less than 30 min
- Myoclonic seizures: It involves shock-like muscle contraction 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]

➢ **PATHOPHYSIOLOGY:**



[7]

➢ **CONVENTIONAL DRUGS USED IN EPILEPSY:**

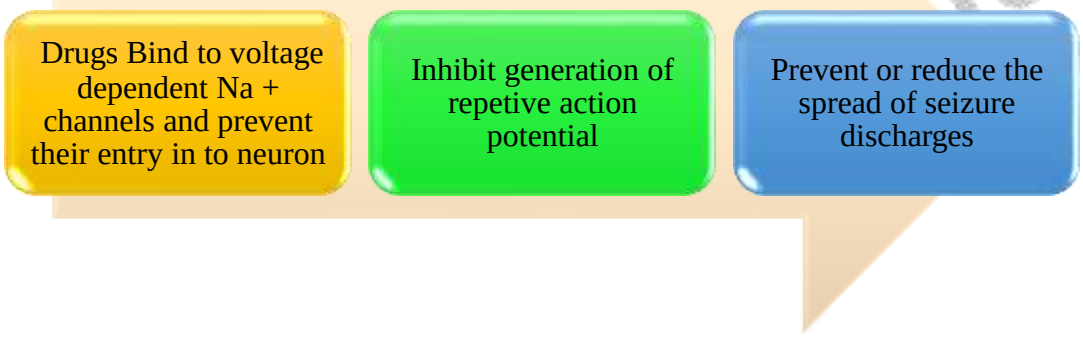
The allopathic approach to managing epilepsy focuses on using conventional medical treatments, primarily medications, to control seizures and improve the quality of life for individuals with this neurological disorder.

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

[7]

- **MECHANISM:**
  - *PROLONGATION OF SODIUM CHANNEL INACTIVATION*

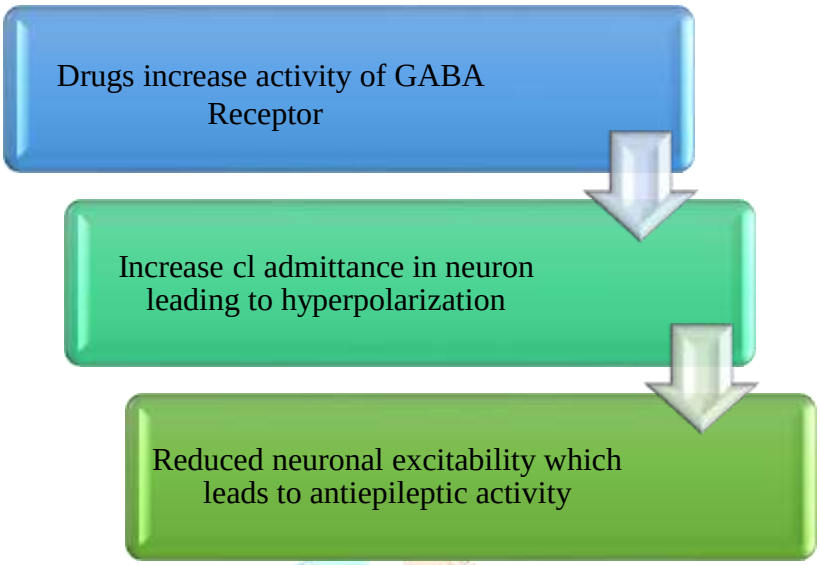


Sodium channels are crucial for the generation and propagation of action potential in neurons. During an action potential, sodium channels open, allowing sodium ions to flow in. As the membrane depolarizes, the channels eventually inactivate, closing and preventing sodium influx. Drugs like Phenytoin, 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 .

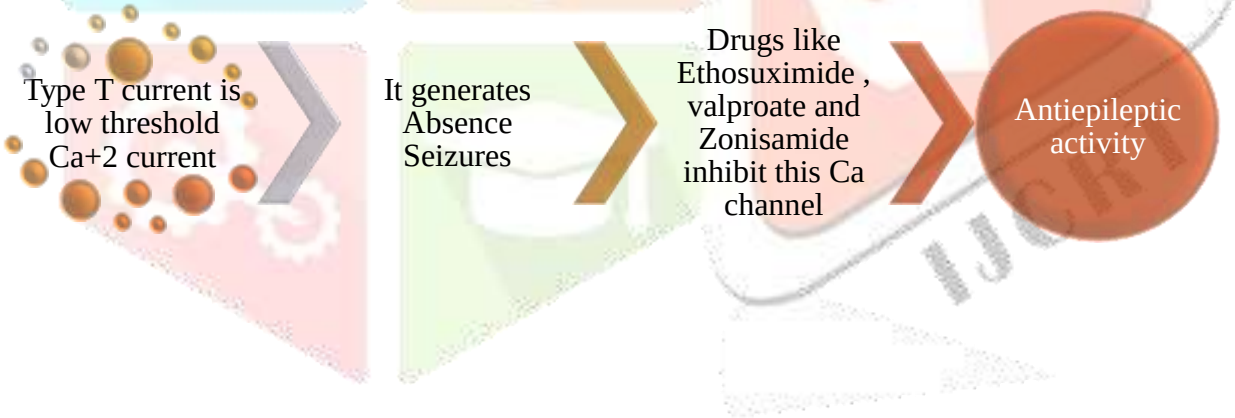
- *FACILITATION OF GABA MEDIATED Cl CHANNEL OPENING*

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.



- *INHIBITION OF T TYPE Ca +2 CURRENT*



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]

➢ 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, West Africa, South Africa	Quercetin	Modulate the activity of GABA, glutamate, and serotonin, Reduce oxidative stress and inflammation, Inhibition of NF-kB, Modulation of ion channels	Ojewole et al., (2007)
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'Gouemo 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 longipeduncu lata 	Polygalace ae	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	Tchoumbou gnang et al., (2009)
45.	Terminalia glaucescens 	Combretac eae	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 	Combretac eae	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 	Combretac eae	Roots, Barks	Savanna belt, Open woodland in Africa	Quercetin, Kaempferol, Luteolin	enhancing GABAergic transmission, Inhibiting voltage-gated Na^+ channels, Exhibiting antioxidant,	Mulaudzi et al., (2013)

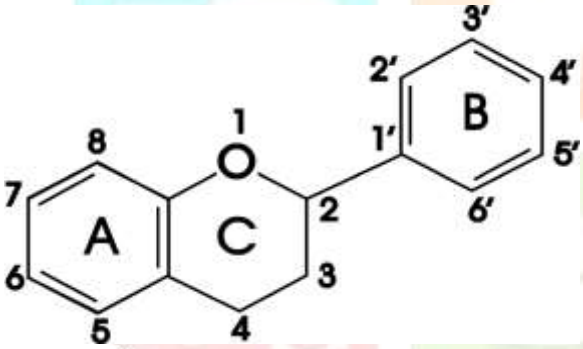
						Anti-inflammatory effects	
48.	Vitellaria paradoxa 	Sapotaceae	Leaves, Barks	Cameroon, Brazil	Naringenin, Quercetin, Kaempferol	Modulating GABA receptors, Inhibiting glutamate release, Exhibiting antioxidant activity, Reducing neuronal excitability	ljeh et al., (2014)

[9]

➢ Flavonoids used as Anti-epileptic Agents

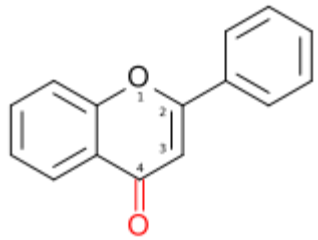
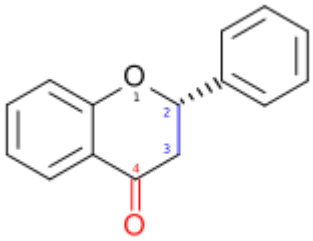
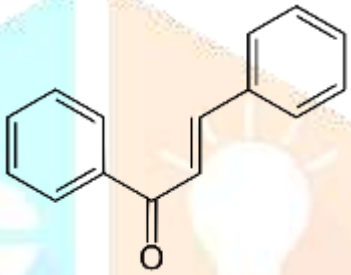
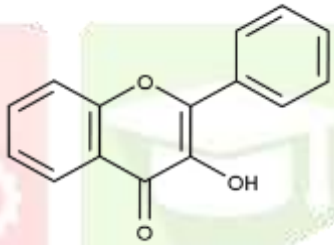
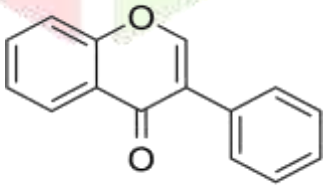
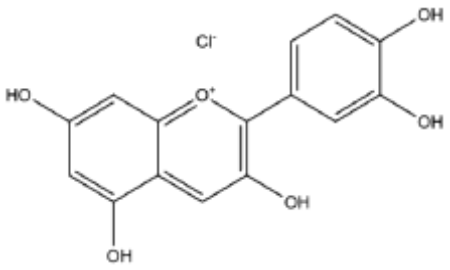
Flavonoids are phyto-nutrients found in almost all plant, vegetables along with Carotenoids which is responsible for colours in fruits, flowers, vegetables. Polyphenols constitute largest group of phytochemicals distributed amongst plant kingdom which covers flavonoids, Non-flavonoids and phenolic acids.

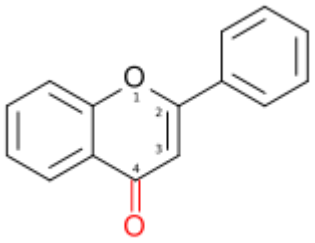
Flavonoids compounds are found as C_6-C_3-C_6 compounds (fifteen carbon skeleton). Flavonoids compounds usually occur in plants as glycosides in which one or more of phenolic hydroxyl groups are compound with sugar residues. Hydroxyl group are found in position 5 and 7 in ring A whereas hydroxyl or alkoxy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



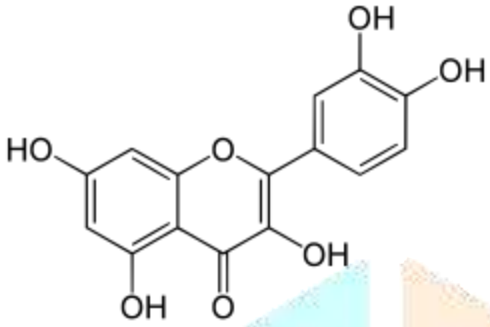
Flavonoids consist of aromatic ring A, condensed to heterocyclic ring C attached to second aromatic ring B. this structure is also know as flavonoid diphenyl propane skeleton. Flavonoids divided into anthocyanins and anthoxanthins. Anthocyanins is the glycosides of anthocyanindin which is the most important 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]

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

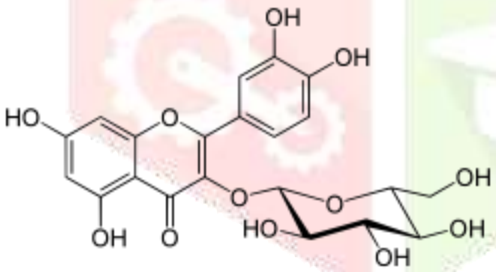
7.	Flavone		Apigenin Baicalein Luteolin Diosmetin Tangeretin

1. Quercetin



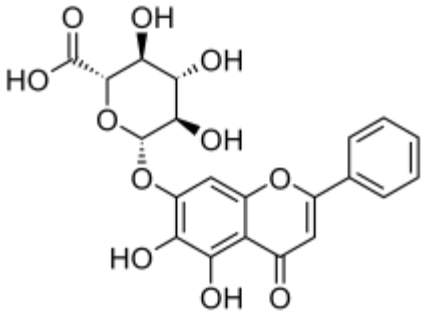
Quercetin, a flavonol belonging to the flavo noid class of polyphenols, has been known by its name since 1857, which originates from the Latin term "quercetum," meaning oak forest. Typically, people consume around 25-50 milligrams of quercetin per day.

2. Isoquercetin



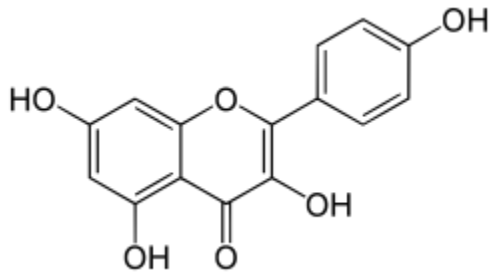
Isoquercetin, also referred to as isoquercitrin or isotrifoliin, is a naturally occurring flavonoid compound that can be described as the 3-O-glucoside derivative of quercetin.

3. Baicalin



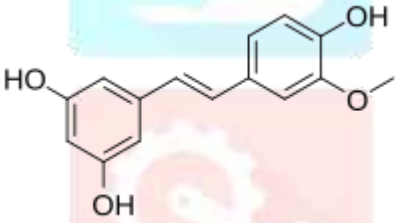
Baicalin is classified as a flavonoid, specifically a flavone glycoside, and can be described as the glucuronic acid conjugate of baicalein.

4. Kaempferol



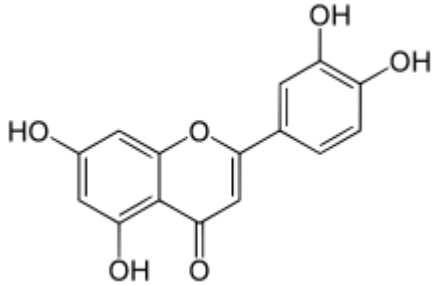
Kaempferol, a naturally occurring flavonol, is a type of flavonoid compound. This yellow crystalline substance has a melting point range of 276–278 °C and exhibits limited solubility in water, while being highly soluble in hot ethanol, ethers, and dimethyl sulfoxide (DMSO). The compound is named in honor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

5. Isorhapontigenin



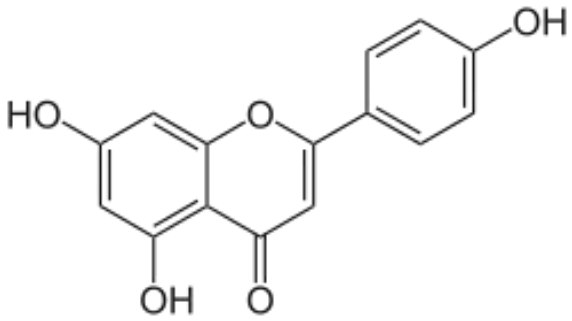
Isorhapontigenin is a stilbenoid compound characterized by its tetrahydroxylated structure and methoxy group. This compound is an isomer of rhapontigenin and shares similarities with resveratrol. Isorhapontigenin can be found in various plant sources, including the Chinese herb Gnetum cleistostachyum, 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



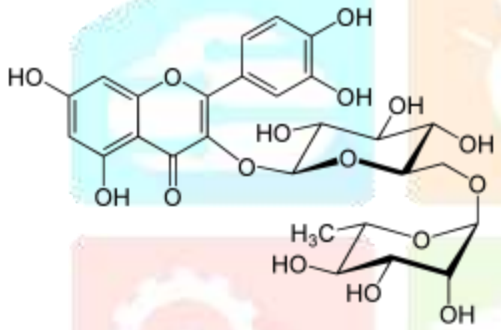
Luteolin is a flavonoid compound that belongs to the flavone subclass, characterized by its distinctive yellow crystalline form. The isolation and naming of luteolin in its pure form date back to 1829, when French chemist Michel Eugène Chevreul first identified it.

7. Apigenin



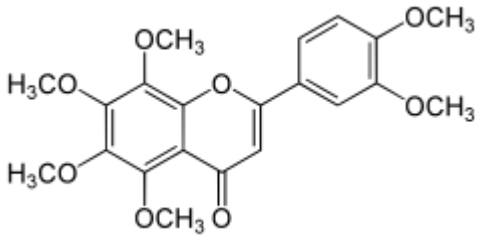
Apigenin, a naturally occurring compound found in various plant species, is a flavone-class molecule that serves as the aglycone for several glycosides. This yellow crystalline substance has been utilized as a dye for wool, showcasing its vibrant color properties.

8. Rutin



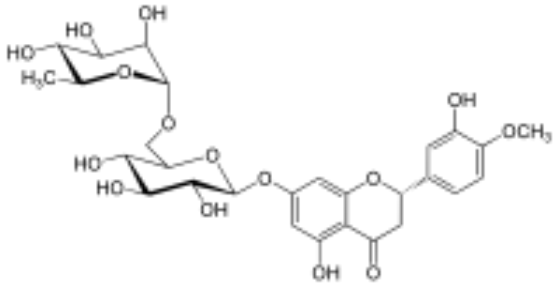
Rutin, also known as rutoside or sophorin, is a glycoside formed by the combination of the flavonol quercetin and the disaccharide rutinose. This flavonoid glycoside is widely distributed in various plant species, including citrus fruits, and is composed of a quercetin molecule bonded to a rutinose disaccharide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

9. Nobiletin



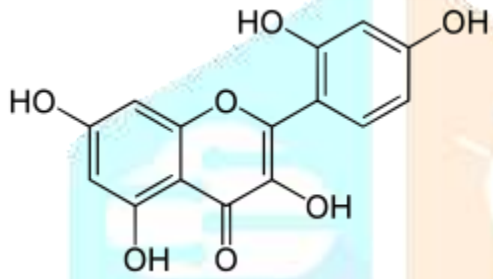
Nobiletin is a flavonoid compound that can be extracted from the peels of citrus fruits, and is characterized as an O-methylated derivative of flavone.

10. Hesperidin



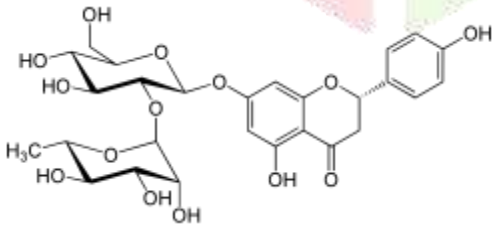
Hesperidin is a type of flavanone glycoside that occurs naturally in citrus fruits, with hesperetin serving as its aglycone. The name "hesperidin" originates from the term "hesperidium," which refers to the fruit of citrus trees. French chemist M. Lebreton first extracted hesperidin from the inner white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

11. Morin



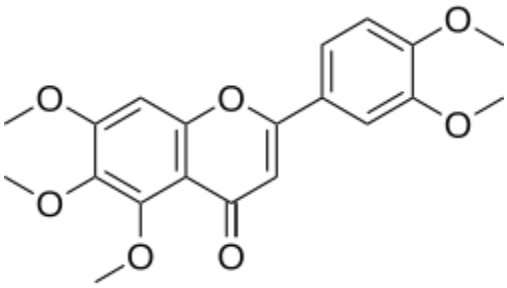
Morin is a yellow-colored compound that can be extracted from various plant sources, including the Osage orange (Maclura pomifera), old fustic (Maclura tinctoria), and the leaves of the common guava (Psidium guajava). Notably, morin forms glycosides with certain sugars, such as arabinose and lyxose,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

12. Naringin



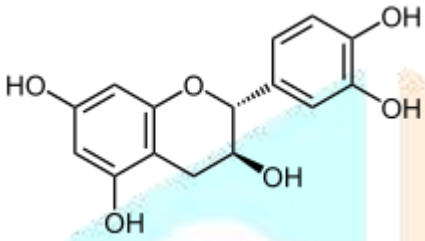
Naringin is a flavanone glycoside formed by the combination of naringenin and the disaccharide neohesperidose. This compound features a core flavonoid structure with a rhamnose and glucose unit attached to the 7-carbon position of its aglycone, naringenin.

13. Sinensetin



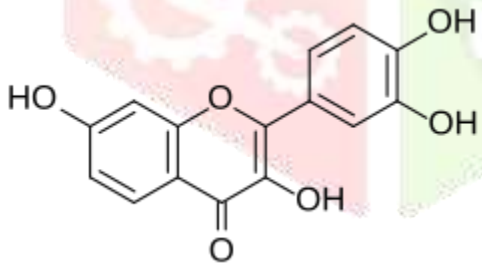
Sinensetin is a flavone compound characterized by its O-methylated structure, and it has been identified in the plant Orthosiphon stamineus and also in the essential oil of oranges.

14. Catechin



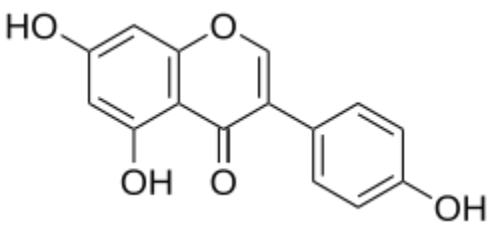
Catechin is a flavan-3-ol compound, a type of secondary metabolite that plays a crucial role in plant antioxidant defenses. As a member of the flavonoid subgroup, catechin is classified as a polyphenol. The term "catechin" originates from the word "catechu," which refers to the tannin-rich extract derived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

15. Fisetin



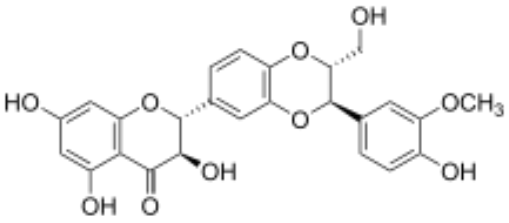
Fisetin, a flavonol compound, is a member of the polyphenol family and is found in various plant species, where it functions as a yellow pigment. The chemical structure of fisetin was initially elucidated by Austrian chemist Josef Herzig in 1891.

16. Genistein

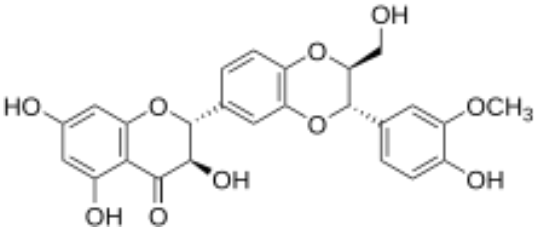


Genistein, a naturally occurring compound with the chemical formula C15H10O5, falls under the category of isoflavones. Its origin dates back to 1899, when it was initially extracted from the plant Genista tinctoria, also known as dyer's broom, which is where it gets its name.

17. Silibinin



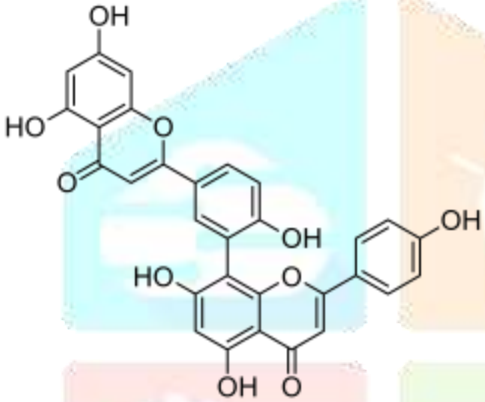
Silibinin A



Silibinin **B**

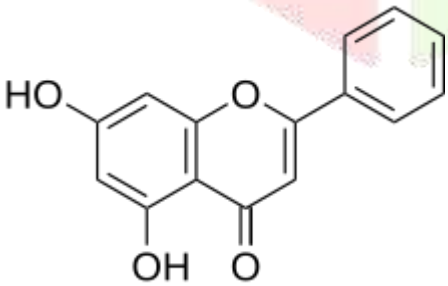
Silibinin, also referred to as silybin, is the primary active component of silymarin, a standardized extract derived from the milk thistle plant. Silymarin is a complex mixture of flavonolignans, including silibinin, isosilibinin, silychristin, and silidianin, among others. Notably, silibinin itself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

18. Amentoflavone



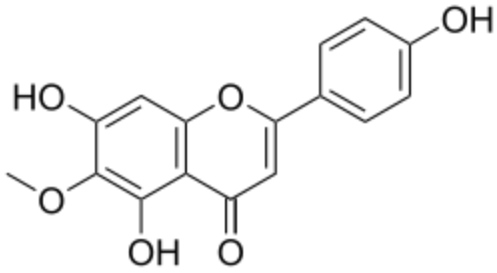
Amentoflavone is a biflavonoid compound, specifically a dimer of apigenin, where two apigenin molecules are linked at the 8 and 3′ positions, forming a 3′,8″-biapigenin structure.

19. Chrysin



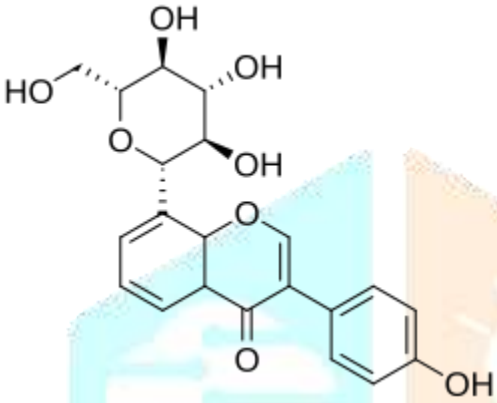
Chrysin, a naturally occurring flavone also known as 5,7-dihydroxyflavone, has limited bioavailability and is quickly eliminated from the body.

20. Hispidulin



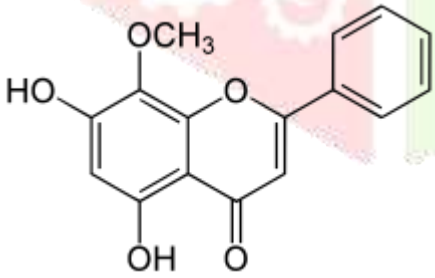
Research has shown that hispidulin, a naturally occurring flavone compound, exhibits potential antiepileptic properties in animal models, including rats and gerbils.

21. Puerarin



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



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]

➢ 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]

➢ 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]

➢ 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]

➢ 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]

➢ MOA

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]

➢ References

1. Seizures and epilepsy: An overview for neuroscientists/ www.perspectivesinmedicine.org
2. www.ILAE.org
3. Journal of personalise medicine review state of art and challenges in epilepsy- a narrative review
4. Current classification of seizures and epilepsies scope, limitation and recommendation for future action /www.ILAE.org
5. Epilepsy foundation- Epilepsy spasms/ https://www.epilepsy.com/what-is-epilepsy/seizures-types/epileptic-spasms

6. Pharmacology-Module-3 /GDC classes Page no-18-19
7. Natural medicines for the treatment of epilepsy: bioactive component, pharmacology: https://pubmed.ncbi.nlm.nih.gov/33746751
8. Pharmacology-Module-3/ GDC Classes/ Page no 21-24
9. Natural medicines for the treatment of epilepsy: bioactive component, pharmacology: https://pubmed.ncbi.nlm.nih.gov/33746751
10. https://en.m.wikipedia.org/wiki/Flavonoid
11. Flavonoids as therapeutic agents for epilepsy: unveiling anti-inflammatory and antioxidant pathway for novel treatments https://pmc.ncbi.nlm.nih.gov/articles/PMC11424894/
12. A review on novel pharmaceutical approaches of herbal drugs in derma care https://juniperpublishers.com
13. Isoflavonoids an overview of their biological activities and potentials health benefits https://www.pubmed.com
14. Isoflavonoids an overview of their biological activities and potential health benefits https://pmc.ncbi.nlm.nih.gov/articles/PMC2984117
15. Perspective: Therapeutic Potential of Flavonoids as Alternative Medicines in Epilepsy https://pmc.ncbi.nlm.nih.gov
16. Flavonoids as GABA receptor modulators and anticonvulsants https://pmc.ncbi.nlm.nih.gov/articles/PMC4306219/