International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2020): 7.803

Herbal Drugs Used In Anti - Psychotic Activity: A Review

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Running title: *Herbal Drugs Used in Anti - Psychotic Activity*

Abstract: ***This review confirms that herbal is convincingly more effective than allopathy drugs in reducing the various activity. Herbal is one of such inherited tradition of health and longevity. A wide variety of plants have been found to have effective against number of various activity. In this review the information is recorded as common name, scientific name, family, part used & reference of the plants used in treatment of various activity. This review helps the researcher to develop new formulations and toxicity studies which will beneficial for the society in future era. However, further neurochemical studies are warranted to explore the actual mechanism of action of herbal drugs as a promising novel herbal agent.***

Keywords: Herbal, Anti - Psychotic and Herbal agents

1. Introduction

Natural products, including plants, animals and minerals have been the basis of treatment of diseases from time immemorial. The future of natural products drug discovery will be more holistic, personalized and involve wise use of ancient and modern therapeutic skills in a complementary manner so that maximum benefits can be accrued to the patients and the community. [1] Traditional remedies invariably involve crude plant extracts containing multiple chemical constituents, which vary in potency from highly active to very weak. In contrast, orthodox medicine relies heavily on single (or a very small member of) chemically well - characterized active ingredients exhibiting selective activities at, in many cases, well - established biological targets. These medicines are generally very potent and many exhibit fairly narrow windows between an effective and a toxic dose. Orthodox medicines are formulated into doses that are carefully standardized for bioavailability. [2] The World Health Organization has estimated that 80% of the earth's inhabitants rely on traditional medicine for their health care needs, and most of this therapy involves the use of plants extracts or their active components. Therefore, therapeutic approach of several traditional medicines is rather more holistic. [3]

Anti - psychotic drugs available in the markets which are in use today, the safety profile is not so promising considering the fact that it has to be continued lifelong. The main and serious adverse effects of these drugs include hypotension and extrapyramidal side effects. The impact of the adverse effect is such that the drug needs to be discontinued after a few years due to some serious extra pyramidal side effects like akathesia, acute muscle dystonia, tardive dyskinesia. Need for drugs with negligible adverse effect specially when used for a prolonged period of time, is increasing for incurable psychotic disorders, where only symptomatic treatment can be given. Herbal drugs are known to have very minimal adverse effect, so it's well worth a therapy for chronic CNS diseases which is virtually incurable. [4]

India is a country where Ayurveda has been practiced from the Vedic ages very successfully. Some plant sources have been searched which is known to have some kind of CNS activity but those were never studied for their antipsychotic activity. An effort will be made to isolate the plant extract of those plants with specific solvent which is known to have CNS activity. [5]

Herbal medicines are gaining growing interest because of their cost - effective, eco - friendly attributes and true relief from disease condition. It has been dealt with in detail in "SHRUSHRUTHA SAMHITHA". [6]

Recent research literature on the use of antipsychotics and dementia examines a range of overlapping issues. These include studies of efficacy, comparative risks of typical versus atypical, non - pharmacological alternatives to manage symptoms, and the challenges of caring for persons with dementia within residential care settings. Research in this area also reports increasingly high rates of use of antipsychotics for dementia as new medications become available. Much of the literature also recommends that other approaches be used before medication. This recommendation is common to clinical guidelines in this area. [7]

Psychosis is a chronic recurrent neuropsychiatric disorder that alters the quality of life of the sufferers and it has been a major public health concern. Current drug treatments are limited by poor efficacy and tolerability. Since psychiatric disorders are on the rise, clinicians are looking for alternative remedies and herbal medications for the treatment of neurobehavioral disorders. [8]

Central nervous system (CNS) is vital organ system. Hence, the drugs acting on the CNS are very important by both

perspective i.e. their effects and adverse effects. Drugs acting in the central nervous system (CNS) were among the first to be discovered by primitive humans and are still the most widely used group of pharmacologic agents. In addition to their use in therapy, many drugs acting on the CNS are used without prescription to increase one's sense of well - being. The mechanisms by which various drugs act in the CNS have not always been clearly understood. Since the causes of many of the conditions for which these drugs are used (schizophrenia, anxiety, etc) are themselves poorly understood. [9]

Mental disorders have become highly prevalent due to ambitious lifestyle, urbanization, and stressful environment. Psychosis is a one of the most debilitating, complex, and costly illness. The meaning of "psyche" is mind or soul, and word " - osis" corresponds to an abnormal condition in Greek. Hence, psychosis is often described as involving a "loss of contact with reality. " These illnesses alter a person's ability to think clearly, make good judgments, respond emotionally, communicate effectively, understand reality, and behave appropriately. It is characterized by three general types of symptoms: Positive symptoms, negative symptoms, and cognitive symptoms. Positive symptoms refer to a loss of contact with reality and comprise of hallucinations, delusions, bizarre behavior, and positive formal thought disorders. Negative symptoms refer to a diminution in or absence of normal behaviors and include flat affect, alogia, avolition, and anhedonia. Cognitive symptoms manifest as deficits in attention, learning, memory, concentration, and executive functions. [10]

To treat psychosis antipsychotic agents are used. Antipsychotics (also called neuroleptics) a first generation of antipsychotics, known as antipsychotics, while second generation, known as atypical antipsychotics. The typical antipsychotics are classified according to their chemical structure while the atypical antipsychotics are classified according to their pharmacological properties. These include serotonin - dopamine antagonists, multi - acting receptor - targeted antipsychotics, and dopamine partial agonists, which are often categorized as atypicals. Typical antipsychotics are also sometimes referred to as the major tranquilizers common antipsychotic drug are haloperidol, promazine, chlorpromazine, etc. Although atypical antipsychotics are generally considered to be more effective and to have reduced side - effects compared to typical antipsychotics. [11]

All antipsychotic drugs tend to block D2 receptors in the dopamine pathways of the brain. This means that dopamine released in these pathways has less effect. Excess release of dopamine in the mesolimbic pathway has been linked to psychotic experiences. It is the blockade of dopamine receptors in this pathway that is thought to control psychotic experiences. [12]

2. Mechanism of Action

Most antipsychotic drugs bind to D2 dopamine receptors and block the action of dopamine. However, drug binding to the receptors does not account for antipsychotic effects because binding occurs within a few hours after a drug dose, and antipsychotic effects may not occur until the drugs have been given for a few weeks. Manifestations of hyperarousal (eg, anxiety, agitation, hyperactivity, and insomnia, aggressive or combative behavior) are relieved more quickly than hallucinations, delusions, and thought disorders. One view of the delayed effects is that the blockade of dopamine receptors leads to changes in the receptors and post receptor effects on cell metabolism and function. With chronic drug administration (i.e., chronic blockade of dopamine receptors), there is an increased number of dopamine receptors on postsynaptic and possibly presynaptic nerve cell membranes (up - regulation). Clozapine (Clozaril) and other atypical agents interact with dopamine, serotonin, and glutamate receptors. Overall, the drugs re - regulate the abnormal neurotransmission systems associated with psychosis. Herbs have been highly valued and used regularly for thousands of years by the peoples of the world as the medicine of the masses. Man has always searched for that herb that heals the body and soothes the mind and there has never been a shortage of vegetation to investigate with some 20, 000 species that have been used by various cultures. Medicinal plants have been used to treat such psychotropic and behavioral conditions as anxiety, depression, seizures, poor memory, dementia, insomnia, and drug intoxication.

The antipsychotic drugs (antipsychotics) are used in a range of conditions. They are the mainstay of the treatment of schizophrenia and will be discussed below in that context. However, they are also the mainstay of the management of delusional disorder, psychosis which occurs in dementia, they have a place in the management of delirium, and they must be added to antidepressants for the successful management of psychotic depression. The antipsychotics have a central place in the management of acute mania (even in the absence of delusions and hallucinations). Olanzapine and aripiprazole have recently gained acceptance as mood stabilizers (prophylactic agents in mood disorders). Quetiapine has recently been approved by the FDA (USA) as a treatment for bipolar depression [12]. In rare cases antipsychotics are used in the management of insomnia and anxiety [13], but this is not recommended and is best left to experts.

Both typical and atypical antipsychotics are effective in reducing the positive symptoms of schizophrenia (hallucinations, delusions and positive thought disorder). The negative symptoms of schizophrenia include social withdrawal, self - neglect, loss of energy and drive, and poverty of thought. It has been construed that the negative symptoms are composed of two subgroups of symptoms: primary negative symptoms (being part of the illness process), and secondary negative symptoms (being apparent rather than actual symptoms of the disorder, instead, being secondary to drug treatment). Claims are made that the atypical may produce no secondary negative symptoms, and go some way in relieving primary negative symptoms [14].

3. Conclusion

This review confirms that herbal is convincingly more effective than allopathy drugs in reducing the antipsychotic activity. Herbal is one of such inherited tradition of health and longevity. A wide variety of plants have been found to

have effective against number of antipsychotic activity. In this review the information is recorded as common name, scientific name, family, part used & reference of the plants used in treatment of antipsychotic activity. This review helps the researcher to develop new formulations and toxicity studies which will beneficial for the society in future era. However, further neurochemical studies are warranted to explore the actual mechanism of action of herbal drugs as a promising novel antipsychotic agent.

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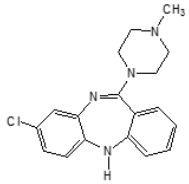
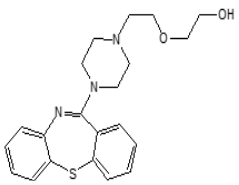
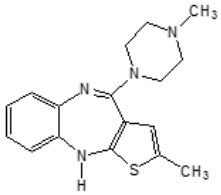
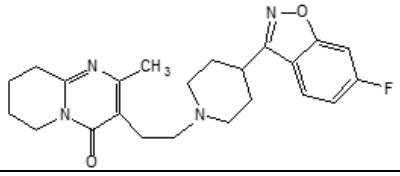
Table 1: Structure of Drugs with their Class

S. No.	Class	Drugs	Structures
1.	Diebenzazepines	Clozapine	
		Quetiapine	
2.	Thienobenzodizepine	Olanzapine	
3.	Benzisoheterazoles	Risperidone	

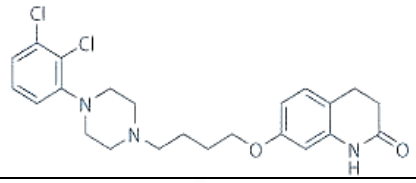
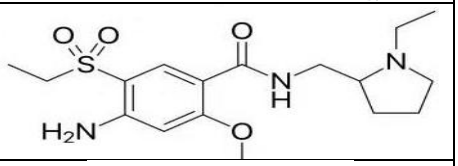
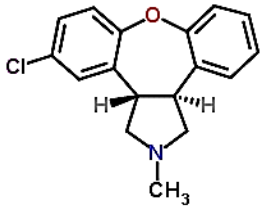
4.	Quinolinone	Aripiprazole	
5.	Benzamide	Amisulpride	
6.	Dibenzo - oxepino pyrrol	Asenopine	

Table 2: Various Extracts of Drug Used in Anti - Psychotic Activity

S. No.	Plant name (Family)	Part used	Extraction	Models	Chemical constituents
1.	Moringa oleifera (Moringaceae)	Leaves	Ethanol	Elevated plus maze model The Light/Dark Box Test. [15]	Alkaloids Diterpenoid Lactones Glycosides Steroids Sesquiterpenoid Phenolics Aliphatic compounds Polysaccharides
2.	Abutilon indicum (Malvaceae)	Leaves	Ethanol	Elevated plus maze model. [16]	Alkaloids Glycosides Tannins Polysaccharides Flavonoids
3.	Plectranthus amboinicus (Lamiaceae)	Leaves	Aqueous solvent Ethanol	Elevated plus maze model The Light/Dark Box Test. [17]	Alkaloids Resins Tannins Saponins Polysaccharides
4.	Coriandrum sativum (Apiaceae)	Fruits	Hydroalocoholic	Elevated plus maze Test Open Field Test The Light/Dark Box Test Social interaction test. [18]	Alkaloids Tannins Flavonoids Resins Carbohydrates
5.	Ficus hispida Linn (Moraceae)	Leaves	Methanol	Elevated plus maze model Zero maze Hole board Rota rod paradigm. [19]	Alkaloids Glycosides Tannins Polysaccharides Flavonoids
6.	Pulsatilla nigricans Stoerck (Ranunculaceae)	Whole plant	Petroleum ether Chloroform Methanol Water	Elevated plus maze model Open field actophotometer. [20]	Alkaloids Glycosides Tannins Polysaccharides Flavonoids
7.	Citrus paradise var. D uncan (Rutaceae)	Leaves	Petroleum ether chloroform Ethanol Water	Elevated plus maze model. [21]	Diterpenoid Lactones Glycosides Steroids Sesquiterpenoid Phenolics Aliphatic compounds
8.	Echium italicum L. (Boraginaceae)	Aerial Parts	Aqueous solvent Ethanol	Prolongation Effect on Pento barbital - Induced Sleeping Time Motor coordination test by rota rod Open Field Test Elevated plus maze Test. [22]	Alkaloids Glycosides Tannins Polysaccharides Flavonoids
9.	Curculigo orchioides (Amaryllidaceae)	Root	Hexane Dichloromethane Ethyl Acetate Methanolic	Elevated plus maze Test Dark &light. [23]	Saponin Carbohydrate Flavonoides Tannins

			Water		
10.	Achyranthes aspera (Amaranthaceae)	Leaves	Methanol	Elevated plus maze Test Hole - board test Open Field Test Dark &light. [24]	Saponin Carbohydrate Flavonoides Tannins
11.	Allium ascalonicum Linn. (Liliaceae)	aerial part	hydroethanolic	Elevated plus maze Test Hole - board test Stair case Dark &light Open Field Test social interaction test. [25]	Alkaloids Glycosides Tannins Polysaccharides Flavonoids
12.	Valeriana jatamansi jones (Valerianaceae)	Whole Plant	Aqueous ethanol Ethanol	Elevated plus maze Test Dark &light. [26]	Glycosides Steroids Sesquiterpenoids Phenolics
13.	Mangifera indica (Anacardiaceaae)	Leaves	Aqueous solvent	Elevated plus maze Test Stair case. [27]	Saponin Carbohydrate Flavonoides Tannins
	Catunargaom spinosa (Thumberacea)	Fruits	Alcoholic, Hydrochloric, Aqueous	Behavior test [28]	Saponin Carbohydrate Flavonoides Tannins

Table 3: Herbal Drugs Used in Antipsychotic Activity

S. No.	Herbal Drug	Biological source/ Family	Uses	Chemical constituents
1.	Saffron	Crocus sativus / Iridaceae	It is used in anticarcinogenic antimutagenic, immuno modulating, antioxidantlike properties, macular degeneration and retinitis pigmentosa. [31]	Flavonoids Tannins Resins Alkaloids
2.	Jyotishmati	Celastrus paniculatus / Celastraceae	It sharpening the memory and improving concentration, cognitionenhancing properties and antioxidant properties. [32]	Flavonoids Tannins Resins Alkaloids Glycosides
3.	Brahmi	Bacopa monniera / Scrophulariaceae	It is used in the treatment of memory loss, its potential benefit in the treatment of Antipsychotic activity. [33]	Flavonoids Tannins Alkaloids Glycosides
4.	Ashwagandha	Withania somnifera / Solanaceae	It is used in antioxidant activity, free radical scavenging activity, and an ability to support a healthy immune system, central nervous system, Antipsychotic activity. [34]	Flavonoids Resins Alkaloids Glycosides
5.	Shankhpushpi	Convolvulus pluricaulis / Convolvulaceae	It is used in psychostimulant, tranquilizer, brain tonic, alterative, febrifuge, fever, nervous debility, loss of memory, also in syphilis, loss of memory, Antipsychotic activity. [35]	Flavonoids Tannins Resins Alkaloids Glycosides
6.	White mulberry	Morus alba/ Moraceae	Anti - microbial, anti - oxidant, anti - HIV, neuroprotective, and anti - stress. [31]	Flavonoids Alkaloids Glycosides
7.	Undirkana or mushakparni	Ipomoea reniformis / Convolvulaceae	Anti - diabetic, anti - inflammatory, anti - epileptic, anti - oxidant, anxiolytic, neuroprotective and anti - microbial. [36]	Flavonoids Tannins Resins Alkaloids Glycosides
8.	Marijuana	Cannabis sativa / Cannabaceae	Anti - epileptic, anti - pyretic, anti - parasitic, and anti - emetic. [37]	Flavonoids Tannins Resins Alkaloids Glycosides
9.	Bushweed	Securinega virosa / Euphorbiaceae	Anti - diabetic, anti - oxidant, anti - rheumatism, anti - diarrheal, and anti - epileptic. [38 - 39]	Flavonoids Tannins Resins Alkaloids Glycosides
10.	Bargad	Ficus benghalensis Linn. / Moraceace	Anti - strees and cns activity. [40]	Flavonoids Tannins Resins Alkaloids Glycosides
11.	Morinda citrifoliaLinn. /Holdi Kachu, Noni	Morinda citrifolia /Rubiaceae	Antipsychotic activity [41]	Flavonoids Tannins Glycosides

12.	Cannabis Sativa L. /Bhang, Siddhi	Cannabis Sativa (Cannabaceae)	Anti - strees and cns activity. [42]	Flavonoids Tannins Resins Alkaloids Glycosides
13.	Datura metel L. /Dhutura	Datura metel L. (Solanaceae)	Anti - microbial, anti - oxidant, anti - HIV, neuroprotective, and anti - stress. [43]	Flavonoids Tannins Resins Alkaloids Glycosides
14.	Vitex negundo L. /Nishinda	Vitex negundo (Lamiaceae)	Anti - diabetic, anti - epileptic, anxiolytic, neuroprotective. [44]	Flavonoids Glycosides

Table 4: Classes of Natural Product with Antipsychotic Activity

S. No.	Class	Chemical Constituent
1.	Anthocyanins	• Cyaniding • Carboxypyranocyanidine • Peonidin glycosides
2.	Phenolic acid	• Caffeic • Sinapic • p - Coumaric • Protocatechuic acids
3.	Coumarin and Furanocoumarin	• Xanthotoxin • Psoralen • Coumarin
4.	Saponins	• Bacosides • Asiaticoside • Panaxosides
5.	Flavonoids	• Rutin • Hesperidin • Quercetin • Quercetin - 3 - galactosid • Isorhamnetin • Taxifolin
6.	Tannins	• Gallic acid • Ellagic acid • Catechol • Catechin
7.	Terpenoids	• Terpinine • Eugenol • Coriandrol • Nardostachone • Jatamanson
8.	Alkaloids	• Atropine • Cocaine • Hyoscyamine • Reserpine • Strychnine

Figures of chemical constituents present in herbal drugs used for antipsychotic activity

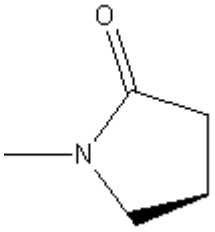


Figure 1: N- methyl pyrrolidone

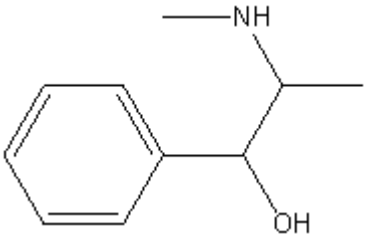


Figure 2: Epherdrine

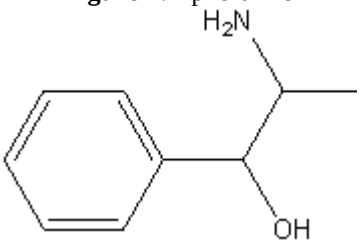


Figure 3: Nor- ephedrine

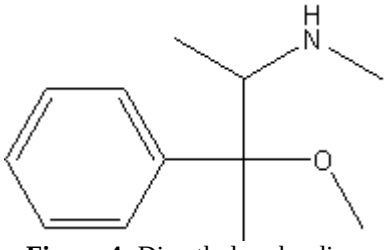


Figure 4: Dimethyl- epherdine

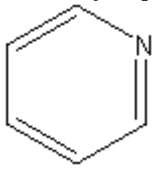


Figure 5: Pyridine

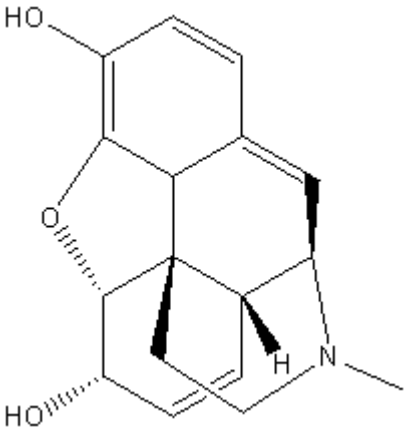


Figure 6: Morphine

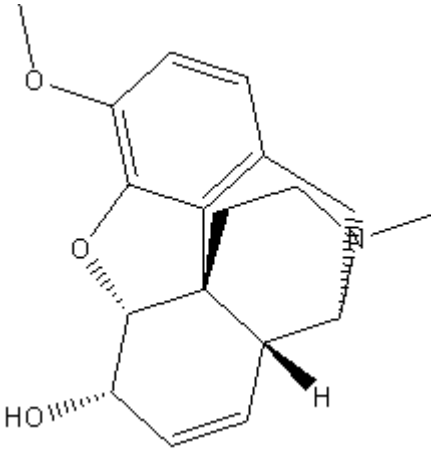


Figure 7: Codine

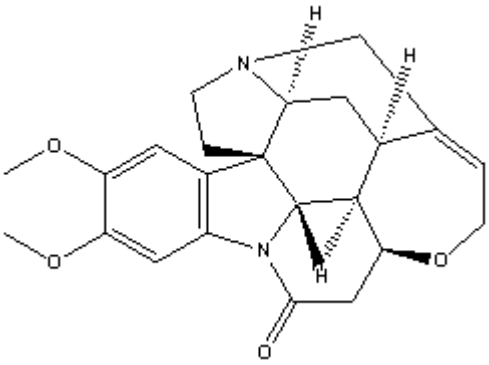


Figure 8: Brucine

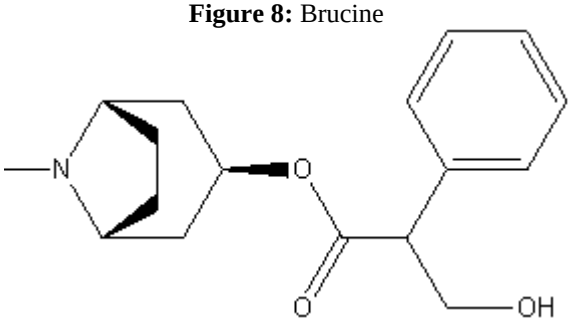


Figure 9: Hyoscyamine

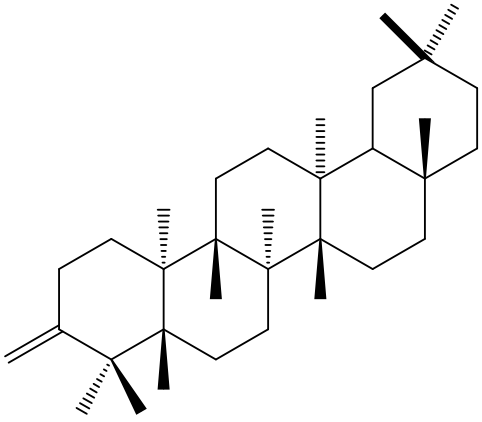


Figure 10: Friedelin

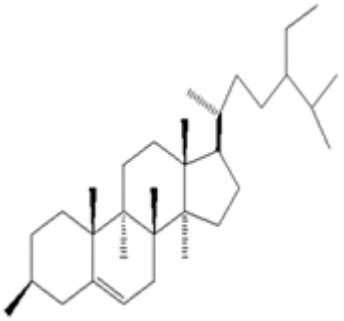


Figure 11: β - sitosterol

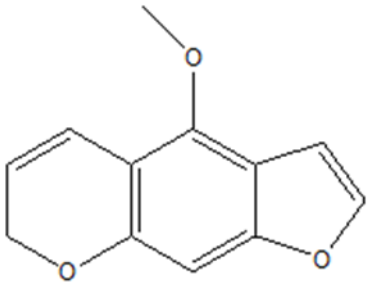


Figure 12: Bergapten

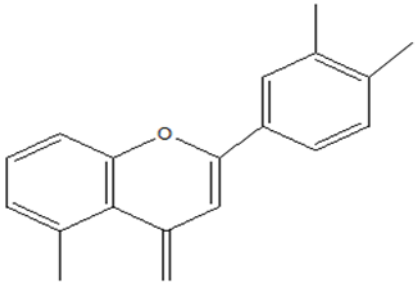


Figure 13: β – amyrin

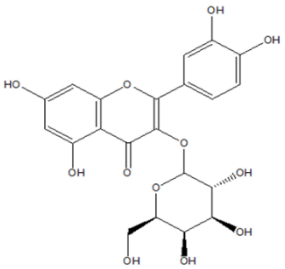


Figure 14: Quercetin - 3 - galactoside

Table and Figure

Table 1: Structure of drugs with their class
Table 2: Various extracts of drug used in anti - psychotic activity
Table 3: Herbal drugs used in antipsychotic activity
Table 4: Classes of natural product with antipsychotic activity
Figures of chemical constituents present in herbal drugs used for antipsychotic activity