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Exploring the Landscape of Mental Health: Progress in Psychosis Treatment and the Therapeutic Potential of Phytochemicals

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Abstract

Mental illness is a critical aspect of human health that significantly affects individuals' emotional and psychological well-being. The present study focused on the "Current status of mental health which highlights both advancements and persistent challenges." About 10% of people worldwide suffer from psychosis, a mental illness characterized by severe distortions in cognition, behavior, perception (delusions and hallucinations), and the ability to identify reality. The growing interest in natural remedies for mental health issues in recent years is indicative of a move toward more comprehensive methods of treating ailments including stress, anxiety, and depression. Numerous genetic, nutritional, microbial, and environmental variables are involved in this complex illness. However, several conditions are included under psychotic illnesses. Although they are pharmacologically categorized as dopamine receptor antagonists, many of them also act on other targets, such as 5-hydroxytryptamine (5-HT) receptors, which may contribute to some of their therapeutic efficacy. The activation of the immune system, neuro-inflammation, endocannabinoid receptors, neurotransmission, cell signaling pathways, and oxidative stress status are all changed and modified by these phytochemicals. Most phytochemicals with anti-schizophrenic properties include flavonoids, alkaloids, terpenoids, polypropanoids, lactones, and glycosides.

Keywords: Psychosis, Phytochemicals, Medications, Receptors, Schizophrenia, Disease, Anti-psychotics

1 Introduction

Psychosis is the mental disorder, with serious distortion of thought, behavior and capacity to recognize reality and of perception (delusions and hallucinations), affecting approximately 10% of world's population. Antipsychotic potency has demonstrated a strong link with its ability to bind to the D2 receptor, and all clinically effective antipsychotics (with the exception of Clozapine-like) exhibit strong post-synapse dopaminergic D2 receptor inhibiting action. Blockade of dopamine action in corpus striatum is responsible for the extrapyramidal symptoms (EPS) so often associated with antipsychotic drugs[1].

Unconventional thinking, delusions, hallucinations, improper mood, and decreased psychosocial functioning are all hallmarks of schizophrenia, a diverse syndrome. Following Kraepelin's 1896 description of dementia praecox, the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) was released in 2000. Since then, the disease's definition has undergone constant change. Future research on the physiology, pathophysiology,

and genetics of the central nervous system (CNS) will probably extend our understanding of schizophrenia[2].

Research has shown a number of abnormalities in the structure and function of the brain, despite the fact that the exact cause of schizophrenia is unknown. But not everyone with a diagnosis of schizophrenia experiences similar changes, and there is still much to understand about the pathophysiology of the disorder. It is likely that a number of pathophysiologic disorders contribute to the development of the comparable but distinct clinical presentations that we call schizophrenia[3].

The etiology of schizophrenia has been explained by a neurodevelopmental theory. This is supported by the fact that most studies on the brains of people with schizophrenia reveal abnormal neuronal migration. This "schizophrenic lesion" may result in abnormalities in cell shape, location, symmetry, connection, and function in addition to abnormal brain circuit creation. In addition to aberrant brain circuit formation, this "schizophrenic lesion" may cause anomalies in cell shape, location, symmetry, connection, and function[4].

In certain studies, respiratory tract infections during the second trimester of pregnancy have been linked to an increased risk of schizophrenia, and these changes are consistent with an aberration in cell migration during that time. Premature births or low oxygen levels in the newborn are linked to schizophrenia, according to some research. Due to the accompanying period of neuronal growth, it is believed that the secondary "synaptic disorganization" that results from such injuries does not cause overt clinical signs of psychosis until adolescence or early adulthood[5].

According to studies, the brains of many people with schizophrenia have thinner cortical walls and larger ventricles, although this isn't necessarily the case when there is widespread gliosis; it can also happen when there isn't. It is believed that gliosis, or the growth of glial cells, happens as a compensatory alteration in brain degenerative illnesses. The dendritic pruning is a typical aspect of the neurodevelopmental process[6].

In a healthy individual, middlescence prunes around 35% of the maximal number of dendrites at the age of 2. According to certain research, people with schizophrenia exhibit a higher rate of pruning. Furthermore, synaptic pruning is the main function of glutamatergic dendrites. or other foetal harm may result in a reduction in the number of basal neurons initially, and glutamatergic stimulation may exacerbate the pruning process. Numerous studies have demonstrated that early children who subsequently develop schizophrenia exhibit cognitive problems, impaired ability to meet typical motor milestones, and aberrant movements[7].

A fact that brain abnormalities exist well in anticipation of the onset of psychotic symptomatology is empirical evidence that connects schizophrenia to neurodevelopmental disorders. However, a growing number of patients' increasing clinical deterioration raises the possibility that this condition may potentially include a neurodegenerative component. Recent brain imaging studies that reveal cumulative brain alterations in patients who experience relapses frequently are consistent with this[8].

Schizophrenia may have a neurodegenerative tendency based on a vulnerable neurodevelopmental predisposition that codes for trophic factors and neurodevelopment, rather than being neurodevelopmental or neurodegenerative in origin. For instance, the chromosome contains the neurodevelopmental protein gene dysbindin[9].

2 Etiology and Pathogenesis of Schizophrenia

Schizophrenia's precise cause is unknown; however, it is thought to result from a combination of environmental and genetic causes. Numerous susceptibility genes have been found by genetic linkage studies; however, it is evident that no single gene is to blame. There are strong correlations between specific gene polymorphisms and the risk of schizophrenia, although many of these correlations are not very strong, and no single gene seems to have a dominant effect[10].

The first and strongest correlation was discovered with the neuregulin-1 gene, which affects the expression of NMDA receptors and is involved in synaptic formation and plasticity. In some ways, the phenotype of transgenic mice that under express neuregulin-1 is similar to that of human schizophrenia. Following this discovery, roughly eight more susceptibility genes were found, some of which had some connection to glutamate-mediated transmission. Genetic investigations have not yet identified a specific neurochemical defect underpinning the schizophrenia phenotype, except than highlighting glutamate and establishing the probable participation of amines like dopamine[11].

Since these structural alterations are likely not progressive and are seen in people with schizophrenia who are presenting for the first time, it is more likely that they reflect an early, irreversible abnormality in brain development than a slow neurodegeneration. Research on post-mortem schizophrenia brains reveals evidence of abnormally shaped cortical neurons that are misplaced. Schizophrenia seems to occur in specific individuals due to a combination of social, environmental, and developmental variables, as well as hereditary elements. Cannabis use is one of the environmental elements that are now believed to be important[12].

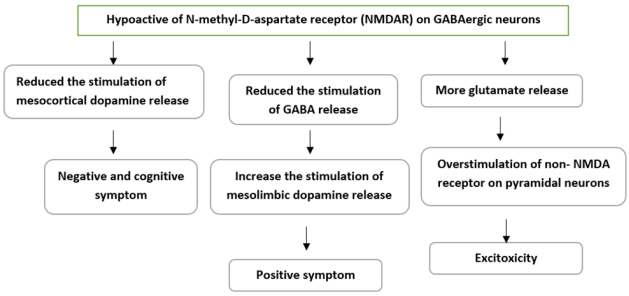

Fig. 1: Contributing Factors of Psychosis

3 Theories of Neurochemistry

Current theories on the neurochemical mechanisms behind schizophrenia are primarily based on pharmacological, not neurochemical, analysis of the effects of antipsychotic medications. The contrary happened: medications that were discovered by accident to be effective have given the primary hints regarding the nature of the condition, rather than neurochemical theory serving as the foundation for logical pharmacological treatment. For many years, a thorough search for neurochemical anomalies in schizophrenia remained fruitless, as neither post-mortem brain material nor other samples from living patients contained any molecular indicators. Although other mediators, like 5-HT, are now gaining attention, dopamine and glutamate remain the main focus of neurochemical hypotheses[13].

3.1 Dopamine Theory

In 2000, Carlson, who was awarded a Nobel Prize, proposed the dopamine theory based on indirect pharmacological evidence from humans and experimental animals. Doctors who treat drug users are well aware that amphetamine causes the release of dopamine in the brain and can cause a behavioural condition in people that is identical to an acute schizophrenia episode. Dopamine release causes a particular pattern of stereotyped behaviour in animals, which is comparable to the repeated behaviours sometimes seen in people with schizophrenia. Strong D2-receptor agonists, such apomorphine and bromocriptine, exhibit similar effects in animals and exacerbate schizophrenia symptoms in humans, just like amphetamine does. Dopamine antagonists, such as reserpine, and drugs that block neuronal dopamine storage are also useful in managing the positive symptoms of schizophrenia and halting amphetamine-induced behavioural abnormalities[14].

There is no conclusive physiological proof that increased dopamine synthesis or release occurs in schizophrenia. Furthermore, even though prolactin production could be abnormally low if dopaminergic transmission were activated, it is normal in patients with schizophrenia. The fact that almost all schizophrenia patients get medication that is known to alter dopamine metabolism while the non-schizophrenic control group does not present a challenge for the interpretation of such investigations. Imaging studies provide the strongest evidence for elevated dopamine release in individuals with schizophrenia. A particular antagonist's binding to striatal D2-receptors (raclopride) was measured using a radioligand imaging approach. When amphetamine was injected, dopamine was released, which caused raclopride to be displaced and the signal intensity to decrease[15].

The decline in schizophrenia subjects was at least twice as large as in control patients, indicating that amphetamine produced a greater amount of dopamine. Dopamine release is clearly associated with symptomatology; in individuals with schizophrenia, this effect was most pronounced during acute episodes and non-existent during spontaneous remissions. However, genetic research has not found any connection between D4-receptor polymorphism and schizophrenia. Furthermore, clinical trials showed that a particular D4-receptor antagonist was unsuccessful. According to a different version of the dopamine hypothesis, schizophrenia is caused by an imbalance between the deficiency of cortical D1-receptor activation (which results in negative symptoms) and the excessive activation of D2-receptors in subcortical regions (which results in positive feelings)[16].

3.2 Glutamate Theory

As a result, another transmitter connected to the pathophysiology of schizophrenia is glutamate. One of the only somewhat consistent findings is that post-mortem schizophrenia brains exhibit lower glutamate concentrations and glutamate receptor density. Human psychotic symptoms, such as hallucinations and cognitive problems, are brought on by NMDA receptor antagonists, such as phencyclidine, ketamine, and dizocilpine. According to this viewpoint, glutamate and dopamine excitatory and inhibitory effects are mediated by GABAergic striatal neurons, which form a sensory 'gate' and project to the thalamus. When dopamine or glutamate levels are too high, the gate is deactivated, allowing unfiltered sensory information to access the cortex[17, 18].

It is also proposed that the cognitive deficiency, which is becoming more widely acknowledged as a key characteristic of schizophrenia and partially responsible for its negative symptoms, may be caused by aberrant glutamate activity, notably decreased NMDA-receptor activation. Therefore, a specific hypothesis is that a majority of positive symptoms are caused by excessive dopamine receptor activity, while the majority of negative symptoms are caused by insufficient NMDA receptor activation. This concept, although clearly simplified, is what motivates present attempts to create new antipsychotic medications that enhance NMDA-receptor activation[19].

4 Synthetic Approach for the treatment of psychosis

Antipsychotic medications, formerly known as neuroleptic medications, antischizophrenic medications, or significant tranquillizers, are typically used to treat schizophrenia, one of the most prevalent and incapacitating types of mental disease. However, psychotic illnesses encompass a variety of disorders. Although many of them also act on other targets, including 5-hydroxytryptamine (5-HT) receptors, which may contribute to their clinical success, pharmacologically speaking, they are classified as dopamine receptor antagonists. Existing medications have numerous problems with their effectiveness and adverse effects. As new medications are created, little gains are being made, but drastic new strategies will likely have to wait until we have a better grasp of the disease's still poorly known biochemical basis[20].

5 Classification of Antipsychotic Drugs

- **First-Generation ('Typical') Antipsychotics:** Chlorpromazine, Haloperidol, Fluphenazine, Flupentixol, Clopenthixol
- **Second-Generation ('Atypical') Antipsychotics:** Clozapine, Risperidone, Sirtinol, Quetiapine, Amisulpride, Aripiprazole, Zotepine

6 Pharmacological Effects of Antipsychotic Drugs

In experimental animals, antipsychotic medications have a wide range of behavioural effects; yet no single test can clearly differentiate them from other psychotropic drug classes. Larger doses of antipsychotic medications promote catalepsy, a condition in which an animal remains immobile even when placed in an abnormal position, and they also decrease spontaneous motor activity. While these medications' propensity to cause catalepsy is similar to extrapyramidal symptoms, their inhibition of amphetamine-induced hyperactivity is similar to their antipsychotic effects. Extrapyramidal actions are linked to dopamine inhibition in the striatonigral pathway, whereas antipsychotic effects most likely reflect D2-receptor antagonism in the mesocortical/mesolimbic route[21, 22].

As a result of their action on D2-receptors, all first-generation antipsychotic medications prevent amphetamine-induced behavioural alterations. Certain atypical medications are less active in these models, as well as in the catalepsy model, since they have less activity on D2-receptors. However, in conditioned avoidance tests, they are just as effective as the earlier medications. Furthermore, both conventional and non-traditional medications lessen the hyperactivity brought on by phencyclidine, a glutamate antagonist that gives people a schizophrenia-like condition. Therefore, phencyclidine and conditioned avoidance tests in animals are used to predict antipsychotic action in people[23].

6.1 Mechanism of Action

The D1 type, which includes D1 and D5, and the D2 type, which includes D2, D3, and D4, are the two functional classes into which the five subtypes fall. The main mechanism behind the therapeutic benefits of antipsychotic drugs is D2-receptor blockade. As previously mentioned, around 80% of D2-receptors must be blocked for antipsychotic effects to occur. The suppression of amphetamine-induced stereotypic behaviour and apomorphine-induced turning behaviour in experimental rats with unilateral striatal lesions is indicative of antagonism at D2-receptors. By preventing a radioactive D2 antagonist, such as spiroperidol, from attaching to pieces of brain membrane, these in vivo effects are replicated in vitro[24].

While some of the more recent medicines (such as sulpiride, amisulpride, and remoxipride) are extremely selective for D2-receptors, the first-generation drugs exhibit some preference for D2 over D1-receptors. Clozapine has a strong affinity for D4 but is somewhat non-selective for D1- and D2-.24. The electrical activity of midbrain dopaminergic neurons in the substantia nigra and ventral tegmentum, as well as the release of dopamine in areas with dopaminergic nerve terminals, is first increased and then decreased by all antipsychotic medications in animal experiments. Variations in dopamine receptor expression may be the cause of these changes. The mesolimbic/mesocortical dopamine pathways are expected to be affected by antipsychotic effects, whereas the nigrostriatal pathways are thought to be affected by antipsychotic drugs' unwanted motor side effects[25].

Antipsychotic medications block receptors instantly, but like many neuroactive substances, they require weeks to start working. Chronic administration of antipsychotic medications causes a brief rise in dopaminergic cell activity that is followed by inhibition after roughly three weeks, at which point both the biochemical and electrophysiological indicators of activity start to decrease[26].

Proliferation of dopamine receptors, as seen by a rise in haloperidol binding, is another delayed impact of long-term antipsychotic medication use. This phenomenon is similar to denervation super sensitivity in terms of pharmacological sensitivity to dopamine. It is unclear how these delayed effects work and how they relate to the clinical response. Some antipsychotic medications have a high affinity for 5-HT2 and/or D4 receptors, whereas others exhibit different patterns of selectivity in their receptor-blocking activities. Despite a lot of good debate, it is still unclear how their receptor specificity relates to their functional and therapeutic effects[27].

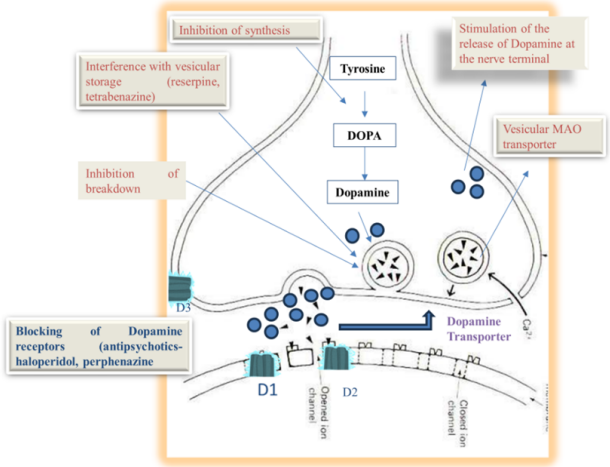

Fig. 2: Mechanism of action of Antipsychotic Drugs

7 Phytocompounds having anti-psychotic property

All sections of plants, but especially flowers, contain alkaloids. These are mostly helpful in the treatment of various neurodegenerative illnesses[28]. By altering acetylcholine concentrations, raising GABA, blocking NMDA receptors, exhibiting anti-oxidant and anti-amyloid properties, and averting neuro-inflammation, these phytochemicals are beneficial against schizophrenia. Nowadays, a number of alkaloids are being studied for their potential to treat schizophrenia. Pyridine alkaloid arecoline has demonstrated muscarinic receptor affinity as a cholinergic agonist and has been found to alleviate cognitive symptoms in schizophrenia patients. In order to lessen memory impairment, it also has antioxidant properties and keeps the cerebral white matter from demyelinating29.

Glycosides are another type of phytocompound with anti-psychotic properties. The "offense and defence" components of plants are glycosides, which are secondary metabolites. By boosting vesicular glutamate transporter 2 in the cingulate gyrus region, bacosides A and B from *Bacopa monnieri* have been demonstrated to mitigate cognitive deficits in the schizophrenia model[30].

Sulforaphane is one example of an isothiocyanate that exhibits antioxidant action via boosting electrophilic response elements, detoxifying phase 2 enzymes, and activating the Nrf2 pathway to exhibit antipsychotic activity. Hypericin, also known as naphthodianthrone, has antioxidant properties. Since it inhibits D3/D4 receptors, it is one of the possible drugs for treating schizophrenia[31].

The byproducts of phytosterol oxidation, oxy phytosterols and phytosterols, are naturally produced by a wide variety of plants. Exposure to these natural agents is rising as a result of an increase in the consumption of plant-based foods boosted with phytosterol and oxy phytosterol[32]. By reducing oxidative stress and inflammation and modifying dopaminergic, acetyl cholinergic, and GABAergic neurotransmission, it controls psychosis[33].

GABA-A receptors and glycinergic activity are inhibited by the sesquiterpene tutin. Furthermore, the glutamate and dopamine pathways are impacted by the monoterpenoid 1,8 cineole. Clinical trials for schizophrenia are effectively examining caryophyllene, a sesquiterpene that is derived from essential oils and acts as a phytocannabinoid[34].

Safranal and crocins, the active compounds in saffron (*Crocus sativus* L.), have shown considerable promise in treating a variety of central nervous system disorders, such as depression, anxiety, and memory loss[35]. By regulating brain-derived neurotrophic factor (BDNF) in the hippocampus, a carotenoid known as crocin has shown promise as an antipsychotic drug. Crocins, at doses of 15–50 mg/kg, reduced the memory impairment, hypermotility, and social isolation that rats suffered from ketamine, according to mounting preclinical studies[36].

Alpha asarone, an essential oil belonging to the polypropanoids class, has anti-schizophrenic properties because it inhibits dopamine D2 and/or D1 receptors. The amino acid glycine decreased the unpleasant symptoms of schizophrenia in a human open trial. It has been shown to be helpful against negative symptoms, treatment-resistant schizophrenia, and cognitive deficits when taken as an adjuvant to other medical therapy[37]. Another amino acid that reduces schizophrenia symptoms is leucine, which works on dopaminergic receptors[38].

8 Conclusion

The treatment of mental illness through both natural and synthetic drugs offers a multifaceted approach to managing and alleviating symptoms. Natural phytocompounds can complement conventional treatments by providing holistic support and minimizing side effects. Meanwhile, synthetic drugs, including various classes of antidepressants and antipsychotics, are pivotal in offering targeted relief and stabilizing mood disorders through precise mechanisms. Combining these approaches can enhance therapeutic outcomes, with natural treatments potentially reducing the reliance on higher doses of synthetic drugs and improving overall well-being. However, patients must collaborate closely with healthcare providers to personalize therapies to their specific needs, establishing a balanced and effective strategy for managing mental health disorders.

References

1. Calabrese J, Al Khalili Y, Shaheen K. *Psychosis (nursing)*. 2023 May. StatPearls Publishing.
2. Adityanjee, Aderibigbe YA, Theodoridis D, Vieweg WV. Dementia praecox to schizophrenia: The first 100 years. *Psychiatry and Clinical Neurosciences*. 1999;53(4):437-448. Available from: 10.1046/j.1440-1819.1999.00584.x
3. Orsolini L, Pompili S, Volpe U. Schizophrenia: A Narrative Review of Etiopathogenetic, Diagnostic and Treatment Aspects. *Journal of Clinical Medicine*. 2022;11(17):5040. Available from: 10.3390/jcm11175040
4. Blakemore SJ, Frith CD. Functional Neuroimaging Studies of Schizophrenia. *Brain Mapping: The Disorders*. 2000;:523-544. Available from: 10.1016/b978-012481460-8/50024-x
5. Brown AS, Derkits EJ. Prenatal Infection and Schizophrenia: A Review of Epidemiologic and Translational Studies. *American Journal of Psychiatry*. 2010;167(3):261-280. Available from: 10.1176/appi.ajp.2009.09030361
6. Cannon TD. Neurodevelopmental influences in the genesis and epigenesis of schizophrenia: An overview. *Applied and Preventive Psychology*. 1998;7(1):47-62. Available from: 10.1016/s0962-1849(98)80021-8
7. Boksa P. Abnormal synaptic pruning in schizophrenia: Urban myth or reality?. *Journal of Psychiatry and Neuroscience*. 2012;37(2):75-77. Available from: 10.1503/jpn.120007
8. Woods BT. Is Schizophrenia a Progressive Neurodevelopmental Disorder? Toward a Unitary Pathogenetic Mechanism. *American Journal of Psychiatry*. 1998;155(12):1661-1670. Available from: 10.1176/ajp.155.12.1661
9. Jun R, Zhang W, Beacher NJ, Zhang Y, Li Y, Lin DT. Dysbindin-1, BDNF, and GABAergic Transmission in Schizophrenia. *Frontiers in Psychiatry*. 2022;13:876749. Available from: 10.3389/fpsyt.2022.876749
10. Gejman PV, Sanders AR, Duan J. The Role of Genetics in the Etiology of Schizophrenia. *Psychiatric Clinics of North America*. 2010;33(1):35-66. Available from: 10.1016/j.psc.2009.12.003
11. Mei L, Xiong WC. Neuregulin 1 in neural development, synaptic plasticity and schizophrenia. *Nature Reviews Neuroscience*. 2008;9(6):437-452. Available from: 10.1038/nrn2392
12. Brown AS. The environment and susceptibility to schizophrenia. *Progress in Neurobiology*. 2011;93(1):23-58. Available from: 10.1016/j.pneurobio.2010.09.003
13. Singh S, Khanna D, Kalra S. Role of Neurochemicals in Schizophrenia. *Current Psychopharmacology*. 2020;9(2):144-161. Available from: 10.2174/2211556009666200401150756
14. Reynolds GP. Beyond the Dopamine Hypothesis. *British Journal of Psychiatry*. 1989;155(3):305-316. Available from: 10.1192/bjp.155.3.305
15. Meltzer HY, Stahl SM. The Dopamine Hypothesis of Schizophrenia: A Review*. *Schizophrenia Bulletin*. 1976;2(1):19-76. Available from: 10.1093/schbul/2.1.19
16. Seeman P. Dopamine receptors and the dopamine hypothesis of schizophrenia. *Synapse*. 1987;1(2):133-152. Available from: 10.1002/syn.890010203
17. Coyle JT. NMDA Receptor and Schizophrenia: A Brief History. *Schizophrenia Bulletin*. 2012;38(5):920-926. Available from: 10.1093/schbul/sbs076
18. McCutcheon RA, Krystal JH, Howes OD. Dopamine and glutamate in schizophrenia: biology, symptoms and treatment. *World Psychiatry*. 2020;19(1):15-33. Available from: 10.1002/wps.20693
19. Van Berckel BN. Glutamate and Schizophrenia. *Current Neuropharmacology*. 2003;1(4):351-370. Available from: 10.2174/1570159033477026
20. Gardner DM, Baldessarini RJ, Waraich P. Modern antipsychotic drugs: a critical overview. *Canadian Medical Association Journal*. 2005;172(13):1703-1711. Available from: 10.1503/cmaj.1041064
21. Wetchateng T, Piyabhan P. EPA-0117 – The use of bacosides a and b to prevent a cognitive deficit in schizophrenia rat models resulting in increased vesicular glutamate transporter 2 (VGLUT2) in the cingulate gyrus. *European Psychiatry*. 2014;29:1. Available from: 10.1016/s0924-9338(14)77591-1
22. Shadkami F, Jones ADs. Nontargeted Profiling of Specialized Metabolites of*Digitalis purpurea*with a Focus on Cardiac Glycosides. *ACS Symposium Series*. 2012;:185-205. Available from: 10.1021/bk-2012-1093.ch011
23. Yadav M, Jindal DK, Dhingra MS, Kumar A, Parle M, Dhingra S. Protective effect of gallic acid in experimental model of ketamine-induced psychosis: possible behaviour, biochemical, neurochemical and cellular alterations. *Inflammopharmacology*. 2018;26(2):413-424. Available from: 10.1007/s10787-017-0366-8
24. Jie F, Yang X, Wu L, Wang M, Lu B. Linking phytosterols and oxyphytosterols from food to brain health: origins, effects, and underlying mechanisms. *Critical Reviews in Food Science and Nutrition*. 2022;62(13):3613-3630. Available from: 10.1080/10408398.2020.1867819
25. Kucerova J, Tabiova K, Drago F, Micale V. Therapeutic Potential of Cannabinoids in Schizophrenia. *Recent Patents on CNS Drug Discovery*. 2014;9(1):13-25. Available from: 10.2174/1574889809666140307115532
26. Georgiadou G, Grivas V, Tarantilis PA, Pitsikas N. Crocins, the active constituents of Crocus Sativus L., counteracted ketamine–induced behavioural deficits in rats. *Psychopharmacology*. 2014;231(4):717-726. Available from: 10.1007/s00213-013-3293-4
27. Sun X-J, Zhao X, Xie J-N, Wan H. Crocin alleviates schizophrenia-like symptoms in rats by upregulating silent information regulator-1 and brain derived neurotrophic factor. *Comprehensive Psychiatry*. 2020;103:152209. Available from: 10.1016/j.comppsych.2020.152209
28. Heresco-Levy U, Ermilov M, Lichtenberg P, Bar G, Javitt DC. High-dose glycine added to olanzapine and risperidone for the treatment of schizophrenia. *Biological Psychiatry*. 2004;55(2):165-171. Available from: 10.1016/s0006-3223(03)00707-8
29. Leiderman E, Zylberman I, Zukin SR, Cooper TB, Javitt DC. Preliminary investigation of high-dose oral glycine on serum levels and negative symptoms in schizophrenia: an open-label trial. *Biological Psychiatry*. 1996;39(3):213-215. Available from: 10.1016/0006-3223(95)00585-4
30. Hudepohl NS, Nasrallah HA. Antipsychotic drugs. *Handbook of Clinical Neurology*. 2012;:657-667. Available from: 10.1016/b978-0-444-52002-9.00039-5
31. Miyamoto S, Merrill DB, Fredrik Jarskog L, Wolfgang Fleishhacker W, Marder SR, Lieberman JA. Antipsychotic Drugs. *Psychiatry*. 2015;:2088-2128. Available from: 10.1002/9781118753378.ch104
32. Strange PG. Antipsychotic Drugs: Importance of Dopamine Receptors for Mechanisms of Therapeutic Actions and Side Effects. *Pharmacological Reviews*. 2001;53(1):119-133. Available from: 10.1016/s0031-6997(24)01483-2
33. Palermo-Neto J. Dopaminergic systems: dopamine receptors. *Psychiatric Clinics of North America*. 1997;20(4):705-721. Available from: 10.1016/s0193-953x(05)70341-5
34. Schaus JM, Clemens JA. Chapter 5. Dopamine Receptors and Dopaminergic Agents. *Annual Reports in Medicinal Chemistry*. 1985;:41-50. Available from: 10.1016/s0065-7743(08)61031-3
35. Meltzer HY. The Mechanism of Action of Novel Antipsychotic Drugs. *Schizophrenia Bulletin*. 1991;17(2):263-287. Available from: 10.1093/schbul/17.2.263
36. Davis JM, Casper R. Antipsychotic Drugs. *Drugs*. 1977;14(4):260-282. Available from: 10.2165/00003495-197714040-00002
37. Porsolt RD, Moser PC, Castagné V. Behavioral Indices in Antipsychotic Drug Discovery. *The Journal of Pharmacology and Experimental Therapeutics*. 2010;333(3):632-638. Available from: 10.1124/jpet.110.166710
38. Rang HP, Dale MM, Ritter JM, Flower RJ. Rang and Dale's Pharmacology. 6th edition Churchill Livingstone Publishers. 2007;:545-556. Available from: 10.1016/b978-0-443-06911-6.50043-8