



Review Article

Use of Nutraceuticals in Psychiatry

Himasree Thakuria¹, Deepanjali Medhi¹

¹Department of Psychiatry, Gauhati Medical College and Hospital, Guwahati, India

***Corresponding author:**

Dr. Himasree Thakuria,
MBBS, Department of
Psychiatry, Gauhati Medical
College and Hospital,
Guwahati, India.

himasreethakuria@gmail.com

Received: 24 October 2023

Accepted: 27 December 2023

Epub Ahead of Print :
10 February 2024

Published: ****

DOI

10.25259/ABMH_21_2023

Quick Response Code:



ABSTRACT

The term “nutraceutical” refers to a food or part of a food providing health or medical benefits that include prevention and treatment of a disease. It reinforces the concept of health in everyday diet as a part of nourishment and serves to functionalize food. Archaeological evidence shows that people began using plants as medicine some 60,000 years ago. Nutraceuticals are said to take part in the signal transduction pathways, maintenance of mitochondrial integrity, gene expression, and to have antioxidant effects. There are a number of nutraceuticals currently being used in the treatment of psychiatric disorders, with positive results. However, they are not patent-protected and not government-sanctioned; thus, there is a lack of regulation on their production. Nevertheless, the integration of nutraceuticals into psychiatric care represents a promising avenue for enhancing mental health treatment.

Keywords: Nutraceuticals, Food, Phytomedicines, Market, Mental health treatment

“Optimum nutrition is the medicine of tomorrow.”

----- Dr. Linus Pauling

INTRODUCTION

“Nutraceuticals” are currently gaining wide popularity in the treatment of multiple disorders across multiple specialties of medical science. The word “nutraceutical” comes from two terms, namely, “nutrition” and “pharmaceutical”. Coined by the American chairman and founder of the “Foundation for Innovation in Medicine” “Dr. Stephen De Felice” in 1989, the term has no regulatory definition. However, in Dr. Stephen’s words, “nutraceutical refers to a food or part of a food providing health or medical benefits that includes prevention and/or treatment of a disease”.^[1]

Nutraceuticals are different from dietary supplements because in addition to nutritional supplementation of diet, they also aid in the prevention and treatment of a disease.^[1] It reinforces the concept of health in everyday diet as a part of nourishment and serves to functionalize food. These products have been successfully used in the treatment of numerous diseases, including cancer, diabetes, heart diseases, and also many psychiatric and neurological disorders. In terms of mental health, they have yielded positive results in a number of studies.

NUTRACEUTICALS IN HISTORY

From time immemorial, there has been a relation between food and medicine as a part of classical traditions. Archaeological evidence shows that people began using plants as medicine some

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2024 Published by Scientific Scholar on behalf of Academic Bulletin of Mental Health

60,000 years ago, dating back to the Paleolithic period.^[2] The Chinese, Sumerians, and the Egyptians have used food as medicine. Phytomedicines are plant preparations that have been used to treat many ailments for centuries. Hippocrates recognized the importance of the relationship between food and health and emphasized on the differences in diseases due to varied nutritional habits. The father of modern medicine quoted “If we could give each person the correct amount of exercise and nourishment, not very little and not very much, we would have the safest way to health.” The Indians have also, since ages, been dependent on traditional or folklore medicines derived from food products to treat acute and chronic conditions. The Ayurveda system of medicine, which developed in India between 2500 and 500 BC, has found its mention in the Vedas and Holy scriptures and believes in rejuvenating the body through nutrition and a healthy diet.^[3]

With the rise of the modern nutraceuticals market first in Japan in the 1980s, the public health authorities have always considered nutraceuticals as a necessary tool in preventing and treating diseases so as to ensure longer, better, and healthier lives. Nutritional supplements started gaining importance in the treatment of psychiatric disorders around the mid-1990s. The mechanism of action of these compounds is not completely understood yet. However, they are said to play a role in signal transduction pathways, maintenance of mitochondrial integrity, gene expression, and to have antioxidant effects.

COMMONLY USED NUTRACEUTICALS

Some of the nutraceuticals used commonly in the treatment of psychiatric disorders include:

Ashwagandha or the **Indian White Cherry**, native to India, is a good antioxidant and has been used for its anxiolytic properties. Withaferin A, which is extracted from the ashwagandha plant, appears to play a role in the treatment of Alzheimer’s disease. It is said to reduce beta amyloid aggregation and inhibit the accumulation of tau proteins.^[4]

Sarpagandha or **Reserpine** is mentioned in the works of Charaka as an antidote to snake bites and insect stings. The plant is also known as Pagal-ki-dawa, as it is believed that a mentally ill person gets cured of his or her insanity by eating the roots. Commonly indicated as an anti-hypertensive after its isolation in 1952, reserpine has also been used to treat psychotic symptoms and agitation due to its vesicular monoamine transporter (VMAT) blocking properties, thus blocking the uptake and storage of norepinephrine and dopamine into synaptic vesicles.^[5]

The **Holy basil** or the **Tulsi**, which is native to the tropics, is known for its aroma and is commonly used to treat the

common cold or any stomach disorders. As per the *Journal of Ayurveda and Integrative Medicine*, holy basil has anxiolytic properties comparable to diazepam and antidepressant actions similar to antidepressant drugs. Regular use of tulsi is said to calm the mind and also to have positive effects on cognition and memory.^[6]

Chewing Betel nuts is still one of the most prevalent cultural activities in the society. Betel nut or areca nut has central nervous system (CNS) stimulating effects and can improve one’s mood.

Kava has also been used as a traditional medicine in ceremonies for relaxation. It is found in the islands of the South Pacific. Data suggest that the kava lactones act by alteration of gamma aminobutyric acid (GABA) channels^[7] and its enantiomeric forms inhibit the reuptake of Norepinephrine and Dopamine.^[8] Kava symptomatically reduces symptoms of anxiety when taken orally. It has sedative and hypnotic properties. Usual doses are 600–800 mg/day. It can, however, potentiate the actions of CNS depressants like alcohol causing confusion. And there is always an associated risk of hepatotoxicity.

Atropa belladonna or the **deadly nightshade**, has anxiolytic properties at 0.05–0.10mg/day; however, it is poisonous and has a strong smell. **Nux vomica** or **poison nut**, at the dose of 0.002–0.005g/day, has antidepressant actions and is lethal at higher doses.

Passion flower has its mention in folklore since long due to its anxiolytic properties. The aerial parts of the plant have been used for its anxiolytic, sedative, and antispasmodic properties. The sedative and anxiolytic properties at 4–8 g/day are related to a specific component called chrysin, which interacts with GABA receptors like benzodiazepines.^[9]

Valerian is an important folk medicine in European and American countries. Its root can be used as flavoring for some beverages and food, and its use primarily lies in the treatment of anxiety and insomnia.^[10] One to two grams per day, is the usual dose, and it is to be avoided with the concomitant use of CNS depressants.

St. John’s wort has been used since biblical times and has found mention in the ancient tales. At that time, it was probably used to treat anxiety and depressive symptoms. Current research suggests that the extracts of St. John’s wort contain compounds named hyperforin and hypericin, which have serotonin reuptake-blocking properties.^[11] A recent Cochrane review has found hypericum to be somewhat effective but not superior to placebo in major depression.^[12] It is recommended to be used at a dosage of 100–950 mg/day. In a study done by Fava et al. in 2005, it was found to be slightly superior to Fluoxetine.^[13] However, there remains

a risk of serotonin syndrome if used together with selective serotonin reuptake inhibitor (SSRIs). It is also an inducer of CYP 450 enzymes.

Ginkgo Biloba, native to the Asian continent, was used in China in ancient times for age-related memory problems. It has been investigated as an adjunct for the management of psychiatric disorders like schizophrenia, depression, and attention deficit hyperactivity disorder and for protection against neural damage caused by antipsychotics. Studies say that there is positive evidence for the effectiveness of ginkgo biloba in the treatment of “cerebral insufficiency.”^[14] It is used at a dose of 120–240 mg/day.

S-adenosylmethionine, which is an active metabolite of L-methionine, is useful for the synthesis and activation of hormones, serotonin, and norepinephrine due to its role in the transmethylation reactions. It can potentially increase the available levels of the monoamines, thus improving one's mood. A meta-analysis found S-adenosylmethionine to be 17–38% more effective compared to placebo, making it comparable to the average antidepressant.^[15] Dosage usually starts at 100–800 mg/day and can be increased up to 1600 mg/day.

Inositol has proven to be superior to placebo in a study, which compared 12 g of inositol and placebo in patients with depressive disorder.^[16] A combination based on SAM and inositol for oral use has been patented as a possible treatment for panic symptoms and depression.^[17] Myoinositol, which is the nutritionally active form of inositol, has been used in the treatment of panic attacks and obsessive compulsive disorder (OCD) too at 12g/day in divided doses.

Acetyl L carnitine, rich in meat, poultry, fish, and dairy products, has antioxidant properties and is used to treat Alzheimer's disease, other cognitive impairments, and in neurodevelopmental disorders. It prevents oxidative damage to the brain^[18] and has neuroprotective effects. It is used at 500 mg–2 g daily in divided doses. It has been used in depression in geriatric patients and also in Down's syndrome.

Recent research has revealed that **Vitamin B12** deficiency is associated with depression as Vitamin B12 is involved in the production of S-adenosylmethionine. It has also long been known that pernicious anemia has neuropsychiatric manifestations and sequelae.

Vitamin B9 and its metabolites also have a significant role in the regulation of the synthesis of monoamines (dopamine, serotonin, and norepinephrine) and in the formation of S-adenosylmethionine. Studies have found that major depressive disorders tend to be associated with lower levels of folic acid in comparison to the healthy population.^[19] Because response to antidepressants is poor in those with low

folate levels, it is often used as an adjunctive treatment for depression in combination with SSRIs. It is given as 15 mg/day and is considered as a medical food by the food and drug administration (FDA).

Omega-3-fatty acids are frequently used in treating psychiatric disorders. They are rich in cold water fish such as salmon and halibut. Used more commonly in cases of dementia and cognitive impairment, a Cochrane meta-analysis of recent studies found that there is evidence of the efficacy of the compounds as an adjunctive in the treatment of bipolar depression.^[20] There is role of omega-3 polyunsaturated fatty acids (PUFAs) in neuronal growth and integrity, their antioxidant protective effect works on the cell membranes, and there is potential neurochemical mechanisms associated with Alzheimer-specific pathology. Doses vary from 1 to 4 g/day. They have been used in the treatment of Attention Deficit Hyperactivity disorder and learning disorders too. Another report also suggests that affective disorders may be related to a deficiency of Omega-3-fatty acid.^[21] Fish oil is said to have a beneficial role in bipolar disorder.

L-Carnosine has gained importance in the treatment of Autism Spectrum Disorder, Attention deficit hyperactivity disorder (ADHD), Alzheimer's dementia, Vascular dementia, Major depressive disorder, OCD, and Schizophrenia. Carnosine facilitates the exportation of lactate from the cells and provides metabolic support for the neurons by buffering protons. It also regulates anti-inflammation activities and reduces reactive oxygen and nitrogen species-related toxicity.

Alpha lactalbumin found in human milk has proven to elevate the mood and also decreases the levels of excess cortisol in subjects who are vulnerable to stress. In experimental rats, it causes an anxiolytic effect and increases the serotonin turnover in the hippocampus.^[22]

N acetyl cysteine, used at doses of 1,200–2,400 mg/day, augments SSRI and has been successfully used in the treatment of depression and OCD as adjunctives. It works by attenuating glutaminergic neurotransmission.^[18] It is also used in the treatment of Trichotillomania.

Glycine activates N-Methyl-D-aspartic acid (NMDA) receptors and may help treat depression by facilitating excitatory neurotransmission in the brain.^[18] It is used at a dosage of 40–90 g/day for schizophrenia and 1 g/day as a supplement.

Citicoline is a choline donor useful for the synthesis of brain phospholipids and acetylcholine.^[18] It is present in nature in high concentrations in meats and animal products such as the liver, brain, and is useful for treating Alzheimer's disease and ischemic brain damage.

Current use of nutraceuticals

The nutraceutical market is growing at an exponential rate and is expected to become an integral part of disease management. As per reports, the Global Nutraceuticals Market Size was USD 353 billion in 2022 and will reach USD 700 billion by 2030 with a compound annual growth rate (CAGR) of 9.4%.^[23] The Indian nutraceutical market also continues to experience significant growth, reaching a valuation of USD 5404.18 million in 2022, and is expected to maintain a strong CAGR of 11.77% till 2028.^[24]

Use of nutraceutical products and dietary supplements for treating psychiatric disorders could possibly encourage more and more people to seek treatment for mental disorders due to the elimination of the stigma associated with the use of typical psychiatric medications. However, it is of utmost importance to keep in mind that these products have not been subjected to much clinical research, and therefore, there remains a chance of having drug interactions with other prescription or nonprescription drugs. Also, these products themselves can cause toxicity many times. There are records of approximately 25,000 hospital admissions in the United States attributed to the adverse effects of nutraceuticals.^[25] Unlike pharmaceuticals, nutraceuticals are not patent-protected and not government-sanctioned; thus, there is a lack of regulation on their production. This may reduce the effectiveness and safety of these products.

CONCLUSION

The integration of nutraceuticals into psychiatric care represents a promising avenue for enhancing mental health treatment. As research continues to unveil the appropriate connection between mental health and these products, incorporating them into prescriptions can provide complementary support to traditional psychiatric interventions. It is crucial to approach this integration with a balanced perspective. The use of nutraceuticals in the evolving landscape of psychiatry holds enormous potential to contribute meaningfully to comprehensive and personalized mental health care.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

Dr. Deepanjali Medhi is on the Editorial Board of the Journal.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

- DeFelice SL. FIM Rationale and Proposed Guidelines for the Nutraceutical Research and Education Act (NREA), November 10, 2002. Foundation for Innovation in Medicine. Retrieved from <http://www.fimdefelice.org> [Last accessed 2024 January 20].
- Alamgir A.N.M. Introduction. In: Therapeutic Use of Medicinal Plants and their Extracts. Progress in Drug Research: Springer; 2017;Volume 1:73.
- Pandey MM, Rastogi S, Rawat AK. Indian Traditional Ayurvedic System of Medicine and Nutritional Supplementation. Evid Based Complement Alternat Med 2013;376327.
- Mikulska P, Malinowska M, Ignacyk M, Szustowski P, Nowak J, Pesta K, *et al.* Ashwagandha (*Withania Somnifera*) - Current Research on the Health-promoting Activities: A Narrative Review. Pharmaceutics 2023;15:1057.
- Yaffe D, Forrest LR, Schuldiner S. The Ins and Outs of Vesicular Monoamine Transporters. J Gen Physiol 150:671–82.
- Cohen Marc Maurice. Tulsi - *Ocimum Sanctum*: A Herb for all Reasons. J Ayurveda Integr Med 2014;5:251–9.
- Jussofie A, Schmitz A, Hiemke C. Kavapyronr Enriched Extract from Piper Methysticum as Modulator of the GABA Binding Site in Different Regions of Rat Brain. Psychopharmacology (Berl) 1994;116:469–74.
- Baum SS, Hill R, Rommelspacher H. Effect of Kava Extract and Individual Kavapyrones on Neurotransmitter Levels in the Nucleus Accumbens of Rats. Prog Neuropsychopharmacol Biol Psychiatry 1998;22:1105–20.
- Wolfman C, Viola H, Paladini A, Dajas F, Medina JH. Possible Anxiolytic Effects of Chrysin, a Central Benzodiazepine Receptor Ligand Isolated from *Passiflora Caerulea*. Pharmacol Biochem Behav 1994;47:1–4.
- Chiappedi Matteo, Vincenzi Silvia de, Bejor Maurizio. Nutraceuticals in Psychiatric Practice. Recent Patents on CNS Drug Discovery 2012;7:163–72.
- Bennett DA Jr, Phun L, Polk JF, Voglino SA, Zlotnik V, Raffa RB. Neuropharmacology of St. John's wort (*Hypericum*). Ann Pharmacother 1998;32:1201–8.
- Linde K, Berner MM, Kristin L. St John's Wort for Major Depression. Cochrane Database Syst Rev 2008;2008:CD000448.
- Fava M, Alpert J, Nierenberg AA, Mischoulon D, Otto MW, Zajecka J, *et al.* A Double-blind, Randomized Trial of St. John's Wort, Fluoxetine, and Placebo in Major Depressive Disorder. J Clinical Psychopharmacology 2005;25:441–7.
- Kleijnen J, Knipschild P. Ginkgo Biloba for Cerebral Insufficiency. Br J Clin Pharmacol 1992;34:352–8.

15. Bressa GM. S-Adenosyl-L-methionine (SAME) as Antidepressant: Meta-analysis of Clinical Studies. *Acta Neurol Scand Suppl* 1994;154:7–14.
16. Levine J, Barak Y, Gonzalves M, Szor H, Elizur A, Kofman O, *et al.* Double-blind, Controlled Trial of Inositol Treatment of Depression. *Am J Psychiatry* 1995;152:792–4.
17. Seneci A, Giovannone D, Zio C. Compositions for Oral use Based on S-Adenosylmethionine and a Process for their Preparation. US20070260660 (2007)
18. Boland Robert, Verduin Marcia L. Kaplan & Sadock's Synopsis of Psychiatry, Twelfth Edition. PA: Wolters Kluwer; 2022.
19. Papakostas GI, Petersen T, Lebowitz BD, Mischoulon D, Ryan JL, Nierenberg AA, *et al.* The Relationship Between Serum Folate, Vitamin B12, and Homocysteine Levels in Major Depressive Disorder and the Timing of Improvement with Fluoxetine. *Int J Neuropsychopharmacol* 1999;51: 527–34.
20. Montgomery P, Richardson Alexandra J. Omega-3 Fatty Acids for Bipolar Disorder. *Cochrane Database Syst Rev* 2008;CD005169.
21. Parker Gordon, Gibson Neville A, Brotchie Heather, Heruc Gabriella, Rees Anne-Marie, Hadzi-Pavlovic Dusan. Omega-3 Fatty Acids and Mood Disorders. *Am J Psychiatry* 2006;163:969–78.
22. Orosco M, Rouch C, Beslot F, Fuerte S, Regnault A, Dauge V. A-lactalbumin-enriched Diets Enhance Serotonin Release and Induce Anxiolytic and Rewarding Effects in the Rat. *Behav Brain Res* 2004;148:1–10.
23. “Nutraceuticals Market Size, Share Global Analysis Report, 2023–2030” (2023) Retrieved from <https://www.fnfresearch.com/nutraceuticals-market/> [Last accessed 2023 October 17]
24. “India Nutraceuticals Market by Application” (2023) Retrieved from <https://www.marketresearch.com/TechSci-Research-v3895/India-Nutraceuticals-Application-Functional-Beverages-33553911/> [Last accessed 2023 October 17]
25. Martin JJ, Pedersen Kim B, Watt James. Adverse Effects of Nutraceuticals and Dietary Supplements. *Annu Rev Pharmacol Toxicol* 2018;58:583–601.

How to cite this article: Thakuria H, Medhi D. Use of Nutraceuticals in Psychiatry. *Acad Bull Ment Health*. doi: 10.25259/ABMH_21_2023