Review Article **Open Access**

FFIMH
Functional Food Ingredients and Mental Health

Sectional study of nutritional psychology to identify the significance of the connection between mental health and nutraceutical functional ingredients

Rajashri Kanad Gutte[1], Vijaya Deshmukh[2]

[1] Institute of Management & Research, MGM university, Aurangabad, MH India 431001; [2]Institute of Management & Research, MGM University, Aurangabad, MH India 431001

***Corresponding Author**: **Rajashri Kanad Gutte,** Research Scholar, Institute of Management & Research, MGM university, Aurangabad, MH India 431001.

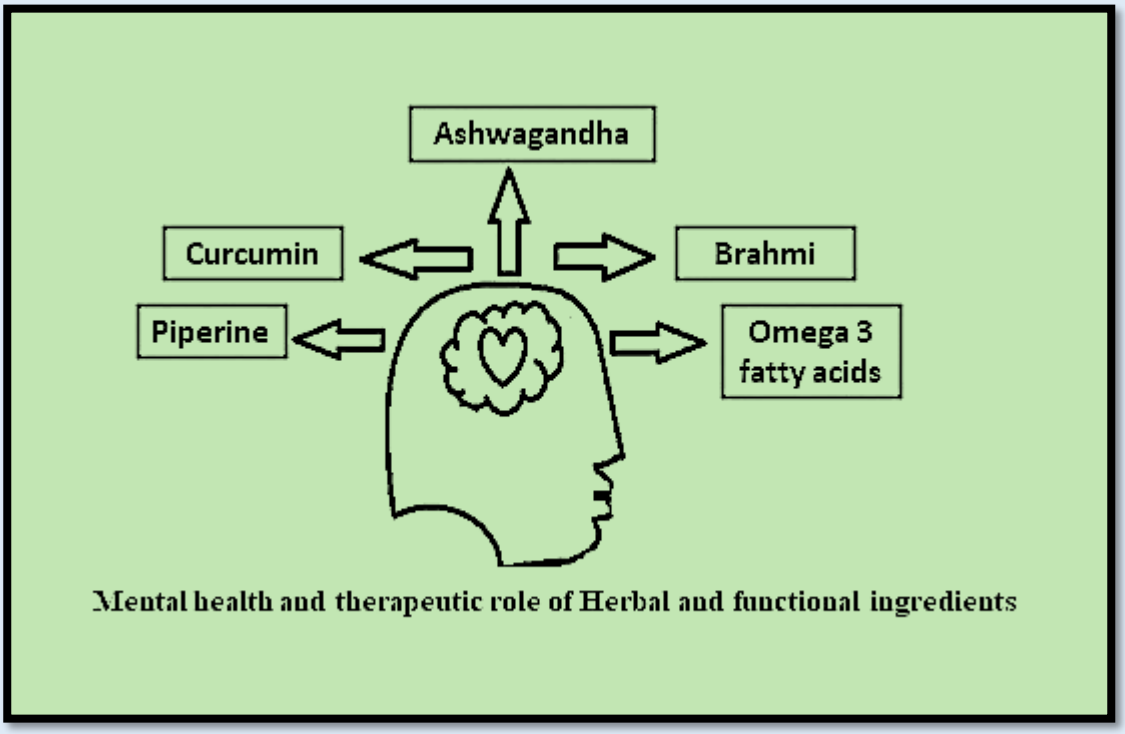
Submission Date: April 6th, 2023; **Acceptance Date:** May 9th, 2023; **Publication Date:** May 11th, 2023

Please cite this article as: Gutte R. K., Deshmukh V. Sectional study of Nutritional Psychology to identify the significance of the connection between mental health and nutraceutical functional ingredients. *Functional Food Ingredients and Mental Health.* 2023; 1(5): 1-13. DOI: https://www.doi.org/10.31989/ffimh.v1i5.1100

ABSTRACT

An individual's good health is often linked to a well-balanced mind, as stated in a famous quote that highlights the impact of the mind on one's overall well-being. The primary goal of this study is to delve deeper into the field of nutritional psychology and functional food ingredients and examine their potential positive impact on mental health. However, the scope of the study is restricted to only five ingredients that have been highly recommended for treating mental health issues. To write this narrative research, we focused on creating comprehensive analysis and review articles. After conducting a thorough literature survey, we assessed the herbal and functional food ingredients commonly used to alleviate psychiatric symptoms or disorders. The most significant findings were related to Omega-3 fatty acids, *Bacopa monnieri* from Brahmi, *Withaniasomnifera* from Ashwagandha, Curcumin from turmeric (*Curcuma longa*) and Piperine from black pepper. The anti-inflammatory and antioxidant properties of these foods showed positive results in preventing and treating mental health problems. Additionally, these foods can promote cell generation in the body. Neurotransmitters such as acetylcholine and monoamines saw significant improvements with the intake of these foods. Hence, it is evident that incorporating these foods into our diet and utilizing them for the development of drugs and nutraceuticals in the foreseeable future can assist in treating various psychiatric issues.

Keywords: Herbal and Functional foods, Mental health, Nutraceutical Ingredients, Nutritional psychology, etc



INTRODUCTION

In contrast to merely being free from illness or infirmity, the World Health Organization (WHO) defines health as a state of full physical, mental, and collective well-being (WHO 2001, p.1) as an essential component of this definition is mental health. WHO defines mental health as a condition of well-being in which a person is conscious of their abilities, able to handle life's typical stresses, work productively and efficiently, and contribute to their community. (WHO 2001a, p.1). [1]

Nutritional psychology is the field of Psychology in which Nutrition will help us to explore the effects of diet and functional nutrients on our physical and mental health. Notably, the relationship between the positive impact of nutraceutical functional food in modifying and maintaining mental health is positively significant.

An intriguing new method for addressing problems that affect our bodies and mental health daily is nutrition psychology. The benefits we receive from the food we consume are more significant than the benefits we anticipate. The study of how nutrients impact mood and behavior is known as nutritional psychology. This field examines the relationship between nutrients or functional ingredients and our internal experience highlighting the bio-physiological mechanisms according to its recommended daily allowances when taken within the limit. [2] Adults must consume appropriate balanced healthy food every day that is rich in natural nutritional ingredients, including enough vital high-quality proteins, amino acids, complex carbohydrates, and vitamins to support adult nutritional needs.

Food supplements have been described as foods and drinks fortified with minerals, vitamins, fatty acids, or protein for purposes of promoting health or preventing disease when included in a regular diet and consumed in typical amounts. The use of herbal and "natural" functional foods to effectively treat mental disorders is

on the rise. Many of these treatment methods are "self-prescribed," though some require a doctor's prescription.

Research on the interconnected links between dietary intake, depression, and anxiety is gathered in the CNP (Centre for Nutritional Psychology which works on the role of diet in supporting mental health) Diet, Depression, and Anxiety Research Category. [3]

WHO estimates that 1 in every 8 people worldwide suffer from a mental disorder. A mental disorder is indicated by a significant clinical impairment in cognition, emotional regulation, or behavior. It is frequently associated with distress or functional limitations in important areas. Mental disorders are also referred to as mental health issues. Anxiety and depressive disorders were the most prevalent mental disorders, affecting 1 in 8 people, or 970 million people worldwide, in 2019. [4] Due to the COVID-19 pandemic, the number of people who suffer from anxiety and depressive disorders significantly increased in 2020. Initial projections indicate a 26% and 28% rise in anxiety and severe depressive disorders, respectively, in just one year. [5]

According to Euromonitor's 2021 Voice of the Consumer: Health and Wellness Survey, modern consumers are most displeased about mental health in the future, followed by diabetes and heart disease. According to Euromonitor, fortified/functional food sales reached $173 billion, and fortified/functional beverages reached $102 billion globally in 2020. Kerry's June 2021 Global Survey (16 countries) found that 42% of consumers worldwide increased their purchases of functional foods and beverages after the pandemic started. According to Innova, the quantity of new functional food and drink launches elevated by 59% between 2016 and 2020. According to the IFIC Food & Health Survey, 2021, energy is the second health aid that American consumers want the most from their foods and beverages, followed by sleep, brain focus (memory, cognition, and focus), and emotional/mental health. [6]

In recent discussions, there has been recognition of the potential benefits that can come from leveraging both modern treatments and natural nutraceutical ingredients to enhance immunity and foster holistic healing. This highlights the importance of ingredients and bioactive components in supporting people's immune systems. [7]

A plethora of research exhibits the interconnections between functional ingredients and all aspects of psychological functioning.

Towards a new mental health landscape: The importance of affecting appetite and satisfaction in "new and beneficial" ways is asserted by many mass-produced food products today. To accomplish this, the primary goal of functional macronutrient substitutes (such as high-intensity sweeteners and fat-replacers) is to assist consumers in enhancing their dietary habits by enabling them to reduce their intake of sugar (17 kJ/g) and/or fat (38 kJ/g), with the short-term goal of controlling energy intake and the long-term goal of weight reduction or weight stability. [8]

To provide a better understanding of nutritional psychology one must study different neurological pathways. Cholinergic, dopaminergic, serotoninergic, and neuroprotective or antioxidant pathways are among the principal neural pathways involved in memory and cognition. [9]

The study of these pathways at the molecular level could be a new revolution in the mental health landscape. The effect of psychosocial stress on biological systems that affect disease pathways is an emerging field of the psychobiology of health and illness. The effectiveness of dietary intervention for reducing the biological response to stress regarding the hypothalamic-pituitary-adrenal (HPA) axis (a major component of the homeostatic response) and sympathetic nervous system has been investigated in

several research including human volunteers and animals. Furthermore, this research has noted enhancements in psychological endpoints including cognitive function, mood, and anxiousness (Mark Hamer et. al. (2005).

The possibilities are endless in this area of psychology for the treatments and therapeutics diagnosed early and on-time treatment is also beneficial for patients and people having a mental illness. [10]

Table 1: Nutraceuticals, their Action, and Adequacy

Nutraceutical Functional Ingredients	**Molecular Action**	**Disorder or symptoms cure**	**Reference**
Omega3 Fatty Acids	Modulate several neurobiological mechanisms that are thought to be involved in the pathophysiology of depression.	Major Depression disorder	11
"Brahmi Saag" (*Bacopa monnieri*) -Bacosides	Increases kinase activity, restores synaptic activity, and eventually improves nerve impulse transmission in the brain to repair injured neurons.	Mental Disorder and neurodegeneration	12
Ashwagandha-Withanoside	It has been discovered that someone, an active metabolite of withanoside IV, phosphorylates the RET (rearranged during transfection) receptor for glial cell-derived neurotrophic factor. improved memory in regular mice	lower morphological plasticity of neurons	12
Curcumin	MAO-A and MAO-B enzyme activity is inhibited by curcumin. The enzyme responsible for norepinephrine, serotonin, and dopamine breakdown is called monoamine oxidase. Curcumin raises the concentration of these neurotransmitters in the synapses by decreasing the activity of the MAO enzyme.	Depression	14

Nutraceutical Functional Ingredients for the Management of Mental Disorders: Recent advancements in our understanding of mental disorders and their molecular mechanisms have indicated that deficiencies in various nutrients such as amino acids, omega-3 fatty acids (O3FAs), vitamins, and minerals are linked to mental illness. [15 and 16] Some of the functional ingredients and their part in mental health are given below.

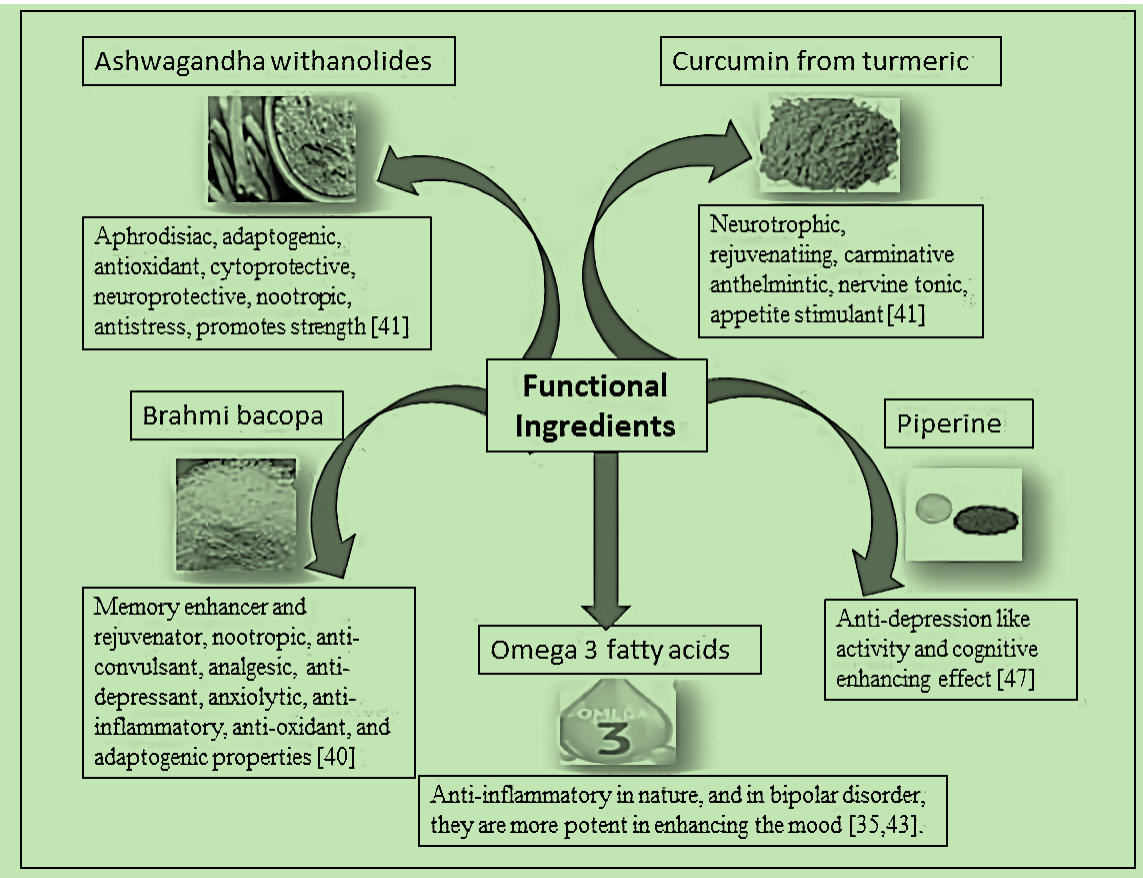


Figure 1: Mental health and therapeutic role of functional ingredients

Omega-3 fatty acids (O3FAs): A sufficient intake of PUFAs (polyunsaturated fatty acids) is essential for brain functioning. The two primary types of PUFAs found in the human body are omega-6 and omega-3 PUFAs. These two groups are formed from the important fatty acid's linoleic acid (LA, 18:2 -6) and alpha-linolenic acid (ALA, 18:3 -3), respectively. [17]They are essential long-chain PUFAs obtained from dietary sources such as marine fish. [18] DHA (Docosahexaenoic acid) and EPA (Eicosapentaenoic acid), found in fish oils, are important n-3 fatty acids linked to a considerable decrease in cardiovascular events in CHD (coronary heart disease) patients. [19] Seaweeds, or edible marine algae, are valuable sources of vitamins, minerals, dietary fiber, long-chain PUFA, protein, and other nutrients. In recent years, many studies have concentrated on marine algae and the components that make them up as nutraceuticals and functional foods for their potential to promote health. This is mostly because of its -3 fatty acids, antioxidants, and other bioactive substances.

Good sources of g-linolenic acid, a type of important n-6 fatty acid, include blackcurrant-seed oil and evening primrose oil.

One of the most encouraging advancements in human nutrition and illness risk reduction over the past three decades is the use of omega-3 oils/long-chain 3 PUFA. Due to its usefulness in the prevention and treatment of mental health issues and neurological function, such as depression and schizophrenia, long-chain 3 PUFA is of significant interest. [20] It also plays a crucial role in the maintenance and expansion of healthy growth, particularly in the brain and retina. [21]

Being anti-inflammatory in nature, Omega 3 fatty acids, in cases of bipolar disorder, are more potent in

enhancing mood. [22 and 23] Epidemiological studies have clearly shown that the prevalence of the onset of a mental disorder decreases with increased consumption of fish. [24 and 25] However, there are many questions about the safety of dietary supplementation with these fatty acids. Several population studies have raised concerns about mortality, cardiovascular incidents, and even cancer. [26] Hydroxytyrosol, one of many phenolics in olives and olive oil, is a potent antioxidant. [27].

Clinical study: It has been investigated how n-3 and n-6 fatty acids affect the stress response in three human involvement studies. In an experiment with 14 healthy volunteers that was random, double-blind, and placebo-controlled, Sawazaki et al. (1999) investigated the impact of fish oil consumption on plasma catecholamine and cortisol responses to a prolonged stress period. During a 9-week assessment period that included 20 stressful medical tests, the participants were given capsules containing either 1•5 g DHA/d or a placebo containing mixed plant oil (a blend of olive oil, rapeseed oil, and soyabean oil). Noradrenaline levels were considerably decreased in the DHA group alone, despite there being no change in adrenaline levels between groups at the start or conclusion of the supplementation period. Surprisingly, however, after the intervention, cortisol levels were considerably lower in the placebo group than in the DHA group. [28]

Brahmi *(Bacopa monnieri):* Ayurvedic works on "Brahmi" (Bacopa monnieri), include "Medhya Rasayana" (a memory booster and rejuvenator) and "Aindra Rasayana" (increasing longevity). It is discovered to have nootropic, anticonvulsant, analgesic, depressive, anxiolytic, anti-inflammatory, antioxidant, and apoptogenic qualities found in the "Charaka Samhita." [9] The triterpenoid saponins, commonly known as Bacosides, are the primary nootropic substances discovered in the Brahmi extract.

B. monnieri has been shown in both preclinical and clinical investigations to be useful in enhancing memory and cognition. In healthy older adults, it has been demonstrated that forgetting newly learned information has significantly decreased, while memory acquisition and retention have improved. This study adds to the body of research showing that B. monnieri may safely improve cognitive function in older people. [29] Different established in vitro assays, including receptor-based assays and enzyme-inhibition assays, were used to evaluate the impact of Bacomind® on various receptors and enzymes. [30]

Clinical studies: In the experimental group of medical students, oral administration of a standardized extract of BM at a dose of 150 mg twice daily for 6 weeks has been demonstrated to improve cognition and performance in several neuropsychological tests, namely digit span backward and logical memory tests. [31]

In a case study of schizophrenia, the addition of 500 mg/day of Brahmi extract for one month reduced psychopathology without causing any treatment-emergent side effects. Despite its early publishing, this case study implies that add-on Brahmi has therapeutic effectiveness in treating schizophrenia, adding a new aspect to its use in complementary medicine. [34]

However, a different study with healthy people (35-60 years) discovered that BM extracts at a dose of 450 mg/day for 12 weeks corresponds to a decreased degree of anxiety in the experimental group but did not enhance cognitive state. [35]

Ashwagandha *(Withaniasomnifera):* Ashwagandha is a member of the Solanaceae plant family. It is categorized as a "Rasayana" in Ayurveda (rejuvenator). Researchers have discovered that ashwagandha leaf extract improves cognition, guards against environmental neurotoxins, and reverses the pathology of Alzheimer's and Parkinson's disease. [36] According to Ayurvedic

traditions, the herb's name ("Ashwa" for horse and "Gandha" for scent) derives from the root's horse-like odor.

Although this plant has been used for ages, only recently have pharmacological and medical research begun to show a significant increase in the global market. Ashwagandha helps the body stay in balance. This is an apoptogenic plant that aids the body in making a successful adjustment to challenging circumstances. One of the few herbs that noticeably I both physiological and psychological components of human functioning is ashwagandha. Some European nations' regulatory organizations only permit the root of the ashwagandha plant, not the leaves. For stress and anxiety, KSM66 Ashwagandha with 5% withanolides root extract is beneficial. Clinical studies have demonstrated the benefits of KSM-66 Ashwagandha in lowering cortisol levels, reducing stress-related food cravings, and improving memory and cognitive performance. For stress and anxiety, KSM66 Ashwagandha with 5% withanolides root extract is beneficial. Clinical studies have also demonstrated the benefits of KSM-66 Ashwagandha in lowering cortisol levels, reducing stress-related food cravings, and improving memory and cognitive performance. [15]

The functional ingredient presents in the Ashwagandha named Withanolide exhibits different neuroprotective functions in the body. Being the eminent one Withanolide A is found to be neuroprotective against beta-amyloid-induced cytotoxicity.[37]

Clinical study: On day 60, scores on all the stress evaluation measures were considerably lower (P0.0001) in the treatment group receiving the high-concentration, full-spectrum Ashwagandha root extract than they were in the placebo group. In comparison to the placebo group, the blood cortisol levels were significantly lower in the ashwagandha group (P=0.0006). There were no documented severe negative events. The results of this study reveal that a high-concentration full-spectrum Ashwagandha root extract increases a person's ability to cope with stress while also enhancing their self-rated quality of life. [17]

Curcumin *(Curcuma longa):* The plant family Zingiberaceae includes the widely used South Asian spice turmeric. The anti-inflammatory and antioxidant effects of turmeric are well-known. Curcumin (diferuloylmethane), a known component of turmeric, has been shown to have strong neuroprotective qualities. Curcuminoids, additional functional monosaccharides, and other substances such as phenolic and flavonoid antioxidants have all been described. Various brain-related illnesses including Alzheimer's disease, Parkinson's disease, autism, multiple sclerosis, and aging-related neurodegeneration may respond well to curcumin therapy. [38]

Huntington's disease (HD) is a persistent, common inherited neurological disorder with no known cure and is brought on by an aberrant amplification of the polyglutamine (poly Q) repeat in the Huntingtin (Htt) protein. In the Drosophila model of Huntington's disease, curcumin greatly reduces polyglutamine-induced cytotoxicity, neuronal dysfunction, and neurodegeneration. [39] It was investigated if curcumin has any positive effects on the intrahippocampal kainate-induced model of TLE (temporal lobe epilepsy). In the kainate-induced model of TLE, it was found that curcumin pre-treatment can reduce certain oxidative stress indicators, attenuate seizures, and prevent hippocampus neuronal loss and MFS (temporal lobe epilepsy). [40] Alcohol consumption-related cognitive impairments are prevented by curcumin in a dose-dependent manner. [41] In addition to increasing the levels of enzymes found to be involved in the synthesis of DHA such as elongase 2 and fatty acid desaturase 2 (FADS2), it also boosts the production of docosahexaenoic acid (DHA) from its precursor compound, alpha-linolenic acid (ALA), in both the liver and brain tissues of rats. [42]

Clinical studies: In adult male patients with severe depressive disorder, curcumin at a dosage of 1000 mg/day for six weeks was observed to reduce depressive symptoms, salivary cortisol, and pro-inflammatory cytokines (IL 1 and TNF), as well as improve the effectiveness of antidepressant therapy. [43]

Piperine: Even till now, it has not been established how piperine, the primary alkaloid from piper nigrum, affects the central nervous system. In the current investigation, male Wistar rats were given piperine at dosages ranging from 5, 10, and 20 mg/kg BW once daily for 4 weeks. The neuropharmacological activity of the animals was then assessed after only one, one, two, and four weeks of therapy. The findings demonstrated that piperine had anti-depressant-like activity and cognitive-enhancing effects at all dose levels tested in this investigation. As a result, piperine has the potential to be a diet that enhances brain function. [44]

Curcumin and Piperine combination: The study states the increase in bioavailability of curcumin when taken with piperine. Treatment with curcumin (20 and 40 mg/kg, for 21 days) substantially restored the behavioral (increased immobility duration), biochemical (increased monoamine oxidase activity), and neurochemical (depletion of brain monoamine levels) changes brought on by chronic unexpected stress. As compared to curcumin's action alone, the bioavailability enhancer piperine (2.5 mg/kg, for 21 days) significantly increased the anti-immobility, neurotransmitter augmentation (serotonin and dopamine), and monoamine oxidase inhibitory (MAO-A) effects of curcumin. This study offered a scientific justification for the use of piperine and curcumin in combination in the treatment of depressive disorders. [45]

Amino acids and Vitamins: Amino acid supplementation serves as a crucial treatment strategy for many mental disorders including depression. Some of the amino acids such as tryptophan, tyrosine, phenylalanine, and methionine have been studied to reduce the incidence of depression.

Serotonin and its precursor, tryptophan, are known to be potent sleep-inducing molecules and are used to restore serotonin levels in patients suffering from depression, significantly reducing their symptoms. [46 and 47] Tyrosine and phenylalanine (via their conversion to dopamine and norepinephrine) [48], and methionine in combination with ATP all provide efficient anti-depressive effects. [49 and 50]

Deficits in folate and vitamin B12 have been linked to bipolar illness and occurrences of depression. The central monoamine metabolism may especially be impacted by folate deficiency, which might worsen depressive disorders. Additionally, homocysteine's neurotoxic effects, which are linked to folate and vitamin B12 deficiencies, may contribute to neurologic and mental problems. [51]

Supplementation with folate and vitamins has effectively reduced the incidence of depressive attacks and manic episodes. Reduced red-cell folate developed in both phases of bipolar disorders. [52] In multiple clinical trials, vitamin B6 and folic acid have been reported as useful in the treatment of anxiety, panic, and even obsessive-compulsive disorders. [34] Supplementation with vitamins C and E has even been shown to prevent the onset of Alzheimer’s disease. Specifically, men given supplements of these vitamins experienced an improved cognitive function and enhanced mental performance. [51 and 52]

Vitamins, minerals, proteins, and carbohydrates are also important in the proper functioning of the physical and mental health of an individual.

The biochemical, electrophysiological, and pharmacological data that suggest cholinergic dysfunction contributes to age-related memory problems are examined. [53]

CONCLUSION

Functional compounds used in nutraceuticals have enormous potential in nutritional psychology. When given to people in therapeutic doses, nutraceuticals are proven to have positive effects on mental health. When compared to other pathological illnesses, the dosage needed to show therapeutic benefits in mental disorders is larger. This study reveals that functional ingredients such as Ashwagandha (Withanolides), Curcumin, Piperine, Brahmi (Bacosides), Amino acids, and Vitamins have the potential of regulating normal physiological, immunological, and neurological functions which are beneficial for positive effects on mental illness and can be considered as important constituents in nutritional psychology. The numerous therapeutic benefits of ashwagandha, Curcumin, Piperine, Brahmi (Bacosides), and Omega 3 fatty acids are thought to be the result of the synergistic action from this varied combination of active ingredients. Nutraceuticals (or dietary supplements as the name suggests) are not meant to be taken as a first-line treatment. They are generally administered as complements to existing drugs as functional means and provide strengthening to the system in a beneficial way.

Functional ingredients interconnect with every aspect of our mental health. Currently, Nutritional psychology offers an innovative approach to alleviating the immense economic, societal, and individual burden of mental illness using formal education and training addressing issues in mental health. More focus on practical studies needs to be conducted by using different functional ingredients for the treatments in mental health for faster recovery with fewer or no side effects.

Therefore, to confirm the validity of the present preliminary data, extremely large definitive randomized controlled studies are required.

FUTURE PERSPECTIVES

There is a growing interest in the potential of nutraceutical ingredients that improve mental health. As research on this topic continues to evolve, there are several future considerations that are worth keeping in mind:

1. More targeted approach: As more research is conducted on this topic, we could see customized formulations which are generated specific to mental health conditions. [56]
2. Natural alternative: The demand for natural nutraceutical ingredients is increasing across the board, consumers are looking for a natural alternative to prescription medications. So, nutraceuticals can be a viable option. [57]
3. Research and development: There is much to be learned in this area about the effect of nutraceuticals on mental health and research and development in this area is likely to continue to grow. Researchers may explore the underlying mechanism of nutraceutical ingredients that affect mental health. Advances in technology in the coming years may benefit scientist to study this and enables them to accurately measure the potential. [58]
4. No more alternative or complementary: In the coming future we may see nutraceutical ingredients as treatments in clinical settings as more clinicians become aware of their potential benefits. [59]

Overall, the future of nutraceutical ingredients looks promising regarding mental health conditions. We may see it as a viable option for addressing various issues and concerns of mental health with continues research and developments.

Author Contributions: The author wrote the entire review article.

Acknowledgments: This research has expert support from co-author and Director and Dean MGMU, Dr. Vijaya Deshmukh. I thank her for providing insights, knowledge, and attention to detail and for their assistance in binding all the data in this paper which greatly assisted the research.

I would like to thank my loving husband Mr. Kanad Gutte, for his exceptional support and encouragement during the study.

Special thanks to anonymous reviewers for their co-insights.

Funding Sources: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declares no conflict of interest.

Abbreviation: CNP - Centre for Nutritional Psychology; WHO - World health organization; COVID-19 - Coronavirus disease; HPA axis- hypothalamic-pituitary-adrenal axis; kJ/g- Kilo Joule per gram; RET - Rearranged during transfection; MAO- Monoamine Oxidase; O3FAs - Omega-3 fatty acids; PUFAs - Polyunsaturated fatty acids; LA - linoleic acid; ALA- alpha linolenic acid; Docosahexaenoic acid (DHA); EPA - Eicosapentaenoic acid; BM extract - Bacopa monnieri; HD - Huntington's disease; Htt - Huntingtin protein; poly Q – Polyglutamine; TLE - temporal lobe epilepsy; FADS2 - Fatty acid desaturase 2; BW – Body weight

REFERENCES

1. WHO Promoting Mental Health. Concepts, Emerging Evidence, Practice. Summary Report. Department of Mental Health and Substance Abuse in collaboration with the Victorian Health Promotion Foundation and the University of Melbourne. World Health Organization, 2004.
2. Marx, W., Moseley, G., Berk, M., & Jacka, F. (2017). Nutritional psychiatry: the present state of the evidence. The proceedings of the Nutrition Society, 76(4), 427-436. DOI: https://doi.org/10.1017/S0029665117002026
3. The CNP, Diet, Depression, and Anxiety Research, https://www.nutritional-psychology.org/research_studies/diet-depression-and-anxiety/
4. Institute of Health Metrics and Evaluation. Global Health Data Exchange (GHDx), [https://vizhub.healthdata.org/gbd-results/] Retrieved 14 May 2022.
5. World Health Organization, News/ COVID-19 pandemic triggers 25% increase in the prevalence of anxiety and depression worldwide, https://www.who.int/news/item/02-03-2022-covid-19-pandemic-triggers-25-increase-in-prevalence-of-anxiety-and-depression-worldwide Retrieved March 2, 2022
6. Nutraceutical World, Minding mental health with nutraceutical: Global Opportunities, Retrieved September 29th 2021
7. Rajashri K. Mundhe, & Dr. Vijaya Deshmukh. ROLE OF NATURAL NUTRACEUTICAL INGREDIENTS IN HOLISTIC RECOVERY OF AFFECTED HUMAN ORGANS DUE TO COVID 19 INFECTION AND ITS TREATMENT. International Engineering Journal For Research & Development, (2022) 7(MGM IOM& R), 13. DOI: https://doi.org/10.17605/OSF.IO/AVY3W
8. Bellisle, F., & Perez, C. Low-energy substitutes for sugars and fats in the human diet: impact on nutritional regulation. Neuroscience and biobehavioural reviews, 1994; 18(2), 197–205. DOI: https://doi.org/10.1016/0149-7634(94)90024-8
9. Aguiar, S., & Borowski, T. Neuropharmacological review of the nootropic herb Bacopa monnieri. Rejuvenation research, 2013; 16(4), 313–326. DOI: https://doi.org/10.1089/rej.2013.1431
10. Wittchen, H. U., Mühlig, S., & Beesdo, K. (2003). Mental disorders in primary care. Dialogues in clinical neuroscience, 5(2), 115–128. DOI: https://doi.org/10.31887/DCNS.2003.5.2/huwittchen
11. Müller, C. P., Reichel, M., Mühle, C., Rhein, C., Gulbins, E., & Kornhuber, J. Brain membrane lipids in major depression and anxiety disorders. Biochimica et biophysica acta, 2015; 1851(8):1052–1065. DOI: https://doi.org/10.1016/j.bbalip.2014.12.014
12. Agrawal, A., Gupta, U., Dixit, S. P., & Dubey, G. P. Management of the mental deficiency by an indigenous drug Brahmi. Pharmacopsychoecologia, 1993; 6(1): 1-5.

13. Tohda C, Joyashiki E. Sominone enhances neurite outgrowth and spatial memory mediated by the neurotrophic factor receptor, RET. Br J Pharmacol. 2009;157(8):1427-1440. DOI: https://doi.org/10.1111/j.1476-5381.2009.00313.x
14. Kulkarni SK, Bhutani MK, Bishnoi M. Antidepressant activity of curcumin: involvement of serotonin and dopamine system. Psychopharmacology (Berl). 2008;201(3):435-442. DOI: https://doi.org/10.1007/s00213-008-1300-y https://ksm66ashwagandhaa.com/ashwagandha/
15. Tapiero H, Ba GN, Couvreur P, Tew KD. Polyunsaturated fatty acids (PUFA) and eicosanoids in human health and pathologies. Biomed Pharmacother. 2002;56(5):215-222. DOI: https://doi.org/10.1016/s0753-3322(02)00193-2
16. Chandrasekhar, et al., A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults. Indian journal of psychological medicine, 2012; 34(3): 255. DOI: https://doi.org/10.4103/0253-7176.106022
17. Reis, L. C., & Hibbeln, J. R. Cultural symbolism of fish and the psychotropic properties of omega-3 fatty acids. Prostaglandins, leukotrienes, and essential fatty acids, 2006; 75(4-5):227–236. DOI: https://doi.org/10.1016/j.plefa.2006.07.014
18. Kris-Etherton, P.M., Harris, W.S., & Appel, L.J. Omega-3 fatty acids and cardiovascular disease: new recommendations from the American Heart Association. Arteriosclerosis, Thrombosis, and Vascular Biology,2003; 23:151–152. DOI: https://doi.org/10.1161/01.ATV.0000057393.97337.AE
19. Barrow, C.& Shahidi F., (Eds.). Marine Nutraceuticals and Functional Foods (1st ed.). CRC Press.2007; Chapter 2, 23, 63 & 91.
20. Anderson, G. J., Connor, W. E., & Corliss, J. D. Docosahexaenoic acid is the preferred dietary n-3 fatty acid for the development of the brain and retina. Pediatric research, 1990; 27(1), 89–97. DOI: https://doi.org/10.1203/00006450-199001000-00023
21. O'Keefe, J. H., & Harris, W. S. Omega-3 fatty acids: time for clinical implementation? The American journal of cardiology, 2000; 85(10):1239–1241. DOI: https://doi.org/10.1016/s0002-9149(00)00735-9
22. Stoll AL, Locke CA, Marangell LB, Severus WE. Omega-3 fatty acids and bipolar disorder: a review. Prostaglandins Leukot Essent Fatty Acids. 1999;60(5-6):329-337. DOI: https://doi.org/10.1016/s0952-3278(99)80008-8
23. Stevens LJ, Zentall SS, Deck JL, et al. Essential fatty acid metabolism in boys with attention-deficit hyperactivity disorder. Am J Clin Nutr. 1995;62(4):761-768. DOI: https://doi.org/10.1093/ajcn/62.4.761
24. Hibbeln, J.R. Seafood consumption, the DHA content of mothers' milk and prevalence rates of postpartum depression: A cross-national, ecological analysis. J Affect Disord, 2002; 69:15-29. DOI: https://doi.org/10.1016/s0165-0327(01)00374-3
25. Hooper, L., Thompson, R. L., Harrison, R. A., Summerbell, et. al. Risks and benefits of omega 3 fats for mortality, cardiovascular disease, and cancer: a systematic review. BMJ (Clinical research ed.), 2006; 332(7544):752–760. DOI: https://doi.org/10.1136/bmj.38755.366331.2F
26. Kris-Etherton, P M., Hecker, K. D., Bonanome, A., Coval, S. M., Binkoski, et.al. Bioactive compounds in foods: their role in the prevention of cardiovascular disease and cancer. The American journal of medicine, 2002; 113, 9B, 71S–88S. DOI: https://doi.org/10.1016/s0002-9343(01)00995-0
27. Sawazaki S, Hamazaki T, Yazawa K, Kobayashi M. The effect of docosahexaenoic acid on plasma catecholamine concentrations and glucose tolerance during long-lasting psychological stress: a double-blind placebo-controlled study. J Nutr Sci Vitaminol (Tokyo). 1999;45(5):655-665. DOI: https://doi.org/10.3177/jnsv.45.655
28. Calabrese, C., Gregory, W. L., Leo, M., Kraemer, D., Bone, K., & Oken, B. Effects of a standardized Bacopa monnieri extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double-blind, placebo-controlled trial. Journal of alternative and complementary medicine (New York, N.Y.), 2008; 14(6), 707–713. DOI: https://doi.org/10.1089/acm.2008.0018
29. Dethe S, Deepak M, Agarwal A. Elucidation of Molecular Mechanism(s) of Cognition Enhancing Activity of Bacomind®: A Standardized Extract of Bacopa Monnieri. Pharmacogn Mag. 2016;12(Suppl 4): S482-S487. DOI: https://doi.org/10.4103/0973-1296.191464
30. Kumar, N., Abichandani, L. G., Thawani, V., Gharpure, K. J., Naidu, M. U., & Venkat Ramana, G. Efficacy of Standardized Extract of Bacopa monnieri (Bacognize®) on Cognitive Functions of Medical Students: A Six-Week Randomized Placebo-Controlled Trial. Evidence-based complementary and alternative medicine,2016 eCAM, 4103423. DOI: https://doi.org/10.1155/2016/4103423
31. Sarkar, S., Mishra, B. R., Praharaj, S. K., & Nizamie, S. H. Add-on effect of Brahmi in the management of schizophrenia. Journal of Ayurveda and integrative medicine, 2012; 3(4): 223–225. DOI: https://doi.org/10.4103/0975-9476.104448

32. Sathyanarayanan V, Thomas T, Einöther SJ, Dobriyal R, Joshi MK, Krishnamachari S. Brahmi for the better? New findings challenging cognition and anti-anxiety effects of Brahmi (Bacopa monniera) in healthy adults. Psychopharmacology (Berl). 2013;227(2):299-306. DOI: https://doi.org/10.1007/s00213-013-2978-z
33. Lerner, V., Miodownik, C., Kaptsan, A., Cohen, H., Matar, M., Loewenthal, U., & Kotler, M. Vitamin B (6) in the treatment of tardive dyskinesia: a double-blind, placebo-controlled, crossover study. The American journal of psychiatry, 2001; 158(9):1511–1514. DOI: https://doi.org/10.1176/appi.ajp.158.9.1511
34. Mental Health and COVID-19: Early evidence of the pandemic's impact. World Health Organization, 2022.
35. Wattanathorn J, Chonpathompikunlert P, Muchimapura S, Priprem A, Tankamnerdthai O. Piperine, the potential functional food for mood and cognitive disorders. Food Chem Toxicol. 2008;46(9):3106-3110. DOI: https://doi.org/10.1016/j.fct.2008.06.014
36. Kurapati, K. R., Atluri, V. S., Samikkannu, T., & Nair, M. P. Ashwagandha (Withania somnifera) reverses β-amyloid1-42 induced toxicity in human neuronal cells: implications in HIV-associated neurocognitive disorders (HAND). PloS one, 2013; 8(10): e77624. DOI: https://doi.org/10.1371/journal.pone.0077624
37. Dutta, Soumam, Roy, Sohini, et al. Functional Foods for Mental Health Promotion, Journal of Mahatma Gandhi Institute of Medical Science, 2020; 25:72-9 DOI: https://doi.org/10.4103/jmgims.jmgims_15_20
38. Chongtham A, Agrawal N. Curcumin modulates cell death and is protective in Huntington's disease model. Sci Rep. 2016; 6:18736. Published 2016 Jan 5. DOI: https://doi.org/10.1038/srep18736
39. Kiasalari, Z., Roghani, M., Khalili, M., Rahmati, B., & Baluchnejadmojarad, T. Antiepileptogenic effect of curcumin on the kainate-induced model of temporal lobe epilepsy. Pharmaceutical biology, 2013; 51(12):1572–1578. DOI: https://doi.org/10.3109/13880209.2013.803128
40. Tiwari V, Chopra K. Protective effect of curcumin against chronic alcohol-induced cognitive deficits and neuroinflammation in the adult rat brain. Neuroscience. 2013; 244:147-158. DOI: https://doi.org/10.1016/j.neuroscience.2013.03.042
41. Wu A, Noble EE, Tyagi E, Ying Z, Zhuang Y, Gomez-Pinilla F. Curcumin boosts DHA in the brain: Implications for the prevention of anxiety disorders. Biochim Biophys Acta. 2015;1852(5):951-961. DOI: https://doi.org/10.1016/j.bbadis.2014.12.005
42. Yu JJ, Pei LB, Zhang Y, Wen ZY, Yang JL. Chronic Supplementation of Curcumin Enhances the Efficacy of Antidepressants in Major Depressive Disorder: A Randomized, Double-Blind, Placebo-Controlled Pilot Study. J Clin Psychopharmacology. 2015;35(4):406-410. DOI: https://doi.org/10.1097/JCP.0000000000000352
43. Wadhwa R, Konar A, Kaul SC. Nootropic potential of Ashwagandha leaves: Beyond traditional root extracts. Neurochem Int. 2016; 95:109-118. DOI: https://doi.org/10.1016/j.neuint.2015.09.001
44. Bhutani, M. K., Bishnoi, M., & Kulkarni, S. K. Anti-depressant like the effect of curcumin and its combination with piperine in unpredictable chronic stress-induced behavioral, biochemical and neurochemical changes. Pharmacology, biochemistry, and behavior, 2009; 92(1), 39–43. DOI: https://doi.org/10.1016/j.pbb.2008.10.007
45. Buist R. The therapeutic predictability of tryptophan and tyrosine in the treatment of depression. Int J Clin Nutr Rev, 1983; 3, 1-3.
46. Agnoli A, Andreoli V, Casacchia M, Cerbo R. Effect of s-adenosyl-l-methionine (SAMe) upon depressive symptoms. J Psychiatr Res. 1976;13(1):43-54. DOI: https://doi.org/10.1016/0022-3956(76)90008-x
47. Kravitz, H.M., Sabelli, H.C., Fawcett, J. Dietary supplements of phenylalanine and other amino acid precursors of brain neuroamines in the treatment of depressive disorders. J Am Osteopath Assoc, 1984; 84(1):119-123 DOI: https://doi.org/10.1515/jom-1984-840928
48. Ruhé, H.G., Mason, N.S., Schene, A.H. Mood is indirectly related to serotonin, norepinephrine and dopamine levels in humans: a meta-analysis of monoamine depletion studies. Mol Psychiatry, 2007; 12(4): 331-359. DOI: https://doi.org/10.1038/sj.mp.4001949
49. Janicak, P. G., Lipinski, J., Davis, J. M., et. al. (1988). S-adenosylmethionine in depression. A literature review and preliminary report. The Alabama journal of medical sciences, 1988; 25(3):306–313.
50. Bottiglieri T. Folate, vitamin B12, and neuropsychiatric disorders. Nutrition reviews, 1996; 54(12), 382–390. DOI: https://doi.org/10.1111/j.1753-4887.1996.tb03851.x
51. Hasanah, C.I., Khan, U.A., Musalmah, M., Razali, S.M. (1997). Reduced red-cell folate in mania. J Affect Disord, 1997; 46(2): 95-9. DOI: https://doi.org/10.1016/s0165-0327(97)00096-7
52. Charlton KE, Rabinowitz TL, Geffen LN, Dhansay MA. Lowered plasma vitamin C, but not vitamin E, concentrations in dementia patients. J Nutr Health Aging. 2004;8(2):99-107. DOI: https://doi.org/10.1016/s0165-0327(97)00096-7
53. Zandi PP, Anthony JC, Khachaturian AS, et al. Reduced risk of Alzheimer disease in users of antioxidant vitamin supplements:

the Cache County Study. Arch Neurol. 2004;61(1):82-88. DOI: https://doi.org/10.1001/archneur.61.1.82

54. Bartus, R. T., Dean, R. L., Beer, B., & Lippa, A. S. The cholinergic hypothesis of geriatric memory dysfunction. Science (New York, N.Y.), 1982; 217(4558), 408–414. DOI: https://doi.org/10.1126/science.7046051.
55. Harvey, A. G., & Gumport, N. B. (2015). Evidence-based psychological treatments for mental disorders: modifiable barriers to access and possible solutions. Behaviour research and therapy, 68, 1–12. DOI: https://doi.org/10.1016/j.brat.2015.02.004.
56. Nasri, H., Baradaran, A., Shirzad, H., & Rafieian-Kopaei, M. (2014). New concepts in nutraceuticals as alternative for pharmaceuticals. International journal of preventive medicine, 5(12), 1487–1499.
57. Das, L., Bhaumik, E., Raychaudhuri, U., & Chakraborty, R. (2012). Role of nutraceuticals in human health. Journal of food science and technology, 49(2), 173–183. DOI: https://doi.org/10.1007/s13197-011-0269-4
58. Tabish S. A. (2008). Complementary and Alternative Healthcare: Is it Evidence-based?. International journal of health sciences, 2(1), V–IX.