

Role of nutrition in depression and other mental illnesses

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Abstract

Nutrients, foods, and dietary components have a significant role in the development and maintenance of depressive disorders as well as the intensity of depression symptoms. Nutritional elements may alter the biomarkers linked to depression and may also influence the onset of depression, obesity, and diabetes. Recent research has identified novel mediators of mood fluctuations and energy balance that operate the gut-brain networks. In this context, a number of healthy foods including olive oil, fish, fruits, vegetables, nuts, legumes, poultry, dairy, and unprocessed meat, have been shown to have a negative correlation with the risk of depression and may even help with the symptoms of depression. The use of sweetened beverages, processed foods, fried foods, processed meat, refined grains, high-fat dairy products, biscuits, snacks, and pastries, on the other hand, has been linked in longitudinal studies to an elevated risk of depression. Nevertheless, it is usually challenging to draw a firm conclusion about a true prospective causal association from this primarily retrospective research since depressed people may also alter their eating habits incidentally as a result of their sadness. Additionally, it has been suggested that some dietary substances, including as calcium, chromium, folate, PUFAs, vitamin D, B12, zinc, magnesium, and D-serine, might be utilised as add-on treatments with antidepressants. In this situation, food and lifestyle changes may be a desired, practical, effective, and non-stigmatizing depression preventive and treatment option. In early randomized controlled clinical studies, a number of drugs that have historically been used to treat metabolic disorders—including pioglitazone, metformin, exenatide, atorvastatin, and gram-negative antibiotics showed some promise for treating depression.

Keywords: Nutrition; Depression; Mental illness; Nutritional deficit

1. Introduction

Few people are aware of the link between nutrition and depression, but the link between nutritional deficits and physical disease is well understood. Depression is frequently assumed to be solely physiological or emotionally driven. On the other hand, nutrition can have a significant impact on the development, intensity and duration of depression. Many of the clearly detectable food patterns that occur before to depression are also present during depression like poor appetite, skipping meals, and a strong craving for sugary foods. [1] Dietary neuroscience is a new field that investigates how nutritional variables affect human cognition, behavior and emotions. Depression, bipolar disorder, schizophrenia, and obsessive compulsive disorder (OCD) are the most frequent mental disorders that are now widespread in many countries. [2] In many Asian and American countries, the general population's food intake pattern reveals that they are commonly low in several nutrients including vital vitamins, minerals, and omega-3 fatty acids. [3] The degree of deficit in these nutrients is a noticeable aspect of the diets of people suffering from mental illnesses. [3] Studies have shown that taking regular doses of essential nutrients might help patients feel better. [4] Amino acid

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supplements have also been reported to help in depression and other mental health issues. [4] An effective therapeutic intervention, namely nutritional treatment, is developing based on accumulated scientific data. These may be useful for treating and preventing depression, bipolar disorder, schizophrenia, eating disorders, anxiety disorders, autism, and addiction. [4] Sometimes, the majority of prescription medications, including antidepressants have side effects. [4] As a result of this, patients frequently fail to take their prescription medicines. Psychiatrists are frequently confronted with such noncompliance. It is important to remember that such noncompliant people with mental illnesses are more likely to commit suicide. In some cases, long-term usage or greater dosages might cause medication toxicity, which can be fatal to the patient. [4] Alternative or complementary dietary therapy is another successful technique for psychiatrists to overcome noncompliance. Although more research is needed to determine the best recommended doses of most nutritional supplements. Psychiatrists can recommend doses of dietary supplements based on previous and current efficacious studies and then adjust the doses based on the results obtained by closely observing the patient's changes. [4]

Some studies analyze the diets of depressed persons. According to these studies, depressed patient's nutrition is insufficient. They make poor dietary decisions and choose items that may lead to depression. Recent research reveals a relationship between low serotonin levels and suicide. [5] Lower levels of this neurotransmitter are thought to contribute to an overall insensitivity to future repercussions that can lead to hazardous, impulsive and violent actions including suicide, which is the ultimate act of inwardly directed impulsive aggression. Depression is a disorder characterized by depressed mood, loss of appetite and lack of interest in pleasurable activities. This illness can have a variety of repercussions if treatment is not provided in a timely manner. Suicidal tendencies are more common in patients suffering from depression, and they are often treated with antidepressants and psychotherapy. [6] Neurotransmitter deficiencies, such as serotonin, dopamine, noradrenaline, and gamma aminobutyric acid (GABA) are frequently linked to depression. [6 – 11] Several studies have shown that the amino acids tryptophan, tyrosine, phenylalanine, and methionine can aid with a variety of mood disorders, including depression. [12–17] Tryptophan, a precursor of serotonin, is normally converted to serotonin when taken alone on an empty stomach. As a result, tryptophan helps in sleep and tranquility. This means that restoring serotonin levels reduces depression caused by serotonin deficits. [8] Dopamine and norepinephrine are produced when tyrosine and its precursor phenylalanine are converted. [18]

Arousal and alertness are caused by dietary supplements containing phenyl alanine and tyrosine. When methionine combines with adenosine triphosphate (ATP) produce S-adenosylmethionine (SAM), which aids in the creation of neurotransmitters in the brain. [19 – 22] More research is needed to provide the daily supplementary dosages of these neuro chemicals that should be eaten to elicit antidepressant effects, according to the current paradigm. The drop in omega-3 fatty acid intake from fish and other sources in most populations have been linked to an increase in the prevalence of serious depression, according to researchers. [23] The two omega-3 fatty acids present in fish oil, eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA) have been demonstrated to have antidepressant benefits in humans. Neurotransmitters are involved for this conversion. The bioconversion of EPA to leukotrienes, prostaglandins and other molecules required by the brain has antidepressant effects. Others believe that EPA and DHA modulate neural signal transduction via activating peroxisomal proliferator activated receptors (PPARs), suppressing G-proteins and protein kinase C, as well as calcium, sodium, and potassium ion channels. Whatever the case may be, epidemiological statistics and clinical trials have conclusively demonstrated that omega-3 fatty acids are useful in the treatment of depression. [24] Daily intake of omega-3 fatty acid dietary supplements containing 1.5 - 2 g of EPA has been demonstrated to improve mood in depressed people. However, higher dosages of omega-3 than 3 gm had no better effects than placebos and may be contraindicated in some situations, such as those taking anticoagulant medications. [25] Vitamin B (e.g., folate) and magnesium deficits, in addition to omega-3 fatty acids, have been associated to depression. [26–28]

According to randomized controlled studies, patients treated with 0.8 mg of folic acid or 0.4 mg of vitamin B12 per day has less depressive symptoms. [27] Furthermore, the findings of many case studies in which patients were given 125 - 300 mg of magnesium (as glycinate or taurinate) with each meal and before night showed that the majority of the patients recovered from serious depression in less than seven days. Nutritional deficits and several mental problems have been linked. [23, 25, 29–32]

Omega-3 fatty acids, vitamin B, minerals, and amino acids that are precursors to neurotransmitters are the most commonly found dietary deficits in people with mental problems. [20, 23, 24, 27, 28, 30, 33] A demographic research suggests a correlation between high fish consumption and a lower incidence of mental problems. This lower incidence rate being due to omega-3 fatty acid consumption. [23, 31, 32] For healthy people, 1 in 2 gm of omega-3 fatty acids per day is recommended, while up to 9.6 gm has been demonstrated to be safe and beneficial for patients with mental problems. [34 – 36] The majority of Asian diets are lacking in fruits and vegetables, which leads mineral and vitamin

deficiencies in the body. The importance of various nutrients in depression and other mental health has been discussed in this study.

2. Carbohydrates

Carbohydrates are naturally occurring polysaccharides that play an important role in an organism's structure and function. Carbohydrates affect the mood and behavior in human body. The release of insulin in the body is triggered by eating a carbohydrate rich meal. Insulin facilitates the entrance of blood sugar into cells, where it may be utilised for energy and it triggers the entry of tryptophan into the brain. The levels of neurotransmitters in the brain are affected by tryptophan.

Because carbohydrate rich diets encourage the production of serotonin and tryptophan, which boost feeling of well being. But low carbohydrate diets tend to produce sadness. Low glycemic index (GI) foods, (such as certain fruits and vegetables, whole grains, pasta etc) are more likely to provide a moderate but lasting influence on brain chemistry, mood, and energy level than high GI foods, such as sweets, which tend to give immediate but temporary relief.

3. Proteins

Proteins are made up of amino acids, which are the essential components for life. Only 12 amino acids are produced by the body itself and remaining the 8 (essential amino acids) must be obtained from diet. All the required amino acids are found in a high quality protein diet. Meats, eggs, milk and other dairy products all are high in good quality protein. One or two essential amino acids may be deficient in plant proteins such as beans, peas and grains. Protein consumption has an impact on brain function and mental wellness because amino acids are used to make several neurotransmitters in the brain.

The amino acid tyrosine is used to make the neurotransmitter dopamine, while tryptophan is used to make the neurotransmitter serotonin. [5] There will be insufficient synthesis of the corresponding neurotransmitters if any of these two amino acids is deficient, which is linked to poor mood and aggression in patients. Excessive amino acid accumulation can potentially cause brain damage and mental impairment. Excessive phenylalanine accumulation can cause brain damage and mental retardation in people who have the condition phenylketonuria.

4. Essential fatty acids

4.1. Omega-3 fatty acids

Brain has highest lipid levels (fats) among all the organs in the body. Brain lipids are composed of fatty acids. These are the structural constituents of membranes. Gray matter is thought to contain 50 % polyunsaturated fatty acids (approximately 33 % of which belong to the omega-3 family), which must be obtained through diet. Omega-3 fatty acids (especially alpha-linolenic acid, ALA) were involved in one of the first experimental demonstrations of the influence of dietary components (nutrients) on the structure and function of the brain. According to a recent research, decreasing plasma cholesterol by diet and medicine promotes depression. The quantity and ratio of omega-6 and omega-3 polyunsaturated fatty acids (PUFA) change the serum lipids and modify the biochemical and biophysical characteristics of cell membranes. It has been suggested that getting enough long-chain PUFAs, particularly DHA, will help prevent depression. [37] Polar phospholipids, spingolipids, and cholesterol are structural and functional components of membrane in cells of the brain, which is a lipid-rich organ. The PUFA derived from the essential fatty acids (EFAs), linoleic acid and alpha-linolenic acid, make up a large component of the glycerophospholipids in the brain. DHA, derived from the omega-3 fatty acid alpha linolenic acid, arachidonic acid (AA), and docosatetraenoic acid, produced from the omega-6 fatty acid linoleic acid, are the most abundant PUFA in the brain. Experiments have shown that diets without omega-3 PUFA cause significant disruptions in neural function. [38] DHA and AA cannot be formed by mammals de novo, according to Marszalek and Lodish's research, despite their abundance in the nervous system. As a result, they or their precursors must be provided through the food and delivered to the brain. Because neurodevelopment happens at such a high rate throughout late pregnancy and the early postnatal period, an adequate supply of PUFAs, particularly DHA, is essential to promote neurite outgrowth as well as proper brain and retinal development. [39]

Dieting-related psychological characteristics were investigated as possible confounders by Bruinsma and Taren of the University Of Arizona College OfPublic Health in Tucson, USA. [40] They debated data that supported and refuted the idea that decreasing plasma cholesterol by diet and drugs causes depression. According to research, a shortage in omega-3 fatty acids and an imbalance in the ratio of EFAs, especially omega-6 and omega-3 fatty acids, may be blame

for the increased depressive symptoms associated with low plasma cholesterol. These connections might explain why the results of cholesterol-lowering treatments and depression trials are so inconsistent. In a similar vein, dietary activities have been linked to mood swings. [41] Omega-3 fatty acids in the diet can help prevent a variety of illnesses, including depression. Their absence can hasten the ageing of the brain by limiting membrane replacement. The relative functions of the vascular component (where the omega-3s are active) and the cerebral parenchyma itself have yet to be determined. It has been proposed that omega-3 has a function in disorders like dyslexia and autism. It was omega-3 fatty acid that was used in the first coherent experimental evidence of the effect of dietary substances on the structure and function of the brain. Experiments were conducted on ex vivo grown brain cells, in vivo brain cells, and ultimately physicochemical, biochemical, physiological, neurosensory and behavioral characteristics. The type of polyunsaturated fatty acids (in particular omega-3) present in formula milks for newborns (both premature and term) improves their visual, cerebral, and intellectual capacities, according to these studies. [16]

5. Vitamins

5.1. B-complex vitamins

A research from neuropsychiatry specialists, suggested that nutrition and depression are related with one another. According to this research, published in Neuropsychobiology,[42] supplementation of nine vitamins at ten times in excess of standard recommended dietary allowance (RDA) for one year increase mood in both men and women. These mood changes after a year happened despite the fact that the blood levels of nine vitamins had reached a plateau after three months. Enhanced vitamin B2 and B6 levels were shown to be significantly linked with improved mood. But vitamin B1 level was connected to bad mood in women, and an improvement in the same after three months was linked to improved mood. Thiamine has been shown to improve cognitive ability especially in the elderly. [43]

5.2. Vitamin B12 (Cynocobalamin)

Vitamin B12 has been shown in clinical trials to postpone the onset of dementia symptoms and blood abnormalities when given in a specific clinical time window, prior to the beginning of the first symptoms. Cobalamin supplementation improves cerebral and cognitive capabilities in the aged individuals. It also improves the function of frontal lobe related components, as well as the language function of persons with cognitive problems. Adolescents with a vitamin B12 deficit on the borderline show symptoms of cognitive abnormalities. [43]

5.3. Folate

Patients with depression have blood folate levels that are 25 % lower on average than healthy controls, according to a research. [44] Low folate levels have also been established as a substantial predisposing factor for poor antidepressant treatment outcomes. A controlled research found that 500 micrograms of folic acid increase the efficacy of antidepressant medication. [45] Various studies have highlighted that depressive symptoms are the most prevalent neuropsychiatric manifestation of folate insufficiency, pointing to folate's crucial function in brain metabolic pathways. [46] It is still unclear that inadequate diet causes folate insufficiency as a symptom of depression or primary folate deficiency causes depression and its symptoms.

6. Minerals

6.1. Calcium

According to a recent study, selective serotonin uptake inhibitors (SSRIs) reduce calcium absorption in the bones. Furthermore, SSRIs might cause patients to have reduced blood pressure, which can lead to falls and broken bones. Doctors' indiscriminate prescribing of SSRIs and their intake by patients at risk of depression or other mental health disorders may enhance their fracture risk. They may be predisposed to osteoporosis due to their age and the fact that they are currently on other drugs. [47]

6.2. Chromium

There are several researches on the role of chromium in human depression [48, 49], demonstrating the importance of this element in mental health.

6.3. Iodine

Iodine is essential for mental well-being. The thyroid hormone provides iodine, which increases the energy metabolism of the brain cells. Iodine deficiency in the diet during pregnancy causes severe brain dysfunction, eventually leading to cretinism.

6.4. Iron

Iron is required for cerebral parenchyma oxygenation and energy production (through cytochrome oxidase), as well as the creation of neurotransmitters and myelin. Children with attention deficit hyperactivity disorder (ADHD) have an iron shortage. The concentrations of iron in the umbilical artery are important during the development of the fetus and in connection to the child's IQ level. Infantile anemia is linked to disturbances in cognitive development. [43] According to a research, twice as many women as men suffer from clinical depression. Not only that this is more prominent among married women between the ages of 25 to 45 who have children. Furthermore, women of reproductive age suffer from depression at a higher rate than women of other ages. These findings suggest that iron deficiency, which is known to produce fatigue and sadness, may play a role in depression. Apathy, sadness, and rapid fatigue when exercising are all symptoms of iron deficiency anaemia. [43]

6.5. Lithium

Johan August discovered and identified lithium in 1817 while doing research on the mineral petalite. Lithium is a monovalent cation. Lithium's importance has been well known in psychiatry. It is a drug of choice for bipolar disorder. Lithium is also used as an enhancing agent in the treatment of depression, scizoaffective disorder, aggressiveness, impulse control problem, eating disorders, attention deficit hyperactivity disorder, and some subgroups of alcoholism. [50] However, while utilising lithium in mentally ill patients certain precautions must be used. Patients with comorbidities in the cardiovascular, renal, endocrine, pulmonary, and dermatological systems can benefit from lithium therapy.

6.6. Selenium

According to a research, inadequate selenium consumption is linked to lowered mood status. [51] It is also reported that, selenium enhances mood and reduces anxiety in patients. [52, 53]

6.7. Zinc

Zinc is involved in the gustation process (taste perception). It is also observed that, zinc levels are lower in those who have depression. [54] Several studies demonstrate that oral zinc might affect the efficacy of antidepressant medication. [55] Zinc also protects brain cells.

Several studies have found that lack of micronutrients might damage a child's complete genetic potential for physical and mental development. When children and adolescents with poor nutritional status experience changes in their mental and behavioral functioning, dietary changes can help, but only to a limited extent. Dietary nutrient composition and meal patterns have been shown to have positive or negative, immediate or long-term consequences. Deficiencies of antioxidants and nutrients (trace elements, vitamins, and non-essential micronutrients like polyphenols) in the diet throughout ageing can lead to brain diseases, which may be caused by a failure of the body's defence mechanisms.

7. Other physiological and psychosocial factors

Another study shows that, diet and depression involves old age, which is a time of vulnerability to unintentional weight loss, a factor that is often linked to increased morbidity and premature death. Anorexia of aging may play a part in this, either by lowering food intake directly or by reducing food intake in reaction to such negative variables as age-related changes in sensory perception (taste and smell), bad dentition, multiple prescription medication usage, and depression. Marcus and Berry [57] reviewed malnutrition in the elderly, is due to refusal to eat. They point to aging-related physiologic changes, mental diseases including dementia, depression, medical, social, and environmental conditions as contributing causes. People are currently using alternative and complementary medicine (CAM) approaches to combat the problem of depression. The National Center for Complementary and Alternative Medicine defines complementary and alternative medicine (CAM) as a collection of medical and health systems, practices, and products that are not currently recognized part of traditional medicine. [58] Mental health providers should be aware that CAM therapies are likely to be used by a significant percentage of their bipolar disorder patients. Some physicians consider these approaches to be appealing and safe alternatives to or complements to standard psychiatric medicines. [59] Current research in psychoneuroimmunology and brain biochemistry suggests that communication pathways may exist,

allowing for a better understanding of the relationship between nutritional intake, central nervous system function, and immune function, all of which influence an individual's psychological health status. These findings may lead to a better recognition of the therapeutic benefits of food intervention in the treatment of depression and other psychological disorders among health practitioners and health care providers.

8. Conclusion

There is a connection between patients' mental health and diet. Correlations between these events and their effects on psychological status are becoming more significant in the context of contemporary trends such as urbanization, globalization, including the food industry, and changes in people's lifestyles and eating habits. Exploring these correlations creates potential opportunities to implement new effective dietary, pharmacological, therapeutic, and above all preventive interventions.

Compliance with ethical standards

Disclosure of Conflict of interest

No Conflict of interest.

References

- [1] Bonny Beardsley. Depression and nutrition. Available from: <http://www.healingwell.com/LIBRARY/depression/beardsley/.asp>.
- [2] Murray CJL, Lopez AD. The global burden of disease. *World Health Organization*. 1996: 270.
- [3] *American psychiatric A: Diagnostic and statistical manual of mental disorders*. 4th ed. Washington DC: 2000.
- [4] ShaheenLakhan SE, Vieira KF. Nutritional therapies for mental disorders. *Nutr Jr*. 2008; 7: 2.
- [5] Available from: <http://diet.hajimeru.biz/category/health/nutritionj>
- [6] Brown GL, Ebert MH, Gover PH, Jimerson DC, Klein WJ, Bunney WE, et al. Aggression, suicide and serotonin: Relationships to CSF amine metabolites. *Am J Psychiatry*. 1982; 139: 741–6.
- [7] Rush AJ. The varied clinical presentations of major depressive disorder. *J Clin Psychiatry*. 2007; 68: 4–10.
- [8] National Institute of Mental Health: Depression. *National Institute of Mental Health*. 2000. (US Department of Health and Human Services, Bethesda (MD) [reprinted September 2002])
- [9] Diehl DJ, Gershon S. The role of dopamine in mood disorders. *Comp Psychiatry*. 1992; 33: 115–20.
- [10] Stockmeier CA. Neurobiology of serotonin in depression and suicide. *Ann N Y Acad Sci*. 1997; 836: 220–32.
- [11] Van Praag HM. Depression, suicide and the metabolism of serotonin in the brain. *J Affect Disord*. 1983; 4: 275–90.
- [12] Firk C, Markus CR. Serotonin by stress interaction: A susceptibility factor for the development of depression? *J Psychopharmacol*. 2007; 21: 538–44.
- [13] Leonard BE. The role of noradrenaline in depression: A review. *J Psychopharmacol*. 1997; 11: S39–47.
- [14] Petty F. GABA and mood disorders: A brief review and hypothesis. *J Affect Disord*. 1995; 34: 275–81.
- [15] McLean A, Rubinsztein JS, Robbins TW, Sahakian BJ. The effects of tyrosine depletion in normal healthy volunteers: Implications for unipolar depression. *Psychopharmacology*. 2004; 171: 286–97.
- [16] Agnoli A, Andreoli V, Casacchia M, Cerbo R. Effects of s-adenosyl-l-methionine (SAME) upon depressive symptoms. *J Psychiatr Res*. 1976; 13: 43–54.
- [17] Bourre JM. Dietary omega-3 Fatty acids and psychiatry: Mood, behavior, stress, depression, dementia and aging. *J Nutr Health Aging*. 2005; 9: 31–8.
- [18] Hoes MJ. L-tryptophan in depression. *J Orthomolecular Psychiatry*. 1982; 4: 231.
- [19] Buist R. The therapeutic predictability of tryptophan and tyrosine in the treatment of depression. *Int J Clin Nutr Rev*. 1983; 3: 1–3.

- [20] Maurizi CP. The therapeutic potential for tryptophan and melatonin: Possible roles in depression, sleep, Alzheimer's disease and abnormal aging. *Med Hypotheses*. 1990; 31: 233–42.
- [21] Ruhe HG, Mason NS, Schene AH. Mood is indirectly related to serotonin, norepinephrine and dopamine levels in humans: A meta-analysis of monoamine depletion studies. *Mol Psychiatry*. 2007; 12: 331–59.
- [22] DeLeo D. S-adenosylmethionines an antidepressant: A double blind trial versus placebo. *Cut Ther Res*. 1987; 41: 865–70.
- [23] Janicak PG, Lipinski J, Davis JM, Comaty JE, Waternaux C, Cohen B, et al. S-adenosylmethionine in depression: A literature Review and preliminary report. *Ala J Med Sci*. 1988; 25: 306–13.
- [24] Hibbeln JR. Fish consumption and major depression. *Lancet*. 1998; 351: 1213.
- [25] Adams PB, Lawson S, Sanigorski A, Sinclair AJ. Arachidonic acid to eicosapentaenoic acid ratio in blood correlates positively with clinical symptoms of depression. *Lipids*. 1996; 31: S157–61.
- [26] Grubb BP. Hypervitaminosis a following long-term use of high-dose fish oil supplements. *Chest*. 1990; 97: 1260.
- [27] Young SN. Folate and depression: A neglected problem. *J Psychiatry Neurosci*. 2007; 32: 80–2.
- [28] Bell IR, Edman JS, Morrow FD, Marby DW, Mirages S, Perrone G, et al. B Complex vitamin patterns in geriatric and young adult inpatients with major depression. *J Am Geriatr Soc*. 1991; 39: 252–7.
- [29] Eby GA, Eby KL. Rapid recovery from major depression using magnesium treatment. *Med Hypotheses*. 2006; 67: 362–70.
- [30] Wurtman R, O'Rourke D, Wurtman JJ. Nutrient imbalances in depressive disorders: Possible brain mechanisms. *Ann NY Acad Sci*. 1989; 575: 75–82.
- [31] Chouinard G, Young SN, Annable L. A controlled clinical trial of L-tryptophan in acute mania. *Biol Psychiatry*. 1985; 20: 546–7.
- [32] Reis LC, Hibbeln JR. Cultural symbolism of fish and the psychotropic properties of omega-3 fatty acids. *Prostaglandin LeukotEssent Fatty Acids*. 2006; 75: 227–36.
- [33] Tanskanen A, Hibbeln JR, Hintikka J, Haatainen K, Honkalampi K, Viinamaki H. Fish consumption, depression, and suicidality in a general population. *Arch Gen Psychiatry*. 2001; 58: 512–3.
- [34] Rudin DO. The major psychoses and neuroses as omega-3 fatty acid deficiency syndrome: Substrate pellagra. *Biol Psychiatry*. 1981; 16: 837–50.
- [35] Von Schacky CA. Review of omega-3 ethyl esters for cardiovascular prevention and treatment of increased blood triglyceride levels. *Vasc Health Risk Manag*. 2006; 2: 251–62.
- [36] Eritsland J. Safety considerations of polyunsaturated fatty acids. *Am J ClinNutr*. 2000; 71: 197S–201S.
- [37] Stoll AL, Severus WE, Freeman MP, Rueter S, Zboyan HA, Diamond E, et al. Omega 3 fatty acids in bipolar disorder: A preliminary double-blind, placebo-controlled trial. *Arch Gen Psychiatry*. 1999; 56: 407–12.
- [38] Sinclair AJ, Begg D, Mathai M, Weisinger RS. Omega-3 fatty acids and the brain: review of studies in depression. *Asia Pac J ClinNutr*. 2007; 16: 391–7.
- [39] Marszalek, Lodish HF. Docosahexanoic acid, fatty acid-interacting proteins and neuronal function: Breast milk and fish are good for you. *Annu Rev Cell Dev Biol*. 2005; 21: 633–57.
- [40] Bruinsma KA, Taren DL. Dieting, essential fatty acid intake and depression. *Nutr Rev*. 2000; 58: 98–108.
- [41] Anita SW, Nicholas WR, Jonathan DE, Laugharne, Ahluwalia NS. Alterations in mood after changing to a low-fat diet. *Br J Nutr*. 1998; 79: 23–30.
- [42] Benton D, Haller J, Fordy J. Vitamin supplementation for one year improves mood. 1995; 32: 98–105.
- [43] Bourre JM. Effect of nutrients (in food) on the structure and function of the nervous system: Update on dietary requirements for brain, Part 1: Micronutrients. *J Nutr Health Aging*. 2006; 10: 377–85.
- [44] Coppen A, Bailey J. Enhancement of the antidepressant action of fluoxetine by folic acid: A randomized placebo controlled trial. *J Affect Disord*. 2000; 60: 121–30.
- [45] Abou-Saleh MT, Coppen A. Folic acid and the treatment of depression. *J Psychosom Res*. 2006; 61: 285–7.
- [46] Alpert JE, Fava M. Nutrition and depression: The role of folate. *Nutr Rev*. 1997; 55: 145–9.

- [47] Golzman D. Canadian study: SSRI increase Bone fracture risk. *Arch Intern Med.* 2007; 167: 188–94.
- [48] Davison K, Abraham KM, Connor, McLeod MN. Effectiveness of chromium in atypical depression: A placebo-controlled trial. *Bio Psychiatry.* 2003; 53: 261–4.
- [49] Docherty J, Sack DA, Roffman M, Finch M, Komorowski JR. A double-blind, placebo-controlled exploratory trial of chromium picolinate in atypical depression: Effect on carbohydrate craving. *J PsychiatPract.* 2005; 11: 302–14.
- [50] Mohandas E, Rajmohan V. Lithium use in special populations. *Indian J Psychiatry.* 2007; 49: 211–8.
- [51] Benton D. Selenium Intake, mood and other aspects of psychological functioning. *NutrNeurosci.* 2002; 5: 363–74.
- [52] Shor-Posner GR, Lecusay, Miguez MJ, Moreno-Black G, Zhnag G, Rodriguez N, et al. Psychological burden in the era of HAART: Impact of selenium therapy. *Int J Psychiatry Med.* 2003; 33: 55–69.
- [53] Duntas LH, Mantzou E, Koutras EA. Effects of a six month treatment with selenomethionine in patients with autoimmune thyroiditis. *Eur J Endocrinol.* 2003; 148: 389–93.
- [54] Levenson CW. Zinc, the new antidepressant? *Nutr Rev.* 2006; 6: 39–42.
- [55] Nowak G, Szewczyk A. Zinc and depression, An update. *Pharmacol Rep.* 2005; 57: 713–8.
- [56] Roberts SB. Energy regulation and aging: recent findings and their implications. *Nutr Rev.* 2000; 58: 91–7.
- [57] Marcus and Berry. Refusal to eat in the elderly. *Nutr Rev.* 1998; 56: 163–71.
- [58] National Center for Complementary and Alternative Medicine - National Institutes of Health. 2002.
- [59] Andreescu C, Mulsant BH, Emanuel JE. Complementary and alternative medicine in the treatment of bipolar disorder: A review of the evidence. *J AffectDisord.* 2008 May 2.