

## Nutraceuticals: As Solutions on Pharmaceuticals

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**ABSTRACT:** Nutraceuticals are merchandise, which other than nutrition also are used as remedy. A nutraceutical product is a substance that gives physiological advantages or prevents chronic disease. Nutraceuticals can be used to show fitness, gradual the getting old technique, save you chronic diseases, extend lifestyles expectancy, and aid the shape and function of the body. Nutraceuticals have currently won popularity due to their capacity nutritional, protection, and therapeutic benefits. Latest research has yielded promising consequences for those compounds in an expansion of headaches. The modern evaluate has made sizable efforts to present new standards approximately nutraceuticals based on disorder-editing warning signs. Emphasis has been made to offer herbal nutraceuticals effective on hard healing disorders related to oxidative pressure, along with hypersensitive reaction, Alzheimer's, cardiovascular, eye sickness, weight problems, hypertension and so on.

**Keywords:** Disease modifiers, oxidative stress, antioxidants, herbal nutraceuticals, as well as nutraceutical products

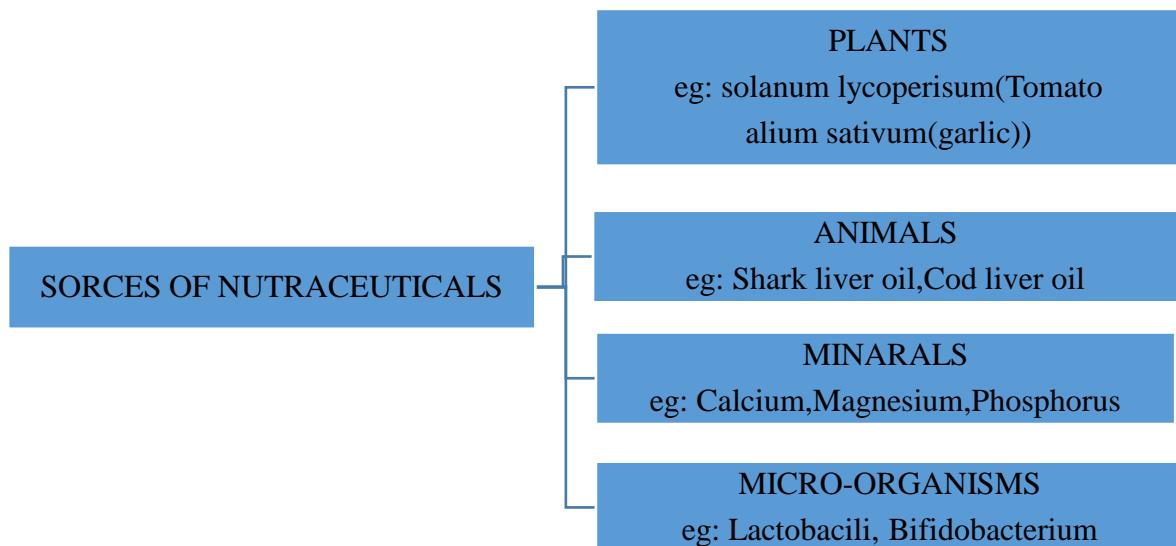
### I. INTRODUCTION:

- Nutraceutical is a time period derived from "nutrition" and "pharmaceutics." The word refers to gadgets which are separated from herbal merchandise, dietary dietary supplements (vitamins), particular diets, and processed meals like cereals, soups, and beverages that serve as medications further to being nutritional supplements.<sup>[1]</sup>
- The goods referred to as "nutraceuticals" are regulated within the USA as medicines, food additives, and nutritional dietary supplements. Whilst definitions of the time period vary by using USA, they normally talk to a product this

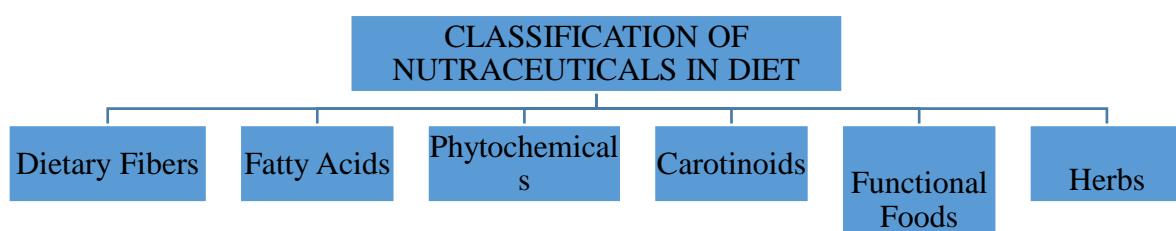
is separated from meals and offered in medicinal bureaucracy unrelated to meals. A substance that has physiological benefits or presents safety in opposition to persistent illnesses can be classified as a nutraceutical product. Nutraceuticals have a possibility to improve properly-being, postpone the growing old system, save you continual illnesses.<sup>[2]</sup>

- Nutraceutical, in evaluation to prescribed drugs, are substances, which usually have now not patent protection. it's far possible to treat or save you illnesses with each pharmaceutical and nutraceutical compounds, however handiest pharmaceutical compounds have official authorities approval.<sup>[3]</sup>
- A nutritional supplement is taken into consideration as a product that bears or contains one or extra of the following nutritional substances: all of those gadgets: a mineral, nutrition, amino acid, medicinal herb or different botanical, dietary complement for human use that raises the daily intake; or concentrates, metabolites, elements, extracts, or mixtures of those substances. amongst those nutritional supplements which can be used for reasons apart from nutrients are nutraceuticals.<sup>[4]</sup>
- The current evaluation has made big efforts to provide new standards about nutraceuticals based totally on sickness-editing symptoms. The emphasis has been on providing herbal nutraceuticals that are effective in difficult-to-treat oxidative pressure problems such as hypersensitive reactions, Alzheimer's, cardiovascular, cancer, diabetes, eye, immune, inflammatory, and Parkinson's diseases, as well as obesity.

- **SOURCES OF NUTRACEUTICALS:**



- **CLASSIFICATION OF NUTRACEUTICALS IN DIET**



- **ADVANTAGE OG NUTRACEUTICALS:**

1. Improve health.
2. Postpone getting older.
3. Available and affordable.
4. Prolongs life.
5. Reduced side effects with desirable outcomes.
6. Holistic methodology.
7. Naturally supply dietary supplements.
8. It provides food for populations with special needs, such as old people who need nutrient-dense food.

- **LIMITATIONS OF NUTRACEUTICALS:**

1. Different testing and regulations apply than for pharmaceuticals.
2. Most US states do not have FDA regulation.
3. Businesses that produce unregulated goods in order to generate large profit margins.

4. Nutrient bioavailability is decreased.
5. Constant reports of toxicity and side effects have been made, resulting from the potential for contamination as well as the nutraceutical itself being consumed.
6. The issue lies in the fact that a lot of these products fail to adequately inform customers about their efficacy and safety, potential side effects, interactions with prescription drugs, and effects on pre-existing medical conditions.
7. The effect could be comparable to a placebo.

<b>PHYSIOLOGICAL NUTRACEUTICALS:</b>	<b>BENEFIT</b>	<b>OF</b>
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1. Cardiovascular agents
2. Antidiabetic agents

3. Antidiabetics
4. Anticancer retailers
5. Immune boosters
6. Chronic inflammatory issues
7. Degenerative illnesses

❖ **TREATMENT OF DISEASE WITH NUTRACEUTICALS :**

**A) CARDIOVASCULAR DISEASES AND NUTRACEUTICALS:**

- The superiority of CVD is growing globally, as are research efforts on this region.<sup>[5]</sup> CVD refers to a variety of heart and blood vessel problems, including coronary heart disorder (heart assault), peripheral vascular disease, cerebrovascular ailment (stroke), high blood pressure, and heart failure.<sup>[6,7]</sup> Low vegetable and fruit consumption is thought to be associated with high CVD mortality.<sup>[8,9,10]</sup> most people of CVDs are preventable. Many research have located that a vegetable and fruit-wealthy weight-reduction plan can shield in opposition to CVD.<sup>[11]</sup>
- To save you and treat CVD, it's miles recommended to eat nutraceuticals inclusive of vitamins, minerals, antioxidants, dietary fibres, and omega-3 polyunsaturated fatty acids (n-3 PUFAs), in conjunction with physical hobby. Polyphenols modify mobile metabolism and signalling, that's thought to reduce arterial disorder.<sup>[12]</sup>
- Flavonoids are extensively distributed in vegetables, onions, endives, cruciferous, grapefruits, apples, cherries, pomegranate, berries, black grapes, and pink wine, and are to be had as flavones, flavanones, and flavonols,<sup>[13]</sup> and play an important function in the prevention and treatment of CVD. Flavonoids inhibit the angiotensin-converting enzyme, cyclooxygenase enzymes that damage down prostaglandins, and platelet aggregation. in addition they defend the vascular machine, which transports oxygen and nutrients to the cells.<sup>[14,15]</sup> Plant foods contain anthocyanins, tannins(proanthocyanidins), tetrahydro-β-carbolines, stilbenes, dietary indoleamines, serotonin, and melatonin, all of which are notion to have health blessings.<sup>[16]</sup> Orange juice containing pulp is excessive in flavonoids. Hesperidin is a flavanone glycoside that belongs to the citrus bioflavonoid class. Citrus sinensis and tangelos are the highest dietary assets of hesperidin. Lemon peel.<sup>[17]</sup>
- Phytosterols compete with dietary cholesterol by way of inhibiting uptake and facilitating excretion from the body. Consequently, they have the ability to reduce the morbidity and mortality from CVD. Phytosterols are observed in maximum plant species, and even as inexperienced and yellow greens comprise great amounts of sterols, their seeds pay attention them.<sup>[18,19]</sup>
- Fish carries omega-three fatty acids, which have an effect on plasma lipids and CVD, along with arrhythmias. Octacosanol, discovered in entire grains, end result, and leaves of many flowers, has lipid-reducing properties and not using a side effects.<sup>[19,20]</sup>

**B) DIABETES AND NUTRACEUTICALS:**

- Type 2 diabetes is the most common, accounting for 95% of all cases, and its miles related to weight problems. notwithstanding the introduction of numerous drugs for diabetes prevention and treatment, the worldwide total quantity of humans with diabetes is growing because of an expansion of things.<sup>[21,22,23]</sup> Diabetes has a sizable financial impact on each individual patients and their households, as well as society as entire.<sup>[24]</sup>
- In current years,a huge variety of natural nutritional supplements and natural medicines have been scientifically validated to gain kind 2 diabetes mellitus in preclinical studies<sup>[25,26]</sup>, however few have been proven to do so in properly-designed randomised medical trials.<sup>[27]</sup>
- Isoflavones are phytoestrogens with structural and practical similarities to human oestrogens. Soy isoflavones have been drastically studied, and their intake has been related to a lower incidence and mortality fee from kind II diabetes, coronary heart sickness, osteoporosis, and sure cancers.<sup>[28]</sup>
- Omega-3 fatty acids have been connected to a reduction in glucose tolerance in diabetes patients. Insulin is vital for the synthesis of lengthy chain n-three fatty acids, making the heart prone to insulin deficiency during diabetes. Ethyl esters of n-three fatty acids may gain diabetics.<sup>[29]</sup>
- Lipoic acid is an antioxidant used in the remedy of diabetic neuropathy and

appears to be effective as an extended-time period dietary complement to defend diabetics from complications.<sup>[30]</sup> Psyllium dietary fibres had been widely used as pharmacological dietary supplements, meals substances, and in processed meals to aid in weight loss, glucose manipulate in diabetic sufferers, and lipid reduction in hyperlipidemia.<sup>[31]</sup> A variety of plant extracts, inclusive of Toucium polium, cinnamon, and sour melon, have been shown to help save you or deal with diabetes.<sup>[32]</sup>

### C) CANCER AND NUTRACEUTICAL:

- Cancer has emerged as a main public-health difficulty in growing countries. Consistent with the arena cancer report, cancer fees are growing, with 15 million new instances predicted by way of 2020, representing a 50% boom. A healthful lifestyle and weight loss program can help save you most cancers.<sup>[33]</sup> Carotenoids are a collection of phytochemicals that are accountable for the numerous colorings of meals. They have got antioxidant properties and are powerful at cancer prevention. current research into carotenoids has targeted at the position of lycopene in human fitness, particularly in most cancers disease.<sup>[34]</sup>
- Flora high in daidzein, biochanin, isoflavones, and genistein inhibit the increase of prostate most cancers cells. Lycopene, that is unsaturated, is a effective antioxidant and a singlet oxygen quencher. Lycopene is concentrated in the prostate, testes, skin, and adrenal glands, in which it protects in opposition to cancer.<sup>[35]</sup> The link between carotenoids and the prevention of cancer and CAD has elevated the importance of greens and fruits in the human weight-reduction plan.
- Lycopene-wealthy greens and fruits reduce oxidative strain and DNA harm, thereby protective towards most cancers.<sup>[36]</sup> Lycopene, one of the major carotenoids, is handiest determined in tomatoes, guava, red grapefruit, watermelon, and papaya.<sup>[36]</sup>  $\beta$ -carotene has antioxidant properties and helps prevent cancer and other diseases.  $\beta$ -carotene is the carotenoid with the highest antioxidant activity. Alpha-carotene has 50-54% of the antioxidant activity as  $\beta$ -carotene, while epsilon-carotene has 42-50%.
- persistent irritation increases the danger of developing most cancers. continual irritation is also connected to immune suppression, a chance aspect for cancer. Ginseng is an instance of an antiinflammatory molecule that targets numerous key gamers inside the irritation-to-cancer pathway.<sup>[37]</sup>
- Cancer-preventive phytochemicals are presently receiving quite a few interest. Chemopreventive components found in end result and veggies might also have anticarcinogenic and antimutagenic residences, further to different health blessings. A extensive variety of phytopharmaceuticals with claimed hormonal interest, called "phytoestrogens," is suggested for the prevention of prostate and breast most cancers.<sup>[38]</sup>
- Citrus fruit flavonoids can assist prevent cancer by performing as antioxidants. Soyfoods are a unique dietary source of isoflavones, polyphenol phytochemicals consisting of epigallocatechin gallate from tea, curcumin from curry, and soya isoflavones, that have most cancers-stopping residences.<sup>[39]</sup>
- Soybeans appear to provide safety against breast, uterine, lung, colorectal, and prostate cancers.  $\beta$ -carotene is present in yellow, orange, and green leafy greens and fruits, such as tomatoes, lettuce, oranges, sweet potatoes, broccoli, cantaloupe, carrots, spinach, and wintry weather squash.
- Saponins have been shown to have antimutagenic and antitumor properties, and they will reduce the hazard of human cancer via inhibiting the growth of most cancers cells. Saponins are phytochemicals observed in peas, soybeans, and some herbs acknowledged for their foaming homes, such as soapberry, soapwort, and soapbark. They can also be found in tomatoes, potatoes, alfalfa, spinach, and clover. Industrial saponins are normally extracted from *Yucca schidigera* and *Quillaja saponaria*.
- Tannins also scavenge free radicals and get rid of cancer causing agents. Tannins discovered in grapes, lentils, tea, blackberries, blueberries, and cranberries had been proven to be anticarcinogenic and are used in alternative medication to prevent most cancers. Walnuts, pecans, strawberries, cranberries, pomegranates, and pink raspberry seeds all incorporate ellagic acid, that's an anticancer agent.<sup>[40]</sup>

#### D) ALZHEIMER'S DISEASE AND NUTRACEUTICALS:

- Alzheimer's disorder (advent) is the most typical form of dementia. there is no remedy for the disorder, which finally causes dying. Alzheimer's sickness is most usually diagnosed in human beings over the age of 65, even though early-onset Alzheimer's can occur a great deal earlier. In 2006, there had been 26.6 million patients worldwide, and it is anticipated to have an effect on one in each eighty five humans with the aid of 2050.<sup>[41]</sup>
- Ladies are more affected than guys, by using nearly 2:1. Several traces of evidence point to an association among oxidative stress and a ramification of neurodegenerative disorders, inclusive of Alzheimer's disorder. Nutraceutical antioxidants like curcumin, lutein, lycopene, turmerin, and  $\beta$ -carotene can fight oxidative strain and potentially gain specific diseases.
- The developing popularity of nutraceuticals stems from the belief that those compounds can postpone the improvement of dementias consisting of Alzheimer's disease.<sup>[30]</sup> several recent papers have demonstrated the beneficial outcomes of numerous nutriceutical plants on Alzheimer's disease, studying, and memory, which includes Zizyphus jujube and Lavandula officinalis.<sup>[42]</sup>

#### E) ALLERGY AND NUTRACEUTICALS:

- Hypersensitive reactions are immune-system hypersensitivity disorders. An allergy is generally brought about whilst someone's immune machine reacts to normally innocent substances. Allergic reactions are prominent via immoderate activation of specific white blood cells known as mast cells and basophils by means of an antibody called immunoglobulin E. This reaction causes an inflammatory reaction that can range from uncomfortable to dangerous.<sup>[43]</sup>

#### F) OBESITY AND NUTRACEUTICALS:

- Obesity is now a worldwide public fitness problem,

affecting approximately 315 million people. Weight increase the danger of a diffusion of sicknesses, which includes hypertension, congestive coronary heart failure, angina pectoris, hyperlipidaemia, respiratory disorders, osteoarthritis, most cancers, renal vein thrombosis, and reduced fertility.<sup>[44]</sup>

#### ❖ FUTURE SCOPE:

Nutraceuticals are the destiny of pharmaceuticals, and the worldwide preference to be more healthy is using the marketplace. • Soyprotein vitamins, useful food components which include lutein, lycopene, omega-3 fatty acids, probiotics, and sterol esters, essential minerals calcium and magnesium, natural extracts garlic and green tea, and non-herbal extracts chondroitin, glucosamine, and coenzyme Q10 are all predicted to look giant increase in the coming years.

#### II. CONCLUSION:

Nutraceuticals may be described as materials that have physiological blessings or protect towards continual diseases. Nutraceuticals may be used to enhance fitness, gradual the ageing procedure, prevent continual sicknesses, enlarge lifestyles expectancy, and aid the shape and feature of the frame. Nutraceuticals have these days won recognition because of their capacity nutritional, protection, and healing blessings. Current studies has yielded promising results for those compounds in a variety of complications. in this evaluate, a lot attempt has been made to offer ailment-modifying warning signs associated with oxidative strain, along with hypersensitivity, Alzheimer's, cardiovascular, cancer, diabetes, eye, immune, inflammatory, and Parkinson's diseases, as well as obesity.

#### REFERENCES:

- [1]. Kalra EK. Nutraceutical – Definition and introduction. AAPS Pharm Sci. 2003;5:E25. [PMC free article] [PubMed] [Google Scholar]
- [2]. Zhao J. Bentham Science Publishers; 2007. [Last accessed on 2012 Mar 24]. Nutraceuticals, Nutritional Therapy, Phytonutrients, and Phytotherapy for Improvement of Human Health: A Perspective on Plant Biotechnology

- Application. Available from: <http://www.benthamscience.com/biot/samples/biot1-1/Zhao.pdf>. [PubMed] [Google Scholar]
- [3]. Chauhan B, Kumar G, Kalam N, Ansari SH. Current concepts and prospects of herbal nutraceutical: A review. *J Adv Pharm Technol Res.* 2013;4:4–8. [PMC free article] [PubMed] [Google Scholar]
- [4]. Zeisel SH. Regulation of “nutraceuticals” *Science.* 1999;285:18535. [PubMed] [Google Scholar]
- [5]. Ghorbani A, Rafieian-Kopaei M, Nasri H. Lipoprotein (a): More than a bystander in the etiology of hypertension? A study on essential hypertensive patients not yet on treatment. *J Nephropathol.* 2013;2:67–70. [PMC free article] [PubMed] [Google Scholar]
- [6]. Behradmanesh S, Nasri P. Serum cholesterol and LDL-C in association with level of diastolic blood pressure in type 2 diabetic patients. *J Renal Inj Prev.* 2012;1:23–6. [PMC free article] [PubMed] [Google Scholar]
- [7]. Nasri H. Comment on: Serum cholesterol and LDL-C in association with level of diastolic blood pressure in type 2 diabetic patients. *J Renal Inj Prev.* 2012;1:13–4. [PMC free article] [PubMed] [Google Scholar]
- [8]. Asgary S, Keshvari M, Sahebkar A, Hashemi M, Rafieian-Kopaei M. Clinical investigation of the acute effects of pomegranate juice on blood pressure and endothelial function in hypertensive individuals. *ARYA Atheroscler.* 2013;9:326–31. [PMC free article] [PubMed] [Google Scholar]
- [9]. Nasri H, Sahinfard N, Rafieian M, Rafieian S, Shirzad M, Rafieian-kopaei M. Effects of Allium sativum on liver enzymes and atherosclerotic risk factors. *J HerbMed Pharmacol.* 2013;2:23–8. [Google Scholar]
- [10]. Rafieian-Kopaei M. Medicinal plants and the human needs. *J HerbMed Pharmacol.* 2012;1:1–2. [Google Scholar]
- [11]. Hu FB, Willett WC. Optimal diets for prevention of coronary heart disease. *JAMA.* 2002;288:2569–78. [PubMed] [Google Scholar]
- [12]. Iriti M, Faoro F. Grape phytochemicals: A bouquet of old and new nutraceuticals for human health. *Med Hypotheses.* 2006;67:833–8. [PubMed] [Google Scholar]
- [13]. Behradmanesh S, Nasri H. Association of serum calcium with level of blood pressure in type 2 diabetic patients. *J Nephropathol.* 2013;2:254–7. [PMC free article] [PubMed] [Google Scholar]
- [14]. Hajivandi A, Amiri M. World kidney day 2014: Kidney disease and elderly. *J Parathyroid Dis.* 2014;2:3–4. [Google Scholar]
- [15]. Shahbazian H. World diabetes day; 2013. *J Renal Inj Prev.* 2013;2:123–4. [PMC free article] [PubMed] [Google Scholar]
- [16]. Asgary S, Sahebkar A, Afshani M, Keshvari M, Haghjooyjavanmard SH, Rafieian-Kopaei M. Clinical evaluation of blood pressure lowering, endothelial function improving, hypolipidemic and anti-inflammatory effects of pomegranate juice in hypertensive subjects. *Phytother Res.* 2013 [PubMed] [Google Scholar]
- [17]. Gharipour M, Ramezani MA, Sadeghi M, Khosravi A, Masjedi M, Khosravi-Boroujeni H, et al. Sex based levels of C-reactive protein and white blood cell count in subjects with metabolic syndrome: Isfahan Healthy Heart Program. *J Res Med Sci.* 2013;18:467–72. [PMC free article] [PubMed] [Google Scholar]
- [18]. Khosravi-Boroujeni H, Mohammadifard N, Sarrafzadegan N, Sajjadi F, Maghroun M, Khosravi A, et al. Potato consumption and cardiovascular disease risk factors among Iranian population. *Int J Food Sci Nutr.* 2012;63:913–20. [PubMed] [Google Scholar]
- [19]. Khosravi-Boroujeni H, Sarrafzadegan N, Mohammadifard N, Sajjadi F, Maghroun M, Asgari S, et al. White rice consumption and CVD risk factors among Iranian population. *J Health Popul Nutr.* 2013;31:252–61. [PMC free article] [PubMed] [Google Scholar]
- [20]. Iriti M, Faoro F. Grape phytochemicals: A bouquet of old and new nutraceuticals for human health. *Med Hypotheses.* 2006;67:833–8. [PubMed] [Google Scholar]
- [21]. Gita C. Functional food attributes of n-3 polyunsaturated and conjugated linoleic acid enriched chicken eggs. *Curr Top*

- Nutraceutical Res. 2004;2:113–21. [Google Scholar]
- [22]. Khosravi-Boroujeni H, Mohammadifard N, Sarrafzadegan N, Sajjadi F, Maghroun M, Khosravi A, et al. Potato consumption and cardiovascular disease risk factors among Iranian population. *Int J Food Sci Nutr.* 2012;63:913–20. [PubMed] [Google Scholar]
- [23]. Sidhu KS. Health benefits and potential risks related to consumption of fish or fish oil. *Regul Toxicol Pharmacol.* 2003;38:336–44. [PubMed] [Google Scholar]
- [24]. Heidarian E, Rafieian-Kopaei M, Ashrafi K. The Effect of hydroalcoholic extract of Allium latifolium on the liver phosphatidate phosphatase and serum lipid profile in hyperlipidemic rats. *J Babol Univ Med Sci.* 2013;15:37–46. [Google Scholar]
- [25]. Bahmani M, Zargaran A, Rafieian-Kopaei M, Saki M. Ethnobotanical study of medicinal plants used in the management of diabetes mellitus in the Urmia, Northwest Iran. *Asian Pac J Trop Med.* 2014;7:348–54. [PubMed] [Google Scholar]
- [26]. Roshan B, Stanton RC. A story of microalbuminuria and diabetic nephropathy. *J Nephropathol.* 2013;2:234–40. [PMC free article] [PubMed] [Google Scholar]
- [27]. Tavafi M. Diabetic nephropathy and antioxidants. *J Nephropathol.* 2013;2:20–7. [PMC free article] [PubMed] [Google Scholar]
- [28]. Baradaran A. Lipoprotein (a), type 2 diabetes and nephropathy; the mystery continues. *J Nephropathol.* 2012;1:126–9. [PMC free article] [PubMed] [Google Scholar]
- [29]. Rahimi-Madiseh M, Heidarian E, Rafieian-kopaei M. Biochemical components of Berberis lycium fruit and its effects on lipid profile in diabetic rats. *J HerbMed Pharmacol.* 2014;3:15–9. [Google Scholar]
- [30]. Rafieian-Kopaei M, Nasri H. Ginger and diabetic nephropathy. *J Renal Inj Prev.* 2013;2:9–10. [PMC free article] [PubMed] [Google Scholar]
- [31]. Tolouian R, T Hernandez G. Prediction of diabetic nephropathy: The need for a sweet biomarker. *J Nephropathol.* 2013;2:4–5. [PMC free article] [PubMed] [Google Scholar]
- [32]. Tavafi M. Diabetic nephropathy and antioxidants. *J Nephropathol.* 2013;2:20–7. [PMC free article] [PubMed] [Google Scholar]
- [33]. Sirtori CR, Galli C. N-3 fatty acids and diabetes. *Biomed Pharmacother.* 2002;56:397–406. [PubMed] [Google Scholar]
- [34]. Coleman MD, Eason RC, Bailey CJ. The therapeutic use of lipoic acid in diabetes: A current perspective. *Environ Toxicol Pharmacol.* 2001;10:167–72. [PubMed] [Google Scholar]
- [35]. Singh B. Psyllium as therapeutic and drug delivery agent. *Int J Pharm.* 2007;334:1–14. [PubMed] [Google Scholar]
- [36]. Momeni A. Serum uric acid and diabetic nephropathy. *J Renal Inj Prev.* 2012;1:37–8. [PMC free article] [PubMed] [Google Scholar]
- [37]. Nasri H, Rafieian-Kopaei M. Herbal medicine and diabetic kidney disease. *J Nephropharmacol.* 2013;2:1–2. [PMC free article] [PubMed] [Google Scholar]
- [38]. Kazemi S, Asgary S, Moshtaghian J, Rafieian M, Adelnia A, Shamsi F. Liver-protective effects of hydroalcoholic extract of Allium hirtifolium boiss. In rats with alloxan-induced diabetes mellitus. *ARYA Atheroscler.* 2010;6:11–5. [PMC free article] [PubMed] [Google Scholar]
- [39]. Willis MS, Wians FH. The role of nutrition in preventing prostate cancer: A review of the proposed mechanism of action of various dietary substances. *Clin Chim Acta.* 2003;330:57–83. [PubMed] [Google Scholar]
- [40]. Kruger CL, Murphy M, DeFreitas Z, Pfannkuch F, Heimbach J. An innovative approach to the determination of safety for a dietary ingredient derived from a new source: Case study using a crystalline lutein product. *Food Chem Toxicol.* 2002;40:1535–49. [PubMed] [Google Scholar]
- [41]. Shirzad H, Kiani M, Shirzad M. Impacts of tomato extract on the mice fibrosarcoma cells. *J HerbMed Pharmacol.* 2013;2:13–6. [Google Scholar]

- [42]. Stahl W, Sies H. Bioactivity and protective effects of natural carotenoids. *Biochim Biophys Acta*. 2005;1740:101–7. [\[PubMed\]](#) [\[Google Scholar\]](#)
- [43]. Shirzad H, Taji F, Rafieian-Kopaei M. Correlation between antioxidant activity of garlic extracts and WEHI-164 fibrosarcoma tumor growth in BALB/c mice. *J Med Food*. 2011;14:969–74. [\[PubMed\]](#) [\[Google Scholar\]](#)
- [44]. Shirzad H, Shahrani M, Rafieian-Kopaei M. Comparison of morphine and tramadol effects on phagocytic activity of mice peritoneal phagocytes *in vivo*. *Int Immunopharmacol*. 2009;9:968–70. [\[PubMed\]](#) [\[Google Scholar\]](#)
- [45]. Limer JL, Speirs V. Phyto-oestrogens and breast cancer chemoprevention. *Breast Cancer Res*. 2004;6:119–27. [\[PMC free article\]](#) [\[PubMed\]](#) [\[Google Scholar\]](#)
- [46]. Thomasset SC, Berry DP, Garcea G, Marczylo T, Steward WP, Gescher AJ. Dietary polyphenolic phytochemicals – Promising cancer chemopreventive agents in humans? A review of their clinical properties. *Int J Cancer*. 2007;120:451–8. [\[PubMed\]](#) [\[Google Scholar\]](#)
- [47]. Li H, Wang Z, Liu Y. Review in the studies on tannins activity of cancer prevention and anticancer. *Zhong Yao Cai*. 2003;26:444–8. [\[PubMed\]](#) [\[Google Scholar\]](#)
- [48]. Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Forecasting the global burden of Alzheimer's disease. *Alzheimers Dement*. 2007;3:186–91. [\[PubMed\]](#) [\[Google Scholar\]](#)
- [49]. Rabiei Z, Rafieian-Kopaei M, Heidarian E, Saghaei E, Mokhtari S. Effects of *Zizyphus jujube* extract on memory and learning impairment induced by bilateral electric lesions of the nucleus basalis of Meynert in rat. *Neurochem Res*. 2014;39:353–60. [\[PubMed\]](#) [\[Google Scholar\]](#)
- [50]. Grammatikos AP. The genetic and environmental basis of atopic diseases. *Ann Med*. 2008;40:482–95. [\[PubMed\]](#) [\[Google Scholar\]](#)
- [51]. Caterson ID, Gill TP. Obesity: Epidemiology and possible prevention. *Best Pract Res Clin Endocrinol Metab*. 2002;16:595–610. [\[PubMed\]](#) [\[Google Scholar\]](#)