

Nutraceuticals: A Review

Simran Vij*, Rajesh Kumar, Ajeet Pal Singh, Amar Pal Singh & Prachi Sharma

Department of Pharmaceutics, St.Soldier Institute of Pharmacy, Lidhran Campus Behind NIT(R.E.C) Jalandhar-Amritsar by Pass, Nh-1, Jalandhar-1440011, Punjab, India.

Abstract

Nutraceuticals have garnered significant attention due to their perceived safety, encompassing foods or food components that offer medicinal or health advantages, including disease prevention and treatment. These products play a crucial role in addressing prevalent health issues such as obesity, cardiovascular disease, cancer, and diabetes. Unlike traditional medications, nutraceuticals often boast natural origins and a reduced risk of side effects. Categorized into nutrients, herbals, and dietary supplements based on their natural sources and chemical composition, the industry has witnessed notable growth rates, particularly in dietary supplements and herbal products. The global nutraceutical market is projected to reach USD 404.8 billion by 2025. Regulatory measures, such as a FDA oversight in the US and the Food Safety and Standard Act in India, ensure the safety and quality of these products. Herbal nutraceuticals, in particular, play a vital role in supporting overall health and combating nutrition-related ailments. This article emphasizes the importance of adhering to established healthy benefits, and understanding the mechanism behind their actions. It serves as a valuable resource for staying updated on recent advancements in nutraceutical research.

1. INTRODUCTION



a. Definition of Nutraceutical

- Nutraceuticals are derived from the combination of “nutrition” and “pharmaceutics”.
- They include products isolated from herbal sources, dietary supplements, specific diets, and processed foods like cereals, soups, and beverages.
- These products, apart from providing nutrition, also have medicinal uses.

b. Benefits of Nutraceuticals

- Nutraceuticals offer physiological benefits and against chronic disease.
 - They can improve health, delay aging, prevent diseases, increase life expectancy, and support body structure and function.
- #### c. Importance and Interest in Nutraceuticals
- Nutraceuticals have gained considerable interest due to their nutritional, safety, and therapeutic effects.
 - Recent studies show promising results for nutraceutical compounds in various diseases.

d. Therapeutic Effects of Nutraceuticals

- Nutraceuticals have therapeutic effects on diseases related to oxidative stress, including allergy, Alzheimer's cardiovascular diseases, cancer, diabetes, eye disorders, immune disorders, inflammatory conditions, Parkinson's and obesity.

e. Sources of Information

- Scientific sites like Medline, Pubmed, and Google scholar were used to gather information about nutraceuticals and their effects on different diseases.

f. Regulatory status and Definition of Nutraceuticals

- In the US, nutraceutical products are regulated as drugs, food ingredients, and dietary supplements.
- Nutraceuticals lack patent protection unlike pharmaceuticals but are used for similar therapeutic purposes.
- Dietary supplements contain various ingredients like minerals, vitamins, amino acids, medical herbs, and botanicals, and are considered a subset of nutraceuticals.

g. Popular Nutraceuticals

- Examples of popular nutraceuticals include ginseng, Echinacea, glucosamine, omega-3, lutein, folic acid, and cod liver oil.
- Many nutraceuticals have multiple therapeutic properties.

h. Market Growth and Potential

- The global nutraceutical market is projected to reach USD 722.49 billion by 2027, with an expected compound annual Growth Rate of 8.3%.
- Markets like Japan and Canada are also forecasted to grow significantly in the nutraceutical sector.

i. Therapeutic Potential of Nutraceuticals

- Nutraceuticals have shown promising results in treating conditions like diabetes, atherosclerosis, cardiovascular diseases, cancer, and neurological disorders by targeting changes in the body's redox state.

- Their antioxidant properties make them valuable for promoting health and preventing life-threatening diseases.

2. **FACTORS DIVIDED THE SHIFT TOWARDS NUTRACEUTICALS**

a. Therapeutics Coverage:

Nutraceuticals encompass a wide range of therapeutics areas including anti-arthritis, cold and cough, sleeping disorders, digestion, and prevention of certain cancers, osteoporosis, blood pressure, cholesterol control, pain management, depression, and diabetes.

b. Dissatisfaction with Pharmaceuticals:

Dissatisfaction with pharmaceutical agents in promoting health has led people to turn towards nutraceuticals for improving health and preventing chronic diseases.

c. Future Potential:

Nutraceuticals show significant potential as therapeutic agents with both preventive and curative properties, suggesting a promising future.

d. Allopathic Medicine Alternatives:

Individuals with chronic disease who have not found solutions in allopathic medicines are turning to nutraceuticals.

e. Replacement of Pharmaceuticals:

Nutraceuticals are rapidly replacing pharmaceuticals in the preventive and management of acute and chronic health problems.

f. Economics Considerations:

Economically challenged patients and those who prioritize prevention over cure are embracing nutraceuticals.

g. Rising Healthcare Costs Concerns:

Increasing numbers of consumers are concerned about rising healthcare costs, further driving the shift towards nutraceuticals.

3. **CATEGORIZATION OF NUTRACEUTICALS**

a. Natural Sources

- Carbohydrate & Fiber
- Fat & Essential Fatty Acids
- Protein
- Vitamins

- Minerals (Macro minerals & Trace minerals)
- Water
- Other Nutrients like Antioxidants, Phytochemicals & Intestinal Bacterial Flora
- b. Pharmacological Conditions
- Dietary supplements
- Functional Food
- Medicinal Food
- Pharmaceuticals
- c. Chemical Constitution
- Liquid Form
- Capsule Forms
- Powder Form
- Pill Form
- d. Regulation by FDA
- Dietary supplements are regulated by the FDA as foods, but their regulation differs from drugs and other foods.

1. Non-Traditional Nutraceuticals

- A. Fortified Nutraceuticals-
- Enriched with vitamins and minerals, often up to 100% of the Dietary Reference Intake for that nutrient.

- Examples include:
 - Orange juice fortified with Calcium
 - Cereals with added vitamins or minerals
 - Flour with added folic acid
 - Milk with added cholecalciferol
- B. Recombinant Nutraceuticals:
 - Produced through biotechnology, including genetic engineering, enzyme/ fermentation technologies.
 - Examples of products:
 - Probiotics
 - Bioactive components extracted using biotechnological methods.
 - Energy- providing foods like bread, alcohol, fermented starch, yogurt, cheese, vinegar, etc.

2. Traditional Nutraceuticals

Traditional nutraceuticals are simply natural with no changes to the food. Food contains several natural components that deliver benefits beyond basic nutrition, such as lycopene in tomatoes, omega-3 fatty acid in salmon or saponins in soys.

A. PROBIOTIC MICRO-ORGANISMS:

ROLE	SOURCES
Crowding out pathogens	Yogurt is rich source of probiotics
Symbiotic relationship	Kefir (A fermented milk drink)
Anti-Microbial effects	
Production of antitoxins	
Reversal of infection consequences	

B. PROBIOTICS

“Probiotics” are a more recent addition to our vocabulary and are the substances which when consumed are not digested by us.

- They act as a nutrient source for the good probiotic bacteria.
- They encourage the probiotic bacteria to grow in favourable environment, which in turn reduces the chances that harmful microbes may start to grow in our digestive tract.
- Example: Insulin has been widely used probiotic used in processed foods. It is a type

of fibre obtain from the root of such plants; chicory, Jerusalem artichoke, and even dandelions.

C. CHEMICAL CONSTITUENTS:

1. **HERBAL:** Nutraceutical holds a great promise to improve health and prevent chronic disease with the help of herbals. **E.g.-** Aloe vera gel, Ephedra, Garlic, Liquorice, Ginger etc.
2. **PHYTOCHEMICALS:** It is plant nutrients with particular biological activities in supporting human health and fight against

many harmful diseases of the human body.

E.g.- Carotenoids, Legumes, Sulphides etc.

D. NUTRACEUTICAL ENZYMES:

- Enzymes are an essential part of life, without which our bodies would cease to function. Those individuals who are suffering from medical conditions such as diabetes, digestive problems and obesity etc.
- Enzymes are derived from microbial, plant and animal sources.

EXAMPLES:-

- **Xylanase enzyme** - derived from *Trichoderma* sp.
- **Papaine enzyme** – widely used in nutraceutical industry as a protease enzyme to help protein digestion.
- **Lactase enzyme** – derived from *Aspergillus* sp. Lactose

1. Commercial Nutraceuticals

New molecule is difficult to discover and are more expensive and risky than ever before. Many pharmaceutical companies are now trying to manufacture nutraceutical because there is undoubtedly a very huge and growing market. Recognition of health benefits from consumption of omega-3 rich seafood is one of the most promising developments in human nutrition and disease prevention research in the past three decades.

A. DIETARY SUPPLEMENTS:

Dietary supplements are products containing concerned nutrients derived from food, often in liquid or capsule form. They encompass various dietary ingredients, including vitamins, minerals, herbs, amino acids and substances like enzymes and organ tissues.

○ TYPES & FORMS:

Available in multiple forms such as tablets, capsules, soft gels, liquids, powders and gel caps. It includes extracts, concentrates and formulations like tablets, capsules, gummies, drinks, and energy bars.

○ COMMONLY USED INGREDIENTS:

Popular supplements encompass a wide range of nutrients, including vitamins (e.g., D and B12), minerals (e.g., calcium and iron), herbs (e.g.,

echinacea and garlic), and specific products like glucosamine, probiotics, and fish oils.

○ FUNCTIONAL BENEFITS:

Dietary supplements serve various purposes, including detoxification, addressing vitamin and mineral deficiencies, and promoting healthy digestion and dietary habits.

B. FUNCTIONAL FOODS:

- Functional foods offer health benefits beyond basic nutrition.
- They're eaten in their natural state rather than as supplements.
- Nutrifaction enhances or restores nutrient levels in processed foods.
- Additional nutrients may be added, like vitamin D to milk.
- Health Canada defines them as food with added components for health benefits.
- In Japan, functional foods must meet specific criteria.
- Examples include fruits like berries and bananas, vegetables like broccoli and spinach, nuts like almonds and cashews, and seeds like chia and flax.

C. MEDICINAL FOOD:

- DEFINITION: Medicinal food plants are those whose consumed parts are recognized as therapeutic in traditional medicine, ethnomedicine, or biomedicine.
- HOLISTIC CONCEPT: Medicinal foods not only provide essential nutrients but also contain bioactive ingredients that help reduce nutrition-related diseases and promote overall well-being.
- NUTRACEUTICALS vs. MEDICINAL FOODS: Nutraceuticals provide medical benefits and can be consumed in non-food matrix forms like pills, while medicinal foods are integrated into normal dietary patterns.
- EXAMPLES: Spices like turmeric, garlic, peppermint, thyme, and sage have been traditionally used for their medicinal properties, such as antioxidant, anti-inflammatory, and digestive benefits.

D. PHARMACEUTICALS:

- DEFINITION: Pharmaceuticals or drugs are formulated to treat, cure, or prevent diseases and are not naturally part of our physiology.
- POTENCY: Pharmaceuticals have higher potency or biological activity compared to phytochemicals ingested in small amounts in the diet, exerting physiological effects over extended use.

4 TOP 10 NUTRACEUTICAL PRODUCTS

This industry is continuing to grow and expand as health-conscious customers look for ways to stay healthy and fit. Here, we've taken a closer look at the top 10 nutraceutical products on the market right now:

- 1) LIQUID PRENATAL VITAMINS – A hot trend in Nutraceuticals.
- 2) VITAMIN D3 – Important for Health and wellness.
- 3) GARCINIA CAMBOGIA - A leading product in weight loss supplements.
- 4) RASPBERRY KETONES – A powerful fat-burning supplement
- 5) GREEN TEA SUPPLEMENTS – A popular antioxidant choice
- 6) ECHINACEA – Versatile uses against infections and skin conditions
- 7) PROBIOTICS – Supporting gut health and digestion
- 8) OMEGA 3 FATTY ACIDS – Essential for overall health
- 9) ALPHA-LIPOIC ACIDS – A natural aid for various health benefits
- 10) VITAMIN B12 – Enhancing metabolism and energy levels.

5. NUTRACEUTICAL MARKET IN DIFFERENT COUNTRIES

A. SEGMENTS OF THE NUTRACEUTICAL INDUSTRY:

- 1) Herbal/Natural Products
- 2) Dietary Supplements
- 3) Functional Foods

B. GROWTH TRENDS:

- Herbal/natural products and dietary supplements are the fastest-growing segments.

- Research and development in the nutraceutical field are currently at their peak.

C. SCIENTIFIC NEED:

- Standardization of nutraceutical compounds/products is crucial.
- Rigorous clinical studies are required to support health claims.

D. REGIONAL MARKET INSIGHTS (ASIA PACIFIC):

- Projected to experience the fastest growth.
- Factors driving growth include busy lifestyles, increased consumption of convenience foods and rapid economic growth.
- Transformation of the food & beverages market due to urbanization, diet diversification, and liberalization of foreign direct investment.
- Rising income and demand for nutritional & healthy products contribute to market expansion.

E. KEY PLAYERS IN THE GLOBAL MARKET:

- Dominated by pharmaceuticals and FMCG companies.
- Major players include Dabur India, GlaxoSmithKline Consumer Healthcare, Cadila Healthcare, Zandu Pharmaceuticals, EID Parry, Himalaya Herbal Healthcare, Sami Labs, Ranbaxy, Elder Pharmaceuticals.

F. REGIONAL MARKET SEGMENTATION:

- North America, Europe, Asia Pacific, Latin America, Middle East & Africa.

G. TYPES OF NUTRACEUTICAL PRODUCTS:

Various types of Nutraceutical Products are available in market:

- i. FOOD – Snacks, confectionery products, bakery products, infants products.
- ii. BEVETAGES – Health drinks, energy drinks, juices.
- iii. DIETARY SUPPLEMENTS – Tablets, liquid, powder, other (gummies, chewable products)

H. DISTIBUTION CHANNELS:

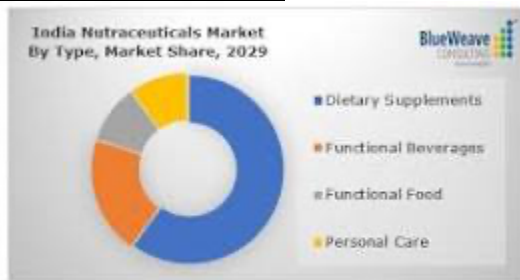
- i. Conventional Stores:

Grocery stores, mass merchandisers, warehouse clubs, online retailers.

ii. Specialty Stores:

Bakery stores, confectionery stores, gourmet stores, health centers.

6. THE GROWING NUTRACEUTICALS MARKET IN INDIA



Source: BlueWeave Consulting

- A. The nutraceuticals market in India is growing rapidly, expected to reach \$18 billion by 2025.
- B. It includes functional foods, beverages, and dietary supplements with the latter dominating the market.
- C. Major players like Amway, Himalaya, Dabur, and Emami compete in the dietary supplements segment.
- D. Factors driving the demand include undernourishment (15% of the population), government initiatives, and rising healthcare costs.
- E. India's GDP growth, coastal location, FDA-approved plants, low labour costs, and ample ingredient availability contribute to its strong market position.
- F. Increased internet penetration boosts nutraceuticals visibility and availability.
- G. Nutraceutical create opportunities for pharmaceutical and food companies to develop consumer-oriented products.
- H. Foreign investment are encouraged, with 100% FDI allowed in manufacturing and retail sectors.
- I. Domestic and global companies, like Patanjali and Nestle, are capitalizing on the growing market.

- J. The success of ventures like Patanjali and entry of global brands highlight the market's potential.

7. NUTRACEUTICALS AND DISEASES

Nutraceuticals have been claimed to have a physiological benefits or provide protection against the following diseases:

- A. Cardiovascular disease
- B. Diabetes
- C. Obesity
- D. Parkinson's disease
- E. Alzheimer's disease
- F. Cancer
- G. Allergy
- H. Osteoarthritis
- I. Eye disorders
- J. Immune disorders
- K. Inflammation

• TOXICITY POTENTIAL OF NUTRACEUTICALS

- Nutraceuticals, like medicinal plants, are believed to be safe remedies for health issues.
- While they generally have fewer side effects than pharmaceuticals, some can still have side effects.
- Conventional medicine views herbal medicines as drugs with potential side effects.
- Many nutraceuticals lack extensive safety studies, and some are poorly understood.
- Conservation efforts are needed to protect wild plants used for nutraceutical purposes.

• ANTI-TOXICITY OF NUTRACEUTICALS

- Synthetic drugs often have toxic properties, but herbal nutraceuticals are being explored for their ability to counteract toxins and drug toxicity.
- Oxidative stress plays a key role in drug toxicity, and many plants have antioxidant properties that can reduce oxidative stress.
- Nutraceuticals, especially medicinal plants, are studied for their protective effects on organs like the kidneys and liver, which are often affected by drug toxicity.

- Research shows promising results in using nutraceuticals to combat toxins and reduce the toxic effects of synthetic drugs.

8. CONCLUSION

Nutraceuticals play a significant role in both the food and pharmaceutical sectors, deriving from mineral, animal, or vegetable sources such as gamma terpenes, beta carotene, and curcumin. These components are formulated into various dosage forms like creams, tablets, and herbal formulations, offering diverse health benefits including anti-diabetic, anti-inflammatory, and anti-cancer properties. While nutraceuticals are increasingly favoured for their perceived natural benefits and cost-effectiveness compared to pharmaceuticals, further collaboration among health professionals, nutritionists, and toxicologists is essential to fully explore their potential. Despite their promising therapeutic properties, nutraceuticals require extensive scientific research and regulatory frameworks such as the proposed Nutraceutical Research and Education Act (NREA) to ensure their efficacy, affordability, and accessibility to all. Looking ahead, the nutraceutical market is poised for substantial growth, driven by rising concerns over lifestyle-related diseases and a shift towards preventive healthcare, with projections indicating significant market expansion in the coming years, reaching a value of USD 578.23 Billion by 2025 according to Grand View Research.

Reference:

1. Kalra EK, Nutraceutical – Definition and introduction. *AAPS Pharm Sci.* 2003;5:E25.
2. 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.
3. Zeisel SH, Regulation of “nutraceuticals” *Science.* 1999;285:1853-5.
4. Hardy G, Nutraceuticals and functional foods: Introduction and meaning. *Nutrition.* 2000;16:688-9.
5. Prevesh Kumar, Nirdesh Kumar and Tushar Omer, Nutraceuticals- critical supplement

For building a healthy India, *World Journal Of Pharmacy And Pharmaceutical Sciences,* 2016; 5(3): 579-594.

6. Olaiya C. O, Soetan K. O, Esan A. The role of nutraceuticals, functional foods and value added food products in the prevention and treatment of chronic diseases M. 1, *African Journal of Food Science,* 2016; 10(10): 185-193.
7. NamdeoShinde, BhaskarBangar, Sunil Deshmukh, Pratik Kumbhar. Nutraceuticals: A Review on current status. *Research J. Pharm. And Tech,* 2014; 7(1): 110-113.
8. Kharb S, Singh V. Nutraceuticals in health and disease prevention. *Indian J. Clin. Biochem,* 2004; 19(1): 50-53.
9. JeroenHugenholtz, Eddy J Smid, Victor Ladero, Pascal Hols. Metabolic engineering of lactic acid bacteria for the production of nutraceuticals. *Antonie van Leeuwenhoek,* 2002; 82: 217-235.
10. Vouloumanou EK, Makris GC, Karageorgopoulos DE. Probiotics for the prevention of respiratory tract infections: a systematic review. *Int J Antimicrob Agents,* 2009; 34:e1-e10.
11. Montrose DC, Floch MH: Probiotics used in human studies. *J ClinGastroenterol,* 2005; 39(6): 469-484.
12. N Borkar, SS Saurabh, KS Rathore, A Pandit, KR Khandelwal; An Insight on Nutraceuticals; *Pharma Tutor,* 2015; 3(8): 13-23.
13. Enhancing Nutraceutical Performance Using Excipient Foods: Designing Food Structures and Compositions to Increase Bioavailability David Julian McClements, Liqiang Zou, Ruojie Zhang, Laura Salvia-Trujillo, TahaKumosani, and Hang Xiao, *Comprehensive Reviewsin Food Science and Food Safety,* 2015; 14: 824-847.
14. Nasri H, Motamedi P, Dehghani N, Nasri P, Taheri Z, Kinani F, et al. Vitamin D and immune system. *J Renal Endocrinol.* 2014;1:5-7.

15. Asgary S, Kelishadi R, Rafieian-Kopaei M, Najafi S, Najafi M, Sahebkar A. Investigation of the lipid-modifying and antiinflammatory effects of *Cornus mas* L. supplementation on dyslipidemic children and adolescents. *PediatrCardiol*. 2013;34:1729-35.
16. Iriti M, Faoro F. Grape phytochemicals: A bouquet of old and new nutraceuticals for human health. *Med Hypotheses*. 2006;67:833-8.
17. Garg A, Garg S, Zaneveld LJ, Singla AK. Chemistry and pharmacology of the Citrus bioflavonoid hesperidin. *Phytother Res*. 2001;15:655-69.
18. Rafieian-Kopaei M, Baradaran A, Rafieian M. Plants antioxidants: From laboratory to clinic. *J Nephrothol*. 2013;2:152-3.
19. Ghayur MN, Gilani AH, Afridi MB, Houghton PJ. Cardiovascular effects of ginger aqueous extract and its phenolic constituents are mediated through multiple pathways. *VasculPharmacol*. 2005;43:234-41.
20. Bahmani M, Vakili-Saatloo N, Gholami-Ahangaran M, Karamati SA, Khalil-Banihabib E, Hajjgholizadeh GH, et al. A comparison study on the anti-leech effects of onion (*Allium cepa* L) and ginger (*Zingiberofficinale*) with levamisole and triclabendazole. *J HerbMedPharmacol*. 2013;2:1-3.
21. Nasri H, Nematbakhsh M, Ghobadi SH, Ansari R, Shahinfard N, Rafieian-kopaei M. Preventive and curative effects of ginger extract against histopathologic changes of gentamicin-Induced tubular toxicity in rats. *Int J Prev Med*. 2013;4:316-21
22. 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.
23. Roshan B, Stanton RC. A story of microalbuminuria and diabetic nephropathy. *J Nephrothol*. 2013;2:234-40. And antioxidants. *JNephrothol*
24. Tavafi M. Diabetic nephropathy and antioxidants. *J Nephrothol*. 2013;2:20-7.
25. Baradaran A. Lipoprotein (a), type 2 diabetes and nephropathy; the mystery continues. *J Nephrothol*. 2012;1:126-9.
26. Rahimi-Madiseh M, Heidarian E, Rafieian-kopaei M. Biochemical components of *Berberislycium* fruit and its effects on lipid profile in diabetic rats. *J HerbMedPharmacol*. 2014;3:15-9.
27. Rafieian-Kopaei M, Nasri H. Ginger and diabetic nephropathy. *J Renal Inj Prev*. 2013;2:9-10.
28. Tolouian R, Hernandez G. Prediction of diabetic nephropathy: The need for a sweet biomarker. *J Nephrothol*. 2013;2:4-5.
29. Caterson ID, Gill TP. Obesity: Epidemiology and possible prevention. *Best Pract Res ClinEndocrinolMetab*. 2002;16:595-610.
30. Rubin SA, Levin ER. Clinical review 53: The endocrinology of vasoactive peptides: Synthesis to function. *J ClinEndocrinolMetab*. 1994;78:6-10.
31. Boozer CN, Nasser JA, Heymsfield SB, Wang V, Chen G, Solomon JL. An herbal supplement containing Ma Huang-Guarana for weight loss: A randomized, double-blind trial. *Int J ObesRelatMetabDisord*. 2001;25:316-24.
32. Lusso JN. Targeting excessive angiogenesis with functional foods and nutraceuticals. *Trends Food Sci Technol*. 2003;14:455-68.
33. Anwar F, Latif S, Ashraf M, Gilani AH. *Moringaoleifera*: A food plant with multiple medicinal uses. *Phytother Res*. 2007;21:17-25.
34. Glenville M. Nutritional supplements in pregnancy: Commercial push or evidence based? *CurrOpinObstet Gynecol*. 2006;18:642-7.
35. Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Forecasting the global burden of Alzheimer's disease. *Alzheimers Dement*. 2007;3:186-91.
36. 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.
37. 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;39:353-60.4
38. Rabiei Z, Rafieian-Kopaei M, Mokhtari S, Alibabaei z, Shahrani M. The effect of pretreatment with different doses of Lavandulaofficinalisethanolic extract on memory, learning and nociception. *Biomed Aging Pathol.* 2013.
39. 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.*
40. Wilis M\$, Wians FH. The role of nutrition in preventing prostate cancer: A review of the proposed mechanism of action of various dietary substances. *ClinChimActa.* 2003;330:57-83.
41. Shirzad H, Kiani M, Shirzad M. Impacts of tomato extract on the mice fibrosarcomacels. *J HerbMedPharmacol.* 2013;2:13-6.
42. Stahl W, Sies H. Bioactivity and protective effects of natural carotenoids. *BiochimBiophysActa.* 2005;1740:101-7.
43. Shirzad H, Taji F, Rafieian-Kopaei M. Correlation between antioxidant activity of garlic extracts and WEHI-164 fibrosarcomatumor growth in BALB/c mice. *J Med Food.* 2011;14:969-74.
44. Shirzad H, Shahrani M, Rafieian-Kopaei M. Comparison of morphine and tramadol effects on phagocytic activity of mice peritoneal phagocytes in vivo. *IntImmunopharmacol.* 2009;9:968-70.
45. Limer JL, Speirs V. Phyto-oestrogens and breast cancer chemoprevention. *Breast Cancer Res.* 2004;6:119-27.
46. Grammatikos AP. The genetic and environmental basis of atopic diseases. *Ann Med.* 2008;40:482-95.
47. 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 ChemToxicol.* 2002;40:1535-49.
48. 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.
49. Brouns F. Soya isoflavones: A new and promising ingredient for the health foods sector. *Food Res Int.* 2002;35:187-93.
50. Ardalan MR, Rafieian. Kopaei M. Antioxidant supplementation in: hypertension. *J Renal InjPrev* 2014;3:39-40.
51. Gupta P, Andrew H, Kirschner BS, Guandalini S. Is lactobacillus GG helpful in children with Crohn's disease? Results of a preliminary, open-label study. *J PediatrGastroenterolNutr.* 2000;31:453-7.
52. Fuller R. Probiotics in human medicine. *Gut.* 1991;32:439-42.
53. Rafieian-Kopaei M. Identification of medicinal plants affecting on headaches and migraines in Lorestan Province, West of Iran. *Asian PacJ Trop Med.* 2014;7:376-9.
54. Jang M, Cai L, Udeani GO, Slowing KV, Thomas CF, Beecher CW, et al. Cancer chemopreventive activity of resveratrol, a natural product derived from grapes. *Science.* 1997;275:218-20.
55. Rouhi-Broujeni A, Heidarian E, Darvishzadeh-Borojeni P, Rafieian- Kopaei M, Gharipour M. Lipid lowering activity of moringapergerina seeds in rat: A comparison between the extract and atorvastatin. *Res J Biol Sci.* 2013;8:150-4.
56. Nasri H, Ardalan MR, Rafieian-Kopaei R. On the occasion of world hypertension day 2014. *J Parathyr Dis.* 2014;2:19-20.
57. Baradaran A, Madihi Y, Merrikhi A, Rafieian-Kopaei M, Nematbakhsh M, Asgari

- A, et al. Nephrotoxicity of hydroalcoholic extract of *Teucrium polium* in Wistar rats. *Pak J Med Sci.* 2013;29:329-33.
58. Ateyyat MA, Al-Mazra'awi M, Abu-Rjai T, Shatnawi MA. Aqueous extracts of some medicinal plants are as toxic as Imidacloprid to the sweet potato whitefly, *Bemisia tabaci*. *J Insect Sci.* 2009;9:15.
59. Baradaran A. Beyond mineral metabolism, the bright immunomodulatory effect of vitamin D in renal disease. *J Nephrofarmacol.* 2012;1:17-8.
60. Nasri H, Behradmanesh S, Ahmadi A, Rafieian-Kopaei M. Impact of oral vitamin D (cholecalciferol) replacement therapy on blood pressure in type 2 diabetes patients; a randomized, double-blind, placebo controlled clinical trial. *J Nephropathol.* 2014;3:29-33.
61. Nasri H, Shirzad H. Toxicity and safety of imedicinal plants. *J HerbMedPharmacol.* 2013;2:21-2.
62. Heidarian E, Rafieian-Kopaei M. Protective effect of artichoke (*Cynarascolymus*) leaf extract against lead toxicity in rat. *Pharm Biol.* 2013;51:1104-9.
63. Nasri H, Ahmadi A, Baradaran A, Nasri P, Hajian S, Pour-Arian A, et al. A biochemical study on ameliorative effect of green tea (*Camellia sinensis*) extract against contrast media induced acute kidney injury. *J Renal Inj Prev.* 2014;3:47-9.