## Nutrient rich foods and their their toxicity

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**Introduction**

In twenty first century, the life style has extensively changed with the rapid increase in world population which has resulted in the increase in leisure and consequently the purchasing power has also increased. These changes has resulted in the decline in physical activities and had an explicit impact on food consumption pattern of general public. It is a fact that the shift towards the utilization of nourishment with tall sugar levels and saturated fats appear hindering impacts on wellbeing with course of time. This shift has led to sudden rise in chronic diseases such as coronary heart maladies, hypertension, weight, cancer, diabetes etc. So it has become necessary to keep up a sound way of life for most individuals. It is well known that great wellbeing is unequivocally related with eat less and numerous other variables such as heredity qualities, environment, way of life propensities and physical activity. Now a day’s, people are profoundly concerned almost selecting solid nourishments with a wide extend of therapeutic values to diminish their chance of chronic diseases. So nutraceuticals can play an important role to control the deficiencies caused due to the consumption of tall sugar levels and saturated fats.

About 2500 years ago, Hippocrates—who is regarded as the founder of modern medicine—established the connection between nutrition and its importance in the treatment of various diseases in a very traditional manner that yielded unique advantages (Yapijakis, 2009). The terms "Ceutical derived from Pharmaceutical" and "Nutra derived from Nutrition" combine to form the word "Nutraceutical," which was coined by Dr. Stephen De-Felice in 1989. Any material that is classified as food, or a portion of food, and provides benefits for prosperity or restoration, including the prevention and treatment of disease, is called a nutraceutical (Chauhan*et al., 2013)*. Nutraceuticals may be utilized to move forward wellbeing, delay the aging process, and avoid persistent illnesses, increment life hope, or work of the body (Zhao, 2007). Pharmaceuticals in contrast with nutraceuticals are the drugs utilized for the treatment of disease and have the legislative endorse but nutraceuticals are the nutrients that may prevent the disease and have not ordinarily obvious security (Chauhan *et al., 2013)*.

**Classification of Nutraceuticals**

Nutraceutical may be broad and common term utilize to depict any nourishment determined item that in addition to having fundamental wholesome esteem within the food. There are different diverse sorts of food items that come beneath the category of nutraceuticals which as listed as:

1. ***Dietary Supplements***

Dietary supplements are the items that contain supplements extracted from food products that are concentrated in fluid or capsule frame. These incorporate vitamins and minerals like calcium and iron; herbs such as Echinacea and garlic; and specialty products like glucosamine, probiotics, and fish oils. There are different criteria on which dietary supplements can be defined based on the Dietary Supplement Health and Education Act of 1994 which are as:

* Implies an item (other than tobacco) expecting to supplement the calories that bears diet which contains one or more of the following dietary ingredients:

 a) a vitamin b) a mineral c) a herb or other botanical product d) an amino acid e) a dietary substance for use by man to supplement the diet by increasing the total dietary intake.

* Means a product which is not represented for use as a conventional food or as a sole item of a meal or the diet; and
* Does include an article that is approved as a new drug, certified as an antibiotic or licensed as a biological marketed as a dietary supplement or as a food prior to such approval, certification, or license (unless the Secretary of Health & Human Services waives the provision) (Dietary Supplement Health and Education Act of 1994).
1. ***Functional Foods***

Functional foods are outlined to permit eating enhanced nourishments near to their common state, instead of by taking dietary supplements fabricated in fluid or capsule frame (Namdeo*et al., 2014)*. These include yogurts, omega-3 milk, canola oil, oats, bran, psyllium and lignins.

1. ***Medical Foods***

For nutrition and dietary control of a disease, medicinal foods are specially designed and formulated. It has distinctive nutritional value than the normal foods. These include health bars, transgenic cows and lacto-ferrin, Transgenic plants for oral vaccination. The classification of various nutraceuticals based on various elements is shown in table 1:

**Table 1: Categorization of different nutraceuticals**

|  |  |  |
| --- | --- | --- |
| **Chemical constituent** | **Source** | **References** |
| **Isoprenoids, or carotenoids** |  |  |
| Lycopene | Tomatoes, pink grapefruit, guava papaya and watermelon  | Mourvaki et al., 2005 |
| Lutin | Corn, avocado, egg York and spinach  | Abdel-Aa et al., 2013 |
| β-Caroteneα-Caroteneα-CryptoxanthinZeaxanthin | Carrots, various fruits and vegetables Oranges and tangerinesCorn and avocado  | Abdel-Aa et al., 2013 |
| **Dietary fibres** |  |  |
| Solubefibre | Legumes, oats, barley and some fruits  | Dhingra et al., 2012 |
| Insoluble fibre | Whole grain foods wheat, nuts and corn bran  | Dhingra et al., 2012 |
| **Polyphenolic compounds** |  |  |
| Flavonones | Anti-cancer, citrus fruits and antioxidants | Ronis et al., 2018 |
| Flavones | Soybean, fruits and vegetables, | Ronis et al., 2018 |
| Flavonols | Broccoli, tea, onions and apples | Ronis et al., 2018 |
| Anthocyanins | Black raspberries, blackberries and blueberries, | Ronis et al., 2018 |
| Phenolic acids | Berries andlegumes | Ronis et al., 2018 |
| Resveratrol | Berries, catechins and red grapes | Ronis et al., 2018 |
| Curcumin | Turmeric root | Ronis et al., 2018 |
| **Fatty Acids** |  |  |
| Omega-3 fatty acids (poly unsaturated fatty acids) | Salmon and Flax seed  | Rodriguez-Leyva et al., 2010 |
| Mono-saturated fatty acids | Tree nuts  | King et al., 2008 |
| **Isothiocyanates** |  |  |
| Sulporaphane | Broccoli, cauliflower, cabbage and horse-radish  | Yagishita et al., 2019 |
| **Plant Stanols/Sterols** |  |  |
| Stanol/sterol esters | Stanol ester dietary supplements and fortified table spreads  | Ojansivu et al., 2015 |
| **Tocotrienol** |  |  |
| Isoprenoids | Grains and palm Oil |  Ahsan et al., 2005 |
| Saponins | Chickpeas and soybeans |  Ahsan et al., 2005 |
| **Probiotics/Prebiotics** |  |  |
| Lactobacilli/bifidobacteria | Yogurt, other dairy and non-dairy applications | Pandey et al., 2015 |
| **Minerals** |  |  |
| Calcium, selenium, potassium, zinc and copper | Food |  |
| **Gulcosinolates** |  |  |
| Gulcosinolates | Cruciferous vegetables and cauliflowers | Kassie et al., 2004 |
| **Phytoestrogens** |  |  |
| Isoflavanes (genistein, daidzein) | Soybeans and legumes | Desmawati et al., 2019 |
| Liganans | Flaxseed, rye, vegetables | Desmawati et al., 2019 |
| **Alkaloids** |  |  |
| Quinine | Cinchona | Egamberdieva et al., 2019 |
| Tropane alkaloids | Solanaceous members: deadly night shade and datura | Egamberdieva et al., 2019 |
| Morphine  | Opium poppy | Egamberdieva et al., 2019 |
| Ergot alkaloids | Fungus: (Clavicepspurpurea) | Egamberdieva et al., 2019 |
| Vincristine | Periwinkle | Egamberdieva et al., 2019 |
| Vinblastine | Periwinkle | Egamberdieva et al., 2019 |
| Fenugreekine | Fenugreek | Egamberdieva et al., 2019 |
| **Non-carotenoid terpenoids** |  |  |
| Saponins | Legumes  | Hock et al., 2016 |
| Perillyl alcohol | Cherries and mints | Hock et al., 2016 |
| Terpenelimonoids | Peels and citrus fruits membranes | Hock et al., 2016 |
| Terpenol | Carrots | Hock et al., 2016 |
| **Anthraquinones** |  |  |
| Senna | Legumes and pulses | Nida, 2019 |
| Barbaloin | Aloe | Nida, 2019 |
| Capsaicin | Capsicum  | Nida, 2019 |
| Piperine | Black peppers and jalapeno peppers | Nida, 2019 |
| **Terpenes** |  |  |
| Menthol  | Mint family plants | Cox-Georgian et al., 2019 |
| Borneol | Pine oil | Cox-Georgian et al., 2019 |
| Santonin | Wormwood | Cox-Georgian et al., 2019 |
| Gossypol | Cotton | Cox-Georgian et al., 2019 |

**Relationship of nutraceuticals with different diseases and their mode of action**

***Prevention of cardio-vascular diseases (CVD):*** The phrase "cardiovascular malady" refers to conditions involving the heart and blood vessels, including stroke, coronary supply, peripheral vascular disease, and route illness. It is well recognised that most CVDs are preventable and that a high CVD mortality rate is associated with low consumption of natural foods and vegetables (Rafieian, 2012). A nutritious diet rich in fruits and vegetables protects against cardiovascular diseases, as shown by numerous studies (Hu*et al.,* 2002*;*Behradmanesh*et al.,* 2013; Hajivandi *et al.,* 2014). Nutraceuticals—such as vitamins, minerals, dietary fibres, antioxidants, and omega-3 polyunsaturated fatty acids—along with active work are suggested for the prevention and treatment of cardiovascular disease. Certain components, like polyphenols, change how cells digest and move in order to reduce blood vessel disease (Shahbazian, 2013).

Flavonoids are commonly present in vegetables, onion, endives, cruciferous, grapefruits, apples, cherries etc. play a major role in cardiovascular disease prevention and curing. Flavonoids piece the chemical such as angiotensin protein, cyclo-oxygenase that break down prostaglandins and check the conglomeration of platelets. The vascular system that transports oxygen and nutrients to cells is also covered (Nasri*et al.,* 2014).

***Treatment of Cancer:*** The Global Cancer Report estimates that by 2020, there will be 15 million new cases of cancer due to rising cancer rates. Eating well and leading a healthy lifestyle are key to preventing cancer. Plants rich in isoflavones, genistein, biochanine, and daidzein prevent the growth of prostate cancer cells (Kruger*et al.,* 2002). Lycopene, found in tomatoes, guava, pink grapefruit, water melon, and papaya, reduces oxidative stress and guards against DNA damage, which may cause cancer (Shirzad*et al.,* 2013). By preventing the growth of cancer cells, saponins have been shown to have anti-mutagenic and anti-tumor properties, which can lower the risk of cancer in humans (Li*et al.,* 2003).

***Treatment of Diabetes:***Type 2 diabetes is the most common type of the disease, accounting for 95% of cases and being associated with obesity. Despite the development of numerous drugs for the prevention and treatment of diabetes, the global population with diabetes is becoming more diversely afflicted (Bahmani*et al.,* 2014). Many herbal dietary supplements have been clinically shown to help type-2 diabetes mellitus in preclinical trials (Rahimi*et al.,* 2014; Tolouian*et al.,* 2013), but not many have held up in well-designed randomised clinical trials. Omega-3 fatty acids have been proposed as a way to reduce glucose tolerance in diabetic patients. Since long-chain n-3 fatty acid synthesis requires insulin, diabetes deficiency may put the heart at risk (Sirtori*et al.,* 2002). An antioxidant like lipoic acid, which also functions well as a long-term dietary supplement to shield diabetics from complications, can be used to treat diabetic neuropathy (Coleman*et al.,* 2001)**.**

***Enhancement of Immune system:***

Numerous nutraceuticals have been shown to play significant roles in resistance status and exposure to specific medical conditions. Coneflower extracts, or certain *Echinacea* herbs like *Echinacea angustfolia, Echinacea pillida*, and *Echinacea purpurea*, are a class of resistant boosters that are important for enhancing immune function. Probiotic supplements, such as strains *of Lactobacillus, Bifidobacterium* sp., and occasionally *Streptococcus*, provide the balance between master and anti-inflammatory cytokines and provide lymphoid tissue maturational signals (Limer*et al.,* 2004; Fuller, 1991; Ziegler and Filer, 1996).Table 2 represents some of the nutraceuticles are their toxic effects

**Table 2: Toxic effects of nutraceutical**

|  |  |  |
| --- | --- | --- |
| **Nutraceutical** | **Toxic effect** | **References** |
| Vitamins and Mineral Supplements | * Higher dosages (> of vitamin B6 leads to photosensitivity and neurotoxicity in elderly patients
* Higher dosages of vitamin E supplements leads to bleeding correlated with antiplatelet action, and causes diarrhea, fatigue and blurred vision.
* unfavourable impacts on bone wellbeing, counting low bone mineral thickness and expanded fracture risk, are associated with excess vitamin A supplementation.
 | * Ziegler et al. 1996
* Melhus et al. 1998
 |
| Fish oils and omega 3 fatty acids | * They can intensify anticoagulation and advance bleeding in patients.
 | Gross et al. 2017 |
| Green tea | Active catechol in green tea extract is alleged to increase oxidative stress and have been related to liver injury. | Mazzanti et al. 2009 |
| Isoflavone supplements | Intake of Isofalvone supplements have resulted endometriosis in women and increased risk of estrogen sensitive cancers in consumers of these products  | Mahady et al. 2003 |
| Soy products | Increment the chance of kidney stones since they contain huge sums of a bunch of chemicals called oxalates. | Ferraro et al. 2020 |
| Saponins | Effects metabolism in a various ways like erythrocyte haemolysis, lessening of blood and liver cholesterol, discourgement of growth rate.  | Chauhan et al. 1999 |
| Probiotics | * People with compromised immune systems or treating from cancer chemotherapy taking probiotics may actually increase one's chances of getting sick.
* Temporary increase in gas and bloating.
* Constipation and increased thirst
* Probiotic supplements can produce histamine inside the digestive tract of humans.
* Probiotics can enter the bloodstream and cause infections in people with suppressed immune systems, prolonged hospitalizations.
 | * Salminen et al. 2004
* Williams, 2010
* Karpa et al. 2007
* Pugin et al. 2017
* Boyle et al. 2006
 |



**Figure 1.** Toxicity due to nutraceuticals(Saad et al., 2006)

**Normal dosages for nutracuticals**

The normal dosages/day of some nutraceutical was given by National Institute of Nutrition in association with ICMR (Indian Council of Medical Research) in 2020 and is given in Table 3:

**Table 3: Normal dosages of nutraceuticals**

|  |  |
| --- | --- |
| **Nutraceutical** | **Daily Intake** |
| Vitamin B6 | 2-4 mg |
| Vitamin E | 10-12 mg |
| Vitamin A | 600 µg |
| Calcium | < 2000 mg/day |
| Magnesium  | < 420 mg/day |
| Potassium  | < 3400 mg/day |
| Dietary Fibers | 20–35 g/day |
| Polyunsaturated Fatty Acids | 2- 3 g/day |
| Phytosterols | ~ 150-450 mg/day |
| Isoflavones | 25 to 50 mg/day  |
| Probiotics | 1-10 Billion CFUs |

**Regulatory Aspects of Nutraceuticals**

Given the dire and somewhat disparate definitions of nutraceuticals in various countries, direction poses a significant challenge to the globalisation of this industry (Ronis*et al.,* 2018). Nutraceuticals are governed by a different set of laws in the USA than those that govern "conventional" foods and drug products, as overseen by the Food and Drug Administration (FDA). The Dietary Supplement Health and Education Act (DSHEA) of 1994 states that before a nutraceutical is promoted, the manufacturer must ensure that it is safe. In the European Union, the European Food and Safety Authority (EFSA) oversees food regulations, with a significant portion falling under its purview. The focus of this legislation is on "food supplements," which are defined as concentrated sources of nutrients and other substances that have a beneficial effect on health. In India, the administrative body which legalizes nutraceutical products is the Food safety and standards authority of India (FSSAI), which has created for playing down science, based guidelines for articles of food and regulates their manufacture, storage and dissemination (.

**Global Nutraceutical Market**

The global nutraceuticals market is expected to experience enormous growth over the next ten or so years. Important developed nations that prioritise health are primarily responsible for this. But consumers in developing markets are also becoming increasingly aware of the advantages of these products. In addition, the average population's expandable wages are rising rapidly in many developing nations, such as India (The Associated Chambers of Commerce and Industry of India).

In few years, world will have more the 1 billion population 70% of this populace live in developed countries and remaining 30% in developing countries. The demand for nutraceutical will expand at a relentless rate in developed countries. The US has been the leading nutraceutical market till date and nearly completely mature. Between 2010 and 2015, it developed from $ 50 Bn to $ 65 Bn, a compounded development of 10% every year. The US market comprises of functional food and Refreshments (65%) and Dietary Supplements (35%). The European market has developed from $ 35 Bn in 2010 to $ 40 Bn in 2016. It is anticipated to develop to $ 51 Bn by 2021. This demonstrates a yearly development of 5% (The Associated Chambers of Commerce and Industry of India). The Indian nutraceuticals market is anticipated to develop from $ 4 Bn in 2015 to $ 10 Bn in 2022, this speaks to a gigantic development of 21% development yearly (The Associated Chambers of Commerce and Industry of India) because the normal urban and semi-urban Indian is getting to be more cognizant around wellbeing and wellness. This can be giving an enormous development opportunity for nutraceuticals in India.

**Conclusion**

Over the past few years, interest in nutraceuticals—which improve health and can be used instead of prescription drugs—has grown. Long-term potential for nutraceuticals is considerable because they are beneficial for modern lifestyles. Customers' curiosity about the connection between nutrition and health has increased demand for nutraceutical information. Even though nutraceuticals hold great promise for improving human health and preventing disease, long-term clinical researchers must experimentally support the use of nutraceuticals in a variety of therapeutic conditions. Nutraceuticals will soon overtake prescription drugs as our preferred treatment in the long run.

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