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OVERVIEW ON: NUTRACEUTICAL, ARE MEDICINE OR HEALTH FOOD IN THE TREATMENT OF HUMAN DISEASES

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ABSTRACT
Nutraceuticals have received significant attention because of their supposed safety and potential nutritional and therapeutic effects". The concept of nutraceuticals was stared from the review in U.K., Germany and France which determined that diet is rated more highly by consumers than exercise or genetic factors for completing good health. Due to this, the nutraceutical market has become a million dollar manufacturing at a global level. The era of development of nutrients as medicines in the pharmaceutical world is of great importance and draws attention of scientists and researchers toward the significant benefits. The history and detection has explored many facts about the curiously profound therapeutic happenings of such agents. As a result, interdisciplinary approaches are now been applied to design and develop various dosage forms to deliver these herbal products relative to their applications. The entire world is rebellious diseases characteristic of the modern age such as obesity, osteoporosis, cancer, diabetes, allergies, and dental problems. With a global increase in the pervasiveness of obesity, both nutrition and exercise play key roles in its anticipation and treatment. Nutrients, herbals and dietary supplements are major constituents of nutraceuticals which make them instrumental in maintaining health, act against various disease conditions and thus promote the quality of life. Using food products to encourage health and cure disease is celebrated. Currently most of the drug molecules available in the formulations were anciently used in their crude form.

KEY WORDS: *Nutraceuticals, interdisciplinary, anticipation, instrumental, ncourage*

I. INTRODUCTION

A nutraceuticals word is comprises of 'Nutrient' and 'Pharmaceuticals'. According to AAFCO, 1996, 'Nutrient' means a feed constituent in a form and at a level that will help, support a life of human being or animal while 'Nutraceutical' means any non-toxic food component that has scientifically proven health benefits including prevention and treatment of disease. Products isolated or purified from food are sold in medicinal forms not usually associated with food. A nutraceutical have a physiological benefit that it provides protection against chronic diseases. [1, 2] The link between food and health was established long ago. Hippocrates once said, "Let food be thy medicine and medicine be thy food." Traditional medicine in Europe, Asia, Africa and pre-Columbian America is rife with examples of foods used to prevent and cure disease. Under the influence of rationalistic Western medicine, however, food has come to be viewed chiefly as a source of nutrition (that is energy, protein and fat) to the exclusion of other purposes. Yet as changing demographics accelerate the proliferation of chronic diseases, a growing body of evidence suggests that targeted nutrition using naturally occurring substances might be able to stabilize or even cure many of the most challenging health problems. The term "Nutraceutical" was coined by combining the terms "Nutrition" and "Pharmaceutical" in 1989 by Dr Stephen DeFelice, Chairman of the Foundation for Innovation in Medicine. "Nutraceutical" is a marketing term developed for nutritional supplement that is sold with the intent to treat or prevent disease and thus has no regulatory definition. Hence a "nutraceutical" is any substance that may be considered a food or part of a food and provides medical or health benefits, encompassing, prevention and treatment of diseases. Such products may range from isolated nutrients, dietary supplements and diets to genetically engineered "designer" foods, herbal products and processed foods such as cereals, soups and beverages. [3]

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Table No.01: Fortified Foods With Their Ayurvedic Nutraceuticals

Fortified Foods	Ayurvedic Nutraceuticals
Calcium Enriched Edli	Antioxidants and bone density enhancer
Probiotic fortified yogurt	Curcumin
Buttermilk	Green tea extract
Omega-3-fortified health drinks and baby foods	Fish oil, Brahmi, Senna, Lutein Sugar free ayurvedic supplement

Global market for nutraceutical vitamin ingredients will increase 6 percent annually to over $13 billion in 2014. Due to imbalance and deficiencies in national medical delivery system, it keeps large number of population dependent on natural and alternative medicines in India. Popularity of Indian Ayurvedic therapies boost the export opportunities for formulations based on ashwagandha, haldi, ginger, tulsi etc. Vitamin D will see the fastest growth in demand due to increasing clinical evidence of swine flu, cancer, and other preventive medicine benefits. Global demand for herbal and non-herbal extracts is increasing continuously. Green tea for weight loss and cancer treatment, while Ginkgo biloba for improving cognitive function, has been widely used as nutraceuticals. Glucosamine generate strongest growth in demand due to its usefulness on treatment of Arthritis. The nutraceutical industry in the US is about $ 86 billion. This figure is slightly higher in Europe and, in Japan, represents approximately a quarter of their $6 billion total annual food sales – 47 % of the Japanese population consumes nutraceuticals11.

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Concepts of Nutraceuticals [5]

In the pharmaceutical progress process, it is a condition to have clinical test results from animal tests and studies, for authentication of the effects. On the other hand, in the case of nutrition, there was no verification method for foods in averting diseases in the past. In recent years however, as food conformation has been scientifically proven to cause lifestyle-related diseases, and has become a social issue.

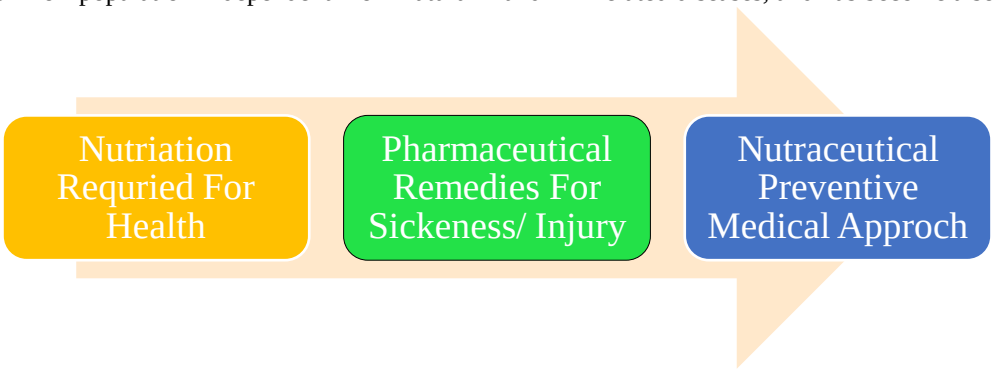

Figure 01: Concept of Nutraceuticals Benefits 0f Nutraceuticals

History & Rediscovery of Nutrients as Nutraceuticals

"Food may possess the ability to prevent diseases or treatment of ailment" this belief is couple of centuries old-proclaimed by our ancestors. The ancient writings and artworks of Egyptians, Romans, and Greek civilizations depicted the medicinal and spiritual applications of plants. The idea arose 3000 years ago when Hippocrates developed a relationship between food for health and therapeutic applications of it. The principal truth depicted in his statement that "Let food be thy medicine and medicine be thy food" is widely applied nowadays. Thus, from such finding, it could be believed that our nature and surroundings have much of the natural therapies to offer. One such finding presents the botanicals, which are in use from ancient times for the treatment of cancer. Similarly, there are many plant derived chemotherapies which consist of Vinca and Taxus brevifolia species to treat cancer and related problems. Furthermore, Ginseng has been another such traditional drug which is in use from past 2000 years in China. It was from the time of Liang dynasty of China that the chemotherapy features of ginseng were discovered and applied even in today's time. From the documented history, Egyptians identified the medicinal importance of coriander, fennel, juniper, cumin, garlic, turmeric,

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thyme, curry, and dried mint found in pyramids. The value of such medicinal sources was so high that even cinnamon was considered more precious in comparison to gold in Egypt. Due to the explored properties of plants, the Roman emperor Heliogabalus made use of cinnamon, clove, and pepper in meals which are used in cuisines and soft drinks until present time. In addition, there were many other plants and food additives identified such as honey and certain vitamins. Honey has always been given prime importance since ancient period. It was referred in Sumerians tablet writing as one of the remedies for health problems. According to Bible, the wise Solomon has said. [6, 7]

II. CLASSIFICATION AND CATEGORIZATION OF NUTRACEUTICALS

The aim of achievement of maximal state of well-being is alarmingly increased with the introduction of nutraceuticals. The term nutraceuticals, itself is a wide class which include many categories and subcategories under it. To understand the applications, the nutraceuticals are needed to be classified. The classification into various classes depending on their uses are:

a) Traditional nutraceuticals
b) Nontraditional nutraceuticals
c) Fortified nutraceuticals
d) Recombinant nutraceuticals
e) Potential and established nutraceuticals
f) Phytochemicals
g) Herbals
h) Functional foods
i) Dietary supplements and dietary fibers
j) Probiotics and prebiotics.

Traditional Nutraceuticals

The category consists of the food which does not undergo any manual changes. The components are natural and are having some potential which are actively involved in health benefits. Lycopene, a constituent of tomatoes is an example of this category.[8.9]

Nontraditional Nutraceuticals

Boosting of nutritional content by addition of nutrients, dietary components for improvement of quality of nutrition comprise this category of nutraceuticals. Beta carotene enriched rice is an example of this class. [8, 9]

Fortified Nutraceuticals

Fortification of food components is the process of addition of micronutrients (essential trace elements and vitamins) to food for enhancing the effectiveness and nutritional value. Its example includes milk fortified with cholecalciferol used in Vitamin D deficiency. [10, 11]

Recombinant Nutraceuticals

It involves the application of biotechnology and genetic engineering in the production of energy providing foods such as yoghurt and cheese or extraction of bioactive components by enzymatic or fermentation technology. Gold kiwifruit is genetically modified for a high level of ascorbic acid, Carotenoids, and Lutein and Zeaxanthin. [10, 11]

Potential and Established Nutraceuticals

Potential nutraceuticals hold an assurance of medicinal benefits. These nutraceuticals have become established medicines only after sufficient data demonstration and clinical testing for their efficacy and safety. All nutraceuticals are potential nutraceuticals but all potential nutraceuticals are not established ones. [12]

Phytochemicals

These are the chemical constituents of plants with distinct biological action. These are been reported to have active components which exerts their effects toward the metabolism and biochemical reactions in living beings and thus, provide health benefits. [13]

Herbals

The herbs possessing medicinal values to be implicated in treatment and prevention of ailments are been included in the class. Botanical products may consist of fresh plant used or any part such as dried leaf, fruit, stem, seeds, roots, or concentrated extract. [14]

Dietary supplements and dietary fibers

A dietary supplement is a product which comprises a supplementary dietary ingredient added as a remedy to deficiencies or diseases. The inclination toward dietary supplements has raised many folds to improve health, fitness, tonic to delay aging, improve performance, and body building. A dietary ingredient is one which enhances the food and its nutritional assessment. Vitamins and minerals as dietary supplements exist in multiple ingredients or single ingredient products in the market. Demand of dietary supplements is alarmingly increasing in developing countries such as Brazil, China, India, and Russia and it has already reserved its place in developed parts of many countries. Dietary supplements other than vitamins and minerals also involve herb, botanicals, amino acids, pure extracts, concentrate or combination of number of ingredients gland extracts, and organ tissues. [15]

Functional Foods

Functional foods are the source of absolutely necessary nutrients providing more than the quantities required for maintenance, growth, and development. The term is specially retained for food or food components that carry the evidence to provide an advantageous factors for health beyond basic nutrition. The class of functional food includes many further subclassed such as cereals, legumes, and fermented food. The potentiality of the functional food including cereals such as rice, corn, wheat, millets, sorghum, and buckwheat has been found in many ways to eliminate the risk of coronary heart disease, tumor incidence, and lowering of blood pressure. Similar to cereals, legumes are the other subclass of functional foods which form a chief element in traditional and modern dietary patterns. These are highly

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nutritious and rich in biologically valuable proteins, bioactive peptides, and amino acids. [16]

III. NUTRACEUTICALS AND DISEASES

1. **Diet Related Diseases**
   In Western societies, the incidence of diet-related diseases is progressively increasing due to greater availability of hyper caloric food and a sedentary lifestyle. Obesity, diabetes, atherosclerosis, and neurodegeneration are major diet-related pathologies that share a common pathogenic denominator of low-grade inflammation. Functional foods and nutraceuticals may represent a novel therapeutic approach to prevent or attenuate diet-related disease in view of their ability to exert anti-inflammatory responses. In particular, activation of intestinal T regulatory cells and homeostatic regulation of the gut micro biota have the potential to reduce low-grade inflammation in diet-related diseases. [17]
2. **Diabetes**
   Ethyl esters of n-3 fatty acids may be beneficial in diabetic patients. Docosahexaenoic acid modulates insulin resistance and is also vital for neurovisual development. Lipoic acid, an antioxidant, for treatment of diabetic neuropathy. Dietary fibers from psyllium have been used for glucose control in diabetic patients and to reduce lipid levels in hyperlipidemia. [18]
3. **Obesity**
   Obesity is a global public health problem and is defined as accumulation of unhealthy amount of body fat. It is a well-established risk factor for many disorders like angina pectoris, congestive heart failure (CHF), hypertension, hyperlipidemia, respiratory disorders, renal vein thrombosis, osteoarthritis, cancer and reduced fertility. [19]
4. **Heart attack and lung cancer**
   Corn's contribution to heart health lies not just in its fiber, but in the significant amounts of folate that corn supplies. Corn maintains the homocysteine, an intermediate product is an important metabolic process called the methylation cycle. Homocysteine is directly responsible for damage of blood vessel heart attack, stroke, or peripheral vascular disease. [20]
5. **Alzheimer's disease**
   β-carotene, curcumin, lutein, lycopene and turmerin may exert positive effects on specific diseases by neutralizing the negative effects oxidative stress mitochondrial dysfunction, and various forms of neural degeneration. [21]
6. **Cancer**
   Flavonoids which block the enzymes that produce estrogen reduces the estrogen-induced cancers. Prevent prostate/breast cancer a broad range of phyto-pharmaceuticals with a claimed hormonal activity, called "phytoestrogens" is recommended. Soyfoods source of isoflavones, curcumin from curry and soya isoflavones possess cancer chemopreventive properties. Lycopene concentrates in the skin, testes, adrenal and prostate where it protects against cancer. [22]
7. **Anti-inflammatory activities**
   Curcumin (diferuloylmethane) which is a polyphenol of turmeric possesses anticarcinogenic, antioxidative and anti-inflammatory properties. Top of Form Beet roots, cucumber fruits, spinach leaves, and turmeric rhizomes, were reported to possess anti-tumor activity. Gamma linolenic acid (found in green leafy vegetables, nuts, vegetable oils i.e. evening primrose oil, blackcurrant seed oil and hemp seed oil, and from spirulina, cyanobacteria) are used for treating problems with inflammation and auto-immune diseases. [23]

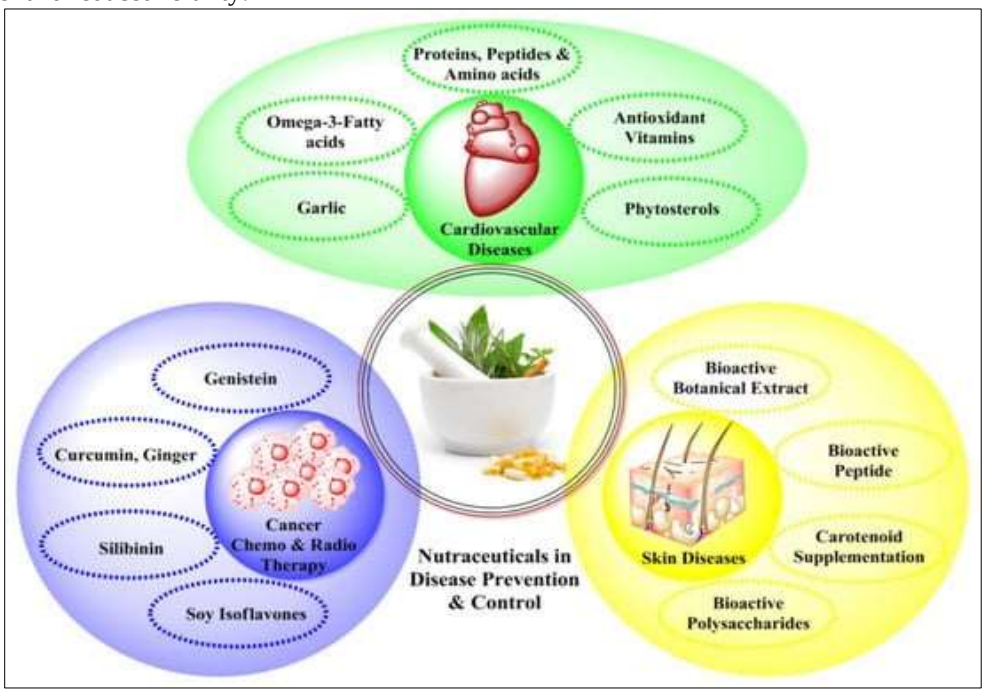

Figure 02: Nutraceuticals in prevention of Disease

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IV. ADVANCEMENT IN DRUG DELIVERY SYSTEMS WITH MEDICATED HERBS

The increasing preferences of consumers to eat healthy food products and the nutraceuticals showing up to be favorable in preventing as well as curing many diseases impelled scientists and researchers to look for efficient delivery systems. The use of novel drug delivery system to deal with the efficacy issues of the products is drawing more and more attention of the researchers.

- **Liposomes**
  Liposomes are the spherical vesicles composed of phospholipids consisting lipid bilayer. These are spherical in shape and can be formulated using cholesterol and natural phospholipids. Liposomes are also preferred to be an advanced delivery system for nutraceutical products. Intranasal quercetin liposomes is one of the examples which have been reported to enhance the penetration of quercetin through blood brain barriers and increase the therapeutic anticancer efficacy of the product. Similarly, buccal liposomal formulation of silymarin has also been proved to offer hepatoprotective effect with enhanced bioavailability of the product resulting into better therapeutic response. The antigout topical liposomal preparation of colchicine has also been proven very effective in the treatment of gout. [24, 25]
- **Phytosomes**
  Phytosomes are the complex of phospholipids and the biologically active ingredients. Oral formulation of Ginseng Phytosomes, prepared using phospholipid Complexation has been found to overcome the problem related to the low solubility of Ginseng and results in the increased absorption in the body which enhances the therapeutic effect of Ginseng as an immunomodulator. Oral phytosomal preparation of Hawthorn (Flavonoid) having cardioprotective and antihypertensive properties has also been reported to offer enhanced efficacy. Quercetin, possessing the properties of an anticancer as well as an antioxidant compound was also subjected to the oral preparation of Quercetin phytosomes providing better therapeutic efficacy of the drug. [26]
  better therapeutic efficacy of the drug. [26]
- **Microspheres**
  Microspheres are the spherical vesicular particles falling within the diameter range of 1-1000 μm. Due to their small size, microspheres can be ingested or injected, can be adjusted to any desired release profile and can also exhibit site-specific as well as organ targeted drug delivery. Intravenous preparation of camptothecin (natural product) loaded microspheres, formulated using oil-in-water evaporation method has been reported to provide prolonged anticancer effect. [27]

V. FORMULATION CHALLENGES [24,25]

Drug interactions may be described as the situation when the activity of one active constituent is affected due to presence of other constituents. It may be food–drug interaction or drug–drug interaction. The pharmacological response may alleviate, lessen or induce side effects.

a) **Garlic (alicin)** exhibits a hypotensive property and a hypocholesterolemic effect, acts as an anti-inflammatory agent and possess anti-bacterial as well as anti-fungal properties. When it is administered with anticoagulants (such as warfarin), it may lead to increased bleeding. With hypoglycemic drugs, such asinsulin or glipizide, it may cause hypoglycemia. With protease inhibitors (such as indinavir or saquinavir), garlic decreases their blood levels and effectiveness.

b) **Green tea** (polyphenols) improves mental alertness and thinking. It is also used to treat a plethora of other medical conditions, including Crohn's disease, Parkinson's disease, cardiovascular disease, diabetes, hypotension, chronic fatigue syndrome (CFS), tooth decay, kidney stones and skin conditions. Consuming green tea with stimulant medications could have dangerous consequences, such as elevated heart rate and blood pressure. Bortezomib (Velcade) may not be as effective against some cancers if used with green tea. Consuming green tea may reduce the effectiveness of warfarin.

c) **The leaf extract** of Gingko biloba is effective in the treatment of Alzheimer's disease and other forms of dementia, Raynaud's syndrome, peripheral vascular disease, vertigo and dizziness, premenstrual syndrome (PMS) and improving color vision in people with diabetes. Ginkgo, when administered with anticoagulants/with NSAIDs, it may increase the risk of bleeding. When administered with anticonvulsants, it may reduce the effectiveness in preventing seizures.

d) **Kava root** (kava-lactones) medicine, native to South Pacific, is used to calm anxiety, stress and to treat insomnia. It is also used in the treatment of attention deficit hyperactivity disorder (ADHD), depression, migraines and other headaches, chronic fatigue syndrome (CFS), epilepsy, psychosis, common cold and other respiratory tract infections, muscle pain, tuberculosis and cancer prevention. Kava is applied to the skin for some skin disorders such as leprosy, to promote wound healing. It is also used in urinary tract infections (UTIs), pain and swelling of the uterus, menstrual discomfort and hot flushes in women with menopause. It is also used as pain reliever in toothaches. When co-administered with barbiturates and benzodiazepines, it may prolong or intensify their effects

e) **Chamomile (tea extract)** is used as tea or dietary supplement for stomach cramps, to treat irritation from chest colds. It is also used for slow healing wounds, abscesses, gum inflammation, and skin conditions such as eczema, chickenpox and diaper-rash. The risk of bleeding increases when it is co-administered with anti-coagulants.

VI. CONCLUSIONS AND FUTURE PROSPECTS

To conclude, nutraceuticals area potentially growing sector and are engaged in both the fields, either medical treatment or nutrition so as to assure integrated medical assistance. These act as potential dietary supplements, prevention of diseases such as CVD, the support and treatment of various types of cancer, and

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other healthcare benefits. It is also advantageous over other therapies in terms of cost. The studies reveal the fact that nutraceuticals exert different types of biological activities in mechanized manner. These properties ultimately lower the age related and chronic diseases. Presently, large numbers of such potential nutraceuticals are undergoing the phases of research and development. The marketing graph of nutraceuticals is also rising all over the world. The market values reported depicts the public behavior of giving more emphasis on the use of nutraceuticals which ultimately is related to the brighter scope of nutraceutical industry.

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