**Review Article** 

# NUTRACEUTICALS AND ITS HEALTH BENEFITS: A REVIEW

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#### ABSTRACT

Nutraceuticals are the food supplements which are used by humans to provide some basic nutrients to prevent them from chronic diseases and improve the quality of life by fulfilling basic needs of body. These products are generally consumed without prescription and supervision. In recent years, people interest in nutraceuticals are increasing day by day because of their nutrition and pharmaceutical activity. They are the best alternative for modern medicines. Global nutraceuticals market is growing very vastly due to their high demands in public. Nutraceuticals can be obtained from various sources like plants, animals, microbes and even they can be modified by using biotechnology. Nutraceuticals can be used in preventing chronic diseases like, cancer, diabetes, inflammation and they are even playing role as immunity enhancer and antioxidants in the corona virus disease or COVID-19.

## **1. INTRODUCTON**

Nutraceutical are the products that are separated from herbal products, dietary supplements etc. *Stephen Defelice* gave the term" Nutraceutical" in 1989. Stephen Defelice was the founder and chairmen of foundation and innovation in medicine, which is an American organization that promotes the medical health.[1]

Nutraceutical is composed of two words – *Nutrient* and *Pharmaceutical*. Nutraceutical are scientifically proven food supplements that are non-toxic and help in prevention and treatment of several diseases. These food supplements keep the body healthy and provides required nutrients for various metabolic processes to regulate body functions and thus keeps the body free from diseases. [2] Nutraceuticals are artificial foods that not even prevents the body from various chronic diseases like cancer, diabetes, Cardiovascular diseases, COVID-19 but also keeps the body healthy, improve the quality of life. [3]

Nutraceutical are more than a food and less than a pharmaceutical i.e., they are the product that are separated or extracted from herbal products, dairy products and food. They are sold in medicinal dosage forms which are generally not related with

food. Examples of nutraceuticals are dietary supplements, natural foods, vitamins, citrus fruits, genetically modified foods (like rice, canola), herbal products, cereals. [4] Under, Dietary Supplement, Health and Education Act (DSHEA) in 1994, Dietary supplements are those supplements that are given with diet which have one or more of these dietary ingredients: like herbs, minerals, an amino acid, etc. These are the products that are used or intake by humans to supplement their diet to improve their health and prevents them from diseases and enhance life expectancy.[5] These are available in various medicinal dosage forms like capsule, tablet, pills and liquid forms. These supplements should not be taken as a conventional food of a meal or diet. It is known as a "dietary supplement".[6]

## 2. HISTORY

The idea of Nutraceutical was arising three thousand years ago. Hippocrates who was known as a father of western medicine (460-377 B.C) misquoted that '*LET FOOD BE THE MEDICINE AND MEDICINE BE THE FOOD*' thus manufacturers started adding iodine to salt to prevent Goiter. Long before the development of the distinct scientific discipline

of nutrition, philosophers and later physicians paid close attention to the role of the daily diet in individual and public health.[8] Ayurveda, the 5000 yr old health science have mentioned benefits of food for therapeutic purposes.

## **3. GLOBAL MARKET**

Based on the increase in demand for nutraceuticals in the western world, it is predicted that China, Brazil, Japan, India, Mexico, Poland, Russia, and South Korea will evolve as the largest producers of Nutraceuticals by 2020. Every year about 1000 new nutraceutical products become available, and in US, approx. 29,000 dietary supplements become available. At least one type of Nutraceuticals are used highly by Japanese(47%) and Americans(66%) annually. Industry amounting to 60 billion\$ annual food seals in Japan. Market of nutraceutical in China is growing very vastly, followed by other countries like Turkey (U.S. \$207million in 2006), Brazil (U.S. \$881 million in 2006. Maximum growth of nutraceuticals market took place in last 10 years. Global nutraceutical market is increasing enormously, and expected to reach 176.7 billion US\$ from 117 billion US\$ with a compound annual growth rate (CAGR) of 7.4%.[9]

According to current reports, the total market for nutraceutical is growing at approx. 22% annum in India.[10]



Fig. 1 Market of Nutraceutical in various countries. [11]



Fig. 2 Global Nutraceutical market in \$ millions. [12]

## 4. INDIAN MARKET

India has high inheritance of herbs and its supplements which have found place in our mythology and folklore. The growth of nutraceuticals market in India is large because of the increased affluence and lifestyle diseases and change in consumer perception and mind set. The Indian nutracautical market was expected to grow to \$2,731 million in 2016. It is expected to have 3.5% of global market share till 2023It is expected to increase frpm 4 to 18 billion US\$ till 2025, with increasing the demand of nutraceuticals in Indian families.[13] Nutraceutical or bioceuticals are ingredients with basic health benefits for humans to improve quality of life. In 2007, Indian nutraceutical market was INR 18.75 billion.[14]

- The Indian nutraceutical market is assumed to reach 10 billionUS\$ in 2022. This represent the a huge growth of 21% growth annually . In 2014, the global nutraceuticals market was dominated by APAC and Europe.[15]
- In India, 13% growth of Dietary products, vitamins was noted in 2016.
- And, 16% growth is noted of Fish oils/omega 3- fatty acids in 2016.



• Amway play the role of a leader in market share.[16]

Fig. 3 Nutraceuticals market in India [17]

# **5. CLASSIFICATION OF NUTRCEUTICALS:**

## 5.1 According to food source

In this classification, nutraceuticals are classified based on their source from which they are obtained. Like Conjugated linoleic acid (CLA) obtained from the fat of beef, lamb. Many Nutraceuticals can be obtained from the animals, plants as well as microbes. For example, choline and phosphatidylcholine are found in plants, animals and microbes. [18,19,20]

S. No.	Source	Examples
1.	Plant source	β-glucan, Ascorbic acid, Quercetin, luteolin, cellulose, Lutein, Gallic acid Perillyl alcohol, Indole 3-carbonol, Pectin, Hemicelluloses, Lignin, β- carotene,γ- tocotrienol.[21,22]
2.	Animal source	Conjugated linoleic acid (CLA), DHA, choline, lecithin, calcium, zinc, creatine, and minerals.[23]
3.	Microbial source	Saccharomyces boulardii (yeast), Bifido bacterium bifidum, B. longum[24,25]

### **Table 1:** Example of nutraceutical according to food source.

## 5.2 According to mechanism of action

Nutraceuticals can also be classified as per their mechanism of action. Such nutraceuticals include antioxidants, anti-bacterial, anti-hypertensives, anti-hypercholesteremic, anti-inflammatory, etc. [26]

Anticancer	Positive influence on blood lipid Profile	Antioxidant	Anti-Inflammatories	Osteogenesis or Bone Protectives
Capsaicin	B-Glucan	CLA	Linoleic acid	CLA
Genestein	γ - Tacotrienol	Ascorbic acid	EPA	Soy protein
Daidzein	α- Tacotrienol	B – Carotene	DHA	Genestein
α-Tacotrienol	MUFA	Tacotrienols	GLA	Daidzein
$\gamma$ – Tacotrienol	Querceitin	Polyphenoles	Capsaiein	Calcium
CLA	Guar	Indole -3- carbonol	Querceitin	Inulin
Letobacillus acidophilus	□ -3 PUFAs	α- Tacotrienol	Curcumin	
Ajoene	resveratrol	Lycopene		
Glycyrrhizin	Tannins			
Lutein	Pectin			

 Table 2: Examples of Nutraceuticals according to mechanism of action. [27,28,29]

# 5.3 According to their chemical nature

Different nutraceuticals have different chemical nature. So, they are arranged according to their chemical nature (table given below). They are categorized under molecular and elemental groups.

 Table 3: Different nutraceuticals with different chemical nature [30,31,32]

CLASSES/COMPONENTS	SOURCE	POTENTIAL BENEFITS
Carotenoids		
(a) α – carotene	Carrots	Neutralizes free radicals which may cause damage to cells.
(b) $\beta$ –carotene	Various fruits and vegetables	Neutralizes free radicals.
(c) lutein	Green vegetables	Maintenance of healthy Vision.
(d) lycopene	Tomatoes and tomato products	Reduce the risk of cancer.
(e) Zeaxanthin	Eggs, citrus, and corn	Maintenance of healthy vision.
Collagen Hydrolysate	Gelatin	Improve some symptoms associated with osteoarthritis.
Dietary fiber		
(a) Insoluble fiber	Wheat bran	Reduce risk of breast/ colon cancer.
(b) $\beta$ – Glucan	Oats	Reduce the risk of cardiovascular disease (CVDs).
(c) Soluble fiber	Psyllium	Reduce the risk of CVDs.
(d) Whole brans	Cereal grains	Reduce the risk of CVDs.
Fatty Acids		
(a) omega-3-fatty acids (DHA/EPA)	Tuna fish and marine oils	Reduce the risk of CVDs; and improve mental health.
(b) conjugated Linoleic acid (CLA)	Cheese and meat products	Improve body composition; and decrease the risk of certain cancers.

D1 1			
Phenois			
(a) Caffeic acid	Fruits, vegetables, citrus	Antioxidant-link activities; and reduce the risk of degenerative	
(b) Ferulic acid		diseases, heart diseases and eye diseases.	
Flavonoids			
(a) Anthrocyanidins	Fruits	Neutralise free radicals and reduce the risk of cancer.	
(b) Catechins	Tea	Neutralize free radicals and reduce the risk of cancer.	
(c) Flavanones	Citrus	Neutralize free radicals and reduce the risk of cancer.	
(d) Flavones	Fruits and Vegetables	Neutralize free radicals and reduce the risk of cancer.	
Plant sterols and stanol ester	Corn, soy, wheat, wood oils.	Lower blood cholesterol levels by inhibiting cholesterol	
		absorption.	
Prebiotics and probiotics			
(a) Fructoligosscharides (FOS)	Jerusalem antichokes, onion	Improve Gastrointestinal health.	
(b) Lactobacillus	powder. Yogurt & other dairy products	Improve GI health.	

### 5.4 According to food available in market



Fig. 4 Types of nutraceutical according to food available in market. [33]

## 5.4.1 Traditional nutraceuticals

Traditional nutraceuticals are those which are obtained from nature directly, and use as it is in their natural form without doing any changes examples are resveratrol in grapes, lycopene in the tomatoes, saponins in soy are used to improve health.

Table 4:	Examples	of traditional	nutraceuticals.	[34]
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NUTRACEUTICALS	EFFECTS
n - 3 P U F A s (polyunsaturated fatty acids)	Prevents several disorders affecting lungs and airways.
ASU (non-saponified residues of avocado and soybean oils)	Stimulates synthesis of aggrecan and extracellular matrix component as type 2 collagen by reducing the production of catabolic (MMP-3) and pro inflammatory (IL-8 AND IL-6) mediators in OA (osteoarthritis).
CLA (conjugated linoleic acid)	Significantly improves AHR (Airway Hyper Responsiveness) associated with reduction in leptin/adiponectin ratio in mild asthma.
MUFAs (monounsaturated fatty acids)	Lowers cardiovascular disease risk and metabolic syndrome.

Resvesterol	Chemosensitizers tumor by modulating drug transporters, cell survival proteins, cell proliferative proteins and members of NF-кB and STAT3 signaling pathways.
Fortified wheat flour	Reduces prevalence of NTDs (Neural tube defects) at birth; increases blood folate concentrations.
Calcitriol	Regulates the levels of p21 and p27 and increases expression of BRCA-1 and -2 tumor suppressor genes contributing in DNA repair mechanism.

# 6. TRADITIONAL NUTRACEUTICALS ARE CATEGORISED INTO

### 6.1 (a) Chemical constituents

### These are of following types

Nutrients: These nutraceuticals are basic are primary metabolites. For e.g., fatty acids, vitamins, minerals, amino acids have nutritional functions. Vitamins like- vitamins A, D, E, K are fat soluble vitamins. *Vitamin A* have antioxidant property thus prevent from cancer, maintains healthy vision, skin and required for growth and development of body. Vitamin D required in calcium absorption for bones and teeth. Vitamin K required for blood clotting. Water soluble vitamins includes- vitamin C, B1, B2, B3, B6 and B12. Vitamin C have antioxidant property, maintains gums, teeth, skin and also prevent from common cold thus required mainly in this corona pandemic. Vitamin B12 helps in RBC formation, genetic material production, metabolism of fat and proteins. Nutraceuticals can be present in many vegetables, cereals, fruits and various animal products, dairy products which have the nutrients to treat and cure various chronic diseases, eye diseases, cancer etc.

**Herbals:** Herbal nutraceutical products that are obtain from plants are very useful in treating various chronic diseases and helps to improve the quality of life by maintaining the diet. Cardiovascular diseases, cancer, inflammation and other diseases can be treated or prevented by these nutraceuticals. Various herbs like- Aloe-vera for anti-inflammatory, emollient. Garlic for antibacterial, antifungal, anti-inflammatory, ginger as carminative are used as nutraceuticals. Herbal nutraceutical is very good choice in prevention various chronic diseases. Peppermint (*Mentha piperita*) treats flu and cold. Salicin (Salix nigra) have anti-inflammatory action. Flavonoids like psoralen have diuretic, carminative, and antipyretic action. [35]

### Phytochemicals

Phytochemicals are those chemical compounds that are produced by plants in their primary or secondary metabolism. They are bioactive in plants and help in defense, growth and development.

These are classified according to chemical constituents present i.e.; Phytochemicals. Tocotrienols, topophones, carotenoids, legumes, phytosterols, flavonoids are some examples of phytochemicals.

Flavonoids obtain from grapes and wines- antiallergic, antiinflammatory, antioxidant.

Isoflavanoids obtain from soyabean - anti cancerous activity.

Carotenoids from vegetables and fruits - Anti cancer, antioxidant.

Phenolic acids present in blueberries, tomatoes, other citrus fruits and have anti-inflammatory, antioxidant, anticancer property.

## 6.1(b) Probiotic microorganism

'PROBIOTIC' term was coined by Metchnikoff. Probiotics are the good live bacteria and yeast that are that helps in healthy digestion and nutrients absorption. They should be consumed by host in sufficient amount to keep digestive system healthy. They help in treating diarrhea, reduce possibility of intestinal infections, treat irritable bowel syndrome, reduce UTI and shows antimicrobial effect. Uses of probiotics are increasing because of their intestine friendly nature which helps in absorption and metabolism of nutrients. Examples are oligofructose, lactobacillus acidophilus, L.lactis, bacillus bulgaricus etc. [36]

# 6.1 (c) Nutraceuticals Enzymes

Enzymes are proteins which act as biocatalyst. Biocatalyst means biological catalyst which enhances the metabolic reactions in the body by binding with substrate to give a metabolic product .it enhances the metabolic processes of body and play essential role in breaking complex molecules in to simpler products. Various diseases like hypoglycemia, diabetes, digestive problems etc. can be treated by adding enzymatic supplements in diet. Enzymes can be obtaining from animals, microbes, plant source.

## 6.2 Non-traditional nutraceuticals

Non- traditional nutraceuticals are prepared by using some techniques like agricultural breeding in fortified food and biotechnology in recombinant nutraceuticals. These are artificial foods with high nutrition content than original foods.

## **6.3 Fortified nutraceuticals**

These nutraceuticals are fortified foods, with some added nutrients or ingredients in it which do not naturally present in them. Nutrients are added by using agricultural breeding and this process is called fortification. Examples include milk is fortified with vitamin D, Orange juice fortified with calcium, salt with iodine, Calcium, iron, and folic acid are added in flour, Cereals with added vitamins or minerals. Banana fortified with soybean ferritin gene is used in iron deficiency.[37]

## 6.4 Recombinant nutraceuticals

Recombinant nutraceuticals are produced by using the biotechnology and genetic engineering. several nutraceuticals like yogurt, cheese, gold kiwi fruit, vinegar, fermented starch, etc are the examples of recombinant nutraceuticals.

# 7. DISEASE THAT ARE TREAED AND PREVENTED WITH NUTRACEUTICALS

## 7.1 Nutraceuticals in Covid-19

COVID-19 is a respiratory disease. It is viral disease caused by "novel corona virus", which is a xenobiotic (foreign substance or pathogen) for our body. Our body reacts to it by activating body's immune response and showing some allergic symptoms. COVID-19 stands for Corona virus disease 2019. The first case of COVID-19 was detected in December 2019, in Wuhan, China.

Major symptoms of COVID-19 are-

- Fever
- Shortness of breath
- Chest pain
- Fever
- Dry cough
- Sore throat
- Tiredness
- Headache
- Loss of taste and smell [38].

As of 4 January 2021, over 2,09,04,701 confirmed cases have been found in USA and caused more than 3,58,682 deaths. Whereas, In India 10.3 million cases have been reached from which 1.5 lakh deaths have been recorded.

Chronic respiratory diseases are also known as pulmonology. These diseases cause systemic inflammation and shortness of breath, leading to irreversible endothelial dysfunction. COVID-19 also influences the immune system of the body. COVID-19 stimulates the body's immune response thus, increase the release of cytokines, such as interleukins (IL-1, IL-6), Interferons (IFN-  $\gamma$ ), chemokines, and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), IL-6 level rises in COVID-19. has been seen in the progression phase of COVID-19. These changes contribute in the formation of cytokine storm. Virus activated the "cytokine storm syndrome", which could be a clinical predictor for fatal outcome in these patients.



Fig. 5: Mechanism of endothelial involvement in COVID-19. [39]

As we know that, there is no cure of COVID-19 so, prevention is better than cure. That is why Nutraceuticals are widely used in prevention and treatment of covid-19 now a days. And also, no vaccine is available till 30 December 2020. So various types of nutraceuticals are used prevention of COVID-19 like, Vitamins D, C, E and dietary minerals, amino acids, probiotics, omega 3- fatty acids, several minerals, carotenoids etc. provide medical health benefit. Curcumin can be used in treatments of virus infections, including COVID-19.[40]

## 7.2 Cardiovascular Diseases (CVDs)

Cardiovascular disease (CVD) is the diseases related to heart and blood vessels, veins and arteries. Congestive heart failure (CHF), coronary heart disease (heart attack), atherosclerosis, peripheral vascular diseases, stroke, arrhythmia(irregular heartbeat) hypertension, heart failure, and so on. In CVDs heart muscles become damaged and lose their ability to contract effectively. Deficiency in nutrients and lifestyle factors can be the major cause for CVD.[41].

Nutraceuticals reduces the risk of CVDs by- decreasing the LDL level in blood, neutralize the free radicals i.e.: antioxidants, reduce the plaque. Proper diet with sufficient nutrients reduces the CVDs risk. Dietary fiber, Vitamins, minerals physical exercise are preferred in prevention and treatment of CVD [42].

- · Flavonoids have antineoplastic, cardioprotective activity.
- Ginger (zingiber officinalis) found in foods and beverages help in reducing palpitation and hypertension.
- · Polyphenol (in grape) prevent and control arterial diseases,
- Flavonoids group of phenolic compounds found in grapes, red wine, apples. It blocks the Angiotensin converting Enzyme (ACE) and enhance lipoprotein metabolism, inhibit platelet aggregation.

Phytosterols, Dietary fibers, turmeric, spirulina also have property to reduce the risk of CVDs. [43]

## 7.3 Cancer and Nutraceuticals

Cancer is a disease which is characterized by abnormal or uncontrolled growth of cells which produces tumor.

Tumor is of 2 types-

- If tumor have potential to spread other parts of body, called as malignant tumor.
- If tumor which do not have the potential to spread over the parts of body, called as benign tumor. Symptoms include- Fatigue, pain, fever, unusual bleeding.

Cancer is a big health problem in developing countries. According to the (WCR)World Cancer Report the number of cancer cases are increasing enormously. Approx 16 million new cases were reported in year 2020. [44] Preventions are better than cure, so healthy lifestyles and exercises play major role in prevention of cancer. Carotenoids are mainly found in vegetables, diets and fruits are the groups which imparts different colors of the foods.  $\alpha$ - carotene,  $\beta$ - carotene, lutein, lycopene, zeaxanthin are the examples of some carotenoids. Among all the above examples of carotenes, most anti-oxidant activity is seen in  $\beta$ -carotenes. Whereas  $\alpha$ -carotene shows appx 55% of  $\beta$ -carotene antioxidant activity. [45,46]

Lycopene is another carotenoid, with antioxidant activity and prevent cancer. It is present in high amount in tomatoes, guava, pink grapefruit, water melon and papaya. Lycopene found in body in high concentrates in the prostate, testes, skin, where it protects the them from cancer.the antioxidant nature of lycopene is because of its unsaturated nature. [46,48



Fig. 6 Nutraceuticals action in cancer. [47]

## 7.4 Diabetes and Nutraceuticals

Diabetes is a group of metabolic disorder which is caused by abnormal metabolism and due to hyperglycemia. Diabetes is a chronic disease. There are two type of diabetes- Type 1 DM and Type 2 DM. Type 2 is most common, from which 95% is associated with obesity. Diabetes cannot be cured; it is only treatable. Symptoms include-

- Weight loss
- Increased urination
- Increase thrust, hunger
- Headache

- Blurred vision
- Fatigue
- Increase blood glucose level.

Herbal drugs have major effect in managing type 2 diabetes. Dietary fibers, magnesium level is used in diabetes. [49] Omega-3 fatty acids helps in reducing glucose tolerance, Lipoic acid act as an antioxidant treat diabetic neuropathy. [50,51]

#### 7.5 Nutraceuticals and their uses in Eye Diseases

Eye diseases include cataract,glaucoma, diabetic retinopathy, night blindness, colour blindness. Healthy lifestyle and balanced diet with all nutrients help to prevent the various eye diseases. Nutraceuticals like- Vitamin A(retinol) prevents night blindness, Vitamin E maintains effective vision and should be intake with vit. C,A and zinc.Vitamin B2, vitamin C are some vitamins that helps in maintaining healthy eye vision.Polyphenolic flavonoids, Vitamins C and E, have antioxidant properties. Astaxanthin, zeaxanthin, lutein is used in prevention of eye diseases.

### 7.6 Nutraceuticals and Parkinsonism

Parkinsonism is a extrapyramidal disorder. Symptoms include-

- Rigidity
- Tremor
- Hypokinesia
- Defective posture
- Expressionless face, etc.

It is a motor disorder in which dopamine-generating cells are damaged in the substantia nigra, with unknown causes due to which there is imbalance of Ach and DA. Depression, sensory, emotional and sleep problems are also some symptoms in parkinsonism. It is common in elderly patients. Vitamin E, glutathione, and Creatine help in prevention of Parkinsonism disease. [54,55]

#### 7.7 Inflammation and Nutraceuticals

Inflammation is an organized local tissue response that are formed in vascularized living tissues. It is a series of immune response of our body against any foreign substance in absence of inflammation process we are not able to eliminate the virus and pathogen.

Five signs of inflammation are- redness, heat, swelling, pain and loss of function. Inflammation can be acute and chronic. Acute inflammation is a primary response against xenobiotics. Ginger, soybean, Unsaponifiable, glucosamine, chondroitin, S-adenosyl methionine are useful in osteoarthritis, Vitamins C and D are also having an anti-inflammatory property to reduce these symptoms.

The anti-inflammatory action of such herbal nutraceuticals act by decreasing the activation of NF- $\kappa$ B . it blocks the expression of TNF- $\alpha$  and IL-1. It also decreases the phospholipase A2, COX-2.

The omega-3 fats are obtained from fish, nuts play a vital role to

treat the inflammation. Whereas some omega-6 fats series plays role in promoting inflammation by generating prostaglandins, leukotrienes, and interleukins. Turmeric is also effective in reducing the inflammation, treating the wounds and in liver diseases. Gamma linolenic acid (GLA) is fatty substance obtained from plant seed oil. As it is also a nutraceutical and it is also use to treat inflammation, skin allergies and other autoimmune diseases. Ginger also has anti-inflammatory properties and used in treating headaches, infections as well as stomach upset. Gentianine, Bromolain, turmeric, pineapple, teas and curcumin have anti-inflammatory activity.[56]

#### 8. CONCLUSION

Nutraceuticals are the food supplements that have proven health benefits in prevention of various chronic diseases, maintain the health of individual. with varying concentration. They are best alternative for modern medicines.

Nutraceuticals can be obtained from various food sources and classified according to their chemical nature, source, disease they treat etc. nutraceuticals are playing major role in preventing various chronic diseases as well as prevent individual from COVID-19 in this pandemic. Nutraceuticals can also be modifying by using recombinant technology and fortified food.

Global nutraceutical market is increasing day by day, it will reach appx US\$ 280.96 billion till 2021. The development of nutraceutical is depending on its quality, safety, long term adverse effects and clinical trials in humans. Nutraceuticals are performing major role in treating and preventing various diseases. Even in the phase of pandemic of COVID-19 these nutraceuticals are acting as immunity enhancers.

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