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Neutraceuticals: Functional Food and Dietary Supplements

			
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ABSTRACT

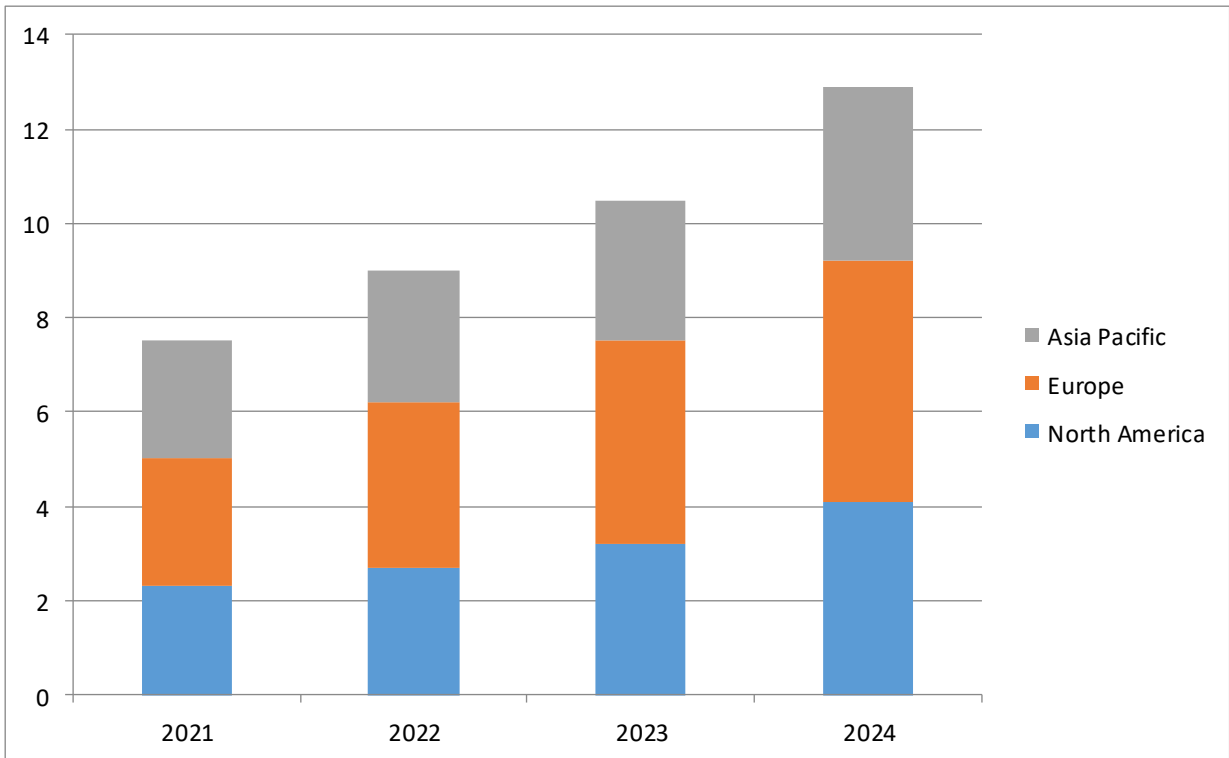
Numerous internal and environmental factors, such as biological cell ageing, ultraviolet (UV) radiation, cigarette use, nutritional inadequacies, and hormonal imbalances that cause skin cell degeneration, all have an ongoing impact on skin ageing. Free radicals and inflammation damage the skin's natural defences, which lead to the breakdown of collagen and elastic fibres. Roughness, wrinkles, pigmentation changes, telangiectasias, loss of elasticity, and decreased firmness are all signs of ageing skin that are accentuated by these internal and environmental variables. Nutraceuticals have been researched throughout the years to prevent and counteract these internal and environmental causes, many of which are present in naturally eaten foods and by-products. There is a therapeutic influence of nutraceuticals on human health. It consists of herbal items, probiotics and prebiotics, medicinal foods intended for illness prevention and treatment, and food supplements. The nutraceutical market is having drifting growth in India, USA and European countries. The motive of the review is to refer dermatologists, to the mechanism of action in neutraceutical in anti-aging and skin health.

INTRODUCTION

The largest organ in the body, the skin, ages continuously due to both internal and external forces [1]. The external variables, such as ultraviolet (UV) radiation, tobacco, inadequate nutrition, and hormone imbalances, might speed up the internal factors, which are a part of the natural ageing process within cells. These outside elements produce free radicals and inflammation, which damage and destroy collagen and elastic fibres [2]. These internal and environmental factors together cause the skin to become more rough, wrinkle, alter in pigmentation, develop telangiectasias, lose elasticity, and become less firm with time, giving the skin an aged appearance [2,3].

The words “nutrient” and “pharmaceuticals” make up the phrase “nutraceuticals.” AAFCO (1996) defines a nutrient as a feed component that will assist support a human or animal’s life, while a nutraceutical is any non-toxic food ingredient with medically proven health advantages, such as the prevention and treatment of disease [4]. The purpose of this review is to assist dermatologists in comprehending the mechanism of action of well-known nutraceuticals and their potential usefulness in antiaging and skin health. No new experiments using human or animal subjects were conducted by any of the writers for this article; instead, it is based on research that has already been done.

The below chart indicates the nutraceutical product marketed by region (USB Billion).



The obstacles in the awareness and consumption of nutraceuticals

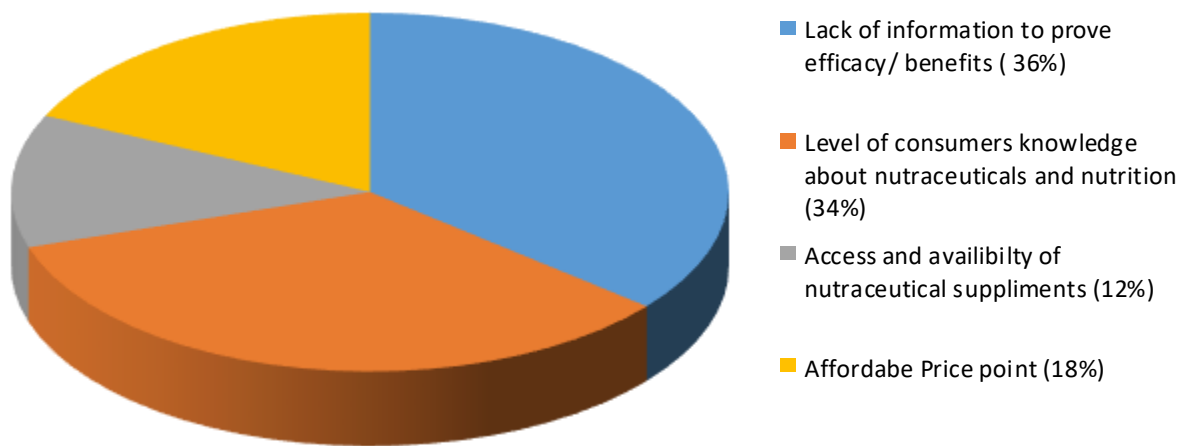


Table 1: Fortified foods with their Ayurvedic nutraceuticals

Sr.no	Fortified Foods	Ayurvedic Nutraceuticals
1.	Calcium enriched idli	Antioxidant and increase bone density
2.	Dal and Atta noodles	Sugar free ayurvedic supplement low calorie sweeteners
3.	Probiotic fortified yogurt	Curcumin
4.	Buttermilk	Green tea extract

One of the most revered tonics in Ayurveda is Triphala. Three significant herbs, Terminalia bellerica (Combretaceae), Terminalia chebula (Combretaceae), and Emblica officinalis, are combined to create it (Phyllanthaceae). These herbs all function as nutritional tonics. Nearly all of our body's organs and systems benefit from Triphala, but the skin, liver, eyes, digestive system, and respiratory system in particular.) The most well-known and well-established therapeutic uses of this compound include its immunomodulating, antibacterial, antimutagenic, and adaptogenic properties [5,6]. The curry ingredient turmeric, a yellow powder from South Asia, is well renowned for its curative properties. It has a strong antibacterial, antifungal, antiviral, and parasitic effect [7,8].

Type of nutraceutical based on the source, nature and application

Traditional, non-traditional, fortified, recombinant, phytochemical, herbal, functional foods, dietary supplements, probiotics, and prebiotics are the different categories of nutraceuticals based on how they are used [9,10]. Due to the similarities of their chemical components and ways of providing health benefits, the definitions and classifications of nutraceuticals frequently overlap. Functional foods are “foods and dietary components that provide a health benefit beyond basic nutrition,” according to the Institute of Food Technologists (IFT). Examples could include ordinary foods, dietary supplements, or foods that have been fortified, enriched, or enhance [11]. Traditional nutraceuticals are characterised as whole foods with possible health benefits, such as fruits, vegetables, grains, fish, dairy, and animal products [12]. Traditional foods or nutraceuticals can improve health by boosting the immune system and reducing the risk of cancer and heart disease [13-15].

Traditional nutraceutical and products

Functional foods

1. Functional foods go beyond supplying nutrition to also help health improvement and illness prevention [16,17]. These foods have components that boost antioxidant and anti-inflammatory effects, both of which are useful in preventing disorders like type 2 diabetes [18]. For a particular population, these foods are made readily available for everyday consumption and are of a comparable calibre to other conventional foods available on the market [19,20]. The majority of people's initial food choice is rice, which has a high nutritional value as a source of carbohydrates with low levels of fat, salt, and sugar because all varieties of rice are gluten-free and include resistant starch, which promotes the growth of good gut flora [21]. The third layer of wholegrain wheat is made up of the endosperm, which is the third layer of the grain, and the germ, which may be processed to make wheat bran and wheat germ. Wheat is the second most common staple food consumed worldwide [22]. Additionally, carrots and broccoli are examples of functional foods due to their active components such as sulforaphane, and lycopene [23]. Carotenoids, collagen hydrolysate, dietary fibres, and fatty acids are some of the active ingredients found in functional foods. These substances have a variety of health advantages, including the ability to reduce inflammation and boost immunity. The nature and numerous health advantages of these functional components will be covered in the following subsections.

Sr.no	Example	Uses
1.	Yogurts	Used as a probiotics for intestinal health.
2.	Omega-3 milk	Used in prevention of heart disease
3.	Canola oil with lowered triglycerides	Used for cholesterol reduction
4.	Oats, bran, psyllium and lignin's	Used for heart disease and colon cancer
5.	Prebiotics	oligofructose for control of intestinal flora
6.	Stanols (Benecol)	Used in reduction of cholesterol adsorption

A] Carotenoids

Carotenoids are natural compounds and sources of pigmentation that accumulate abundantly in plants, fruits and vegetables, and algae. A wide range of carotenoid derivatives are found in the human diet, including α -carotene, β -carotene, β -cryptoxanthin, lutein, lycopene, zeaxanthin, crocetin, fucoxanthin and astaxanthin[24,25]. About 20 of the over 600 fat-soluble plant pigments known as carotenoids are found in human tissues and blood[26,27]. Skin carotenoids concentrations rise when the ingredients are consumed, but fall with oxidative stress and UV exposure [26]. Due to the many conjugated C=C bonds that make up their chemical structure, carotenoids are also well known for their antioxidant properties. Carotenoids may interact with free radicals thanks to their structure, making them potent antioxidants [28].

B] b-Carotene

A precursor to vitamin A is b-carotene. By preventing lipid damage brought on by free radicals and singlet oxygen, it defends cells from harm [26]. Additionally, it contains photoprotective qualities that raise the minimal erythema dose (MED), guard against sunburn development, and prevent immune system photo suppression [26,27,29]. Green leafy vegetables, orange root vegetables, and yellow or orange fruits are foods high in b-carotene [26]. The RDA is established by vitamin A consumption since b-carotene is a precursor to vitamin A. The recommended daily allowance (RDA) for vitamin A for adults is 700 μ g for women and 900 μ g for men, according to the Food and Nutrition Board of the Institute of Medicine [30]. Long-term beta-carotene supplementation has been linked to one the increased risk of lung cancer, more research is needed to determine the optimal daily dose considering the health risks of supplements [29].

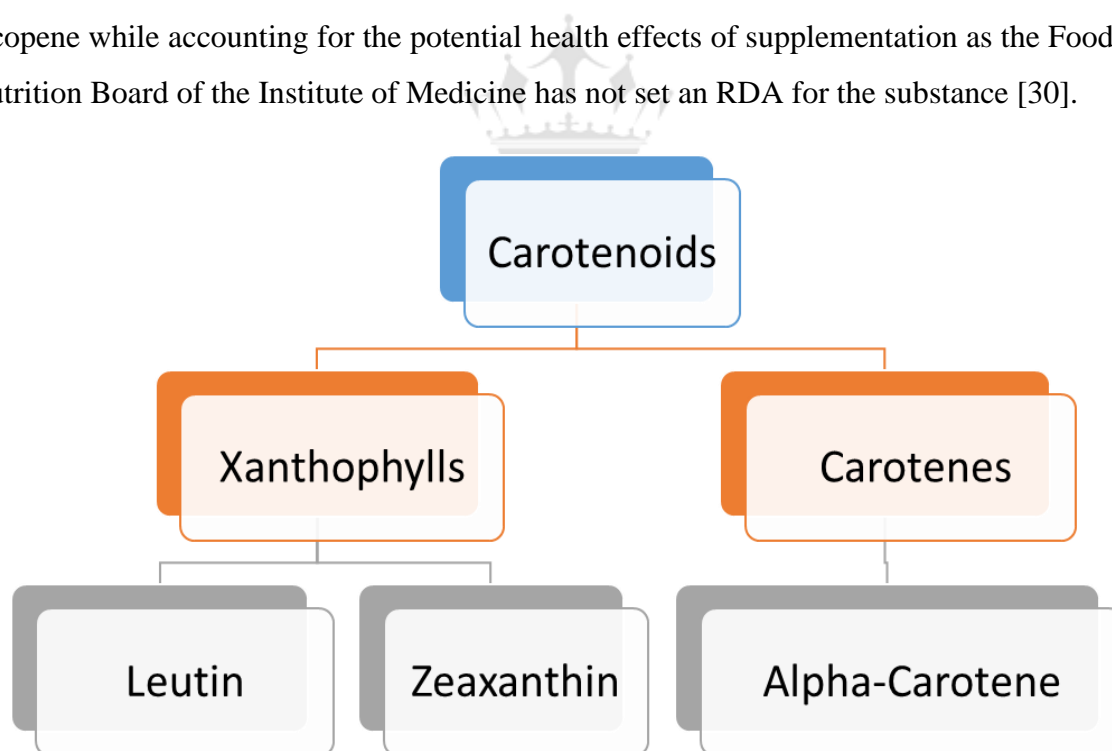
C] Lutein and Zeaxanthin

Lutein and zeaxanthin are the two major xanthophyll carotenoids in the retina and are widely believed to benefit eye health. However, significant amounts of both are found in human skin[31]. In both skin and eyes, these carotenoids act as blocking fillers and antioxidant that protects against harmful blue wavelengths and free radical damage [31,32]. Other studies have demonstrated that lutein and zeaxanthin prevent ECM breakdown by blocking MMPs, delaying the effects of UV radiation-induced photoaging, and reducing lipid peroxidation in the skin[31,33]. Lutein and zeaxanthin oral supplements, topical applications, or both at once

for maximum benefit can produce these skin benefits [31,33]. Zeaxanthin and lutein must be received exogenously because humans cannot manufacture them [30]. Although the Food and Nutrition Board of the Institute of Medicine has not yet defined lutein and zeaxanthin RDAs, 6–10 mg of lutein and 2 mg of zeaxanthin per day have been suggested in earlier studies [30,32,34]. Notably, in order to potentially lower the incidence of age-related macular degeneration and cataract, the American Optometric Association suggests taking 10 mg of lutein and 2 mg of zeaxanthin per day if one is not getting enough through food alone[35].

D] Lycopene

Although it has no vitamin A action, the carotenoid family's strongest singlet oxygen quencher is lycopene[26]. Lycopene has been proven in vitro experiments to be able to stop the growth of a variety of cancer cells by arresting the cell cycle and inducing apoptosis [26]. Additionally, there is a strong link between lycopene levels in skin that are higher with a reduction in skin roughness[26]. Watermelon, tomatoes, and pink grapefruit are among the foods high in lycopene. Further research is required to define the ideal daily amount for lycopene while accounting for the potential health effects of supplementation as the Food and Nutrition Board of the Institute of Medicine has not set an RDA for the substance [30].



E] Collagen Hydrolysate

In mammals, collagen is a major protein that may be obtained from the connective tissues of cows, including their skin, bone, cartilage, and tendons. By exposing it to hot water, collagen can be extracted, resulting in the partially hydrolyzed substance known as gelatin. Enzymatic

hydrolysis is used to thoroughly hydrolyze gelatin in order to create collagen hydrolysates. The positive effects of collagen hydrolysates include antioxidant, anti-ageing, anti-tumour, anti-inflammatory, and anti-obesity properties [36,37]. Collagen hydrolysates from domestic yak (*Bos grunniens*) bone have been proven to have immune-enhancing properties and have the ability to enhance mice's adaptive and innate immunity [38]. An investigation into the health advantages of collagen hydrolysate in females with photoaged skin also revealed a striking improvement in skin hydration, wrinkles, and suppleness [39].

F] Dietary Fibers

According to numerous studies, fibres are plant-based non-starch carbohydrates that are difficult to digest and provide a number of health benefits. They are naturally present in a variety of foods, such as fruits, vegetables, wheat bran, oats, and ispaghula husk [40-42]. Based on their solubility in hot water, ability to hold onto water, and viscosity, dietary fibres can be divided into more than just soluble and insoluble fibres. Viscous elements like fructans and β -glucans as well as non-viscous fibres like hemicellulose are found in soluble fibres. While soluble fibres tend to prolong stomach emptying time, insoluble fibres tend to speed it up, helping to relieve constipation. Insoluble fibres tend to lose their characteristic of viscosity and are insoluble in water [43].

G] Fatty Acid

Animal fats, fish oil supplements, seeds, olive oil, and coconuts all include fatty acids as a component of their oils and fats. In addition to their function in energy storage, they have also been shown in numerous studies to have anti-inflammatory and immunomodulatory properties. In one study, patients with rheumatoid arthritis (RA) who received omega-3 polyunsaturated fatty acids (PUFAs) at a dose of >2.7 g/day for at least three months reported less severe RA symptoms. Long-chain polyunsaturated fatty acids, or omega-3 and omega-6, are two categories that make up essential fatty acids. Linolenic acid is the source of omega-3 fatty acids, while linoleic acid is the source of omega-6 fatty acids (LA). Alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid are the three most prevalent types of omega-3 essential fatty acids (DHA) [45].

Classification of nutraceuticals based on the mode of action

Nutraceuticals are thought to improve human health and lengthen lifespan along with numerous other mechanisms that slow down ageing and ward off chronic diseases [46].

Numerous nutraceutical supplements have demonstrated a beneficial effect on immune system functions, diabetes, obesity, cancer, cardiovascular disease, and cancer[47-49]. In general, nutraceutical modes of action involve raising functional components that will improve health[50].

1] Anti-cancer activity

According to research on the use of nutraceuticals as chemo-preventative agents, they have the potential to both prevent and treat cancer. It has been demonstrated that nutritional supplements from many sources have anti-cancer properties. Many plants, including garlic, ginseng, curcumin, ginger, and green tea extract, have been found to inhibit oncogenesis. These pathways include promoting autophagy and intrinsic apoptosis, as well as inhibiting DNA alkylation, tumour initiation, proliferation, and metastasis[51]. Numerous studies have been conducted to determine the mechanisms of action of nutraceuticals against different types of cancer, and it has been discovered that a wide variety of nutraceuticals exhibit anti-cancer properties against oral cancer, prostate cancer, breast cancer, lung cancer, and colon cancer cells[52]. Cell cycle arrest, apoptosis, and anti-angiogenesis are brought on by the activation of the vitamin D receptor (VDR) [53,54]. Organs and tissues contain this nuclear receptor, which is intracellular. The growth arrest gene and DNA damage-inducible gene are activated when the active form of vitamin D binds to VDR[53,54]. This leads to the conclusion that while vitamin D sufficiency benefits in illness prevention, vitamin D insufficiency would result in a variety of disorders. Additionally, the possibility of vitamins including vitamin A, C, and D as anti-cancer agents has been researched. On the other hand, gemcitabine and the complementary treatment supplement *Clinacanthus nutans* have both been studied. The use of *C. nutans*, either alone or in conjunction with gemcitabine, was discovered to have an anti-proliferative impact on pancreatic cancer cells. The overexpression of Bax and the downregulation of Bcl-2, cIAP-2, and XIAP in human pancreatic cancer cells sum up this combinatory therapy[55]. Numerous studies have been done on how prebiotics and probiotics affect colorectal cancer (CRC). It is thought that both prebiotics and probiotics are helpful in supporting human health, particularly in the gastrointestinal tract. High fibre consumption increases the number of short chain fatty acids (SCFAs), which produces bacteria and lowers the number of colon tumours, according to research on the anti-cancer effects of prebiotics[56]. Prebiotic and probiotic diet promotes lactic acid-producing bacteria, which in turn expresses its anti-cancer action in colorectal cancer. These substances also have immunomodulatory and anti-inflammatory effects. Green tea's polyphenols, in particular,

have been demonstrated to target cancers of the liver, lung, breast, prostate, and skin. Green tea is rich in catechins, which have anticancer properties including antioxidant, anti-inflammatory, antiproliferative, and antiangiogenic effects[57]. According to a study looking at habitual green tea consumption in humans, epigallocatechin gallate (EGCG) lowers the incidence of prostate cancer[58]. Additionally, a study showed that long-term treatment with resveratrol at high doses promoted apoptosis and inhibited the proliferation of malignant cells in human non-small cell lung cancer[59]. In general, functional foods and nutraceuticals act as chemosensitizing or chemopreventive agents in the treatment of cancer.

2] Probiotics in kidney health

If the waste products are not effectively expelled, they can become extremely toxic when they reach high concentrations in the blood and can seriously harm various organ systems[60]. The overworked and damaged kidneys cause a buildup of toxic wastes in circulation. Urea, uric acid, creatinine, and other toxins can be used as nutrition by some probiotic microbes to thrive[60]. As they grow in number, more uremic toxins are diffused into the intestine from the circulating blood and over the lining of the intestinal walls. The faeces, which typically include 50% germs by weight, are expelled along with the increased microbial development. With the help of bacteria, enteric toxin reduction technology turns the colon into a blood-cleansing agent that, indirectly, eliminates toxic wastes and aids in their elimination as faeces. As a result, using Kibow® Biotics orally can help you maintain a healthy kidney function.

3] Anti-Inflammatory Activity

Nutraceuticals have anti-inflammatory effects that aid in the treatment and prevention of chronic disorders linked to inflammation[61]. Nutraceutical usage as complementary alternatives to anti-inflammatory therapeutic medications results in a reduction in drug dosage, which lowers side effects. This is another advantage of using nutraceuticals as anti-inflammatory agents[62]. After taking a strong anti-inflammatory like curcumin, inflammatory cytokines such as interleukins, TNF-, and cyclooxygenase-2 (COX-2) can be suppressed[63]. Curcumin has the ability to decrease the inflammation caused due to cutaneous complications and helps to the betterment of a patient's health and high-sensitivity c-reactive protein (hs-CRP)[64]. One class of dietary supplements that have been demonstrated to treat inflammatory diseases is PUFAs[65]. Treatment with PUFA decreased NF-B expression. Additionally, Duchenne muscular dystrophy patients showed a decrease in

proinflammatory markers and a rise in the anti-inflammatory marker IL-10[66]. Lycopene, an anti-inflammatory chemical found in tomatoes that helps shield the heart and fend off cardiovascular conditions including atherosclerosis and myocarditis, is another illustration of a nutraceutical component[67,68]. Probiotics with anti-inflammatory properties control the NF-B signalling pathway, inflammatory cytokines, and the regulatory T cell response to produce their anti-inflammatory effects[69]. The anti-inflammatory properties of lycopene, ginger, cinnamon, and peppermint have also been demonstrated. Ginger and its components have anti-inflammatory properties that can help to lessen inflammation[70]. In a study, ginger was given orally to newborn rats with necrotizing enterocolitis. The rats' TNF-, IL-1 and IL-6 levels decreased, indicating a significant decrease in inflammation[70].

Table of the anti-inflammatory mode of action along with their benefits

Mode of action	Nutraceuticals	Benefits	Reference
Reduce the synthesis of nitric oxide (NO), interleukin-1 (IL-1), nuclear factor kappa B (NF-B), tumour necrosis factor (TNF), and iNOS.	Resveratrol	Neuroprotective	[71]
Limit the inflammatory response, including ICAM-1, MCP-1, Cox-2, TNF-, IL-1, and IL-6	Baicalin	Improvement of trinitrobenzene sulphonic acid (TNBS) induced colitis	[72]
IL-10 levels should rise while TNF-, COX-2, 5-LOX, and IL-6 expression is decreased.	Flavocoxid	Protects from sepsis	[73]

Reduces the expression of TNF α , IL-1 β and reduces myeloperoxidase (MPO) activity	Curcumin	Enhances dextran sulfate sodium (DSS)-induced colitis	[74]
TNF-, IL-1, and IL-6 expression were decreased, however IL-10 expression was increased. decreases the expression of TLR-2 and TLR-4 inhibits I-B, p65, p38, ERK, and JNK from becoming phosphorylated.	Piperine	Reduces inflammatory injury in Staphylococcus aureus endometritis.	[75]
Inhibits NF-kappa B p65 subunit activation, which decreases the production of cytokines and inflammatory cells.	Eucalyptol	Potential treatment for acute lung irritation brought on by cigarette smoke.	[76]
NF-kB and p38 are inhibited, and TNF- and IL-1 levels are decreased.	Ortho-eugenol	Treatment of pain and inflammation.	[77]

4] Nutraceuticals against Alzheimer's disease (AD)

The most common type of dementia is Alzheimer's disease (AD), also known as senile dementia of the Alzheimer's type (SDAT), primary degenerative dementia of the Alzheimer's type (PDT), or simply Alzheimer's. The following are some of the several dietary supplements that are used to treat Alzheimer's disease:-

Antioxidants: Because most chronic diseases have a significant oxidative stress component, antioxidants are absolutely essential in the treatment of practically all disorders. A major factor in neurodegenerative illnesses like phosphatidylserine is oxidative stress[78]. The compound phosphatidylserine is quite intriguing. The main phospholipid in the brain, phosphatidylserine, is responsible for the fundamental structure of the cell membrane. Phospholipids and membrane phosphatidylserine are crucial for cell-to-cell communication and the delivery of biochemical letters to the cell. The oral supplement phosphatidylserine improves neuronal membranes, cell metabolism, and certain neurotransmitters, including acetylcholine, nor-epinephrine, serotonin, and dopamine [79].

5] Anti-Lipid activity

The condition known as hypercholesterolemia refers to an elevated level of low-density lipoproteins in the blood[80]. This section will explore the impact of nutraceuticals on various illnesses linked to increased lipid levels because research has been done on how they can lower lipid profiles in hypercholesterolemic patients. Nutraceuticals have the ability to significantly reduce levels of total cholesterol (TC) and low-density lipoprotein (LDL) when used as hypolipidemic drugs. Based on how they work, lipid-lowering nutraceuticals can be divided into three classes. These processes consist of preventing the synthesis and absorption of cholesterol as well as the excretion of LDL[80].

First off, a variety of mechanisms contribute to the lipid-lowering effects of the majority of nutraceuticals: When combined with diet, medication, or other nutraceuticals, they may be candidates for increasing the effects of lipid-lowering since they have the ability to work simultaneously on several phases of lipid-induced vascular damage[81]. Foods or supplements containing plant sterols have been shown useful in decreasing lipid levels. Plant sterols have been shown to alter lipid profiles by reducing the intestinal absorption of cholesterol[82]. It has been discovered that consuming plant sterols had a positive impact on lipid profiles by reducing the levels of triglycerides and LDL in people who were either at risk for or had type-2 diabetes[83]. Further research on the additive effects of plant sterols with lipid-lowering treatments revealed that adding plant sterols to atorvastatin or ezetimibe led to further decreases in total and low-density cholesterol[84]. The selected nutraceuticals were berberine, RYR, monacolin K, policosanol, and folic acid. A study was done to evaluate the capacity of a collection of nutraceuticals to change lipids. According to the findings, RYR dramatically reduced TC and LDL[85]. When liposomal berberine, curcumin, and fermented

red rice were combined, it significantly reduced inflammatory markers and improved lipid profiles in those with hypercholesterolemia[86]. In conclusion, the ability of numerous nutraceuticals and functional foods to control lipid profiles has been demonstrated. Nutraceuticals can either decrease cholesterol synthesis, decrease cholesterol absorption, or increase cholesterol excretion depending on how they work. Each of the aforementioned nutraceuticals may have one or more mechanisms of action, lowering TC and LDL.

Nutraceutical safety on consumer

Only a small percentage of the nutraceuticals available on the market are detrimental to human health and are therefore not generally harmful when consumed by humans. When administered in the right, regulated levels, studies have demonstrated that numerous frequently used nutraceuticals have many health advantages with relatively little harm. Anthocyanins, polyphenols, and catechins are examples of common nutraceuticals that are safe for human consumption when employed under controlled conditions. Only a small number of research have shown how these compounds are bad for human health. However, research on nutraceuticals has demonstrated that the risks are outweighed by the benefits, and they are universally accepted for usage in humans when taken in the right amounts and dosages[87]. Misuse and excessive usage of these products, however, could be harmful to people's health. The kind, duration, and quantity of use are the main determinants of these nutraceuticals' safety for customers. Some dietary supplements, especially when taken by someone who is on medicine, may interact with the medication in a way that has highly negative effects on the body[88]. In other words, the use of nutraceuticals has significantly expanded for both human and veterinary products. Because there are no extensive analyses of their safety and effectiveness in clinical studies, the toxicity concerns related to their use are also elevated. Additionally, ensuring correct pharmacokinetics and minimising fluctuations and adulterants such as heavy metals, agricultural chemicals, and mycotoxins.

CONCLUSION

Patients who eat a healthy, balanced diet and use the bulk of the nutraceuticals described here are probably getting enough of these nutrients to get the skin advantages mentioned above. Numerous Indian enterprises have established themselves as suppliers of plant extracts and phytochemicals on a local and international level, which will support the growth of the nutraceuticals industry in the near future. It is unquestionably possible to improve health and avoid various diseases with the use of nutraceuticals, some of which have shown efficacy

comparable to that of traditional medications. Comparing nutraceuticals to both complementary treatments and traditional pharmaceuticals, there are generally fewer side effects, unfavourable effects, and medication interactions. Several pharmaceutical companies, notably Ranbaxy and Abbott, have taken the initiative to provide a variety of nutraceutical products for customers of various ages. Therefore, more thorough research about their safety and effectiveness is required from both academia and the pharmaceutical industry. Additionally, the application of cutting-edge and high-throughput technologies can aid in our understanding of the underlying mechanisms of action and expand the boundaries of this fascinating field of study for the benefit of humanity in terms of both economic and health results.

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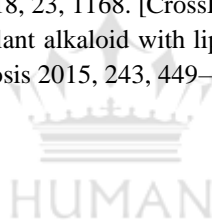
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