



“A COMPREHENSIVE REVIEW ON NUTRACEUTICAL AND ITS APPLICATION”

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ABSTRACT:-

Nutraceuticals—which are basically **nutritional supplements**—have become incredibly popular, largely because people think they're safe. Plays major role in prevention of diseases.

These supplements are used to boost overall **health**, help slow down **aging**, **prevent** diseases, and make the human body functioning proper. They're achieving popularity because they offer both **nutritional and medicinal benefits**.

Nutraceuticals can be classified on based on their source: they can be **dietary supplements** or substances taken from **herbs** (like bioactive compounds). The herbal kind, in particular, are great for maintaining health and promoting a long, high-quality life.

These products have shown promising results in helping to manage a several types of serious conditions, including **cancer**, **neurological disorders**, and **heart disease**, among others.

This is why there's a strong focused on researching them, looking at things like:

What they are: determining the different beneficial substances that act as nutraceuticals, such as specific **carbohydrates**, **fats**, **edible flowers**, **alkaloids**, and **compounds from medicinal plants**.

The Big Picture: Understanding the need for people to eat better diets and the health problems that arise when they don't stick to healthy eating guidelines.

Innovation: Development of new nutraceuticals, functional foods, and food supplements that offer new health advantages.

Science: Understanding exactly **how** these products work inside the body (their mechanisms of action).

The Rules: Defining and understanding the testing, formulation, and **regulatory** aspects of bringing these supplements to market.

Ultimately, a key use of nutraceuticals being explored is their role in **prevention** of certain diseases.

Keyword:- Nutraceutical, Dietary supplements, Herbal bioactive compounds, Application

Introduction :- What Exactly Are Nutraceuticals?

The term "nutraceutical" was actually created in **1989** by **Stephen L. Defelice**, the founder and chairman of the Foundation of Innovation Medicine. It is a mixture of two words **nutrition** and **pharmaceutical**.

Simply put, nutraceuticals are **food-based products** that claims to provide health benefits *beyond* the basic nutrients you get from eating. Depending on where you live, these products might promise to prevent long-term diseases, promote overall health, slow down aging, extend your lifespan, or support specific body functions or structures.

These are essentially active biological compound present in food that act like both **nutrients** and **medicine**. Nutraceuticals are natural, bioactive, or chemical compounds that just being a nutritional supplement, also have properties that can **promote health**, **cure**, or **prevent disease**. They are supplements that contain essential ingredients like **lipids (fats)**, **vitamins**, **carbohydrates**, **proteins**, and **minerals**.

Health Benefits

Nutraceuticals are being recognized as potent helpers in the treatment of a wide variety of conditions, including:

- **Heart Disease** (cardiovascular disease)^{2,3}
- **Diabetes**^{4,5}
- **Atherosclerosis** (hardening of the arteries)^{6,7}
- **Cancer**^{8,9}
- **Neurological Disorders** (brain/nerve conditions)^{10,11}

The increasing popularity of nutraceuticals is happening for several reasons¹²⁻¹⁶:

Most of the people becoming are worrying about the increasing cost of healthcare. Some individuals are not satisfied with using traditional pharmaceuticals to stay healthy, so they are choosing to nutraceuticals to improve their well-being and help prevent chronic diseases as well as acute problems. Healthcare professionals are recognizing that our food supply is often heavily processed as well nutrition is declined in our food. They understand that foods grown using chemical fertilizers, pesticides, and genetically modified seeds might be missing the key nutrients we need for optimal health. There is a growing trust in preventing sickness before it starts, rather than just treating it. People dealing with chronic diseases, who haven't found relief from conventional medicine, are looking for alternatives. For patients with tight budgets, nutraceuticals can be a more affordable option as compared to modern treatment.

Bioactive Compounds as Nutraceuticals

Bioactive compounds are natural substances which is present in small amounts within foods, especially in fruits, vegetables, and whole grains. Beyond just providing basic nutrition, these compounds provides a various types of health benefits and show significant promise for their therapeutic properties. Based on their origin, bioactive compounds are typically grouped into two main categories: those from herbal sources and those found in dietary supplements (Table 1).

Table 1 Bioactive ingredients

Herbal bioactive ingredients	Dietary supplements
Bitters	Prebiotics
Essential oil	mushroom
Flavonoids	Probiotics
Carotenoids	Vitamins
Tannins	Lipids
Alkaloids	Proteins
Anthraquinones	carbohydrates

Herbal Bioactive Ingredients

Therapeutic Plants Herbs have gain more attention for centuries, and for good reason. They are much more than just seasoning; they possess a wonderfully diverse range of scents and flavour and potent for prevention of diseases. This diversity has made them incredibly valuable, not only in the kitchen as a staple for cooking but also in traditional and modern medications.

A major category of nutraceuticals comes directly from these therapeutic plants (Medicinal plants) the Herbal Bioactive Substances **17, 18**. These are the potent compounds tucked away inside herbs, and they include a long list of beneficial molecules such as:

- Carotenoids
- Coumarins
- Flavonoids
- Lignans
- Phthalates
- Plant sterols
- Polyphenols
- Saponins
- Sulphides
- Terpenoids

Alkaloids:- Alkaloids are truly a unique family of chemical compounds **19**. They can be defined as a heterocyclic chemical structure containing nitrogen, and they are essential players in the fundamental biological processes of plants, animals, and even microorganisms. Because they're abundantly present in the natural herb and heavily utilized in medicine, and ecology.

They provide significance health benefits to human beings. When alkaloids comes in contact with cells and molecules within organisms, they can induce powerful changes, which is why they've been so widely adopted as curative medications throughout the pharmaceutical industry **20**.

Extensive care is required for some varieties can be exceedingly harmful even in small concentrations **21**. Generally, they dissolve easily in organic solvents.

In the world of medicine, plant-derived alkaloids are workhorses **22, 23**. They serve as:

- Anti-malarial agents (like quinine and chloroquine)
- Anti-cancer treatments (such as vinblastine, vincristine, and taxol).
- Drugs to increase blood circulation (e.g., vincamine for the brain).
- You probably consume pharmacologically active alkaloids every day! Take, for instance, a comforting cup of black tea, which contains

theophylline, or your morning coffee, which contains caffeine cite:24. Both are essential components of the human diet.

Other well-known sources of alkaloids include the spice rack. Piperine, an alkaloid, is found in long pepper (*Piper longum* L.) and black pepper (*Piper nigrum* L.), two spices frequently used in Indian and other cuisines 25.

We can also find significant amounts of alkaloids in various *Capsicum* peppers, which include:

- Chili and red pepper (*Capsicum annuum* L.)
- Bird pepper or tabasco (*Capsicum frutescens* L.)
- Peruvian pepper (*Capsicum bac catum* L.)
- Aji pepper (*Capsicum Chinese* Jacq.)
- Rocoto pepper (*Capsicum pubescens* Ruizet Pav.)

research indicates that piperine specifically has significant physiological activity and is not harmful 26.

Saponins

Steroid saponins are natural compounds which are present in wide variety of plants, as well as some microorganisms and even animals 27. You can find them in many types medicinal plants, including:

- Aubergines (*Solanum aethiopicum* L.)
- *Capsicum* peppers (*Capsicum annuum*)
- Ginseng (*Panax ginseng*)
- Yucca (*Yucca schidigera*) 28

Saponins are incredibly crucial and play an essential role in numerous pharmacological processes 29. They boast a wide range of health benefits, such as:-

- Hypoglycemic activity (helping to lower blood sugar).
- Reducing both LDL cholesterol (the "bad" cholesterol) and overall serum cholesterol.
- Inhibiting the growth of cancer cells.
- Stimulating the cell-mediated immune system.
- Exhibiting strong antioxidant and antifungal activity.
- Offering neurotrophic and neuroprotective activity.
- Providing viricidal effects (killing viruses).

Tannins

Tannins are a collection of substances made up of phenolic and polyphenolic chemicals 30, 31, 32. In your body, they primarily function as astringents by causing tissues to contract and shrinking the structural proteins found in the skin and mucosa. Beyond this, tannins are vital for:

- Preventing lipid peroxidation.
- Stopping the production of super-oxides.
- Completing crucial free radical scavenging activity.
- Tannins are widely used to treat conditions like ulcerative colitis because they offer a host of beneficial health features, including 33, 34
- Anti-inflammatory and antimicrobial actions.
- Immunomodulatory effects.
- Analgesic (pain-relieving) and antidiarrheal properties.
- Neuroprotective and antihypertensive actions.
- They are even used in livestock feed to protect against parasites like gastrointestinal worms 35.

Bitters

Bitters are mixture of chemical compounds that, as the name suggests, have a strong, bitter taste and are present in many therapeutic herbs 36.

Common herbs containing significant amounts of bitter compounds include:

- Yarrow (*Achillea millefolium*)
- Chamomile (*Matricaria chamomilla*)
- Horehound (*Marrubium vulgare*)
- Peppermint (*Mentha piperita*)
- Rue (*Ruta*)
- Milk thistle (*Silybum marianum*)

➤ Dandelion (*Taraxacum*)

These bitter compounds target the digestive system and majorly triggers the stomach to release digestive enzymes and helps facilitate the flow of bile from the liver. This dual action increases your appetite and allows for better nutrient absorption from your food **36**.

Bitters are prescribed to patients who face issues like poor appetite, liver and gallbladder problems, gastritis, sluggish bowels, and post-flu symptoms **37**. Not only digestion, bitters offer other pharmacological advantages, including the ability to cite:38:

- Treat cancer.
- Calm the nervous system.
- Provide antioxidant, anti-inflammatory, antibacterial, and anti-diabetic properties.
- Despite their disagreeable taste, the beneficial effects of bitters start right in the mouth, meaning oral use is necessary to achieve the best results. Some potent bitters described in Indian Ayurveda include:
- Guduchi (*Tinospora cordifolia*)
- Manjista (*Rubia cordifolia*)
- Neem (*Azadirachta indica*)
- Turmeric (*Curcuma longa*)

Due to their affection for the liver and spleen, these are mostly used in Ayurvedic medicine to treat various diseases **39**.

Carotenoids

Carotenoids are the vibrant, colorful compounds responsible for orange, yellow, and red colors we observe in many fruits, vegetables, and seafood **40**. These pigments are synthesized naturally by plants, algae, bacteria, and fungi.

Animals, including humans, cannot produce carotenoids by their own. This means we have to obtain them through our diet and then metabolize them for our body to use in various metabolic actions **41**. In the biological world, carotenoids are vital **42**:

- They act as antioxidants.
- They help regulate membrane fluidity.
- In plants, they are auxiliary light-harvesting components in photosynthesis.
- You can get these vital compounds from many common foods. For example cite:43, 44:
- Apricots (*Prunus armeniaca*) and broccoli are great sources of β -carotene and lutein.
- Carrots and tomatoes offer excellent amounts of β -carotene and lycopene.
- Pumpkin (*Cucurbita* spp.) is a good source of β -carotene, β -cryptoxanthin, lutein, and zeaxanthin.
- Green leafy vegetables provide both lutein and β -carotene.

Out of the approximately 600 discovered carotenoids, only about 50 has provitamin A property. The three most significant ones are α -carotene, β -carotene, and β -cryptoxanthin cite:43, 44. Consuming these specific carotenoids is important because they can help protect us from serious eye conditions **43, 44**.

Finally we could say carotenoids are powerful because they function as antioxidants and significantly improve resistance to oxidative stress across all species cite:45. They are also recognized for having notable anti-cancer properties **46**.

Flavonoids

Flavonoids are significant compounds found abundantly in nature, also present as glycosides and, notably, as vital antioxidants **47**.

You can easily incorporate them into your diet, as they are major components of:

- Vegetables like broccoli, green pepper, kale, onion, spinach, and tomato.
- Fruits such as orange, grapefruit, apple, and grape.
- Various herbs including *Citrus grandis*, *Hypericum perforatum*, and *Sophora japonica*.
- Soybeans **47**.

Flavonoids offer a wide spectrum of health benefits **48**. They have been shown to possess:

- Antiviral properties.
- Antiallergic effects.
- Anticholinesterase activity.
- Anticancer and, of course, strong antioxidant properties.
- Crucially, they provide a protective impact against coronary heart disease.

Because of their dynamic profile, a variety of products containing flavonoids are being developed or already present in market functional foods and

dietary supplements **49**.

However, there is a challenge: published research has gained less attention to the ADME (Absorption, Distribution, Metabolism, and Excretion) properties of flavonoids in animals **49**. There is not so much data makes it harder to accurately predict their biological effects, which finally limits their full potential for use as food sources.

Essential Oils

Essential oils are the concentrated, naturally present mixtures of aromatic chemicals that give plants their particular scent **50**. They can be made from nearly every part of a plant:

- Buds and flowers
- Bark and wood
- Fruits and leaves
- Roots, seeds, twigs, and herbs

These precious oils are extracted using traditional methods like steam or solvent extraction method **51**. Some , advanced techniques, such as subcritical water extraction, have also been successfully used to harvest essential oils from plant materials like *Thymbra spicata* leaf **51**.

Chemically, these volatile oils are a mixture of terpenes, aldehydes, esters, ketones, and phenolic chemicals **52**. They often contain significant levels of terpenoids, which gives them their impressive antiseptic and antibacterial properties **52**. By enhancing the body's natural defense mechanisms, essential oils help protect us against a number of infectious diseases.

Moreover, they have significant beneficial effects across the body **53**

- They are anti-cancer, anti-inflammatory, and antispasmodic (e.g., yarrow and chamomile).

Certain oils, like rosemary, ginger, and thyme, are known to have positive effects on the heart and circulatory system.

Anthraquinones

Anthraquinones are certain group of molecules, each carrying having biological characteristics **54**.

One of their most general properties is a laxative effect, which occurs because they stimulate muscle contraction in the digestive tract. You can find high concentrations of anthraquinones in several plant species, including **55, 56, 57**.

- Aloe vera (*Aloe barbadensis* Miller)
- Cascara (*Rhamnus purshianus*)
- Dock (*Rumex crispus*)
- Rhubarb (*Rheum palmatum*)
- Senna (*Senna alexandrina*)

Researchers have focused on the significantly anti-cancer action **55, 56, 57**

Aloe-emodin, a hydroxyanthraquinone found in aloe vera, has been shown to limit the growth of various tumor cell lines, including lung cancer, hepatoma, and leukemia cells **55, 56**.

Similarly, emodin and rhein from *Rheum rhabarbarum* (rhubarb) also demonstrate anti-cancer effects **57**.

In fact, aloe-emodin has been specifically reported to have anti-neuroectodermal tumor properties in both in-vivo and in-vitro studies **58**.

The latex of the Aloe plant also contains significant amounts of anti-inflammatory anthraquinones, known for their ability to heal and stop pain cite **59**.

Interestingly, anthraquinone production isn't limited to plants! It's also found in marine life. Recently, researchers discovered two anthraquinones with anti-tumor capabilities—Lupinacidin A and Galvaquinone B—in a sea anemone from Easter Island, suggesting a novel source for nutraceutical development **59**.

Dietary Supplements

Probiotics

Probiotics have become a hot topic in health research. They are essentially helpful microorganisms that, when consumed in the right amounts (as a single or mixed live culture), provide therapeutic benefits to human health **60**.

The journey to understanding probiotics began with the Russian immunologist Elie Metchnikoff. He observed that Bulgarian peasants, who regularly consumed fermented milk containing beneficial *Lactobacillus* bacteria, often lived long and healthy lives. This observation led to the hypothesis—and the subsequent development—of probiotics. Years later, we now know that bacteria in our bodies are far from static; they are dynamic, symbiotic co-residents **60**. Some modern health issues, like the increase in inflammatory and allergic disorders, are even attributed to consuming fewer helpful microbes compared to our ancestors **61**.

The three species most commonly used to create commercial probiotics are *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces cerevisiae* **62**.

Consuming these beneficial microbes has been shown to offer several important health improvements **62**

- Enhancing immune defense against pathogens.
- Suppressing auto-immune responses.
- Shortening the duration of infectious diarrhea.
- Increasing gastrointestinal tolerance to antibiotics.
- Improving the treatment of women with bacterial vaginosis.
- Lessening the symptoms of Irritable Bowel Syndrome (IBS).
- Decreasing the incidence of dental caries (cavities).

Prebiotics

If probiotics are the good bacteria, then prebiotics are their food! They are food ingredients that, even in small amounts, stimulate the growth of beneficial bacteria **63**. When these beneficial bacteria colonize the host, they have a positive impact on overall health.

You can think of prebiotics as the essential nourishment for the various bacterial species, like *Lactobacillus* and *Bifidobacterium*, that live inside humans and are crucial to our health and well-being **63**. These probiotic bacteria consume the prebiotic fiber as a substrate.

To determine how well a prebiotic compound works in a variety of hosts, including humans, they often undergo a wide range of in-vivo and in-vitro testing **64, 65**. The fermentation characteristics being examined are usually linked to healthy colon function and metabolism.

Many food items contain fermentable fiber that is suitable for human nutrition cite:66. While a substance's ability to ferment might be the only factor considered when selecting it as a prebiotic **67**, some researchers caution against using this as the sole criterion. This is because food matrices are complex and offer a variety of metabolic and nutritional advantages **68**. When qualifying a substance as a prebiotic, it's also essential to consider the fermentation products themselves, as they can be either advantageous or harmful **66**. Currently, the two most popular and recognized sources of prebiotics are resistant starch and fructans.

Proteins

Proteins are fundamental building blocks of our diet, playing several crucial roles **69**. They are key components of food, contributing to organoleptic properties (especially texture), acting as a valuable source of nutrition for tissue building, and offering a wide array of other health benefits.

There's a growing trend toward using plant-derived nutrients to develop healthier, novel, and safer foods **69**. This shift is beneficial from both an economic standpoint and an environmental perspective. Accordingly, demand for plant proteins is increasing, particularly for use in food matrices to boost the nutritional and health profiles of these products.

A great contemporary example is the use of legume proteins as food ingredients. Historically, legumes were primarily used to derive oils and fats. Among all legumes, Lupin (*Lupinus albus* L.) stands out as the richest source of protein, with a content equivalent to soybean—nearly 35% of its dry weight **70**. Interest in dietary proteins sourced from seeds has surged globally due to their nutritional value **71, 72**. These proteins possess several therapeutic activities, including:

- Hypoglycaemic (blood sugar-lowering) activity.
- Hypolipidemic (fat-lowering) effects.
- Anti-cancer and anti-obesity activities.
- Clearly, plant proteins have a vital role to play in improving human health **71, 72**.
- Beyond plants, egg protein is recognized as an essential source in a balanced diet **73**.

It also delivers its own set of health benefits, such as:

- Anti-cancer and antihypertensive (blood pressure-lowering) properties.
- Antimicrobial and antioxidant activity.
- Immunomodulatory and protease inhibitor actions.

Finally, even waste products are being utilized: a protein isolate prepared from the by-products generated during the milling of pigeon pea has been reported as both a good source of nutraceuticals and a useful encapsulating material with bioactive properties **74**.

Carbohydrates

Carbohydrates are the most abundant and widespread class of nutrients, playing a profoundly important role in the human body **75**. These molecules in our diet vary widely, from tiny simple sugars to complicated starches. Dietary guidelines recommend that carbohydrates should make up at least 5% of the total calories we consume in a balanced diet **75**.

They are absolutely critical for human physiology and metabolic activity. Furthermore, adequate carbohydrate intake helps in the prevention of a number of chronic diseases, including:

- Cancer
- Cardiovascular disease
- Diabetes

- Obesity
- Gastrointestinal disorders

Starchy carbohydrates are a primary source of energy and are necessary for maintaining a healthy digestive tract. There is still huge, untapped potential in the research of applying bioactive carbohydrates within functional foods **76**.

For example, certain carbohydrates act as food for beneficial gut bacteria cite **77**

Inulin (fructans), fructose, and other oligosaccharides actively promote the growth rate of health-promoting bacteria, such as Bifidobacteria.

These beneficial microbes can limit the proliferation of potentially hazardous anaerobic bacteria in the gut.

They also act as immunomodulators, helping to balance the immune system.

Other specific carbohydrates, like Chitosan and chitin, have been used as functional dietary additives with potential anti-obesity activity **78**. A study even found that consuming carbohydrates along with a suitable amount of protein has a positive impact on the overall gut bacteria count, yielding numerous health benefits for humans **79**.

Therefore, utilizing carbohydrates as a nutraceutical source holds great promise for improving human health.

Lipids

Lipids are a broad category of organic compounds known for being soluble in organic solvents but insoluble in water **80**. In the past, dietary fats often got a bad reputation, with many people assuming they only caused weight gain and other health issues.

However, modern technology has advanced significantly, allowing us to combine the beneficial effects of fatty acids with triacylglycerol molecules to actually increase the nutritional value of lipids **80**. These engineered structured fats play a clear role in lowering the caloric value of the food they are added to, all while providing specific medical benefits. Research has even focused on the link between lipid nutrition and the position of fatty acids, suggesting that a process called acidolysis could be used to improve the nutrition profiles of triacylglycerols. Given these advantages, more research is needed to make lipid manufacturing cost-effective **80**.

Some of the most prominent nutraceuticals already on the market contain high levels of phytosterols, phytosteranols, and their fatty acid esters cite: **81**. Examples include products like Take Control®, Becel Proactiv, and Flora Proactiv by Unilever, CookSmart® by Procter & Gamble, and Danacol® by Danone.

Furthermore, recent studies highlight that flaxseed is an excellent source of beneficial lipids and should be utilized as a nutraceutical **82**. It is projected that consuming flaxseed may reduce the risk of cancer and cardiovascular disease, help relax artery smooth muscles, and lower cholesterol levels **82**.

Vitamins

Vitamins are essential for human health, and thanks to their strong anti-oxidant properties, they are widely used as nutraceuticals cite: **83**. These nutraceutical products can be particularly helpful for individuals on special diets or for smokers, as both groups are often prone to vitamin deficiencies. These deficiencies usually arise from insufficient food intake, poor absorption by the body, or inadequate utilization **83**.

Seaweeds, for instance, are a remarkably rich source of vitamins **83**. Their nutrient profiles contain:

- Adequate concentrations of the B complex vitamins
- Provitamins A and E.

Carotenoids.

Consuming these can have a profoundly beneficial effect, including a positive impact on lung and cervical malignancies and an aid in reducing deaths caused by cerebrovascular illnesses **84**.

Specifically:

- Red algae (*Porphyra* sp.) are a rich source of Vitamin B 12, a vitamin often lacking in vegan diets **85**.
- People who consume diets rich in Vitamin C generally have a lower risk of acquiring stomach cancer compared to those with regular diets **85**.
- A study suggests that combining the herbal compound Shilajit with B-complex vitamins is effective in preventing Alzheimer's disease **86**.
- For treating symptoms of dry eye, it is beneficial to use oral supplementation of nutraceuticals containing vitamins, minerals, omega-3 fatty acids, and antioxidants **87**.
- As a result, vitamins demonstrate immense potential, and their addition to the diet as a nutraceutical is a simple, effective way to promote better human health.

Mushrooms

For centuries, humans have recognized the value of mushrooms, utilizing them for both culinary and medicinal purposes **88**. Their applications have significantly expanded to include nutraceuticals, cosmeceuticals, and traditional medicines.

Out of the approximately 12,000 diverse mushroom species, around 2,000 are suitable for human consumption **88**. While only about 35 different species are commercially produced worldwide (with *Agaricus bisporus* being the most common) **41**, nearly 200 different wild species are actively used for their therapeutic benefits **89**.

Mushrooms are nutrient powerhouses **90, 91**. Their fruiting bodies typically contain: Between 50 and 65 percent carbohydrates. 20 to 30 grams of

unsaturated fatty acids per kilogram of dry mass.

Beyond their basic nutritional content, edible mushrooms contain a wide array of vital active ingredients, including:

Polysaccharides (β -glucans)

Peptides

Minerals

Dietary fiber

Terpenes, glycoproteins, and alcohols

Antioxidants

Mushrooms are considered excellent functional foods because key components like ergothioneine, selenium, Vitamin B 12 and vitamin D are highly bioavailable when consumed **92, 93**.

Medically, mushrooms are highly significant because their unique, biologically active compounds help boost the immune system to treat and prevent life-threatening disorders such as **92, 93**.

- Cancer
- Heart disease
- Cerebral stroke
- Hypertension

Their therapeutic qualities are extensive, encompassing antibacterial, anti-diabetic, anti-tumor, anti-fungal, anti-inflammatory, antithrombotic, antiviral, and hypolipidemic (fat-lowering) effects **92, 93**.

Application of Nutraceuticals

For over two decades, researchers have been actively working to establish the link between phytochemicals and potential health advantages cite:94. The evidence is strong: consistently consuming fruits and vegetables significantly lowers the incidence of numerous disorders, including cancers of the esophageal, stomach, lung, endometrial, oral cavity, pancreatic, pharyngeal, and colon **94**.

The primary phytochemicals that play a protective role in disease prevention include: allium compounds, beta carotene, dietary fibers, flavonoids, folic acid, D-limonene, dithiolthiones, indole-3-carbinol, inositol hexaphosphate, isoflavones, isothiocyanates, lutein, lycopene, phytosterols, selenium, and saponin.

Cardiovascular Disease (CVD)

Cardiovascular diseases (CVD) refer to problems affecting the heart and blood vessels **95**. It's well-documented that a low intake of fruits and vegetables is strongly associated with an increased risk of CVD **95**. Conversely, countless studies have highlighted the beneficial effects of a diet rich in these foods for CVD prevention.

For both preventing and treating CVD, nutraceuticals are often recommended alongside physical activity **96**. These supplements include:

- Minerals and Vitamins
- Dietary fibers and Antioxidants
- Omega-3 polyunsaturated fatty acids
- The mechanism of action is often complex:
- Polyphenols decrease the likelihood of vascular disease by modifying cellular communication and metabolism cite:96.
- Flavonoids are also crucial for preventing CVD. They help prevent platelet aggregation by inhibiting enzymes like angiotensin-converting enzyme and cyclooxygenase **97**.

Cancer

Cancer remains one of the main public health challenges globally. Nutraceuticals with strong antioxidant properties are particularly valuable in prevention **98**.

Carotenoids, such as lycopene and others, provide a significant protective role against cancer **98**.

Lycopene-rich fruits and vegetables have an anti-cancer effect primarily by reducing oxidative stress and DNA damage **99**. Excellent sources of lycopene include: tomatoes, pink grapefruit, guava, watermelon, and papaya.

Pectin, a soluble fiber found in apples, has been shown to be protective against prostate cancer by preventing cancer cells from sticking to healthy cells in the body **97**.

Natural phenolic substances with anti-cancer properties include: gallic acids, curcumin, ferulic acid, and caffeic acid **97**.

Curcumin, derived from *Curcuma longa* (turmeric), is well-known for its anti-inflammatory, anti-oxidative, and anti-carcinogenic effects.

Obesity :-Obesity is a global health crisis linked to numerous severe illnesses, including hypertension, angina pectoris, congestive heart failure, certain cancers, hyperlipidemia, osteoarthritis, respiratory issues, and renal vein thrombosis **97, 100**. A major contributing factor is the consumption of high-fat foods.

The potential of nutraceuticals to assist with obesity management is an active area of study. Nutraceuticals believed to have beneficial anti-obesity effects include **97, 100**

Capsaicin

- Conjugated linoleic acid (CLA)
- Momordica charantia (bitter melon)
- Citrus aurantium (bitter orange)
- Psyllium fiber
- Additionally, herbal stimulants commonly used to support weight loss include ephedrine, caffeine, chitosan, and green tea.

Conclusion

- Nutraceuticals represent an exciting, natural alternative to traditional treatments cite:**100**. They offer a different source of treatments that can not only help manage but also potentially prevent a wide spectrum of fatal illnesses. Their popularity is surging largely because they are generally perceived as more affordable and accessible than conventional prescription medications.
- However, the field is still maturing. Long-term, rigorous study is essential to fully define the precise role that nutraceuticals play in maintaining health and treating diseases. Specifically, more research is needed to understand exactly how these compounds affect disease activity and its underlying development (pathogenesis).
- We also need to delve into the chemistry: research must explore how bioactive compounds interact with other components in food and how these interactions influence their ability to act as therapeutic agents.
- Furthermore, there are practical challenges in product development:
- Sensory Qualities: Depending on the type and quantity of bioactive compounds added to food products, their sensory qualities—such as look, body, flavor, color, and texture—can be significantly impacted. This ultimately affects how consumers accept the product as a whole.
- Stability: The microbial instability of these functional elements once they are incorporated into a food matrix is another obstacle that needs to be overcome.
- To boost the trustworthiness and global market acceptability of these products, clinical studies must be conducted more swiftly, precisely, and uniformly.

REFERENCES

1. Singh J, Sinha S. Classification, regulatory acts and applications of nutraceuticals for health: A review. *Int J Pharm Biol Sci.*, 2012; 2(1):177-187.
2. Ashwlayan V, Nimesh S. Nutraceuticals in the management of diabetes mellitus. *Pharm Pharmacol Int J.*, 2018; 6:114-120. <https://doi.org/10.15406/ppij.2018.06.00166>
3. Aquila G, Marracino L, Martino V, Calabria D, Campo G, Caliceti C, Rizzo P. The use of nutraceuticals to counteract atherosclerosis: The role of the notch pathway. *Oxid Med Cell Longev.*, 2019; 5470470. <https://doi.org/10.1155/2019/5470470>
4. McClements DJ. Nutraceuticals: Superfoods or superfads. In *Future Foods*. Copernicus Chem., 2019; 167-201. https://doi.org/10.1007/978-3-030-12995-8_6
5. Sarris J, Byrne GJ, Stough C, Bousman C, Mischoulon D, Murphy J, et al., Nutraceuticals for major depressive disorder-more is not merrier: An 8-week double-blind, randomised, controlled trial. *J Affect Disord.*, 2019; 245:1007-1015. <https://doi.org/10.1016/j.jad.2018.11.092>
6. Hussain SA, Panjagari NR, Singh RR, Patil GR. Potential herbs and herbal nutraceuticals: Food applications and their interactions with food components. *Crit Rev Food Sci Nutr.*, 2015; 55(1):94-122. <https://doi.org/10.1080/10408398.2011.649148>
7. Dureja H, Kaushik D, Kumar V. Developments in nutraceuticals. *Indian J Pharmacol.*, 2003; 35(6):363-372.
8. <https://www.globenewswire.com/newsrelease/2019/01/29/1706747/0/en/Global-nutraceuticals-Market>
9. <http://publication.assochem.tv/data/product-file/88>.
10. Sharma A, Kumar P, Sharma P, Shrivastav BA. Comparative study of regulatory registration procedure of nutraceuticals in India, Canada and Australia. *Int J Pharm Qual Assur.*, 2013; 4(4):61-66.
11. Smarta RB. Paradigm shift from pharmaceuticals to nutraceuticals, *Nuffoods Spectrum*. 2017.
12. Maxwell J, Smith D, Brewster M, Eggleton S. Food as pharma as wellness products evolve, the distinction between food and medicine blurs. *R&C worlds express*. 2012.
13. Biotech for wellness: driving successful R & D and licensing in nutraceuticals through new business models and collaboration, research and markets, 2010.
14. Kumar P, Kumar N, Tushar O. Nutraceuticals- critical supplement for building a healthy India, *World J Pharm Pharma Sci.*, 2016; 5(3):579-594.
15. Olaiya CO, Soetan KO, Esan A. The role of nutraceuticals, functional foods and value added food products in the prevention

- and treatment of chronic diseases M. I, *African J Food Sci.*, 2016; 10(10):185-193. <https://doi.org/10.5897/AJFS2015.1402>
16. Sosnowska B, Penson P, Banach M. The role of nutraceuticals in the prevention of cardiovascular disease. *Cardiovasc Diagn Ther.*, 2017; 7(1):S21-S31. <https://doi.org/10.21037/cdt.2017.03.20>
 17. Roy A, Jauhari N, Bharadvaja N. Medicinal plants as a potential source of chemopreventive agents. *anticancer plants: natural products and biotechnological implements*; Springer, 2018;109- 139 https://doi.org/10.1007/978-981-10-8064-7_6
 18. Kapoor VK, Dureja J, Chadha R. Herbals in the control of ageing. *Drug Discov Today.* 2009; 14(19-20):992-998. <https://doi.org/10.1016/j.drudis.2009.06.014>
 19. Debnath B, Singh WS, Das M, Goswami S, Singh MK, Maiti D, Manna K. Role of plant alkaloids on human health: A review of biological activities. *Mater.Today Chem.*, 2018; 9:56-72. <https://doi.org/10.1016/j.mtchem.2018.05.001>
 20. Sottorff I, Künzel S, Wiese J, Lipfert M, Preuke N, Sonnichsen FD, Imhoff JF. Antitumor anthraquinones from an easter isl and sea anemone: Animal or bacterial origin. *Mar. Drugs*, 2019; 17(3):154. <https://doi.org/10.3390/md17030154>
 21. Kumar S. Alkaloidal drugs-A review. *Asian J Pharm Sci.*, 2014; 4(3): 2014.
 22. Isah T. Anticancer alkaloids from trees: Development into drugs. *Pharmacogn Rev.*, 2016; 10(20):90-99. <https://doi.org/10.4103/0973-7847.194047>
 23. Alasvand M, Assadollahi V, Ambra R, Hedayati E, Kooti W, Peluso I. Antiangiogenic effect of alkaloids. *Oxid Med Cell Longev.*, 2019; 2019:9475908. <https://doi.org/10.1155/2019/9475908>
 24. Aniszewski T. Alkaloids-secrets of life: alkaloid chemistry, biological significance, applications and ecological role; Elsevier, 2007.
 25. Gorgani L, Mohammadi M, Najafpour GD, Nikzad M. Piperine-the bioactive compound of black pepper: From isolation to medicinal formulations. *Compr Rev Food Sci Food Saf.*, 2017; 16(1):124-140. <https://doi.org/10.1111/1541-4337.12246>
 26. Srinivasan K. Black pepper and its pungent principle-piperine: A review of diverse physiological effects. *Crit Rev Food Sci Nutr.*, 2007; 47(8):735-748. <https://doi.org/10.1080/10408390601062054>
 27. Podolak I, Galanty A, Sobolewska D. Saponins as cytotoxic agents: A review. *Phytochem Rev.*, 2010; 9(3):425-474. <https://doi.org/10.1007/s11101-010-9183-z>
 28. Moreira R, Pereira DM, Valente P, Andrade PB. Pyrrolizidine alkaloids: Chemistry, pharmacology, toxicology and food safety. *Int J Mol Sci.*, 2018; 19(6): 1668. <https://doi.org/10.3390/ijms19061668>
 29. Ding X, Zhang W, Li S, Yang H. The role of cholesterol metabolism in cancer. *Am J Cancer Res.*, 2019; 9(2):219-227.
 30. Ying W, Seigny MB, Chen Y, Swanson RA. Poly(ADPribose) glycohydrolase mediates oxidative and excitotoxic neuronal death. *Proc Natl Acad Sci USA*, 2001; 98(21):12227-12232. <https://doi.org/10.1073/pnas.211202598>
 31. Bors W, Michel C. Chemistry of the antioxidant effect of polyphenols. *Ann N Y Acad Sci.*, 2002; 957(1):57-69. <https://doi.org/10.1111/j.1749-6632.2002.tb02905.x>
 32. Wei L, Chuncheng Y, Huafeng Z, Rugang Y. Preparation of aloe- herbs health beverage. *Food Sci China*, 2004; 25:207-209.
 33. Roy A, Bharadvaja N. Effect of various culture conditions on shoot multiplication and GC-MS analysis of *Plumbago zeylanica* accessions for plumbagin production. *Acta Physiol Plant.*, 2018; 40(11):190. <https://doi.org/10.1007/s11738-018-2766-9>
 34. Roy A, Bharadvaja N. Establishment of root suspension culture of *Plumbago zeylanica* and enhanced production of plumbagin. *Ind Crops Prod.*, 2019; 137:419-427. <https://doi.org/10.1016/j.indcrop.2019.05.007>
 35. Hoste H, Sotiraki S, Mejer H, Heckendorn F, Maurer V, Thamsborg S. Alternatives to synthetic chemical antiparasitic drugs in organic livestock farming in Europe. *Organic farming, prototype for sustainable agricultures*; Springer: Dordrecht, 2014; 149-169. https://doi.org/10.1007/978-94-007-7927-3_8
 36. Dhinra D, Michael M, Rajput H, Patil RT. Dietary fibre in foods: A review. *J Food Sci Technol.*, 2012; 49(3):255-266. <https://doi.org/10.1007/s13197-011-0365-5>
 37. Liao H, Banbury LK, Leach DN. Antioxidant activity of 45 Chinese herbs and the relationship with their TCM characteristics. *Evid Based Complement Alternat Med.*, 2008; 5(4):429-434. <https://doi.org/10.1093/ecam/nem054>
 38. McMullen MK, Whitehouse JM, Towell A. Bitters: Time for a new paradigm. *Evid Based Complement Altern Med.*, 2015; 670504. <https://doi.org/10.1155/2015/670504>
 39. Manohar SR, Paul R, Priya S. A Brief review of synonyms and properties of Guduci (*Tinospora cordifolia* (Thunb.) Miers) from selected nighantus (ayurvedic drug lexicons). *Phcog J.*, 2018; 10(6s) <https://doi.org/10.5530/pj.2018.6s.2>
 40. Sugawara T, Yamashita K, Asai A, Nagao A, Shiraishi T, Imai I, Hirata T. Esterification of xanthophylls by human intestinal Caco-2 cells. *Arch Biochem Biophys.*, 2009; 483(2):205-212. <https://doi.org/10.1016/j.abb.2008.10.007>
 41. Okada T, Nakai M, Maeda H, Hosokawa M, Sashima T, Miyashita, K. Suppressive effect of neoxanthin on the differentiation of 3T3-L1 adipose cells. *J Oleo Sci.*, 2008; 57(6):345-351. <https://doi.org/10.5650/jos.57.345>
 42. Umeno D, Tobias AV, Arnold FH. Diversifying carotenoid biosynthetic pathways by directed evolution. *Microbiol Mol Biol Rev.*,

- 2005; 69(1):51-78. <https://doi.org/10.1128/MMBR.69.1.51-78.2005>
43. Tang G, Russell RM. Carotenoids as provitamin A. Carotenoids; Birkhäuser Basel, 2009; 149-172. https://doi.org/10.1007/978-3-7643-7501-0_8
 44. Carrillo-Lopez A, Yahia EM, Ramirez-Padilla GK. Bioconversion of carotenoids in five fruits and vegetables to vitamin A measured by retinol accumulation in rat livers. Am J Agric Biol Sci., 2010; 5(2):215-221. <https://doi.org/10.3844/ajabssp.2010.215.221>
 45. Yeum KJ, Aldini G, Russell RM, Krinsky NI. Antioxidant/pro-oxidant actions of carotenoids. Carotenoids; Birkhäuser Basel, 2009; 235-268. https://doi.org/10.1007/978-3-7643-7501-0_12
 46. Linnewiel-Hermoni K, Khanin M, Danilenko M, Zango G, Amosi Y, Levy J, Sharoni Y. The anti-cancer effects of carotenoids and other phytonutrients resides in their combined activity. Arch Biochem Biophys., 2015; 572:28-35. <https://doi.org/10.1016/j.abb.2015.02.018>
 47. Chao PDL, Hsiu SL, Hou YC. Flavonoids in herbs: biological fates and potential interactions with xenobiotics. Yao Wu Shi Pin Fen Xi, 2002; 10(4):23-28.
 48. Panche AN, Diwan AD, Chandra SR. Flavonoids: An overview. J Nutr Sci., 2016; 5e47. <https://doi.org/10.1017/jns.2016.41>
 49. Prasad R, Prasad SB. A review on the chemistry and biological properties of Rutin, a promising nutraceutical agent. Asian J Pharm Sci., 2019; 5(S1): 1-20. <https://doi.org/10.31024/ajpp.2019.5.s1.1>
 50. Brenes A, Roura E. Essential oils in poultry nutrition: Main effects and modes of action. Anim Feed Sci Technol., 2010 158(1-2):1-14. <https://doi.org/10.1016/j.anifeedsci.2010.03.007>
 51. Ozel MZ, Gogus F, Lewis AC. Subcritical water extraction of essential oils from *Thymbra spicata*. Food Chem., 2003; 82(3):381-386. [https://doi.org/10.1016/S0308-8146\(02\)00558-7](https://doi.org/10.1016/S0308-8146(02)00558-7)
 52. Bansod S, Rai M. Antifungal activity of essential oils from Indian medicinal plants against human pathogenic *Aspergillus fumigatus* and *A. niger*. World J Med Sci., 2008; 3(2):81-88.
 53. Christaki E, Bonos E, Giannenas I, Florou-Paneri P. Aromatic plants as a source of bioactive compounds. Agriculture, 2012; 2(3):228-243. <https://doi.org/10.3390/agriculture2030228>
 54. Srinivas G, Babykutty S, Sathiadevan PP, Srinivas P. Molecular mechanism of emodin action: Transition from laxative ingredient to an antitumor agent. Med Res Rev., 2007; 27(5):591-608. <https://doi.org/10.1002/med.20095>
 55. Lee HZ, Hsu SL, Liu MC, Wu CH. Effects and mechanisms of aloe-emodin on cell death in human lung squamous cell carcinoma. Eur J Pharmacol., 2001; 431(3):287-295. [https://doi.org/10.1016/S0014-2999\(01\)01467-4](https://doi.org/10.1016/S0014-2999(01)01467-4)
 56. Yeh FT, Wu CH, Lee HZ. Signaling pathway for aloe emodin-induced apoptosis in human H460 lung nonsmall carcinoma cell. Int J Cancer, 2003; 106(1):26-33. <https://doi.org/10.1002/ijc.11185>
 57. Huang Q, Lu G, Shen HM, Chung MC, Ong CN. Anticancer properties of anthraquinones from rhubarb. Med Res Rev., 2007; 27(5):609-630. <https://doi.org/10.1002/med.20094>
 58. Elshohly MA, Gul W, Avula B, Khan IA. Determination of the anthraquinones aloe-emodin and aloin-A by liquid chromatography with mass spectrometric and diode array detection. J AOAC Int., 2007; 90(1):28-42. <https://doi.org/10.1093/jaoac.90.1.28>
 59. Sottorff I, Künzel S, Wiese J, Lipfert M, Preußke N, Sönnichsen FD, Imhoff JF. Antitumor anthraquinones from an Easter Island sea anemone: Animal or bacterial origin. Mar Drugs, 2019 17(3):154. <https://doi.org/10.3390/md17030154>
 60. Eckburg PB, Bik EM, Bernstein CN, Purdom E, Dethlefsen L, et al., Diversity of the human intestinal microbial flora. Science, 2005; 308(5728):1635-1638. <https://doi.org/10.1126/science.1110591>
 61. Guarner F, Bourdet-Sicard R, Brandtzaeg P, Gill HS, McGuirk P, Van Eden W, Versalovic J, Weinstock JV, Rook GA. Mechanisms of disease: the hygiene hypothesis revisited. Nat Clin Pract Gastroenterol Hepatol., 2006; 3(5):275-284. <https://doi.org/10.1038/ncpgasthep0471>
 62. Kechagia M, Basoulis D, Konstantopoulou S, Dimitriadi D, Gyftopoulou K, Skarmoutsou N, Fakiri EM. Health benefits of probiotics: A review. ISRN Nutr., 2013; <https://doi.org/10.5402/2013/481651>
 63. Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health. Nutrients, 2017; 9(9):1021. <https://doi.org/10.3390/nu9091021>
 64. Tokunaga T. Novel physiological function of fructooligosaccharides. Biofactors, 2004; 21(1-4):89-94. <https://doi.org/10.1002/biof.552210117>
 65. Forchielli ML, Walker WA. The role of gut-associated lymphoid tissues and mucosal defence. Br J Nutr., 2005; 93(S1):S41-S48. <https://doi.org/10.1079/BJN20041356>
 66. Priebe MG, Vonk RJ, Sun X, He T, Harmsen HJ, Welling GW. The physiology of colonic metabolism. Possibilities for interventions with pre- and probiotics. Eur J Nutr., 2002 41(1 Suppl. 1): I2-I10. <https://doi.org/10.1007/s00394-002-1101-8>

67. Blaut M. Relationship of prebiotics and food to intestinal microflora. *Eur J Nutr.*, 2002; 41(1 Suppl. 1):I11-I16. <https://doi.org/10.1007/s00394-002-1102-7>
68. Slavin J. Why whole grains are protective: Biological mechanisms. *Proc Nut. Soc.*, 2003; 62(1):129-134. <https://doi.org/10.1079/PNS2002221>
69. Lonnie M, Hooker E, Brunstrom JM, Corfe BM, Green MA, Watson AW, et al., Protein for life: Review of optimal protein intake, sustainable dietary sources and the effect on appetite in ageing adults. *Nutrients*, 2018; 10(3):360. <https://doi.org/10.3390/nu10030360>
70. Melini F, Melini V, Luziatelli F, Ruzzi M. Current and forward- looking approaches to technological and nutritional improvements of gluten-free bread with legume flours: A Critical Review. *Compr Rev Food Sci Food Saf.*, 2017; 16:1101-1122. <https://doi.org/10.1111/1541-4337.12279>
71. Das L, Bhaumik E, Raychaudhuri U, Chakraborty R. Role of nutraceuticals in human health. *J Food Sci Technol.*, 2012; 49(2):173-183. <https://doi.org/10.1007/s13197-011-0269-4>
72. Drewnowski A, Dwyer J, King JC, Weaver CM. A proposed nutrient density score that includes food groups and nutrients to better align with dietary guidance. *Nutr Rev.*, 2019; 77(6):404-416. <https://doi.org/10.1093/nutrit/nuz002>
73. Réhault-Godbert S, Guyot N, Nys Y. The golden egg: nutritional value, bioactivities, and emerging benefits for human health. *Nutrients*, 2019; 11(3):684. <https://doi.org/10.3390/nu11030684>
74. Tapal A, Vegarud GE, Sreedhara A, Kaul TP. Nutraceutical protein isolate from pigeon pea (*Cajanus cajan*) milling waste by product: Functional aspects and digestibility. *Food Funct.*, 2019; 10(5):2710-2719. <https://doi.org/10.1039/C8FO01933A>
75. Galanakis CM. *Nutraceutical and Functional Food Components, Effects of Innovative Processing Techniques*, 1st ed.; Elsevier Inc., B.V., 2017. <https://doi.org/10.1016/B978-0-12-805257-0.00001-6>
76. Slavin J, Carlson J. Carbohydrates. *Adv Nutr.*, 2014; 5(6):760-761. <https://doi.org/10.3945/an.114.006163>
77. Lattimer JM, Haub MD. Effects of dietary fiber and its components on metabolic health. *Nutrients*, 2010; 2(12):1266-1289. <https://doi.org/10.3390/nu2121266>
78. Hayes M, Carney B, Slater J, Brück W. Mining marine shellfish wastes for bioactive molecules: Chitin and chitosan-Part A: extraction methods. *Biotechnol J.*, 2008; 3(7):871-877. <https://doi.org/10.1002/biot.200700197>
79. Hayes M, Tiwari BK. Bioactive carbohydrates and peptides in foods: An overview of sources, downstream processing steps and associated bioactivities. *Int J Mol.Sci.*, 2015; 16(9):22485-22508. <https://doi.org/10.3390/ijms160922485>
80. Tomova A, Bukovsky I, Rembert E, Yonas W, Alwarith J, Barnard ND, Kahleova H. The effects of vegetarian and vegan diets on gut microbiota. *Front Nutr.*, 2019; 6:47. <https://doi.org/10.3389/fnut.2019.00047>
81. Misurcova L, Ambrozova J, Samek D. Seaweed lipids as nutraceuticals. *Advances in food and nutrition research*; Academic Press, 2011; 64:339-355. <https://doi.org/10.1016/B978-0-12-387669-0.00027-2>
82. Kumar S, Sharma B, Bhadwal P, Sharma P, Agnihotri N. Lipids as nutraceuticals: A shift in paradigm. *Therapeutic Foods*; Academic Press, 2018; 51-98. <https://doi.org/10.1016/B978-0-12-811517-6.00003-9>
83. Skrovankova S. Seaweed vitamins as nutraceuticals. *Advances in food and nutrition research*; Academic Press, 2011; 64:357-369. <https://doi.org/10.1016/B978-0-12-387669-0.00028-4>
84. Hoang BV, Lee J, Choi JJ, Kim YW, Ryu KW, Kim J. Effect of dietary vitamin C on gastric cancer risk in the Korean population. *World J Gastroenterol.*, 2016; 22(27):6257-6267. <https://doi.org/10.3748/wjg.v22.i27.6257>
85. Carrasco-Gallardo C, Fariás GA, Fuentes P, Crespo F, Maccioni RB. Can nutraceuticals prevent Alzheimer's disease? Potential therapeutic role of a formulation containing shilajit and complex B vitamins. *Arch Med Res.*, 2012; 43(8):699-704. <https://doi.org/10.1016/j.arcmed.2012.10.010>
86. Gatell-Tortajada J. Oral supplementation with a nutraceutical formulation containing omega-3 fatty acids, vitamins, minerals, and antioxidants in a large series of patients with dry eye symptoms: results of a prospective study. *Clin Interv Aging*, 2016; 11:571-578. <https://doi.org/10.2147/CIA.S98102>
87. Aghajanzpour M, Nazer MR, Obeidavi Z, Akbari M, Ezati P, Kor NM. Functional foods and their role in cancer prevention and health promotion: A comprehensive review. *Am J Cancer Res.*, 2017; 7(4):740-769. 88. Rathore H, Prasad S, Sharma S. Mushroom nutraceuticals for improved nutrition and better human health: A review. *Pharma Nutrition*, 2017; 5(2):35-46. <https://doi.org/10.1016/j.phanu.2017.02.001>
89. Aida FMNA, Shuhaimi M, Yazid M, Maaruf AG. Mushroom as a potential source of prebiotics: A review. *Trends Food Sci Technol.*, 2009; 20(11-12):567-575. <https://doi.org/10.1016/j.tifs.2009.07.007>
90. Arora S, Tandon C, Tandon S. Evaluation of the cytotoxic effects of CAM therapies: An in vitro study in normal kidney cell lines. *Sci. World J.*, 2014 <https://doi.org/10.1155/2014/452892>
91. Rahi DK, Malik D. Diversity of mushrooms and their metabolites of nutraceutical and therapeutic significance. *J Mycol.*, 2016. <https://doi.org/10.1155/2016/7654123>
92. Chaturvedi VK, Agarwal S, Gupta KK, Ramteke PW, Singh MP. Medicinal mushroom: Boon for therapeutic applications. *Biotech.*, 2018; 8(8):334. <https://doi.org/10.1007/s13205-018-1358-0>

93. Badalyan SM, Barkhudaryan A, Rapior S. Recent progress in research on the pharmacological potential of mushrooms and prospects for their clinical application. Medicinal Mushrooms; Springer: Singapore, 2019; 1-70. https://doi.org/10.1007/978-981-13-6382-5_1
94. Bradbury KE, Appleby PN, Key TJ. Fruit, vegetable, and fiber intake in relation to cancer risk: Findings from the European Prospective Investigation into Cancer and Nutrition (EPIC). Am J Clin Nutr, 2014; 100(suppl): 394S-398S. <https://doi.org/10.3945/ajcn.113.071357>
95. Rafieian-Kopaei M. Medicinal plants and the human needs. J Herbmed Pharmacol., 2012; 1(1):1-2.
96. Asgary S, Sahebkar A, Afshani MR, Keshvari M, Haghjooyjavanmard S, Rafieian-Kopaei M. Clinical evaluation of blood pressure lowering, endothelial function improving, hypolipidemic and anti-inflammatory effects of pomegranate juice in hypertensive subjects. Phytother Res., 2014; 28(2):193-199. <https://doi.org/10.1002/ptr.4977>
97. Nasri H, Baradaran A, Shirzad H, Rafieian-Kopaei M. New concepts in nutraceuticals as alternative for pharmaceuticals. Int J Prev Med., 2014; 5(12):1487-1499.
98. Willis MS, Wians FH. The role of nutrition in preventing prostate cancer: A review of the proposed mechanism of action of various dietary substances. Clin Chim Acta., 2003; 330(1-2):57- 83. [https://doi.org/10.1016/S0009-8981\(03\)00048-2](https://doi.org/10.1016/S0009-8981(03)00048-2)
99. Shirzad M, Kordyazdi R, Shahinfard N, Nikokar M. Does Royal jelly affect tumor cells. J Herbmed Pharmacol., 2013; 2(2):45-48.
100. De Freitas Junior LM, De Almeida EB. Medicinal plants for the treatment of obesity: Ethnopharmacological approach and chemical and biological studies. Am J Transl Res., 2017; 9(5):2050-2064