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Bioactive phytochemicals on humanoid endurance & advancement of herbal medicine

Abstract

The Indian traditional system of conventional medication includes an enormous lexis of herbal preparations and medicinal plants. They are optional nutrients that are mostly produced by plants as a form of defence. These items may include isolated nutrients, nutritional supplements, particular diets, herbal products, processed foods, and drinks. They may also include genetically modified designer foods. Phytochemicals are naturally occurring compounds that can be found in a variety of foods, including legumes, fruits, vegetables, whole grains, and herbs. These substances include polyphenols, flavonoids, isoflavonoids, anthocyanidins, phytoestrogens, terpenoids, carotenoids, limonoids, phytosterols, glucosinolates, and fibers. Phytochemicals are known to have a significant impact on human health, with potential medical benefits that can help prevent and treat a range of illnesses and physiological abnormalities.

Phytochemicals have been shown to have various pharmacological effects on human health, including acting as powerful antioxidants, antibacterial and antifungal agents, anti-inflammatory and anti-allergic compounds, antispasmodic agents, chemo preventive agents, hepatoprotective agents, neuroprotective agents, as well as hypolipidemic and hypotensive agents. Therefore, these compounds are of great interest in the fields of medicine, nutrition, and health science. They also induce apoptosis, act as a diuretic, stimulate the central nervous system, modulate the immune response, and act as a carminative, analgesic. It is necessary for herbal products to undergo quality control, thorough testing to determine their efficacy and safety, and reliable clinical trials. To give improved health care services to the public, the meticulous and scientific integration of India's traditional system of herbal medicine into evidence-based clinical illness management is crucial. Thus, this chapter focuses on the integration and advancement of herbal-based medicines through the scientific validation of some clinically important bioactive phytochemicals.

Keywords: phytochemicals, nutraceutical, traditional medicine, herbal drug, antioxidants, diseases

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Introduction

India possesses the richest biodiversity and accounts for 8% of global biodiversity, with around 49,000 plant species of which 5,150 species are endemic.[1] The Himalayan range, Western Ghats, North-Eastern Indian hills (Khasi and Mizo hills), and Vindhya and Satpura mountains of Northern India host a rich diversity of higher plant species. This abundance of flora is noteworthy and indicative of the region's unique ecological characteristics. It is important to recognize the significance of this diversity and to study and conserve these ecosystems to ensure their preservation for future generations. Herbal medicine has special importance in the society, culture, and traditional medicine of India.[2] Plant-based medicines are at the root of the modern healthcare system and are acknowledged for their economic importance.[3] In biological research and drug development, traditional medical knowledge and botanicals are crucial components. In addition to being utilized directly as therapeutic agents, herbal medicines and their phytoconstituents are also used as lead molecules in the development of novel drugs. Current research and understanding suggest that the use of phytochemicals or crude drugs can confer real benefits on health when used long-term.[4]

The prevalence of synthetic drug adverse effects and the rising population both contribute to the rise in popularity of alternative therapies. According to the World Health Organization, achieving the goal of "Health for All" is impossible without the use of herbal medicines. This highlights the increasing demand for various herbal products such as medicinal plants, health products, pharmaceuticals, food supplements, and cosmetics worldwide, indicating the widespread belief and acceptance of herbal remedies by the general public. This in turn has created great scope for India to utilize its traditional knowledge of herbal medicine and repository of medicinal plants in the service of the world population and for the economic growth of India.[5,6]

The recent notion of 'customized' or 'personalized' medicine and diet is comprehensive to the field of nutrition and can be used to delay the onset of disease and to sustain optimum human health.[7]

The word nutraceuticals, coined by Dr. Stephen de Felice, derived from the words "nutrition" and "pharmaceutical", is a food or food product that provides health and medical benefits, including the prevention and treatment of disease.[8] A potential nutraceutical is one that holds a promise of a particular health or medical benefit; such a potential nutraceutical only becomes an established one after there is sufficient clinical data to demonstrate such a benefit.[9] A nutraceutical demonstrates physiological benefits or offers protection from chronic disease as a result. The assortment of goods in question encompasses a diverse array of items, including but not limited to, singular nutrients, dietary supplements, specialized regimens, genetically modified sustenance, herbal products, as well as processed comestibles such as cereals, soups, and beverages. The phytochemicals, which are their bioactive components, support or promote health and are found where the food and pharmaceutical sectors converge. Such substances may range from isolated nutrients, dietary supplements, and specific diets to genetically engineered designer foods, herbal products, processed foods, and beverages.[7]

Nutraceuticals are chemically classified into three distinct groups, namely isoprenoid derivatives (which include terpenoids, carotenoids, saponins, tocotrienols, tocopherols, and terpenes), phenolic compounds (such as coumarins, tannins, lignins, anthocyanins, isoflavones, flavanones, and flavonoids), and carbohydrate derivatives (including ascorbic acid and oligosaccharides). They are essential for maintaining a healthy immune system, thus inadequate or excessive intakes might have a detrimental effect on health. In the mainstream of medical education and health, regulating authorities all over the world have recognized nutraceuticals as potential nutraceutical therapies. The healthcare sector showed how a growing population was moving away from prescription drugs for cancer treatment and toward over-the-counter nutraceuticals for cancer management and prevention. The growing awareness of nutraceutical benefits and the shift of healthcare economics in favour of nutraceuticals brought nutraceutical medicine into the spotlight of government health policy on the systematic use of nutraceuticals in the prevention and/or control of various chronic diseases.[8]

This chapter delves into the impact of the abundance of information available on the development and utilization of phytochemicals as nutraceuticals. The focus will be on providing a comprehensive overview of the supporting evidence that underscores the protective and health-promoting effects of phytochemicals. These substances may be incorporated into food or supplements as nutraceuticals, or used in the production of pharmaceuticals. It would also focus on the integration and advancement of herbal-based medicines through the scientific validation of some clinically important bioactive phytochemicals.

Herbal medication and modernism: Can Indian customary medicinal methods demonstrate the route advancing?

Many rural and ethnic communities preserve ancient plant-based medicine through active participation. A renaissance of herbal medicine is overdue. Achieving modern safety and efficacy requirements while integrating herbal medicine into the actual mainstream of modern healthcare is a difficult undertaking.

The consumption of dietary phytochemicals, which are present in whole grains, beans, fruits, vegetables, and herbs, can potentially prevent the onset of chronic degenerative illnesses such as cancer, cardiovascular disease, and neurological disorders. This dietary practice may provide substantial health benefits to individuals. Table 1. Among these, fruits and vegetables make up a considerable portion of the phytochemical sources. Phytochemicals present in food possess a significant value in the treatment of various diseases, either as standalone therapies or in combination with other treatments. These compounds exhibit a positive impact on human health by providing protection against a diverse range of ailments, including cancer, coronary heart disease, diabetes, hypertension, inflammation, microbial, viral, and parasitic infections, psychotic disorders, spasmodic conditions, ulcers, and more. The nutraceutical properties of phytochemicals render them indispensable for maintaining optimal health. The National Cancer Institute has recently made efforts to raise public knowledge about alternative cancer prevention methods, focusing on lifestyle, preventative, and controllable health measures, eating habits, and dangerous toxins with a number of successful attempts using antioxidants, garlic, and vitamins. The major nutraceuticals were reviewed and reported as vitamins and minerals, phytochemicals. The vitamins A, B_6, B_{12}, D, E, and folate have been reported as anti -cancer, immune-protective, and reducing cancer risk in the population at risk of cancer and individuals who used self-medication.[10]

Epidemiological and animal research has shown that regular consumption of fruits, vegetables, and whole grains can effectively reduce the risk of chronic diseases caused by oxidative damage (Cieslik et al., 2006). It is widely recommended that individuals incorporate these foods into their diets as a preventative measure against such health issues. The natural antioxidants carotenoids, tocopherols, ascorbates, lipoic acids, and polyphenols are potent and can scavenge free radicals. There are a variety of natural antioxidants that work synergistically to eliminate free radicals within the body. These antioxidants include superoxide dismutase (SOD), catalase, glutathione peroxidase, glutathione reductase, minerals such as selenium, manganese, copper, and zinc, in addition to vitamins A, C, and E, carotenoids, limonoids, and polyphenols.

Table 1 Phytochemical power: A closer look at their health benefits

Phytochemicals	Source Plant	Health Benefits
α−linolenic acid (ALA)	Flax seeds	Preventing cancer and lowering the risk of coronary heart disease.
Allicin	Garlic, onion	These are some of the beneficial properties associated with certain substances: they may be antibacterial, anticancer, antifungal, anti-inflammatory, chemo-preventive, hepato-protective, hypolipidemic, hypotensive, or neuroprotective.
Anthocyanins	Blackberry, cherry, orange, purple corn, raspberry, red grapes	This item has anti-allergic, anti-inflammatory, antioxidant, and pigment properties.
Apigenin	Apple, artichoke, basil, celery, cherry, grapes, nuts, parsley	These are the potential benefits of the substance: anti-inflammatory, antioxidant, antispasmodic, chemo-preventive, ability to induce apoptosis, and inhibition of breast and ovarian cancers.
Caffeic acid	Artichoke, pear, basil, oregano	This product has properties that can help with inflammation, fatigue, and stress.
Carotene	Carrots, Leafy greens, red, orange, and yellow vegetables, pumpkin	Anti-carcinogenic compounds stimulate the release of immunogenic cytokines, IL-1 and TNF-alpha, provide protection to the cornea against UV light, and enhance DNA repair enzymes.
Catechins	Tea	Antioxidant, CNS stimulant, and Diuretic
Curcumin	Turmeric	This substance has properties that help lower blood pressure, reduce inflammation, provide antioxidants, and may help prevent cancer.
Diosgenin	Fenugreek seeds	Hypolipidemic

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Table 1 Continued...

Phytochemicals	Source Plant	Health Benefits
Ellagic acid	Cranberry, grapes, pecans, pomegranates, raspberry, strawberry, walnuts	Anticancer, and antioxidant
Ferulic acid	Oats, rice, orange, pineapple, peanut	To safeguard against cancer, bone degeneration, and menopausal symptoms like hot flashes, take necessary precautions.
Gallic acid	Tea, mango, strawberries, soy	The following are some noteworthy activities of the substance: cytotoxic and antioxidative, anti-leukemic, antioxidant, anticancer, anti-neoplastic, anti-inflammatory, and anti-diabetic.
Genistein	Alpha-alfa sprouts, red clover, chickpeas, peanuts	It has various health benefits such as functioning as a phytoestrogen, antioxidant, anti-cancer agent, and promoting heart health. Additionally, it can aid those with metabolic syndrome.
Lutein	Kale, spinach, red pepper, mango, papaya, kiwi, peaches, squash, honeydew melon, plum, avocado	This product absorbs harmful blue light and provides protection against colon cancer.
Lycopene	Apricots, papaya, pink guava, tomato, watermelon	Reduced risk of developing atherosclerosis and prostate cancer.
Momorbicin	Karela (Bitter gourd)	Anti-diabetic medication or treatment for diabetes.
Myristicin	Nutmeg	Hypolipidemic (Note: This word refers to a substance that reduces lipid levels in the blood.)
Piperine	Pepper	This substance possesses properties such as being aromatic, analgesic, hepato-protective, and stomachic.
Quercetin	Red onions, buckwheat, red grapes, green tea, apple skin	This substance is a potent antioxidant that can reduce LDL oxidation, as well as act as a vasodilator and blood thinner.
Resveratrol	Blueberry, peanuts, red grapes, and red wine	This substance is an antioxidant that can help prevent the onset of aging, cancer, diabetes, and heart disease.
Rutin	Asparagus, buckwheat, and citrus fruits	This helps to strengthen the walls of your capillaries.
Silymarin	Milk thistle *(Silybum marianum*)	This helps to guard against UVB-induced cancer and provides protection for the liver.
Stigmasterol	Soybean	This pertains to the prevention of cancer, lowering of lipid levels, and preventing osteoporosis.
Sulforaphane, Glucosinolates	Broccoli sprouts, cabbage, cauliflower, collards, cruciferous vegetables, kale, radish, turnip	Consuming antioxidants can help prevent damage to DNA, which in turn lowers the risk of developing breast and prostate cancers.
Ursolic acid	Apple, basil, cranberry, lavender, Oregano, rosemary	The substance has anti-inflammatory, antimicrobial, and antitumor properties.
Withaferin, Withanolides	*Withania somnifera*	This substance has properties that can combat cancer and also modify the immune system.
Zingiberene	Ginger	The substance has antibacterial, antifungal, carminative properties, and also useful in treatment of dizziness

The food and pharmaceutical industries can benefit from synthetic antioxidants such butylated hydroxy anisole (BHA) and butylated hydroxy toluene (BHT) (Kondratyuk and Pezzuto, 2004). In-vitro antioxidants and in-vivo antioxidants are the two primary divisions of the natural antioxidant system.

The success of nutraceuticals is largely reliant on self-prescription and personal experiences. However, it is far to realize the phenomenal benefits of nutraceuticals unless controlled clinical trials support the evidence and facts of nutraceutical preventive therapeutic efficacy.[8]

Phytochemicals in plants: A key to optimal health

Polyphenols

Polyphenols, which are natural substances, can be found primarily in fruits, vegetables, cereals, and various drinks. The consumption of polyphenols is also increased by legumes and chocolate. These compounds are produced by plants as secondary metabolites and are typically used in pathogen or UV radiation defence. Basic studies and epidemiological studies have demonstrated an inverse relationship between the consumption of a diet high in polyphenols and the risk of degenerative illnesses. A diet high in antioxidants is linked to a lower prevalence of degenerative diseases, according to epidemiological studies. There are a variety of foods that are rich in dietary polyphenols, including cereals, legumes (like barley, corn, nuts, oats, rice, sorghum, wheat, beans, and pulses), oilseeds (such as rapeseed, canola, flaxseed, and olive seeds), fruits, vegetables, and beverages (like fruit juices, tea, coffee, cocoa, beer, and wine). Some fruits, such as apples, grapes, pears, cherries, and different types of berries, contain 200-300mg of polyphenols for every 100g of fresh weight. Like this, 100 mg of polyphenols are present in a cup of coffee, tea, or a glass of red wine. Their total dietary intake may be about 1g per day, which is about 10 times higher than that of vitamin C and 100 times higher than those of vitamin E and carotenoids.[11]

Secondary metabolites known as plant polyphenols are widely found in higher plants. Their special qualities include intermolecular complexation, water solubility, and antioxidant capacities. They are

categorized as tannins, galloyl and hexahydroxydiphenoyl esters and derivatives, or condensed proanthocyanidins. Nutritionists have traditionally seen polyphenols as anti-nutrients since some polyphenols, like tannins, have detrimental effects such as lowering the activities of digestive enzymes, energy, protein and amino acid availability, mineral uptake, and having other adverse repercussions. The discovery of numerous polyphenols' antioxidant properties has united opinion on the health advantages that many of these substances offer. The most important dietary phenolics are the hydroxybenzoic and hydroxycinnamic acids, polyphenols (hydrolyzable and condensed tannins), and flavonoids, the latter of which is the subject of the greatest investigation. Plants are shielded from oxidative damage by phenols. They have also been studied extensively as antioxidant protectants for human beings and play beneficial role in reducing the risk of coronary heart disease, diabetes, hypertension, and some types of cancer.[11]

The major components of tea polyphenols are flavonols (catechin, epicatechin, catechingallate, and epigallocatechingallate), flavanols (quercetin, kaempferol, and their glycosides), flavones (vitexin, isovintexin), and phenolic acids (gallic acid, chlorogenic acid). They can make up up to 30% of the dry weight of the green leaves and 9–10% of the dry weight of the black tea leaves, respectively. Ferulic acid is related to dietary fiber that is connected to the cell wall's hemicellulose via ester bonds. Apples, pears, and grapes frequently contain coumaric acids and caffeoyl esters, which are forms of caffeine. In addition, apples, pears, and grapes are high in gallic acid and chlorogenic acid, respectively. Among fruits, apples have the highest concentrations of quercetin. Products made from grains are particularly essential in the diet of humans because they have a higher concentration of phenolic acids in the outer layers of the kernel that make up the bran. The majority of phenolic acid derivatives are tannins that can be hydrolyzed and are typically esterified with glucose. Citrus fruits are a significant source of flavonoids, and orange juice contains large amounts of hesperidin (120–250 mg/liter).

Quercetin occurs in its glycosylated form as rutin in fruits, vegetables, and particularly onions are its rich source.[12] The pigments anthocyanins range in quantity in fresh berries from 0.15 to 4.5 mg/g and are found in fruits like cherries, plums, strawberries, raspberries, blackberries, and red currants (Table 1). Some flavonoids are only found in a few foods, but soy, which has genistein and daidzein concentrations of about 1 mg/g, is the largest source of isoflavonoids. These compounds have drawn a lot of interest because of their potential to fight cancer and osteoporosis. Prostate, breast, and uterine cancer are uncommon in people who follow traditional diets heavy in soy and tea.

Although there are a range of potentially anti-mutagenic fruits, vegetables, and cereals their intake is generally below the level essential to protect from various mutagens.[13] Since ancient times, Silybum marianum extracts have been utilized to treat liver diseases in folk medicine. The major flavonoid in this plant's silymarin combination, silibinin, has demonstrated beneficial effects on the liver. In addition to being hepatoprotective, silibinin has been amply demonstrated in human lung, bladder, and prostate cancer models to induce apoptosis, decrease and/or inhibit cell proliferation, and promote tumor angiogenesis. Kolaviron from seeds of the *Garcinia kolu* and hispidulin from *Buccuris frimeru* have also been reported as hepatoprotective.[11]

Flavonoids

The most prevalent class of plant polyphenols are flavonoids. The minor flavonoids (flavanones and dihydroflavonols), flavones, and flavonols constitute a subclass of plant phenols known as flavonoids. The most common flavonoids in foods are flavonols. The two primary members of this category are quercetin and kaempferol. They are typically present at 15–30 mg/kg of fresh weight, which is a relatively low concentration. Flavonols are abundant in onions, curly kale, leeks, broccoli, and blueberries. Tomatoes and several other fragrant plants, like mint (Mentha piperita), contain flavanones, but only citrus fruits have them in significant quantities. The primary flavanones include eriodictyol in lemons, hesperetin in oranges, and naringenin in grapefruit. A vast amount of recent literature proposes that the stilbenes provide beneficial health effects.[14] According to recent research, stilbenes exhibit direct antioxidant action much like other polyphenols do. However, because to their relative dynamic health benefits, stilbenes outperform other polyphenols. Resveratrol (3, 4', 5-trihydroxystilbene) is one of the most well-studied naturally occurring polyphenols. Red wine, which is created from these grapes, contains the most resveratrol of any food. The anti-carcinogenic and anti-inflammatory properties of resveratrol are well recognized. Recently, evidence suggests that stilbenes may act as a signalling molecule within tissues and cells to modulate the expression of genes and proteins.[15]

Most plant tissues contain flavonoids, which are frequently found in vacuoles. Because they have a higher concentration of phenolic acids in the outer layers of the kernel that make up the bran, products manufactured from grains are especially important in human diets. In addition to acting as direct chemical protectors, the proposed mechanisms for their health advantages include modulatory effects on a number of metabolic and signaling enzymes. It has been demonstrated that flavonoids suppress the cyclooxygenase, which produces prostaglandins, the angiotensin converting enzyme (ACE), which raises blood pressure, and the estrogen-producing enzymes.

In addition to inhibiting estrogen synthase, which binds estrogen to receptors in a variety of tissues, these in vitro inhibitory effects have the potential to prevent platelet aggregation, which would reduce the risk of heart disease and thrombosis and also lower the risk of cancers associated with estrogen. It is well known that flavonoids possess bioactive properties such as the ability to scavenge free radicals, inhibit hydrolytic and oxidative enzymes, and have anti-inflammatory and antiviral effects. Dietary flavonoids have been shown to have anti-proliferative effects on disorders like cancer, cardiovascular disease, and inflammatory diseases. The ability of flavonoids to scavenge hydroxyl, superoxide anion, and lipid peroxy radicals is a sign of their potential for health benefits. The top three sources of flavonoids are tea (61%) onions (13%) and apples (10) with cherry, tomato, broccoli, black grapes, and blueberries rounding out the top ten.

Consumption of flavonoids and death from coronary heart disease are inversely correlated. Consuming foods high in flavonoids seems to lower the chance of dying from coronary heart disease. Some flavonoids have also been reported to be mutagenic, despite the fact that flavonoid intake has been linked to a lower risk of death from coronary heart disease. The potency of flavonoids as antioxidants depends on their chemical structure. The position of hydroxyl groups and other features of the chemical structure of flavonoids are critical for the antioxidant and free radical scavenging properties of these substances.

Quercetin, the most abundant dietary flavonol, is a potent antioxidant because it has all the right structural features for free radical scavenging activity.[11] Luteolin possesses anti-bacterial, anti-mutagenic, and anti-inflammatory properties. Similar to the dietary pigmented polyphenol curcumin, apigenin inhibited

12-O-tetradecanoylphorbol-3-acetate (TPA)-mediated tumor development of mouse skin, perhaps by inhibiting protein kinase C activity and nuclear oncogene expression. In addition to relaxing smooth muscle, apigenin has antimicrobial, anti-inflammatory, diuretic, and hypotensive properties. Hexahydroxyflavone myricetin possesses anti-gonadotropic and antibacterial properties, although it does not appear to be mutagenic. The widely consumed flavonol kaempferol is directly mutagenic and has anti-inflammatory and antibacterial properties. The most common flavonoid in higher plants, quercetin, appears to contribute to kaempferol's mutagenicity in the presence of microsomal metabolizing systems.

Numerous enzymes, smooth muscle contraction, and rat lymphocyte proliferation are all inhibited by quercetin. Despite having anti-inflammatory, antibacterial, antiviral, and anti-hepatotoxic effects, it is also mutagenic and allergic. Major sources of catechins and gallic acids include grapes, berries, chocolate, and green tea. Gallic acid esters like epicatechin, epicatechingallate, and epigallocatechingallate (EGCG) are abundant in tea. Numerous investigations have revealed that these substances offer protective advantages by their capacity to scavenge free radicals and by inhibiting the generation of eicosanoids and platelet aggregation. Prostate cancer is prevented by drinking green tea.[15] Wine has an astringent flavor because to catechins and procyanidins. Red wine's potential to guard against atherosclerotic cardiovascular disease is assumed to be in part due to catechin, one of the principal phenolics present in red wine and grapes.

Isoflavonoids

They belong to the phenolic phytonutrients subclass. Fabaceae (Leguminosae) family members virtually exclusively produce isoflavonoids. Tofu, soy flour, soybeans, and soy cheese are their primary food sources. Dietary isoflavones, such as genistein and daidzein, are primarily obtained from soy, and soybeans are an incredibly concentrated source of these substances. Soy isoflavones constitute an activity of numerous phytochemicals known as phytoestrogens and have attracted a lot of research because they bind to the estrogen receptor class of molecules. Most hormone-dependent and hormone-independent cancer cells, including colon cancer cells, are inhibited by genistein from growing in culture.

Isoflavones have received considerable attention as potentially preventing and treating cancer and osteoporosis.[8] Consuming soybean products in mice prevented the development of experimental prostate cancer and changed tumor biomarkers linked to angiogenesis. Even while epidemiological statistics indicate that soy may reduce the risk of breast and prostate cancer, there isn't much proof that it also protects against colon cancer.

Antioxidant and anti–proliferative properties of isoflavones offer additional, important mechanisms for their protection against many prevalent chronic diseases.[14] Cellular damage resulting from oxidative stress is believed to be a major contributor to the etiology of cardiovascular disease through the oxidation of LDL, and cancer by causing DNA strand breaks that may lead to mutations.[11] The soy isoflavone genistein selectively engaged the beta-oestrogen receptor and reduced binding to the alpha-receptor by a factor of 20 according to recent interesting mechanistic studies.

Anthocyanidins

These are aglycones of anthocyanins, which are water-soluble flavonoids. One of the main pigments in fruits and flowers is made up of these substances.[16] These pigments' colors are affected by pH and metal ion complexes. Anthocyanidins, a kind of flavonoid, have antioxidant effects in vitro and may also have antioxidative and antimutagenic properties in vivo. In the ferric-reducing ability experiment, they were discovered to have strong antioxidant activity for isolated anthocyanidins (aglycons and glycosides) and complex plant samples; however, in HT29 clone 19A cells, these compounds were unable to prevent the hydrogen peroxide-induced oxidation of DNA bases.

In leaf cells, anthocyanins frequently appear red, but depending on their chemical composition, vacuole pH, and interactions with other pigments, they can also generate pink, purple, blue, orange, brown, or even black leaf colours. Many of the published articles on plant defensive colouration have assumed red foliage to be the outcome of the production of anthocyanins, even though other pigments– carotenoids, apocarotenoids, betalains, condensed tannins, quinones and phytomelanins– can also contribute to plant vermilion.[16]

Phytoestrogens

These non-steroidal phytochemicals share structural and physiological similarities with gonadotropin-releasing hormone. They offer a hormone replacement treatment (HRT) alternative that has positive benefits on the cardiovascular system and might possibly help with menopausal symptoms. In hormone replacement treatment (HRT), they can take the place of synthetic selective estrogen receptor modulators (SERMs). They have antioxidant effects due to their polyphenolic nature, anti-carcinogenic, modulation of steroid metabolism or of detoxification enzymes, interference with calcium-transport and favourable effects on lipid and lipoprotein profiles.[17] According to chemical composition, Flavonoids, isoflavonoids, coumestans, stilbenes, and lignans are different types of phytoestrogens. Either plants or their seeds contain them. While the soy sprout is a powerful source of coumestrol, the main coumestan, the soybean is high in isoflavones.

Due to their structural resemblance to estrogen, flavonoids can have both estrogenic and anti-estrogenic effects. They may also offer some protection against heart disease and bone loss. The precursors to these compounds are widely distributed across the plant world but are primarily found in the family Leguminosae. They are particularly prevalent in soybean and its products, legumes, berries, whole grains, and cereals. They are structurally similar to estrogen in that they include specific hydroxyl groups that can be arranged in a stereochemical alignment that is almost identical to estrogen. According to estimations, women in China, Japan, Taiwan, and Korea consume more isoflavones than women elsewhere, and as a result, they report lower incidences of osteoporosis and associated health problems such hot flushes, cardiovascular disorders, and hormone-dependent breast and uterine malignancies. Red wine and peanuts, both of which contain resveratrol, are the main dietary sources of phytoestrogenic stilbenes. Both the cis and trans isomers of resveratrol exhibit estrogenic effects, although only the trans isomer has been identified. Trans-resveratrol is only present in the skin of red grapes; very small levels can also be found in white wine and green grapes. Sprouting legumes like soy and alfalfa are the main dietary sources of cumestans; however, small amounts have also been found in brussel sprouts and spinach. The largest quantities are reportedly found in clover and soybean sprouts. A broad class of phenylpropanoid dimers and oligomers are referred to as lignans. Secoisolariciresinol and matairesinol are two lignan dimers that, while not naturally estrogenic, easily transform into the oestrogenic mammalian lignans enterodiol and enterolactone. These are of great interest because of their estrogenic, anti-carcinogenic, antiviral, antifungal and antioxidant activities.[18]

In large quantities, the Phyto lignans are present in flaxseed, asparagus, whole grains, vegetables, and tea. Apart from strawberries

and cranberries, fruits also have modest levels. In humans, after consumption of plants rich in isoflavones and lignans, enzymatic metabolic conversions occur in the gut, by microflora, and the mammalian lignans are readily absorbed.[18]

Terpenoids

The greatest class of phytonutrients found in grains and green vegetables are terpenes, sometimes referred to as isoprenoids. Higher plants, mosses, liverworts, algae, and lichens, as well as insects, microorganisms, and sea organisms, all contain these substances. Terpenoids are derived from a common biosynthetic pathway based on mevalonate as parent, and are named terpenoids, terpenes or isoprenoids with the subgroup of steroids among them as a class.[19] Their significance to plants stems from the need for them to use photosensitizing pigments in photosynthetic reactions to fix carbon. It is now understood that the presence of these molecules in animal tissues also provides a degree of defence against some illnesses, particularly those linked to chronic damage and growth dysregulation. Animals have evolved to use these compounds for hormonal and growth regulatory functions (vitamin A).

Gibberellins, among other terpenoids, are classified as hormones (as are carotenoids and phytol), photosynthetic pigments (as are ubiquinone and plastoquinone), electron carriers (as are ubiquinone and plastoquinone), mediators of polysaccharide assembly, as well as communication and defence processes. Diterpenes have been linked to several biological processes, such as antibacterial, antifungal, anti-inflammatory, anti-leishmanial, cytotoxic, and antitumor properties. Currently, a variety of terpenoids that are useful for human health care can elicit in humans a wide range of biological responses.

Different terpenoid molecules have antimicrobial, antifungal, antiparasitic, antiviral, antiallergenic, antispasmodic, anti-hyperglycemic, anti-inflammatory, chemotherapeutic, and immunomodulatory properties [20]. Terpenes can be employed as natural pesticides, skin penetration enhancers, and storage protection agents for agricultural products. Terpenes interact with free radicals to produce an unusual antioxidant function. Because of their lengthy carbon side chains, they react with free radicals by dividing into fatty membranes. Tocotrienols and tocopherols are the terpene antioxidants that have been investigated the most. They affect cancer cells and are naturally present in whole grains. Tocotrienols effectively induce apoptosis in human breast cancer cells. The impact of a diet of fruits, vegetables and grains on reduction of cancer risk may be explained by the actions of terpenes *in vivo*.[20]

Carotenoids

They are prevalent in fruits and vegetables and are highly pigmented in the colors of yellow, orange, and red. When taken by birds, they are also absorbed into the yolk of their eggs. Carotenes and xanthophylls are the two types of molecules that make up carotenoids. All carotenoids share a poly-isoprenoid structure, a long-conjugated chain of double bonds, and approximately bilateral symmetry around the central double bond as common chemical traits. Carotenoids can be converted to cis-trans isomers through isomerization because they contain conjugated double bonds. The biological importance of carotenoid isomerization in relation to human health is little understood, even though the trans-isomers are more prevalent in foods and more stable.

Beta-carotene contains vitamin A activity, but carotenes have biological activities that are tissue specific. An association between increased food intake and tissue concentrations of carotenoids and a reduced risk of chronic illnesses is suggested by epidemiological studies. Carotene and lycopene have been shown to be inversely related to the risk of cardiovascular diseases and a number of cancers, in contrast to lutein and zeaxanthin, which have been associated with eye problems. Lutein can guard against cancers of the lungs, prostate, breast, colorectal, and uterine. Additionally, they may protect against the risk of gastrointestinal cancer. The xanthophyll forms of carotenoids shield additional antioxidants, and these shields may also be tissue-specific. Zeaxanthin, cryptoxanthin and astaxanthin are members of the xanthophyll group.[21] It has been proposed that the primary mechanism by which carotenoids provide their positive effects is through their antioxidant capabilities. Recent studies are also showing that carotenoids may mediate their effects via other mechanisms such as gap junction communication, cell growth regulation, modulating gene expression, immune response and as modulators of Phase I and II drug metabolizing enzymes.[22] Extensive research has been conducted on the antioxidant properties of certain carotenoids. Other processes, such as their pro-vitamin A activity, immunological, endocrine, and metabolic activities, as well as their regulation of cell cycle, apoptosis, and cell differentiation, are being investigated in ongoing studies. Future research will delve into their bioavailability, metabolism, mechanisms of action, and safety.

Limonoids

Limonoids, which are terpenes found in citrus fruits, have gained the attention of natural product and synthesis chemists due to their diverse structures and wide range of bioactivities. Citrus juice and tissues both contain significant concentrations of these highly oxygenated triterpenoid chemicals, which are known as important physiologically active natural substances. They can be found in the form of water-soluble limonoid glucosides or water-insoluble limonoid aglycones in seeds. Recent studies have shown that certain citrus limonoids possess noteworthy anticancer properties. In fact, it was shown that five limonoid aglycones significantly increased glutathione-S-transferase levels in mice, a crucial detoxifying enzyme system that catalyzes the conjugation of glutathione with several carcinogenic substances. Furthermore, two limonoid aglycones were shown to reduce the incidence of tumours in mice by more than 50% at a dose of 10mg. These promising findings suggest that citrus limonoids may have substantial anticancer effects and are safe for animal models. Natural fruit, citrus enriched with limonoids, and purified forms of limonoids can all be utilized to fight human cancer. By suppressing Phase I enzymes and activating Phase II detoxifying enzymes in the liver, they operate as chemotherapeutic agents. D-Limonene, the commonest monocyclic monoterpene, found within orange peel oil, inhibits pancreatic carcinogenesis induced in experimental models and also provides protection to lung tissue.[23] Though the preliminary studies are encouraging, they have primarily been carried out on cell cultures and animal subjects. To ascertain the efficacy of limonoids in cancer prevention or treatment in humans, additional research is required. The primary step involves assessing the compounds' bioavailability for humans, encompassing factors such as absorption rates following ingestion, their distribution in blood and tissues, and the duration of their presence therein. If limonoid compounds are found to be bioavailable, further human studies will be needed to assess the effects of limonoid ingestion on biomarkers related to cancer.[24]

Phytosterols

This information is about an important subclass of terpenes. Most commonly, seeds, nuts, fruits, and vegetables contain phytosterols. On average, seeds have 120 mg of plant sterols per 100g of wet weight, compared to 20 mg for vegetables and 15 mg for fruit. The most abundant phytosterols in nature are sitosterol, campesterol, and

stigmasterol, which make up 65%, 30%, and 3% of dietary phytosterol intake, respectively. Animals respond well to the anti-inflammatory, anti-neoplastic, anti-pyretic, and immuno-modulating effects of beta-sitosterol and its glycoside, which are produced by plants. According to research, phytosterols inhibit inflammatory enzymes and outcompete cholesterol for absorption in the intestine, assisting with the body's removal of cholesterol. In the colon, plant sterols are first solubilized into micelles before being delivered to enterocytes. They are made into chylomicrons, esterified inside the enterocyte, and then secreted into the lymphatics before being eliminated by the biliary system. The sterolin pumps made up of the ATP-binding cassette proteins ABCG5 and ABCG8 convey un-esterified phytosterols back into the intestinal lumen. These are expressed in the mucosal cells and the canalicular membrane, and they re-secrete sterols, especially absorbed plant sterols, back into the intestinal lumen and from the liver into bile.[25] Studies show that saturated phytosterols are more effective than unsaturated compounds in reducing cholesterol levels in the body. This is due to their ability to decrease both total cholesterol and LDL cholesterol in the blood. It's not surprising that they compete with cholesterol for absorption in the intestine, as their structure is similar. However, in mammals, phytosterols are not as easily absorbed and are more quickly excreted from the liver and metabolized to bile acids compared to cholesterol. While animal studies suggest that phytosterols can reduce atherosclerosis, human studies have mixed results and do not definitively link serum phytosterol levels with an increase in atherosclerotic risk. It is reassuring that vegetarians who consume considerable plant sterols are at decreased risk of ASCVD, but it is impossible to separate the effects of phytosterol excess from animal fat reduction in this population.[26]

Glucosinolates

Cruciferous vegetables contain chemicals that activate liver detoxification enzymes, which contribute to their pungent aroma and bitter taste. Eating these vegetables can provide a natural defence against cancer, mutagens, and other harmful substances. Some sprouts of crucifers, such as broccoli and cauliflower, have higher levels of glucoraphanin (a type of glucosinolate) than mature plants. Crucifer sprouts may protect against the risk of cancer more effectively than the same quantity of mature vegetables of the same variety.[27] Cruciferous vegetables contain glucosinolates that break down into biologically active compounds like indoles, nitriles, thiocyanates, and isothiocyanates when prepared, chewed, and digested. Two of the most commonly studied compounds for their anticancer properties are indole-3-carbinol and sulforaphane. It has been demonstrated through research that eating brassica vegetables lowers the risk of malignancies of the rectum, colon, stomach, and lungs. It is thought that the thioglucosides present in these plants are responsible for this. These dietary glucosinolates are known to block the formation of carcinogens, both endogenous and exogenous, which can prevent the initiation of carcinogenesis. Through the induction of Phase 2 detoxification enzymes and the inhibition of Phase 1 carcinogen-activating enzymes, which can affect several processes related to chemical carcinogenesis, including metabolism, DNA binding, and mutagenic activity of promutagens, the protective effects are achieved. According to studies, indoles and brassica vegetables have a good impact on human health when consumed in realistic levels by rats, mice, and humans alike. In mouse models, the glucosinolate metabolite indole-3-carbinol has also been shown to prevent organ-site carcinogenesis. Its preventive effect on human mammary carcinogenesis may be due in part to its ability to regulate cell cycle progression, increase the formation of anti-proliferative estradiol metabolite and induce cellular apoptosis.[28]

Fibres

Numerous plant-based foods are rich in indigestible residues that were once labelled as crude fibre. However, they are now recognized as dietary fibre (DF) and non-starch polysaccharides (NSP). DF is a collection of intricate polysaccharides such as cellulose, gums, mucilage, hemicellulose, and lignin, each with distinct chemical, physiochemical, and physiological characteristics. According to research, these dietary fibers help manage cardiovascular disease, lower blood cholesterol levels, control blood glucose levels in diabetics, and prevent colon cancer. The disease-preventing potential of DF will depend upon the proportion and actual quantities of different polysaccharide components present in each food.[29] The positive impact of dietary fiber components stems largely from their ability to expand and prolong transit time in the small intestine. They are therefore beneficial as a treatment technique for some types of diabetes (such as non-insulin-dependent diabetic mellitus) since the release and absorption of glucose are slowed down as a result. Additionally, these ingredients work with bile salts to encourage the body's elimination of cholesterol and lower blood cholesterol levels. They also connect with food toxins in the gut, lessening their toxicity. They can also have some adverse nutritional effects by binding dietary calcium, magnesium, zinc, and iron, thereby reducing their bioavailability.[30]

Consuming a diet high in meat and fat has been associated with an increased risk of colon cancer. However, the consumption of dietary fibre can provide protection against colorectal diseases. This is because fibre can alter the colon's environment, making it less conducive to cancer growth. Moreover, fibre can increase the bulk of faeces, reducing bile acid concentrations that are elevated by high-fat diets. Studies have shown that dietary sugar beet fibre and short-chain fatty acids like butyric acid can reduce cholesterol production in rat livers and intestines. Due to how different dietary fibres are digested into short-chain fatty acids, particularly butyric acid, in the colon, they may have different effects on cancer risk. Butyric acid has been shown to inhibit the growth of colonic epithelial and tumour cells, as well as induce apoptosis (cell death) in vitro. Butyric acid may help to control the apoptotic process in the mucosa of the colon. An intriguing topic of study is how butyric acid and its derivatives may be produced by the fermentation of fiber. Its enrichment through food products, such as fibre and starch, may emerge as a molecular-based strategy that provides significant health.[30]

Polysaccharides

Polysaccharides are essential biomolecules found in a variety of organisms, including plants, microorganisms, algae, and animals. They play crucial roles in many life processes, including cell communication, adhesion, and molecular recognition in the immune system. Biochemistry and pharmacology have recently begun to pay more attention to natural sources of bioactive polysaccharides. Particularly plant polysaccharides have shown a variety of biological actions, including improving wound healing and enhancing the immune system. They have also been used in traditional medicine as hypoglycemic and anti-inflammatory agents. While traditionally used as thickening, emulsifying, and stabilizing agents, there is now a growing market for healthy compounds produced from controlled enzymatic degradation of polysaccharides, such as starch, to create oligo- or monosaccharide syrups. Some of them possess interesting biological properties e.g., oligodextrins (anti-ulcer agents, lowering serum cholesterol in low saturated fat diet), fructooligosaccharides (prebiotics, dietary fibre, stimulate mineral absorption, enhance defense mechanism).[32]

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Saponins

Saponins are a type of compound that can be found in various plant species as a natural defense mechanism against pathogens and pests. These compounds are initially stored in the plant cells as inactive precursors, but can be activated by plant enzymes when under attack. Interestingly, saponins are widely used across various industries including the production of drugs, foaming agents, sweeteners, taste modifiers, and cosmetics. Saponins are glycosylated and can be classified into three groups: triterpenoid, steroid, or steroidal glycoalkaloid. Triterpenoid saponins are predominantly found in dicotyledonous plants, while steroid saponins are mainly found in monocots. However, oats contain both triterpenoid and steroid saponins. Finally, it's important to note that steroidal glycoalkaloids are primarily found in members of the Solanaceae family, such as potatoes and tomatoes. Among these, α-tomatine is the major saponin found in tomatoes and is present even in healthy plants with a concentration of approximately 1 mM in tomato leaves. This saponin is potent enough to inhibit the growth of several non-pathogens of tomato. Therefore, it would be expected that this molecule could protect the tomato leaves from fungal pathogens.[34]

The importance of phytochemicals for health and disease prevention

According to epidemiological evidence, it is widely believed that phytochemicals may serve as a key factor in safeguarding against cancer and cardiovascular disease. This inference is based on the observation that individuals who consume a higher number of fruits and vegetables have a lower chance of developing these illnesses. As a result, nutritionists are actively researching the specific phytochemicals present in these foods that offer such protective benefits. Experimental evidence that phytochemicals influence many cellular mechanisms which may optimize health has highlighted the need to identify clearly which effects may be of greater health significance.[35]

The emergence of nutraceuticals, or foods that offer potential health benefits, has had a significant impact on consumer behavior. The efficacy of these functional foods hinges on their health claims and the presence of specific phytochemicals, which are natural compounds found in plants with medicinal properties that can help to treat a range of disorders. For years, pharmaceutical companies have explored natural plant products in their quest for new drugs. Phytochemicals play important role in human health as antioxidants, antibacterial, antifungal, anti-inflammatory, anti-allergic, antispasmodic, chemopreventive, hepatoprotective, hypolipidemic, neuroprotective, hypotensive agents, and help in preventing aging, diabetes, osteoporosis, cancer and heart diseases, induce apoptosis, diuretic, CNS stimulant, analgesic, protects from UVB-induced carcinogenesis, immuno-modulator and carminative.[36]

Red pepper and ginger contain capsaicin, which has been found to have anti-carcinogenic and anti-mutagenic properties. Curcumin, another phytochemical found in plants, has been shown to be an effective anti-inflammatory and cancer preventative. In a study on mice, dietary soy phytochemical concentrate, genistein, decreased tumor volumes by 40% to 48%, while dietary soy protein isolate decreased them by 37%. Major isoflavonoid genistein, which is present in soy, has been shown to have anti-proliferative effects on mitogen-stimulated proliferation in cultured human breast cancer cells. Carcinogen-induced rat models of breast cancer have shown that soy isoflavonoid conjugates have chemopreventive activity.

Osteoporosis can be caused by aging, hormone deficiency, and diet. Studies have indicated that phytoestrogens, which are present in plants, can help treat osteoporosis and related conditions while also helping postmenopausal women retain their bone mineral density. According to evidence from numerous human research, dietary phytoestrogens can have estrogenic effects on postmenopausal women's vaginal cytology and hot flushes, among other things. Cardiovascular illnesses are the main killers of postmenopausal women in the US and Europe. Isoflavonoids have been discovered to lower total and LDL cholesterol and boost HDL cholesterol, lowering the risk of cardiovascular illnesses. They can be found in soy products, soy protein, and flaxseed. There is evidence to support the hypothesis that phytoestrogen consumption contributes to the lower incidence of CVDs in Asian countries and in vegetarians and that they may also be cardio-protective.[35]

According to numerous scientific research, those who consume more isoflavonoids (phytoestrogens) in their diet have decreased incidences of various cancers, including breast, prostate, and colon cancer. Breast cancer risk is associated with enterolactone, a mammalian lignan, levels in the circulation. Like this, there are associations between isoflavonoids and lignans in the diet and breast, thyroid, and ovarian malignancies in both pre-and postmenopausal women. In Asia and Eastern Europe, where the use of phytoestrogens is higher than in Western countries and among vegetarians, hormone-dependent cancers are less frequent. Breast, ovarian, prostate, and colon cancer show a negative link with phytoestrogen intake when compared to cancer mortality rates. According to the information gathered from epidemiological, animal, and cell-line studies, phytoestrogens may act as a preventative measure against the occurrence of prostate and breast cancer. It has been reported that increased consumption of beans, lentils and peas, tomatoes, and dried fruits was associated with significantly decreased prostate cancer risk.[36]

Consuming diets that are high in phytonutrients can provide various phytoestrogens like isoflavones, resveratrol, and lignans, which can produce a range of pharmacological effects. The overall quality of life can be negatively impacted by several estrogen-related illnesses that affect women, including osteoporosis, cardiovascular and cognitive decline, higher risk of breast cancer, and other symptoms. The strongest evidence for the physiological effects of phytoestrogens on humans comes from studies on the effects of soy protein supplements on lipids, lipoproteins, and vascular function. Therefore, postmenopausal women who have the greatest breast cancer risk should be encouraged to increase their phytoestrogen intake (Figure 1).[35]

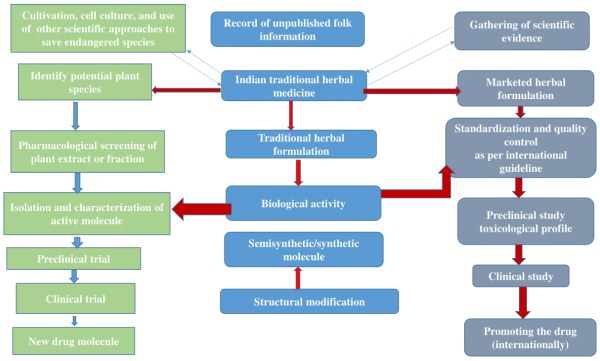

Figure 1 Plan for advancing and incorporating conventional herbal medicine into contemporary medicine.

Challenges facing the resurgence of traditional herbal medicine in India and the role of Indian organizations

The use of phytochemicals from traditional Indian medicine, specifically Ayurveda, is gaining global attention. Significant efforts

are being made to integrate these herbal remedies into modern medicine. India has ample resources for research in this area, with institutions such as the Central Drug Research Institute (CDRI), Council of Scientific and Industrial Research (CSIR), Central Institute of Medicinal and Aromatic Plants (CIMAP), National Botanical Research Institute (NBRI), Regional Research Laboratories (RRL), and National Chemical Laboratory (NCL) all playing important roles. Several government and non-governmental organizations from different countries have actively started researching plants and formulations described in Ayurveda.[38]

Products from Ayurveda have been successfully evaluated in clinical trials for the treatment of bronchial asthma, rheumatoid arthritis, ischemic heart disease and cancer; amongst other illnesses.[39] Indian medicinal herbs (e.g., Ashwagandha, Guggulu, Haridra, Kutki, Shatavari, Atmaupta, Amruta, Brahmi, Guduchi, Amla, Ginger) and complex herbal formulations (Rasagenthi Lehyam, Brahma Rasayana, Semecarpus Lehyam, Triphala, and other Rasayanas) were evaluated through preclinical studies and reported to possess positive effect.[40]

The US National Center for Complementary and Alternative Medicine has funded several research works based on Ayurvedic medicine, for example, use of curcuminoids in cardiovascular diseases; a compound from *M. pruriens* (L.) used against the side effects of anti-Parkinson's drugs; use of three plants (ginger, turmeric, and *Boswellia*) to cure arthritis and asthma, and to validate the effect of *Centella asiatica* (L.) against Alzheimer's disease.[41]

The effectiveness of *Withania somnifera* (L.) and *Asparagus racemosus* wild as vaccine adjuvants has been evaluated in experimental systems, indicating their potential in immunobiological preparations. However, it is crucial to conduct controlled clinical trials to establish the effects of these drugs and compare their potency with allopathic medicines. While encouraging clinical trials have been conducted on Indian traditional medicines, more trials are necessary. For instance, clinical studies have been successful in evaluating piperine, a bio-enhancer from pippali. According to a multi-center investigation, Vijaya Sar (an aqueous decoction of *Pterocarpus marsupium* Roxb) works well as an anti-diabetic and hypoglycemic medication. A US patent for the creation of a herbal anti-psoriatic medication including *Argemone mexicana* (L.) has been approved, and Lupin Ltd (Mumbai, India) has submitted an Investigational New Drug (IND) application. The CDRI has also created a product for the treatment of hyperlipidemia and atherosclerosis that contains a portion of Gugu lipid from *Commiphora weightii*.

Boswellia serrata Roxb. gum resin has been commercialized by Regional Research Laboratories (Jammu) as a non-steroidal anti-inflammatory drug, which also demonstrates hypolipidemic effect.[42,43] A double-blinded clinical trial has been carried out with "arogyawardhini" (an Ayurvedic product containing Amla, Bahera, Harar, Guggulu, Kutki, Neem, Chitrak Mool) in viral hepatitis, while effects of *M. pruriens, Phyllanthus amarus*, and *Tinospora cordifolia* have been investigated in the treatment of Parkinson's disease, hepatitis, and obstructive jaundice, respectively.[44]

A standardized *Bacopa monnieri L*. plant extract that has been enhanced with bacoside has been created by the CSIR and CDRI. The extract is used to improve memory and learning and is marketed under various brand names in Asia and Europe. Brahmi is described in the Charak Samhita and Sushruta Samhita and has been used as a brain tonic for 3,000 years.[45]

Customary therapeutic preparations comprising medicinal plants

A clinical trial of a well-known classical Ayurvedic formulation, "triphala", which is prepared by combining the fruits (without seeds) of *Terminalia chebula* Retz., *Terminalia bellerica* Roxb., and *Emblica officinalis* Gaertn., showed potent effects against constipation and other gastric problems.[46]

A standardized formulation prepared with purified extract of ashwagandha (*W. somnifera*), guggulu (*B. serrata*), and haldi (*Curcuma longa*) was effective in improving a joint swelling condition and has a good safely profile when given to people suffering from rheumatoid arthritis.[7]

Prostalyn, a herbal formulation for treating benign prostate hyperplasia, contains two traditional Indian medicinal plants - *Murraya koeniggi* and *Tribulus terrestris*.

A short-term clinical trial demonstrated that "tarika", an Ayurvedic pimple remover herbal powder (containing *T. chebula fruit, T. bellerica fruit, Santalum album heartwood powder, Curcuma aromatica rhizome, Embelia ribes fruit, Berberis aristata dried stem, Acorus calamus rhizome, Embelica officinalis fruit, Taxus baccata leaf, Myristica officinalis fruit endosperm*, and *Cyperus rotundus* rhizome) has good effect in patients suffering from moderate to severe degrees of acne vulgaris.[48]

"Guduchyadi ghrita medhya rasayana", clinical trials have shown promising outcomes for a combination of Indian medicinal plants, including guduchi, apamarga, vidanga, shankhapushpi, vacha, haritaki, kushtha, and shatavari. It has been found to enhance mental health, memory, and alleviate stress and depression, making it a possible solution for slowing down the aging process.

"Amalki rasayana", an Ayurvedic herbal product, has showed promising effects in patients suffering from age related macular degeneration.[49]

The CSIR has developed several traditional plant-based formulations. Some of these are α, β arteether (E-mal – which was included in India's National Malaria Control Programme) and elubaquine (Aablaquin) as antimalarial drugs; Asmon® to cure asthma; Sallaki® of *B. serrata* to treat rheumatoid arthritis and osteoarthritis; Livzon poly-herbal formulation, which has been evaluated as a hepatoprotective agent; and immines, a multi-herbal drug to provide immunomodulatory activity.[50]

Several Siddha herbal formulations like Gly Cyn Neu ointment against diabetic neuropathic symptoms, combination of amukkara choornam and linga chenduram, and two other poly-herbal (for internal and external use) formulations against rheumatoid arthritis have also undergone successful clinical trials.[51,52]

Throughout history, ISMs have utilized various herbal remedies to treat jaundice and viral hepatitis. Currently, there are more than 6,000 herbal medicines available worldwide that are used to manage liver disorders. Of these, approximately 40% are composed of poly-herbal formulations, which include extracts from *Silybum marianum* L. Gaertn. seed, *Picrorhiza k*urroa Royle ex Benth, and various *Phyllanthus sp*. plants, as well as glycyrrhizin preparation. These formulations consist of a combination of ninety-three Indian herbs and are available in the Indian market.[53]

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Modern medicines like tablets, capsules, powders, syrups, ointments, and gels contain patented and proprietary herbal medicines such as Arishtas, Churnas, Rasayanas, Ghrits, and Ras. According to a survey, more than 70% of all drugs sold as Ayurvedic medicine in the Indian market are branded editions – patented and proprietary medicines.[54]

The Government of India has created the Traditional Knowledge Digital Library (TKDL) to compile and preserve traditional medicinal knowledge that is available to the public.

Currently, a number of botanicals are undergoing clinical trial using reverse pharmacology processes to find new drugs to cure/prevent hepatotoxicity, viral hepatitis, cancer, diabetes, and arthritis based on the traditional knowledge of India.[53] ISMs have described herbal medicines and medicinal plants as a great source of new drugs, including folk medicine.

Conclusion

For many years, indigenous people have used medicinal plants to treat various illnesses. Recently, scientific research has shown the nutritional and medical benefits of phytonutrients/phytochemicals for preventing and treating diseases. These "novel" nutraceuticals from plants could become an essential part of dietary disease prevention. Although nutraceuticals have the potential to promote human health and prevent diseases, health professionals, nutritionists, and regulatory toxicologists must work together to regulate them appropriately for maximum health and therapeutic benefits. Long-term clinical studies are necessary to scientifically validate nutraceuticals for different medical conditions.

Further studies are needed to determine the role of various phytochemicals in preventing chronic degenerative diseases and their interactions with food and drugs. It is also important to understand the effects of different processing methods on the biological availability and effectiveness of nutraceuticals. Like drugs, nutraceuticals should be subject to strict regulatory controls.

Future nutraceuticals from both plant and animal sources offer the food sector great chances to develop cutting-edge food items. To attract investors and consumers, the food industry must emphasize the monetary rewards and unique benefits of nutraceuticals while also creating products that appeal to consumers' tastes.

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Conflicts of interest

Author declares that there is no conflict of interest.

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