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Review Article

Mustard-derived secondary metabolites and human health

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ABSTRACT

Plant secondary metabolites (PSMs) are essential for human health and are the building blocks of many pharmaceuticals. Indeed, PSMs account for 25% of all medications. Access to natural resources, particularly medicinal plants, remains one of the ongoing hurdles for the drug discovery and pharmaceutical industry. Even if they exhibit biological hits, endangered animals barred from collecting large samples are more severely affected by this bottleneck. Cultivating the organism outside its typical habitat may be possible, but this is not always possible. A solution may be to cultivate pharmaceutically exciting plant species. Abiotic stressed plants offer a viable alternate source for novel medication development. Plants may defend themselves by creating a variety of PSMs to resist abiotic environmental stresses.
In most cases, plants either create new chemicals from scratch or boost the concentration of already-existing ones, such as the well-known bioactive lead compounds morphine, camptothecin, catharanthine, epicatechin-3-gallate (EGCG), quercetin, resveratrol, and kaempferol. Most PSMs are plant defence compounds with anti-inflammatory and antioxidant properties, produced under diverse abiotic stress conditions. Terpenoids, alkaloids, and phenolic chemicals are the three main PSM categories. Animals' health benefits and production increase when they consume forages with PSMs in pastures and rangelands. This has significance for improving meat and dairy biochemical richness for human consumption. Producers may be able to manage their lands more effectively, use fewer inputs, and have less environmental impact. This is if they better grasp PSMs and their functional roles in agroecology. PSMs to maintain a healthy human and animal population and a robust ecosystem are covered in this review paper.

Keywords- *No poverty, Zero hunger, Plant Secondary Metabolites, Human health, Sustainable agriculture, Immune system*

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Introduction

Because of their capacity to produce secondary metabolites with potential biological activity, plants have long been influential in the development of medicine. Plants were utilized in traditional medicine in various ways to treat a wide range of conditions. According to the World Health Organization, over 80% of the world's population still uses traditional and folk medicine, primarily based on plant remedies. Drugs made from plants that are used in conventional medicine are frequently less expensive, more readily available, and have fewer side effects than their synthetic counterparts. A recent analysis of numerous traditional medicinal plants using more advanced techniques has resulted in the discovery of numerous promising compounds. These plant-derived substances can alter already-existing medications [1-3]. Plants produce secondary metabolites to help them defend themselves. Secondary metabolites serve as physical barriers against predators, aiding in plant survival and species expansion. For instance, slugs are poisoned by the lactucin in chicory leaves. Slugs are discouraged from eating and harming the species of their presence in leaves [4 - 6]. Other plants in the same species can receive alerts from some secondary metabolites that danger is nearby. Other metabolites draw pollinators because of their pleasing color. Secondary metabolites are essential for plant survival but also significantly impact human health. A diet high in plants has terrific health benefits because secondary metabolites benefit humans. A few of the many secondary metabolites we can ingest to benefit our health are listed below. Small molecules known as plant secondary metabolites (PSMs) have a variety of chemical structures and biological functions. PSMs are secondary metabolites that are neither required for primary life functions nor have high-energy bonds, in contrast to primary metabolites, which are the primary drivers of vital life processes, including cell formation (7–10). However, PSMs perform crucial secondary physiological and biochemical roles that guarantee plant fitness and survival, especially their interactions with the environment and ability to deal with biotic and abiotic stress (11–14). These variables, particularly abiotic stressors (nutrient deficiency, seasonality, salinity, wounding, drought, light, U.V. radiation, temperature, greenhouse gases, and climate change), significantly alter chemotypes and levels of PSMs production. For example, UV-B radiation causes tree foliage to produce more phenolic acids and flavonoids as protective pigments, and high temperatures cause plants to produce more terpenoids (15–18). Flavonoids and phenols are well-known for having anti-inflammatory and antioxidant properties (19–22). Similarly, under elevated O3 levels, the production of antioxidative substances like glutathione, g-aminobutyric acid (GABA), terpenoids, and volatile organic compounds (VOCs) rises (20,23–25). PSMs are the foundation of many pharmaceutical drugs and are essential to human health. Indeed, PSMs account for more than 25% of all currently available medications (26–31). The most widely used PSMs-derived medications include aspirin, morphine (Papaver somniferum), digitoxin (from Digitalis purpurea), taxol (from Taxus baccata), artemisinin (from Artemisia annua), quinine (from Cinchona officinalis), vinblastine and vincristine

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(From Catharanthus roseus), as well as digitoxin, quinine, and artemisinin (first isolated as salicylic acid from Filipendula ulmaria). Natural product researchers and pharmaceutical companies have an opportunity to investigate the biochemical responses of plants to climatic stress for the development of numerous novel therapeutics because plants exposed to various abiotic stress conditions produce many PSMs in higher concentrations as their coping mechanism (4). No thorough literature review examines the range of plants impacted by abiotic stresses for drug discovery.

Plant Secondary Metabolites and Human Health

Higher plants naturally produce secondary metabolites called polyphenols, which have important uses in industrial and medical applications (32–37). The large molecules known as polyphenols, with a molecular weight of about 800 Daltons, allow them to pass through the cell membrane and access or occupy space in intracellular sites as pigment or phytochemicals (38–43). Most polyphenols comprise flavonoids, polyphenolic amides, lignans, stibines, and phenolic acids. Flavonoids such as flavonols, isoflavones, flavones, anthocyanins, and proanthocyanins are examples of flavonoids, and lignans are compounds that are derived from phenylalanine found in cereals or seeds (44–50). The chemical structure, sugar rings, composition, and synthesis pathways categorize these secondary metabolites. For example, phenolic compounds typically comprise simple sugars containing benzene, oxygen, and hydrogen. There is growing evidence from clinical trials that these polyphenols are effective in the pre-treatment and prevention of many chronic diseases, such as osteoporosis, cancer, type-2 diabetes, degenerative diseases, immune-related cardiovascular (CVD), and cancer (51–56). These polyphenols display numerous antimicrobial, antibacterial, antioxidant, and virucidal properties (57–61). Polyphenols help to maintain blood sugar levels by promoting the release of insulin, which also improves glucose tolerance and insulin sensitivity. A diet high in polyphenols may lower cholesterol levels and low-density lipoprotein (LDL), ultimately affecting blood pressure (62–69). Polyphenols also prevent blood clots, slow the growth of tumors, boost immunity, and reduce the risk of pulmonary embolism. Alkaloids, phenolic compounds, terpenoids, and sulfur-containing compounds are some of the four classes of plant-based secondary metabolites, and they all have a variety of medical or industrial uses (70–77). From an industrial standpoint, polyphenols can be used as pharmanutrients for synthesising medicines, as a coloring or dyeing agent, for tanning leather, as an encapsulating medium, or as another beneficial food ingredient (78–83). By using various extraction methods, such as chromatography (thin or paper), Soxhlet, microwave, heat reflux, ultrasonic, liquid-liquid extraction, supercritical fluid extraction, and ultra-high pressure extraction, the polyphenols from various origins can be obtained. Additionally, nuclear magnetic resonance (NMR), reverse phase liquid chromatography (RPLC), high-performance liquid chromatography (HPLC), and other spectroscopic techniques can be used to analyze the identification (qualitative or quantitative) of polyphenols (84–89). Sunlight continuously irradiates plants. They have therefore created a variety of defense mechanisms against UVR harm. Creating secondary metabolites with UVR protection activity and antioxidant properties is one of these mechanisms (90–97). Because of these molecules, plants are a significant source of compounds to prevent photoaging, UVR damage, and other diseases like skin cancer (98–105).

Plant Chemical Defenses

The significance of plant secondary metabolites in ecology typically differs from their potential for use in medicine, yet they are essential to all aspects of plant-environment interactions. Despite the adverse environmental conditions brought on by biotic factors like invading diseases, herbivores, and competitors, chemical and physical defenses—crucial for plants to survive in plant communities—have enabled their survival. Plant species have different chemical defenses that represent their individual evolutionary histories. This allows for classifying plant species through chemical taxonomy according to the distinct variety of secondary metabolite families they create. Among plants' most prevalent protective chemicals are benzoic and cinnamic acids, phenolic derivatives, flavonoids, terpenoids, alkaloids, long-chain hydrocarbon compounds, derived alcohols, carbonylic and carboxylic compounds. Less prevalent substances include glucosinolates, amines, thiophenes, cyanogenic glycosides, disulfures, and sulfoxides restricted to particular genera. The nutraceutical value of foods derived from plants has also been shown to be impacted by environmental circumstances, which alter chemical defense synthesis (106–114). We have provided information on the influence of biotic and abiotic environmental factors on the production of secondary metabolites by various plant species (98,101–108). Abiotic variables commonly affecting phytochemical development include nutrients, light, water shortages, and severe temperatures. Soil quality plays an essential role in this process. Chenopodium album synthesizes phytotoxins when pH, soil aggregate mean weighted diameter and extractable phosphorus are deviated from their ideal values in Argentinean continuously cultivated soil. Consumed in American countries as an alternate source of nutrients, this edible weed demonstrates cross and multiple resistances to synthetic pesticides and causes financial losses in agricultural production (2,5,38,46,74,7,10,12,14,27,29,32,35). We also noted a rise in its flavonoid production under similar circumstances, which raised its nutraceutical value and supported its use as a source of phytochemicals that scavenge free radicals (Chludil et al., 2008) (fig. 1)

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Fig.1 Role of P.M.s under stress conditions

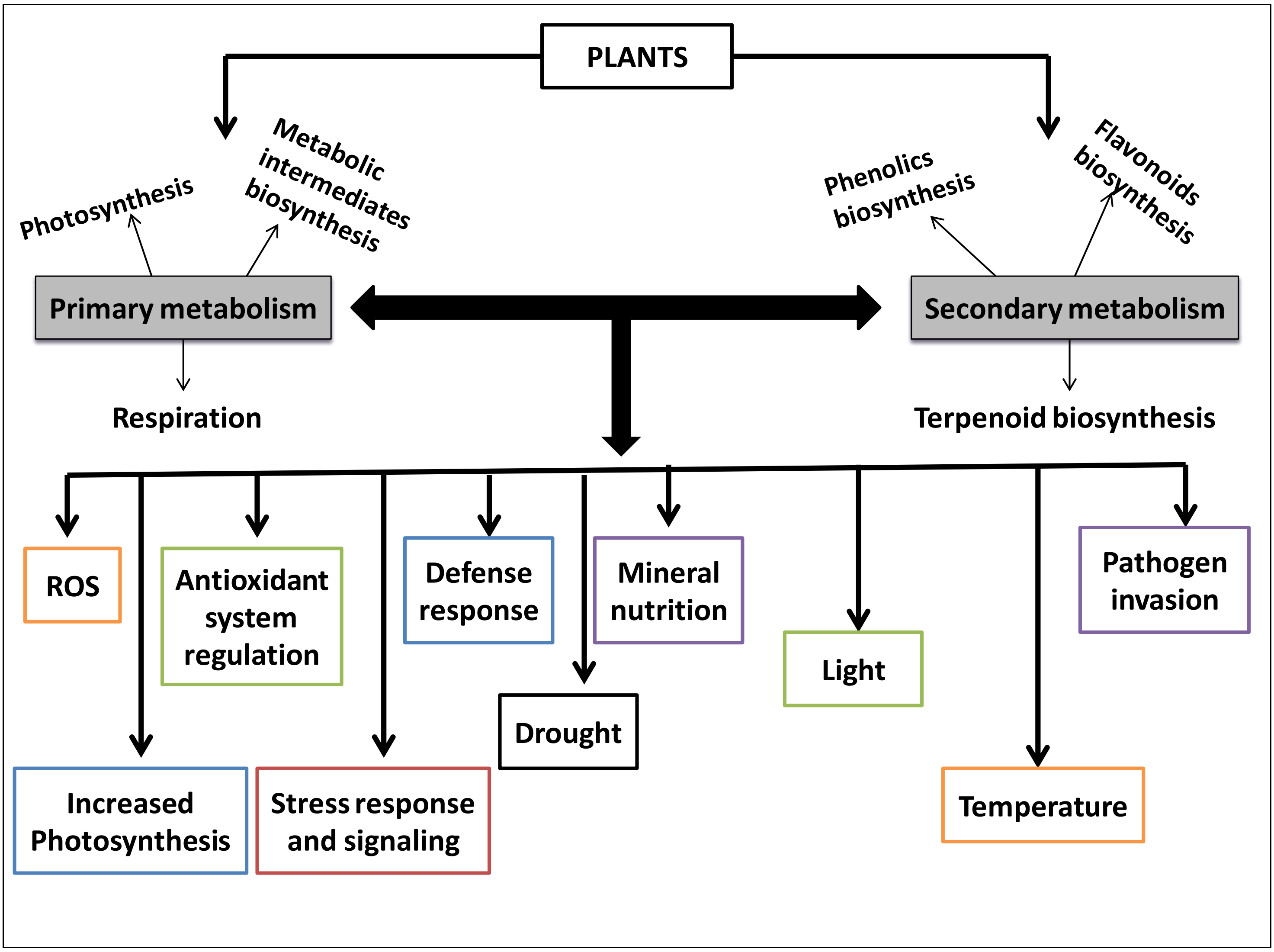
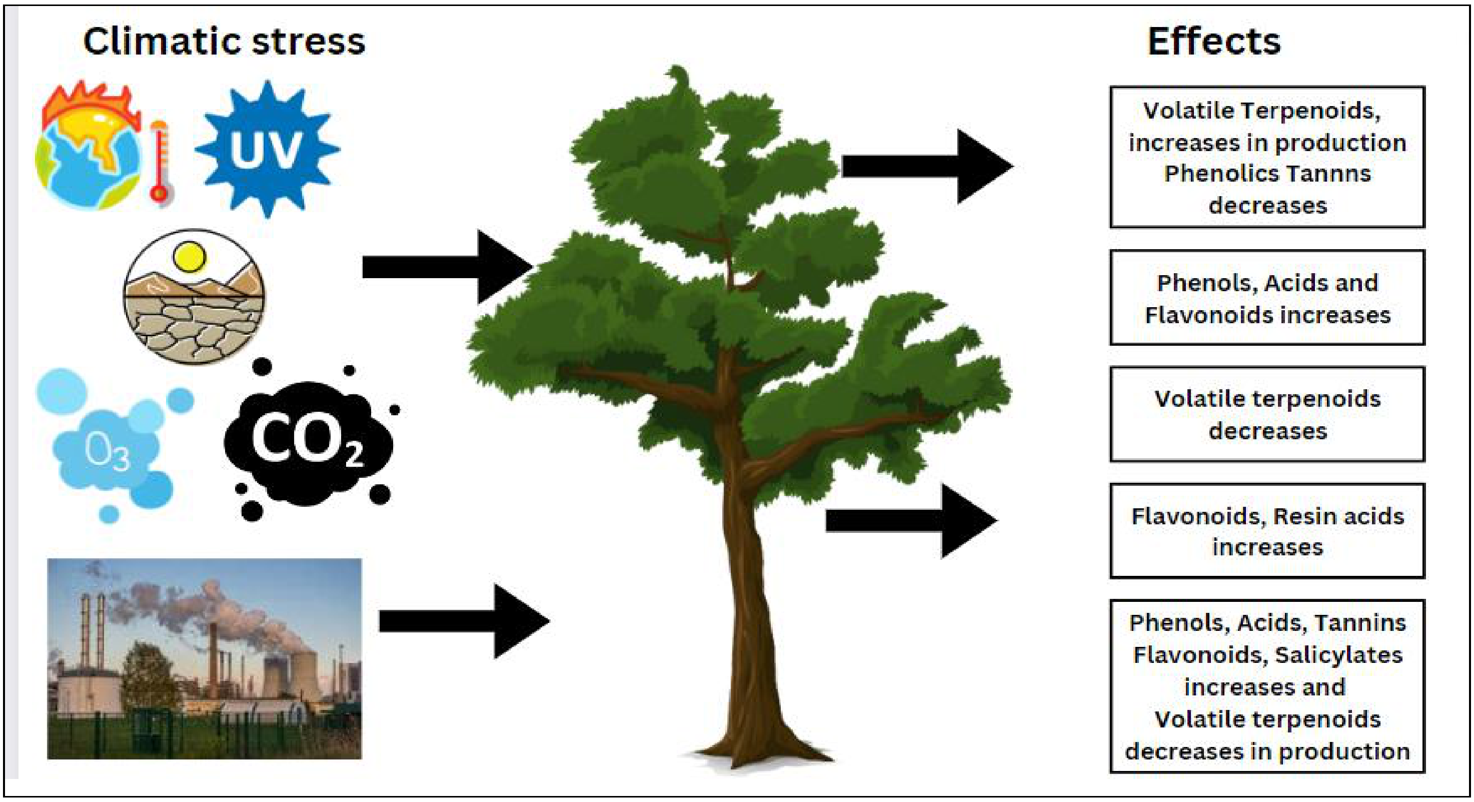


Fig.2. Factors affecting PSMs production in plants



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Factors Influencing Psms Production in Plants

It has been suggested that two possible processes are involved in responding to external stressors (40,57,61,63–66,74): membrane stabilization and direct antioxidative scavenging of reactive oxygen species (ROS) that are generated when the plant is under stress, as well as the attraction of pollinators to the plant (73–76,84,88,89,91). Superoxide dismutase, catalase, and peroxidase are enzymes that plant used to either directly catalyze ROS to less damaging chemicals or to facilitate the enzymatic regeneration of antioxidants while under oxidative stress (e.g., monodehydroascorbate reductase, dehydroascorbate reductase, and glutathione reductase). The non-volatile isoprenoids, such as tocopherols, zeaxanthin, and carnosic acid, can directly scavenge reactive oxygen species (ROS) through hydroxyl radical-mediated mechanism (101–103,105,109–111,113). A recent study has found that rising global temperatures, as well as other environmental factors including air O3, UV-B radiation, and the concentration of air CO_2, can increase plant stress and, as a result, either augment or limit the synthesis of PSM as a way to deal with these stresses. Yeshi and Wangchuk say tri-trophic interactions between plants and herbivorous and carnivorous arthropods and wounding cause plants to emit volatile organic compounds (VOCs). These emissions are also influenced by various environmental factors, such as temperature, light, moisture, and pollutants (2,3,109,111,4,5,36,40,101,103,104,106). Depending on how high these levels are, individual plant stress levels specifically impact the formation of PSMs. Compounds are encouraged or inhibited from being synthesized or emitted to accomplish this. There is a wide variety of purposes for PSMs in plants, but many factors affect how they are produced (2,8,10,13) (fig 2).

Natural Products in Medicine

Modern lifestyles, poor diets, and numerous stressors have been linked to the development of diseases such as diabetes, atherosclerosis, coronary heart disease, and cancer. Proinflammatory cytokines, whose release is controlled by nuclear factor-kappaB, are involved in most of these diseases. As a result of long-term oxidative stress produced by reactive oxygen species (ROS) and reactive nitrogen species (RNS), DNA, proteins, and lipids are damaged, and cellular antioxidant capacity is reduced, which affects several metabolic pathways and induces inflammation. As a result of oxidative stress, complex lipids, an essential component of neural tissue, can be damaged, leading to the development of neurodegenerative diseases such as Alzheimer's and Parkinson's (2–4,7,9). A variety of bioactive natural compounds have been used to treat human ailments. These compounds' stereochemical and functional properties are determined by their biological functions and the enzymes involved in their biosynthesis. Based on a space-filling model, phytochemicals complement enzyme active sites due to their distinctive shape, and their carefully placed functional groups allow them to interact with biological surfaces in noncovalent ways, such as hydrogen bonding, stacking, hydrophobic interactions, and dipolar interactions. When using natural goods as medicines, it is also essential to consider their easy biological transformation and potential cytotoxicity. The chemical properties of most representative groups of secondary metabolites involved in illness prevention and therapy will be reviewed later in this chapter. Chemoprotective phytochemicals have been used for many years to prevent undesirable cellular activity brought about by abnormal proinflammatory signal transmission. Many can decrease chronic inflammation by inhibiting NF-kB activation (19,21,23,25). Natural antioxidants, primarily polyphenolic derivatives, interfere with a variety of targets in the oxidative sequence; they reduce localized oxygen concentrations, scavenge ROS and RNS, bind metal ions associated with their generation and the transformation of lipid peroxides into peroxyl and alkoxyl radicals, and break chains by scavenging intermediate radicals, preventing continued hydrogen abstraction (1–4,7–10). Several decades of research have demonstrated that phenolic derivatives enhance cellular antioxidant capacity and inhibit cancer development. They serve as blockers (affecting the start stage) or suppressors (affecting the upcoming promotion and progression stages). These compounds may also protect lipids from oxidative damage by inhibiting specific stages (1–4,7–10), such as scavenging free radicals, stopping chain reactions, and chelating divalent cations that initiate oxidative reactions.

Phenolic Compounds

Flavonoids and benzoic and cinnamic acid derivatives are plants' most common phenolic compounds. Through the shikimate pathway (C6–C3), phenylpropanoid building blocks C6-C3 contribute to other plant phenolic backbones, including flavonoids, anthocyanidins, and coumarins. Cinnamonic acids are produced as part of the biosynthesis of polyphenolic units. Benzoic acid derivatives, such as gallic and ellagic acids, are also produced through this metabolic route (C6-C2-C6). Various biological targets are affected by their polyphenolic antioxidant activity, which is attributed to their chemical structure. Polyphenols have been shown to possess antioxidant and free radical scavenging properties based on the quantity and positioning of hydrogen-donating hydroxyl groups (O.H.). As glycosylation occurs, antioxidant capacity typically decreases, and conjugated double bonds and hydrogen-donating groups such as amino and thiol further reduce antioxidant capacity. The ability of polyphenols to delocalize electrons turns them into stable radicals, which explains their role as hydrogen-supplying molecules and radical scavengers. Several polyphenols block topoisomerases or phosphate tidylinositol kinases, two enzymes involved in free radical formation. However, they may chelate metal ions in the reverse direction, strengthening their catalytic potential for free radical production (1–4,7–10). Their ability to chelate metal ions implicated in free radical creation has also been described. Exogenous antioxidants' beneficial benefits become harmful when given in large doses. The ability of some polyphenols to behave as an antioxidant or a prooxidant depending on the concentration, the target molecule, and the oxidative oxidant source is a factor in polyphenol cytotoxicity. They can cause considerable oxidative damage to primary metabolites under specific circumstances (1–4,7–10). They can maintain and re-establish redox equilibrium, ensuring biological systems' health at optimum concentrations (1–4,7–10). (Table 1).

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Table 1: Classification, Types, and Examples of plant secondary metabolites

Classification	Types	Example
Terpenes	Monoterpenes	Geraniol
	Sesquiterpenes	Humulene
	Diterpenes	Cafesol
	Sesterpenes	Geranylfarsol
	Tetraterpenes	Lycopene
	Polyterpenes	Gutta-percha
Phenolics	Coumarin	Hydroxycoumarins
	Lignin	Resveratrol
	Flavonoids	Quercitin
	Isoflavonoids	Genistein
	Tannins	Tannins acid
N containing compounds	Alkaloids	Cocaine
	Cyanogenic glucosides	Dhurrin
	Non-protein amino acids	Canavanin
S containing compounds	Glutathione	
	Glucosinulate	Beta-D-Glucopyrinose
	Thionins	
	Defensins	

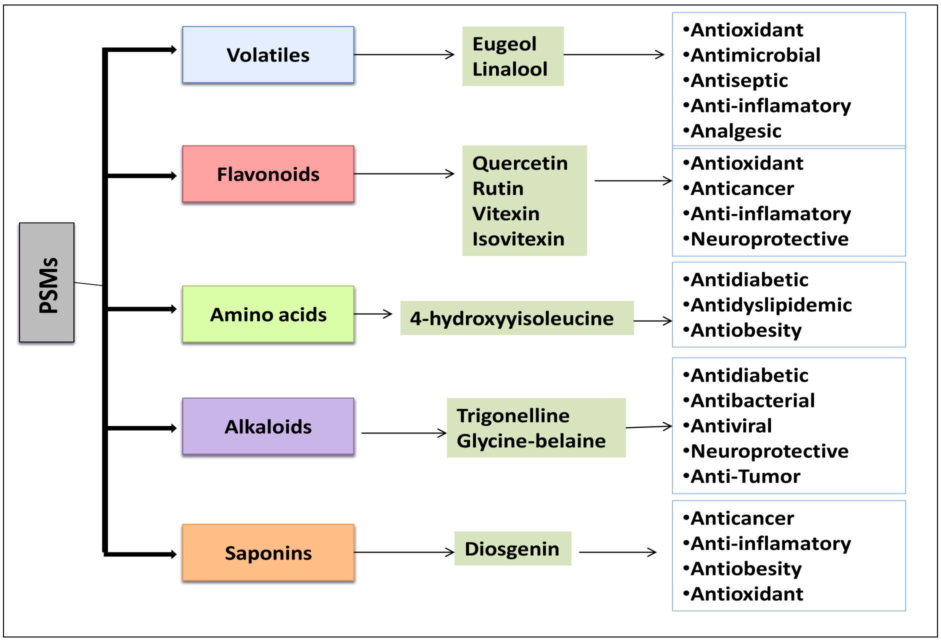
CAROTENOIDS: Carotenoids are naturally occurring tetraterpenes in plants, algae, and bacteria that photosynthesize light. Carotenoids are primarily found in fruits and vegetables in the average person's diet. Red, orange, and yellow carotenoids produce the vibrant colors of pumpkins, sweet potatoes, cantaloupes, papayas, and tomatoes. Leafy greens like spinach supply the body with carotenoids. Carotenoid pigments are hidden by chlorophyll, which prevents them from appearing red, orange, or yellow. Two important carotenoids are lycopene and zeaxanthin. The antioxidant properties of zeaxanthin and lycopene could help prevent cancer because they clean the body of reactive oxygen and nitrogen species (1,2,13,14,3,4,7–12). Carotenoids are tetraterpenoids with single and double bonds alternating with various cyclic or acyclic end groups (2,3,7,8,10). Their photoprotective properties include their ability to absorb U.V. rays, quench radicals generated during photo-oxidation, and inhibit lipid peroxidation due to their extended conjugated double-bond system that inhibits lipid peroxidation. It has been shown that dietary carotenoids have a photoprotective effect (1,2,13,14,3,4,7–12). Researchers claim that lycopene is the most potent inhibitor of the singlet oxygen radical (ROS), the most harmful ROS produced in the skin after exposure to sunlight (1,2,13,14,3,4,7–12). Lycopene protects against UVB photodamage by suppressing ornithine decarboxylase (ODC) and myeloperoxidase activity. Furthermore, it prevents caspase-3 cleavage in the apoptotic pathway and inflammation (1,2,13,14,3,4,7–12). It has been shown that a topical sunscreen cream containing lycopene-rich tomato extract is effective.

Furthermore, lycopene protects against phototoxicity when taken orally. As a result of daily consumption of 16 mg of lycopene, skin erythema caused by sun radiation decreased by 40% for ten weeks (38,45–48,50).It is moreover, adding -carotene (24 mg/day) or a carotenoid combination of -carotene, lutein, and lycopene (8 mg each/day) to the diet for 12 weeks protected against UV-induced erythema (38,45–48,50).

GLUCOSINOLATES: Several substances are derived from amino acids that are called glucosinolates. Among the most important sources of dietary fibre are cruciferous vegetables like broccoli, collard greens, cabbage, and mustard. To prevent cancer, glucosinolates induce apoptosis in the cells. It is believed that glucosinolates can help control the proliferation of cells in an area of uncontrollable cell growth. Furthermore, they possess antioxidative properties, crucial in defending the body against oxidative stress (38,45–48,50).

CAFFEINE: In plants, such as tea leaves, the alkaloid caffeine is produced in the plant's young leaves. There are two dietary sources of caffeine in the form of tea made from the Camellia sinensis plant and coffee made from the seeds of the Coffea arabica plant. As a stimulant, caffeine positively affects the mind and body, improving mental and physical well-being. The mechanism by which caffeine works is that it inhibits the adenosine receptors. When there is adenosine in the brain, the nerves in the brain are less active. Adenosine is also responsible for controlling neurotransmitters such as dopamine, which can lead to increased brain activity due to the release of adenosine. Despite being a drug, caffeine positively affects mood and productivity when consumed in moderation (38,45–48,50).

Fig. 3. Effects of different plant secondary metabolites on human health



SAPONINS: Allium species, including onions and garlic, contain saponins, which are terpenoids found in plants. In addition to that, they are also rich in spinach, tea, and legumes. This is because saponins help maintain heart health by attaching to and removing cholesterol from cell membranes. There is a decrease in the elasticity of the cell membrane due to LDL cholesterol intercalating into them and stiffening them. There is an increased risk of heart damage if the vascular system is rigid. Saponins can prevent this by attaching to that cholesterol and removing it from the arterial membranes by binding to it and removing it. As well as improving heart health, consuming saponins is also one way of enhancing it (38,45–48,50). In addition to supporting human health, secondary metabolites also play a significant role in plant defense. A secondary metabolite can significantly affect health promotion,

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disease prevention, and aesthetic qualities. To discover more about the properties of plant compounds and how they affect human health in the future, our natural resources must be protected because there are still undiscovered plant species.

FLAVONOIDS: Carotenoids cause the vibrant colors of pumpkins, sweet potatoes, cantaloupes, papayas, and tomatoes. Leafy greens like spinach provide the body with the majority of its carotenoids. Due to the high chlorophyll content, the carotenoid pigments do not appear red, orange, or yellow. Two important carotenoids are lycopene and zeaxanthin. In addition to their antioxidant properties, zeaxanthin and lycopene may improve cancer prevention (53–56,58–60). Several authors have studied plant flavonoids for their structure-activity correlations and pharmacological potential (73–76). There are several types of flavonoids, and the most common is 2-phenyl benzopyrene, which has a benzene ring (A) condensed with a heterocyclic six-membered ring (C) containing g-pyrone, pyran, or pyridinium. The phenyl ring (B) is substituted at C-2 and C-3 in flavonoids and isoflavonoids. The significant flavonoids are also classified into flavones, isoflavones, flavonols, flavanones, flavanols (catechins), and anthocyanidins, with flavones and catechins being the most potent anti-ROS compounds. Kaempferol, quercetin, morin, myricetin, and rutin are flavonol derivatives whose antioxidant activity has been implicated in anti-inflammatory, antiallergenic, antiviral, and anticancer properties. It has been demonstrated that apigenin, kaempferol, and quercetin activate the cellular antioxidant system by increasing glutathione levels (88,89,91–94).

FLAVONOLS: It has been shown that flavonols have cardioprotective effects on animals, lowering postischemic cardiac damage in rats and preventing the oxidation of low-density lipoprotein (LDL). Cheating redox-active metals, activating antioxidant enzymes, decreasing alpha-tocopherol radicals, and inhibiting oxidases can minimize peroxynitrite toxicity and ROS damage (1). Certain flavonols might enhance calcium homeostasis balance by binding to sarco/endoplasmic reticulum Ca2+-ATPase and altering its shape (98,103,105,106,108). Several extracts from Combretum very podophyllum are potent against Vibrio cholera and Enterococcus faecalis, including apigenin, genkwanin, kaempferol, rhamnazin, 30-Dimethylether, and rhamnocitrin. Antimicrobials are also present in other substances. These agents also worked well against Shigella and Micrococcus luteus (Martini et al., 2004). The ability of flavonols to scavenge free radicals depends on the pattern of substitutions they undergo; a significant positive effect has been reported for the B ring O-dihydroxy substitution (catechol arrangement), which increases the stability of the ortho-semiquinone radical.

The methylation of hydroxyl groups on the B ring significantly reduces antioxidant capacity; methylation of kaempferol's (one hydroxyl group at the B ring) scavenging capacity results in a 50% decrease in activity. It has been shown that rutin, the most prevalent glycoside in C. album with a catechol moiety, has substantially better scavenging capability than the similar kaempferol glycoside without one (66–68,71). It has also been noted that luteolin, which has a catechol arrangement at the B ring, is a more effective peroxyl radical scavenger than kaempferol, which displays a 3-OH group at the C ring. Quercetin which possesses both structural characteristics, behaves as a significantly more effective free radical scavenger than luteolin. This demonstrates the importance of the C-3 hydroxyl group. Most flavonols found in plants are glycosides and the type of sugar group they belong to influences how they are digested after consumption. Glucosides have been demonstrated to be nearly five times greater than that of rutinoside. This indicates that they can be actively absorbed from the small intestine. This contrasts with rutinosides, which appear absorbed from the colon after losing their glycosidic moiety (1,2,4,7,8). By replacing hydrogen atoms with methyl ones, flavonoids are significantly reduced in their antiparasitic activity. According to reports, caustic in has six times the activity against T. cruzi and more than double that against L. infantum of attempting (1,2,4,7,8) (Table 2).

Table 2: Different classes of Flavonoids and dietary sources

Class	Name	Dietary source
Flavones	Chrysin	Fruit skins
	Apigenin	Parsley, celery
Flavonones	Naringin	Citrus, grapefruits
	Naringenin	Citrus fruits
	Taxifolin	Citrus fruits
	Eriodictyol	Lemon
	Hesperidine	Oranges
Flavonol	Quercetin	Onion, Lettuce, tea, berries, tomato, apple, olive oil
	Kaenpferol	Grapefruit, leek, broccoli, black tea
	Rutin	Buckwheat, tomato skin, citrus, red pepper, red wine
Anthocyanidins	Cyanidin	Cheery, grape, strawberry
	Epigenidin	Stored fruits
	Delphinium	Dark fruits

Source: 1,2,4,7,8

ANTHOCYANINS: The majority of naturally occurring water-soluble pigments are anthocyanins, which are O-glycosides of flavilium cations and have one or more glycosidic moieties at C-3, C-5, or C-7 (1,2,4,7,8). The most prevalent glycosidic unit is glucose, while other sugars such as rhamnose, xylose, galactose, arabinose, and the disaccharide rutinose (6-O-L-rhamnosyl-D-glucose) can also be found (1,2,4,7,8). The most prevalent anthocyanins in nature are cyanidin, delphinidin, petunidin, peonidin, pelargonidin, and malvidin (17,21,25,28,32,36,41). Their antioxidant, anti-inflammatory, and detoxifying properties support their preventative actions against cancer and cardiovascular illnesses. They have been shown to neutralize a-tocopherol radicals, which improve fatty acid stability, and to scavenge superoxide and lipid peroxyl radicals much more quickly than flavonoids. They have been shown to inhibit digestive enzymes (a-glucosidase, b-amylase, protease, and lipase), which are therapeutic targets in the management of type II diabetes and obesity, as well as induce apoptosis, exhibit antiangiogenic and antiproliferative activities.

Additionally, anthocyanins have been shown to have anti-aging properties, lower the likelihood of developing degenerative diseases like Alzheimer's, and have inhibitory effects on HIV-1 (25,27,59,60,65,28–30,37,45–47,57). The quantity and location of free hydroxyl groups in an organic compound determine its antioxidant potential, which is caused by its capacity to generate stable radicals after scavenging harmful ones. Additionally, the catechol structure at the B ring improves its capacity to bind metal ions (25,27,59,60,65,28–30,37,45–47,57). However, it depends on variables like pH and reactive species (2,3,5,25); at a moderate pH, they can use a B ring to chelate metal ions (1–4,8). After passing via the liver and experiencing methylation and glucuronide reactions, certain anthocyanin glycosides are absorbed from the stomach and enter the bloodstream before being delivered to the intestine. Others travel to the small intestine, transforming a mixture of chalcone and quinonoid forms. It has also been proposed that additional absorption occurs in the jejunum, where microbiota may metabolize

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anthocyanins by disrupting the C ring, producing phenolic acids and aldehydes. After cyanidin-3-glucoside and rutinoside are transformed, protocatechuic acid (3,4-dihydroxybenzoic acid) has been described as a significant metabolite (1–4,8). The biological effects of anthocyanins, such as their antioxidant, antiobesity, cardiovascular protection, and anti-inflammatory capabilities, have been attributed to it. The human large intestine also produces phenolic derivatives such as syringic acid, 2,4,6-trihydroxybenzaldehyde, and 3-O-methylmalonic acid.

QUINONES: Quinones have dehydrogenating or oxidizing properties and, after reaction, become an utterly aromatic system. Others lack phenolic hydroxyl groups; among the latter, thymoquinone from Nigella sativa volatile oil has been demonstrated to have anti-inflammatory and antineoplastic properties. Some of these natural compounds are phenolic derivatives. It has been found to influence the immune system by modifying inflammatory mediators' levels and triggering apoptosis by p53-dependent and p53-independent pathways in cancer cell lines. This bioactive benzoquinone has been demonstrated to improve the therapeutic index and protect non-tumour tissues from chemotherapy-induced harm when combined with anticancer medications (1–4,8). It has been noted that naphthoquinones, which contain phenolic hydroxyl groups, exhibit antiprotozoal effects; several of them have been suggested as potential leads for drug development (1–4,8). Plumbagin, a 1,4-naphthoquinone, can cause oxidative stress in Trypanosoma congolense and T. cruzi after being converted to semi-quinone radicals by trypanothione reductase, a crucial enzyme in the antioxidant thiol metabolism of trypanosomes. It has been noted that diospyrin and a few semi-synthetic derivatives show proapoptotic and anticancer properties (1–4,8). On T. brucei bloodstream forms, it has also exhibited antitrypanosomal activity in vitro; semi-synthetic monomethylated derivatives have been reported to be more effective than the parent molecule (1–4,8). Leishmania donovani promastigote growth has also been inhibited by diospyrin, likely due to the parasite DNA topoisomerase I catalytic activity (1–4,8). Mansonone F, a nonphenolic sesquiterpene o-quinone generated by Mansonia altissimo and Ulmus pumila, has been shown by (1–4,8) to have antibacterial and antiproliferative properties. Mansonone F has exhibited efficacy against anti-methicillin-resistant S. aureus due to its quinone moiety and tricyclic structure, with the 2, 3-olefin being somewhat beneficial. According to SAR tests on numerous synthesized analogues with various substituents, lipophilicity is crucial to bolster its action against this resistant bacterium by (1–4,8).

Impact of Plant Secondary Metabolites on Foraging Animals

Because some PSMs have been shown to harm animals potentially, herbivores reduce their intake of plants containing PSMs based on the number of metabolites in them (26,32–37,39). Paracelsus (1493–1541) wrote, "All substances are poisons; there is none, not a poison." The correct dose differentiates a poison from a remedy" (12–19). Alkaloids are secondary metabolites of plants that are toxic to ruminants. The binding or other mechanisms by which alkaloids and terpenes act can, however, be reduced by supplementing animals with alkaloids or terpenes in plants such as tall fescue (Schedonorus arundinaceous) and sagebrush (Artemisia tridentata), either by binding or through other mechanisms (23–25,27–31). Phytochemicals have antioxidative and cancer-fighting properties(7–12). The protein-binding properties of condensed tannins make them similar to bypass proteins commonly found in ruminant nutrition, which improve amino acid absorption. Ruminants' internal parasites and worms are suppressed by condensed tannins (1–6,8). Saponins are similar to tannins in precipitating proteins and decreasing animal cholesterol (1–6,8). In addition to boosting rumen-microbial protein synthesis, saponins may decrease protozoa in the rumen and improve growth efficiency (1–6,8). These metabolites have historically been bred out of plants used as crops and forages because of the concentration in monoculture cultivation and the impact of PSMs on lowering forage consumption (1–6,8). When given a variety of forages with various kinds and amounts of PSMs, foraging animals eat more and perform better (24,25,27,30). PSMs positively affect foraging animals' health when administered in the right proportions (9–15). Animals eat 50–75 species at once. It has historically been the case that researchers and producers focused on the three to five species that contribute the most calories and protein to livestock. In addition to the meat and dairy we get from these 50–75 additional plant species, they are just as crucial for the health of humans and animals (18,19,29,20–25,27,28).

Plant Secondary Metabolites, Herbivores, and Human Health

Various PSMs improve the health of foraging animals and the taste, richness, and quality of cheese, milk, and meat intended for human consumption (18,19,29,20–25,27,28). Animals' diets are, therefore, related to our health through the chemical properties of the plant species they eat. Antioxidants, immunomodulators, anti-inflammatory, and antibacterial agents in plants protect humans and animals from diseases and infections (2,3,12,13,4–11). In livestock, phytochemicals are transformed into biochemicals incorporated into meat and fat consumed by humans. In the human body, these biochemicals become healthy biochemicals. Herbs, spices, vegetables, and phytochemically rich fruits also offer these benefits (2–5). Substances that reduce oxidative stress and inflammation associated with cancer, cardiovascular disease, and metabolic syndrome may benefit humans and animals. Plants have historically provided medication to all animals, including humans. Many medications (such as antibiotics, analgesics, and fever reducers) are made from plants that naturally contain these compounds. Numerous reviews describe PSMs' health-promoting properties for animals, including humans (2,3,12,13,4–11). By reintegrating plants with various PSMs into our crops and forages, we can reconsider these compounds' fundamentally important role in health before modern medicine (2–5).

Pharmacological Activities of Secondary Metabolites

Plants produce a vast and varied range of S.M. They include numerous bioactive compounds that serve as plant defence agents. These chemicals neutralize bacteria or animal cells by interacting with specific targets within those structures. However, plants' various metabolic routes to produce S.M. ensures unique structures in these defense molecules. These structures can be used to create effective medications and pharmaceuticals. Because of this, plants are a significant source of compounds that can enhance health and treat ailments. Plant anticancer, antioxidant, and antibacterial properties are among their positive pharmacological effects (2–5). Plants synthesize a large and varied array of S.M. Many of these are bioactive compounds that plants employ as defense chemicals. These

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chemicals exhibit biological activity that neutralizes them by interacting with particular targets in animal or microbial cells.
On the other hand, the variety of metabolic routes plants use to produce S.M. ensures the presence of particular structures in these defensive molecules. These structures are helpful for the development of novel medications and therapeutic products. Plants are a significant source of compounds that can enhance health and treat ailments, which is why they are so beneficial. Among the advantageous pharmacological properties of the plants, anticancer, antioxidant, and antibacterial properties stand out (10–12). Antimicrobial resistance is another health issue examined in medicinal plants. According to estimates, some 25,000 patients in the European Union die each year from diseases brought on by resistant bacteria. Estimates show 77 thousand deaths are caused by resistant bacteria annually in the United States. These figures make it abundantly evident that the pharmaceutical industry needs and prioritizes novel compounds with antibacterial action. Plant extracts have bacterial-fighting properties against Gram-positive and Gram-negative bacteria (7–9).
Additionally, scientists have mentioned a potential synergy between antibiotics and plant extracts (11–13). Polyphenols' antibacterial action is based on their capacity to prevent microbes' development, reproduction, respiration, and other essential functions. This effect is caused by the oxidation of particular enzymes, inhibiting several vital processes like respiration. Additionally, polyphenols inhibit bacteria protein creation by binding to DNA chains. Some scientists say polyphenols may rupture microorganism cell membranes, leading to cell apoptosis (11–13). Due to their lipophilic character, monoterpenes interact with phospholipids in bacterial cell membranes. Cell lysis results from disrupting the ordered structure of the membranes (11–13). Plant extracts have also been investigated for antioxidant properties. Polyphenols or phenolic chemicals are primarily responsible. Since the missing electrons are more delocalized in flavonoids' structure than in other compounds, they serve as buffers that trap free radicals. This produces the less reactive flavin radical. Reactive oxygen species are prevented from forming by flavonols like quercetin's ability to bind transition metal ions like iron or copper (11–13).

Conclusion

Significant progress has been made in understanding plant secondary metabolites and their function in human health. Numerous investigations are being carried out to comprehend PSM function in various physiological processes and metabolisms. Other studies demonstrate the importance of secondary metabolites in preventing diseases, including CVD (cardiovascular disease), diabetes, and stress, as well as in treating diseases and enhancing health. A few more studies have also demonstrated the beneficial effects of regular consumption of vegetables high in polyphenols on people's general health. According to research and studies, plant secondary metabolites are promising future micronutrients, and evidence supports this claim. They may cure disorders. According to numerous studies, PSM extracts benefit human health because of their antioxidant, anti-inflammatory, and antibacterial properties. However, additional research is required before PSMs can be categorized as vital dietary supplements packed with bioactive components. They can also be commercialized as a vital nutrient for overall health and lead a holistic lifestyle.

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