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Plant secondary metabolites as defenses: A review

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Abstract: Plant secondary metabolites have a variety of functions, including mediating relationships between organisms, responding to environmental challenges, and protecting plants against infections, pests, and herbivores. In a similar way, through controlling plant metabolism, plant microbiomes take part in many of the aforementioned processes indirectly or directly. Researchers have discovered that plants may affect their microbiome by secreting a variety of metabolites, and that the microbiome could likewise affect the metabolome of the host plant. Pesticides are agrochemicals that are employed to safeguard humans and plants from numerous illnesses in urban green zones, public health initiatives, and agricultural fields. The careless use of chemical pesticides is destroying our ecology. As a result, it is necessary to investigate environmentally benign alternatives to pathogen management, such as plant-based metabolites. According to literature, plant metabolites have been shown to have the ability to battle plant pathogens. Phenolics, flavonoids, and alkaloids are a few of the secondary metabolites of plants that have been covered in this study.

Keywords: alkaloids, flavonoids, phenolics, plant pathogens, secondary metabolites

INTRODUCTION

Since natural systems present plants with a variety of conflicting forces, plants have developed an extensive defensive system to cope with abiotic and biotic stresses [UL HAQ *et al.* 2019]. Because a multitude of stress factors interact to impact plants, every alteration in plant metabolic physiology cannot be attributed to a single stress component [GAŁCZYŃSKA *et al.* 2019; HEDJAL *et al.* 2018]. Various response pathways are activated in response to a particular stress, and there are several interconnections between signaling routes for herbivorous and pathogens insects [BODENHAUSEN, REYMOND 2007]. Some of these response mechanisms are activated independently of the antimicrobial nature, whereas others are triggered by infection [MANNIELLO *et al.* 2021]. Other plant defensive mechanisms include the creation of polymeric barriers to prevent pathogen entry and the production of pathogen cell wall destroying enzymes (PCWDEs) [Belair *et al.* 2022; Tyśkiewicz *et al.* 2022]. Plant pathogens generate PCWDEs as a subgroup of carbohydrate-active enzymes to deteriorate plant cell walls. Plants release PCWDE inhibitor proteins (PIPs) to limit the effect of PCWDEs [Prasanth *et al.* 2022]. Plants also have unique signaling and identification mechanisms that allow them to quickly identify pathogen entry and mount an appropriate defensive response [Waheed *et al.* 2022]. In the event that they become infected, plants have developed to adapt to further microbial attacks [Tsuda, Katagiri 2010; Wu *et al.* 2014]. Secondary metabolism, which is distinct from primary metabolism, describes metabolic pathways and the tiny molecules they produce as byproducts that are not necessary for the growth and reproduction of the organism [Dixon *et al.* 2010]. Plant secondary metabolites (PSMs) are a diverse group of substances that are produced by secondary metabolic pathways in plants [Divekar *et al.* 2022]. PSMs contain a significant number of structurally varied chemicals that were either produced as intermediates in the biosynthetic pathways of these primary metabolites or as primary metabolites themselves [Jamloki *et al.* 2021; Yeshi *et al.* 2022]. A wide range of secondary metabolites are produced by plants that shield them from microbes and predators, as well as deter herbivores and microbes, depending on their poisonous nature. Certain secondary metabolites aid plant communication with other organisms, while others defend plants against abiotic stress such as metal toxicity, ozone, and ultraviolet (UV)-B, making secondary metabolites crucial for development and growth [Chakraborty, Acharya 2017; Koza *et al.* 2022]. CO_2 fixation enzymes, nitrogen metabolism, motility, pigmentation, survival, and growth are all known to be harmed by UV-B [Pandey *et al.* 2020].

CLASSIFICATION

PSMs are typically categorized into six broad molecular families, depending on their biosynthesis pathways: phenolics, terpenes, steroids, alkaloids, and flavonoids [Zhang *et al.* 2021]. Sulphur/nitrogen (S/N), terpenes, and phenolics-containing compounds are the principal categories of secondary metabolites generated by plants (Fig. 1).

The greatest class of PSMs are terpenes. Some terpenes, such as gibberellins and brassinosteroids, are engaged in basic processes, such as plant growth and development, even though the majority of terpenes are crucial for plant defense [Ninkuu *et al.* 2021; Sharma *et al.* 2022]. A total of 25,000 different compounds are classified as terpenes, and they serve a variety of purposes such as preventing oviposition, feeding, or direct toxicity [Ansari, Akhtar 2019]. Terpenes have the ability to draw pollination insects. They have a fundamental unit called 5-C isoprene (isoterpenes, C_5H_8), which is toxic to herbivores [Galili *et al.* 2005; Hillier, Lathe 2019].

Nearly 10,000 different secondary metabolites make up the diverse category of chemicals known as plant phenols [Bartwal *et al.* 2013]. Secondary metabolites with a hydroxyl functional group (phenyl group) attached to an aromatic ring are known as phenolics. They are the most widely dispersed secondary metabolites [Verma, Shukla 2015]. Simple phenols (such as catechols and derivatives of hydroxybenzoic acid), lignins, condensed tannins, stilbenes, catechol melanins, and flavonoids are all examples of phenolic compounds [Cheynier *et al.* 2013]. Phenolics are a diverse group of molecules due to their unique chemical structures. In addition to aggressively deterring herbivores, these metabolites also actively entice pollinators to plants [Badri *et al.* 2013]. Herbivores can be directly poisoned by phenols, or phenols can be oxidized by enzymes like polyphenol oxidases or peroxidases to produce toxic compounds that interfere physiologically with insect development and growth [Hammer, Bowers 2015].

Glucosides, which are mostly found in the Brassicaceae and Capparales plant taxa, are sulfur-containing secondary metabolites [War *et al.* 2020]. About 120 structural structures of the derivatives of amino acids known as glucosides were identified. The kind of glucoside is often determined by the side chain's amino acid precursor [Blažević *et al.* 2020]. Younger leaves and plant reproductive parts have been found to have higher levels of

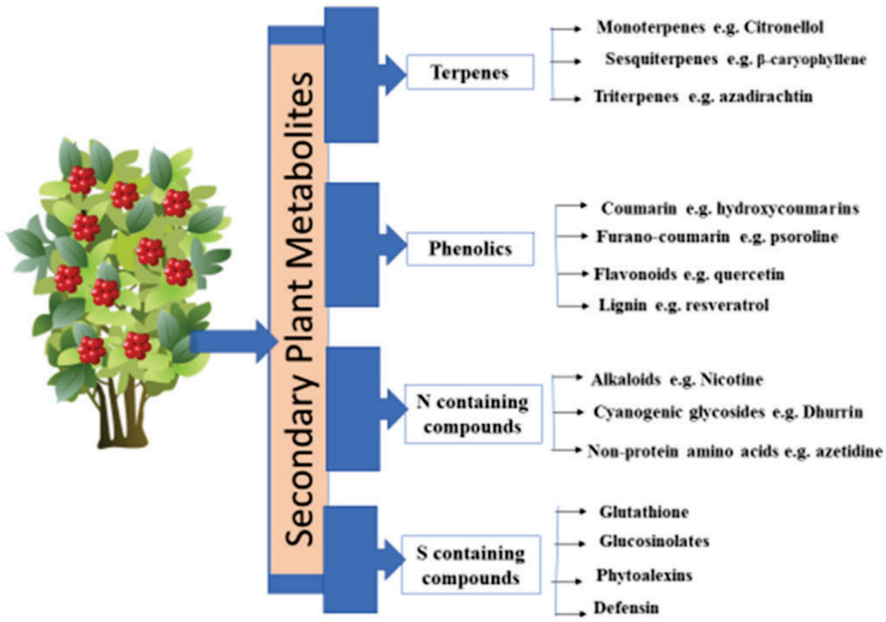

Fig. 1. Types of secondary metabolites; source: Garcia-Mier *et al.* [2019]

glucosinolate [Tsunoda *et al.* 2017]. Usually, glucosinolates are found in the vacuoles of cells, where myrosinases have a protective coating over them (thioglucosidase). Damage caused by herbivores leads to the breakdown of plant cells, which in turn causes myrosinases to convert glucosinolates into poisonous compounds such as isothiocyanates, thiocyanates, and nitriles. These glucosinolate breakdown products have been demonstrated to be just as efficient as synthetic insecticides at deterring herbivorous insects from feeding by being extremely poisonous to them [Keith, Mitchell-Olds 2017].

Alkaloids are among the second-generation metabolites that contain nitrogen [Michael 2016]. The plant kingdom has reported about 10,000 distinct alkaloid compounds to date. On the basis of biosynthesis, alkaloids are separated into three classes: (a) proto-alkaloids, (b) pseudo-alkaloids, and (c) true alkaloids [Kilgore, Kutchan 2016]. Proto-alkaloids and real alkaloids both originate from amino acids. Pseudo-alkaloids, however, are not made from amino acids [Lichman 2021; Rajput *et al.* 2022]. True alkaloids share a heterocyclic ring with nitrogen and are derived from amino acids. Because alkaloids interfere with DNA replication, enzyme activity, and protein synthesis, they are poisonous to herbivores and disrupt neural signal transduction [Bribi 2018].

Amino acids are the primary sources of sulphur and nitrogen-containing compounds [Rodrigues-Corrêa, Fett-Neto 2019]. *In vitro* studies of plants whose secondary metabolite expression was altered using current methods have demonstrated the defensive significance of secondary metabolites [Li *et al.* 2020]. the result of plant pathogen interactions over millions of years are secondary metabolites, and more than one hundred thousand metabolites are thought to be involved in the plant protection mechanism; thus, the situation is still unclear. Whereas large concentrations of secondary metabolites are expected to make plants better able to withstand biotic and abiotic stressors, for plant growth and reproduction, their synthesis is known to be costly [Piasecka *et al.* 2015]. Numerous investigations revealed that hundreds of plant chemicals have chemical and ecological defense functions, spawning a new field of study called ecological biochemistry [Kuhlisch, Pohnert 2015; Nelson, Whitehead 2021; Shear 2015; Stanley *et al.* 2016]. PSMs provide a variety of functions, including disease, insect, and herbivore defense, stress response, and modulating organismal relationships [Barak 2022]. Plant microbiomes, on the other hand, regulate plant metabolism and so play a role in many of the above-mentioned activities. Plants may influence their microbiome by secreting different metabolites, according to studies, and the microbiome, in turn, can alter the host plant's metabolome. However, little is understood about the interactions that influence phenotypic alterations [Singh *et al.* 2019]. Phenolics, flavonoids, and alkaloids are a few of the secondary metabolites of plants that have been covered in this study.

PLANT DEFENSE THROUGH PSMs

Flavonoids and phenylpropanoids, which have distinct modes of action, are broadly dispersed chemicals in the plant defense system [Hildreth *et al.* 2022]. Lots of antifungal agents address only six processes, the majority of which function in tandem with cell signaling molecules and have physiological effects or target pathogen components such as reproductive system, DNA alkylation, and enzyme inhibition, etc. [Le Roy *et al.* 2016]. The majority of these compounds include phenolics with hydroxyl groups that are prone to disintegrate into phenolate ions [Hadacek 2002]. Because phenolic hydroxyl groups establish hydrogen and ionic connections with protons and peptides, the larger their number, the more denaturing and astringent the product [Wink 2018]. Proteins cannot function effectively without confirmation, i.e., a good three-dimensional structure. Any alteration in protein conformation alters the characteristics of the protein, preventing interaction with other RNA/DNA and proteins [Marsafari *et al.* 2020]. Secondary metabolites engage with free amino-, OH-, or SH- groups to form a covalent link, which changes the 3D structure of proteins, resulting in a change in protein turnover or loss of function [Tiwari *et al.* 2016]. Stronger ionic bonds and hydrogen bonds are formed by polyphenols [Han *et al.* 2020]. The protein's flexibility is altered whenever these weak non-covalent bonds form at the same time and interact with a protein, resulting in protein inactivation. Since phenols' polar nature reduces their absorption after oral ingestion, they are less hazardous compounds [Wang *et al.* 2019]. A wood degradation test using stilbene impregnated birch and aspen samples was used to investigate pinosylvin's influence and resveratrol fungal growth [Seppänen *et al.* 2004]. Resveratrol stimulates the development of fungal growth at pinosylvin concentrations that are sufficient to prohibit fungal growth [Goyal *et al.* 2012; Salehi *et al.* 2018].

PSMs AS ANTIVIRAL, ANTIFUNGAL, AND ANTIBACTERIAL COMPOUNDS

Flavonoids, phenolics, and alkaloids, among other secondary plant metabolic products have antiviral properties [Hussein, El-Anssary 2018]. Alkaloids have various physiologically active molecules that affect living beings due to their diverse architectures. Antiviral activities have been discovered in over 18,000 alkaloids found in traditional Chinese herbs [Jubair *et al.* 2021]. The plantain lily (*Hosta plantaginea*) alkaloid 7-deoxy-trans-dihydronarciclasine (named E144) has an anti-TMV activity with a minimum IC50 value of 1.80 μM [Yang, He 2021]. Furthermore, Bruceine-D, which may be found in the Brassica javanica extract, has an inhibiting effect against TMV, CMV, and PVY [Mao *et al.* 2019]. White goosefoot (*Chenopodium amaranticolor*) extract embedded with 100 $\mu g \cdot dm^{-3}$ Bruceine-D has been shown to suppress more than 90% of CMV and PVY infection after 15 minutes of treatment [Aliev, Kurbanova 2022].

According to research, the majority of secondary metabolites are thought to have antifungal properties [Basile *et al.* 2015]. Allied flavonoids and phenolics make up a wide set of phytochemicals [Velu *et al.* 2018]. As indicated in Table 1, these chemicals are found in large quantities in the leaves and skins of fruits and play a role in plant disease resistance, UV resistance, and defense against pigmentation.

Phenolics have been shown to alter microbe cell permeability and induce functional and structural distortion of membrane proteins, causing membrane bonded enzymes, ATP generation and preservation system, pH gradient, and substrate consumption for ATP synthesis to be disrupted [Benhamou *et al.* 1996]. The pathogens' development in the apoplast is slowed by

Table 1. List the antifungal properties of phenolic compounds

Fungus	Chemical compound
Phytophthora infestans	vanillic acid
Phytophthora	oleuropein
Phoma tracheiphila	nobiletin
Penicillium digitatum	naringin
Monilinia fructicola	genistein
Helminthosporium sativum	hordatin A
Fusarium oxysporum	chlorogenic acid
Eutypa lata	salicylic acid
Colletotrichum circinans	protocatechuic acid
Botrytis cinerea	benzaldehyde
Aspergillus	flavones

Source: own elaboration based on literature.

antimicrobial substances [Kwon *et al.* 2008]. Secondary metabolites may have antibacterial properties, according to one research [Helmann *et al.* 2022]. Legume leaf extracts in liquid form, such as *Zapoteca portoricensis*, were also shown to contain flavonoids. The antimicrobial substances' defensive role in the study of *Arabidopsis* root exudates infected with *Pseudomonas syringae* was identified in the root exudates as a defense mechanism against this bacterium [Helmann *et al.* 2022]. It was discovered that plants infected with strains that are not pathogenic produce a greater quantity of secondary metabolites than plants inoculated with virulent strains and that *P. syringae* is unable to infect *Arabidopsis* in seven out of eight strains [O'Malley, Anderson 2021; Valette *et al.* 2020]. Non-pathogenic bacteria have a mild antibacterial effect on non-infecting strains. Infecting strains had no effect on root exudation's antibacterial efficacy [Guo *et al.* 2021].

CONCLUSIONS

Due to their significant role in the physiology of plant stress, secondary metabolites have attracted a lot of attention. Even in challenging circumstances, these metabolites have the potential to preserve the health and productivity of food crops with little loss. By increasing the synthesis of numerous enzymes involved in the production of secondary metabolites and raising the expression of various genes involved in plant resistance mechanisms, PSMs mediate a variety of defensive functions. In this work, in order to control bacterial, viral, fungal, and insect diseases, we have highlighted the most recent developments in the use of secondary metabolites. With the passage of time, plants acquired defense systems against a variety of abiotic and biotic stressors. Apart from secondary metabolites that are either shown to be produced or caused by infection, sophisticated techniques are needed to accurately examine the relationship between crop resistance management and nitrogen and sulphur treatment. Previous research has shown that the quantity of certain substances in the growing medium affects the formation of N- and S-containing secondary metabolites, implying that an optimal amount of these nutrients is necessary for healthy plant development and resistance to environmental and microorganisms' challenges.

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