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Secondary Metabolites as Health Building Functional Compounds

Shivam Sharma, D. R. Chaudhary

Department of Vegetable Science,
CSK HPKV Palampur,
Himachal Pradesh, India.

Viveka Katoch

Department of Seed Science and Technology,
CSK HPKV Palampur,
Himachal Pradesh, India.

Shubham Verma

Department of Genetics and Plant Breeding,
CSK HPKV Palampur,
Himachal Pradesh, India.

Anuj Choudhary

Department of Botany,
Punjab Agriculture University,
Ludhiana, Punjab.

Sahil Mehta

School of Agricultural Sciences,
K.R. Mangalam University,
Gurugram, Haryana, India.

Himanshu Thakur

Department of Entomology,
CSK HPKV Palampur,
Himachal Pradesh, India.

Sahil Negi

Department of Biotechnology,
CSK HPKV Palampur,
Himachal Pradesh, India.

Abstract:

Secondary metabolites are known to access extra health benefits in addition to basic nutrition and their biological activities are well reported and documented from time to time about their effectiveness and reliability. Currently, most heated debate due to prevalence of pandemic COVID-19 is to discover novel secondary metabolites having potency to battle severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Cancer, diabetes and obesity are most fatal widespread disease across the globe with fact of interest that obesity along with type-2 diabetes have been related with more probability of cancer. Moreover, health ailments due to overconsumption of secondary metabolites also need attention for risk assessment of the same. But at present, very limited literature is available on toxicity, risk assessment and health safety. Therefore, this chapter is focused on classification, source, plant function, biological significance and toxicity of plant secondary metabolites available till date.

Keywords: *COVID-19. SARS-CoV-2, PSMs.*

3.1 Introduction:

Organic compounds synthesized by plant can be categorized into primary metabolites directly involved in plant growth and metabolic processes whereas, secondary metabolites are metabolic byproducts or intermediates which are not necessary for plant's normal growth and development but are essential for the interaction of plants with their environment and are often generated in response to stress (Yang et al. 2018). Due to structurally diverse group of low-molecular weight these are known as plant secondary metabolites (PSMs) having origin from either primary metabolites or biosynthetic pathway intermediates (Piasecka et al. 2015).

Highly diverse set of pathogen-inducible metabolic pathways that have led to the accretion of thousands of distinct metabolites and having major role in the adaptation of plants (Isah, 2019). It is now well evident that secondary metabolites are active and important components of defence mechanisms, particularly in the chemical warfare between plants and their pathogens. Some of these substances have also been shown to have roles in warding off herbivores, attracting pollinators, acting as allelopathic agents, protecting against toxicity, UV radiation and other abiotic and biotic stresses, and signal transduction (Pang et al. 2021). The increased importance in these compounds is sparked by their commercial relevance as dyes, medicines, polymers, waxes, glues, fibers, antibiotics, herbicides, and insecticides (Lu et al. 2017). In humans, they possess various health benefits; many of them exhibit anti-microbial, anti-inflammatory, and anti-allergic actions due to their antioxidant activity and are able to prevent illnesses (Pedro et al. 2016).

Their role is indispensable in several human diseases for example. Sulforaphane a glucosinolate found in cruciferous vegetables like broccoli, and cabbage, showed anti-inflammatory effects against SARS-CoV-2 respiratory infections (Ordonez et al. 2022). Their multifaceted involvement has led to reevaluating their potential functions, particularly in ecological interactions, was prompted by the increased awareness in plant and human life.

3.2 Classification, Source and Role of Secondary Metabolites in Plant Functions:

As per biosynthetic pathways, these can be grouped into four bigger molecular families: terpenes, phenols, glycosides and alkaloids (**Fig.1**; Kessler and Kalske, 2018). Terpenoids are volatile compounds responsible for fragrance such as carotenoids, sterols, limonene and pinene. Phenolics act as antioxidants, structural polymers (lignins), attractants and UV shield (flavonoids), signaling molecules (salicylic acid) and defense response chemicals (tannins and phytoalexins). Glycosides having both sugar and non-sugar aglycone moiety such as cyanogenic glucosides whereas alkaloids contain at least one nitrogen atom and are highly reactive for biological activity such as caffeine, morphine, papaverine and coaine etc. PSMs performs crucial functions of repelling pests and pathogens and serving as symbiosis signals between plants and microorganisms (**Table 3.1**; Guerrieri et al. 2019).

Table 3.1: Classification source and role of secondary metabolites in plant functions

Sr. No.	Secondary metabolite	Source	Class	Plant Function	Reference
1.	Taxanes	*Taxus spp.*	Diterpene	Repress growth and cell cycle progression	Sharma et al. 2014
2.	Camptothecin	*Camptotheca acuminata*	Monoterpene indole	Cytotoxic to invader pathogens	Mazumder et al. 2022
3.	Baicalin	*Scutellaria baicalensis*	Flavonoids	Induces apoptosis and prevent signal pathways	Hu et al. 2022
4.	Isoflavones and saponins	*Glycine max*	Flavonoids	Association with rhizobia	Hartman et al. 2017
5	Flavones	*Laccaria bicolor*	Flavonoids	Germination of *Pisolithus and Suillus* enhanced	Pei et al. 2020
6	7, 4′-dihydroxyflavone	*Medicago sativa*	Flavonoid	Increase in soil *Acidobacteria*	Szoboszlay et al. 2016
7	Hydroxycinnamic acid amide	Potato	Flavonoid	Plant cell wall reinforcement to resist *Phytopthora infestans*	Yogendra et al. 2015
8	Steroidal glycoalkaloid	Tobacco *and C. roseus*	Glycoalkaloid	Defend against phytopathogens and insect infestation	Cardenas et al. 2016
9	Phytoalexins	*Brassica* sp.	Phenolics	Resist pathogenic colonization	Ahuja et al. 2012
10	Triterpenes saponins	*Medicago truncatula*	Triterpenes	Abiotic and biotic stress response	Mertens et al. 2016
11	Proanthocyanidins (PA)	Norway spruce	Flavonoid	Resistance against *Heterobasidion annosum*	Danielsson et al. 2011

3.3 Biological Activities and Significance:

Wide range of biological activities exhibited by secondary metabolites has been reported and documented well from time to time via different researcher **(Table 3.2)** and many yet to come. Currently, most heated debate due to prevalence of pandemic COVID-19 is to discover novel secondary metabolites having potency to battle severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Recently, family Brassicaceae; nearly cole crops which are known as 'Crown Jewel of Nutrition' and specifically Broccoli due to presence of sulforaphane showed promising results with anti-inflammatory activity to battle SARS-CoV-2 (Ordonez et al. 2022). On the same note, myricetin inhibited SARS-CoV-2 viral replication and ameliorated pulmonary inflammation (Xiao et al. 2021).

Cancer, diabetes and obesity are most fatal widespread disease across the globe with fact of interest that obesity along with type-2 diabetes have been linked with more chances of cancer incidence (Scully et al. 2021). Indeed, certain secondary metabolites viz., glucoraphanin, naringenin, luteolin, lutein and cyanindin-3-glucoside revealed their effectiveness in treatment and management of the same. Glucoraphanin a glucosinolate of sulforaphane in numerous studies (Gupta et al. 2022; Tian et al. 2020; Xu et al. 2018; revealed and confirmed antidiabetic activities.

Table 3.2: Biological activity and significance of plant secondary metabolites

Sr. No.	Secondary metabolite	Class	Biological activity and significance	Reference
1	Sulforaphane	Glucosinolate	Anti-cancerous, antidiabetic and anti-cardiovascular	Zhang et al. 2022; Rhoden et al. 2021
2	Glucoraphanin	Glucosinolate	Antiobesity, antidiabetic	Xu et al. 2018
3	Indole-3-carbinol	Glucosinolate	Leukaemia therapeutic agents	Karimabad et al. 2022
4	Isothiocyanates	Glucosinolate	Anti-cancerous and chemopreventive	Mitsiogianni et al. 2019
5	Sinigrin	Glucosinolate	Antimicrobial	Tarar A & Peng, 2022
6	Glucoerucin, erucin	Glucosinolate	Antiobesity	Lucarini et al. 2019; Chaea et al. 2015
7	Quercetin	Flavonols	Anti-cancerous	Veiga et al. 2022
8	Catechin	Flavonols	Antiviral i.e., severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)	Chourasia et al. 2021
9	p-coumaric	Flavonols	Anti-inflammatory and antimicrobial	Aldaba-Muruato et al. 2021
10	Gallic acid	Flavonols	Anti-fungal activity against *Candida albicans*	Liberato et al. 2022
11	Ferulic acid	Flavonols	Antioxidant	Adeyemi et al. 2020
12	Myricetin	Flavonols	Antiviral (SARS-CoV-2)	Xiao et al. 2021
13	Kaempferol	Flavonols	Anticancerous	Govindaraju et al. 2019

Sr. No.	Secondary metabolite	Class	Biological activity and significance	Reference
14	Naringenin	Flavonols	Antiobesity & antidiabetic	Navya et al. 2020
15	Apigenin	Flavones	Anticancerous	De and Blay, 2021
16	Luteolin	Flavones	Antidiabetic	Sangeetha, 2019
17	Cyanidin-3-glucosides	Anthocyanin	Antioxidant, antidiabetic and neuroprotection	Cásedasa et al. 2019
18	Astaxanthin,	Carotenoids	Antioxidant, antiaging	Mahendra and Kamaludeen, 2022; Tominaga et al. 2017
19	Lycopene	Carotenoids	Antioxidant, anticancer	Khathuria et al. 2020
20	Crocin	Carotenoids	Antioxidant	Yaribeygi et al. 2019
21	Lutein	Carotenoids	Antidiabetic, prevention of macular degeneration and eye related disease	Kotagiri et al. 2022; Saisugun et al. 2019
22	Betanidin	Betacyanins	Antioxidant	Ramirez-Velasquez et al. 2022
23	Atropine	True alkaloids	Anticholinergic	Schmoll et al. 2022
24	Morphine	True alkaloids	Narcotic and anesthetic	Kim et al. 2017

3.4 Toxicity and Health Safety:

In spite of numerous progressions in synthetic drug chemistry, medicine and antibiotics, till date plants continue to be major source of drugs for treating multiple human ailments. Therefore, risk assessment through lethal dose 50 (LD50) methodology of secondary metabolites is must to ensure health safety. Another side of coin revealed health ailments due to overconsumption of secondary metabolites enriched crops. For instance, Ma and co-workers (2018) conducted a cohort study based on 200,907 type-2 diabetic free population (88, 293 man and remaining women) in which higher glucosinolate consumption was positively correlated with 19 % high risk of incidence of type-2 diabetes. Although in majority of studied literature carotenoids are known for their beneficial antioxidant and eye sight improving characteristics but despite all, Mikkelsen and co-workers (2009) reported adverse effect of excessive beta-carotene consumption in diabetic persons.

So, to conclude its truthfulness and reality more clinical trials are needed. Among phenols, Rocha et al. 2009 in resveratrol for hepatic oxidative stress and Suh et al. 2009 in epigallocatechin-3-gallate for oxidative cell damage.

3.5 Future Perspective and Conclusion:

Secondary metabolites are known to access extra health benefits in addition to basic nutrition and their biological activities are well reported and documented from time to time about their effectiveness and reliability. But at present, very limited literature is available on toxicity, risk assessment and health safety. Therefore, further clinical trial and evidences

are required before reaching up to a satisfactory inference about adverse effect of plant secondary metabolites on human health. Despite availability of synthetic drugs, plants continue to be major source of drugs on which human population relies across the globe. So, discovering and identifying novel techniques of phytoextraction is a need of hour. Moreover, genetic engineering and new biotechnological interventions of genome editing such as CRISPR-Cas9 and TALENs are thought to revolutionize next generation nutrition breeding by enhancing status of secondary metabolites within plant system.

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