The role of phytoalexins in promoting human health: A review

Maha Ebrahim Irzoqy
Ministry of Education, Mosul, Iraq

* Corresponding Author: **Maha Ebrahim Irzoqy**

Article Info

ISSN (online): 2582-8940
Volume: 05
Issue: 03
July-September 2024
Received: 12-05-2024;
Accepted: 15-06-2024
Page No: 16-20

Abstract
Phytoalexins are a defense group and are low molecular weight compounds of antimicrobial nature produced by plants in response to attacking pathogens. Phytoalexins are considered diverse in their chemical nature, but have a common function, that is, the defense of the plant. With climate change and the development of pure-line crop varieties, the properties of phytoalexins are the accumulation at the sites of infection and inhibit the growth of pathogenic microbes making them potential antimicrobial agents, which may be exploited to resist the disease. Since many genes that encode enzymes involved in their biopath are well studied, phytoalexins are also useful in promoting human health. Some of them are known to possess various biologically active properties such as antioxidants, anticancers, antidiabetic, anti-paratopia, heart and growth preparation.

DOI: https://doi.org/10.54660/IJMBHR.2024.5.3.16-20

Keywords: phytoalexins, human health, disease

1. Introduction

Phytoalexins are a class of low molecular weight compounds which are synthesized in response to stressful conditions, mainly caused by microbial challenges or other environmental factors. Functionally, phytoalexins are toxic to microbial agents that can infect plants. Hence, they possess vital roles in the resistance of plant systems to various phytopathogens. In plants, these agents produce co-evolutionary damage that has been recognized to generate novel bioactive compounds. Prominent phytoalexins possess antimicrobial or antifungal properties. They are also called secondary metabolites of plants, which are well-known as alkaloids, terpene derivatives, flavonoids, tannins, phenolic compounds, and phytoalexins. These functions can motivate us to study their potential pharmacological activities and explore potential novel applications of these resources. (Ahmed & Kovinich, 2021, Sharma *et al*.2022, Sashankar & Chakraborty, 2023) [1, 2, 3].

1.1. Definition and Types of Phytoalexins

The participation of biogenic substances in the development and evolution of the plant world is currently very important to plant protection. Plants are able to synthesize a wide variety of substances with varied chemical structures that are the products of biosynthesis pathways specific to plants. Besides components of primary metabolism, various small-molecular secondary metabolites, such as phytohormones, phytoalexins, and components involved in plant defense responses, are also products of primary metabolic pathways. Phytoalexins are low molecular weight defensive compounds preferentially induced by plant pathogens. The term 'phytoalexin' refers to antibiotic compounds of low molecular weight that are synthesized by plants in response to microbial infection. It is commonly accepted that phytoalexins are formed in the resistance response of higher plant tissues, as a result of the biological activity of classical defensive substances. (Tiku, 2020, Bizuneh, 2021, Ninkuu *et al*. 2022) [4, 5, 6].

The role of phytoalexins is often associated with the health status of humans. The importance of phytoalexins for humans is mainly due to their antioxidant, antibacterial, and antifungal activities. Phytoalexins are low molecular weight secondary metabolites serving as a defense against pathogenic microorganisms in higher plants. Initially, phytoalexins were discovered in

plants as antibiotics. Over time, compounds with biological activities similar to those of phytoalexins were discovered in fungi, cancer cells, and other organisms. Phytoalexins are used in certain crops as a potential means to promote resistance to pathogens, resulting in lower levels of pesticide usage and maintaining ecological balance. The consumption of edible plants providing beneficial substances including phytoalexins is more important than using medicinal supplements. (Bizuneh, 2021, Sharma *et al*.2022) [2, 5].

2. Biological Functions of Phytoalexins

Besides resveratrol, flavonoid plant quiescence phenol compounds such as quercetin, via its antioxidant function, can scavenge excessive ROS formation, enhance apoptosis in orthologous cancer cells, down-regulate Bcl-2 expression, and block a cell cycle. Because of their high antioxidant activity in cancer cells, polyphenolic compounds derived from food plants are often included in dietary recommendations. Recent research found that the method through which polyphenolic antitumor compounds exert their biological function occurs only after digestion and metabolism by gut microbiota. Furthermore, beneficial bacterial microbiots are vital for the biological activity of polyphenols. Gut molecules bind polyphenols, temporarily protecting them from enzymatic breakdown in the gut. Then, upon impact, these molecules release polyphenols and facilitate contact with the bacterial enzyme, allowing breast anthocyanin intestine-mediated release of polyphenol into the body, while other classes of polyphenols are metabolized by gut bacterial enzyme colonic microbiota using diverse mechanisms. Taken together, these data suggest that polyphenols have their activity in the human body as post inflammatory mediators. We can't talk about the biological function of polyphenolics in human health without evaluating their inflammatory metabolites. (Kayacan *et al*.2021, Zhang *et al*.2021, Das *et al*.2022) [7, 19, 9].

2.1. The roles of phytoalexins in human health

The primary biological function of phytoalexins is to promote the health of plants against microbial invasion or in response to abiotic stimuli. Humans and other animals, however, repeatedly ingest phytoalexins, which are produced in plants. What are the roles of phytoalexins in promoting human health? Bioinformatic analysis showed that polyphenols are common as antioxidant compounds in the human body, whereas phytoalexins are relatively uncommon in the human body. In general, polyphenols - resveratrol is the best-known example - are considered ALA component compounds derived by the human body from ingested food sources. Several studies have demonstrated the beneficial effects of resveratrol on human health. For example, found that resveratrol can induce the interleukin-1 receptor-associated kinase M, mediate sphingomyelinase-dependent apoptosis in estrogen receptor-negative breast cancer cells. Reviewed the pros and cons of resveratrol in treating chronic obstructive pulmonary disease (COPD). (Tiku, 2020, Sharma *et al*. 2024, Ahmed & Kovinich, 2021) [4, 1, 10].

2.2. Antioxidant Properties

Plant cells are also exposed to free radicals that can be generated in different occasions. Several types of ROS can be produced also in the cells of phytoalexitic compounds, like stilbenes, flavonoids, or glucosinolates. To counteract the production of radicals, plant cells produce different enzymatic constituents, such as the superoxide dismutase (SOD), catalase (CAT), or the ascorbate peroxidase (APX). However, despite an array of enzymatic constituents, plant cells also require non-enzymatic constituents which assist the enzymatic levels when there is a significant production of ROS. These non-enzymatic constituents can be flavonoids, betalains, anthocyanins, carotenoids, and ascorbic acid. The plant synthetic process should always guarantee the presence of these important given constituents, not only to use them in favor of the plant cell metabolism, but also to store these exogenous regulators in the extracellular matrix. (Tiku, 2020, Bizuneh, 2021, Dev *et al*. 2024) [4, 5, 11].

The first line of defense to counteract the production of ROS in human cells is the production of antioxidant compounds. Although there is a whole range of endogenous antioxidant agents in human cells, the diet is a potential source of many other antioxidant agents. When these compounds come from a diet, they are called exogenous antioxidants. These molecules have a common property: they are able to scavenge free radicals and to prevent oxidative damages to important biomolecules like lipids, proteins, and nucleic acids. A lack of defenses against oxidation phenomena could lead to inflammatory processes, with the production of free radicals. (R2020, Gulcin, 2020) [13].

3. Phytoalexins in Disease Prevention

It has been known for a long time that natural products are potent inhibitors of diseases. Consumption of plants such as fruits, vegetables, and tea has been linked to reduced risks of cardiovascular diseases, diabetes, obesity, and cancer. For example, it has been shown that consumption of grapefruit and its juice, which are rich in specific flavonoids, is negatively correlated with the incidence of coronary heart diseases (CVD). Natural products are not just serving as food nutrients to meet human daily requirements, but also as important 'chemical weapons', through which plants can repel or even kill a variety of microbial pathogens, including fungi, bacteria, and viruses. Reactive oxygen species have proven particularly effective as antimicrobial agents against microbial pathogens which are confronted at all stages of the infection process whether in flowers, leaves, or roots. When plants are infected by some avirulent pathogens, the production of ROS is significantly increased within a few minutes after infection. As part of the defense, plants are also capable of synthesizing a diverse set of substances to counteract members of these pathogen types. Figure 1 Most examples of natural product function as antimicrobial defense agents come from medicinal herbs, such as onion, garlic, and ginger. Decorator Response: Phytochemicals that are produced by any means of tissue manipulation have been used for centuries as traditional medicine in the treatment of human diseases and were then mainly derived from those herbal material. The ability of legumes to synthesize potent anti-microbial compounds was discovered half a century ago. Then began the era of resveratrol as insect-resistance agents and at the same time its function as a cancer-protective agent in mammals from the 1990s. Task Deliverable: These observations support previous epidemiological findings, which show that consumption of some fruits, vegetables, and tea has been linked to reduced risks of coronary heart disease and cancer. Multiple lines of evidence therefore suggest that the plant products capable of protecting plants also protect human health as well. For further discussion, the components of the elicitor mix might provide targets for developing

expected substances that will be induced from our understanding of the structure of disease resistance gene products by the comparison with the structures of the components. This article focuses more on the products of 'susceptibility phenotypes', phytoalexins, for a better understanding of the mechanisms of compound defense and possible secondary metabolic pathway design as well. (Wang *et al*. 2021, Krga *et al*. 2022, Ruxton & Myers, 2021, Bhatt *et al*., 2024, Khalil *et al*. 2022) [14, 15, 16, 17, 18].

3.1. Anticancer Potential

Plant phytochemicals disrupt oxidative damage, inflammation, cancer of different types, and other chronic diseases by preventing the deleterious influence of the molecules derived from oxygen (ROS), reactive nitrogen (RNS) species, disrupting pro-inflammatory mediator activation related to cancer formation and oncoproteins, or providing them protective abilities. The aforementioned abilities are correlated with protective advantages, preventing several complications and contributing to the decreased incidence of a number of chronic diseases, notably cancer. Anticancer activity of a wide variety of phytoalexins and phytochemicals is evaluated in the current review. However, it should be noted that the bioavailability of many potential phytochemicals is very low and, as such, the dietary consumption of natural bioavailable compounds could hold a significant impact in anticancer activities. These phytochemicals activate a number of signal transduction pathways beneficial in maintaining redox balance and also have a large anti-inflammatory effect, not all of it easily explainable. (Guan *et al*. 2021, He *et al*. 2023, Ruhee & Suzuki, 2020) [19, 23, 21].

It is well documented that certain natural compounds found in food sources have the potential to obstruct invasion, angiogenesis, metastasis, and programmed cell death (apoptosis) that lead to cancer. It is well known that a diet replete with fresh fruits, vegetables, and whole grains can reduce the risk of developing cancer, since they are enriched with various phytochemicals that have a cancer prevention role. Chemoprotective activities are developed through different pathways. The processes that have been explored are activation of transcription and mRNA stability of tumor suppressor genes, suppression of proto-oncogenes, apoptosis of several different cancerous cells, and inhibition of angiogenesis. Chemoprotective responses are achieved through antioxidant properties, activation of pro-inflammatory mediators, inhibition of cell proliferation, antiproliferative effect, carcinogen inactivation, metal sequestration, and immune-stimulatory properties. (Farvid *et al*., 2021, Jideani *et al*. 2021, Wallace *et al*. 2020) [22, 23, 24].

4. Phytoalexins in Food and Nutrition

Not all dietary components passively provide health benefits; some are produced in response to stimulation by herbivores or pathogens and function as antimicrobial compounds. These compounds are called phytoalexins, since they are produced endogenously by plants to inhibit the growth and colonization of a broad range of pathogens. Some of these compounds are critical components of plants' responses to pathogen attack and are at the heart of the molecular arms race between plants and their pathogens. Advances in these areas will provide insights into the mechanism and modification of plant defense responses and will allow the passive uptake of these valuable compounds to promote human health. (Tiku, 2020, Ahmed & Kovinich, 2021, Bizuneh, 2021) [4, 1, 5].

For thousands of years, the beneficial properties of certain dietary components have been appreciated because of their "curative" value in the management of various disorders. These components were isolated and are known by different names such as essential nutrients, antibiotics, immunomodulators, allergens, anti-stress factors, adaptogens, and antioxidants. Because they are derived mainly from plants, they are often termed phytochemicals. With the identification of their mechanisms of action and associated health benefits, interest in phytochemicals has increased. There are over a thousand nutrients, which serve to prevent various human diseases. These findings have led to important advances in human nutrition and a greater appreciation of regular consumption of complex mixtures of essential nutrients, known commonly as a balanced diet. (Guan *et al*. 2021, Balakrishnan *et al*. 2021, Bag *et al*., 2022) [19, 25, 26].

4.1. Sources of Phytoalexins in the Diet

In relation to this last section, it is especially relevant to underline that the human body is not able to synthesize lignans itself, and for that reason, it is precisely their tree character that justifies the importance of lignans' place in the diet. (Bach *et al*. 2020) [27].

Precisely, all these types of natural compounds can exert negative effects on human health thanks to their respective antioxidant, anti-inflammatory, cardioprotective, chemoprotective, photoprotective, and neuroprotective effects. In addition, they participate in the reduction of the risk of suffering from certain diseases such as diabetes, obesity, cardiovascular diseases, cancer, visual disturbances, cognitive deficit, and alterations in the gut microbiota. (Sivakumar & Deepa, 2023, Arora *et al*., 2020) [28, 29].

With respect to the botanical origin of some of the most known and studied phytoalexin families, it is necessary to detail, frequently, if not exclusively, the families of flavonoids (subclass of flavonols), stilbens (particularly resveratrol), isoflavones, and lignans (enterolactone and enterodiol). (Dev *et al*. 2024, Marant *et al*. 2024) [11, 30].

After explaining what phytoalexins are, it is necessary to mention that these compounds are synthesized and accumulated in countless species of plants, especially in the skin of fruits and in the outermost part of plants. Moreover, the concentration and content of these biologically active compounds are generally higher in the most unfavorable circumstances, such as after the attack, for example, of phytopathogens or ultraviolet radiation. (Ishihara, 2021, Sharma & Gupta, 2020) [31, 32].

5. Conclusion and Future Directions

Phytoalexins are characterized as low molecular weight metabolites, often with antimicrobial activity. Originally, phytoalexins were considered ubiquitous in resistant plants under attack by pathogens. However, present evidence suggests that phytoalexins contribute to plant disease resistance but may also play roles in plant development and cell signaling. It has been suggested that flavonoids, auxins, and other phenolic compounds are de facto signaling molecules and that their defensive properties against pathogens may be a type of side effect of their primary function as growth regulators. Accurately determining the roles of specific phenolic compounds, such as the

isoflavonoid phytoalexins, in plant disease interaction is difficult due to their overall low abundance, structural diversity, and lower ultraviolet (UV) absorbance. Nevertheless, characterization of phenolic metabolites provides useful insights for the prevention and control of numerous mycotoxin-producing organisms, as well as other microbial contaminants, which affect humans, animals, and agriculture.

Phytoalexins are well known for their affiliation with plants in fighting against disease-causing agents. They are present in numerous crops and regulate the microbiomes, particularly bacteria and fungi. When the microbiome is altered, they play a role in morphogenesis, maintaining balance, and restoring the normal status of new niches. Phytoalexins have been proven to be integral for health, with their anticancer, antimicrobial, and antiviral properties. Their existence in numerous foods and medicinal herbs is quoted as a previously unknown health benefit. With the help of advanced technologies, it is believed that phytoalexins and their relatives will be used in the development of several novel therapeutics through modern technologies.

6. References

1. Ahmed S, Kovinich N. Regulation of phytoalexin biosynthesis for agriculture and human health. Phytochemistry Reviews; c2021. Available from: yorku.ca
2. Sharma I, Thakur A, Sharma A, Singh N, Kumar R, Sharma A. Phytoalexins: Implications in plant defense and human health. In: Plant Secondary Metabolites: Physico-Chemical Properties and Therapeutic Applications. Singapore: Springer Nature Singapore; 2022:329-53. Available from: researchgate.net
3. Sashankar P, Chakraborty B. Phytoalexins from Poaceae: their types, biosynthesis, role in biotic and abiotic stress adaptation and application in human health. Journal of Mycopathological Research; c023. Available from: imskolkata.org
4. Tiku AR. Antimicrobial compounds (phytoanticipins and phytoalexins) and their role in plant defense. Co-evolution of Secondary Metabolites; c2020. Available from: [HTML].
5. Bizuneh GK. The chemical diversity and biological activities of phytoalexins. Advances in Traditional Medicine; c2021. Available from: researchgate.net
6. Ninkuu V, Yan J, Fu Z, Yang T, Ziemah J, Ullrich MS, *et al*. Lignin and its pathway-associated phytoalexins modulate plant defense against fungi. Journal of Fungi. 2022;9(1):52. Available from: mdpi.com
7. Kayacan S, Yilancioglu K, Akdemir AS, Kaya-Dagistanli F, Melikoglu G, Ozturk M. Synergistic effect of apigenin and curcumin on apoptosis, paraptosis and autophagy-related cell death in HeLa cells. Anticancer Research. 2021;41(3):1271-82. Available from: iiarjournals.org
8. Zhang J, Duan D, Song ZL, Liu T, Hou Y, Fang J. Small molecules regulating reactive oxygen species homeostasis for cancer therapy. Medicinal Research Reviews. 2021;41(1):342-94. Available from: researchgate.net
9. Das SS, Sarkar A, Chabattula SC, Verma PRP, Nazir A, Gupta PK, *et al*. Food-grade quercetin-loaded nanoemulsion ameliorates effects associated with Parkinson's disease and cancer: Studies employing a transgenic *C. elegans* model and human cancer cell lines. Antioxidants. 2022;11(7):1378. Available from: mdpi.com
10. Sharma A, Sharma A, Sharma A, Kumar Y, Sharma P, Bhardwaj R, Sharma I. Polyphenol phytoalexins as the determinants of plant disease resistance. In: Plant Phenolics in Biotic Stress Management Book. Singapore: Springer Nature Singapore; 2024:243-74. Available from: [HTML].
11. Dev M, Dev V, Singh KP, Pant P, Rawat S. Role of phytoalexins in plant disease resistance. Biorationals and Biopesticides: Pest Management; 2024:127. Available from: [HTML].
12. Dias RT, Martin-Hidalgo D, Silva BM, Oliveira PF, Alves MG. Endogenous and exogenous antioxidants as a tool to ameliorate male infertility induced by reactive oxygen species. Antioxidants & Redox Signaling. 2020;33(11):767-85. Available from: [HTML].
13. Gulcin İ. Antioxidants and antioxidant methods: An updated overview. Archives of Toxicology; c2020. Available from: [HTML]
14. Wang Y, Gallegos JL, Haskell-Ramsay C, Lodge JK. Effects of chronic consumption of specific fruit (berries, citrus and cherries) on CVD risk factors: A systematic review and meta-analysis of randomised controlled trials. European Journal of Nutrition. 2021;60:615-39. Available from: springer.com
15. Krga I, Corral-Jara KF, Barber-Chamoux N, Dubray C, Morand C, Milenkovic D. Grapefruit juice flavanones modulate the expression of genes regulating inflammation, cell interactions and vascular function in peripheral blood mononuclear cells of postmenopausal women. Frontiers in Nutrition. 2022;9:907595. Available from: frontiersin.org
16. Ruxton CHS, Myers M. Fruit juices: are they helpful or harmful? An evidence review. Nutrients; c2021. Available from: mdpi.com
17. Bhatt P, Kumar V, Malik MK, Kumar T. Citrus flavonoids: Recent advances and future perspectives on preventing cardiovascular diseases. The Flavonoids; c2024. Available from: [HTML].
18. Khalil MN, Farghal HH, Farag MA. Outgoing and potential trends of composition, health benefits, juice production and waste management of the multi-faceted Grapefruit *Citrus X paradisi*: A comprehensive review for maximizing its value. Critical Reviews in Food Science and Nutrition. 2022;62(4):935-56. Available from: hu.edu.eg
19. Guan R, Van Le Q, Yang H, Zhang D, Gu H, Yang Y, *et al*. A review of dietary phytochemicals and their relation to oxidative stress and human diseases. Chemosphere. 2021;271:129499. Available from: [HTML]
20. He WJ, Lv CH, Chen Z, Shi M, Zeng CX, Hou DX, Qin S. The regulatory effect of phytochemicals on chronic diseases by targeting Nrf2-ARE signaling pathway. Antioxidants; 2023. Available from: mdpi.com
21. Ruhee RT, Suzuki K. The integrative role of sulforaphane in preventing inflammation, oxidative stress and fatigue: A review of a potential protective phytochemical. Antioxidants; c2020. Available from: mdpi.com
22. Farvid MS, Barnett JB, Spence ND. Fruit and vegetable consumption and incident breast cancer: a systematic review and meta-analysis of prospective studies. British

Journal of Cancer; c2021. Available from: nih.gov
23. Jideani AI, Silungwe H, Takalani T, Omolola AO, Udeh HO, Anyasi TA. Antioxidant-rich natural fruit and vegetable products and human health. International Journal of Food Properties. 2021;24(1):41-67. Available from: tandfonline.com
24. Wallace TC, Bailey RL, Blumberg JB, Burton-Freeman B, Chen CO, Crowe-White KM, *et al*. Fruits, vegetables, and health: A comprehensive narrative, umbrella review of the science and recommendations for enhanced public policy to improve intake. Critical Reviews in Food Science and Nutrition. 2020;60(13):2174-211. Available from: tandfonline.com
25. Balakrishnan R, Azam S, Cho DY, Su-Kim I, Choi DK. Natural phytochemicals as novel therapeutic strategies to prevent and treat Parkinson's disease: current knowledge and future perspectives. Oxidative Medicine and Cellular Longevity. 2021;2021(1):6680935. Available from: wiley.com
26. Bag S, Mondal A, Majumder A, Banik A. Tea and its phytochemicals: Hidden health benefits & modulation of signaling cascade by phytochemicals. Food Chemistry; c2022. Available from: [HTML]
27. Bach Knudsen KE, Nørskov N, Bolvig AK, Hedemann MS, Lærke HN. Lignans. In: Dietary Polyphenols: Their Metabolism and Health Effects; 2020:365-406. Available from: [HTML].
28. Sivakumar T, Deepa B. Phytoalexins: defend systems of plants and pharmacological potential-a systematic review. International Journal Of Engineering Technology And Management Sciences; c2023. Available from: researchgate.net
29. Arora B, Sindhu RK, Arora S. Journal of Pharmaceutical Technology Research and Management; c2020. Available from: semanticscholar.org
30. Marant B, Crouzet J, Flourat AL, Jeandet P, Aziz A, Courot E. Key-enzymes involved in the biosynthesis of resveratrol-based stilbenes in *Vitis* spp.: A review. Phytochemistry Reviews; 2024:1-21. Available from: urd-abi-agroparistech.com
31. Ishihara A. Defense mechanisms involving secondary metabolism in the grass family. Journal of Pesticide Science; c2021. Available from: jst.go.jp
32. Sharma S, Gupta N. Defense signaling in plants against micro-creatures: do or die. Indian Phytopathology; c2020. Available from: [HTML]