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Fruit-derived phytochemicals in chronic disease management: Epigenetic modulation, molecular mechanism, and therapeutic potential

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Abstract

The bioactive compounds known as phytochemicals which exist in fruits, have become increasingly important for their probable role in disease prevention and management. Various biological responses emerge from these compounds since they demonstrate antioxidant activity and anti-inflammatory effects as well as neuroprotective mechanisms to promote metabolic control and immune system adjustment and wellness. Phytochemicals influence gene expression and epigenetic modifications, making them crucial in the treatment of cancer, neurodegenerative disorders, and metabolic diseases. The benefits that phytochemicals confer to the entire body are significantly enhanced through their essential interactions with gut microbiota. Clinical use of phytochemicals is currently restricted by multiple obstacles which include their insufficient absorption rates and fast breakdown patterns as well as the need for additional medical approval. Advancements in nanotechnology, such as phytosomes and nanoparticles, offer promising solutions to enhance phytochemical absorption and efficacy. Phytochemicals when included in dietary guidelines represent an entire-system method to stop diseases and support human wellness sustainably. Further research should focus on elucidating phytochemicals' mechanisms of action, optimizing formulation strategies, and conducting comprehensive clinical studies to validate their efficacy and safety for evidence-based healthcare.

1. Introduction

Medical research into phytochemical disease management mechanisms obtained from fruits stands at the core of current nutrition and health sciences investigations. Active compounds in these substances provide extensive protective properties through their ability to control biological responses that relate to oxidative stress and inflammatory responses while managing metabolic processes. Phytochemicals specifically flavonoids phenolics and carotenoids function as key components in battling reactive oxygen species because they serve as primary agents against chronic conditions such as cardiovascular diseases diabetes and cancer (Zhang *et al.,* 2015). These compounds have an additional benefit beyond their antioxidant functions since they regulate immune system response and reduce inflammation. Strawberry phenolic compounds show their anticarcinogenic and anti-inflammatory properties by signaling pathway regulation thus controlling cellular apoptosis and proliferation (Giampieri *et al.,* 2017). These bioactive constituents show potential as a natural therapeutic when used to prevent and control chronic diseases because they manage the connection between oxidative stress and inflammation in disease development (Serafini and Peluso, 2017).

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Viewpoints about epigenetic regulation suggest that fruit-derived phytochemicals function as agents which modify gene expression, and this occurs through DNA methylationand histone modification. Cancer risk reduction stems from these processes because they control oncogene and tumor suppressor gene activation (Carlos Reyes *et al.,* 2019). The cellular signaling pathways for metabolism and immune response and oxidative defense get targeted by specific phytochemicals known as flavonoids and terpenes (Murakami and Ohnishi, 2012). Polyphenols and anthocyanins are compounds that work *via* PPAR and Nrf2 transcription factors to control metabolic homeostasis in lipid metabolism and antioxidant responses (Li *et al.,* 2022). Research shows that phytochemicals work in combination when eaten as whole foods to improve their body absorption and to create better health results through diets featuring abundant fruit consumption (Nema *et al.,*2022; Jaworsky *et al.,* 2023).

2. Overview of fruit derived phytochemicals

The essential phytochemical grouping in fruits consists of polyphenols that contain both flavonoids together with phenolic acids. The compounds demonstrate robust antioxidative properties by both eliminating free radicals and reducing oxidative stress which serves as a crucial factor in initiating multiple chronic diseases (Donno *et al.,* 2018). The phytochemical compounds quercetin together with kaempferol and myricetin which exist in apples and berries alongside grapes regulate oxidative stress through NRF2 pathways and suppress inflammation by blocking NF-κB activation. The cardioprotective properties along with anti-inflammatory actions and life-span extension are explained through this mechanism. Two important compounds in blueberries and blackcurrants named cyanidin along with delphinidin and malvidin activate brain-derived neurotrophic factor (BDNF) production to protect the nervous system and improve cognitive function.Whole fruit consumption provides superior biological effects than individual phytochemical supplement use because phytochemicals enhance their activity when combined (Donno *et al.,* 2018).

Among fruit-derived phytochemicals, carotenoids are well known for their antioxidant properties and vibrant colors. The prostate cancer preventive properties of tomato and papaya lycopene have been validated through its ability to capture free radicals and change cellular communication processes through gap junctions (Campestrini *et al.,* 2019). Individuals who consume mangoes or citrus fruits obtain vital compounds including β-carotene, lutein and zeaxanthin because these nutrients support vision functions in addition to immune protection and skin health maintenance. The described mechanisms demonstrate potential uses for these ingredients in both eye health supplement products and functional beverages and cosmeceuticals applications.

Fruits contain terpenes that perform critical functions regarding metabolic health as well as disease prevention. The compounds limonene, carvacrol, and linalool show anti-inflammatory and antimicrobial as well as neuroprotective properties in citrus fruits, plums, and persimmons. These compounds affect apoptosis through p53 signaling mechanisms and reduce MMP-9 expression levels which enhances both chemo preventive and neuroprotective effects (Serafini and Peluso, 2017).

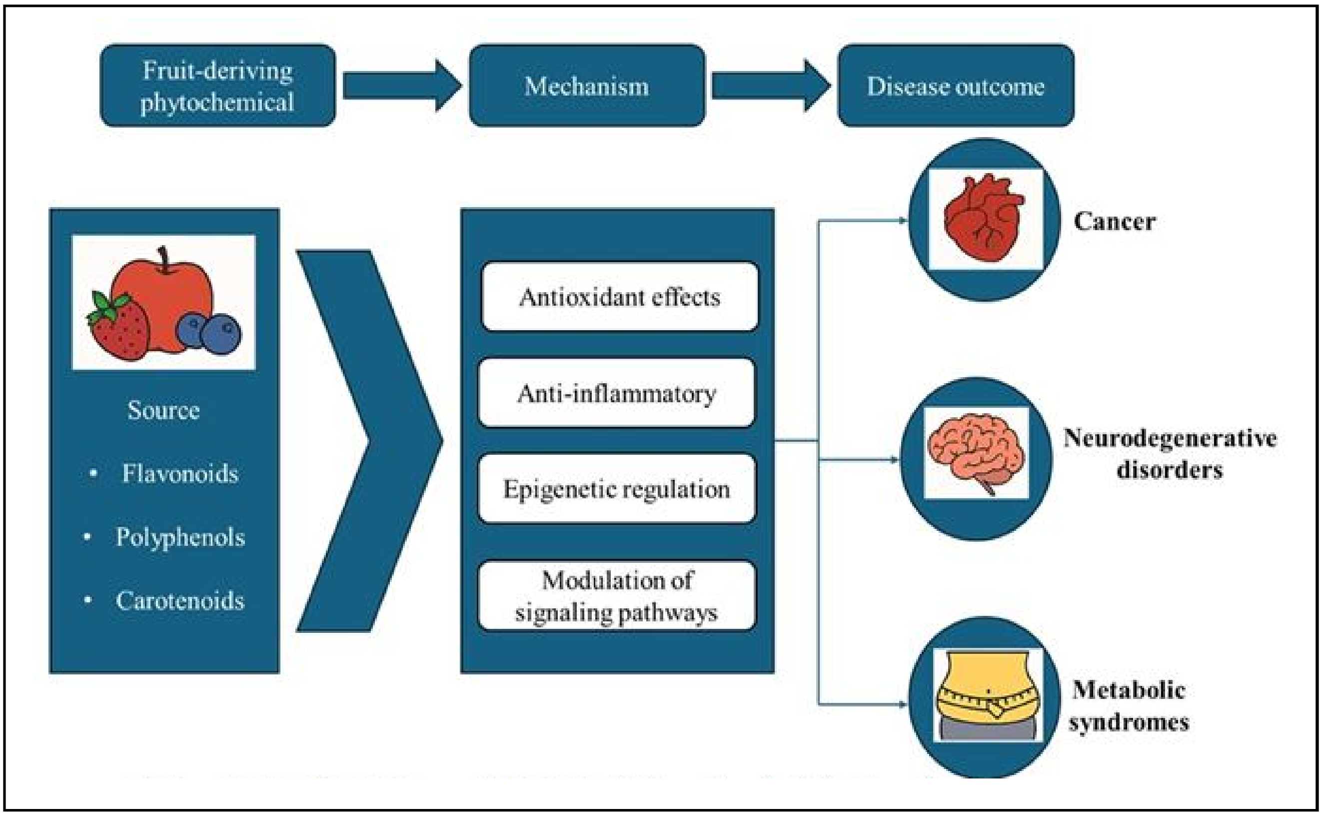

Figure 1: Graphical abstract fruit derived phytochemicals in chronic disease management

Both ellagitannins and proanthocyanidins from pomegranates and cranberries and black grapes exhibit antimicrobial effects through their ability to prevent bacterial adherence while stopping lipid peroxidation. Such mechanisms enable potential use in probiotics as well as natural antimicrobial and oral health products (Lee *et al.,* 2021). The organic acids found in sea buckthorn affect metabolic regulation when combined with their derivatives while strengthening antioxidant capabilities which improve both metabolic functions and reduce oxidation stress (Alsuhaymi *et al.,* 2023). Research performed by scientists has confirmed that phytochemicals from fruits can affect cellular operations and gene expression patterns. The alkaloids berberine, Harman and Solas dine contained in bananas and citrus fruits, and passionfruit activate the AMPK pathway to provide metabolic regulation and anticancer effects by inhibiting DNA topoisomerases (Li *et al.,* 2022). The sterols β-sitosterol and diosgenin along with saponins that exist in avocados, olives, and figs block the absorption of cholesterol while managing steroid hormone functions to improve cardiovascular health and lipid regulation. Among the numerous health-modulating compounds found in black goji berries stands a complex polyphenolic profile according to research conducted by (Li *et al.,*2022). The evaluation demonstrates phytochemical substances in food regulate the expression of microRNA while they help fight different diseases including obesity and cancer according to Srivastava *et al.* (2015) Figure 1.

3. Classification and bioavailability of fruit derived phytochemicals

Phytochemicals in fruits Figure 2 contribute to health benefits through distinct biochemical mechanisms. Polyphenols, such as flavonoids (anthocyanins, flavanols, flavanones) and phenolic acids, are abundant in berries, apples, and grapes, demonstrating strong antioxidant and anti-inflammatory properties with a high correlation (up to 0.92) between phenolic content and antioxidant activity (Golovinskaia and Wang, 2021; Blank *et al.,* 2018). Carotenoids, responsible for the vibrant hues of mango, papaya, and dragon fruit, include beta-carotene, lutein, and lycopene, which have been linked to reduced chronic disease risks, including cancer (Samtiya *et al.,* 2021; Singh *et al.,* 2022). Terpenes, such as limonene and myrcene in citrus fruits, contribute to aroma and offer anti-inflammatory and antimicrobial benefits (Desai *et al.,* 2022). Vitamins and minerals, particularly vitamins C and E, enhance phytochemical bioactivity by modulating absorption and efficacy (Weber *et al.,* 2021). Organic acids play a crucial role in taste, stability, and antioxidant activity while also influencing phytochemical bioavailability (Lee *et al.,* 2021).The bioavailability of these phytochemicals determining their absorption and utilization depends on factors such as food matrix, processing, and physiological conditions. Whole fruits exhibit enhanced bioavailability due to synergistic interactions among phytochemicals, optimizing health benefits (Park *et al.,* 2015; Samtiya *et al.,* 2021). Advanced extraction techniques, as observed in kiwi fruit studies, maximize antioxidant yield (Weber *et al.,* 2021; Park *et al.,* 2015), while freeze-drying preserves bioactive compounds in fruits like passion fruit (Silva *et al.,* 2016; Gonzalez *et al.,* 2020). Additionally, individual dietary habits and gut microbiota, *e.g.*, Lactobacillus, Bifido bacterium composition play a vital role in phytochemical metabolism, emphasizing the influence of the microbiome on disease prevention (Golovinskaiaand Wang, 2021).

4. Antioxidant mechanisms and oxidative stress modulation

Phytochemicals from fruits exhibit antioxidant activity through multiple mechanisms, including ROS elimination, endogenous enzyme protection, synergistic antioxidant effects, and oxidative stress pathway regulation.Three key antioxidant compounds in phenolic compounds and flavonoids together with carotenoids deactivate ROS which reduces oxidative stress damage to cells. Research findings show *Diospyros mespiliformis* possesses high nitric oxide (NO) radical scavenging ability thus demonstrating potential for reducing oxidative harm according to (Danzomo *et al.,* 2024). Phytochemicals achieve antioxidant protection of the body through mechanisms that build up natural defenses. Research testing tomato plants shows that adding melatonin supplements enhances antioxidant capacities of the fruit through better reducing power in situations of plant stress hence humans could potentially experience equal health benefits by consuming these compounds (Debnath *et al.,* 2018). The multiple phytochemical components found in fruits create conditions through which different compounds unite to strengthen overall antioxidant capacity. The scientific study by Feei *et al.* (2019) shows that the diverse compounds in Goji berries produce stronger protection against oxidative stress than what single antioxidants can achieve. The phytochemical compounds modify oxidative stress-related routes by stimulating the activation process of nuclear factor erythroid 2–related factor 2 (Nrf2) that oversees antioxidant protein production. Tests revealed that phenolic acids and flavonoids activate Nrf2 pathway functions which strengthens cellular redox equilibrium while preventing damage from long-term oxidative stress (Zhang *et al.,* 2015).

Phytochemical antioxidants display variable bioavailability levels because of their molecular composition together with food structure elements and human body functioning and food processing treatments. Antioxidants found in various fruits show varying effectiveness in target tissue antioxidant concentration based on how the body absorbs and processes them. According to Carlsen *et al.* (2010) antioxidant-rich foods might not result in higher antioxidant metabolite levels because their bioavailability stands as variable. Statement from Serafini and Peluso (2017) shows that the complete consumption of whole berries enhances antioxidant activity better than individual supplement components because the food matrix plays an essential role in raising compound effectiveness. Composite gut microbiota and the digestive system exert additional effects on antioxidant intake by the body. Research based interventions demonstrate that greater consumption of fruits and vegetables leads to enhanced antioxidant conditions in the body thus showcasing how dietary choices affect oxidative stress levels (Talegawkar *et al.,* 2009). The methods used for food processing dramatically affect how antioxidants are available in the human body. The bioactive compound effectiveness is influenced when processing methods like freeze-drying and juicing either maintain or break down the compounds. Freeze-drying methods preserve phytochemical chemicals because they function better than excessive heat during juicing processes damages specific antioxidants (Tesoriere *et al.,* 2004). Knowledge about these aspects forms the basis for improving the intake of antioxidants from fruits to achieve maximum health advantages.

5. Anti-inflammatory pathways of fruit phytochemicals

Nutritional research and disease prevention sciences show strong interest in the anti-inflammatory aspects of phytochemicals that stem from fruits. Plenty of anti-inflammatory bioactive compounds exist in fruits and these compounds work against inflammation through distinct mechanisms. This review describes major biological paths affected by phytochemicals from fruits while studying their anti-inflammatory effects. Plants derived from fruits hinder the production of pro-inflammatory cytokine molecules TNF-α, IL-1β, and IL-6. Flavonoids along with phenolic acids present in fruits diminish inflammatory response by reducing cytokine secretion in the body. Flavonoids of the *Garcinia xanthochymus* ethanolic extract inhibit prostaglandin synthetase to reduce inflammatory mediator release according to Winata *et al.* (2018). The proper management of cytokine activity enables the treatment of persistent inflammatory diseases. The significant mechanism directing ROS removal leads to this pathway. The antioxidant compounds polyphenols and carotenoids found throughout numerous fruits successfully eliminate ROS molecules which drive oxidative stress and inflammatory reactions Akter *et al.,* (2022). Among the prominent components found in pomegranate juice ellagic acid demonstrates excellent antioxidant properties which strengthen its anti-inflammatory response according to Akter *et al.* (2022). Consequently, the modulation of nitric oxide (NO) production serves as a vital mechanism. Activated macrophages release elevated NO levels that result in stronger inflammatory signals. Laboratory studies prove that *Phyllanthus emblica* fruit extracts intervene powerfully with NO synthesis thus supporting their use as antichronic inflammatory treatment options according to (Li *et al.,* 2022). The reduction of NO levels by fruit phytochemicals aids in protecting tissues from damage during extended inflammatory events. Phytochemicals from fruit cause significant reduction of NF-κB signaling pathway activation which stands as a primary target for fruit-derived chemicals in their anti-inflammatory effects. The activation of NF-κB triggers inflammation-causing genes which intensifies inflammatory responses. Phytochemicals from dragon fruit have been proven to lessen the activity of NF-κB while limiting the release of cytokines and chemokines according to Yuna *et al.* (2023); Kim *et al.* (2011). Such dietary pathway control suggests that fruits could provide solutions for managing inflammatory disorders. Some phytochemicals not only suppress inflammation but contribute to its natural termination. *Eugenia jambolana* contains compounds which show potential for treating inflammation and liver damage in individuals with cholestatic conditions thus making them important for homeostasis restoration (Donepudi *et al.,* 2011) Table 1, Figure 2.

Table 1: Molecular mechanisms and therapeutic potential of fruit derived phytochemicals

Phytochemical class	Major compounds	Source fruits	Molecular mechanisms	Health benefits	Potential applications	References
Flavonoids	Quercetin, Kaempferol, Myricetin	Apples, Berries, Grapes	Regulates oxidativestress *via* NRF2 pathway, inhibits inflammation by suppres -sing NF-κB	Antioxidant, Anti-inflammatory, cardioprotective	Functional foods, Nutraceuticals, Anti-ageing formulations	Khan *et al.,* 2021
Anthocyanins	Cyanidin, Delphinidin, Malvidin	Blueberries, Cherries, Blackcurrants	Modulates gut microbiota, Enhances brain-derived neu-rotrophic factor (BDNF) expression	Neuroprotection, Cognitive enhance-ment, Diabetes management	Brain health supplements, Antidiabetic formulations	Patel, 2014
Carotenoids	β-Carotene, Lycopene, Lutein, Zeaxanthin	Mangoes, Pap-ayas, Tomatoes	Scavenges free radicals, Enh-ances intercellular communi-cation *via* gap junctions	Vision health, Im-mune modulation, Anticancer	Eye health supple-ments, Cosmece-uticals, Functional beverages	Yahia *et al.,* 2017
Phenolic acids	Caffeic acid, Ferulic acid, Gallic acid	Grapes, Apples, Pomegranates	Inhibits pro-inflammatory enzymes (COX-2, LOX), Modulates histone deacety-lases (HDACs)	Anti-inflammatory, Anti-atherosclerotic, Longevity promotion	Anti-ageing products, Cardiovascular health supplements	Sadiq *et al.,* 2024
Tannins	Ellagitannins, Proanth-ocyanidins	Pomegranates, Cranberries, Black Grapes	Reduces bacterial adhesion, Inhibits lipid peroxidation	Antimicrobial, Anti-cancer, Gut health enhancement	Probiotics, Natural antimicrobials, Oral health products	Joshi *et al.,* 2022
Alkaloids	Berberine, Harman, Solasodine	Bananas, Citrus, Passion fruit	Activates AMPK pathway, Inhibits DNA topoisomerases	Metabolic regulation, Antidiabetic, Anti-cancer	Diabetes manag-ement, Metabolic syndrome treatments	U *et al.,* 2023
Terpenoids	Limonene, Carvacrol, Linalool	Citrus fruits, Plums, Persimmons	Modulates apoptosis *via* p53, Inhibits MMP-9 expression	Anticancer, Neuropro-tection, Antimicrobial	Chemopreventive drugs, Neuroprote-ctive formulations	Monisha *et al.,* 2015
Sterols and saponins	β-Sitosterol, Diosgenin	Avocados, Olives, Figs	Inhibits cholesterol absorp-tion, Modulates steroid hor-mone pathways	Cardiovascular health, Hormonal balance, Lipid metabolism regulation	Cholesterol-lowe-ring supplements, Functional foods	Dini, 2018

The examination of these benefits demonstrates how these phytochemicals work as multiuse agents promoting both inflammatory reduction and recovery processes. Food phytochemicals play a fundamental role in maintaining healthy gut function which directly controls the severity of inflammation in the body. The active compounds work to regulate gut microbial groups to keep the gut barrier strong and minimize whole-body inflammation (Santa *et al.,* 2023). The production of anti-inflammatory mediators rises when microorganisms in a balanced gut environment multiply thus strengthening the anti-inflammatory effects of consuming fruits.

Multiple important phytochemicals obtained from fruits showcase their anti-inflammatory properties. The inflammatory enzyme activity receives inhibition from biological compounds like quercetin and kaempferol in addition to their ability to downregulate inflammatory mediators (Hipni *et al.,* 2024; Dwiwina *et al.,* 2023). Pomegranates and strawberries contain ellagic acid which regulates pro-inflammatory cytokines along with showing extensive anti-inflammatory effects (Akter *et al.,* 2022). Research by Yuna *et al.* (2023) together with Hipni *et al.* (2024) demonstrates that betacaine anti-inflammatory effects in dragon fruit peel arise from modifying oxidative stress. Anthocyanins present in berries reduce inflammation through their ability to block nitric oxide production and prevent NF-κB signaling according to Cassidy *et al.* (2013); Islam *et al.* (2016).

6. Epigenetic modulation and gene regulation

The therapeutic mechanism of phytochemicals operates through epigenetic regulation which changes expression patterns of genes as well as cell functions. The therapeutic potential of dietary compounds relies on DNA methylation since they modify tumour suppressor gene and oncogene methylation patterns to control their regulatory function Figure 3. The Prostate cancer cell study at Shu *et al.* (2011) demonstrated that curcumin from turmeric reverses epigenetic silencing of Neurog1 gene by demethylating it. DNA remodelling processes depend heavily on histone modifications because these modifications determine how genes become accessible or inaccessible. The compounds in extra virgin olive oil known as oleuropein directs histone deacetylase activity of HDAC2 and HDAC3 downward to create an open chromatin pattern which enables better transcription of anti-inflammatory genes (Bordoni *et al.,* 2019; Munoz-Garcla*et al.,* 2022). Phytochemicals manipulate gene expression through microRNA regulation which supports both tumour-suppressing microRNA activation and blocking oncogenic microRNA expression as part of preventive health strategies (Kapinova *et al.,* 2018). The disease preventing effects and therapeutic advantages become possible due to these epigenetic modifications. Phytochemicals control NF-κB signaling pathways and NRF2 oxidative stress elements to prevent chronic inflammation which leads to tumorigenesis according to (Chou *et al.,* 2024; Lee *et al.,* 2013). The anti-inflammatory characteristics of phytochemicals reach immune regulation through mechanisms that activate epigenetic factors whereby compounds such as thymoquinone in *Nigella sativa* regulate inflammatory cytokine activity to manage diseases like rheumatoid arthritis and inflammatory bowel disease (Bordoni *et al.,* 2019; Saleh *et al.,* 2021). Neurological health advantages from phytochemicals have gained more prominence because these compounds affect both neuroinflammatory activities and pathways related to ageing and neurodegenerative diseases. Studies indicate these bioactive compounds have therapeutic value for prevention and treatment of Alzheimer's and Parkinson's diseases through their control of epigenetic markers (Corbi *et al.,* 2016). After research advances, scientists must study phytochemical epigenetic interactions to establish targeted dietary intervention methods and therapeutic strategies.

Nachman bioactive compounds from fruits control multiple metabolic pathways that affect oxidative stress management as well as lipid regulation and pancreatic insulin response and cellular self-destruction and intestinal microbial populations. Bioactive compounds from fruits use their power to neutralize free radicals as their primary mechanism of effect. Anthocyanins together with flavonoids and polyphenols specifically found in berries perform as free radical interceptors that fight oxidative stress which leads to metabolic disorders like cardiovascular diseases and metabolic syndrome and specific cancers (Ciumarnean *et al.,* 2020; Makhaik *et al.,* 2021).

7. Metabolic regulation and disease prevention

Studies demonstrate that bilberries contain high levels of anthocyanins, and they enable both reductions of oxidative stress and improvements of metabolic balance (Vanekova and Rollinger, 2022; Vladimir Knezevic *et al.,* 2023).

The metabolism of lipids receives influence from phytochemicals through their ability to manage cholesterol amounts while promoting fatty acid break down. Research indicates bilberries reduce LDL plasma cholesterol although they improve fatty acid metabolism through cholesteryl ester transfer protein (CETP) activity according to Vanekova and Rollinger (2022). The results imply that phytochemicals from fruits have potential as dietary therapy solutions for dyslipidaemia which remains a primary risk factor for heart disease. Their influence on insulin sensitivity together with glucose metabolism is extremely important. Scientific studies demonstrate that curcumin which comes from turmeric possesses the ability to reduce insulin resistance, so it functions as a viable dietary substance for type 2 diabetes patients (Akintunde *et al.,* 2019; Forni *et al.,* 2019). Regular berry consumption functions as a means to improve glycaemic control according to Essa *et al*. (2014) in their study about metabolic health management.

Cellular autophagy exists as a vital cellular process which phytochemicals control to degrade cellular elements and clear them for reuse. Medical experts agree that boosted autophagy protects against both obesity-related disorders and neurodegenerative diseases. Scientific research shows that polyphenolic substances produce autophagic activation which leads to an improvement in metabolic homeostasis (Limanaqi *et al.,* 2019). Across metabolic regulation the modulation of gut microbiota relies heavily on phytochemicals found in food which affect the microbial composition of the gut. The relationship between polyphenols in the gut microbiota results in better fat metabolic performance and lessened inflammatory responses. The fermentation products from polyphenols which gut bacteria produce create insulin sensitizing metabolites that reduce inflammation markers (Duda Chodak *et al.,* 2015; Wang *et al.,* 2024). Several phytochemicals in our food help maintain healthy body metabolism by establishing favorable microbial soil in our digestive tract.

The disease prevention capability of phytochemicals from fruits applies across the metabolic spectrum. The dietary consumption of fruits dense with phytochemicals shows potential to enhance blood glucose regulation and lipid profile management which helps decrease disease development possibilities (Ciumarnean *et al.,* 2020; Forni *et al.,* 2019) within metabolic syndrome and diabetes contexts. Studies show that cardiovascular protection exists within fruit-sourced polyphenols because grapes and apples release compounds that boost endothelial function and minimize oxidative stress while decreasing systemic inflammation (Ciumarnean *et al.,* 2020; Torres Ossandon *et al.,* 2020). Neurodegenerative diseases can be protected by fruit phytochemicals which enable berry compounds to control signaling processes that affect neuroplasticity and oxidative stress while protecting cognitive function from age-related decline (Essa *et al.,* 2014). The ability of fruit phytochemicals to prevent cancer represents an important sector where their potential emerges as significant. These bioactive compounds help lower the risks of different cancers especially breast cancer and digestive tract cancers by both reducing oxidative stress alongside blocking inflammatory pathways driving tumorigenesis (Limanaqi *et al.,* 2019; Palafox-Carlos *et al.,* 2011; Rangarajan *et al.,* 2020).

8. Gut microbiome interactions and immune modulation

The immune system control functions of the gut microbiome affect both adaptive and innate immunity components. A greater microbial diversity determines immune function according to research which shows immunotherapy treatment for non-small cell lung cancer patients achieves better results with increased microbial diversity (Jin *et al.,* 2019). Using this research we can understand that immune system strength depends on having various types of microbiota. Immunomodulation arises from metabolic digestive products known as short-chain fatty acids (SCFAs) which consist of butyrate along with propionate and acetate. The immune response improves through SCFAs which develop anti-inflammatory pathways while affecting T cell differentiation and boosting regulatory T cell functionality (Dang and Marsland, 2019). The gut microbiota establishes contact with dendritic cells (DCs) to trigger adaptive immunity functions while DCs serve as essential antigen presentation elements for T cell activation. The immune responses to checkpoint inhibitors enhance when people have Lactobacillus bacteria in their intestinal ecosystem according to Katayama *et al.* (2019). Scientists have discovered that microbial dysbiosis which represents an abnormal bacterial population distribution associates with multiple autoimmune and inflammatory disorders. Research shows that Proteobacteria pathobionts drive inflammatory bowel disease (IBD) and rheumatoid arthritis by causing excessive inflammatory reactions and immune system dysfunction according to Lim *et al.* (2022). The gut microbiome impacts systemic immunity by sending metabolites from the gut to various organs including lungs and liver which enhances the concept of gut-lung axis (Li *et al.,* 2020). The diet determines how gut microbiota distributes and function in relation to immunity because diets rich in dietary fiber and polyphenols expand microbial diversity and produce short-chain fatty acids which reduce inflammation (Jin *et al.,* 2019; Durack and Lynch, 2018). Research shows that the detailed relationship between gut microbiome and human health drives scientists to investigate therapeutic methods based on probiotics and dietary changes for immune improvement (Durack and Lynch, 2018).

Table 2: Molecular mechanisms of fruit derived phytochemicals in chronic disease management

Phytochemical class	Key compounds	Major fruit sources	Molecular mechanisms	Target pathways	Chronic diseases	References
Polyphenols	Flavonoids, Resveratrol, Curcumin	Berries, Grapes, Pomegranate	Antioxidant (ROS scavenging, Nrf2 activation), Anti-inflammatory (NF-κB inhibition), Epigenetic regulation	↓ ROS, ↓ IL-6, ↓ TNF-α, ↑ Nrf2	CVD, cancer, neurodegeneration	Magrone *et al.,* 2019
Carotenoids	β-Carotene, Lycopene, Lutein	Carrots, Tomatoes, Papaya, Mango	Lipid peroxidation prevention, Neuroprotection (mitochondrial stability)	↓ MDA, ↑ BDNF, ↓ Aβ plaques	Alzheimer's, eye disorders, CVD	Milani *et al.,* 2016
Terpenes and alkaloids	Limonene, Berberine	Citrus fruits (Lemon, Orange), Bananas	Metabolic regulation (AMPK activation), Anti-inflammatory (COX-LOX inhibition)	↓ LDL, ↓ TG, ↑ HDL, ↑ AMPK	Diabetes, obesity, metabolic syndrome	Sharma *et al.,* 2022
Organosulfur compounds	Allicin, Sulforaphane	Garlic, Onions, Cruciferous vegetables	Gut microbiome modulation, Detoxification (Keap1/Nrf2 activation)	↑ SCFAs, ↓ LPS, ↑ GALT immunity	Cancer, gut disorders	Nosrati *et al.,* 2017
Anthocyanins	Delphinidin, Cyanidin	Blueberries, Blackberries, Cherries	Neuroprotection (neurogenesis, anti-inflammatory), Vascular protection	↓ β-Amyloid, ↑ NO, ↓ ICAM-1	Stroke, Parkinson's, hypertension	Camara *et al.,* 2022

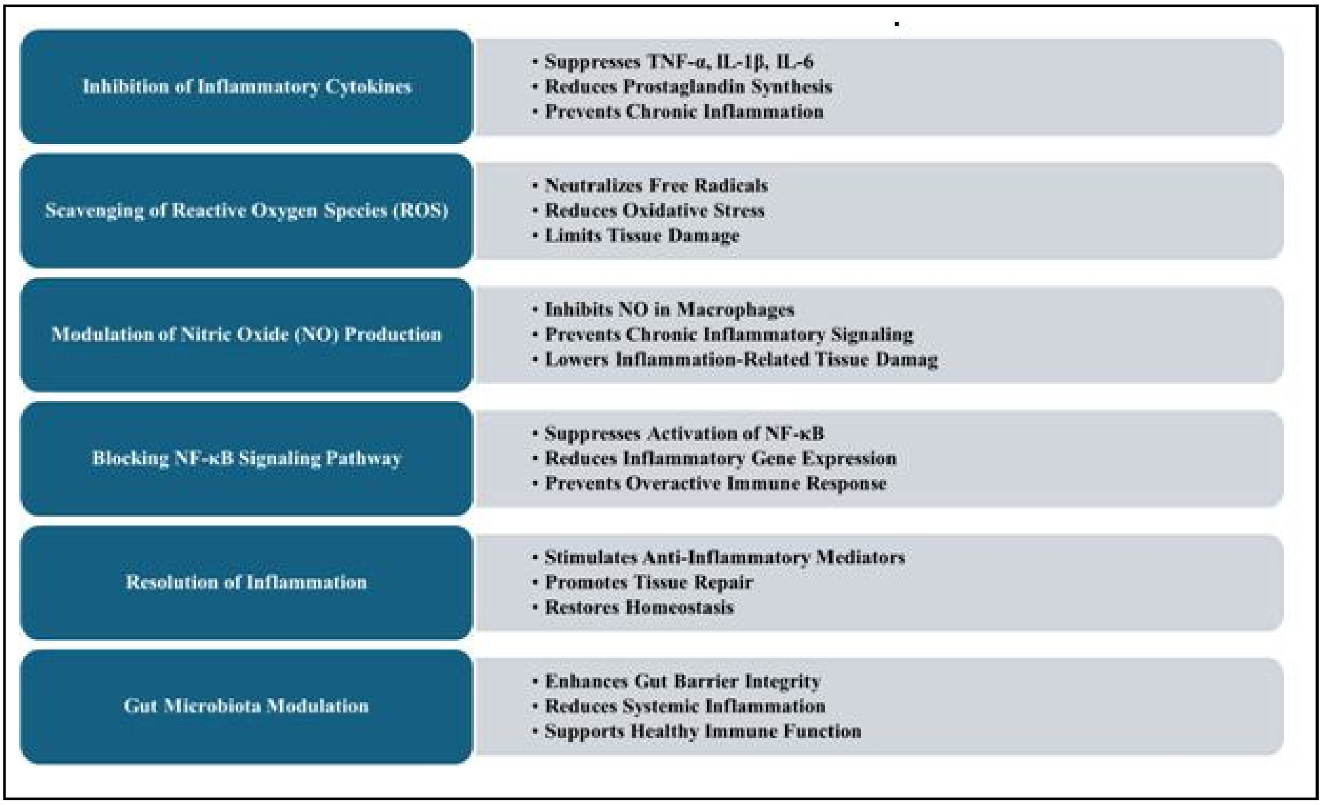

Figure 2: Fruit phytochemicals.

9. Neuroprotective and cognitive benefits of phytochemicals

Phytochemicals serve as essential neuroprotective compounds through their ability to decrease oxidatory pressure and minimize inflammation in the brain structures while supporting neural cells for survival. Phytochemicals function as antioxidants by converting reactive oxygen species (ROS) into harmless elements that control the progression of Alzheimer's and Parkinson's diseases. Phytochemical compounds activate Bcl-2 and Nrf2 pathways through their mechanism which improves both cognitive function and neuronal resilience in the brain (Trivedi, 2024; Zhang *et al.,* 2017). When content reaches the brain these ingredients control microglial activation to reduce pro-inflammatory cytokines while maintaining synaptic connections to enhance memory function (Kumar and Khanum, 2012; Limanaqi *et al.,* 2019). Phytochemicals regulate the expression of neurotrophic factors through an enhancement of brain-derived neurotrophic factor (BDNF) function because this factor supports neurogenesis and enables synaptic plasticity. Scientific research indicates that *Curcuma longa* polyphenolic compounds together with Bacopa Monnier polyphenols boost BDNF expression to protect brain health (Naoi *et al.,* 2017). The gene expression regulatory action of phytochemicals occurs through epigenetic markers where they manage DNA methylation and histone acetylation to improve neural resistance (Ganeshpurkar *et al.,* 2014). Phytochemicals protect mitochondria because they improve their membrane potential and stop cell death in toxic brain environments (Hasan *et al.,* 2024).

The protective properties of phytochemicals towards brain health create valuable potential in stopping cognitive deterioration and degenerative neural disorders as we age. Research based on epidemiology shows that eating flavonoids and polyphenols together with other phytochemicals decreases dementia risk while improving brain function (Wang *et al.,* 2018; Katayama and Nakamura, 2018). Research in clinical environments has demonstrated that phytochemicals show promise as supplementary treatments for improving neurological results (Kim *et al.,* 2019). The neuroprotective effects of *Corema album* berry juice emerge from metabolic interactions among multiple phytochemicals found in whole-food sources according to (Canoyra *et al.,* 2024). Phytochemicals show strong potential as a brain health-supporting intervention because they have dual capabilities to control inflammation with their neuroprotective properties.

10. Translational applications of phytochemicals in medicine

The translational potential of phytochemicals continues to expand as researchers explore their applications in cancer treatment and neuroprotection. Specific bioactive compounds target cancer stem cells (CSCs) and tumor microenvironments, thereby enhancing standard cancer treatments without increasing side effects (Gupta *et al*., 2021). The combination of phytochemicals shows potent anti-cancer effects so optimized formulations may lead to better clinical results (Gano *et al.,* 2023). The blood-brain barrier-crossing ability of phytochemicals allows them to offer protection for brain cells during neurodegenerative diseases including Alzheimer's and Parkinson's (Liu *et al.,* 2022). The clinical adoption of phytochemicals meets barriers from poor drug absorption that requires nanotechnology-based delivery systems such as phytosomes and nanocarriers to improve their therapeutic values (Chen *et al.,* 2022; Alharbi *et al.,* 2021). The implementation of phytochemicals in medical practice encounters major difficulties because of poor bioavailability and inconsistent pharmacokinetics. Human clinical trials for these substances remain sparse owing to Ojha *et al.* (2016) observations. Healthcare practitioners need to bridge pharmacokinetic research gaps and perform clinical trials of adequate design to establish these phytochemicals as medical practice options. The scientific knowledge of phytochemical interactions matters because these substances either enhance but sometimes block the therapeutic effects together (Rathod *et al.,* 2022). Phytochemicals present in diets fulfil two essential functions by delivering clinical benefits as well as acting to boost health while reducing disease chances when flavonoid intake increases (Sahoo *et al.,* 2023). The complete therapeutic potential of phytochemicals can become visible when medical professionals use a comprehensive strategy that joins clinical pharmacological methods with dietary interventions

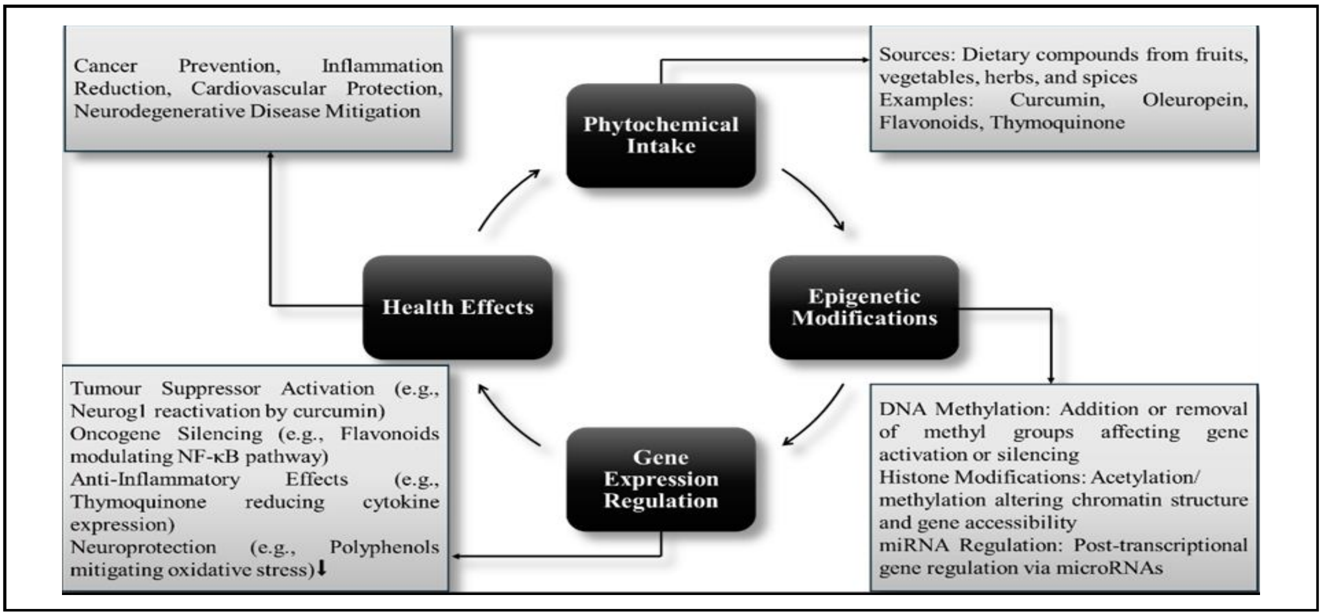

Figure 3: Epigenetic modulation cycle by phytochemicals.

11. Conclusion

Certain phytochemicals in fruits and vegetables have proven therapeutic strength to fight chronic diseases and study data shows these substances perform three essential tasks that benefit the body by fighting inflammation and being antioxidants and controlling metabolism processes. Studies show the importance of phytochemicals increases because they play a role in the relationship between gut microbiome and cellular pathways. Phytochemicals function as protective elements for the nervous system through epigenetic control of gene expression and through modifications of main signaling networks that make them appealing agents to prevent diseases. Phytochemicals demand specific delivery systems for absorption because they prove hard to absorb biologically. Public health has an opportunity because of the growing chronic disease epidemic to implement phytochemicals through diet since whole foods demonstrate better effects than supplements due to synergic effects between multiple substances. Future research must conduct well-regulated human population tests for validity assessment and investigate chemical activities to provide standardized dietary guidance. Such bioactive compounds offer therapeutic advantages for the development of new dietary interventions to enhance health results and increase life quality among different population groups.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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