Egypt. J. Chem. **Vol. 69**, No. 3 pp. 47 - 68 (2026)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

The Effects of Plant Extracts on Gene Expression: Mechanisms and Therapeutic Potential

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Abstract

Plant extracts have been shown to influence gene expression in various biological systems, exhibiting potential therapeutic potential against multiple diseases, including cancer, cardiovascular diseases, and neurological conditions. This paper reviews shows the mechanisms through which plant-derived bioactive compounds modulate gene expression, focusing on the transcriptional regulation, epigenetic modifications, and small, non-coding RNA molecules, which is known as microRNA (miRNA), involvement. In addition, the health-related impacts of plant extracts, particularly their anti-inflammatory, antioxidant, anticancer properties, and their impact on various signaling pathways that control gene expression were discussed in this paper reviews. Through a deeper understanding of the molecular interactions between plant compounds and genetic material, we explore the future applications of variety of plant extracts as a natural resource in personalized medicine for human health and disease, as well as in crop biotechnology. Ultimately, advancing this field depend on integrative approaches that combine molecular biology, pharmacology, and clinical research to fully realize the therapeutic potential of plant-based compounds.

Keywords: Plant extracts; Gene expression; bioactive compounds; transcription factors; inflammation; cancer; epigenetics; antioxidant; miRNA.

1. Introduction

Plants are an abundant source of bioactive molecules that have been widely utilized in traditional medicine for centuries. In recent decades, advances in molecular biology and high-throughput screening have revealed that many of these compounds exert therapeutic effects through direct modulation of gene expression and signalling pathways. Unlike conventional drugs that often target a single molecule, plant extracts typically contain multiple phytochemicals acting synergistically on diverse molecular targets, offering a broad spectrum of biological activities **[1].**

Regulation of gene expression by plant-derived compounds occurs through several mechanisms, including transcriptional regulation, modulation of transcription factors, epigenetic modifications (DNA methylation, histone acetylation), post-transcriptional regulation via non-coding RNAs, and direct effects on protein translation **[2]**. For instance, polyphenols such as curcumin and resveratrol have been shown to influence key regulatory pathways like NF-κB, Nrf2, and p53, thereby modulating genes involved in inflammation, oxidative stress response, and apoptosis [**3]**. Similarly, alkaloids and terpenoids from medicinal plants exhibit regulatory effects on oncogenes and tumor suppressor genes, highlighting their potential in cancer prevention and therapy [**4]**.

The therapeutic potential of plant extracts is increasingly linked to their ability to reprogram cellular gene expression profiles, thereby restoring homeostasis in pathological conditions such as cancer, metabolic disorders, cardiovascular diseases, and neurodegenerative diseases **[5]**. Moreover, understanding the molecular mechanisms underlying these effects provides opportunities for the rational design of phytochemical-based therapeutics, functional foods, and nutraceuticals with enhanced efficacy and safety profiles.

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Received date 29 September 2025; Revised date 15 November 2025; Accepted date 19 November 2025
DOI: 10.21608/EJCHEM.2025.428057.12403

This review explores the mechanisms by which plant extracts regulate gene expression, focusing on transcriptional, epigenetic, and post-transcriptional pathways. It further discusses the therapeutic potential of these regulatory effects in the context of human health and disease.

2. Bioactive Compounds in Plant Extracts

Bioactive compounds are phytochemicals present in foods that can influence metabolic processes and contribute to improve the health. They demonstrate inhibition or induction of enzymes, suppression of receptor activities, and modulation of gene expression **[6]**, they are categorized into phenolic and non-phenolic compounds and pigments, or into various groups such as polyphenols, phytosterols, terpenoids, carotenoids, saponins and other compounds [**7**].

Medicinal plants are rich in polyphenols, which include flavonoids, phenolic acids, lignans, and stilbenes [**8, 9]**. Polyphenols are a large group of natural compounds that contain multiple phenolic groups **[11]**, in addition to vitamins (C and E) and carotenoids (likexanthophylls and carotenes), which make up most plant-based antioxidants [**10, 8**]. These compounds are common in plants, where they help defend against pathogens and support normal cell function. In humans, polyphenols protect against cardiovascular diseases, metabolic disorders, and aging [**12**], and slowing tumor growth, spread, and blood vessel formation [**13–15**]. Polyphenols and carotenoids, have antioxidants, anti-inflammatory, antibacterial, antiviral, anti-aging, and anticancer properties **[23, 8, 24-33].** Flavonoids, carotenoids, and alkaloids have antioxidant activities [**16]**, anti-inflammatory [**17]**, anticancer properties [**18]**, and antimicrobial effects [**19]**.

2.1- Polyphenols

2.1.1 Flavonoids

Most edible fruits and vegetables contain flavonoids (flavanones, flavonols, catechins, flavones, anthocyanidins, and isoflavonoids) [**34- 36]**, In addition to their anti-inflammatory and antioxidant properties **[20]**, flavonoids also have anti-proliferative, anticancer, anti-angiogenic, antimicrobial, antiviral, antimalarial, and neuroprotective properties **[21, 22].** Flavonoids (fruits, wine, vegetables, and tea) [**37]**. Reduce oxidative stress and inflammatory reactions by influencing a number of signalling cascades, including phosphoinositide 3-kinase (PI3K)/ the activated protein kinase (Akt), ERK, mitogen activated protein kinase (MAPK), and other protein kinase pathways. They have anticancer, neuroprotective, and cardioprotective effects through these mechanisms. Chrysin may help treat epilepsy and depression and has been shown to reduce neuroinflammation **[21].** Likewise, isoflavones, flavanols, and anthocyanins are linked to a decreased risk of cardiovascular disorders. Furthermore, Brazil nuts flavonoids have shown promise in lowering the risk of cancer and promoting heart health **[38].** As shown in Fig.1, flavonoids have been demonstrated to exhibit anti-inflammatory effects by reducing chemokine and COX-2 expression, modulating immune cell function, suppressing cytokine release, and inhibiting pro-inflammatory transcription factors such as PI3K/Akt and IKK/JNK [**39,40**].

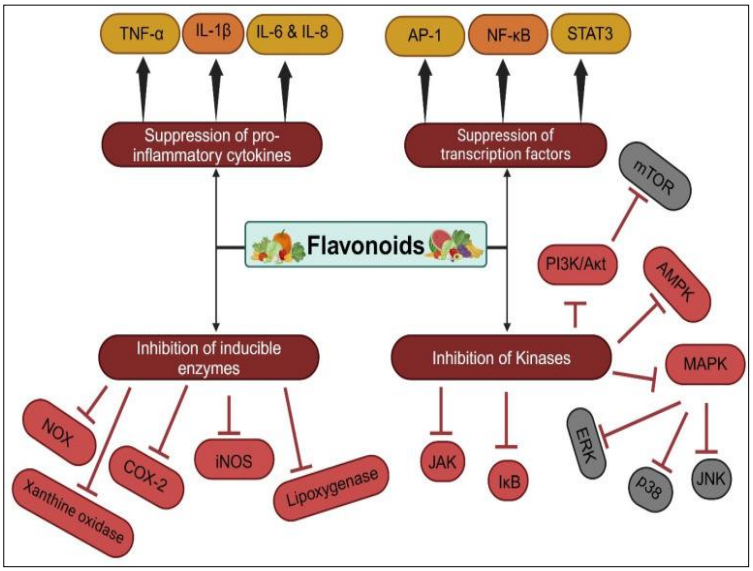

Figure 1: The targets of flavonoids in inflammatory processes according [**41]**.

In edible plants like onions, quercetin, Kaempferol (broccoli), isorhamnetin (onion), and myricetin (berries), fisetin, silymarin, and rutin are flavonols, and they are present in lettuce, saffron, tomatoes, apples, grapes, berries, onions, kale, red wine, and tea [**36]**. Kaempferol damage DNA in cancer cells, inhibits the proliferation and progression of cancer cells and induces apoptosis

[**42]**. The quercetin sources are broccoli, apples, grapes, and tea, can influence the proliferation of various cancers, such as breast, lung, liver, colon, and gastric cancer [**43]**. Apigenin, luteolin, and tangeretin are flavones present in sweet red pepper, parsley, chamomile, celery, Ginkgo biloba, and mint **[36]**, found in apple, cabbages, carrots, broccoli, and herbs. Apigenin has anticancer actions by modulating key signaling pathways [**44].** Also, Luteolin hss anti-inflammatory and antioxidant effects and can inhibit the development of cancer cells and induce apoptosis [**45, 46].**

Green tea, , grapes and chocolate contain epigallocatechin gallate (EGCG), and catechin [**47**]. Flavanols encompass a range of compounds from the simple monomer catechins and epicatechin to more complex structures such as epigallocatechin, epigallocatechingallate, gallocatechin, epicatechingallate, and procyanidin that in green and black tea, and fruits (bananas, peaches, apples and blueberries) [**36]**, they can affect gene expression and cell signaling and can inhibit the metastasis and proliferation of cancer cell [**48]**.Also, EGCG can suppress angiogenesis, inhibit proliferation and metastasis, and induce apoptosis of cancer cells types [**49, 50**]. Citrus fruits, (tomatoes, and potatoes) vegetable contain flavanones that influence both cell signaling and gene expression in manners that enhance the effects of anti-inflammation and antioxidant. As an example, hesperidin prevents the growth of tumors and promotes apoptosis and naringenin have breast and skin anticancer effects [**51, 52**], and potential methods for augmenting its anticancer efficacy for medical use have been investigated [**53**].

Phytoestrogens are a class of flavonoids that are primarily found in soy-based foods like tofu and roasted soy nuts have structural similarities to oestrogen **[36].** The most prevalent isoflavones among them are genistein and daidzein, which are well known for their phytoestrogenic properties **[34, 54, 55].** These substances suppress the growth and metastasis of cancer cells, alter gene expression, and have anti-inflammatory and antioxidant qualities **[56].** Specifically, genistein has been shown to increase cisplatin's anticancer effectiveness in cervical cancer cells, indicating that it may play a part in enhancing the results of chemotherapy **[57].**

Anthocyanins as malvidin, pelargonidin, delphinidin, cyanidin, and peonidin, are responsible for colour of fruits asred grapes, merlot grapes, strawberries, blackberries, cranberries, blueberries, bilberries, and raspberries [**36**].

2.1.2 Phenolic acids

Utilize benzoic acid–derived compounds (including gallic and hydroxybenzoic acids) and cinnamic acid–derived compounds (like p-coumaric, ferulic, and caffeic acids). In edible plants, hydroxycinnamic acids are more prevalent than hydroxybenzoic acids [**8]**.

2.1.3. Stilbenes

Grapes, peanuts, and red wine contain resveratrol, has anti-inflammatory, antioxidant and cardioprotective properties [**58**].

2.1.4. Lignans

Such as secoisolariciresinol and matairesinol, are present in legumes, seeds (particularly flaxseed), and grains, transformed into enterolignans by gut microbiota, which demonstrate both estrogenic and antioxidant properties [**59**].

2.2. Carotenoids

Are potent antioxidants that promote human health [**60**]. These compounds can work in conjunction with vitamin E as antioxidants to strengthen membranes and prevent the oxidative degradation in lipid-rich environments. Some carotenoids, such as β-carotene, serve as precursors to vitamin A, essential for immune function, cellular communication, and vision [**61**]. Carotenoids offer a wide range of health benefits that extend beyond their antioxidant roles. β-Carotene, which is a provitamin A compound, plays a crucial role in maintaining healthy skin and vision, while lutein and zeaxanthin accumulate in the macula to protect against age-related macular degeneration (AMD) [**62, 63**]. Lycopene is associated with a reduced risk of disease of heart and prostate cancer, due to its ability to reduce the oxidative damage of DNA and modulate NF-κBsignaling pathways [**64**].

2.3. Vitamins C and E

Vitamins C and E are vital micronutrients that are crucial for maintaining human health [**65**], these vitamins help safeguard both water-soluble and lipid parts from damage caused by oxidative stress. Vitamin C acts to neutralize reactive oxygen species (ROS), restore other antioxidants (such as vitamin E), and shield biomolecules, including DNA, lipids, and proteins, from oxidative stress [**66**]. Vitamin C can regenerate oxidized vitamin E within cell membranes, enabling it to maintain its antioxidant function, thus establishing an efficient redox cycle that boosts overall antioxidant defense [**67**]. Both vitamins may

play a role in reducing the risk of chronic diseases as specific cancers neurodegenerative conditions and cardiovascular associated with oxidative stress, Vitamin E is associated with lower LDL oxidation and enhanced vascular health, while vitamin C is linked to improved endothelial function and stronger immune response [**68**].

2.4. Alkaloids

Possess antioxidant, antibacterial, and anti-inflammatory properties. Examples of alkaloids with notable antioxidant effects include caffeine, berberine, and theobromine. Caffeine, found in coffee and tea, inhibit lipid peroxidation, and effectively scavenge hydroxyl radicals [**69**]. Berberine, which is derived from Coptischinensis, and *Berberis vulgaris* activating AMP-activated protein kinase (AMPK) pathways and reducing oxygen reactive species (ROS) production to modulate oxidative stress, indicating potential benefits for metabolic and neurological disorders. Important modulators of cellular redox homeostasis are organosulfur compounds found in Allium plants (garlic and onion) and cruciferous vegetables (broccoli and cabbage). Bioactive components of garlic, such as diallyl sulphide, S-allyl cysteine, and allicin, as well as sulforaphane from broccoli sprouts, are known to activate the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway. This pathway's activation boosts the body's natural antioxidant systems and increases the expression of phase II detoxification enzymes **[70]**. Sulforaphane has drawn the most attention of these substances because of its well-established ability to enhance cellular resistance to oxidative stress, suppress inflammatory signalling, and boost antioxidant defences. Its potential as a dietary agent to reduce the risk of chronic diseases is highlighted by these qualities. By directly scavenging reactive oxygen species and affecting the activities of antioxidant enzymes, terpenoids also contribute to the maintenance of redox balance. Antioxidant and anti-inflammatory properties of molecules like ursolic acid and oleanolic acid support their protective role against age-related functional decline and metabolic disorders **[71].** Saponins, a class of glycosylated metabolites widely distributed in foods such as legumes, spinach, quinoa, and ginseng, also exhibit antioxidant properties. Their protective effects are largely mediated through the suppression of lipid peroxidation and the enhancement of endogenous enzymes, particularly glutathione peroxidase (GPx) and catalase (CAT) **[72]**. These phytochemicals are consumed daily habits and have been increasingly advocated as a natural approach to disease prevention and management, particularly in early-stage diseases and collectively contribute to the potential health-promoting effects of plant-based diets. Ongoing research continues to uncover new mechanisms by which phytochemicals exert their health-promoting effects, highlighting their potential as therapeutic agents in both preventive and therapeutic strategies against various ailments [**73**]. Phytochemicals found in fruits and vegetables offer a wide range of therapeutic benefits.

Several naturally occurring bioactive compounds including, resveratrol, curcumin, astaxanthin, sulforaphane, indole-3-carbinol, quercetin, epigallocatechin-3-gallate (EGCG), anthocyanins, lycopene, ellagic acid, fisetin, capsaicin, and ginger-derived phytochemicals have been reported to target different therapeutic areas and have the capability to modulate gene expression [**74-76**].

3.Mechanisms of Gene Expression Regulation by Plant Extracts

The ability of plant-derived compounds to modulate gene expression underlies much of their therapeutic potential. These effects occur through diverse molecular mechanisms that span transcriptional regulation, epigenetic modifications, and post-transcriptional modulation.

3.1. Transcriptional Regulation

Many plant extracts can influence the activity of transcription factors, which are proteins that bind to DNA and regulate the transcription of specific genes. For example:

3.1.1. Nuclear Factor kappa B (NF-κB): Some plant extracts (e.g., from curcumin and green tea polyphenols) can suppress the activation of NF-κB, which is involved in inflammation and immune responses.

3.1.2 Activating Protein-1 (AP-1): Plant compounds can either upregulate or downregulate AP-1 activity, which is associated with stress response and apoptosis.

3.1.3. Nuclear erythroid 2-related factor 2 (Nrf2): Nrf2 regulates antioxidant genes, and plant extracts rich in flavonoids or polyphenols can activate Nrf2, leading to enhance antioxidant responses. Phytochemicals can directly or indirectly modulate transcription factors, thereby altering gene transcription. For example, curcumin and resveratrol suppress activation of nuclear factor-kappa B (NF-κB), a transcription factor that controls genes associated with inflammation and oncogenesis [**77, 78**]. Similarly, nuclear factor erythroid 2–related factor 2 (Nrf2), activated by flavonoids which stimulates the expression of antioxidant response element (ARE)-regulated genes that combat oxidative stress [**73, 79**]. Terpenoids, such as ursolic acid, have been shown to influence peroxisome proliferator-activated receptors (PPARs), thereby regulating lipid metabolism and glucose homeostasis [**80**].

The activity of transcription factors can be modulated by curcumin, which inhibits NF-κB, AP-1, STATs, HIF-1, Notch-1, Egr-1, and β-catenin, but stimulates Nrf2 activation **[81].** In diabetic patients, quercetin improves insulin sensitivity by inhibiting NF-κB signaling in adipose tissue, which results in decreased secretion of tumour necrosis factor alpha (TNF-α) and interleukin-6 (IL-6) **[82].** Likewise, anthocyanins, the natural pigments found in berries and red grapes, suppress NF-κB activation and reduce circulating levels of C-reactive protein (CRP), a recognized marker of systemic inflammation **[83].**

Flavonoids modulate key cellular signaling pathways such as Nrf2, MAPKs, and NF-κB, thereby exerting cytoprotective and anti-inflammatory effects **[84]**. Resveratrol, a polyphenol present in grapes and red wine, activates Nrf2—the central regulator of antioxidant defense—promoting the expression of enzymes like superoxide dismutase (SOD) and catalase (CAT), which protect pancreatic β-cells and insulin-responsive tissues from oxidative injury **[85**]. Lycopene has been associated with a reduced

risk of cardiovascular disease and certain cancers, particularly prostate cancer, through its ability to limit oxidative DNA damage and modulate NF-κB signaling pathways **[86]**.

3.2. Epigenetic Modifications

Some plant extracts can induce epigenetic modifications such as DNA methylation, histone modification, or regulation of microRNA expression. These changes affect gene expression without altering the DNA sequence itself.
One important way that plant extracts influence gene expression over an extended period of time is through epigenetic regulation, which includes histone modification, DNA methylation, and chromatin remodelling. Polyphenols such as EGCG from green tea inhibit DNA methyltransferases (DNMTs), resulting in re-expression of tumor suppressor genes in cancer cells that had been silenced [**87**]. The processes of epigenetic, reverse DNA methylation in tumor suppressor genes can be influenced by catechins found in green tea, which can also enhance their relative transcription rates. Moreover, they influence DNA methylation and lessen the impact of DNA methyltransferase 1 (DNMT1) through mechanisms such as inhibition enzymatic directly and indirectly, reduced the expression and translation of DNMT1**[88]**. Another way in which epigenetic regulation can occur involves the antioxidant and redox-related activities of green tea catechins, particularly their ability to suppress histone deacetylase (HDAC) activity **[89].** In studies of gastric carcinoma, elevated consumption of EGCG has been linked to decreased of the CDX2 and BMP-2 genes methylation, demonstrating a measurable epigenetic effect compared with placebo groups **[90]**. In addition, EGCG has been shown to enhance the expression of tissue inhibitors of metalloproteinases (TIMPs), such as TIMP-3. This factor is crucial because it interferes with the gelatinase activity of MMP-2 and MMP-9, enzymes that play a role in metastatic processes. EGCG is considered a modulator of metalloproteinase activity, providing advantages in oncological contexts [8591]. Furthermore, in acute promyelocytic leukemia (APL), EGCG contributes to tumor suppression by limiting cellular proliferation and inducing programmed cell death **[92].**

Curcumin has been reported to alter histone acetylation by modulating histone acetyltransferases (HATs) and histone deacetylases (HDACs), thereby influencing genes involved in cell cycle regulation and apoptosis [**93**]. Curcumin has been reported to modulate patterns of methylation DNA and modifications of histone, influencing genes expression involved in inflammation and cancer. Curcumin is well-known for its antioxidant, anti-inflammatory, and anticancer effects, as well as its role as an epigenetic modulator [**94**]. Curcumin serves as an epigenetic regulator through several mechanisms: it alters histones by controlling the activity of histone deacetylase (HDAC) and histone acetyltransferase (HAT); it affects DNA methylation by blocking DNA methyl transferase (DNMT); it modifies microRNAs by upregulating tumor-suppressive miRNAs like miR-15a, miR-16, miR-22, miR-26a, miR-34a, miR-145, miR-146a, and let-7 **[95,96]**; it downregulates oncogenic miRNAs (miR19a, b, miR-21, miR-27a, miR-130a, and miR-186) **[97]**; and it activates transcription factors, cytokines, and the genes of tumour suppression **[98].** Targeting the methylation of DNA is an effective treatment strategy because acute myeloid leukaemia (AML) is largely caused by the inactivation of genes caused by DNA methylation. Both in vitro and in vivo, curcumin has been shown to suppress DNMT1 expression in AML cell lines **[99]**. Curcumin may reduce the expression of DNMT1's positive regulators, Sp1 and p65. In AML cell lines, this decrease is correlated with a decrease in these transcription factors' binding to the DNMT1 promoter. Curcumin has the potential to treat AML because of these characteristics **[100]**. Moreover, dietary isothiocyanates such as sulforaphane promote histone acetylation and activate detoxification genes, contributing to their chemopreventive effects [**106**].

3.3. Post-transcriptional via microRNA modulation

MicroRNAs (miRNAs) constitute a class of small non-coding RNAs that fine-tune gene expression at the post-transcriptional level by modulating mRNA stability and translation. Several plant extracts can influence miRNA profiles, thus indirectly regulating gene expression.
Both EGCG and curcumin have change miRNA expression, which in turn regulates genes involved in inflammation, cell survival, and cancer.
A single phytochemical may simultaneously influence transcriptional, epigenetic, and post-transcriptional processes. For example, curcumin not only inhibits NF-κB (transcriptional effect) but also modulates HDACs (epigenetic effect) and regulates miRNAs (post-transcriptional effect) [**93, 124**]. This integrative regulation underscores the multi-target nature of plant extracts, distinguishing them from single-compound pharmaceuticals and enhancing their potential in managing complex diseases.

Curcumin, the bioactive polyphenol obtained from the rhizome of *Curcuma longa*, has been pleiotropic properties (antioxidant and anti-inflammatory actions, as well as anticancer and antimicrobial activities), underscoring its therapeutic relevance across diverse pathological conditions **[125]**.The antitumor effects of curcumin may stem from several mechanisms, including the downregulation of gene expression that inhibits growth, the induction of apoptosis, and regulation of various signaling

pathways and oncogene expression. Gene expression regulated by curcumin plays a crucial role in the f cellular signaling pathways regulation (Akt, MAPK, NF-κB), and others. miRNAs can also regulate these signaling pathways. Curcumin was found to target the transcription factor SP1 and the estrogen receptor ESR1 in human pancreatic cells, leading to an up-regulation of miRNA-22 and a down-regulation of miRNA-199a* expression. These curcumin-regulated miRNAs played a crucial role in its anti-tumor efficiency [**124**]. Furthermore, after treating several breast cancer cell lines with curcumin, both (miR-181b, miR-34a, miR-16, miR-15a, and miR-146b-5p) up-regulation and down-regulation (miR-19a and miR-19b) was observed **[126].**

3.4. Modulation of Signaling Pathways

Plant extracts may impact various signaling pathways that control gene expression. For instance:

3.4.1MAPK/ERK pathway: Some extracts, such as those from ginger, can influence on the MAPK pathway, which is important in cell differentiation, growth, and response to stress.
A bioactive substance found in *Coptis chinensis* and *Berberis vulgaris*, berberine helps control oxidative stress by reducing ROS levels and activating AMPK signalling. As such, it may be used to treat metabolic and neurological conditions. Maintaining cellular redox balance is a key function of organosulfur compounds, particularly those found in cruciferous vegetables (like broccoli and cabbage) and Allium species (like garlic and onion) **[111]**. The development of insulin resistance and inflammation are largely influenced by the MAPK cascade, which is made up of the p38, JNK, and ERK kinases. By inhibiting p38 MAPK and JNK phosphorylation, curcumin reverses these effects and reduces cytokine-driven insulin resistance **[112]**.

3.4.2.PI3K/Akt pathway: Certain plant compounds like those in cannabis or flaxseed may modulate the phosphoinositide 3-kinase (PI3K)/Akt signaling axis, that is fundamental to the regulation of metabolism, survival, and tumor progression.In addition to this axis, dietary phytochemicals also engage other regulatory networks such as MAPK/ERK 1/2, Wnt, and Hedgehog, which orchestrate processes including proliferation, differentiation, and programmed cell death. When disrupted, these pathways contribute to the onset and progression of multiple diseases **[113, 114]**. By modifying the function of proteins embedded within these signalling cascades, phytochemicals may influence cellular behavior in ways that provide therapeutic benefit. This broad mechanistic capacity has led to growing interest in dietary phytochemicals as supportive agents for the prevention and treatment of cancer, metabolic disorders, and neurodegenerative diseases **[115, 116]**.

The anti-inflammatory, anti-amyloid, anti-hyperphosphorylation, and antioxidant properties of phytochemicals have made them valuable tools as therapeutic candidates for neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's **[117]**. These substances are known in cancer biology to disrupt important molecular pathways that control the development and spread of tumours. Enhancing antioxidant defences, deactivating carcinogens, preventing unchecked cell division, triggering cell cycle arrest and apoptosis, and affecting immune system activity are some of their actions **[118]**.
STAT proteins tightly regulate transcription factors that control decisions about cell fate, including Bcl-2, p53, interleukin-6 (IL-6), and cyclin D **[119]**. Following their activation by Janus kinase (JAK) signalling, STATs undergo phosphorylation and move into the nucleus, where they affect the transcription of genes related to cell survival, proliferation, and apoptosis. This emphasises how crucial they are to maintaining cellular homeostasis and the onset of disease **[120]**. Numerous cancers, including those of the lung, breast, colon, blood, ovary, brain, and skin have been closely linked to dysregulation of the Wnt/β-catenin pathway. Likewise, the anticancer defence depends on the tumour suppressor protein p53, which cooperates with other signalling cascades **[114, 121]**. A bioactive isothiocyanate found in cruciferous vegetables, sulforaphane, has potent anticancer properties by altering the PI3K/Akt signalling pathway. By inhibiting Akt phosphorylation and downregulating PTEN in xenograft mouse models, sulforaphane has been demonstrated in experimental studies to inhibit the progression of lung cancer. Due to these characteristics, sulforaphane is regarded as a potentially effective natural therapeutic agent for the treatment of lung cancer **[122]**. Mixture of natural plants extracts may be combined with chemotherapy to induce its activity or decrease its side effects thus improve cancer patient's life quality. Incorporating natural products into conventional oncology may yield more effective, tailored, and comprehensive approaches for lung cancer treatment. **[123].**

4.Therapeutic Potential of Plant Extracts via Gene Expression Modulation

The ability of plant-derived compounds to regulate gene expression has profound therapeutic implications. By modulating signaling pathways, transcription factors, epigenetic regulators, and non-coding RNAs, phytochemicals exert pleiotropic effects across diverse disease contexts.

4.1. Cancer Prevention:

Apoptosis-related Genes: Compounds derived from plants, like ginseng and garlic, have been shown to alter the ratio of pro-apoptotic (like Bax, p53) to the genes of anti-apoptotic (like Bcl-2), which in turn controls programmed cell death, a mechanism of interest in cancer treatment. Specifically, quercetin increases the expression of Bax, p53, caspase-3, and caspase-9, which together activate the pathway of mitochondrial apoptotic and fortify pro-apoptotic responses **[105, 106]**. Grape seed extract has been shown to influence the expression of p21 and cyclin D1, genes that play a role in regulating the

cell cycle, which may slow cancer cell growth. Another important feature of quercetin is its ability to halt the cycle of cell in the phase of G1 by decreasing the ratios of (D1/Cd4 and E/Cdk2) and p21 activation [**107, 108**]. Quercetin also inhibits carcinogenesis and metastasis, according to evidence, in part by stabilising p53, a key regulator of cell survival and apoptosis in cancer treatment [**109**].

Many plant extracts are studied for their potential anticancer properties by altering the cell cycle regulation, apoptosis, and metastasis genes expression. For example: Green tea extract (rich in catechins) has been shown to inhibit the expression of genes that promote tumorigenesis and metastasis. In liver, prostate, and lung cancer, EGCG plays a significant role in regulating microRNAs associated with cancer. It upregulates miR-16, miR-210, and miR-330 while reducing the expression of miR-21 and miR-98-5p [**124**].

Some plant extracts, including those from cruciferous vegetables (e.g., broccoli, cabbage) and green tea, have compounds like sulforaphane and EGCG that influence genes involved in tumor suppression, apoptosis, and cell cycle regulation. For example, sulforaphane activates the Keap1-Nrf2 pathway, which leads to the expression of phase II detoxifying enzymes and may reduce the risk of cancer. Polyphenols are used as anti-inflammatory, antihypertensive, antidiabetic, and anticarcinogenic properties **[127]**.

Nrf2 transcription factor is essential for cellular defense reactions **[132]**. By preventing cell transformation and tumour growth, Nrf2 helps prevent cancer by activating antioxidant pathways. For instance, sulforaphane inhibits NF-κB signalling and increases Nrf2 activity, which reduces pro-inflammatory mediators and inhibits the growth of cancer cells **[133–140].**

The NF-κB pathway is significant because it controls multiple pro-inflammatory genes, including cyclooxygenase (COX-2) and iNOS, and inflammation is a defining feature of many cancers and chronic illnesses. Because they inhibit NF-κB, compounds such as indole-3-carbinol (I3C) and its derivative diindolylmethane (DIM) have anti-inflammatory properties by downregulating COX-2) , iNOS, CXCL5, and interleukin-6 (IL-6) **[141].** Naturally occurring in cruciferous vegetables like broccoli and cabbage, glucosinolates (GLSs) also have positive health effects. Antioxidant and detoxifying properties, along with their impact on epigenetic regulation, are thought to contribute to their anticancer potential. These impacts include changing histone structure, controlling microRNA expression, and changing CpG methylation in genes linked to cancer **[142, 143].**

The main catechin found in green tea is epigallocatechin-3-gallate (EGCG), a powerful polyphenol with strong anti-inflammatory and antioxidant **[144]**. EGCG inhibits the growth of cells and induces apoptosis in order to suppress acute promyelocytic leukaemia (APL) **[145]**. EGCG suppresses tumour growth by causing apoptosis and controlling proliferation via pathways like MAPK/ERK and growth factors like IGF1, IGF, and Insulin-like growth factor binding protein-3 (IGFBP-3) in both cultured cells and animal models of prostate, breast, skin, liver, bladder, lung, and gastrointestinal cancers. Additionally, it enhances apoptosis by interfering with the PI3K/AKT/p-BAD survival signalling cascade. Furthermore, EGCG inhibits vascular endothelial growth factor (VEGF) activity, invasion, and angiogenesis **[146]**. The modulation of cancer-related microRNAs is another important function of EGCG; in liver, prostate, and lung cancers, it downregulates miR-21 and miR-98-5p while upregulating miR-16, miR-210, and miR-330 **[147].** EGCG, reactivate silenced tumor suppressor genes by inhibiting DNA methyltransferases **[131]**.

Curcumin activates the cellular antioxidant defense by inducing epigenetic modifications in the Nrf-2 gene. Increased expression of Nrf-2 and its downstream target NQO1 at the transcript and protein levels was linked to curcumin-induced demethylation of the Nrf-2 gene in TRAMP C1 prostate cancer cells **[148]**. Additionally, curcumin inhibits STAT3 phosphorylation, which is a crucial mediator in oncogenic signalling pathways **[149**]. Additionally, it significantly suppresses NFκB, which encourages cell apoptosis **[150]**. Furthermore, curcumin decreases the anti-apoptotic regulators Mcl-1 and Bcl-2 activation while increasing the pro-apoptotic protein Bax expression. Additionally, it alters pathways linked to apoptosis that involve the proteins p38, p53, and NF-κB **[151]**. Curcumin's anticancer effects are primarily attributed to its ability to reduce the expression of cyclin-dependent kinases (CDKs), which regulate of the cell-cycle progression **[152]**. Curcumin can inhibit breast cancer cell lines by suppressing the human epidermal growth factor receptor 2, a tyrosine kinase (HER2-TK). **[153]**. By downregulating the PI3K/AKT signalling cascade, curcumin has been demonstrated to have anticancer effects **[154**]. Additionally, it alters a variety of transcription factors, increasing the activity of protective factors like Nrf2 while suppressing NF-κB, AP-1, STAT proteins, HIF-1, Notch-1, Egr-1, and β-catenin **[155, 156].** Transcriptional factors are important targets of curcumin because they control important aspects of tumour development, such as proliferation, survival, angiogenesis, invasion, and inflammation. Their dysregulation is frequently observed in malignancies **[156]**. Curcumin suppresses NF-κB and STAT3 pathways, leading to reduced transcription of oncogenes and inflammatory mediators **[129**].

Due to its strong anti-inflammatory qualities, curcumin has been shown to slow the growth of some cancers by inhibiting the expression of pro-inflammatory mediators like iNOS, lipoxygenase-2, COX-2, and other cytokines [157]. Additionally, by scavenging free radicals and preventing their further generation, curcuminoids demonstrate their antioxidant capacity [158]. Curcumin increases the activity of antioxidant enzymes such as SOD, CAT, GST, and GSR, according to experimental data from both in vitro and in vivo studies. This process lessens the buildup of reactive species like hydrogen peroxide, nitric oxide

radicals, and superoxide anions. Additionally, by increasing the enzymes that break down xenobiotics, curcumin helps the detoxification system and helps prevent the development of cancer [159]. Curcumin's gene-regulatory effects inhibit inflammation, enhance antioxidant defenses, and prevent cancer, but deeper mechanistic insights and optimized delivery are needed for clinical translation.

Resveratrol causes cells to undergo apoptosis in a number of ways. Among these are cyclin-dependent kinase inhibitors, apoptosis-related cytokines, receptor signalling, and the start of mitochondrial pathways and caspase cascades. Pro-survival proteins like survivin, XIAP, cIAPs, cFLIP, Bcl-XL, and Bcl-2 are also suppressed, and transcriptional regulators like NF-κB, AP-1, HIF-1α, and STAT3 are downregulated, along with survival-associated kinases like MAPK, PI3K/AKT, PKC, and EGFR kinase. Resveratrol eventually causes programmed cell death by triggering one or more of these pathways **[160, 161]**. Furthermore, it alters important regulators of DNA synthesis and the cell cycle progression, such as p53, CDKs, Rb/E2F, and their inhibitors. The substance also affects the activity of transcription factors, particularly NF-κB, AP-1, and EGR1, that are connected to stress responses and proliferation. MAPK and tyrosine kinases like SRC are one mechanism behind these processes. They affect cell survival and apoptosis by controlling elements like Bcl-2 proteins, apoptosis inhibitors, and carcinogenesis-related enzymes (like COX, NOS, and phase I/II enzymes) **[160]**. Furthermore, it has been demonstrated that resveratrol alters the expression and function of co-transcriptional regulators, particularly SIRT1 and p300 [**162]**. Antioxidant and anticancer benefits have been linked to regular consumption of cruciferous vegetables, which include broccoli, cabbage, Brussels sprouts, cauliflower, and kale. Numerous studies suggest that the main bioactive substances in these vegetables that provide these protective benefits are glucosinolates (GLSs) **[163].** Resveratrol induces p53-mediated apoptosis and regulates miRNAs that inhibit tumor growth **[130].**

Quercetin, a flavonoid from the flavonols group, is found in different type of fruits—as apples, grapes, olives, and citrus fruits like oranges, as well as vegetables including tomatoes, onions (*Allium cepa* L.), broccoli, and capers, and in beverages like tea and red wine **[164]**. Quercetin exhibits anticancer activity against a number of cancers, including those of the breast, prostate, kidney, colorectal, ovarian, gastric, nasopharyngeal, and pancreatic regions, according to both in vitro and in vivo studies. Its antitumor mechanisms include controlling the cell cycle, preventing tumour metastasis, and inhibiting angiogenesis and cell proliferation **[165]**. By upregulating pro-apoptotic factors like (caspase-3, BAX, caspase-9, and p53), and activating the pathway of mitochondrial apoptotic, quercetin increases programmed cell death and apoptosis [**166, 167**]. Quercetin's capacity to stop the cycle of cell at G1 phase, mainly by p21activation and downregulating the D1/Cdk4 and E/Cdk2 complexes is another noteworthy effect [**107, 108].** Quercetin has been shown in multiple studies to have the ability to suppress carcinogenesis and metastasis in cancer. Additionally, it can stabilize p53, a crucial molecule in cancer treatment that regulates cell death and survival **[168]**.

It has been demonstrated that quercetin suppresses the expression of particular genes, which is linked to a reduction in cell invasion, migration, and viability. By disrupting the regulation of uPA/uPAR systems, AMPKα, NF-κB, ERK1/2, and PKC-δ, it exhibits antimetastatic activity in gastric cancer **[169]**. By inhibiting the AKT signalling pathway and triggering the c-Jun N-terminal kinase (JNK) pathway, quercetin reduces cell viability and triggers apoptosis in colorectal cancer cells with KRAS mutations **[170]**.

By lowering androgen receptor (AR) transcription and AR-driven PSA expression, quercetin prevents the growth of prostate cancer tumours. Additionally, it induces apoptosis in a dose-dependent manner and inhibits the survival protein Akt **[171]**. Additionally, quercetin decreases IGF1 levels and elevates IGFBP3 levels, which is linked to enhanced pro-apoptotic effects and decreased levels of anti-apoptotic proteins such as BCL2 and B-cell lymphoma extra-large (BCLXL) **[172]**.

The epigenetic effects of quercetin involve the suppression of Janus kinase 2 (JAK2), leading to reduced invasion, proliferation, and cancer cells migration **[173]**, promote apoptosis via its ability to demethylate DNA. Due to enhanced proteasomal degradation, quercetin inhibits the expression of class I HDAC in leukemia cells **[174]**. It is well known that quercetin is a powerful nutraceutical that can improve human health by lowering the production of pro-inflammatory and free radical molecules. Research has also shown that quercetin can alter the expression of microRNAs in various cancer types by downregulating oncogenic miRNAs like (miR-155, miR-27a, miR-21, and miR-148c,miR-19b) and upregulating tumor-suppressive miRNAs like (miR-15a, miR-let-7, miR-16, miR-22, miR-26, miR-200b-3p, miR-142-3p, miR-146a, miR-330 , and miR-217) **[175].**

Lycopene can increase the fluidity of cellular membranes and exhibits strong antioxidant activity. It has been demonstrated that carotenoids, along with their metabolites and oxidation products, improve gap junction communication (GJC), a crucial cancer prevention mechanism. Restoring GJC function can aid in suppressing unchecked cell proliferation, as it is frequently compromised in a variety of cancers **[176]**. Lycopene modulates the expression of genes associated with inflammation, apoptosis, and cancer progression, thereby diminishing the risk of prostate cancer [**[177].** Adequate lycopene consumption may lower the risk of prostate cancer **[178].** Fig. 2. show the gene expression and antitumor activity of curcumin.

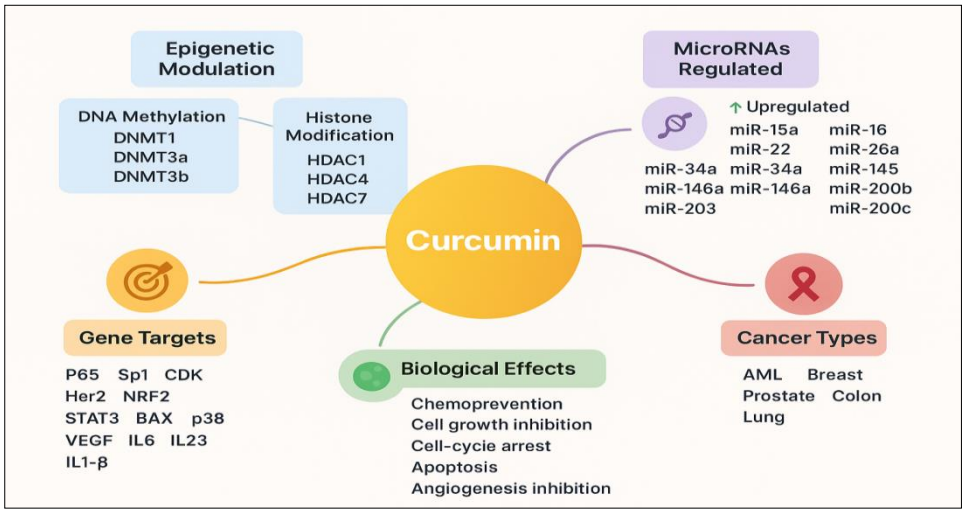

Figure 2: Summary of the gene expression and antitumor activity of curcumin**4.2. Cardiovascular diseases**

Flavonoids, including quercetin, suppress NF-κB activity and reduce the expression of adhesion molecules implicated in atherosclerosis **[179]**. Terpenoids such as ursolic acid enhance PPAR signaling, thereby improving lipid profiles, and reducing hyperlipidemia **[180]**.

4.3. Neurodegenerative Diseases

The neurodegeneration seen in many neuro-inflammatory diseases is closely linked to microglia activation. Numerous pathogens, including bacteria, viruses, lipopolysaccharides, and amyloidβ, can cause neuro-inflammation **[182].** A variety of phytochemicals may suppress distinct neuroinflammatory signaling pathways. Alkaloids, essential oil components, and isoflavones that were separated from medicinal plants shown both increased anti-inflammatory efficacy and decreased inflammatory signaling **[184, 181, 185, 186].**

Ginsenosides modulate anti-apoptotic gene expression and attenuate neuroinflammation, offering therapeutic potential in Parkinson's disease **[188]**. Alzheimer's and Parkinson's disorders are among the age-related illnesses that frequently contribute to neuroinflammation **[183]**. Resveratrol induces SIRT1, a longevity gene that protects neurons and mitigates Alzheimer's pathology **[187].** Research suggests that the compound may offer protection against neurodegenerative conditions like Alzheimer's disease and age-related cardiovascular disorders **[188].** Additionally, its ability to modulate cellular pathways may contribute to the prevention of age-related meabolic disoreders, such as diabetes **[189]**. While the concentrations of resveratrol in natural sources as red grapes may vary in dietary sources. However, it's essential to note that the benefits of resveratrol are most effective when it is considered part of a holistic approach to health, including an active lifestyle and a balanced diet **[190].** As research continues to unravel the intricate mechanisms behind these effects, nutraceuticals such as resveratrol hold promise as potential allies in the pursuit of prolonged health and vitality.

4.4. Antioxidant, Inflammatory and Immune-Related Disorders

4.4.1. Antioxidant Effects

1.Antioxidant Genes: Many plant extracts, such as those from green tea and grapes, upregulate genes responsible for antioxidant protection, such as catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx);

Through a variety of strategies, polyphenols combat oxidative stress: (1) neutralising free radicals by their hydroxyl groups; (2) chelating transition metals to stop Fenton-type reactions that produce hydroxyl radicals; and (3) enhancing cellular antioxidant defences like GPx, SOD, and CAT, which are frequently triggered by activation of the Nrf2 pathway [**96102**]. They can also inhibit the production of ROS by enzymes such as xanthine oxidase and NADPH oxidase. Flavonoids are a significant class of polyphenols that exhibit antioxidant activity through multiple processes, including direct neutralization of free radicals, sequestration of transition metals such as Fe^{2+} and Cu^{2+}, regulation of endogenous defence enzymes like SOD, CAT, and GPx, and inhibition of pro-oxidant enzymes such as NADPH and xanthine oxidase **[103, 104]**.

At low moderate concentrations, reactive oxygen species (ROS) are essential for cell signalling and homeostasis **[191]**. Nevertheless, overproduction of ROS can harm proteins, lipids, and nucleic acids, which can lead to cellular dysfunction and the emergence of several chronic illnesses **[192]**. When ROS production surpasses antioxidant defences, oxidative stress results, which can damage proteins, lipids, and DNA and is a major factor in the development of disease **[193]**.

Numerous substances derived from plants, such as polyphenols, flavonoids, carbohydrates, glycosides, alkaloids, saponins, peptidoglycans, minerals, and vitamins, have shown promise in preventing oxidative damage to cells. These substances have the ability to either directly neutralise free radicals or alter signalling pathways and the expression of genes related to redox balance **[194, 195]**.

Resveratrol has strong anti-inflammatory and antioxidant qualities. By acting early in oxidative reactions, partly by chelating copper and preventing it from catalysing harmful reactions, it exhibits stronger antioxidant activity than flavonoids [**196**]. Beyond its direct scavenging effects, resveratrol affects the expression of genes linked to oxidative stress: it downregulates prooxidant genes, including those linked to NADPH oxidase, and upregulates antioxidant enzymes, such as SOD1 and GPX1, in a concentration-dependent manner **[197]**. Resveratrol effectively neutralises reactive species, incluede hydrogen peroxide (H_2O_2), superoxide (O2−), hydroxyl radicals (OH−), nitric oxide (NO), and nitrogen dioxide (NO2), according to studies **[198, 199]**. Nonetheless, direct scavenger activities are not common, partly because of the reduced in vivo half-life of this molecule. In vivo, resveratrol's antioxidant properties stem from its role as gene expression regulator. Resveratrol, downregulation of NADPH-oxidase, resulting in the reactive oxygen species (ROS) to decrease. Moreover, the expression of various antioxidant enzymes is enhanced by hyperstimulation of tetrahydrobiopterin-GTP-cyclohydrolase. According to **[200]**, some genes that control resveratrol's impact are mediated by Nrf2.

4.4.2. Anti-inflammatory Effects

Inflammation-related Genes: Compounds such as curcumin (from turmeric) and boswelliagingerse can downregulate NF-κB pathway and the inflammatory cytokines expression (e.g., TNF-α, IL-6) and chemokines.

A common characteristic of many chronic illnesses, including cancer, is inflammation. The expression of important pro-inflammatory mediators like COX-2 and iNOS is largely regulated by the transcription factor NF-κB. It has been demonstrated that I3C and its derivative DIM both decrease inflammation by inhibiting the expression of COX-2, iNOS, CXCL5, and IL-6, most likely by preventing NF-κB activation **[104].**
Curcumin suppresses COX-2 and iNOS transcription, reducing chronic inflammation **[201]**. According to **Dharmadeva et al. [202]** and **Otunola&Afolayan [203]**, inflammation is a process of biological defensive that allows the living cells to defend themselves against diseases caused by fungi, bacteria, viruses, physical agents, and compromised immune systems. Naturally, there are two types of inflammation: acute (the first level of inflammation) and chronic (out of proportion to protective dam age) **[204]**. To preserve human health, the body's innate immune system uses both acute and chronic inflammatory reactions as important defense mechanisms **[205].** Inflammatory processes are characterized by the increased production of mediators such as reactive oxygen species (ROS), reactive nitrogen species (RNS), pro-inflammatory cytokines including interleukins (ILs) and tumor necrosis factor-α (TNF-α), as well as enzymes like cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). These molecules not only act as effectors of the inflammatory cascade but also represent key biomarkers for assessing the extent of the host inflammatory response **[206].** Many flavonoids have biological properties such as anti-inflammatory, antiviral, antioxidant, and anticancer properties [**207-209].**

Medicinal plant phytochemicals are important in the treatment of several inflammatory conditions **[210]**. For instance, berberine and hyoscine, which are derived from *Berberis vulgaris* and Datura stramonium, respectively, were noted as licensed alkaloid compounds that are available for sale as possible anti-inflammatory agents **[211].** It is often advised to use medicinal plant extracts as an alternative treatment approach to treat inflammatory agents **[212].** Numerous inflammatory illnesses have been reported to be treated by secondary metabolites that have been extracted from different portions of medicinal plants **[213]**. Living organs like the skin, liver, heart, joints, stomach, brain, and lungs are all impacted by inflammatory illnesses **[214].** Cytokines drive inflammation by promoting enzyme activation, stimulating mediator release, inducing vascular changes such as fluid extravasation and vasodilation, facilitating immune cell recruitment, and contributing to tissue injury **[215].** EGCG, kaempferol and berberine, have been proven effective in causing cancer cells to undergo apoptosis by blocking pathways essential for the survival and cancer cells growth [**216**]. These results highlight the adaptability and therapeutic potential of phytochemicals, stimulating further investigation into their uses in the prevention and treatment of illness as well as their function in enhancing general health and wellbeing. Developing innovative treatments and preventive measures for a variety of medical disorders will depend on ongoing studies into their mechanisms of action and therapeutic potential **(Table 1)**. [**217**].

Table 1: Phytochemical with their targeted pathways and outcomes in biological models [217]

Sl No.	Plant scientific name	Photochemical	Associated Disease(s)	Target Protein/Pathway	Approach/Model	Outcome	Reference
1	*Allium sativum*	Allicin	Hypercholesterolemia	HMG-CoA reductase pathway	Cholesterol synthesis Assay in liver cells	Inhibits HMG-CoA reductase, lowers cholesterol synthesis	[218]
			Hypoxia-related conditions	HIF-1αpathway	Hypoxia model in cells	StabilizesHIF-1α, enhances cellular adaptation to hypoxia	[219]
2	*Berberis vulgaris*	Berberine	Metabolic syndrome	AMPK pathway	Metabolic syndrome	Activates AMPK, improves glucose and lipid metabolism	[220]
			Metabolic syndrome	AMPK pathway	Human clinical trial	Activates AMPK, improves lipid metabolism in metabolic syndrome	[221]
3	*Brassica oleracea*	Kaempferol	Cancer	PI3K/Akt/mTOR pathway	Cancer cell proliferation assay	InhibitsPI3K/Akt/mTOR Signaling, induces apoptosis	
				Akt/mTOR pathway	Cancer cell line viability assay	Inhibits Akt/mTOR Signaling, Induces apoptosis	[222]
		Sulforaphane	Neurodegenerative diseases	Keap1/Nrf2pathway	Oxidative stress Model in neuronal cells	ActivatesNrf2, enhances Antioxidant defenses	[223]
4	*Cannabis sativa*	Cannabidiol (CBD)	Pain management	TRPV1receptor	Pain perception study in humans	ModulatesTRPV1activity, reduces pain sensitivity	[224]
5	*Camellia sinensis*	Epigallocatechin gallate (EGCG)	Cancer	Bcl-2familyproteins	Apoptosis in cancer cells	Induces apoptosis by modulating Bcl-2familyproteins	[225]
			Obesity	FAS pathway	Obesity model in mice	Inhibits FAS activity, reduces adipose tissue formation	[226]
		Catechins (from green tea)	Alzheimer's disease	β-amyloid aggregation pathway	Alzheimer's disease model(mice)	Inhibitsβ-amyloid aggregation, Improves cognitive function	[227]
		Epicatechin	Muscle wasting disorders	Myostatin pathway	Skeletal muscle cell culture	Inhibits myostatin expression, promotes muscle growth	[228]
6	*Capsicum annuum*	Quercetin	Cancer	PI3K/Akt pathway	Cancer cell line assay	InhibitsPI3K/Akt Signaling, suppresses cancer growth	[229]
			Inflammatory bowel disease	PI3K/Akt pathway	Inflammatory bowel disease	SuppressesPI3K/Akt Signaling, ameliorates inflammation	[230]
			Skin cancer, skin damage	MAPK pathway	UV-induced damage	Inhibits MAPK activation, protects Against UV-induced skin damage	[231]
			Obesity	PPAR-γ pathway	Adipocyte differentiation	Activates PPAR-γ, promotes adipocyte differentiation	[232]

n myeloid (U-937), macrophages, dendritic cells, epithelial (HeLa), and Jurkatcells stimulated by LPS, TNF-α, or PMA, resveratrol primarily reduces inflammation by suppressing NF-κB **[233, 234]**. This substance targets IκB kinase to stop NF-κB activation **[235]**. Furthermore, resveratrol downregulates iNOS and COX-2 expression in human primary airway epithelial cells activated by cytokines like TNF-α, IL-1, or IFN-γ **[236]** and inhibits COX-2 transcription in PMA-stimulated human mammary epithelial cells **[237]**. Additionally, it inhibits splenic lymphocytes and macrophages from producing pro-inflammatory cytokines like TNF-α, IL-12, IFN-γ, IL-1, and IL-6 **[233, 238].**

According to Roy et al. [**239**], one of the most frequent causes of liver damage or malfunction is inflammatory illness. By blocking or modifying the signalling pathways that cause liver inflammation, extracts and isolated compounds from medicinal plants are particularly useful in the treatment of liver diseases [**240**]. Liver stress was significantly reduced by some flavonoids derived from a methanol extract of *B. vulgaris'* aerial portion **[241].** According to Zhang et al. [**242**], ageniposide molecule that was extracted from *G. jasminoides* fruit was shown to reduce CYP2E1 expression and prevent liver fibrosis.
The primary chemical components of the aqueous extract of the floral portion of *M. recutita*, matricin, α-Bisabolol, luteolin apigenin-7-glucoside, and apigenin, suppress the formation of leukotrienes and prostaglandins **[243]**. According to Wedler et al. **[244]**, TNF-α stimulates epidermal cells to produce the chemokine interleukin-8 (IL-8) and vascular endothelial growth factor (VGEF), which lead to skin inflammation. Curcumin (*C. viticella* and *C. longa*) extracts reduce NO and TNF-α release and is utilized to modulate skin disruption in humans **[245, 246]**.

According to Maione et al. [**242],** cardiovascular inflammations are linked to factors that enhance endothelial function, activate enzymes that play a significant role in the development of an atherosclerosis, and boost transcriptional messengers. Quercetin, ferulic acid, allicin, gensenosides, myricetin, and kaempferol are found in the aqueous extract of *G. biloba* leaves, these chemicals inhibit the angiotensin-converting enzyme and reduce the inflammatory effects on the cardiovascular system **[247]**. To regulate cardiovascular inflammation, the diterpene chinone found in the rhizome portion of *S. miltiorrhiza* shown the ability to prevent the stimulation of the MAPK and NF-κB pathways **[248].**

Phytochemicals prevent the production of leukotrienes by inhibiting LOX-5, NF-κB activation, and the production of proinflammatory cytokines that lead to joint deterioration and swelling **[249, 250].** According to Murugananthan et al. [**251**], oxyacanthine and berberine, which were separated from the root extract of *B. vulgaris*, showed a decrease in chronic joint inflammation. Sinomenine, the isolate of stem part of *S. acutum*, displayed modulation of angiogenesis **[252]**. Alkaloids, flavone aglycones, gallic tannins, and saponins from the bark portion of *F. sycomorus* showed a decrease in skeletal muscular contraction **[253].**
The antibacterial action that indirectly lowers gastrointestinal inflammation is caused by polyphenols and quercetin glycoside **[254].** Quercetin glycoside that was separated from the root and leaf extracts of *A. sylvestris and V. vinifera*, respectively, inhibite the generation of inflammatory mediators such IL-8 **[255, 256]**. By lowering myeloperoxidase activity, 1,8-cineole has been shown to have an anti-inflammatory effect on gastrointestinal inflammation **[257]**.

The ability of anti-inflammatory medicinal plants to alter gene expression has been studied. These plants and the compounds they produce primarily target signal transduction-related protein kinases, specifically protein kinase C (PKC) and mitogen-activated protein kinase (MAPK), to influence cellular regulation. The expression of particular genes is controlled by blocking these enzymes, which also modifies the capacity of transcription factors like nuclear factor-kappa B (NF-κB) and activator protein-1 (AP-1) to bind DNA. A number of signal transduction kinases are known to be inhibited by flavonoids; for example, some flavonoid derivatives have the ability to block PKC and protein tyrosine kinase. In signalling pathways, MAPKs are also essential. In macrophages, lipopolysaccharide (LPS) activates three different MAPK types: p38 MAPK, Jun N-terminal kinase/stress-activated protein kinase (JNK/SAPK), p38 MAPK, and extracellular signal related kinase (ERK). A naturally occurring plant flavonoid called quercetin has been shown to downregulate p38 MAPK, which lowers the expression of iNOS. Furthermore, it has been demonstrated that quercetin inhibits AP-1-DNA binding by reducing TNF-α production in LPS-stimulated RAW cells. It seems to affect TNF-α at the post-transcriptional level by modulating p38 MAPK and ERK1/2 activity differently. Moreover, quercetin inhibits p38 and ERK kinases, which suppresses NF-κB activation. Research continuously shows that anti-inflammatory phytochemicals can partially inhibit the activation of transcription factors that are important for the expression of different inflammatory proteins and enzymes, including AP-1 and NF-κB. The inhibition of several protein kinases involved in signalling pathways most likely mediates these effects **[258, 259]**.

Phytochemicals are thought to operate by alleviating inflammation stress through enhance the release of systematic mediators, cytokines, and chemokines, thereby fostering cellular infiltration to resolve inflammatory responses and reestablish tissue coordination **[260]**. At the cellular and molecular levels, the mechanism of anti-inflammatory activity is widely employed **[261].** By targeting important regulatory enzymes like phospholipase A2, cyclooxygenases, lipoxygenases, protein kinases, and phosphodiesterases, as well as by modifying histamine production and transcriptase activation, phytochemicals can lower the levels of prostanoids and leukotrienes. Numerous substances have shown anti-inflammatory properties in vitro, including flavonoids, polyphenols, alkaloids, saponins, tannins, and terpenes [**262**]. For instance, quercetin efficiently inhibits the enzymes COX-2 and 5-LOX, which are crucial in the transformation of arachidonic acid into eicosanoids. By suppressing activated immune cells, controlling eicosanoid synthesis, and halting the release of pro-inflammatory mediators, resveratrol also modifies the inflammatory process [**263**]. In addition, it is recognized that flavonoids, curcumins, and tannins have anti-inflammatory properties due to their ability to inhibit proinflammatory enzymes via free radical scavenging **[264].**

Conclusion and challenges
Plant-derived extracts exert significant influence on gene expression by modulating key molecular pathways such as oxidative stress regulation, inflammation, apoptosis, and cell proliferation. Bioactive compounds like polyphenols, flavonoids, and alkaloids interact with transcription factors including NF-κB, AP-1, and Nrf2, thereby contributing to immunomodulatory and protective effects against chronic diseases in modern drug development and. exhibit a wide range of pharmacological activities such as anti-inflammatory, antioxidant, anticancer, and cardioprotective effects. Curcumin effectively targets the NF-κB and mTOR pathways which has demonstrated efficacy in managing inflammatory diseases and cancer; resveratrol, known for its potential in combating cardiovascular diseases and quercetin, which shows promise in addressing cancer and inflammatory bowel diseases.

Challenges and future directions; Challenges: Low bioavailability and poor solubility are significant hurdles for efficacy. Solutions: Innovative formulation strategies are being developed to overcome these issues.Future needs: Translating these molecular findings into clinical applications requires further rigorous investigation, standardization of extracts, and comprehensive safety evaluations. An integrative approach combining molecular biology, pharmacology, and clinical research is essential for full realization of their therapeutic potential.

Conflicts of Interest
The author reports no conflicts of interest.

References

1. Efferth T, Koch E. Complex interactions between phytochemicals. The multi-target therapeutic concept of phytotherapy. Curr. Drug Targets. 2011;12 (1): 122–132. doi: 10.2174/138945011793591626. PMID: 20735354.

2.Liu R H, Hu F B, Wang, Y. Phytochemicals and gene expression in chronic diseases. Crit Rev Food Sci Nutr. 2018, 58(8): 1300–1311. doi: 10.3390/metabo13020243. PMID: 36837862; PMCID: PMC9966918.

3.Aggarwal B B, Harikumar K B. Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. Int. J. Biochem. Cell Biol. 2009;41(1): 40–59. doi: 10.1016/j.biocel.2008.06.010. Epub 2008 Jul 9. PMID: 18662800; PMCID: PMC2637808.

4.Patel S, Rauf A, Khan H, Khalid S. Natural alkaloids as potential cancer therapeutics: Current progress and future perspectives. Biomed. pharmacother. 2021;143: 112110. 10.1016/j.ejphar.2019.172472. Epub 2019 Jun 19. PMID: 31228447.

5.Shen T, Wang X N, Lou H X. Natural products as regulators of gene expression. Chin J Nat Med. 2020; 18(8):554–566

10.1016/j.ejphar.2019.172472.

6.Correia RT, Borges KC, Medeiros MF, Genovese MI. Bioactive compounds and phenolic-linked functionality of powdered tropical fruit residues. Food Sci Technol Int. 2012 Dec;18(6):539-47. doi: 10.1177/1082013211433077. Epub 2012 Sep 26. PMID: 23014856

7.Makkar R, Behl T, Kumar A, Nijhawan P, Arora S. Emerging therapeutic effects of herbal plants in rheumatoid arthritis. Endocr Metab Immune Disord. (2021) 21:617–25. 10.2174/1871530320666200620232828 [DOI]

8. Manach C, Scalbert A, Morand C, Remesy C, Jimenez L. Polyphenols: Food sources and bioavailability. Am. J. Clin. Nutr. 2004; 79: 727–747. doi: 10.1093/ajcn/79.5.727. PMID: 15113710.

9.Tsimogiannis D, Oreopoulou V. Classification of phenolic compounds in plants. In Polyphenols in plants. Amsterdam: Elsevier. 2019: 263–84. DOI:10.1016/B978-0-12-813768-0.00026-8

10. Baiano A, del Nobile M.A. Antioxidant compounds from vegetable matrices: Biosynthesis, occurrence, and extraction systems. Crit. Rev. Food Sci. Nutr. 2015; 56: 2053–2068/ doi: 10.1080/10408398.2013.812059. PMID: 25751787.

11.Kozikowski A P, Tückmante lW, Böttcher G, Romanczyk LJ Jr. Studies in polyphenol chemistry and bioactivity. 4.1 Synthesis of trimeric, tetrameric, pentameric, and higher oligomeric epicatechin-derived procyanidins having all-4beta,8-interflavan connectivity and their inhibition of cancer cell growth through cell cycle arrest. JOC. 2003,68 (5):1641–1658.

12.Santos-Buelga, C, González-Paramás A M, Oludemi T, Ayuda-Durán B, González-Manzano S. Plant phenolics as functional food ingredients. Adv Food Nutr Res. 2019; 90:183–257. doi: 10.1016/bs.afnr.2019.02.012. 31445596.

13.Fantini M, Benvenuto M, Masuelli, Frajese GV, TresoldiI, Modesti A, Bei R. In vitro and in vivo antitumoral effects of combinations of polyphenols, or polyphenols and anticancer drugs: perspectives on cancer treatment. Int. J. Mol. Sci**.** 2015;16 (12):9236–9282. doi: 10.3390/ijms16059236. PMID

14.Thyagarajan A, Forino A S, Konger R L, Sahu R. P. Dietary polyphenols in cancer chemoprevention: implications in pancreatic cancer. Antioxidants.2020;9 (8) 651. **https://doi.org/10.3390/antiox9080651**

15.Sajadimajd S, BahramsoltaniR, Iranpanah A, et al. Advances on natural polyphenols as anticancer agents for skin cancer. Pharmacol Res. 2020;151: 104584 doi: 10.1016/j.phrs.2019.104584. Epub 2019 Dec 3. PMID: 31809853.

16. Thuphairo K, Sornchan P, Suttisansanee U. Bioactive Compounds, Antioxidant Activity and Inhibition of Key Enzymes Relevant to Alzheimer's Disease from Sweet Pepper (*Capsicum annuum*) Extracts. Prev Nutr Food Sci. 2019 Sep;24(3):327-337. doi: 10.3746/pnf.2019.24.3.327.

17.Villarreal-Soto S A, Beaufort S, Bouajila J.; et al. "Impact of Fermentation Conditions on the Production of Bioactive Compounds with Anticancer, Anti-Inflammatory and Antioxidant Properties in Kombucha Tea Extracts. Process Biochem.2019; 83: 44–54.

18.Wu MS, Aquino L B B, Barbaza MY U, Hsieh CL, Castro-Cruz KA, Yang LL, Tsai PW. Anti-Inflammatory and Anticancer Properties of Bioactive Compounds From *Sesamum indicum* L.—A Review. Molecules.2019;24(24): 4426.

19. Gosset-Erard C, Zhao M, Lordel-Madeleine S, Ennahar S. "Identification of Punicalagin as the Bioactive Compound Behind the Antimicrobial Activity of Pomegranate (*Punica granatum* L.) Peels." Food Chem.2021; 352:129396

20.FerrazCR, Carvalho TT, ManchopeM.F, Artero N.A, Rasquel-Oliveira F.S. FattoriV Casagrande R, VerriWA, Jr. Therapeutic Potential of Flavonoids in Pain and Inflammation: Mechanisms of Action, Pre-Clinical and Clinical Data, and Pharmaceutical Development. Molecules.2020; 25:762. 10.3390/molecules25030762.

21. Ullah A, Munir S, Badshah SL, Khan N, Ghani L, Poulson BG, Emwas AH, Jaremko M. Important Flavonoids and Their Role as a Therapeutic Agent. Molecules. 2020 Nov 11;25(22):5243. doi: 10.3390/molecules25225243. PMID: 33187049; PMCID: PMC7697716.

22.Crozier A, Jaganath I.B, Clifford MN. Dietary Phenolics: Chemistry, Bioavailability and Effects on Health. Nat. Prod. Rep. 2009; 26:1001–1043.

23.Peng C, Wang X, Chen J, Jiao R, Wang, L, Li YM, Zuo Y, Liu Y, Lei L, Ma KY, et al. Biology of ageing and role of dietary antioxidants. BioMed Res. Int. 2014; 2014:831841

24. Jenab M, Riboli E, FerrariP, SabateJ, Slimani N, Norat T, Friesen M, T jonneland A, Olsen A, Overvad, K, et al. Plasma and dietary vitamin C levels and risk of gastric cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST). Carcinogenesis 2006;27: 2250–2257

25. Li AN, Li S, Zhang YJ, XuX.R, Chen YM, Li HB. Resources and biological activities of natural polyphenols. Nutrients 2014; 6: 6020–6047.

26. Arathi BP, Raghavendra-Rao Sowmya, P, Vijay K, Baskaran V, Lakshminarayana R. Metabolomics of carotenoids: The challenges and prospects—A review. Trends Food Sci. Technol. 2015; 45: 105–117.
27.Zhang, YJ, Gan RY, Li S, Zhou Y, Li AN, Xu DP, Li H.B. Antioxidant phytochemicals for the prevention and treatment of chronic diseases. Molecules 2015; 20: 21138–21156.
28.Wojtunik-Kulesza KA, Oniszczuk A, Oniszczuk T, Waksmundzka-Hajnos M. The influence of common free radicals and antioxidants on development of Alzheimer's disease. Biomed.Pharmacother.2016; 78: 39–49.
29. BalmusI M, Ciobica A, Trifan A, Stanciu C. The implications of oxidative stress and antioxidant therapies in inflammatory bowel disease: Clinical aspects and animal models. Saudi J. Gastroenterol.2016; 22:3–17.
30. Prasad KN. Simultaneous activation of Nrf2 and elevation of antioxidant compounds for reducing oxidative stress and chronic inflammation in human Alzheimer's disease. Mech. Ageing Dev. 2016; 153: 41–47.
31.Salomone F, Godos J, Zelber-Sagi S. Natural antioxidants for non-alcoholic fatty liver disease: Molecular targets and clinical perspectives. Liver Int. 2016; 36: 5–20
32.Zhou Y, Zheng J, Li Y, Xu DP,LiS,ChenYM,Li H.B. Natural polyphenols for prevention and treatment of cancer. Nutrients 2016; 8: 515.
33.. Zheng J, Zhou Y, Li Y, XuD. P, LiS, LiHB. Spices for prevention and treatment of cancers. Nutrients. 2016;8: 495.
34. Erlund I. Review of the flavonoid's quercetin, hesperetin, and naringenin. Dietary sources, bioactivities, bioavailability, and epidemiology.Nutr.Res. 2004; 24: 851–874.
35. Serafini M, Peluso I Raguzzini A. Flavonoids as Anti-Inflammatory Agents. Proc. Nutr. Soc. 2010; 69: 273–278.
36. Farzaei MH, Singh AK, Kumar R, Croley CR, Pandey AK, Coy-Barrera E, Kumar Patra J, Das G, Kerry RG, Annunziata G, Tenore GC, Khan H, Micucci M, Budriesi R, Momtaz S, Nabavi SM, Bishayee A. Targeting Inflammation by Flavonoids: Novel Therapeutic Strategy for Metabolic Disorders. Int J Mol Sci. 2019 Oct 8;20(19):4957. doi: 10.3390/ijms20194957. PMID: 31597283; PMCID: PMC6801776.
37. Shen N, Wang T, Gan Q, Liu, S, Wang L,Jin B. Plant flavonoids: classification, distribution, biosynthesis, and antioxidant activity. Food Chem. 2022; 383:132531.
38.YangJ. Brazil nuts and associated health benefits: A review. LWT.2009; 42:1573–1580.
39.Panche AN, Diwan AD, Chandra SR. Flavonoids: An overview. J. Nutr. Sci. 2016;5:e47. doi: 10.1017/jns.2016.41. [DOI] [PMC free article] [PubMed] [Google Scholar]
40 Chirumbolo S, Bjørklund G, Lysiuk R, Vella A, Lenchyk L, Upyr T. Targeting Cancer with Phytochemicals via Their Fine Tuning of the Cell Survival Signaling Pathways. Int. J. Mol. Sci. 2018; 19:3568. doi: 10.3390/ijms19113568. [DOI] [PMC free article] [PubMed] [Google Scholar
41 Zahra M, Abrahamse H, George BP. Flavonoids: Antioxidant Powerhouses and Their Role in Nanomedicine. Antioxidants (Basel). 2024 Jul 29;13(8):922. doi: 10.3390/antiox13080922. PMID: 39199168; PMCID: PMC11351814.
42.Da J, Xu M, Wang, Y, Li, W, Lu M, Wang Z. Kaempferol promotes apoptosis while inhibiting cell proliferation via androgen-dependent pathway and suppressing vasculogenic mimicry and invasion in prostate cancer. Anal.Cell. Pathol. 2019;10 doi: 10.1155/2019/1907698.
43.Tang S M, X.T, Zhou J, Li Q P, Ge X X, Miao L. Pharmacological basis and new insights of quercetin action in respect to its anti-cancer effects. Biomedicine & Pharmacotherapy. 2020;121. doi: 10.1016/j.biopha.2019.109604.
44. Sharma A, Ghani A, Sak K, Tuli HS, Sharma AK, Setzer WN, Sharma S, Das AK. Probing into Therapeutic Anti-cancer Potential of Apigenin: Recent Trends and Future Directions. Recent Pat Inflamm Allergy Drug Discov. 2019;13(2):124-133. doi: 10.2174/1872213X13666190816160240. PMID: 31418666.
45. Yin H, Wang L, Wu M, Liu Y, Li N, Chen T. "Cyanidin-3-O-glucoside chloride acts synergistically with luteolin to inhibit the growth of colon and breast carcinoma cells," Pharmazie. 2019,74, 1, 54–61. doi: 10.1691/ph.2019.8746.
46. Jang C H, Moon N, OhJ, Kim J. S. "Luteolin shifts Oxaliplatin-induced cell cycle arrest at G0/G1 to apoptosis in HCT116 human colorectal carcinoma cells," Nutrients.2019; 11: 4, 770,
47.Garg S.K, Shukla A, Choudhury S. Polyphenols and flavonoids. In Nutraceuticals in veterinary medicine. Cham: Springer International Publishing. 2019; 187–204. 10.1007/978-3-030-04624-8_13
48.Martin M, Ramos S. Impact of cocoa flavanols on human health. Food Chem Toxicol. 2021; 151:112121
49. Gan R Y, Li H B, Sui Z Q, Corke H. Absorption, metabolism, anti-cancer effect and molecular targets of epigallocatechin gallate (EGCG): An updated review. Crit Rev Food Sci Nutr. 2018;58(6):924–941. 10.1080/10408398.2016.
50.. Xu X Y, Zhao C N, Cao S Y, Tang G Y, Gan R Y, Li H. B. Effects and mechanisms of tea for the prevention and management of cancers: an updated review. Crit Rev Food Sci Nutr. 2020;60 (10): 1693–1705. 10.1080/10408398.2019.1588223.
51. Qi Z, Kong S, Zhao S, Tang Q. "Naringenin inhibits human breast cancer cells (MDA-MB-231) by inducing programmed cell death, caspase stimulation, G2/M phase cell cycle arrest and suppresses cancer metastasis," Cell. Mol. Biol., 2021; 67(2): 8–13. 10.14715/cmb/2021.67.2.2.
52. Kumar R. and Bhan, A. Tiku. "Naringenin suppresses chemically induced skin cancer in two-stage skin carcinogenesis mouse model. Nutrition and Cancer.2020; 72(6): 976–983. 10.1080/01635581.2019.1656756.
53. Akhter M H, Kumar S, Nomani S. Sonication tailored enhance cytotoxicity of naringenin nanoparticle in pancreatic cancer: design, optimization, andinvitrostudies. Drug Dev. Ind. Pharm.2020;46 (4): 659–672. doi: 10.1080/03639045.2020.

54.. Deis L, Quiroga AM, De Rosas MI. Coloured compounds in fruits and vegetables and health. In Psychiatry and Neuroscience Update: From Epistemology to Clinical Psychiatry. 2021, IV, 343-358. Cham: Springer International Publishing
55. Liggins J, BluckL.J.C, Runswick S, Atkinson C, Coward WA, Bingham SA. Daidzein and genistein contents of vegetables. Br. J. Nutr. 2000; 84: 717–725.
56.Křížová L, Dadáková K, Kašparovská J, Kašparovský T. Isoflavones," Molecules. 2019;24 (6):1076
57. Liu H, Lee G, Lee JI, Ahn TG, Kim SA. Effects of genistein on anti-tumor activity of cisplatin in human cervical cancer cell lines. Obstet Gynecol Sci. 2019 Sep;62(5):322-328. doi: 10.5468/ogs.2019.62.5.322.
58. Vikal A, Maurya R, Bhowmik S, Khare S, RaikwarS, Patel P, Kurmi BD. Resveratrol: a comprehensive review of its multifaceted health benefits, mechanisms of action, and potential therapeutic applications in chronic disease. Pharmacol Res-Nat Prod. 2024;3.
59. Senizza A, Rocchetti G, Mosele JI, Patrone V, Callegari ML, Morelli L, Lucini L. Lignans and Gut Microbiota: An Interplay Revealing Potential Health Implications. Molecules. 2020 Dec 3;25(23):5709. doi: 10.3390/molecules25235709. PMID: 33287261; PMCID: PMC7731202.
60. Ranganath KG. Pigments that colour our fruits: an overview Erwerbs-obstbau 2022; 64: 535–47
61.Gürbüz M, Aktaç Ş. Understanding the role of vitamin A and its precursors in the immune system Nutr Clin Metab 2022; 36: 89–98
62. Kumar P, Banik SP, Ohia SE, Moriyama H, Chakraborty S , Wang C-K Song Y S ,Goel A ,BagchiMBagchi D Current insights on the photoprotective mechanism of the macular carotenoids lutein and zeaxanthin: safety efficacy and bio-delivery J Am NutrAssoc 2024 ;43: 505–18.
63. Faisal Z, Irfan R, Akram N, Manzoor H M I , Aabdi MA, Anwa r M J, Khawar S ,SaifAShah YA ,Afzaal M. The multifaceted potential of fenugreek seeds: from health benefits to food and nanotechnology applications Food Sci Nutr 2024; 12: 2294–310. 10.1002/fsn3.3959.
64. Tripathi AK, Das R, Ray AK, Mishra SK, Anand S. Recent insights on pharmacological potential of lycopene and its nanoformulations: an emerging paradigm towards improvement of human health Phytochem Rev 2024; 24 :1091–118.
65. ChuCCChewSCLiewWC Nyam K L. Review article vitamin E: a multi-functional ingredient for health enhancement and food preservation J Food Meas Charact 2023; 17: 6144–56. 10.1002/fsn3.3959.
66. Charlton NC, Mastyugin M, Török B, Török M. Structural Features of Small Molecule Antioxidants and Strategic Modifications to Improve Potential Bioactivity. Molecules. 2023 Jan 20;28(3):1057. doi: 10.3390/molecules28031057. PMID: 36770724; PMCID: PMC9920158.
67. Singh P, Kesharwani RK, KeservaniRK Antioxidants and vitamins: roles in cellular function and metabolism In Sustained energy for enhanced human functions and activity. Cambridge: Academic Press2017; 385–407
68. Clemente-Suárez VJ, Bustamante-Sanchez Á , Mielgo-Ayuso J , Martínez-Guardado I , Martín-Rodríguez A , Tornero-Aguilera JF Antioxidants and sports performance Nutrients 2023 ;15:2371
69. Phull AR, Nasir BulHaqI, Kim SJ. Oxidative stress consequences and ROS mediated cellular signaling in rheumatoid arthritis Chem-Biol Interact 2018 ;281: 121–36. doi: 10.1016/j.cbi.2017.12.024.
70. Goncharov NV, Belinskaia DA, Ukolov A I, Jenkins RO, Avdonin PV. Organosulfur compounds as nutraceuticals In Nutraceuticals Amsterdam: Elsevier 2021; 911–24. https://doi.org/10.1016/B978-0-12-802147-7.00041-3
71. Alves I, Araújo E M Q, Dalgaard LT, Singh S , Børsheim E , Carvalho E. Protective effects of sulforaphane preventing inflammation and oxidative stress to enhance metabolic health: a narrative review Nutrients 2025; 17 :428.
72. Chaudhary P, Janmeda P, Docea A O, Yeskaliyeva B, AbdullRazis A F ,Modu B ,CalinaD , Sharifi-Rad J Oxidative stress free radicals and antioxidants: potential crosstalk in the pathophysiology of human diseases Front Chem 2023; 11: 1158198
73.Pereira G C, Application of biotechnology in producing plant bio-active compounds, in: M.S. Akhtar, M.K. Swamy (Eds.), Natural Bio-Active Compounds: Volume 3: Biotechnology, Bioengineering, and Molecular Approaches, Springer, Singapore, 2019, pp. 59–78, https://doi.org/10.1007/978-981-13-7438-8_3.
74. Parsaei P, Karimi M, AsadiSY, Rafieian-kopaei M Bioactive components and preventive effect of green tea (Camellia sinensis) extract on post-laparotomy intra-abdominal adhesion in rats IntJ Surg2013; 11: 811–815
75. Santini A, Tenore GC, NovellinoE Nutraceuticals: A paradigm of proactive medicine Eur J Pharm Sci 2017; 96: 53–61
76. Lachance PA, Das YT Nutraceuticals In Comprehensive Medicinal Chemistry II, Taylor J B Triggle D J Eds, Elsevier: Oxford UK 2007; 449–461
77. Jobin C, Bradham CA, RussoMP, Juma B, NarulaAS, Brenner DA, SartorRB Curcumin blocks cytokine-mediated NF-κB activation and proinflammatory gene expression by inhibiting inhibitory factor I-κB kinase activity J Immunol1999; 163 (6): 3474–3483
78. Aggarwal BB, Harikumar KB Potential therapeutic effects of curcumin the anti-inflammatory agent against neurodegenerative cardiovascular pulmonary metabolic autoimmune and neoplastic diseases Int J Biochem Cell Biol 2009 41 ;1: 40–59.
79. Kweon M H, Jung ST, KimJS Chemopreventive effects of dietary flavonoids on Nrf2-mediated antioxidant enzyme induction. Food Sci Biotechnol 2006 ;15 (2): 217–221.
80. Liu J Pharmacology of oleanolic acid and ursolic acid J Ethnopharmacol **2019**; 120 (3): 292–300
81. Nagoor NH, Aggarwal B Cancer-linked targets modulated by curcumin IntJBiochemMol Biol.2012; 3: 328–351

82. Clemente-Suárez VJ, Peris-Ramos HC, Redondo-Flórez L , Beltrán-Velasco AI. Martín-Rodríguez A David-Fernandez S Yáñez-Sepúlveda R Tornero-Aguilera J F. Personalizing Nutrition Strategies: Bridging Research and Public Health JPersMed 2024; 14: 305

83. Li P, Ding L, Cao S, Feng X, Zhang Q, Chen Y, Zhang N ,Qiu F. Curcumin Metabolites Contribute to the Effect of Curcumin on Ameliorating Insulin Sensitivity in High-Glucose-Induced Insulin-Resistant HepG2 Cells JEthnopharmacol 2020; 259:113015. doi: 10.1016/j.jep.2020.113015.

84. Jazvinšćak Jembrek MOršolić N , MandićL ,Sadžak A ,ŠegotaS Anti-oxidative anti-inflammatory and anti-apoptotic effects of flavonols: targeting Nrf2 NF-κB and p53 pathways in neurodegeneration Antioxidants (Basel) 2021; 10: 1628

85. Huang YC, Huang LT, Sheen J M, Hou CY, YehYT, Chiang CP ,LinIC ,Tiao MM ,TsaiCC ,Lin Y J Chen CC TainYL, YuHR.Resveratrol Treatment Improves the Altered Metabolism and Related Dysbiosis of Gut Programed by Prenatal High-Fat Diet and Postnatal High-Fat Diet Exposure JNutrBiochem 2020;75: 108260

86. Tripathi AK, Das R, Ray A K, Mishra S K, Anand S. Recent insights on pharmacological potential of lycopene and its nanoformulations: an emerging paradigm towards improvement of human health PhytochemRev 2024; 24: 1091–118

87. Fang M Z, Wang Y, Ai N ,HouZ ,Sun Y ,LuH ,Welsh W ,YangCS Tea polyphenol (−)-epigallocatechin-3-gallate inhibits DNA methyltransferase and reactivates methylation-silenced genes in cancer cell lines Cancer Res 2003; 63(22): 7563–7570

88. Yiannakopoulou EC Targeting DNA methylation with green tea catechins Pharmacology 2015; 95: 111–116

89. Khan MA, Hussain A, Sundaram MK, Alalami U ,GunasekeraD ,Ramesh L ,HamzaA ,Quraishi U (-)-Epigallocatechin3-gallate reverses the expression of various tumor-suppressor genes by inhibiting DNA methyltransferases and histone deacetylases in human cervical cancer cells OncolRep2015; 33: 1976–1984

90. Henning SM, Wang P, Carpenter CL, HeberD Epigenetic effects of green tea polyphenols in cancer Epigenomics2013; 5: 729

91. Deb G, Thakur VS, Limaye AM, Gupta S Epigenetic induction of tissue inhibitor of matrix metalloproteinase-3 by green tea polyphenols in breast cancer cells Mol Carcinog 2015; 54: 485–499

92. Borutinskaite V, Virkšait ˙ e A, Gudelyt ˙ e G, Navakauskien ˙ e R Green tea polyphenol EGCG causes anti-cancerous epigenetic ˙ modulations in acute promyelocytic leukemia cells Leuk Lymphoma 2018; 59: 469–478

93. Rahman IBiswasS K, KirkhamPA Regulation of inflammation and redox signaling by dietary polyphenols Biochem Pharmacol2011; 82 (9): 1147–1158

94. Reuter S, Gupta SC, ParkB, Goel A, AggarwalBB Epigenetic changes induced by curcumin and other natural compounds GenesNutr2011; 6: 93

95. Teiten MH, Dicato M, DiederichM Curcumin as a regulator of epigenetic events Mol Nutr Food Res 2013; 57: 1619–1629

96. Yang CH, Yue J, SimsM, Pfeffer LM The Curcumin Analog EF24 Targets NF-κB and miRNA-21 and Has Potent Anticancer Activity In Vitro and In Vivo PLoS ONE 2013; 8: e71130

97. Zhang J, Zhang T, TiX ,Shi J ,WuC ,Ren X ,YinH Curcumin promotes apoptosis in A549/DDP multidrug-resistant human lung adenocarcinoma cells through a miRNA signaling pathway BiochemBiophysRes Commun2010; 399 : 1–6

98. Hassan FU, Rehman M S U, Khan MS, AliMA, Javed A ,NawazA ,Yang C Curcumin as an alternative epigenetic modulator: Mechanism of action and potential effects Front Genet 2019; 10: 514

99. Yu J ,PengY ,Wu LC ,XieZ ,Deng Y ,HughesT ,He S ,MoXK ,Chiu M ,WangQE , et al Curcumin Down-Regulates DNA Methyltransferase 1 and Plays an Anti-Leukemic Role in Acute Myeloid Leukemia PLoS ONE 2013; 8

100. Boyanapalli SSS, Kong A N T "Curcumin the King of Spices": Epigenetic Regulatory Mechanisms in the Prevention of Cancer Neurological and Inflammatory Diseases Curr Pharmacol Rep2015; 1: 129–139

101. MyzakM C ,HardinK ,Wang R ,DashwoodRH ,Ho E Sulforaphane inhibits histone deacetylase activity in BPH-1 LnCaP and PC-3 prostate epithelial cells *Carcinogenesis 2004; 25 (8): 1399–1407

102. Simunkova M, Barbierikova Z, Jomova K, Hudecova L, Lauro P, Alwasel SH, Alhazza I, Rhodes CJ, Valko M. Antioxidant vs. Prooxidant Properties of the Flavonoid, Kaempferol, in the Presence of Cu(II) Ions: A ROS-Scavenging Activity, Fenton Reaction and DNA Damage Study. Int J Mol Sci. 2021 Feb 5;22(4): 1619. doi: 10.3390/ijms22041619. PMID: 33562744; PMCID: PMC7915082.

103. DeisL, Quiroga AM De Rosas MI Coloured compounds in fruits and vegetables and health In Psychiatry and Neuroscience Update: From Epistemology to Clinical Psychiatry–Vol IV 2021 (pp 343-358) Cham: Springer International Publishing

104. Thiraviyam P, Aafreen K ,Kannan D ,Ganapathy PS Evaluation of antioxidant and antibacterial activities of seagrass *Cymodocea serrulata* Discover Plants 2025; 2 :68.. DOI:10.1007/s44372-025-00147-

105. Zhang Q ,Zhao XH ,WangZJ Cytotoxicity of flavones and flavonols to a human esophageal squamous cell carcinoma cell line (KYSE-510) by induction of G2/M arrest and apoptosis Toxicol In Vitro 2009 ;23: 797–807

106. Tan J , Wang B , Zhu L. Regulation of survivin and Bcl-2 in HepG2 cell apoptosis induced by quercetin ChemBiodivers 2009; ,6: 1101–1110

107. Gupta K , Panda D Perturbation of microtubule polymerization by quercetin through tubulin binding: A novel mechanism of its antiproliferative activity Biochemistry 2002;41: 13029–13038

108. Moon SK ,Cho GO ,Jung SY ,Gal SW, KwonTK ,Lee Y C, Madamanchi N R, Kim CH. Quercetin exerts multiple inhibitory effects on vascular smooth muscle cells: Role of ERK1/2 cell-cycle regulation and matrix metalloproteinase-9 Biochem Biophys Res Commun 2003; 301: 1069–1078

109. TanigawaS, Fujii M ,Hou DX Stabilization of p53 is involved in quercetin-induced cell cycle arrest and apoptosis in Hep G2. cells Biosci Biotechnol Biochem 2008; 72:797–804

110. Kim EJ ,Park H , Kim J , Park J H Y 3 3'-diindolylmethane suppresses 12-O-tetradecanoylphorbol-13-acetate-induced inflammation and tumor promotion in mouse skin via the downregulation of inflammatory mediators Mol Carcinog 2010; 49: 672–683

111. Goncharov NV, Belinskaia DA, UkolovAI, Jenkins RO, AvdoninPV. Organosulfur compounds as nutraceuticals InNutraceuticals Amsterdam: Elsevier 2021; 911–24. https://doi.org/10.1016/B978-0-12-802147-7.00041-3

112. Li P , Ding L , Cao S , FengX , Zhang Q, , ChenY ,Zhang N ,Qiu F. Curcumin Metabolites Contribute to the Effect of Curcumin on Ameliorating Insulin Sensitivity in High-Glucose-Induced Insulin-Resistant HepG2 Cells. J Ethno pharmacol 2020; 259: 113015

113. Yap L , Worlikar SA, MacKerell P , Shapiro D , Fletcher S. Small molecule inhibitors of the ERK signalling pathway: towards novel anti-cancer therapeutics Chem Med Chem 2011; 6: 38-48

114. Yu F, Yu C, Li F, Zuo Y, Wang Y, Yao L, Wu C, Wang C, Ye L. Wnt/β-catenin signaling in cancers and targeted therapies Sig Transduct Target Ther 2021; 6: 1-24

115. Huang L, Walter V ,Hayes D, Onaitis N , Hedgehog–GLI M. signaling inhibition suppresses tumor growth in squamous lung cancer Clin Cancer Res 2014; 20: 1566-1575

116. Huang Y, Xiao D , Burton-Freeman B , Edirisinghe M I. Chemical changes of bioactive phytochemicals during thermal processing Reference Module in Food Science Elsevier (2016)

117. Sharifi-Rad J , Rapposelli S , Sestito S , Herrera-Bravo J , Arancibia-Diaz A, SalazarLA,YeskaliyevaB, BeyatliA Leyva-Gómez G, González-Contreras C, Gürer ES, Martorell M Calina D. Multi-Target Mechanisms of Phytochemicals in Alzheimer's Disease: Effects on Oxidative Stress Neuroinflammation and Protein Aggregation J Pers Med 2022 Sep 15 ,12(9):1515 doi: 10 3390/jpm12091515

118. George BP , Chandran R , Abrahamse H. Role of phytochemicals in cancer chemoprevention: insights Antioxidants 2021; 10: 1455

119. Bharadwaj U , Kasembeli MM, Robinson P ,Tweardy D J. Targeting Janus kinases and signal transducer and activator of transcription 3 to treat inflammation fibrosis and cancer: rationale progress and caution Pharmacol Rev2020, 72: 486-526

120. Hu X ,Li J ,Fu M , Zhao X , Wang W The JAK/STAT signaling pathway: from bench to clinic Sig Transduct Target Ther 2021, 6: 1-33

121. Zhang Y Wang X Targeting the Wnt/β-catenin signaling pathway in cancer JHematol Oncol2020 13 165

122. YangM, Wang H ,ZhouM ,Liu W ,KuangP ,Liang H ,YuanQ The natural compound sulforaphene as a novel anticancer reagent targeting PI3K-AKT signaling pathway in lung cancer Oncotarget 2016; 77: 6656–76666

123. El Hawary S S. E., Hadeel N A, Kamel K M , Amira K E, Mouchira A S. Herbal Phytoconstituents: Natural weapon against lung cancer. Egypt. J. Chem. 2025; 68: SI: Z. M. Nofal, 255 - 288. DOI: 10.21608/ejchem.2025.365750.11408

124. Cadieux Z ,Lewis H ,Esquela-Kerscher A Role of Nutrition theEpigenome and MicroRNAs in Cancer Pathogenesis In MicroRNAs in Diseases and Disorders: Emerging Therapeutic Targets , Royal Society of Chemistry: London UK2019 ,pp 1–35 ISBN 9781782621454

125. Sun M ,Estrov Z ,JiY ,Coombes KR ,HarrisDH ,Kurzrock R Curcumin (diferuloylmethane) alters the expression profiles of microRNAs in human pancreatic cancer cells Molecular Cancer Therapeutics 2008; 7 3: 464–473

126. Mirzaei H ,Masoudifar A ,SahebkarA ,Zare N , Sadri Nahand J, Rashid iB , Mehrabian E ,MohammadiM ,Mirzaei HR ,Jaafari MR, Micro RNA. A novel target of curcumin in cancer therapy J Cell Physiol 2018; 233 (4):3004-3015

127. Norouzi S ,Majeed M , Pirro M ,Generali D ,SahebkarA Curcumin as an adjunct therapy and microRNA modulator in breast Cancer Curr PharmDes 2018' 24 (2): 171-177

128. Li W, Chen H, XuB ,Wang Y ,Zhang C , Cao Y ,Xing X Research progress on classification sources and functions of dietary polyphenols for prevention and treatment of chronic diseases J Future Foods 2023; ,3: 289–305

129. 1Shanmugam M K, Rane G ,KanchiMM ,Arfuso F ,ChinnathambiA ,Zayed ME ,AlharbiSA ,Tan BK ,KumarAP ,Sethi G The multifaceted role of curcumin in cancer prevention and treatment Molecules 2015; 20 (2): 2728–2769

130. Tili E, Michaille JJ, AlderH, Volinia S, Delmas D, Latruffe N, Croce CM. Resveratrol modulates the levels of microRNAs targeting genes encoding tumor-suppressors and effectors of TGFβ signaling pathway in SW480 cells Bio chem. Pharmacol 2010; 15 80 (12): 2057–2065.

131. Fang M Z, Wang Y ,AiN ,Hou Z ,SunY ,Lu H ,WelshW ,YangCS Tea polyphenol (−)-epigallocatechin-3-gallate inhibits DNA methyltransferase and reactivates methylation-silenced genes in cancer cell lines Cancer Research 2003 63 (22): 7563–7570

132. Sharifi-Rad J , Seidel V ,Izabela M ,Monserrat-Mequida M ,SuredaA ,Ormazabal V ,ZunigaFA ,Mangalpady SS ,PezzaniR ,Ydyrys A ,TussupbekovaG, MartorellM ,CalinaD , Ch o W C Phenolic compounds as Nrf2 inhibitors: potential applications in cancer therapy Cell Commun Signal 2023; 21: :89

133. SuX, Jiang X ,MengL ,Dong X ,ShenY ,Xin Y Anticancer activity of sulforaphane: the epigenetic mechanisms and the Nrf2 signaling pathway Oxid Med And Cell Longevity 2018)

134. Dickinson S E , Rusche J J ,Bec SL ,HornDJ ,Janda J ,Rim S H et al The effect of sulforaphane on histone deacetylase activity in keratinocytes: differences between in vitro and in vivo analyses MolCarcinogenesis2015; 54: 1513–20

135. Morimitsu Y, Nakagawa Y, Hayashi K ,Fujii H ,KumagaiT ,Nakamura Y , et al A sulforaphane analogue that potently activates the Nrf2-dependent detoxification pathway J Of Biol Chem 2002; 277: 3456–63

136. Guerrero-BeltránCE Calderón-Oliver M Pedraza-Chaverri J Chirino YI Protective effect of sulforaphane against oxidative stress: recent advances Exp Toxicologic Pathol 2012; 64: 503–8
137. Houghton C, Fassett A Coombes JS Sulforaphane and other nutrigenomic Nrf2 activators: can the clinician's expectation be matched by the reality? Oxid Med Cell Longevity (2016) 2016
138. Uddin MS, Mamun AA, Jakaria M, Thangapandiyan S, Ahmad J, Rahman MA, Mathew B, Abdel-Daim MM, Aleya L. Emerging promise of sulforaphane-mediated Nrf2 signaling cascade against neurological disorders. Sci Total Environ. 2020 Mar 10; 707:135624. doi: 10.1016/j.scitotenv.2019.135624.
139. Mao L, Yang T, Li X, Lei X, Sun Y, Zhao Y, Zhang W, Gao Y, Sun B, Zhang F. Protective effects of sulforaphane in experimental vascular cognitive impairment: Contribution of the Nrf2 pathway. J Cereb Blood Flow Metab. 2019 Feb;39(2):352-366. doi: 10.1177/0271678X18764083.
140. Esfandyari S AleyasinANoroozi ZTaheriMKhodarahmianMEslamiMetal The protective effect of sulforaphane against oxidative stress through activation of Nrf2/ARE pathway in human granulosa cells Cell J (Yakhteh) 2021; 23: 692
141. Kim EJ, Park H ,KimJ ,Park J H Y 3 3'-diindolylmethane suppresses 12-O-tetradecanoylphorbol-13-acetate-induced inflammation and tumor promotion in mouse skin via the downregulation of inflammatory mediators MolCarcinog2010; 49: 672–683
142. Fuentes F, Paredes-Gonzalez X,Kong A N T Dietary Glucosinolates Sulforaphane PhenethylIsothiocyanate Indole-3-Carbinol/3 30 -Diindolylmethane: Anti-Oxidative Stress/Inflammation Nrf2 Epigenetics/Epigenomics and In Vivo Cancer ChemopreventiveEfficacyCurrPharmacolRep20151 179
143. Royston KJ, Tollefsbol TO. The Epigenetic Impact of Cruciferous Vegetables on Cancer Prevention CurrPharmacolRep2015;1: 46–51
144. Singh BN, ShankarS, Srivastava RK Green tea catechin epigallocatechin-3-gallate (EGCG): Mechanisms perspectives and clinical applications BiochemPharmacol2011; 82: 1807–1821
145. Borutinskaite V ,Virkšait ˙ e A ,Gudelyt ˙ e G ,Navakauskien ˙ e R Green tea polyphenol EGCG causes anti-cancerous epigenetic ˙ modulations in acute promyelocytic leukemia cells Leuk Lymphoma 2018 ;59 : 469–478
146. Henning SM, Wang P , Carpenter CL , Heber D. Epigenetic effects of green tea polyphenols in cancer Epigenomics 2013; 5 -729.
147. Cadieux Z, Lewis H, Esquela-Kerscher A Role of Nutrition the Epigenome and MicroRNAs in Cancer Pathogenesis In MicroRNAs in Diseases and Disorders: Emerging Therapeutic Targets, Royal Society of Chemistry: London UK2019 ,pp 1–35 ISBN 9781782621454
148. Kho r T O, HuangY, Wu T -Y, Shu L, LeeJ, Kong A -N T. Pharmacodynamics of curcumin as DNA hypomethylation agent in restoring the expression of Nrf2 via promoter CpGs demethylation Biochem Pharmacol 2011; 82: 1073–1078
149. Qadir M, Naqvi S, Muhammad S. Curcumin: A Polyphenol with Molecular Targets for Cancer Control Asian Pac J CancerPrev 2016; 17: 2735–2739
150. Vadukoot AK, Mottemmal S, Vekaria P H. Curcumin as a Potential Therapeutic Agent in Certain Cancer Types Cureus 2022 14 e22825
151. Wang M, Jiang S, Zhou L ,YuF, Ding H,,LiP, Zhou M. Wang K. Potential Mechanisms of Action of Curcumin for Cancer Prevention: Focus on Cellular Signaling Pathways and miRNAs IntJBiolSci 2019; 15 : 1200–1214
152. Kasi PD, Tamilselvam R, Skalicka-Wo´zn
iak K ,NabaviSF ,Daglia M ,BishayeeA ,Pazoki-Toroudi H ,NabaviSM Molecular targets of curcumin for cancer therapy: An updated review TumourBiol 2016 ; 37: 13017–13028
153. Giordano A ,Tommonaro G Curcumin and Cancer Nutrients2019 ;11 : 2376
154. Farghadani R, Naidu R. Curcumin: Modulator of Key Molecular Signaling Pathways in Hormone-Independent Breast Cancer. Cancers (Basel). 2021 Jul 8;13(14):3427. doi: 10.3390/cancers13143427.
155. Nagoor N H, Aggarwal B Cancer-linked targets modulated by curcumin. Int J Biochem Mol Biol. 2012; 3: 328–351
156. Zhou H , Beevers C S..HuangS Targets of curcumin Curr Drug Targets 2011 ; 12: 332
157 Shanmugam MK, Rane G ,Kanchi MM ,ArfusoF ,Chinnathambi A ,ZayedME ,Alharbi SA ,Tan B K H ,Kumar AP ,SethiG The Multifaceted Role of Curcumin in Cancer Prevention and Treatment Molecules2015; 20: 2728–2769
158. Abrahams S, Haylett WL ,JohnsonG ,Carr JA ,Bardien S. Antioxidant effects of curcumin in models of neurodegeneration aging oxidative and nitrosative stress: A review Neuroscience 2019; 406: 1–21
159. RuanD, ZhuYW, Fouad AM, YanSJ, Chen W, ZhangYN, Xia WG ,WangS ,Jiang SQ ,YangL ,Zheng CT Dietary curcumin enhances intestinal antioxidant capacity in ducklings via altering gene expression of antioxidant and key detoxification enzymes PoultSci2019 ;98 : 3705–3714
160. Varoni EM, Lo Faro AF, Sharifi-Rad J, Iriti M. Anticancer Molecular Mechanisms of Resveratrol FrontNutr2016; 3: 8 doi: 10.3389/fnut.2016.00008.
161. Issinger OG, GuerraB Phytochemicals in cancer and their effect on the PI3K/AKT-mediated cellular signaling Biomed Pharmacother 2021 ;139: 111650. doi: 10.1016/j.biopha.2021.111650. Epub 2021 May 1. PMID: 33945911.
162. Signorelli P, GhidoniR. Resveratrol as an anticancer nutrient: Molecular basis open questions and promises J Nutr Biochem2005; 16: 449–466. doi: 10.1016/j.jnutbio.2005.01.017. PMID: 16043028.
163. Connolly EL, Sim M, Travica N, Marx W, Beasy G, Lynch GS, Bondonno CP, Lewis JR, Hodgson JM, Blekkenhorst LC. Glucosinolates From Cruciferous Vegetables and Their Potential Role in Chronic Disease: Investigating the Preclinical and Clinical Evidence. Front Pharmacol. 2021 Oct 26; 12:767975. doi: 10.3389/fphar.2021.767975. PMID: 34764875; PMCID: PMC8575925.
164. Banc R, Loghin F, Miere D , Ranga F , Socaciu C. Phenolic composition and antioxidant activity of red rosé and white wines originating from Romanian grape cultivars Not Bot Horti Agrobot Cluj-Napoca 2020; 48: 716–734.

165. Mirazimi S M A, Dashti F, TobeihaM, Shahini A ,JafariR ,Khoddami M ,SheidaAH ,EsnaAshari P. Aflatoonian AH, Elikaii F , et al. Application of Quercetin in the Treatment of Gastrointestinal Cancers Front Pharmaco l2022 ;13: 921.
166. Zhang Q , Zhao X H ,Wang Z J. Cytotoxicity of flavones and flavonols to a human esophageal squamous cell carcinoma cell line (KYSE-510) by induction of G2/M arrest and apoptosis Toxicol In Vitro 2009; 23: 797–807
167. Tan J, Wang B, Zhu L. Regulation of survivin and Bcl-2 in HepG2 cell apoptosis induced by quercetin Chem Biodivers 2009; 6 :1101–1110.
168. Tanigawa S , Fujii M, Hou D X . Stabilization of p53 is involved in quercetin-induced cell cycle arrest and apoptosis in HepG2 cells Bio sci Biotechnol Biochem 2008 ;72: 797–804
169. Xi L ,Zhang Y ,KongS ,Liang W miR-34 inhibits growth and promotes apoptosis of osteosarcoma in nude mice through targetly regulating TGIF2 expression Biosci Rep2018 ;38 : 20180078
170. Yang Y ,Wang T ,ChenD ,Ma Q ,ZhengY ,Liao S ,WangY ,Zhang J Quercetin preferentially induces apoptosis in KRAS-mutant colorectal cancer cells via JNK signaling pathways Cell Biol Int 2019; 43 : 117–124
171. Ghafouri-FardS, Shabestari FA ,VaeziS ,Abak A ,ShooreiH ,Karimi A ,TaheriM ,Basiri A Emerging impact of quercetin in the treatment of prostate cancer Biomed Pharmacother 2021 ;138 : 111548
172. Vijayababu MR ,Arunkumar A ,KanagarajP ,Arunakaran J. Effects of quercetin on insulin-like growth factors (IGFs) and their binding protein-3 (IGFBP-3) secretion and induction of apoptosis in human prostate cancer cells J Carcinog 2006; 5: 10. doi: 10.1186/1477-3163-5-10. PMID: 16600019; PMCID: PMC1482693.
173. Luo CL, Liu YQ ,WangP ,Song CH ,WangKJ ,Dai LP ,ZhangJY ,Ye H The effect of quercetin nanoparticle on cervical cancer progression by inducing apoptosis autophagy and anti-proliferation via JAK2 suppression Biomed Pharmacother 2016; 82 : 595–605 [CrossRef].
174. Alvarez MC, Maso V, Torello CO, Ferro KP, Saad STO. The polyphenol quercetin induces cell death in leukemia by targeting epigenetic regulators of pro-apoptotic genes. Clin Epigenetics. 2018 Nov 8;10(1):139. doi: 10.1186/s13148-018-0563-3.
175. Kim DH ,Khan H ,UllahH ,Hassan S T S ,Šmejkal K ,EfferthT ,Mahomoodally MF ,XuS ,Habtemariam S ,FilosaR , et al MicroRNA targeting by quercetin in cancer treatment and chemoprotection Pharmacol Res2019 ;147 :104346
176. Aust O , Ale-Agha N ,ZhangL ,Wollersen H ,SiesH ,Stahl W Lycopene oxidation product enhances gap junctional communication FoodChem Toxicol 2003 ; 41: 1399–1407
177. Ilic D, MissoM Lycopene for the prevention and treatment of benign prostatic hyperplasia and prostate cancer: A systematic review Maturitas2012; 72 :269–276
178. Lu Y, Edwards A, Chen Z, Tseng TS, Li M, Gonzalez GV, Zhang K. Insufficient Lycopene Intake Is Associated With High Risk of Prostate Cancer: A Cross-Sectional Study From the National Health and Nutrition Examination Survey (2003-2010). Front Public Health. 2021 Dec 13; 9:792572. doi: 10.3389/fpubh.2021.792572.
179. Li Y,Yao J,Han C, YangJ ,Chaudhry M T, Wang SLiu H &YinY. Quercetin inflammation and immunity Nutrients 2016 ;8 (3): 167
180. Liu J Pharmacology of oleanolic acid and ursolic acid J of Ethnopharmacology 2019; 120 (3): 292–300
181. Lim HS, Kim YJ, Kim BY, Park G, Jeong SJ. The Anti-neuroinflammatory Activity of Tectorigenin Pretreatment via Downregulated NF-κB and ERK/JNK Pathways in BV-2 Microglial and Microglia Inactivation in Mice With Lipopolysaccharide. Front Pharmacol. 2018 May 9; 9:462. doi: 10.3389/fphar.2018.00462.
182. CandiracciM, Piatti E, Dominguez-Barragan ´M , García-Antras ´ D Morgado BRuano D Guti´errez JF ,ParradoJ ,Castano ˜A Anti-Inflammatory Activity of a Honey Flavonoid Extract on Lipopolysaccharide-Activated N13 Microglial Cells JAgric Food Chem 2012; 60 : 12304–12311
183. Christopher J S G, Saswati B, Ezilrani PS Optimization of Parameters for Biosynthesis of Silver Nanoparticles Using Leaf Extract of Aegle marmelosBrazilianArchBiolTechnol 2015; 58 : 702–710 https://doi.org/10.1590/S1516-89132015050106
184.. Khazdair MR, Anaeigoudari A, Hashemzehi M, Mohebbati R. Neuroprotective potency of some spice herbs, a literature review. J Tradit Complement Med. 2018 Apr 30;9(2):98-105. doi: 10.1016/j.jtcme.2018.01.002.
185. Gupta V, Guleri R, Gupta M, Kaur N, Kaur K, Kumar P, Anand M, Kaur G, Pati PK. Anti-neuroinflammatory potential of Tylophora indica (Burm. f) Merrill and development of an efficient in vitro propagation system for its clinical use. PLoS One. 2020 Mar 25;15(3): e0230142. doi: 10.1371/journal.pone.0230142.
186. Qin W, Yang T, Ho L, Zhao Z, Wang J, Chen L, Zhao W, Thiyagarajan M, MacGroganD,Rodgers J T, Puigserver P ,PasinettiGM Neuronal SIRT1 activation as a novel mechanism underlying the prevention of Alzheimer's disease amyloid neuropathology by calorie restriction. J. of Biological Chemistry 2006 ; 281 (31): 21745–21754
187. Radad K, MoldzioR, Rausch WD. Ginsenosides and their CNS targets Neuroscience Research 2011; 68 (4): 285–295 doi: 10.1111/j.1755-5949.
188. Minocha, T H. Birla, A.A. Obaid, V. Rai, P. Sushma, C. Shivamallu, M. Moustafa, M. Al-Shehri, A. Al-Emam, M.A. Tikhonova Flavonoids as promising neuroprotectants and their therapeutic potential against Alzheimer's disease Oxidative Medicine and Cellular Longevity, 2022 (2022), Article 6038996, 10.1155/2022/6038996
189.Tsalamandris, S. Antonopoulos A.S. , Oikonomou E. , G.- Papamikroulis, A. Vogiatzi G., Papaioannou S. , Deftereos S. , Tousoulis D. The role of inflammation in diabetes: Current concepts and future perspectives European Cardiology Review, 2019;14 (1) : 50, 10.15420/ecr.2018.33.1

190 Cowan S, Lim S, Alycia C, Pirotta S, Thomson R, Gibson-Helm M, Blackmore R, Naderpoor N, Bennett C, Ee C, Rao V, Mousa A, Alesi S, Moran L. Lifestyle management in polycystic ovary syndrome - beyond diet and physical activity. BMC Endocr Disord. 2023 Jan 16;23(1):14. doi: 10.1186/s12902-022-01208-y..

191. Phull AR, Nasir B, Haq IU, Kim SJ. Oxidative stress, consequences and ROS mediated cellular signaling in rheumatoid arthritis. Chem Biol Interact. 2018 Feb 1; 281:121-136. doi: 10.1016/j.cbi.2017.12.024. .

192. Jomova K, Raptova R, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, Valko M. Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. Arch Toxicol. 2023 Oct;97(10):2499-2574. doi: 10.1007/s00204-023-03562-9.

193. Bhattacharya S, Heidler P, Varshney S. Incorporating neglected non-communicable diseases into the national health program-A review. Front Public Health. 2023 Jan 10; 10:1093170. doi: 10.3389/fpubh.2022.1093170.

194. Unuofin J O, Lebelo S L. Antioxidant Effects and Mechanisms of Medicinal Plants and Their Bioactive Compounds for the Prevention and Treatment of Type 2 Diabetes: An Updated Review Oxid Med Cell Longev 2020; 2020 :1356893

195. Bharti SK, Krishnan S, Kumar A, Kumar A. Antidiabetic phytoconstituents and their mode of action on metabolic pathways. Ther Adv Endocrinol Metab. 2018 Mar;9(3):81-100. doi: 10.1177/2042018818755019. Epub 2018 Feb 12.

196. Miura T ,Muraoka S ,IkedaN ,Watanabe M ,FujimotoY Antioxidative and prooxidative action of stilbene derivatives PharmacolToxicol2000; 86: 203–208

197. SpanierG, Xu H ,XiaN ,Tobias S ,DengS ,Wojnowski L ,ForstermannU ,Li H Resveratrol reduces endothelial oxidative stress by modulating the gene expression of superoxide dismutase 1 (SOD1) glutathione peroxidase 1 (GPx1) and NADPH oxidase subunit (NOX4) JPhysiol Pharmacol 2009 ;60 : 111–116

198. ValkoM, Leibfritz D ,MoncolJ ,Cronin M T D ,Mazur M ,TelserJ Free radicals and antioxidants in normal physiological functions and human disease Int J Biochem Cell Biol 2007 ; 39 : 44–84

199. Di MeoS ,Reed TT ,VendittiP ,Victor VM Role of ROS and RNS Sources in Physiological and Pathological Conditions OxidMedCellLongev 2016; 2016: 1245049

200. Farkhondeh T, Folgado SL, Pourbagher-Shahri AM, Ashrafizadeh M, Samarghandian S. The therapeutic effect of resveratrol: Focusing on the Nrf2 signaling pathway. Biomed Pharmacother. 2020 Jul; 127:110234. doi: 10.1016/j.biopha.2020.110234. Epub 2020 May 20. PMID: 32559855.

201. Jobin C ,Bradham CA ,RussoMP ,Juma B ,NarulaAS ,Brenner DA ,SartorRB Curcumin blocks cytokine-mediated NF-κB activation and proinflammatory gene expression by inhibiting inhibitory factor I-κB kinase activity J of Immunol 1999 ; 163 (6): 3474–3483

202. Dharmadeva S, Galgamuwa LS, Prasadinie C, Kumarasinghe N. In vitro anti-inflammatory activity of Ficus racemosa L. bark using albumin denaturation method. Ayu. 2018 Oct-Dec;39 (4):239-242. doi: 10.4103/ayu.AYU_27_18.

203. Otunola G A, Afolayan AJ.Chemical Composition Antibacterial and in Vitro Anti-Inflammatory Potentials of Essential Oils from Different Plant Parts of Moringa oleifera Lam AmJBiochemBiotechnol 2018 ;14: 210–220 **DOI:** https://doi.org/10.3844/ajbbsp.2018.210.220

204. Sumathi S, Anuradha R In Vitro Anti-Inflammatory Acitivty of Flower Extract of CouroupitaguianensisAublInnovareJAyurvedicSiences 2016; 4: 4–6

205. Jahangir M ,Baek KKim , E Seok W ,JeongD ,Ho J ,KweonD ,Hyo D ,WoongT ,Kim J In Vivo and in Vitro Anti-Inflammatory Activities of Persicaria chinensis Methanolic Extract Targeting Src/Syk/NF-KB JEthnopharmacol 2015; 159 : 9–16

206. FangkrathokN, Junlatat J, Sripanidkulchai B In Vivo and in Vitro AntiInflammatory Activity of Lentinus polychrousExtractJEthnopharmacol 2013; 147: 631–637

207. Di Carlo G, Mascolo N, IzzoAA, Capasso F Flavonoids: old and new aspects of a class of natural therapeutic drugs LifeSci1999; 65: 337–353

208. Middleton Jr , E Kandaswami C ,TheoharidesTC The effects of plant flavonoids on mammalian cells: implications for inflammation heart disease and cancer Pharmacol Rev 2000 ; 52: 673–751

209. Riboli E, Norat T Epidemiologic evidence of the protective effect of fruit and vegetables on cancer risk AmJClinNutr 2003; 78 : 559S–569S

210. Ayertey F, Ofori-Attah E, Antwi S, Amoa-Bosompem M, Djameh G, Lartey NL, Ohashi M, Kusi KA, Appiah AA, Appiah-Opong R, Okine LK. Anti-inflammatory activity and mechanism of action of ethanolic leaf extract of *Morinda lucida* Benth. J Tradit Complement Med. 2020 Aug 4;11(3):249-258. doi: 10.1016/j.jtcme.2020.07.001.

211. Heinrich M, Mah J, Amirkia V. Alkaloids Used as Medicines: Structural Phytochemistry Meets Biodiversity-An Update and Forward Look. Molecules. 2021 Mar 25;26(7):1836. doi: 10.3390/molecules26071836.

212. Tasneem S, Liu B, Li B, Choudhary MI, Wang W. Molecular pharmacology of inflammation: Medicinal plants as anti-inflammatory agents. Pharmacol Res. 2019 Jan; 139:126-140. doi: 10.1016/j.phrs.2018.11.001.

213. Gonfa YH ,Beshah F ,TadesseMG ,Bachheti A Phytochemical Investigation and Potential Pharmacologically Active Compounds of Rumex nepalensis: An Appraisal Beni-SuefUniv J Basic Appl Sci 2021; 10 : 1–11 https://doi.org/10.1186/s43088-021-00110-1

214. Naz R ,Ayub H ,NawazS ,Islam ZU ,YasminT ,Bano A ,WakeelA ,Zia S ,RobertsTH AntimicrobialActivity Toxicity and Anti-Inflammatory Potential of Methanolic Extracts of Four Ethnomedicinal Plant Species from Punjab Pakistan BMC Complement AlternMed 2017 ;17 : 1–13

215. Devi KP ,Malar DS ,NabaviSF ,Sureda A ,XiaoJ ,Nabavi SM ,DagliaM Kaempferol and Inflammation: From Chemistry to Medicine PharmacolRes 2015; 99 : 1–10\

216.Almatroudi A., Allemailem K S. Alwanian WM, Alharbi BF, Alrumaihi F, Khan A A, Almatroodi SA, Rahmani, AH. Effects and mechanisms of kaempferol in the management of cancers through modulation of inflammation and signal transduction pathways, Int. J. Mol. Sci. 2023;24 8630, https://doi.org/ 10.3390/ijms24108630

217.paul, J. K., Azmal, M., Haque, A. S. N. B., Talukder, O. F., Meem, M., & Ghosh, A. (2024). Phytochemical-mediated modulation of signaling pathways: a promising avenue for drug discovery. *Advances in Redox Research*, *13*, 100113

218 Liu L, Yeh Y.-Y. S-Alk(en)yl cysteines of garlic inhibit cholesterol synthesis by deactivating HMG-CoA reductase in cultured rat hepatocytes, J. Nutr. 2002;132 : 1129–1134, https://doi.org/10.1093/jn/132.6.1129.

219.Wang S-L, Liu D-S., Liang E.-S, Gao Y.-H, Cui Y., Liu Y.-Z., Gao W. Protective effect of allicin on high glucose/hypoxia-induced aortic endothelial cells via reduction of oxidative stress, Exp. Ther. Med. 2015;10: 1394–1400, https://doi. org/10.3892/etm.2015.2708.

220. Li, W, Hua B., Saud S.M, Lin H., Hou W., Matter M.S., Jia L., Colburn N.H., Young M. R., Berberine regulates AMP-activated protein kinase signaling pathways and inhibits colon tumorigenesis in mice, Mol. Carcinog. 2015 ;54 1096–1109, https://doi.org/10.1002/mc.22179.

221. Utami AR, Maksum IP, Deawati Y. Berberine and its study as an antidiabetic compound, Biol. (Basel) 2023;12 973, https://doi.org/10.3390/ biology12070973.

222.Choi EY, Han EJ, Jeon S-J, Lee S.-W., Moon JM, Jung S.-H, Park Y-S, Park B- K., Kim B.-S,- Kim S K, Jung J.-Y. Kaempferol inhibits cervical cancer cells by inducing apoptosis and autophagy via inactivation of the PI3K/AKT/mTOR signaling pathway, Anticancer Res.2024;44:2961–2972, https://doi.org/ 10.21873/anticanres.17108.

223.Kubo E, Chhunchha B, Singh P, Sasaki H, Singh D.P. Sulforaphane reactivates cellular antioxidant defense by inducing Nrf2/ARE/Prdx6 activity during aging and oxidative stress, Sci. Rep. 2017;7: 14130, https://doi.org/10.1038/s41598- 017-14520-8.

224.Louis-Gray K, Tupal S,Premkumar, L.S. TRPV1: a common denominator mediating antinociceptive and antiemetic effects of cannabinoids, Int. J. Mol. Sci. 2022; 23 10016, https://doi.org/10.3390/ijms231710016.

225.Wang J, Xie Y, Feng Y, Zhang L., Huang X, Shen X, Luo, X. (-)-Epigallocatechingallate induces apoptosis in B lymphoma cells via caspasedependent pathway and Bcl-2 family protein modulation, Int. J. Oncol. 2015;46 :1507–1515, https://doi.org/10.3892/ijo.2015.2869.

226. Li F, Gao C, Yan P, Zhang M, Wang Y,Hu Y, Wu X, Wang X, Sheng J. EGCG Reduces Obesity and White Adipose Tissue Gain Partly Through AMPK Activation in Mice, Front. Pharmacol. 2018; 9 : 1366, https://doi.org/10.3389/ fphar.2018.01366.

227.Afzal O, Dalhat MH, Altamimi ASA, Rasool R, Alzarea SI, Almalki WH, Murtaza BN, Iftikhar S, Nadeem S, Nadeem MS, Kazmi I. Green Tea Catechins Attenuate Neurodegenerative Diseases and Cognitive Deficits. Molecules. 2022 Nov 6;27(21):7604. https://doi.org/10.3390/molecules27217604.

228. Gutierrez-Salmean G, Ciaraldi TP, Nogueira L, Barboza J, Taub PR, Hogan MC, Henry RR, Meaney E, Villarreal F, Ceballos G, Ramirez-Sanchez I. Effects of (-)-epicatechin on molecular modulators of skeletal muscle growth and differentiation. J Nutr Biochem. 2014 Jan;25(1):91-4. doi: https://doi.org/10.1016/j. jnutbio.2013.09.007.

229.Shi H, LI X-Y, Chen Y, Zhang X, Wu Y, Wang Z-X, Chen P-H, Dai H-Q, Feng J, Chatterjee S, Li Z-J, Huang X-W, Wei H-Q, Wang J, Lu G-D and Zhou J Corrigendum: Quercetin Induces Apoptosis Via Downregulation of VEGF/Akt Signaling Pathway in Acute Myeloid Leukemia *Cells.* Front. Pharmacol. 202011: https://doi.org/10.3389/fphar.2020.534171.

230.Zhang Q, Wen F, Sun F, Xu Z, Liu Y, Tao C, Sun F, Jiang M, Yang M, Yao J. Efficacy and Mechanism of Quercetin in the Treatment of Experimental Colitis Using Network Pharmacology Analysis. Molecules. 2022 Dec 24;28 (1):146. doi: 10.3390/molecules28010146.

231.Shin EJ, Lee JS, Hong S, Lim TG, Byun S. Quercetin Directly Targets JAK2 and PKCδ and Prevents UV-Induced Photoaging in Human Skin. Int J Mol Sci. 2019 Oct 23 ;20 (21):5262. doi: 10.3390/ijms20215262.

232. Hong SY, Ha AW, Kim W. Effects of quercetin on cell differentiation and adipogenesis in 3T3-L1 adipocytes. Nutr Res Pract. 2021 Aug;15(4):444-455. doi: 10.4162/nrp.2021.15.4.444.

233 Gao X ,Xu YX ,JanakiramanN ,Chapman RA ,GautamSC Immunomodulatory activity of resveratrol: suppression of lymphocyte proliferation development of cell-mediated cytotoxicity and cytokine production BiochemPharmacol 2001 ;62 : 1299–1308.

234. Manna SK ,Mukhopadhyay A ,AggarwalBB Resveratrol suppresses TNF-induced activation of nuclear transcription factors NF-kappa B activator protein-1 and apoptosis: potential role of reactive oxygen intermediates and lipid peroxidation J Immunol2000 ; 164: 6509–6519

235. Holmes-McNary M , Baldwin Jr , A S. Chemopreventive properties of transresveratrol are associated with inhibition of activation of the IkappaBkinaseCancerRes2000; 60 : 3477–3483

236. Donnelly LE ,Newton R ,KennedyGE ,Fenwick PS ,LeungRH ,Ito K ,RussellRE ,Barnes PJ Anti-inflammatory effects of resveratrol in lung epithelial cells: molecular mechanisms AmJPhysiol LungCell MolPhysiol 2004; 287: L774–783

237. SubbaramaiahK, Chung WJ ,MichaluartP ,Telang N ,TanabeT ,Inoue H ,JangM ,Pezzuto JM ,DannenbergAJ Resveratrol inhibits cyclooxygenase-2 transcription and activity in phorbol ester-treated human mammary epithelial cells JBiolChem 1998; 273 : 21875–21882

238. Kowalski J ,Samojedny A ,PaulM ,Pietsz G ,WilczokT Effect of apigenin kaempferol and resveratrol on the expression of interleukin-1beta and tumor necrosis factor-alpha genes in J774 2 macrophages Pharmacol Rep2005; 57 : 390–394
239. Roy A ,Bhoumik D ,SahuRK ,Dwivedi J Medicinal Plants Used in Liver Protection UKJPharmBiosci 2014 ; 2 : 23–33
240. Li X, Sun R, Liu R. Natural products in licorice for the therapy of liver diseases: Progress and future opportunities. Pharmacol Res. 2019 Jun; 144:210-226. doi: 10.1016/j.phrs.2019.04.025.
241. Asadi-SamaniM, Kafash-Farkhad N ,AzimiN ,Fasihi A ,Alinia-Ahandani E ,Rafieian-Kopaei M Medicinal Plants with Hepatoprotective Activity in Iranian Folk Medicine Asian Pac J Trop Biomed 2015 ;5 : 146–157
242. Zhang A, SunH ,Wang X Recent Advances in Natural Products from Plants for Treatment of Liver Diseases EurJMedChem 2013; 63 : 570–577
243. Dawid-Pa´c R Medicinal Plants Used in Treatment of Inflammatory Skin Diseases PostepDermatologii Alergol 2013; 30: 170–177
244. WedlerJ, Daubitz T, Schlotterbeck G , Butterweck V In Vitro AntiInflammatory and Wound-Healing Potential of a Phyllostachys edulis Leaf ExtractIdentification of Isoorientin as an Active Compound PlantaMed2014 ; 80: 1678–1684
245. Maione FRussoR Khan HM ascolo N. Medicinal Plants with Anti Inflammatory Activities Nat Prod Res2016; 6419: 1–10
246.KırmızıbekmezH, ˙ Inan Y ,ReisR ,Sipahi H ,Goren ¨ A C ,Yes¸ilada E2019 Phenolic Compounds from the Maione FRussoRKhanHMascolo N2016 Medicinal Plants with AntiInflammatoryActivitiesNatProd Res 2019 ; 6419: 1–10
247. Liperoti R, Vetrano DL, Bernabei R, Onder G. Herbal Medications in Cardiovascular Medicine. J Am Coll Cardiol. 2017 Mar 7;69 (9):1188-1199. doi: 10.1016/j.jacc.2016.11.078.
248. Li ZM, Xu SW, Liu PQ. Salvia miltiorrhizaBurge (Danshen): a golden herbal medicine in cardiovascular therapeutics. Acta Pharmacol Sin. 2018 May;39(5):802-824. doi: 10.1038/aps.2017.193. Epub 2018 Apr 26.
249. Dragos D, Gilca M, Gaman L, Vlad A, Iosif L, Stoian I, Lupescu O. Phytomedicine in Joint Disorders. Nutrients. 2017 Jan 16;9(1):70. doi: 10.3390/nu9010070.
250. Singh S, Singh TG, Mahajan K, Dhiman S. Medicinal plants used against various inflammatory biomarkers for the management of rheumatoid arthritis. J Pharm Pharmacol. 2020 Oct;72(10):1306-1327. doi: 10.1111/jphp.13326.
251. MuruganantharG, Sudheer KG, Sathya CP, Mohan S Anti-Arthritic and Anti-Inflammatory Constituents from Medicinal Plants JApplPharmSci 2013 ; 3 : 161–164
252. Xia X, May BH, Zhang AL, Guo X, Lu C, Xue CC, Huang Q. Chinese Herbal Medicines for Rheumatoid Arthritis: Text-Mining the Classical Literature for Potentially Effective Natural Products. Evid Based Complement Alternat Med. 2020 Apr 28; 2020:7531967. doi: 10.1155/2020/7531967.
253. Wambugu SN, Mathiu PM ,GakuyaDW ,Kanui TI ,KabasaJD ,Kiama SG Medicinal Plants Used in the Management of Chronic Joint Pains in Machakos and Makueni Counties KenyaJEthnopharmacol 2011; 137 : 945–955
254. Kaymaz K, Hensel A, Beikler T. Polyphenols in the prevention and treatment of periodontal disease: A systematic review of in vivo, ex vivo and in vitro studies. Fitoterapia. 2019 Jan; 132:30-39. doi: 10.1016/j.fitote.2018.11.012.
255. Vogl S, Picker P, Mihaly-Bison J, Fakhrudin N, Atanasov AG, Heiss EH, Wawrosch C, Reznicek G, Dirsch VM, Saukel J, Kopp B. Ethnopharmacological in vitro studies on Austria's folk medicine--an unexplored lore in vitro anti-inflammatory activities of 71 Austrian traditional herbal drugs. J Ethnopharmacol. 2013 Oct 7;149(3):750-71. doi: 10.1016/j.jep.2013.06.007.
256. Sangiovanni ELorenzo C D Colombo E Colombo F Fumagalli M Frigerio G Restani P Agli M D 2015. The Effect of in Vitro Gastrointestinal Digestion on the Anti-Inflammatory Activity of Vitis vinifera Food Funct 2015; 1–11
257. De Cássia da Silveira E Sá R, Andrade LN, Dos Reis Barreto de Oliveira R, de Sousa DP. A review on anti-inflammatory activity of phenylpropanoids found in essential oils. Molecules. 2014 Jan 27;19(2):1459-80.doi: 10.3390/molecules19021459.
258. Dinarello CA. Anti-inflammatory Agents: Present and Future. Cell. 2010 Mar 19;140(6):935-50.doi: 10.1016/j.cell.2010.02.043.
259. Nworu CS, Akah PA. Anti-inflammatory medicinal plants and the molecular mechanisms underlying their activities Afr J Tradit Complement Altern Med 2015; 12: 52–61
260. Dragos D, Gilca M, Gaman L, Vlad A, Iosif L, Stoian I, Lupescu O. Phytomedicine in Joint Disorders. Nutrients. 2017 Jan 16;9(1):70. doi: 10.3390/nu9010070.
261. Hossen MJ, Jeon SH, Kim SC, Kim JH, Jeong D , SungNY , Yang S , BaekKS , Kim JH ,YoonDH. In Vitro and in Vivo Anti-Inflammatory Activity of Phyllanthus acidus Methanolic Extract J Ethnopharmacol 2015 ;168: 217–228
262. Nunes CDR, Barreto Arantes M, Menezes de Faria Pereira S, Leandro da Cruz L, de Souza Passos M, Pereira de Moraes L, Vieira IJC, Barros de Oliveira D. Plants as Sources of Anti-Inflammatory Agents. Molecules. 2020 Aug 15;25(16):3726.doi: 10.3390/molecules25163726.
263. Arifin YF, Hamidah S, Panjaitan S, Suhartono E In Vitro Anti-Inflammatory Activities of Red Gemor (Nothaphoebe Cf Umbelliflora) J Med Bioeng 2015; 4: 312–317
264 Adebayo SA, DzoyemJP, ShaiLJ, Eloff J N. The Anti-Inflammatory and Antioxidant Activity of 25 Plant Species Used Traditionally to Treat Pain in Southern African BMC Complement Altern Med 2015;15: 1–10.