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REVIEW

Bioactive Compounds of *Capsicum* Species and Their Therapeutic Properties: A Comprehensive Review

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ABSTRACT

Hot peppers, belonging to the *Capsicum* genus, are cultivated worldwide not only as spices and vegetables but also as valuable sources of bioactive compounds with potential health benefits. These plants contain a wide range of biologically active molecules, including capsaicinoids, capsinoids, carotenoids, phenolic compounds, vitamins, and peptides. Such compounds have attracted increasing scientific interest due to their antioxidant, anti-inflammatory, analgesic, antimicrobial, metabolic, and anticancer properties. In recent years, advances in phytochemical characterization and pharmacological studies have provided deeper insights into the mechanisms underlying the health-promoting effects of *Capsicum*-derived compounds. Evidence suggests that these bioactives may contribute to disease prevention and therapeutic support by modulating oxidative stress, inflammation, and key metabolic pathways. In this review, we summarize current knowledge on the major bioactive components of *Capsicum* species, with particular emphasis on their absorption, bioavailability, and biological activity. Special attention is given to their potential effects on cardiovascular, metabolic, neurological, gastrointestinal, and immune functions. In addition, emerging applications of hot peppers in the development of nutraceuticals, functional foods, and pharmaceutical products are discussed. Finally, existing limitations in the current literature are highlighted, and future research directions are proposed to better clarify their clinical relevance and safety.

Keywords: Functional Foods; *Capsicum* spp.; Capsinoids; Carotenoids; Therapeutic Properties; Metabolic Health

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1. Introduction

Chili peppers, belonging to the *Capsicum* genus within the *Solanaceae* family, are cultivated worldwide for their culinary, nutritional, and medicinal value. Among more than thirty recognized species, five—*Capsicum annuum*, *C. frutescens*, *C. chinense*, *C. baccatum*, and *C. pubescens*—have been widely domesticated. Originally native to the Americas, these peppers spread globally through trade and cultivation, becoming well-known not only for their characteristic pungency and flavor but also for their various health benefits [1,2].

The *Capsicum* genus contains a wide variety of bioactive compounds, including capsaicinoids, capsinoids, carotenoids, phenolic compounds, flavonoids, and vitamins C, A, and E. Together, these compounds are responsible for a range of biological effects, such as antioxidant, anti-inflammatory, analgesic, antimicrobial, and anticancer activities [3,4].

Among these compounds, capsaicinoids—especially capsaicin and dihydrocapsaicin—have been the most extensively studied. They are known to influence pain perception, thermogenesis, and metabolic regulation primarily through activation of the transient receptor potential vanilloid 1 (TRPV1) receptor [5,6].

Beyond their biochemical properties, epidemiological evidence suggests that regular chili consumption is associated with reduced all-cause mortality and lower incidence of cardiometabolic disorders, although causality remains to be fully established [7]. Such findings are consistent with laboratory and clinical research supporting the potential of chili-derived bioactives in disease prevention and management. Topical formulations of capsaicin are already in therapeutic use for neuropathic pain, while dietary supplements containing pepper extracts are explored for metabolic and cardiovascular benefits.

Given these insights, *Capsicum* species represent a valuable source of bioactive molecules with multifaceted health applications. This review aims to (i) summarize the chemical diversity of Capsicum bioactives, (ii) elucidate their biological mechanisms and therapeutic effects, (iii) critically compare existing findings, and (iv) identify key knowledge gaps and future research directions to advance their development in functional foods and drug formulations.

2. Methodology

2.1. Literature Search Strategy

A comprehensive literature search was conducted across several academic databases, including PubMed, Scopus, Web of Science, and Google Scholar. The search covered publications from January 2000 to January 2025 and was limited to peer-reviewed articles in English. Keywords and MeSH terms such as “Capsicum,” “capsaicin,” “capsaicinoids,” “capsinoids,” “carotenoids,” “bioactive compounds,” “phytochemistry,” “antioxidant activity,” “metabolic syndrome,” and “therapeutic effects” were combined using the Boolean operators AND and OR to refine the results. Additionally, reference lists of the selected studies were manually screened to identify any further relevant publications.

Inclusion and Exclusion Criteria:

Studies were included if they met the following requirements:

- Focused on *Capsicum* species or their isolated bioactive compounds.
- Reported nutritional, pharmacological, biological, or therapeutic outcomes.
- Were based on in vitro, in vivo, animal, human clinical studies, or systematic reviews.
- Provided clearly described methods and measurable outcome data.

Exclusion criteria were:

Studies were excluded if they met any of the following conditions:

❖ Sources that were not peer-reviewed, such as conference papers, theses, reports, or short communications.
❖ Articles that did not specifically focus on *Capsicum* or its bioactive compounds.
❖ Studies that lacked sufficient methodological details or did not provide extractable

2.2. Study Selection Process

The study selection process was conducted following the PRISMA guidelines to ensure methodological transparency (**Figure 1**). A total of 100 records were identified through database searching (PubMed, Scopus, Web of Science, and Google Scholar). In addition, 10 records were identified through other sources, resulting in 110 records initially identified.

After the removal of duplicate records, 30 records remained for further evaluation. Subsequently, 70 records were screened based on their titles and abstracts. During this screening stage, 15 records were excluded due to irrelevance to *Capsicum* species or lack of focus on bioactive compounds and therapeutic outcomes.

Following title and abstract screening, 6 full-text articles were assessed for eligibility. Of these, 20 full-text articles were excluded for reasons including insufficient methodological detail, lack of extractable data, or failure to meet the scope of the review. Ultimately, 20 studies met the inclusion criteria and were included in the qualitative synthesis of this review.

All screening and eligibility assessments were performed by the author(s), and any uncertainties were resolved through discussion and consensus. The overall process of study identification, screening, eligibility assessment, and inclusion is illustrated in the PRISMA flow diagram.

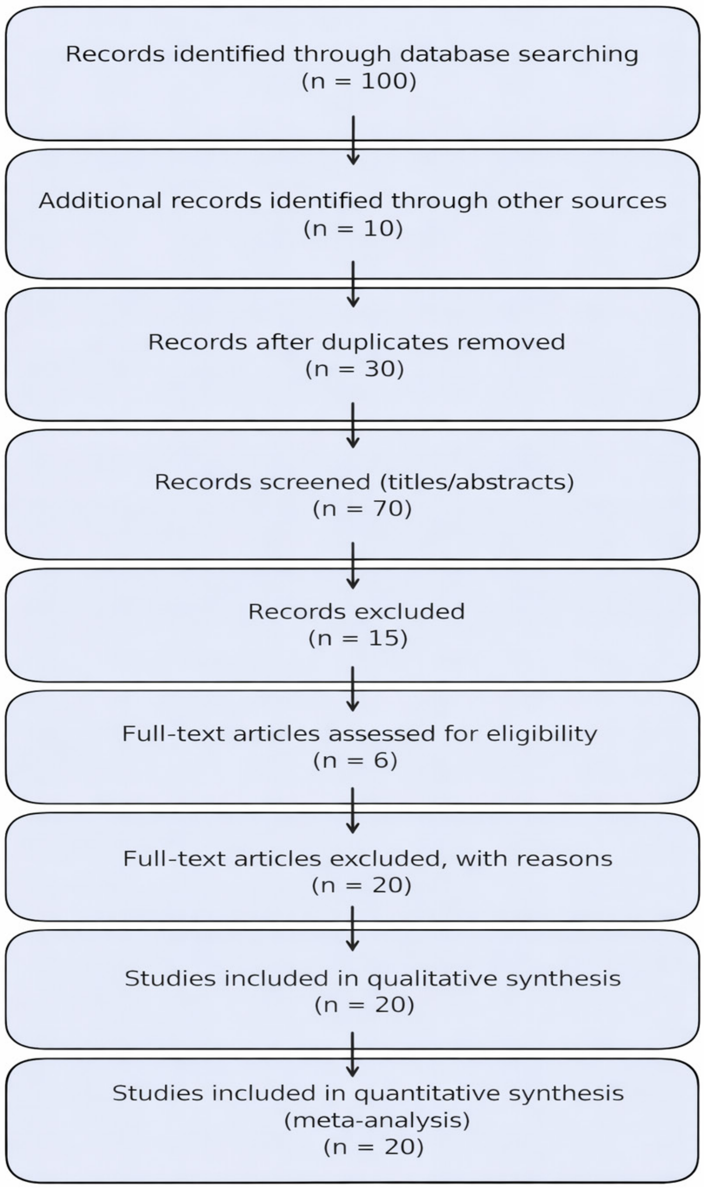

Figure 1. A flow diagram to visually summarize the study selection process (from identification to inclusion/exclusion).

Note: The numerical values reported in the PRISMA flow diagram represent consolidated and filtered records across multiple databases and screening stages, and were rounded for clarity of presentation.

3. Bioactive Compounds of *Capsicum*

3.1. Capsaicinoids and Capsinoids

Capsaicinoids are a distinct group of alkaloid compounds that are produced almost exclusively in *Capsicum* fruits. They are synthesized by the placenta epidermal cells and stored in vesicles within the peppers, where they primarily serve as a chemical defense against herbivores and microbial pathogens. Structurally, capsaicinoids are amides formed from vanillylamine linked to branched-chain fatty acids. To date, more than 20 capsaicinoids have been identified, with capsaicin and dihydrocapsaicin making up roughly 80–90% of the total pungent fraction. Minor compounds such as nordihydrocapsaicin, homocapsaicin, and homodihydrocapsaicin account for the remainder. Although present in smaller amounts, these minor capsaicinoids also exhibit notable biological activity [8,9]. The most well-characterized physiological target of capsaicinoids is the transient receptor potential vanilloid 1 (TRPV1), a selective cation channel expressed in sensory neurons and other cell types. Activation of TRPV1 by capsaicin causes depolarization through the influx of sodium and calcium ions into nociceptive neurons, producing the characteristic burning sensation. This initial excitation is followed by desensitization, which underlies the analgesic effects of capsaicin used in topical treatments for neuropathic and musculoskeletal pain. Beyond its role in pain signaling, TRPV1 activation also affects thermogenesis, energy metabolism, gastric motility, and cardiovascular function, highlighting the broader pharmacological potential of capsaicinoids [10,11].

Capsaicinoids have also been shown to exert systemic biological effects through mechanisms that do not depend on TRPV1. Experimental studies indicate that they possess anti-inflammatory properties by suppressing NF-κB signaling, downregulating the expression of pro-inflammatory cytokines, and inhibiting COX-2 gene expression. Their antioxidant effects arise not only from direct radical scavenging but also through the activation of natural defense pathways, such as the Nrf2-antioxidant response element signaling pathway. Additionally, capsaicinoids have been reported to induce apoptosis in cancer cells, inhibit angiogenesis, and modulate cell cycle progression in cultured cells, although these effects may depend on the dose and cellular context [12,13]. Other than capsaicinoids, peppers produce structurally related capsinoid compounds that are not pungent. Capsinoids such as capsiate, dihydrocapsiate, and nordihydrocapsiate differ from capsaicinoids by possessing an ester bond rather than an amide bond. Capsinoids were first defined from the non-pungent variety *C. annuum* CH-19 Sweet. Capsinoids are not pungent themselves, but they activate TRPV1 receptors in the gastrointestinal system and create identical thermogenic and metabolic effects to capsaicinoids without gastric or oral irritability. For these properties, capsinoid-based weight loss and metabolic health nutraceuticals have been suggested [14,15].

Pharmacokinetic studies prove capsinoids are hydrolyzed faster than capsaicinoids with less systemic bioavailability. Regardless of these findings, they can substantially enhance energy expenditure, improve lipid oxidation, and improve glucose metabolism in animal models and human trials. Capsinoids are tolerated by humans at dosing levels higher than capsaicin and thus are promising candidates for use in functional food enrichment and dietary supplementation.

Relative capsaicinoid and capsinoid concentrations vary across *Capsicum* species and varieties and are controlled by genetic, environmental, and agricultural factors. Breeding and biotechnology enabled scientists to develop bell peppers and pungent pepper varieties with defined pungency profiles and compositions of bioactives, offering potential to balance undesirable effects and health promotion [16,17]. Capsaicinoids and capsinoids are best defined as the most typical and highly researched bioactive compounds from Capsicum plants. Their capability for controlling pain perception, diet-induced heat or thermogenesis, metabolic regulation, inflammation, and carcinogenesis makes them central controllers of *Capsicum* species therapeutics. Future research will focus on enhancing availability, defining dose–response relationships, and converting benchwork into practical applications in nutritional and clinical practices [18,19].

3.2. Carotenoids

Carotenoids are a diverse family of lipophilic pigments that impart yellow, orange, and red hues to ripe

Capsicum fruits. These compounds are isoprenoids synthesized through the plastidial terpenoid pathway. In peppers, more than 30 carotenoids have been identified, and their composition and concentration can vary depending on the species, cultivar, fruit maturity, environmental conditions, and post-harvest handling. Among these, the most abundant and biologically significant carotenoids include capsanthin, capsorubin, β-carotene, zeaxanthin, and lutein [20].

3.2.1. Major Carotenoids in Capsicum

- **Capsanthin**: This carotenoid is the most common phenolic pigment present in *Capsicum annuum,* and it makes up to about 50 percent of the total carotenoid pool. It works as a very effective singletoxygen quencher/peroxyl-radical scavenger, and thus it offers potent antioxidant defense. Besides, modern studies have recordedanti-inflammatory effects of capsanthin and its influence on the homeostasis development of cells, which makes capsanthin a nutrient of special interest in creating functional foods and nutraceutical products [21].
- **Capsorubin**: Typically co-occurs with capsanthin, imparting deep red hues. It enhances antioxidant defense and has been associated with the modulation of inflammatory pathways. Additionally, capsorubin plays a role in protecting cellular structures from oxidative stress and may contribute to overall skin health and immune system support [22].
- **β-Carotene**: a proven provitamin A carotenoid, which is enzymatically-derived to retinol, the factor that is essential to normal vision, somatic development, and cell-mediated immunity [23].
- **Lutein and Zeaxanthin**: These xanthophylls are naturally present in the macular area of the human retina. They play a crucial role in protecting the eyes by counteracting phototoxicity caused by blue light exposure. Their antioxidant properties help reduce the risk of age-related macular degeneration (AMD), thereby promoting long-term eye health. Additionally, these compounds may enhance visual performance by improving contrast sensitivity and reducing glare effects. Regular intake through diet or supplements can support optimal retinal function and overall ocular wellness [24].
- **Violaxanthin and Antheraxanthin**: These pigments occur in immature green peppers and are intermediates in the carotenoid biosynthetic cascade, providing significant antioxidant activity. As the peppers mature, these compounds are further converted into other carotenoids such as capsanthin and capsorubin, which contribute to the vibrant red coloration of ripe peppers and enhance their nutritional profile [25].

3.2.2. Biological and Health Functions of *Capsicum* Carotenoids

Carotenoids derived from *Capsicum* species play diverse and important roles in human health. One of their primary functions is antioxidant defense. These compounds neutralize free radicals and reactive oxygen species, thereby protecting lipids, proteins, and DNA from oxidative damage. Owing to their lipophilic nature, carotenoids are readily incorporated into cell membranes, where they help stabilize membrane structure and prevent lipid peroxidation. Carotenoids are also strongly associated with eye health. Lutein and zeaxanthin accumulate in the macular region of the retina, where they act as optical filters by absorbing high-energy blue light and reducing photo-oxidative stress. Epidemiological studies consistently show that higher dietary intake of these carotenoids is associated with a reduced risk of age-related macular degeneration and cataract formation. In addition to their ocular benefits, carotenoids contribute to immune modulation. Compounds such as β-carotene and capsanthin enhance immune function by influencing cytokine production, supporting T-cell responses, and maintaining mucosal integrity [26–29]. These effects collectively strengthen host defense mechanisms. Carotenoids from *Capsicum* also exhibit anti-inflammatory properties. Capsanthin and capsorubin have been shown to downregulate nuclear factor kappa B (NF-κB) signaling and reduce the expression of pro-inflammatory mediators, suggesting protective roles in chronic inflammatory conditions. Furthermore, emerging evidence from animal and in vitro studies indicates that chili pepper carotenoids may positively influence metabolic health by improving lipid metabolism, reducing adipogenesis, and alleviating insulin resistance, although confirmation in large-scale human studies is still required [30–32].

3.2.3. Bioavailability and Stability

The bioavailability of carotenoids in peppers is affected by various factors:

- **Processing and food matrix**: Heat processing (e.g., cooking, roasting) enlarges the release of carotenoids from their cell walls and hence improves bioaccessibility.
- **Fat content**: Fat present in the diet has the maximum intestinal absorbability because carotenoids are absorbed during gastrointestinal tract passage through incorporation in micelles.
- **Isomerization**: The native trans-isomeric forms of carotenoids are prone to conversion to cis-forms during processing with an attendant impact on bioavailability and antioxidant capacity [33,34].

3.2.4. Applications and Future Prospects

Owing to their stability and intense pigmentation, *Capsicum* carotenoids find routine application as natural food colorants (e.g., paprika oleoresin) in the food industry. There has also been greater interest in their application in nutraceuticals and dietary supplements, especially for eye health and antioxidant applications. Recent advancements in encapsulation technologies and functional food preparations revolve around increasing carotenoid stability and delivery with ultimate bioactivity.

Briefly, chili pepper carotenoids—most notable among them capsanthin, capsorubin, β-carotene, lutein, and zeaxanthin—not only contribute to fruit coloration but also to a whole spectrum of health-promoting activities from antioxidant defense to eye and immunity protection. Clinical trials then follow to demonstrate their therapeutic potential and define the best levels of consumption for disease protection.

3.3. Vitamins and Minerals

In addition to their endowed phytochemical profile comprised of capsaicinoids, carotenoids, and phenolic compounds, *Capsicum* fruits are an excellent dietary source of essential minerals and vitamins. Apart from enhancing the nutrient profile of peppers, these micronutrients also increase their therapeutic potential, comprising prevention of oxidative stress, augmentation of immunity defense, and promotion of metabolic health [35].

3.3.1. Vitamins in *Capsicum*

Capsicum fruits are an excellent source of several essential vitamins that contribute to their nutritional and therapeutic value. Among these, vitamin C (ascorbic acid) is particularly abundant, with concentrations often exceeding those found in citrus fruits. Vitamin C functions as a potent water-soluble antioxidant, scavenging reactive oxygen species and regenerating oxidized vitamin E. It also plays a critical role in collagen synthesis, wound healing, and iron absorption. High dietary intake of vitamin C has been associated with enhanced immune function and reduced risk of cardiovascular disease and certain cancers. *Capsicum* species are also rich in provitamin A carotenoids, including β-carotene, capsanthin, and capsorubin. These compounds are metabolized into retinol (vitamin A), which is essential for vision, epithelial integrity, immune competence, and reproductive health. Given the global prevalence of vitamin A deficiency, peppers represent an important dietary source of this nutrient, particularly in populations with high chili consumption [36].

Vitamin E, present in *Capsicum* mainly as tocopherols, contributes to lipid-phase antioxidant protection by preventing oxidative damage to polyunsaturated fatty acids in cell membranes. This vitamin also supports immune regulation and cardiovascular health by inhibiting low-density lipoprotein oxidation. In addition, peppers contain several B-complex vitamins, including vitamin B6 (pyridoxine), folate, riboflavin, and niacin. These vitamins act as essential cofactors in amino acid metabolism, neurotransmitter synthesis, and cellular energy production, further enhancing the overall nutritional profile of *Capsicum* fruits [37–41].

3.3.2. Minerals in *Capsicum*

Capsicum, commonly known as bell peppers, is a rich source of several essential minerals that contribute to overall health. One of the most abundant minerals in fresh peppers is potassium, an important electrolyte that helps maintain fluid balance, regulate blood pressure, and support proper neuromuscular function.

Magnesium is another key mineral found in capsicum. It plays a vital role in enzyme activity, DNA structure, and muscle and nerve function. Adequate magnesium intake has been associated with a reduced risk of metabolic syndrome and type 2 diabetes, highlighting its importance for metabolic health.

Although present in smaller quantities, calcium in capsicum contributes to bone health, nerve signal transmission, and the proper functioning of blood vessels. Iron is also found in modest amounts, particularly in red peppers, and is essential for the formation of hemoglobin and efficient oxygen transport in the body. The high vitamin C content in capsicum enhances the absorption of non-heme iron, making it easier for the body to utilize this mineral.

Capsicum also contains trace elements such as zinc, copper, and manganese. These minerals serve as cofactors for antioxidant enzymes like superoxide dismutase, which help protect the body against oxidative stress, support immune defense, and regulate various metabolic processes [42].

3.3.3. Biological and Health Contributions

The synergistic action of vitamins and minerals in *Capsicum* enriches its nutrient and therapeutic capabilities. High vitamin C levels increase iron absorbability and immunity, while provitamin A carotenoids and vitamin E strengthen antioxidant protection and eye health. The synergistic antioxidant protection of vitamin C and vitamin E with carotenoids provides broad protection against oxidative stress–related illness such as cardiovascular disease, neurodegeneration, and cancer. Key minerals such as potassium and magnesium also contribute to cardiometabolic regulation, making chili peppers a functional food in cardiovascular medicine [43].

3.3.4. Impact of Ripening and Processing

Vitamin and mineral content of peppers is determined by fruit maturity, genotype, and processing treatments. Vitamin C and carotenoid levels, for example, generally increase with maturity, having their greatest contents in red mature fruit. Heat processing (drying, cooking) reduces vitamin C content due to heat sensitivity, but has the effect of increasing the bioaccessibility of carotenoids due to the breaking of plant cell walls during thermal processing. Mineral composition does not vary considerably with cooking, and peppers are therefore a stable food item across different culinary preparations [44,45].

3.4. Peptides and Other Compounds

Capsicum's bioactive peptides, volatile oils, and fatty acids fortify its antimicrobial and anti-obesity actions, adding strength to the biological effects of known Capsicum phytochemicals. These compounds achieve their combined effect synergistically to boost *Capsicum*'s therapeutic potential, and so it is a novel ingredient to incorporate in functional food products and nutraceutical mixes. Besides, its bioactive structures support enhanced metabolic efficiency, holding potential therapeutic avenues to managing lifetime diseases such as diabetes and heart complaints [46,47].

4. Therapeutic Properties

4.1. Antioxidant and Anti-inflammatory Effects

Peppers are rich in vitamin C, carotenoids, and phenolic compounds, all of which are extremely potent antioxidants. Vitamin C chelates reactive oxygen species (ROS) and assists in the regeneration of other antioxidants, such as vitamin E, and thus safeguards lipids, proteins, and DNA against oxidative damage. This is especially important since oxidative stress plays a part in the etiology of chronic diseases, including cardiovascular disease, neurodegeneration, and cancer. Carotenoids, including capsanthin, β-carotene, lutein, and zeaxanthin, also complement the antioxidant capacity of peppers. Lipid-soluble pigments guard against lipid peroxidation of cellular membranes and augment the body's endogenous antioxidant machinery, including superoxide dismutase (SOD) and glutathione peroxidase. Flavones like quercetin and luteolin also reduce the creation of free radicals and mitigate oxidative stress on a cellular basis. In everyday vegetables, red bell peppers stand out for having an extremely high vitamin C content, and hot peppers contribute capsaicinoids to propoundingly augment antioxidant defenses through mild cellular stress signaling. In addition to the antioxidant activities of peppers, they also have major anti-inflammatory activities. Chronic inflammation is a key causal element of various diseases, such as arthritis, metabolic syndrome, and cardiovascular diseases. Peppers' compounds, notably capsaicin (the pungent component of hot chili peppers), are able to modulate major inflammatory pathways. Capsaicin acts on the TRPV1 receptor of the sensory neurons to induce desensitization and low secretion of neuropeptides such as substance P, responsible for pain and inflammation. At the molecular function, capsaicin and other pepper polyphenols inhibit the expression of pro-inflammatory mediators, including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), cyclooxygenase-2 (COX-2), and the transcription factor NF-κB. This results in a measurable systemic inflammation marker reduction both experimentally and clinically. Additionally, the flavonoids and carotenoids of peppers are capable of regulating immune cell signaling to diminish oxidative stress-mediated inflammation and ensure a balanced immunity. Therapeutic topical preparations of capsaicin are also therapeutically utilized to prevent pain from osteoarthritis and neuropathic diseases, exemplifying the therutic anti-inflammatory applications of substances from peppers [48,49].

4.2. Cardiovascular Health

The consumption of peppers, particularly those rich in capsaicinoids such as capsaicin, has been increasingly associated with improved cardiovascular health. Capsaicin exerts multiple beneficial effects on the cardiovascular system through vasodilatory, anti-atherogenic, and lipid-modulating actions.

4.2.1. Vasodilation and Blood Pressure Regulation

Capsaicin activates the transient receptor potential vanilloid 1 (TRPV1) channels present on sensory neurons and vascular endothelial cells, leading to the release of vasodilatory mediators, notably nitric oxide (NO). This cascade results in relaxation of vascular smooth muscle and enhanced blood flow. Improved endothelial function and vasodilation contribute to lower blood pressure and reduced vascular resistance, thereby decreasing cardiac workload and overall circulatory stress.

4.2.2. Lipid Metabolism and Atherosclerosis Prevention

Dietary intake of capsaicin-rich foods has been shown to positively influence lipid metabolism. Capsaicin enhances adipose tissue lipolysis and increases energy expenditure, supporting a healthier lipid profile. Experimental evidence demonstrates that capsaicin lowers low-density lipoprotein cholesterol (LDL-C) and triglyceride levels while elevating high-density lipoprotein cholesterol (HDL-C). These changes help prevent atherosclerosis by reducing lipid deposition, plaque formation, and oxidative modification of LDL particles.

4.2.3. Improved Circulation and Heart Function

Through enhanced blood circulation and reduced vascular inflammation, capsaicin may provide protection against cardiovascular conditions such as coronary artery disease and hypertension. Regular consumption of capsaicin-containing foods has been associated with improved microvascular perfusion and cardiac output, thereby supporting optimal heart function and vascular health.

4.2.4. Long-Term Cardioprotective Effects

Epidemiological studies indicate that populations with higher consumption of spicy foods exhibit a lower incidence of cardiovascular mortality. Incorporating capsaicin-rich foods into the daily diet may help maintain favorable cholesterol levels, support vascular tone, and mitigate risk factors for cardiovascular disease, thereby promoting long-term heart health and circulatory system integrity [50].

4.3. Metabolic Health and Obesity

Activation of TRPV1 will increase energy expenditure and fat oxidation, burning calories via thermogenic increases in metabolic rate. Over the long-term, this large energy expenditure often results in decreased fat mass. Additionally, TRPV1 activation also modulates pathways involved in appetite regulation, resulting in lower appetite, ultimately leading to decreased daily caloric intake. Human clinical trials have shown that supplementation with either chili or capsaicin products can lead to body weight decreases or improvements in insulin sensitivity, giving substantial evidence for efficacy in treatment through capsaicin in obesity and metabolic syndrome. Intake of capsaicin (the predominant bioactive in chili peppers) has been associated with decreased visceral fat and altered metabolic risk factors. Decreased availability of visceral fat has been found to be especially favorable relative to Triglyceride, glucose, and lipid characteristics of metabolic risk factors. These successes for reduced metabolic risk (decreased triglyceride and improved glycemic responses) are important in categorical cardiometabolic risk [51].

4.4. Anticancer Properties

Capsaicin exhibits pro-apoptotic, anti-proliferative, and anti-angiogenic activity against varying lines of cancer cells. Capsaicin's bimodal effect (protective vs. pro-carcinogenic effect at high concentrations) has been controversial. There is evidence to support the fact that capsaicin triggers apoptosis through mitochondrial targeting and selective modulation of pivotal proteins such as caspases. Capsaicin's capacity to inhibit angiogenesis through suppression of VEGF signaling also holds potential in the inhibition of tumor growth. Capsaicin's effects are found to be dose-dependent, so study of the same is critical to prove safety and efficacy in clinical usage [52].

4.5. Neurological Benefits

Capsaicin possesses analgesic effects, traditionally found in topical creams to relieve neuropathy. Recent studies reveal potential neuroprotective actions against Alzheimer's and Parkinson's diseases. Capsaicin also possesses the ability to elevate cognition through the suppression of inflammation and oxidative stress in the brain. Capsaicin's potential to allow healthy neuronal communication and potentially slow neurodegeneration has scientific novelty [52].

4.6. Antimicrobial and Gastrointestinal Effects

Capsaicinoids inhibit the growth of pathogens such as *H. pylori*, and also have an effect on gut microbiota composition and gastrointestinal well-being. Capsaicinoids also have the capability to induce the growth of beneficial bacteria, which is an aid to keeping the microbiome in balance. Digestive enzyme activity encouraged by them adds to nutrient assimilation as well as gastrointestinal health. High intake, however, has the potential to induce irritation/discomfort in sensitive individuals, so a measure of moderation is necessary. The main bioactive compounds of bell pepper species and their therapeutic effects are presented in **Table 1**.

Table 1. Major Bioactive Compounds of *Capsicum* spp. and Their Therapeutic Effects.

Bioactive Compound	Examples	Biological/Therapeutic Effects	Main Mechanism/Pathway
Capsaicinoids	Capsaicin, Dihydrocapsaicin	Analgesic, anti-inflammatory, metabolic stimulation, weight reduction	TRPV1 receptor activation, NF-κB suppression, thermogenesis enhancement
Capsinoids (non-pungent)	Capsiate, Dihydrocapsiate	Similar effects to capsaicin without gastrointestinal irritation	TRPV1 activation in the gut, increased energy expenditure
Carotenoids	Capsanthin, Capsorubin, β-Carotene, Lutein, Zeaxanthin	Antioxidant, eye protection, immune modulation	ROS scavenging, membrane stabilization, blue-light absorption in the macula
Vitamins	C, A (from β-carotene), E, B6, Folate	Immune enhancement, collagen synthesis, cardiovascular protection	Water- and lipid-phase antioxidant activity, synergy with carotenoids
Minerals	Potassium, Magnesium, Iron, Zinc	Blood pressure regulation, metabolism, hemoglobin synthesis	Electrolyte balance and enzymatic cofactors
Peptides and Volatile Compounds	Bioactive peptides, essential oils	Antimicrobial, anti-obesity effects	Synergistic action with main phytochemicals, improved metabolism

4.7. Critical Comparison of Findings

Although numerous in vitro and animal studies consistently report strong antioxidant, anti-inflammatory, and metabolic regulatory effects of Capsicum bioactives, the translation of these benefits to human clinical outcomes remains inconsistent. For example, several cell and animal model studies demonstrate that capsaicin activates TRPV1, leading to increased thermogenesis and reduced adipogenesis; however, clinical trials show only modest and shortterm effects on body weight, often requiring doses that may not be well tolerated in regular diets. Similarly, carotenoids such as capsanthin and lutein exhibit potent antioxidant activity in controlled laboratory conditions, yet their bioavailability is highly influenced by food matrix, fat intake, and individual metabolic differences, which may explain inconsistent results in epidemiological studies. These discrepancies suggest that while mechanistic evidence is strong, dose standardization, formulation stability, and long-term clinical evaluations are needed before definitive therapeutic recommendations can be made.

5. Bioavailability and Safety Considerations

The bioavailability of Capsicum bioactive compounds varies considerably depending on molecular structure, food matrix, and individual metabolic factors. Capsaicinoids, including capsaicin and dihydrocapsaicin, exhibit low oral bioavailability, with human studies reporting systemic absorption ranging from 6–20 percent of the ingested dose due to rapid first-pass metabolism in the liver and intestinal mucosa. Peak plasma concentrations typically occur 1–3 h after ingestion, followed by rapid clearance.

In contrast, capsinoids, which are non-pungent analogues, show even lower systemic availability, with less than 5 percent absorption, but exert gastrointestinal TRPV1-mediated metabolic effects locally. These differences partly explain why capsinoids may require 2–4 times higher dosing than capsaicin to achieve similar thermogenic outcomes.

Carotenoids from *Capsicum* demonstrate fat-dependent absorption, with co-ingestion with dietary lipids increasing intestinal uptake 2–6 fold. Bioaccessibility studies indicate that 30–50 percent of capsanthin and β-carotene in peppers becomes available for absorption after typical cooking or homogenization processes, compared to less than 15 percent in raw peppers due to intact cell wall structures.

Regarding therapeutic dosing, clinical studies show that 2–10 mg/day of pure capsaicin or 135–250 mg/day of capsinoid extract can produce measurable metabolic and anti-inflammatory effects. However, doses above 8–10 mg/day of capsaicin often produce gastrointestinal discomfort, including burning sensation, reflux, and diarrhea in sensitive individuals.

Safety evaluations indicate that topical capsaicin (0.025–0.075 percent) is well tolerated for neuropathic pain, while oral intake above 30–40 mg/day may cause mucosal irritation. Although no conclusive evidence links dietary capsaicin to carcinogenicity in normal consumption ranges, very high chronic intake (>50 mg/day) has raised concerns in isolated epidemiological contexts, suggesting that dose and duration should be carefully regulated in supplementation.

To improve systemic availability and reduce irritant effects, recent research is investigating nanoencapsulation, liposomal carriers, protein-stabilized emulsions, and biopolymer nano-gels, which have been shown to increase bioavailability 3–10 fold in controlled laboratory models while reducing gastrointestinal irritation.

6. Conclusions

Despite extensive research on Capsicum bioactive compounds, several important questions remain regarding their therapeutic optimization, clinical applicability, and long-term safety. Future research should prioritize improving the bioavailability and stability of compounds such as capsaicinoids and carotenoids, which undergo rapid metabolism and degradation. Innovative delivery strategies, including nanoencapsulation, liposomal carriers, emulsified formulations, and polymer-based slow-release systems, may enhance systemic absorption and therapeutic efficacy. Another promising direction lies in metabolic engineering and precision plant breeding. Advances in genomics and gene editing (e.g., CRISPR-Cas9) could enable the development of pepper cultivars with tailored phytochemical profiles, such as high-capsinoid but low-pungency varieties, or enhanced carotenoid and phenolic content for specific nutritional or therapeutic purposes. These targeted crops have strong potential in the nutraceutical and functional food markets. Furthermore, while mechanistic evidence for anti-inflammatory, cardiometabolic, and neuroprotective actions is strong, there is a clear need for well-designed, long-term clinical trials that establish optimal dosing, safety thresholds, and efficacy in diverse populations. Human trials should also consider potential interactions with medications and metabolic variability among individuals.

Growing evidence suggests that Capsicum compounds may influence gut microbiota composition, which opens a novel avenue for treating metabolic and inflammatory diseases through microbiome-targeted nutrition. Integrating metabolomics and microbiome profiling may help clarify these interactions. Finally, regulatory and commercial frameworks must evolve alongside scientific discovery. Establishing standardized extract formulations, quality control benchmarks, and clinical usage guidelines will be essential for safely translating Capsicum-derived compounds into pharmaceuticals, functional foods, and personalized nutrition strategies.

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References

[1] Jaiswal, V., Gahlaut, V., Kumar, N., et al., 2021. Genetics, Genomics and Breeding of Chili Pepper Capsicum frutescens L. and Other Capsicum Species. In: Al-Khayri, J.M., Jain, S.M., Johnson, D.V. (Eds.). Advances in Plant Breeding Strategies: Vegetable Crops, Volume 9: Fruits and Young Shoots. Springer: Cham, Switzerland. pp. 59–86.

[2] Barboza, G.E., García, C.C., de Bem Bianchetti, L., et al., 2022. Monograph of Wild and Cultivated Chili Peppers (Capsicum L., Solanaceae). PhytoKeys. 200, 1.

[3] Oh, J., Ku, K.-H., Lee, S.-K., et al., 2025. Water and Oil Matrix Effect on the Perceived Spiciness in Chili Pepper Powder. Journal of Sensory Studies. 40(2), e70028.

[4] Variyar, P.S., Suprasanna, P., 2024. Peppers—An Overview on the Bioactives and Their Nutritional, Functional Properties and Post-Harvest Processing. In: Variyar, P.S., Singh, I.P., Adiani, V.A., et al. (Eds.). Peppers: Biological, Health, and Postharvest Perspectives. CRC Press: Boca Raton, FL, USA. pp. 1–15.

[5] Akhtar, A., Asghar, W., Khalid, N., 2021. Phytochemical Constituents and Biological Properties of Domesticated Capsicum Species: A Review. Bioactive Compounds in Health and Disease. 4(9), 201–225.

[6] del Rocio Moreno-Ramírez, Y., Hernández-Bautista, A., López, P.A., et al., 2019. Variability in the Phytochemical Contents and Free Radical-Scavenging Capacity of Capsicum annuum var. glabriusculum (Wild Piquin Chili). Chemistry & Biodiversity. 16(10), e1900381.

[7] Bonaccio, M., Di Castelnuovo, A., Costanzo, S., et al., 2019. Chili Pepper Consumption and Mortality in Italian Adults. Journal of the American College of Cardiology. 74(25), 3139–3149.

[8] Srinivasan, K., 2016. Biological Activities of Red Pepper (Capsicum annuum) and Its Pungent Principle Capsaicin: A Review. Critical Reviews in Food Science and Nutrition. 56(9), 1488–1500.

[9] Popelka, P., Jevinová, P., Šmejkal, K., et al., 2017. Determination of Capsaicin Content and Pungency Level of Different Fresh and Dried Chilli Peppers. Folia Veterinaria. 61(2), 11–16.

[10] Mumpuni, D.R., Putri, H.S., Airlangga, P.S., et al., 2024. Transient Receptor Potential Vanilloid 1 in Acute Pain: A Literature Review. Pharmacognosy Journal. 16(5).

[11] Gannon, N.P., Lambalot, E.L., Vaughan, R.A., 2016. The Effects of Capsaicin and Capsaicinoid Analogs on Metabolic Molecular Targets in Highly Energetic Tissues and Cell Types. BioFactors. 42(3), 229–246.

[12] Abdel-Salam, O.M., Mózsik, G., 2023. Capsaicin, the Vanilloid Receptor TRPV1 Agonist in Neuroprotection: Mechanisms Involved and Significance. Neurochemical Research. 48(11), 3296–3315.

[13] Wang, F., Xue, Y., Fu, L., et al., 2022. Extraction, Purification, Bioactivity and Pharmacological Effects of Capsaicin: A Review. Critical Reviews in Food Science and Nutrition. 62(19), 5322–5348.

[14] Lang, Y., Kisaka, H., Sugiyama, R., et al., 2009. Functional Loss of pAMT Results in Biosynthesis of Capsinoids, Capsaicinoid Analogs, in Capsicum annuum cv. CH-19 Sweet. The Plant Journal. 59(6), 953–961.

[15] Uarrota, V.G., Maraschin, M., de Bairros, A.d.F.M., et al., 2021. Factors Affecting the Capsaicinoid Profile of Hot Peppers and Biological Activity of Their Non-Pungent Analogs (Capsinoids) Present in Sweet Peppers. Critical Reviews in Food Science and Nutrition. 61(4), 649–665.

[16] Batiha, G.E.S., Alqahtani, A., Ojo, O.A., et al., 2020. Biological Properties, Bioactive Constituents, and Pharmacokinetics of Some Capsicum spp. and Capsaicinoids. International Journal of Molecular Sciences. 21(15), 5179.

[17] Lu, M., Ho, C.T., Huang, Q., 2017. Extraction, Bioavailability, and Bioefficacy of Capsaicinoids. Journal of Food and Drug Analysis. 25(1), 27–36.

[18] Whiting, S., Derbyshire, E., Tiwari, B.K., 2012. Capsaicinoids and Capsinoids: A Potential Role for Weight Management? A Systematic Review of the Evidence. Appetite. 59(2), 341–348.

[19] Irandoost, P., Lotfi Yagin, N., Namazi, N., et al., 2021. The Effect of Capsaicinoids or Capsinoids in Red Pepper on Thermogenesis in Healthy Adults: A Systematic Review and Meta-Analysis. Phytotherapy Research. 35(3), 1358–1377.

[20] Kolašinac, S.M., Dajić-Stevanović, Z., Kilibarda, S.N., et al., 2021. Carotenoids: New Applications of "Old" Pigments. Phyton. 90(4), 1041–1062.

[21] Mohd Hassan, N., Yusof, N.A., Yahaya, A.F., et al., 2019. Carotenoids of Capsicum Fruits: Pigment Profile and Health-Promoting Functional Attributes. Antioxidants. 8(10), 469.

[22] Arimboor, R., Natarajan, R.B., Menon, K.R., et al., 2015. Red Pepper (Capsicum annuum) Carotenoids as a Source of Natural Food Colors: Analysis and Stability—A Review. Journal of Food Science and Technology. 52(3), 1258–1271.

[23] Tomlekova, N., Spasova-Apostolova, V., Pantchev, I., et al., 2021. Mutation Associated with Orange Fruit Color Increases Concentrations of β-Carotene in a Sweet Pepper Variety (Capsicum annuum L.). Foods. 10(6), 1225.

[24] Xu, J., Lin, J., Peng, S., et al., 2023. Development of an HPLC-PDA Method for the Determination of Capsanthin, Zeaxanthin, Lutein, β-Cryptoxanthin and β-Carotene Simultaneously in Chili Peppers and Products. Molecules. 28(5), 2362.

[25] Bonaccorsi, I., Cacciola, F., Utczas, M., et al., 2016. Characterization of the Pigment Fraction in Sweet Bell Peppers (Capsicum annuum L.) Harvested at Green and Overripe Yellow and Red Stages by Offline Multidimensional Convergence Chromatography/Liquid Chromatography–Mass Spectrometry. Journal of Separation Science. 39(17), 3281–3291.

[26] Jomova, K., Valko, M., 2013. Health Protective Effects of Carotenoids and Their Interactions with Other Biological Antioxidants. European Journal of Medicinal Chemistry. 70, 102–110.

[27] De la Cruz-Ricardez, D., del Carmen Lagunes-Espinoza, L., Soto-Hernáandez, R.M., et al., 2024. Phytochemical Profile of Capsicum spp. Fruits Related to Ripeness Level, Shading and Harvest Season in the Southeast of Mexico. Chilean Journal of Agricultural Research. 84(2), 211–224.

[28] Agarwal, R., Hong, H.T., Hayward, A., et al., 2020. Carotenoid Profiling of Orange-Coloured Capsicums: In Search of High-Zeaxanthin Varieties for Eye Health. Proceedings of the 1st International Electronic Conference on Food Science and Functional Foods. 70(1), 84.

[29] Li, P., Zhang, X., Liu, Y., et al., 2022. Characterization of 75 Cultivars of Four Capsicum Species in Terms of Fruit Morphology, Capsaicinoids, Fatty Acids, and Pigments. Applied Sciences. 12(12), 6292.

[30] Villa-Rivera, M.G., Ochoa-Alejo, N., 2020. Chili Pepper Carotenoids: Nutraceutical Properties and Mechanisms of Action. Molecules. 25(23), 5573.

[31] Cho, S.Y., Kim, H.W., Lee, M.K., et al., 2020. Antioxidant and Anti-Inflammatory Activities in Relation to the Flavonoids Composition of Pepper (Capsicum annuum L.). Antioxidants. 9(10), 986.

[32] Dludla, P.V., Cirilli, I., Marcheggiani, F., et al., 2023. Bioactive Properties, Bioavailability Profiles, and Clinical Evidence of the Potential Benefits of Black Pepper (Piper nigrum) and Red Pepper (Capsicum annuum) against Diverse Metabolic Complications. Molecules. 28(18), 6569.

[33] Vulić, J., Šeregelj, V., Kalušević, A., et al., 2019. Bioavailability and Bioactivity of Encapsulated Phenolics and Carotenoids Isolated from Red Pepper Waste. Molecules. 24(15), 2837.

[34] Pugliese, A., Loizzo, M.R., Tundis, R., et al., 2013. The Effect of Domestic Processing on the Content and Bioaccessibility of Carotenoids from Chili Peppers (Capsicum Species). Food Chemistry. 141(3), 2606–2613.

[35] Olatunji, T.L., Afolayan, A.J., 2018. The Suitability of Chili Pepper (Capsicum annuum L.) for Alleviating Human Micronutrient Dietary Deficiencies: A Re-

view. Food Science & Nutrition. 6(8), 2239–2251.

[36] Kirana, R., Deswina, P., Dwiatmini, K., 2023. Mapping of Chili Varieties by Vitamin C Levels. In Proceedings of the Conference. IOP Conference Series: Earth and Environmental Science. 1287(1), 012009.

[37] Orobiyi, A., Ahissou, H., Gbaguidi, F., et al., 2015. Capsaicin and Ascorbic Acid Content in the High Yielding Chili Pepper (Capsicum annuum L.) Landraces of Northern Benin. International Journal of Current Microbiology and Applied Sciences. 4(9), 394–403.

[38] Perveen, S., Zafar, S., Iqbal, N., et al., 2021. Provitamin A Carotenoids. In: Zia-Ul-Haq, M., Dewanjee, S., Riaz, M. (Eds.). Carotenoids: Structure and Function in the Human Body. Springer International Publishing: Cham, Switzerland. pp. 775–797.

[39] Buarque, F.S., Soares, M.A., Ribeiro, B.D., et al., 2025. Development of Hydrophobic Eutectic Solvents Composed of Dl-Menthol and Fatty Acids/Alcohols: Application in the Extraction of Capsaicinoids and Carotenoids from Capsicum frutescens. Journal of Molecular Liquids. 417, 126591.

[40] Kim, T.J., Choi, J., Kim, K.W., et al., 2017. Metabolite Profiling of Peppers of Various Colors Reveals Relationships Between Tocopherol, Carotenoid, and Phytosterol Content. Journal of Food Science. 82(12), 2885–2893.

[41] Kantar, M.B., Anderson, J.E., Lucht, S.A., et al., 2016. Vitamin Variation in Capsicum spp. Provides Opportunities to Improve Nutritional Value of Human Diets. PLoS One. 11(8), e0161464.

[42] Zhou, C.X., Zhang, W., Yu, B.G., et al., 2024. Global Analysis of Spatio-Temporal Variation in Mineral Nutritional Quality of Pepper (Capsicum spp.) Fruit and Its Regulatory Variables: A Meta-Analysis. Food Research International. 193, 114855.

[43] Hernández-Pérez, T., Gómez-García, M.D.R., Valverde, M.E., et al., 2020. Capsicum annuum (Hot Pepper): An Ancient Latin-American Crop with Outstanding Bioactive Compounds and Nutraceutical Potential. Comprehensive Reviews in Food Science and Food Safety. 19(6), 2972–2993.

[44] Martínez, S., López, M., González-Raurich, M., et al., 2005. The Effects of Ripening Stage and Processing Systems on Vitamin C Content in Sweet Peppers (Capsicum annuum L.). International Journal of Food Sciences and Nutrition. 56(1), 45–51.

[45] Sanatombi, K., Rajkumari, S., 2020. Effect of Processing on Quality of Pepper: A Review. Food Reviews International. 36(6), 626–643.

[46] Ribeiro, S.F., Carvalho, A.O., Da Cunha, M., et al., 2007. Isolation and Characterization of Novel Peptides from Chilli Pepper Seeds: Antimicrobial Activities Against Pathogenic Yeasts. Toxicon. 50(5), 600–611.

[47] Oliveira, A.P.B.F., Resende, L.M., Rodrigues, R., et al., 2022. Antimicrobial Peptides of the Genus Capsicum: A Mini Review. Horticulture, Environment, and Biotechnology. 63(4), 453–466.

[48] Sanatombi, K., 2023. Antioxidant Potential and Factors Influencing the Content of Antioxidant Compounds of Pepper: A Review with Current Knowledge. Comprehensive Reviews in Food Science and Food Safety. 22(4), 3011–3052.

[49] Oboh, G., Rocha, J.B.T., 2007. Distribution and Antioxidant Activity of Polyphenols in Ripe and Unripe Tree Pepper (Capsicum pubescens). Journal of Food Biochemistry. 31(4), 456–473.

[50] Nandagopal, A., Nemala, A.R., 2024. Role of Capsaicin in Cardiovascular Diseases. In: Swamy, M.K.S., Kumar, A. (Eds.). Capsaicinoids: From Natural Sources to Biosynthesis and Their Clinical Applications. Springer Nature: Singapore. pp. 373–394.

[51] Ferreira, L.G.B., Faria, J.V., Dos Santos, J.P.S., et al., 2020. Capsaicin: TRPV1-Independent Mechanisms and Novel Therapeutic Possibilities. European Journal of Pharmacology. 887, 173356.

[52] Chamikara, M.D.M., Dissanayake, D.R.R.P., Ishan, M., et al., 2016. Dietary, Anticancer and Medicinal Properties of the Phytochemicals in Chili Pepper (Capsicum spp.). Ceylon Journal of Science. 45(3), 5–20.