

Capsicum spp.: A Comprehensive Review of Bioactive Compounds, Health Benefits, and Recent Advances in Emerging Applications

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ABSTRACT

Capsicum spp. (chilli peppers) are globally important horticultural crops recognised for their nutritional value, distinctive pungency, and diverse biological activities. Beyond their culinary applications, *Capsicum* fruits are rich sources of bioactive compounds, including capsaicinoids, carotenoids, flavonoids, phenolic compounds, vitamins, and other phytochemicals that contribute to their antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anti-obesity, cardioprotective, neuroprotective, and anticancer properties. These bioactive constituents exert their effects through the modulation of key molecular pathways involved in oxidative stress, inflammation, lipid metabolism, and glucose homeostasis, highlighting their potential in the prevention and management of chronic diseases. This review provides a comprehensive overview of *Capsicum* spp., covering its taxonomy, botanical characteristics, nutritional composition, major bioactive compounds, therapeutic and pharmacological properties, recommended dosage, safety, toxicity, and current applications in food, nutraceutical, and pharmaceutical industries. Recent advances in extraction technologies and novel delivery systems to improve the stability and bioavailability of capsaicinoids are also discussed. Furthermore, this review identifies current research gaps, including the need for standardised extraction methods, improved clinical validation, and enhanced bioavailability, while highlighting future research directions for the development of *Capsicum*-based functional foods and therapeutic products. Overall, *Capsicum* spp. with significant potential to support human health and the development of innovative value-added products.

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1. Introduction

The genus *Capsicum* currently comprises approximately 43 recognised species, of which five domesticated species—*Capsicum annuum*, *Capsicum baccatum*, *Capsicum chinense*, *Capsicum frutescens*, and *Capsicum pubescens*—are cultivated worldwide and constitute the primary sources of commercial chilli production. *C. annuum* is the most economically important and widely cultivated species because of its broad adaptability, extensive genetic diversity, and diverse applications in the fresh market, processed food industry, and pharmaceutical sectors (Barboza *et al.*, 2022; Carrizo García *et al.*, 2022). Chilli (*Capsicum annuum* L.) is one of the world's most valuable vegetable and spice crops, contributing substantially to global food security, agricultural income, and international trade. Major producing countries include China, India, Indonesia, Mexico, Turkey, and several Southeast Asian nations, where chilli cultivation supports both domestic consumption and export markets. In addition to its economic importance, chilli cultivation contributes significantly to rural livelihoods and the value-added food processing industry (FAOSTAT, 2024; Tripodi & Kumar, 2019). According to the latest FAOSTAT (2024) database, global chilli and pepper production has increased substantially over the past two decades owing to growing consumer demand, expansion of cultivation areas, and improvements in agricultural practices. Fresh chilli production now exceeds 36 million tonnes annually, highlighting its increasing economic importance and the need for sustainable disease management strategies to minimise production losses caused by fungal pathogens (FAOSTAT, 2024). Besides enhancing flavour, colour, and aroma, chilli fruits are excellent sources of bioactive compounds including capsaicinoids, carotenoids, flavonoids, phenolic acids, vitamins A, C and E, and essential minerals. These phytochemicals exhibit antioxidant, antimicrobial, anti-inflammatory, anticancer, anti-obesity, and cardioprotective activities, making chilli an important functional food ingredient with increasing applications in nutraceutical and pharmaceutical industries (Batiha *et al.*, 2020; Barboza *et al.*, 2022). Two chemical groups produced by chilli are capsaicinoids and carotenoids. The capsaicinoids are alkaloids that are responsible for the pungency of chilli pepper. A large number of carotenoids provide high nutritional value and the colour to chilli (Tripodi & Kumar, 2019).

The growing interest in plant-derived therapeutics and functional foods has increased the need for comprehensive evaluations of their efficacy, safety, and potential health applications. In line with the World Health Organization's emphasis on assessing the safety, efficacy, quality, accessibility, and rational use of herbal and traditional medicines, a critical appraisal of *Capsicum* spp. is warranted (Batiha *et al.*, 2020). Although chili pepper has long been recognised for its culinary importance and medicinal value, recent advances in phytochemistry, pharmacology, and nutritional science have generated substantial new evidence that has not been comprehensively synthesised. This narrative review synthesises relevant and recent literature on *Capsicum* spp., with emphasis on bioactive compounds, health-related properties, safety, extraction technologies, delivery systems, and food applications. Although previous reviews have comprehensively described the phytochemistry and biological activities of *Capsicum* spp., fewer reviews have integrated these aspects with recent developments in food processing, extraction technologies, bioaccessibility, delivery systems, safety, and emerging food and nutraceutical applications. Therefore, the present review aims to provide an integrated food-science perspective by connecting the composition and functionality of *Capsicum* bioactive compounds with processing, technological challenges, safety considerations, and strategies for improving their stability and bioavailability. Additionally, the review identifies existing research gaps and highlights future directions for the development of chilli pepper as a safe and effective functional food and therapeutic agent.

2. Taxonomy, Morphology and Nutritional Composition of *Capsicum* spp.

2.1 Taxonomy Classification and Morphological Characteristics

The genus *Capsicum* that belongs to the family Solanaceae have been domesticated for agricultural

production. Originating from Central and South America, *Capsicum* species are now cultivated worldwide and represent one of the most economically important vegetable and spice crops because of their nutritional, culinary, pharmaceutical, and industrial values (Tripodi & Kumar, 2019; Barboza *et al.*, 2022). Recent phylogenetic and genomic studies have considerably improved the understanding of evolutionary relationships among cultivated and wild *Capsicum* species, facilitating germplasm conservation and crop improvement programmes. *Capsicum* species exhibit substantial morphological diversity in plant architecture, leaf morphology, flower structure, fruit size, fruit colour, shape, pungency, and seed characteristics. These variations are primarily determined by genetic background but are also influenced by environmental

conditions, cultivation practices, and developmental stages. Fruit morphology is particularly important because it determines commercial quality, consumer preference, processing suitability, and capsaicinoid accumulation. During fruit maturation, chlorophyll degradation and carotenoid biosynthesis result in characteristic colour changes from green to yellow, orange, or red depending on genotype (Barboza *et al.*, 2022).

2.2 Nutritional Composition

The nutritional composition of chilli peppers varies considerably among cultivars, geographical origin, environmental conditions, cultivation practices, maturity stage, and postharvest processing methods. These factors significantly influence the accumulation of bioactive compounds and determine the overall nutritional and functional quality of chilli fruits. Recent metabolomic analyses have revealed substantial variation in phytochemical profiles among different *Capsicum* species, providing valuable information for breeding programmes aimed at improving nutritional quality and health-promoting properties (Tripodi & Kumar, 2019; Jang *et al.*, 2024). Furthermore, advances in food metabolomics have demonstrated that chilli peppers contain numerous minor phytochemicals, including alkaloids, saponins, terpenoids, and volatile aroma compounds that contribute not only to flavour development but also to antioxidant, antimicrobial, anti-inflammatory, and immunomodulatory activities. Consequently, *Capsicum* fruits are increasingly recognised as valuable functional food ingredients with potential applications in nutraceutical, pharmaceutical, and food industries (Batiha *et al.*, 2020; Mohammadi, 2025).

Chilli peppers are recognised as nutrient-dense vegetables that provide essential vitamins, minerals, dietary fibre, and numerous phytochemicals beneficial to human health. They are particularly rich in vitamin C, provitamin A carotenoids, vitamin E, potassium, magnesium, and folate while containing relatively low caloric content. In addition to essential nutrients, chilli fruits contain abundant phenolic compounds, flavonoids, carotenoids, and capsaicinoids, which collectively contribute to their antioxidant capacity and functional properties (Jang *et al.*, 2024; Maharjan *et al.*, 2024). According to recent FAOSTAT (2024) data, global production of fresh and dried chilli peppers continues to increase owing to expanding consumer demand for functional foods and natural health-promoting ingredients (FAOSTAT, 2024; Hernández-Pérez *et al.*, 2020). The remarkable health-promoting properties of chilli peppers are primarily attributed to their diverse phytochemical composition. Among these compounds, capsaicinoids are considered the principal bioactive metabolites responsible for pungency and many of the reported pharmacological effects (Jayan *et al.*, 2025; Batiha *et al.*, 2020). Other important constituents include carotenoids, flavonoids, phenolic acids, vitamins, tocopherols, phytosterols, and volatile compounds, all of which contribute synergistically to the biological activities of *Capsicum* spp. (Pap *et al.*, 2026).

However, comparisons among studies indicate that the nutritional and phytochemical profiles of *Capsicum* cannot be considered uniform, as reported values vary according to species, cultivar, fruit maturity, growing environment, geographical origin, and analytical methodology (Veiga *et al.*, 2019; Alonso-Villegas *et al.*, 2023). These differences should therefore be considered when comparing the nutritional quality and functional potential of different *Capsicum* materials (Jang *et al.*, 2024; Maharjan *et al.*, 2024). Recent metabolomic investigations further demonstrate that different *Capsicum* cultivars can be distinguished according to their metabolite profiles, supporting the use of metabolomic approaches to characterize chemical diversity beyond measurements of individual compounds (Ramírez-Meraz *et al.*, 2024). Thus, the nutritional value of *Capsicum* should be evaluated based on both major nutrients and the

diversity and relative abundance of its phytochemical constituents (Jang *et al.*, 2024). The nutritional quality and phytochemical composition of chilli peppers are also markedly influenced by postharvest handling and food processing techniques. Drying, roasting, fermentation, freeze-drying, and thermal processing may alter the stability and bioavailability of capsaicinoids, carotenoids, vitamin C, and phenolic compounds. While thermal treatments generally reduce heat-sensitive vitamins such as ascorbic acid, they may improve the extractability and bioaccessibility of carotenoids and certain phenolic compounds through disruption of plant cell structures. Therefore, optimisation of processing conditions is essential to preserve the nutritional value, bioactive stability, and functional integrity of *Capsicum*-derived products (Rezazadeh *et al.*, 2021).

From a food-science perspective, processing should therefore be evaluated not only in terms of compound retention but also in relation to bioaccessibility, food-matrix interactions, sensory properties, and the intended application of the final product (Shahidi & Pan, 2022). Processing conditions may produce different effects on individual compounds; therefore, a treatment that improves the extractability or bioaccessibility of one phytochemical may simultaneously reduce the stability of another (Sanatombi, 2020; Shahidi & Pan, 2022).

2.3 Bioactive Compounds of *Capsicum* spp.

Capsaicin and dihydrocapsaicin account for approximately 90% of the total capsaicinoid content in chilli peppers and are synthesised predominantly in the placental tissues of the fruit. These alkaloids activate transient receptor potential vanilloid 1 (TRPV1), initiating signalling pathways involved in pain perception, thermogenesis, inflammation, glucose metabolism, and lipid homeostasis (Petran *et al.*, 2024). Their concentration varies considerably depending on species, cultivar, fruit maturity, environmental conditions, and cultivation practices (Jayan *et al.*, 2025). Recent transcriptomic and metabolomic studies have demonstrated that capsaicinoid biosynthesis is regulated by a complex network of structural genes and transcription factors, including *Pun1*, *pAMT*, *Kas*, *BCAT*, and *MYB31*, which collectively influence pungency intensity and capsaicinoid accumulation in different *Capsicum* cultivars (Arce-Rodríguez & Ochoa-Alejo, 2017; Tripodi & Kumar, 2019). Phenolic acids and flavonoids are important secondary metabolites that contribute significantly to the antioxidant capacity of chilli peppers. These compounds effectively scavenge reactive oxygen species, inhibit lipid peroxidation, regulate inflammatory mediators, and protect cellular components from oxidative damage. Recent studies have also suggested synergistic interactions between flavonoids and capsaicinoids in enhancing antioxidant and anti-inflammatory activities (Hernández-Pérez *et al.*, 2020; Pap *et al.*, 2026).

The major compounds identified in *Capsicum* include capsaicin and dihydrocapsaicin among the capsaicinoids; quercetin, luteolin, apigenin, and catechin among the flavonoids; and capsanthin, capsorubin, β -carotene, lutein, and zeaxanthin among the carotenoids (Alonso-Villegas *et al.*, 2023). Among these constituents, capsaicin and dihydrocapsaicin together generally account for approximately 80–90% of total capsaicinoids, although their abundance can vary substantially among species, cultivars, maturity stages, and growing conditions (Zhu *et al.*, 2025). The concentrations of nutrients and bioactive compounds vary considerably among *Capsicum* species and cultivars because of differences in genotype, maturity stage, growing conditions, geographical origin, processing, and analytical methodology (Veiga *et al.*, 2019; Alonso-Villegas *et al.*, 2023). Consequently, direct comparison of reported concentrations should be made cautiously unless these experimental factors are comparable. Overall, the available evidence indicates that the functional potential of *Capsicum* is determined by a complex phytochemical profile rather than by capsaicin alone. This compositional diversity provides opportunities for developing *Capsicum*-based functional foods and value-added products, while also presenting challenges for standardisation, stability, bioaccessibility, and reproducibility of bioactive-compound content (Sanatombi, 2023; Altemimi *et al.*, 2021).

In addition to antioxidant activity, flavonoids such as quercetin, luteolin, apigenin, and catechin have demonstrated antimicrobial, anticancer, cardioprotective, and neuroprotective effects, thereby enhancing the therapeutic potential of chilli-derived phytochemicals (Pap *et al.*, 2026). Carotenoids, including capsanthin, capsorubin, β -carotene, lutein, and zeaxanthin, are responsible for the attractive red and orange pigmentation of mature chilli fruits. Besides their colouring properties, these pigments exhibit

potent antioxidant activities and have been associated with reduced risks of cardiovascular diseases, age-related macular degeneration, and several chronic inflammatory disorders. Consequently, carotenoids from chilli peppers are increasingly utilised as natural food colourants and nutraceutical ingredients (Mohammadi, 2025). Recent investigations have also reported that carotenoid biosynthesis is closely associated with fruit ripening and environmental adaptation, making these pigments valuable biomarkers for fruit quality evaluation and genetic improvement programmes (Barboza *et al.*, 2022). In addition to capsaicinoids, phenolic compounds, and carotenoids, *Capsicum* fruits contain several other biologically active constituents, including tocopherols, phytosterols, alkaloids, terpenoids, volatile compounds, and polysaccharides. Although present in lower concentrations, these metabolites contribute synergistically to the antioxidant, antimicrobial, anti-inflammatory, and immunomodulatory activities of chilli peppers. Recent metabolomic studies suggest that the health benefits of *Capsicum* result from the combined action of multiple phytochemicals rather than a single bioactive compound, emphasizing the importance of investigating their synergistic interactions (Salehi *et al.*, 2021; Mohammadi, 2025).

3. Therapeutic and Pharmacological Properties

Increasing evidence demonstrates that *Capsicum*-derived bioactive compounds exert multiple biological activities through the regulation of oxidative stress, inflammatory signalling pathways, cellular metabolism, and immune responses. Consequently, chilli peppers have attracted considerable attention as functional foods with potential applications in the prevention and management of chronic diseases (Ferdowsi *et al.*, 2023). Emerging evidence from experimental, clinical, and epidemiological studies suggests that regular dietary consumption of chilli peppers is associated with reduced risks of metabolic syndrome, obesity, cardiovascular disease, and certain cancers, although further well-designed human intervention studies are required to establish optimal dosage and long-term safety (Pap *et al.*, 2026). Importantly, the strength of evidence differs among these health outcomes: mechanistic and animal studies provide predominantly preclinical evidence, whereas epidemiological studies demonstrate associations rather than causality, and human intervention studies remain comparatively limited (Chopan & Littenberg, 2021; Zhang *et al.*, 2023). Capsaicinoids, phenolic compounds, flavonoids, and carotenoids collectively contribute to the antioxidant capacity of chilli peppers by scavenging reactive oxygen species, enhancing endogenous antioxidant enzyme activities, and reducing lipid peroxidation. These mechanisms protect cellular macromolecules from oxidative damage and may decrease the risk of chronic diseases associated with oxidative stress (Hernández-Pérez *et al.*, 2020; Mohammadi, 2025). Moreover, these antioxidant mechanisms also contribute to mitochondrial protection, maintenance of cellular redox homeostasis, and regulation of oxidative stress-responsive genes, thereby supporting healthy ageing and reducing chronic inflammatory conditions (Pap *et al.*, 2026).

Capsaicin exerts potent anti-inflammatory effects through modulation of NF- κ B, MAPK, COX-2, TNF- α , IL-1 β , and IL-6 signalling pathways. By suppressing the production of pro-inflammatory cytokines and inflammatory mediators, capsaicin may alleviate chronic inflammatory disorders and improve immune regulation (Basith *et al.*, 2016; Mohammadi, 2025). Recent molecular studies further indicate that capsaicin regulates Nrf2 signalling and inhibits activation of the NLRP3 inflammasome, thereby providing additional protection against chronic inflammatory and autoimmune diseases (Varshney *et al.*, 2024). However, these mechanistic findings are primarily derived from cellular and animal models and should not be interpreted as evidence of established clinical efficacy in humans. Experimental and clinical studies indicate that capsaicin improves insulin sensitivity, stimulates glucose uptake, activates AMP-activated protein kinase (AMPK), and regulates glucose homeostasis. These mechanisms suggest that regular dietary intake of chilli peppers may contribute to improved glycaemic control and reduced risk of type 2 diabetes mellitus (Ferdowsi *et al.*, 2023). Human evidence for metabolic effects remains heterogeneous, and reported benefits should therefore be regarded as potential rather than established therapeutic effects. Capsaicinoids improve endothelial function, reduce oxidative stress, regulate lipid metabolism, and improve vascular homeostasis. Collectively, these physiological actions are associated with hypertension, dyslipidaemia, atherosclerosis, and cardiovascular disease (Mohammadi, 2025). Observational studies have reported

associations between chilli consumption and lower cardiovascular or all-cause mortality; however, such findings cannot establish that chilli consumption itself causes the observed reduction in risk (Chopan & Littenberg, 2021).

Moreover, capsaicin exhibits broad-spectrum antimicrobial activity against numerous Gram-positive and Gram-negative bacteria as well as pathogenic fungi. Proposed mechanisms include disruption of microbial membranes, inhibition of biofilm formation, interference with cellular metabolism, and suppression of microbial virulence factors. These findings support the application of chilli-derived compounds as natural antimicrobial agents in food preservation and pharmaceutical formulations (Hernández-Pérez *et al.*, 2020). For food applications, antimicrobial activity should be evaluated according to the target microorganism, compound concentration, food matrix, processing conditions, and sensory acceptability rather than extrapolated directly from in vitro assays to commercial products (Rezazadeh *et al.*, 2021). Recent investigations have demonstrated that capsaicin suppresses tumour progression by inducing apoptosis, promoting cell-cycle arrest, inhibiting angiogenesis, reducing metastatic potential, and modulating oxidative stress and TRPV1-mediated signalling pathways. Although encouraging results have been obtained in experimental models, further clinical investigations are necessary to establish its therapeutic efficacy and safety in cancer patients (Ferdowsi *et al.*, 2023). In addition, preclinical studies have further reported that capsaicin modulates PI3K/Akt/mTOR, STAT3, and Wnt/ β -catenin signalling pathways, thereby suppressing tumour proliferation, invasion, metastasis, and chemoresistance. Nevertheless, additional randomized clinical trials remain necessary before capsaicin-based therapeutics can be translated into routine clinical practice (Wu *et al.*, 2020). Overall, the current evidence supports biological activity of *Capsicum* constituents, but the extent to which these findings translate into clinically meaningful benefits remains dependent on the form of exposure, dose, bioavailability, population, and study design. Figure 1 shows overview the nutritional composition, bioactive compounds, therapeutic mechanisms, industrial applications, safety considerations, and future research directions of *Capsicum* spp.

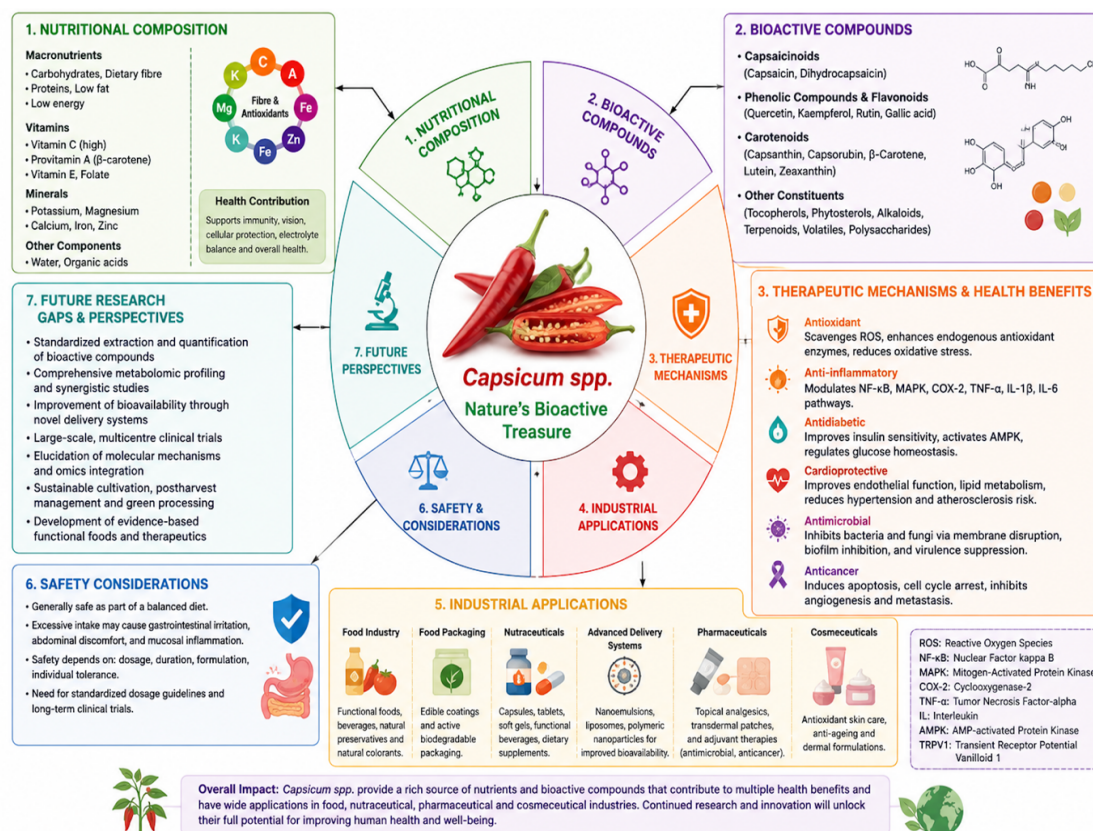


Figure 1. Overview of the nutritional composition, bioactive compounds, therapeutic mechanisms, industrial applications, safety considerations, and future research directions of *Capsicum* spp.

4. Safety, Exposure, Toxicity and Dosage Considerations

Because no universal daily dosage has been established for *Capsicum* spp., this section considers safety according to the form, concentration, route, duration, and intended use of exposure rather than proposing a single recommended dose. The acceptable intake of capsaicin varies depending on the intended application, route of administration, and individual physiological conditions. For dietary consumption, capsaicin is generally considered safe when consumed as part of a normal diet; however, high-dose supplementation or concentrated capsaicin extracts may increase the risk of gastrointestinal irritation, nausea, vomiting, diarrhoea, abdominal pain, and gastric mucosal injury, particularly in individuals with pre-existing gastrointestinal disorders (Salehi *et al.*, 2021; Maharjan *et al.*, 2024). Accordingly, the exposure associated with ordinary culinary consumption should not be directly compared with concentrated extracts or purified capsaicin preparations, because their doses and pharmacokinetic profiles can differ substantially (Maharjan *et al.*, 2024; Jayan *et al.*, 2025). Topical capsaicin formulations, including creams, gels, and transdermal patches containing low (0.025–0.1%) or high (8%) concentrations of capsaicin, have been approved for the management of neuropathic pain and musculoskeletal disorders. While these formulations are generally well tolerated, transient burning sensations, erythema, pruritus, and localized pain are among the most frequently reported adverse effects, which usually diminish following repeated application (Basith *et al.*, 2016). Topical preparations should therefore be considered separately from oral dietary exposure because their route of administration, local tissue concentration, and therapeutic objectives are different. Evidence from clinical studies supports the use of an 8% capsaicin patch for selected neuropathic pain conditions, but this evidence cannot be extrapolated to establish an oral daily intake for *Capsicum* consumption (Mou *et al.*, 2016).

Several experimental studies have demonstrated that excessive or prolonged exposure to high concentrations of capsaicin may induce oxidative stress, epithelial damage, neurotoxicity, and cytotoxic effects under specific experimental conditions. Nevertheless, these adverse outcomes are highly dependent on dose, exposure duration, and experimental model, and are generally not observed at levels achieved through normal dietary consumption (Pap *et al.*, 2026). Experimental toxicity findings should therefore be interpreted in relation to the administered concentration, exposure route, exposure duration, and experimental model, rather than being directly extrapolated to normal food consumption. The bioavailability of capsaicin following oral administration remains relatively low because of its poor aqueous solubility, rapid metabolism, and extensive first-pass hepatic metabolism. Consequently, recent pharmaceutical research has focused on the development of advanced delivery systems, including nanoemulsions, liposomes, polymeric nanoparticles, solid lipid nanoparticles, and microencapsulation technologies, to improve capsaicin stability, controlled release, bioavailability, and therapeutic efficacy while reducing gastrointestinal irritation and systemic toxicity (Mohammadi, 2025). The effectiveness of these delivery systems should nevertheless be evaluated using appropriate food or pharmaceutical matrices because improved chemical stability or apparent bioaccessibility does not necessarily demonstrate improved clinical efficacy (Shahidi & Pan, 2022). Despite promising findings from preclinical and clinical investigations, there is currently no universally accepted recommended daily intake or therapeutic dosage of capsaicin for disease prevention or treatment. Future multicentre randomized controlled trials are required to establish evidence-based dosage guidelines, evaluate long-term safety, investigate potential interactions with pharmaceuticals, and determine safe therapeutic windows for different populations, including children, older adults, pregnant women, and patients with chronic diseases (Maharjan *et al.*, 2024; Jayan *et al.*, 2025). Therefore, claims concerning dosage or therapeutic efficacy should distinguish between whole-food consumption, standardized extracts, purified capsaicin supplements, topical formulations, and experimental preparations. Furthermore, standardisation of chilli-derived extracts with respect to capsaicinoid composition, purity, and manufacturing quality is essential to ensure product consistency, efficacy, and consumer safety. Harmonized regulatory guidelines for nutraceutical and pharmaceutical products containing capsaicin will facilitate their wider clinical application while minimizing safety concerns associated with variable formulations and dosing practices (Basith *et al.*, 2016).

5. Current and Emerging Applications

The multifunctional properties of *Capsicum* spp. have expanded their applications beyond traditional culinary uses. Chilli-derived bioactive compounds are increasingly incorporated into functional foods, nutraceuticals, dietary supplements, pharmaceutical formulations, natural food preservatives, biodegradable active packaging materials, and nanotechnology-based delivery systems designed to improve capsaicin stability and bioavailability. By bridging the gap between agricultural byproduct valorization and high-value compound extraction, these developments significantly advance green chemical processing and economic sustainability (Baiano, 2014; Chemat *et al.*, 2017). These innovations highlight the considerable commercial potential of *Capsicum* as a sustainable source of natural bioactive ingredients for the food, pharmaceutical, and healthcare industries (Jayan *et al.*, 2025). Recent research increasingly emphasises the integration of extraction, stabilization, formulation, and delivery technologies to overcome the low water solubility, pungency, instability, and limited bioavailability of capsaicin, thereby improving its suitability for food and nutraceutical applications (Maharjan *et al.*, 2024; Wang *et al.*, 2025). A comprehensive matrix of these cross-industry implementations is systematically consolidated in Table 1, which outlines the current applications of *Capsicum*-derived bioactive compounds in food, nutraceutical, and pharmaceutical industries.

In the food industry, capsaicinoids and carotenoids are increasingly incorporated into functional foods and beverages owing to their natural antioxidant properties, ability to enhance product shelf life, and potential to replace synthetic preservatives and colourants. Furthermore, these matrix-embedded components effectively mitigate lipid oxidation, thereby preserving the native flavor and sensory profiles of processed food matrices (Shahidi & Ambigaipalan, 2015). However, the technological performance of these compounds depends strongly on the composition and structure of the food matrix, processing conditions, storage environment, and sensory tolerance to pungency (Rezazadeh *et al.*, 2021; Shahidi & Pan, 2022). In addition, chilli extracts have been investigated as natural antimicrobial agents in edible coatings, biodegradable food packaging, and active packaging systems to inhibit foodborne pathogens and delay microbial spoilage, thereby improving food quality and safety (Hernández-Pérez *et al.*, 2020; Silva *et al.*, 2023). This bio-based preservation paradigm directly caters to the growing consumer demand for clean-label products devoid of synthetic chemical additives (Carocho *et al.*, 2014). Nevertheless, further studies are required to optimize the concentration of chilli-derived extracts to achieve antimicrobial efficacy without adversely affecting colour, aroma, taste, and overall consumer acceptability. The nutraceutical industry has extensively explored chilli-derived phytochemicals for the development of capsules, tablets, soft gels, functional beverages, and dietary supplements targeting weight management, metabolic syndrome, cardiovascular health, and immune support. These modern formulations frequently capitalize on the natural synergistic interactions between co-existing capsaicinoids and flavonoids to elicit a more profound metabolic response (Jayan *et al.*, 2025; Yang *et al.*, 2025). Human evidence suggests that capsaicin supplementation may produce modest effects on body weight, body mass index, and waist circumference, but these findings do not establish capsaicin as a stand-alone treatment for obesity (Zhang *et al.*, 2023). Advances in encapsulation technologies, including nanoemulsions, liposomes, and polymeric nanoparticles, have significantly improved the bioavailability, stability, and controlled release of capsaicin, thereby overcoming its limitations associated with poor aqueous solubility and gastrointestinal irritation (Salehi *et al.*, 2021; Mohammadi, 2025). These protective nanostructures insulate the sensitive cargo from early enzymatic degradation in the upper digestive tract, ensuring localized and efficient intestinal uptake (McClements, 2015). Recent delivery-system research further indicates that lipid-, protein-, and polysaccharide-based carriers can improve capsaicin dispersibility, stability, and bioavailability, although their performance remains dependent on carrier composition and formulation conditions (Jayan *et al.*, 2025).

In pharmaceutical applications, capsaicin has been successfully formulated into topical creams, gels, patches, and transdermal delivery systems for the management of neuropathic pain, osteoarthritis, diabetic neuropathy, and post-herpetic neuralgia. Mechanistically, these localized applications achieve therapeutic efficacy by selectively binding to transient receptor potential vanilloid 1 (TRPV1) receptors, desensitizing nociceptive nerve fibers to provide sustained pain relief (Caterina *et al.*, 1997; Anand & Bley, 2011). Recent

pharmaceutical research has further demonstrated the potential of capsaicin as an adjuvant therapeutic agent in antimicrobial and anticancer treatments through its ability to modulate oxidative stress, apoptosis, angiogenesis, and immune signalling pathways. These findings highlight the growing importance of chilli-derived bioactive compounds as promising candidates for precision medicine and natural product-based drug development (Basith *et al.*, 2016; Maharjan *et al.*, 2024; Mohammadi, 2025). However, most anticancer and several other pharmacological applications remain at the preclinical stage and require rigorous clinical validation before therapeutic claims can be established.

Despite these promising applications, several challenges remain, including variability in phytochemical composition among cultivars, low oral bioavailability of capsaicinoids, pungency-related adverse effects, and the lack of standardized extraction and formulation protocols. Moreover, scaling these innovations to an industrial volume remains challenging due to the high energy costs and operational constraints frequently tied to non-thermal, green extraction technologies (Sicaire *et al.*, 2019). In addition, the selection of an extraction technology should consider not only extraction yield but also solvent safety, energy consumption, selectivity, scalability, residual solvent levels, stability of the recovered compounds, and suitability for the intended food or pharmaceutical application (Cardoso *et al.*, 2024; Yang *et al.*, 2025; Zhu *et al.*, 2025). Future research should therefore focus on sustainable extraction technologies, advanced delivery systems, and large-scale clinical trials to fully exploit the industrial and therapeutic potential of *Capsicum*-derived bioactive compounds (Maharjan *et al.*, 2024).

5.1 Bioactive Compound Extraction Technologies

To unlock the industrial and therapeutic potential of *Capsicum*-derived bioactive compounds, efficient and sustainable isolation methods are paramount. Traditional extraction techniques, such as Soxhlet extraction and maceration, heavily rely on petroleum-derived organic solvents like hexane, chloroform, and acetone, which pose substantial environmental risks, safety hazards, and toxicity concerns for food-grade products. Consequently, modern extraction paradigms have shifted toward environmentally benign, intensified green technologies aimed at achieving accelerated mass transfer, reducing processing steps, and lowering energy consumption (Soquetta *et al.*, 2018). Among these green approaches, Ultrasound-Assisted Extraction (UAE) and Microwave-Assisted Extraction (MAE) have emerged as powerful tools for isolating capsaicinoids, capsinoids, and other sensitive antioxidants (Vázquez-Espinosa *et al.*, 2019). These techniques utilise acoustic cavitation or microwave irradiation to rupture plant cell walls, facilitating swift solvent penetration and minimizing the degradation of thermolabile compounds. Furthermore, modern variants have effectively utilised edible vegetable oils (such as soybean oil) as green, non-toxic, and non-volatile co-solvents coupled with UAE to seamlessly yield pre-fortified food-grade systems (Cardoso *et al.*, 2024). To further maximize yield from resilient agricultural byproducts, Enzyme-Assisted Extraction (EAE) using cellulases has been successfully implemented to break down structurally rigid seed cell walls, recovering valuable capsaicinoids and phenolics with high anti-inflammatory and antioxidant activities using pure water as a solvent (Cortes-Ferre *et al.*, 2022).

Supercritical fluid extraction utilising carbon dioxide SFE-CO₂ represents another hallmark advancement in green recovery, providing an inert, highly tunable solvent condition that completely circumvents toxic organic residues. The operational efficiency of SFE-CO₂ is markedly enhanced when coupled with ultrasonic fields; the application of ultrasonic waves induces high-frequency micro-disturbances within the vegetable matrix to dramatically increase mass transfer coefficients without causing structural cracking on the cell wall surfaces (Santos *et al.*, 2015). For target compound purification, crude SFE-CO₂ extracts have been successfully integrated with downstream high-speed countercurrent chromatography (HSCCC) systems to isolate highly pure crystalline capsaicin and dihydrocapsaicin at industrial scales (Yan *et al.*, 2017). Simultaneously, the deployment of Natural Deep Eutectic Solvents (NADES) has emerged as a frontline paradigm for customizing highly selective, biodegradable extraction media. When applied to the pungent placenta tissues of *Capsicum* spp., choline chloride–citric acid systems establish rich intermolecular hydrogen-bonding networks with target capsaicinoids, facilitating superior homogeneous dispersion, enhanced antioxidant capacities, and strong antibacterial activity against pathogens like *Escherichia coli* and *Staphylococcus aureus* (Yang *et al.*, 2025). To overcome physical mass

transfer resistance inside resilient tissues, sophisticated cocktail enzyme-assisted natural deep eutectic solvent (CE-NADES) pre-treatments have been engineered. These systems synergise biological cell-wall depolymerization with low-temperature eutectic dissolution to lower overall matrix decomposition thresholds and dramatically elevate the industrial extractable yield of capsaicin (Zhu *et al.*, 2025). From a comparative perspective, no single extraction technology can be considered universally optimal because extraction performance depends on the target compound, plant tissue, solvent system, temperature, extraction time, and intended end use. Therefore, technological selection should balance recovery efficiency with solvent safety, energy requirements, extract quality, reproducibility, and scalability (Chemat *et al.*, 2017; Cardoso *et al.*, 2024).

Table 1. Current Applications of *Capsicum*-Derived Bioactive Compounds in Food, Nutraceutical and Pharmaceutical Industries.

Industry	Specific Applications	Bioactive Compounds	Key Benefits and Mechanisms	References
Food Industry	Functional foods, functional beverages, natural preservatives, and natural food colourants	Capsaicinoids, carotenoids, phenolic compounds	Provide natural antioxidant activity, enhance nutritional value, extend shelf life, reduce lipid oxidation, and replace synthetic preservatives and colourants.	Hernández-Pérez <i>et al.</i> (2020); Silva <i>et al.</i> (2023); Jayan <i>et al.</i> (2025)
Food Packaging	Edible coatings, biodegradable films, and active food packaging	Chilli extracts, capsaicin, phenolic compounds	Exhibit antimicrobial and antioxidant activities, inhibit foodborne pathogens, delay microbial spoilage, and improve food safety and storage stability.	Hernández-Pérez <i>et al.</i> (2020); Silva <i>et al.</i> (2023)
Nutraceutical Industry	Dietary supplements, capsules, tablets, soft gels, powders, and functional beverages	Capsaicinoids, carotenoids, flavonoids, phenolic compounds	Support weight management, metabolic health, cardiovascular function, immune modulation, antioxidant defence, and anti-inflammatory activity.	Salehi <i>et al.</i> (2021); Mohammadi (2025); Jayan <i>et al.</i> (2025)
Advanced Nutraceutical Delivery Systems	Nanoencapsulation, microencapsulation, nanoemulsions, liposomes, polymeric nanoparticles, and solid lipid nanoparticles	Capsaicin-loaded nanocarriers	Improve aqueous solubility, enhance bioavailability and stability, enable controlled release, increase therapeutic efficacy, and	Salehi <i>et al.</i> (2021); Mohammadi (2025); Jayan <i>et al.</i> (2025)

			reduce gastrointestinal irritation.	
Pharmaceutical Industry (Pain Management)	Topical creams, gels, transdermal patches, ointments, and controlled-release formulations	Capsaicin	Clinically used for the management of neuropathic pain, osteoarthritis, diabetic neuropathy, post-herpetic neuralgia, and musculoskeletal disorders through TRPV1 receptor activation and nociceptor desensitization.	Basith <i>et al.</i> (2016); Maharjan <i>et al.</i> (2024); Mohammadi (2025)
Pharmaceutical Industry (Advanced Therapeutics)	Adjunctive therapy, targeted drug delivery, precision medicine, and natural therapeutic formulations	Capsaicin, dihydrocapsaicin, flavonoids, carotenoids	Exert antimicrobial, anti-inflammatory, antioxidant, cardioprotective, antidiabetic, and anticancer effects by regulating oxidative stress, apoptosis, angiogenesis, inflammatory signalling pathways (NF- κ B, MAPK), and TRPV1-mediated cellular responses.	Basith <i>et al.</i> (2016); Maharjan <i>et al.</i> (2024); Mohammadi (2025)
Cosmeceutical Industry	Anti-ageing creams, antioxidant skin-care products, topical formulations, and cosmetic ingredients	Capsaicin, carotenoids, phenolic compounds	Improve skin microcirculation, provide antioxidant protection, reduce oxidative stress, stimulate collagen synthesis, and contribute to skin rejuvenation and anti-ageing effects.	Salehi <i>et al.</i> (2021); Mohammadi (2025)
Biomedical and Healthcare Applications	Drug delivery systems, wound healing materials, tissue engineering, antimicrobial biomaterials, and medical devices	Capsaicin-based biomaterials, nanoformulations	Enhance wound healing, suppress microbial infections, reduce inflammation, improve targeted drug delivery, and support regenerative	Maharjan <i>et al.</i> (2024); Mohammadi (2025); Jayan <i>et al.</i> (2025)

6. Research Gaps and Future Perspectives

One of the major challenges in *Capsicum* research is the substantial variability in phytochemical composition among species, cultivars, geographical regions, cultivation practices, environmental conditions, fruit maturity, and postharvest processing. This variability complicates the standardisation of bioactive compounds and often results in inconsistent biological activities reported across different studies. Therefore, harmonised cultivation practices, standardised extraction procedures, and validated analytical methods are essential to ensure reproducibility and facilitate comparisons among research findings (Tripodi & Kumar, 2019; Hernández-Pérez *et al.*, 2020; Jang *et al.*, 2024). Future studies should report sufficient information on cultivar identity, maturity stage, growing conditions, sample preparation, extraction procedure, analytical method, and concentration basis to facilitate meaningful comparison among studies. Recent advances in genomics, transcriptomics, proteomics, metabolomics, and artificial intelligence (AI)-assisted bioinformatics have created unprecedented opportunities to better understand the biosynthesis, regulation, and biological functions of capsaicinoids and other phytochemicals. Integrating multi-omics technologies with genome-wide association studies (GWAS) and molecular breeding approaches will accelerate the identification of key regulatory genes controlling capsaicinoid biosynthesis, stress tolerance, disease resistance, and nutritional quality in *Capsicum* species (Barboza *et al.*, 2022; Lozada *et al.*, 2022). Integration of metabolomic data with food-processing and sensory studies may further help identify cultivars with desirable combinations of bioactive content, stability, flavour, pungency, and technological functionality.

Although numerous *in vitro* and *in vivo* studies have demonstrated the therapeutic potential of capsaicin and related phytochemicals, the available clinical evidence remains relatively limited. Future multicentre randomized controlled trials involving diverse populations are required to establish standardized dosage recommendations, evaluate long-term safety, determine pharmacokinetic characteristics, investigate potential drug–nutrient interactions, and confirm clinical efficacy for the prevention and treatment of chronic diseases, including obesity, diabetes mellitus, cardiovascular disease, neurodegenerative disorders, and cancer (Maharjan *et al.*, 2024; Jayan *et al.*, 2025). The available evidence should therefore be interpreted according to study type, with mechanistic and animal findings regarded as preclinical evidence, observational studies interpreted as associations, and conclusions regarding therapeutic efficacy reserved primarily for adequately powered human intervention studies. This evidence-based distinction is particularly important for obesity and metabolic-health claims, for which human trials suggest relatively modest effects despite stronger mechanistic evidence from experimental models (Zhang *et al.*, 2023). Advances in pharmaceutical formulation technologies also provide promising opportunities to overcome the limitations associated with capsaicin, including poor aqueous solubility, low oral bioavailability, rapid metabolism, and dose-dependent gastrointestinal irritation. Emerging delivery systems such as nanoemulsions, liposomes, polymeric nanoparticles, solid lipid nanoparticles, hydrogels, and microencapsulation technologies may improve targeted delivery, controlled release, therapeutic efficacy, and patient compliance while minimizing adverse effects (Basith *et al.*, 2016; Saab *et al.*, 2021; Salehi *et al.*, 2021). Beyond human health applications, future research should also explore the utilisation of *Capsicum*-derived bioactive compounds in sustainable agriculture, active food packaging, natural food preservation, livestock nutrition, and cosmetic formulations. The antimicrobial and antioxidant properties of capsaicinoids and phenolic compounds offer promising alternatives to synthetic preservatives, antibiotics, and chemical additives, thereby supporting the development of safer and more environmentally friendly products (Hernández-Pérez *et al.*, 2020; Rezazadeh *et al.*, 2021; Silva *et al.*, 2023).

For food applications, future research should place greater emphasis on real-food validation, sensory acceptance, compound stability during processing and storage, food-matrix interactions, and regulatory requirements rather than relying predominantly on *in vitro* efficacy measurements. Overall, multidisciplinary collaborations integrating plant science, food science, biotechnology, pharmacology, medicine, nutrition, and systems biology will be essential to translate laboratory discoveries into

commercially viable functional foods, nutraceuticals, pharmaceuticals, and sustainable industrial applications. Such integrated approaches will maximize the economic value and therapeutic potential of *Capsicum* species while ensuring standardisation across global value chains.

7. Conclusion

Capsicum species represent one of the most important horticultural crops worldwide, serving not only as indispensable culinary ingredients but also as valuable sources of bioactive compounds with considerable nutritional and therapeutic significance. The diverse phytochemical composition of chilli peppers, particularly capsaicinoids, carotenoids, flavonoids, phenolic compounds, vitamins, and volatile metabolites, contributes to their antioxidant, anti-inflammatory, antimicrobial, cardioprotective, antidiabetic, neuroprotective, and anticancer properties. Consequently, *Capsicum* has attracted increasing scientific and commercial interest as a promising functional food and natural source of nutraceutical and pharmaceutical ingredients. With increasing consumer demand for plant-based functional foods and natural therapeutic agents, *Capsicum* species are expected to play an increasingly important role in sustainable nutrition and preventive healthcare. Continued advances in multi-omics technologies, precision breeding, green extraction methods, and nanotechnology-based delivery systems will facilitate the translation of laboratory discoveries into commercially viable food, nutraceutical, and pharmaceutical products. Furthermore, interdisciplinary collaboration among plant scientists, food technologists, pharmacologists, clinicians, and industry stakeholders will be essential to accelerate innovation, establish evidence-based health claims, and maximise the global economic and therapeutic potential of chilli-derived bioactive compounds. Future research should prioritise standardised analytical and extraction procedures, well-designed human clinical trials, long-term safety assessment, quantitative characterisation of bioactive compounds, and validation of *Capsicum*-based products in real food matrices. Collectively, these efforts will provide a stronger scientific foundation for the safe and effective development of *Capsicum*-derived functional foods, nutraceuticals, and therapeutic products.

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