Phytochemical and Biological properties of domesticated capsicum species: A Review

ABSTRACT

America is the original home of the *Capsicum genus* (Solanaceae). It is now a significant agricultural crop grown all over the world, not only for its commercial significance but also for the fruits' high nutritional worth. Capsicum and its various variants have many beneficial qualities that set them apart from other vegetables. They are also used as a spice in many foods due to its potent, pungent flavour, which is created during the plant's secondary metabolism. Due to the presence of carotenoids, which can be utilised as a natural colouring agent and antioxidant, capsicum fruit displays a diverse colour profile. Capsaicinoids, one of their phytochemical components, give sharp-tasting cultivars their typical pungency. Capsicum and its capsaicinoids, particularly capsaicin, have also received a lot of research attention due to their health advantages. Additionally, the essential oils from capsicum are used in cosmetics as anti-aging ingredients. Thus, this study covers the scientific literature on Capsicum species and their phytochemicals, which have been shown to have protective effects against cancer, diabetes, gastrointestinal disorders, pain, and metabolic syndrome as well as having antibacterial and antioxidant properties. The chemical and functional characteristics of the bioactive chemicals derived from capsicum and their successful application in the pharmaceutical, food, agricultural, cosmetic, and textile sectors.

Keywords: *Capsicum, capsaicinoids, capsaicin, carotenoids, metabolic syndrome, pungency*

INTRODUCTION

According to [44] medicinal plants are important natural treatments for the treatment of a variety of disorders. According to [33] natural compounds from higher plants may offer a fresh source of therapeutic agents with potentially novel modes of action. Worldwide cultivation and use of Capsicum spp. is common [20]. They are a part of the 2000 species and 90 genera that make up the Solanaceae family. Vegetables like pepper, tomato, and potato are members of this plant family, which is indigenous to the Americas [37]. Capsicum, sometimes known as pepper, is an annual herbaceous plant that belongs to the Solanaceae family. The most frequently cultivated spice in the world is *Capsicum annuum* L., which is renowned for its pungency, scent, and colour qualities. One of the five domesticated species, together with *C. baccatum* L., *C. chinense Jacq*., *C. frutescens* L., and *C. pubescens*, it belongs to the Capsicum genus, which has about 30 species [50] [51]. According to [34], chilli peppers, often known as chiles, chillies, or simply chillies, were the first crops. Furthermore, Aztecs and Mayans have been using Capsicum species in traditional medicine from pre-Hispanic times. Due to its economic significance and the high nutritional content of the fruits, this genus is now grown throughout the world, including in tropical, subtropical, and temperate regions of Africa, Asia, and America as well as the Mediterranean basin (Table 1). *C. chinense*, *C. annuum*, *C. pubescens*, *C. baccatum*, and *C. frutescens* are a few of the five recognised cultivated species of this genus [23], [26]. Vitamins C and E, provitamin A, carotenoids, and phenolic compounds are all abundant in peppers and contribute to the plant food's overall antioxidant activity and bioactive qualities [37]. Capsaicinoids, which are vanillylamine coupled with a branched-chain fatty acid to form capsaicin and dihydrocapsaicin (Figure 1), are the most distinctive phenolic compounds discovered in pepper fruits and are in charge of 90% of the pungency of peppers [12]. The cultivar and species of Capsicum determine how pungent they are. According to [1], the concentration of these chemicals can range from being undetectable in some non-pungent cultivars to 664 mg/100 g in pungent cultivars. Due to its use in traditional medicines to treat conditions including ulcers, toothaches, rheumatism, alopecia, and diabetes, capsicum has been shown to be quite useful [16]. The chemical makeup of the capsicum fruit is likewise distinct because it contains flavonoids, alkaloids, and carotenoids that are phenolic chemicals that have favourable impacts on human health [11]. Due to the existence of numerous chemical compounds with possible medicinal qualities, *C. annuum* has been the focus of pharmacological study in addition to its usage as a food ingredient [41]. However, the chemical profile varies depending on a number of variables, including species, seasonality, climatic conditions, and plant life cycle [4].

Table 1: Nutritional composition of *Capsicum* spp. fruit (per 100 g of edible portion) [46]

Nutrients	Spices, pepper, red or cayenne	Peppers, sweet, green, raw	Peppers, hot chili, green, raw	Peppers, sweet, yellow, raw
Water (g)	8.05	93.89	87.74	92.02
Protein (g)	12.01	0.86	2.00	1.00
Energy (kcal)	318	20	40	27
Carbohydrate (g)	56.63	4.64	9.46	6.32
Calcium (mg)	148	10	18	11
Phosphorus (mg)	293	20	46	24
Selenium (µg)	8.8	0.0	0.5	0.3
Iron (mg)	7.80	0.34	1.20	4
Sodium (mg)	30	3	7	2
Copper (mg)	0.373	0.066	0.30	0.107
Potassium (mg)	2014	175	340	212

Fatty acids, total saturated (g)	3.260	0.058	0.021	0.031
Fatty acids, total monounsaturated (g)	2.750	0.008	0.011	
Total lipids (fat) (g)	17.27	0.17	0.20	0.21
Ash (g)	6.04	0.43	0.60	0.45
Niacin (mg)	8.701	0.480	0.950	0.890
Vitamin C, total ascorbic (mg)	76.4	80.4	242.5	183.5
Thiamin (mg)	0.328	0.047	0.090	0.028
Vitamin B-6 (mg)	2.450	0.224	0.278	0.168
Carotene, beta (mg)	21.84	0.208	0.671	0.120
Cryptoxanthin, beta (mg)	6.252	0.007	0.050	

Composition data obtained from the National Nutrient Database for Standard Reference Release 28, USDA Food Composition database (https://ndb.nal.usda.gov/ndb/; accesed 18/11/2017).

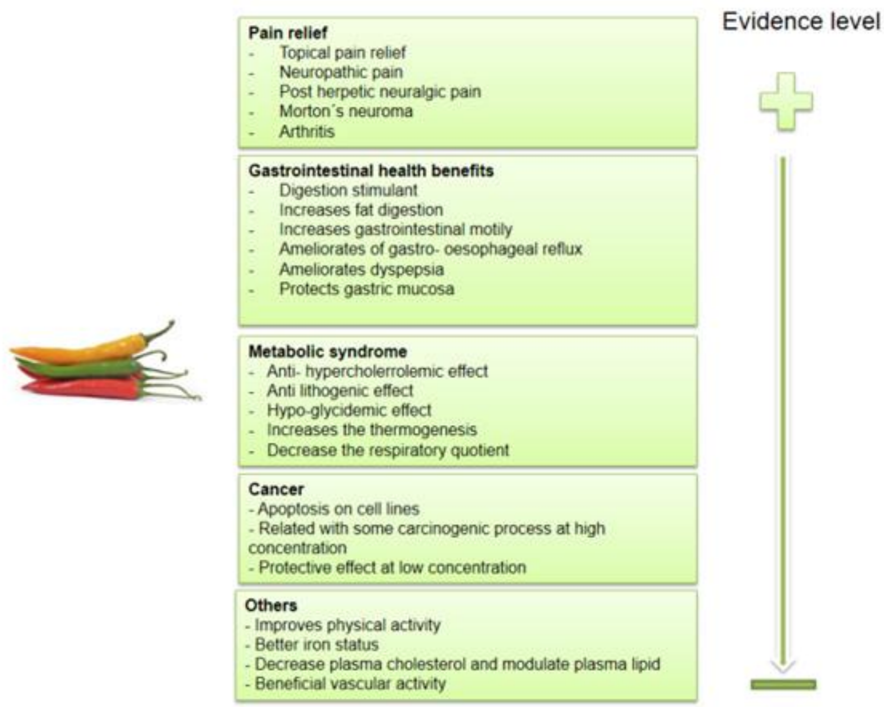


Figure 1. Example of health benefits of the consumption of *Capsicum* spp.

Nearly all types of capsicum, including the green, sweet, and hot forms, are abundant in significant phytochemicals including flavonoids and polyphenols, which are recognised as bioactive food elements. The glycosides and aglycones quercetin, myricetin, luteolin, kaempferol, and apigenin are among the other phytochemicals found in capsicum [24]. While the glycosyltransferase enzymes naturally occur in the secondary metabolites of plants and catalyse the synthesis of glycosides. Aglycone and glycone (the sugar moiety) are two functionally distinct portions of glycosides that are only loosely linked by glycosidic linkage. The most common plant glycosides are O-glycosides, which are generated by the glycosidic bond with oxygen, and C-glycosides, which are formed by the glycosidic bond with carbon and are the most resistant to hydrolysis [7]. Numerous researches have been done to identify carbon and oxygen glycosides utilising methods including ultraviolet spectrum analysis and mass spectrometry fragmentation. These studies' findings point to the presence of four different types of quercetin (3O-rhamnoside, 3-O-glucoside-7-O-rhamnoside, and quercetin glycosylated), two luteolin O-glycosides (apiosyl-acetylglucoside and 7-O-2-apiosylglucoside), five luteolin C-glycosides (6-C-hexoside, 8- In capsicum fruits, the concentration of various bioactive substances varies depending on the species, genetic characteristics, growth and developmental stages, as well as ecological factors. Among all the fruits in this family, the red fruits of cultivars of capsicum have the highest concentration of bioactive chemicals, and the green fruits have high quercetin content. 3-O-R-Lrhamnopyranoside whose concentration decreases as the fruit ripens.

"But in the case of capsicum, the bioactive substances are present in appreciably sufficient amounts and are in charge of numerous cellular and physiological functions. The major anthocyanin found in some species of red and purple capsicums is delphinidin-3 transcoumaroylrutinoside5-glucoside, whereas the total amount of anthocyanin present in fruits ranges from 0.5 mg per 100 g to 28 mg per 100 g in ripe yellow to ripe red fruit, respectively" [40].

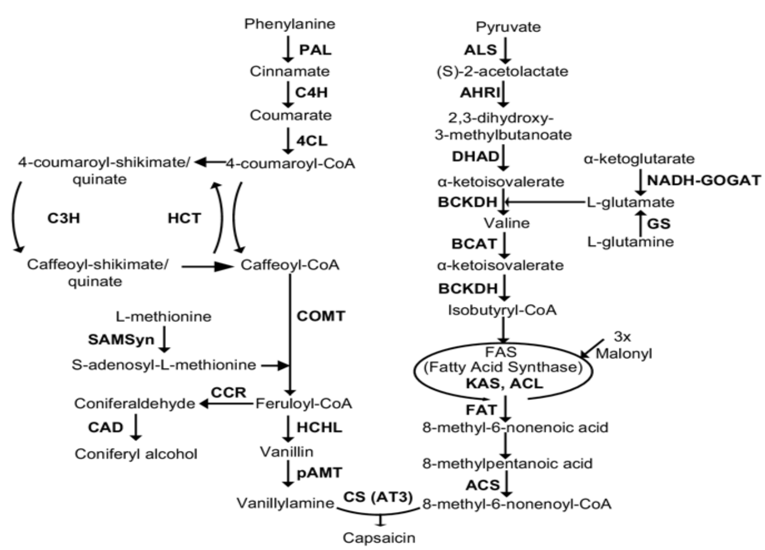
PUNGENCY – a characteristic trait of capsicum

The primary characteristic of almost all types of capsicum is pungency, or "heat," which is due to the popularity of the plant's use as a spice. Pun1 and pAMT have been shown to be the two genes that control the synthesis of pungency in capsicum Tsurumaki and Sasanuma 2019 [45]. "When plants create different helpful compounds for humans via either of the two methods, i.e. the phenylpropanoid system or the branched-chain fatty acid pathway, they develop this appealing quality of pungency in the capsicum plants" Naves *et al.* 2019 [39]. "Capsaicinoids, a type of alkaloids that are biosynthesized and eventually build up in the placental tissue during secondary metabolism in capsicum, are the primary substances accountable for chilli peppers' spiciness. Capsaicin and dihydrocapsaicin are the two main representative families of capsaicinoids involved in pungency" Aza-González *et al.* 2011 [6]. "A hydrophobic, colourless, and odourless molecule known as capsaicin (trans-8-methyl-N-vanillyl-6nonenamide), an HVA derivative, can serve as a deterrent against herbivores as well as microbial and fungal attacks" Basith *et al.* 2016 [8]. "In placental tissue (where the seeds connect), inner membranes, and to a lesser extent, the fleshy sections of the fruit, capsaicin is found in high amounts" Srinivasan 2016 [44]. Nordihydrocapsaicin (7.4%), norcapsaicin, homocapsaicin I, homodihydrocapsaicin I (2%), homocapsaicin II (2%), homodihydrocapsaicin II, and nonivamide are among the minor capsaicinoids discovered in chilli fruits Guillen *et al.* 2018 [18]. The amount of capsaicinoids present directly correlates with the pungency of the capsicum plant; especially they include capsaicins Parvez 2017 [41]. The formation of analogues with various levels of pungency in capsicum fruits has been linked to a variation in the acid component of the capsaicin. The fruit of C. chinense is thought to be the most pungent among the domesticated species of the genus Capsicum Chapa-Oliver *et al.* 2018 [10].

Synthesis and accumulation of pungent compounds:

The placental tissues, pericarp, seeds, and other vegetative organs all synthesise capsaicinoids including the capsicum plant's stems and leaves. The majority of capsaicinoids are created in the first 20 to 50 days after anthesis, when the fruit is developing, and this rate of synthesis rises as the fruit ages. Genotype, fruit ripeness, as well as environmental elements including water availability and solar energy, are other factors that affect the generation of capsaicinoids (Guillen *et al*. 2018) [52]. The phenylpropanoid pathway and the branched-chain fatty acid pathway are the two biosynthetic pathways for capsaicinoids. Valine (or leucine), the primary precursor of the fatty acid pathway, is combined with the primary precursor of the phenylpropanoid pathway, phenylalanine, to create vanillylamine, which is crucial for the formation of capsaicinoids and their eventual accumulation in the placental tissue of the fruit (Arce-Rodríguez and Ochoa-Alejo 2019) [53]. Numerous putative enzymes and genes that code for proteins are thought to be involved in the manufacture of capsaicinoids.

Figure 2. Model pathway of capsaicin (capsaicinoids) biosynthesis in capsicum [53]



Coloring compounds of capsicum:

One of the key markers of quality for both fresh pepper fruit and the food items made from it is colour. The colour of mature and fully ripened fruit of all species in the genus Capsicum is determined by four genes (y, c1, c2, cl), and about 20 carotenoids Mamedov *et al.* 2017 [31].The isoprenoid (or mevalonate) route produces the extremely lipid-soluble terpenoids known as carotenoid colours, which are primarily preserved in the chromoplasts of capsicum fruit. The chemical structure of the carotenoids is made up of 5-carbon isoprenoid groups with an alternate double bond. Carotenoids typically feature a 40-carbon isoprene structural backbone with the aromatic ring structures at one or both ends of the molecule Arimboor *et al.* 2015 [5]. Different types of Capsicum include carotenoids that are present in a variety of colours, including yellow, orange, and red. As the fruit ripens, these carotenoids grow and change colour. The ratio of carotenoids to chlorophyll in capsicum fruit has been found to be 32:68 during the start of fruit ripening, giving the fruits their green colour Mohd Hassan *et al.* 2019 [35].Capsanthin and capsorubin, two important carotenoids, are in charge of the capsicum's red colour, while lutein is in charge of the green and yellow variations. Additionally, the presence of -carotenes, cryptoxanthin, zeaxanthin, violaxanthin, antheraxanthin, and cucurbitaxanthin A is responsible for the yellow to orange colour of capsicum. According to reports, these carotenoids have crucial roles to play. Besides giving the capsicum fruit colour, they also play several biological and health-related aspects Kim *et al.* 2016 [27].

Biological activities of *Capsicum* plant extracts and their constituents: Potential as a functional ingredient

ANTIOXIDANT ACTIVITY

Among the phytochemicals found in capsicum, carotenoids play an important role in colouring peppers and protecting cells and tissues from damaging reactive oxygen species (ROS) by scavenging singlet molecular oxygen, peroxyl radicals, and reactive nitrogen species (RNS). However, a large portion of Capsicum spp.'s total antioxidant activity is linked to its phenolic composition, not just to its vitamin and carotenoid content. In general, the quantity of antioxidants (carotenoids, flavonoids, phenolic acids, and ascorbic acid) increases with fruit maturation in C. annuum, C. frutescens, and C. chinense along with the antioxidant activity measured in vitro. Additionally, compared to other vegetables, capsicum has a stronger antioxidant activity. In this regard, [37] recent study revealed that, among the red 'California' pepper, the 'Fino' lemon, and the red onion all showed the highest antioxidant capacity in the TEAC (trolox equivalent antioxidant capacity), FRAP (ferric ion reducing antioxidant power), and ORAC (oxygen radical absorbance capacity) assays, respectively, of 44 cultivars of fruits and vegetables grown in Andalusia (Spain). Note that the major components of this red pepper are hydroxycinnamic acids and flavonoid glycosides, and that it is nonpungent. In other trials, however, the presence of metal ions may result in a possible pro-oxidant impact of capsicum flavonoids Howard *et al.* 2000 [21]. Additionally, capsaicin has demonstrated antioxidant properties similar to butylhydroxyanisole (BHA), preventing the oxidation of human low density lipoprotein (LDL), which inhibits the lipid peroxidation caused by cooper ions and lessens the production of TBARS Naidu and Thippeswamy 2002 [38].

ANTIMICROBIAL ACTIVITY

Both helpful and harmful bacteria strains have been successfully combated by the polyphenolic chemicals found in capsicum. Standard gram-positive and gram-negative bacterial strains were employed as test organisms to determine antibiotic sensitivity. Salmonella enterica serovar Typhimurium ATCC 13311, Bacillus subtilis ATCC 6633, Listeria monocytogenes sub sp. lactis Bb12, Lactobacillus acidophilus CECT 4529, Lactobacillus plantarum CECT 748, and six wild-type strains of S. aureus (8, 14, 26, 32, 550, 319) are among the bacteria that have been identified Mokhta *et al.* 2017 [36]. In terms of preventing the growth of several bacterial and fungal organisms like L. monocytogenes and Aspergillus flavus, C. annuum ethanol extracts demonstrated remarkable effectiveness Anikwe *et al.* 2017 [3]. The methanolic extract from red pepper was examined and found to be efficient against the drug-resistant Vibrio cholerae strains, according to a study by Yamasaki *et al.* 2011 [48]. According to a different study, *C. frutescens* seed extracts in n-hexane and chloroform were highly effective against a variety of pathogenic microbes, including *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Staphylococcus aureus*, *Candida albicans*, *Candida krusei*, *Alternaria alternata*, and *Aspergillus niger*.

ANTITUMOR PROPERTIES

Regarding its use in a variety of medical applications, capsaicin has attracted a lot of interest. By triggering apoptosis in these cells, it has been discovered to be efficacious and to exhibit protective characteristics against numerous mutagenic and tumor-causing cells. The tumor-associated NADH-oxidase (tNOX) enzyme, which contributes in promoting cellular growth close to the plasma membranes, is responsible for this action of capsaicin Della *et al.* 2017 [14]. Carotenes, which have antimutagenic and anticarcinogenic characteristics, are abundant in chilli peppers. According to the research, using the red pepper extract decreased the genotoxic activity of urethane in yeast cells, bacteria, and mammal cells. According to the findings, carotenoids and capsaicinoids have a significant anti-mutagenic effect Laohavechvanich *et al.* 2006 [28].

It is believed that the i (ICD), a process involving the early surface exposure to calreticulin (CRT), a multifunctional chaperone protein, is the mechanism underlying the activity of capsaicinoids. In a study, it was discovered that the chemotherapeutic drug cisplatin and the capsaicin compounds boosted CRT expression, which increased ICD induction and increased cell death in human osteosarcoma cells (OCs) MG-63. In particular, capsaicin therapy has been linked to the translocation of calreticulin from the internal membranes to the outer cell surface, increasing MG-63 cell phagocytosis and stimulating interferongamma (IFN-) release. As a result, this led to the induction of apoptosis, which ultimately prevented the proliferation of bladder cancer cells by inhibiting their activity. Comprising the sirtuin 1 (SIRT1) protein and the tNOX enzyme. In addition, it was found that capsaicin significantly decreased the expression and activity of numerous proteins linked to cell cycle progression, which in turn decreased the rates of cancer cell proliferation and migration Jin *et al.* 2016; Lin *et al.* 2016 [25] [29]. The majority of the findings published in the literature demonstrated that high doses of capsaicin used to treat malignancies stimulate the proliferation of tumour cells while modest doses of capsaicin used to treat cancers suppress the growth of numerous human cancers

ANTIDIABETIC ROLE

Since capsaicin's alkaloids have been shown to be helpful at controlling blood glucose levels, they may one day be utilised to treat diabetes in people. A study revealed that the capsicum fruit's crude extract assisted in preventing the intestinal absorption of glucose and likely helped lower blood sugar levels. GDM poses a serious health danger to both expectant mothers and their unborn children in the future. 42 women who were between 22 and 33 weeks pregnant participated in a trial in which capsaicin pills (5 mg/day) were given to them. According to the study's findings, capsaicin-rich supplements for chilli helped women with gestational diabetes' postprandial hyperglycemia and hyperinsulinemia as well as their fasting lipid metabolic abnormalities. They also dramatically decreased the incidence of large-forgestational-diabetes [49].

CARDIOVASCULAR ROLE

Dihydrocapsaicin is one of several capsaicinoids that have been shown to lower inflammatory cytokines like interleukin 1 beta (IL-1 beta), IL-6, tumour necrosis factor-alpha (TNF-alpha), and C-reactive protein (CRP), as well as plasma cholesterol, LDL-C, VLDL-C, and triglycerides. Apolipoprotein A1 (apoA1) and high-density lipoprotein cholesterol (HDL-C) levels in plasma also significantly increased. The findings of capsaicinoids inhibited cholesterol absorption by lowering plasma cholesterol levels were further supported by the plasma sterol study. Due to its role in raising HDL levels, dihydrocapsaicin actively enhanced the CRT pathway, which in turn suppressed the formation of atherosclerosis plaques and promoted cholesterol efflux in THP-1 macrophagederived foam cells Hu *et al.* 2013 [22]. The metabolic syndrome, which includes high blood sugar, obesity, dyslipidemia, and hypertension, is frequently considered to be a significant risk factor for the onset of CVDs and subsequent death. The effects of capsaicin on lowering blood cholesterol levels, lowering blood glucose levels, preventing hyperglycemic episodes, and atherosclerosis incidence and prevalence have been the subject of several investigations, both in vivo and in vitro. The findings of the research showed that capsaicin reduced intestinal cholesterol absorption and had an anti-hyperlipidemic impact. The activation of the PPAR, or peroxisome proliferator-activated receptor, may possibly be a part in this impact. Capsaicins' favourable antidiabetic, antihypertensive, and anti-obesity properties make them perfect for use and has the potential to greatly lower the risk of mortality from cardiovascular diseases and the treatment of metabolic syndrome(Sanati *et al.* 2018 [42].

ANTI-INFLAMMATORY ACTIVITY

Inflammation is a biological defence mechanism that can be brought on by a variety of things, including injury, infection, and toxic substances If it persists, inflammation can become a pathological disease. Bioactive chemicals derived from capsicum, such as polyphenols, flavonoids, tocopherols, capsaicinoids, and capsinoids, have been shown in several studies to have anti-inflammatory properties Bhattacharya *et al.* 2010; Luo *et al.* 2010 [9] [30]. The capsicum's ability to reduce inflammation is caused by its ability to inhibit (LOX). Capsicum cultivars showed different levels of lipoxygenase inhibition, with green capsicum recording the greatest level (46.12%), followed by yellow (44.09%), and red capsicum (32.18%). Capsaicin has well-established anti-inflammatory qualities, and it is frequently used in topical gel and cream formulations for pain treatment. Inducing the inflammatory response, capsaicin releases pro-inflammatory mediators that then activate the TRPV1 (transient receptor potential cation channel subfamily V member 1, also known as capsaicin receptors) channels linked to thermoreception and nociception Basith *et al.* 2016; Luo *et al.* 2020 [30]. Capsaicin suppressed the production of prostaglandin E2 (PGE2) hormone by inhibiting the activity of the cyclooxygenase-2 (COX-2) enzyme and the expression of inducible nitric oxide synthase (iNOS), according to a study to assess the anti-inflammatory effect in murine peritoneal macrophages produced by LPS. Capsaicin administration finally resulted in a decrease in inflammation since prostaglandins, COX-2, and iNOS are important proinflammatory mediators Luo *et al.* 2020 [30].

PAIN RELIEF

As topical painkillers, natural capsaicinoids from chilli peppers have drawn a lot of interest. The use of creams, ointments, and patches to treat many types of pain, particularly neuropathic pain, has taken advantage of this distinctive feature of capsaicin Derry *et al.* 2013 [13]. In two studies, topical creams containing 0.075% or 0.025% of capsaicin Deal *et al.* 1991 [15] reduced pain in 21% and 70%, respectively, of individuals with osteoarthritis and rheumatoid arthritis. Topical application of 0.075% capsaicin reduced pain in a trial including 219 men and women with severe diabetic neuropathy and researchers from 12 sites, improving daily activities and improving patient quality of life Group 1992 [17]. Adults appear to experience some alleviation from chronic neuropathic pain when a low dose capsaicin cream (0.075%) or a high dose patch (8%) is applied repeatedly. In individuals with neuropathic pain, a single 60-minute application of a capsaicin 8% patch provided excellent pain relief for up to 12 weeks. This finding suggests that high-concentration capsaicin products offer the advantages of a longer duration of action and a lower risk of systemic side effects. Additionally, lotions containing capsaicin are used to treat psoriasis, lowering swelling and irritation. In post-herpetic neuralgia pain, a painful condition that happens after the dormant herpes zoster virus reactivates, the application of an 8% capsaicin patch has shown to be effective and long-lasting Mankowski *et al.* 2017 [32].

CONCLUSIONS

Different types of capsicum and its derivatives have become more and more popular over the past few years. The capsicum plant has significant uses in a wide range of industries, including food, agriculture, medicine, pharmaceuticals, and cosmetics. It also includes a huge diversity of bioactive chemicals. Historically, the majority of capsicum research has concentrated on the biosynthesis, characterization, and potential extraction techniques of these bioactive components utilizing various solvents. However, more lately, the research agenda has undergone a paradigm change in favour of the idea of using capsicum for a variety of purposes. An effort has been made to highlight the chemical and functional characteristics of capsicum in the writing of this review paper.

FUTURE PROSPECTS

The fruit of the cayenne pepper and its related parts are potential resources that have a wide range of applications. The agro-food and textile industries have both benefited from this plant's byproducts. The importance and possibilities of this plant are numerous as the trend away from synthetic chemicals towards natural substances is accelerating. Due to the presence of capsaicinoids, carotenoids, and polyphenolic chemicals, products generated from capsicum, such as chilli powder, oleoresins, refined extracts, and enhanced fractions, are frequently utilized in food and medicine. To create more adaptable and healthier food items, greater research into these bioactive components is necessary.

Additionally, these items must be standardised in order to improve their marketing from the standpoint of pungency, colour, flavour, and scent, which are now lacking. There are no standardised recommendations in the literature for preserving the stability, security, and quality of goods made from capsicum, particularly those used in food, medicine, and cosmetics. Therefore, further study is needed to develop creative methods for boosting extraction effectiveness, developing bioactive chemical isolation methods, and increasing the uses of these functional components across many industries.

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