Annals of Phytomedicine 13(2): 206-217, 2024

DOI: http://dx.doi.org/10.54085/ap.2024.13.2.20

Annals of Phytomedicine: An International Journal

http://www.ukaazpublications.com/publications/index.php

Print ISSN : 2278-9839 Online ISSN : 2393-9885

Review Article : Open Access

A comprehensive insights on pharmacological and nutritional benefits of Chilli (*Capsicum annuum* L).

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Article Info

Article history

Received 13 July 2024

Revised 29 August 2024

Accepted 30 August 2024

Published Online 30 December 2024

Keywords

Benefits

Chilli

Capsaicin

Nutritional

Risks

Abstract

Chilli or hot pepper (*Capsicum annuum* L.) fruits have been utilized for food flavouring, natural colouring and traditional medicinal purposes. Chilli is a Solanaceous crop which is being utilized both as mature unripe pod as a vegetable crop and ripe pod as a spice. Chilli was first used in cooking in 15th century itself. It was introduced in India by Portuguese traders in 15th century. Chilli, both sweet and spicy are consumed in many different ways around the world. India leads the world in hot pepper production, consumption and exports. This crop holds significant value in the Indian economy and is a vital part of the food. The ingredient that gives hotness to chilli is by an alkaloid called capsaicinoids. In addition, it contains phenols, folates, carotenoids and oxidative products, all of which have a variety of biological functions in human health. Iron, magnesium, potassium, vitamins A, C, B, E and dietary fibres are all found in good amounts in chilli. The primary bioactive ingredient in chilli, capsaicin gives the spice its intense flavour and a host of health advantages. Chilli's nutritious levels varies according to the variety and maturity stage. In addition to its nutritional benefits, chilli possesses pharmacological and antibacterial characteristics, including antioxidants, anti-inflammatory, antiallergenic and anti-carcinogenic effects, are present in chilli. The pharmaceutical industry uses chilli due to its pharmacological properties. Analgesic, anti-inflammatory, antiulcer, antihemorrhagic and immune-boosting properties of chilli are important. Because of its pharmacological qualities, chilli is used in the pharmaceutical sector. It has the ability to lower the cholesterol levels, beneficial for cardiac conditions and functions as a gastro protectant. In this review the nutritional, pharmacological and health benefits and hazards associated with chilli is discussed briefly hereunder.

1. Introduction

Chilli (*Capsicum annuum* L.) is an economically important vegetable cum spice crop being grown all over the world. The most significant crop for spice production, which contributes about 29% of the Nation's entire output and 34% of its total product ion (Rani *et al.,* 2023). Chilli is commonly referred to as bell pepper or chilli pepper or hot pepper, *etc*. This dicotyledonous flowering plant is a member of the Solanaceae family and possesses surplus nutritional and therapeutic benefits (Knapp *et al.,* 2004). Global chilli production reached 36.29 million tonnes in 2022 and reached up to 40.2 million tonnes in 2023. In 2021, China alone produced 16.7 million tonnes (Zulkarnain *et al.,* 2023). *Capsicum annuum*, *C. frutescens*, *C. chinense*, *C. pubescens* and *C. baccatum* are the five domesticated species of chilli. South Central America is said to be the centre of origin. It is highly expensive due to its pungency and its ability to bring unique taste to a broad variety of cuisines (Andrews, 1999). Its uses have expanded over time from its historical use as a medicinal plant and for seasoning of fresh and processed vegetables, spices in dried forms, food colouring, ornamental plant breeding and the creation of extracts for the pharmaceutical and cosmetic industries (Paran and Van Der Knapp, 2007). The colour in chilli is due to the presence of pigments such as green chlorophyll, yellow/orange β-cryptoxanthin, zeaxanthin, purple/violet anthocyanins, lutein and yellow/orange β-carotene. These fruits undergo profound morphological, physiological and metabolic transformations during ripening, which are influenced by factors such as genotype, maturity and growth conditions. In contrast, capsicums exhibit a remarkable diversity and exceptional health-promoting chemical compounds like capsaicinoids which includes capsaicin, flavonoids, vitamins C and E, carotenoids (provitamin A), essential oils and minerals which have antimicrobial, anticancer and antioxidant properties (Del Rocio Gimez-Garcia and Ochoa-Alejo, 2013; Delgado-vargas and Pareded-Lopez, 2002). The nutritional levels may vary depending on the variety and maturity stage (Ozgur *et al.,* 2011). Numerous biochemical and pharmacological characteristics including antioxidant, anti-inflammatory, antiallergenic and anticarcinogenic effects are present in chilli (Nishino, 1998). Furthermore, chilli also possess antibacterial quality (Wahba *et al.,* 2010). The placenta's inner

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membrane contains the pungency or hotness of the chilli which is measured on the Scoville scale. The most valuable spices that are traditionally traded worldwide are those that grow in tropical regions. The main exclusion from this category is the variety of peppers known as chilli, paprika and coriander that are grown in a considerably wider range of tropical and nontropical conditions (Singh *et al*., 2012). Although, the exact date of chilli's arrival is unknown, it is believed to be arrived in Misawa's harbour in around 1520.

Obesity is a global health concern in these days because of lifestyle, unhealthy eating behaviour and other factors such as stress, health condition, medicines and sleep deprivation. Changing one's lifestyle to manage weight rarely results in noticeable or long-lasting weight loss (LeBlanc *et al.,* 2011). A healthy diet must include vegetables in large quantities. Limiting fat, sugar and salt intake while eating a diet rich in fruits and vegetables can potentially lower the risk of cardiovascular illnesses and obesity (Ozturk *et al.,* 2009). As a vegetable, the chilli, a member of the *Capsicum* genus, finds widespread use as a spice. Because of the properties of two special ingredients, capsaicin and capsaicinoids which give hot chilli their strong aroma and are also utilized in therapeutic diets. Besides these properties, it possesses antitumour, anticancer, antioxidant and antiobesity properties which have been the subject of recent studies (Malagarie-Cazenave *et al.,* 2009; Ozturk *et al.,* 2009). Capsaicin has been shown to have antiobesity properties due to its ability to prevent oxidative stress and cell adipogenesis (Leung, 2008). In this review, it is attempted to redefine the importance of nutritional value, health benefits and medicinal properties as possible solutions to create awareness and encourage research works so that it could be properly used to reduce the potential health risks.

2. Nutritional value of *C. annuum*

Chilli is found to have numerous vitamins, minerals and amino acids that are vital to human development and health and all the qualities that makes them suitable for consumption (Pawar *et al.,* 2011). The vitamin C found in fresh chilli helps to repair damaged cells and boost the immune system. Besides it also contains vitamin A, C and B_1 and nutraceutical compounds like capsaicin, rutin and also have bioactive compounds like ascorbic acid (Pidigam *et al*., 2022). Riped red chilli is a fantastic source of β-carotene, tryptophan, lysine and phenylalanine which are the essential amino acids for the human being that cannot be synthesized and supplied in diet for which chilli is one of the source used to reduce degenerative diseases (Abdul Salam, 2015). Chillies are rich source of vitamins and in particular vitamin B (Ganguly *et al*., 2017). In addition, hot peppers are abundant in calcium, phosphorus, magnesium, iron and potassium. In Chilli, there are hundreds of varieties and species and their nutritional and antioxidant contents vary depending on whether they are consumed as dried fruits, riped red or other colours or as fresh, unriped fruits (Howard et al., 2000). The water soluble vitamin C, which has antioxidant properties is present in significant amounts in capsicum fruits. Its concentration can range from 20 to 247 mg/100 g fresh weight and can rise as the fruit ripens. Variations in the fruit's environmental growing condition and genetic makeup can also impact its content. Certain chilli hybrids grown under water stress in greenhouses had lower vitamin C levels. Moreover, red-fruited chillies have twice as much vitamin C as green-fruited chillies. Chilli loses much of its vitamin C as it dries. Vitamin C stimulate immune system and heal cellular damage. The ascorbic acid concentration of chilli is directly correlated with their pungency.

Table 1: Nutritional value of hot green chilli, green sweet chilli and hot red chilli per 100 g of edible portion (Bal *et al*., 2022)

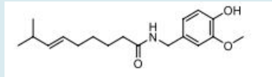
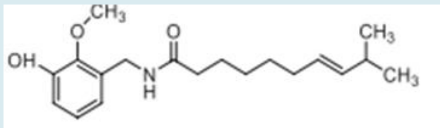
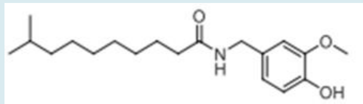
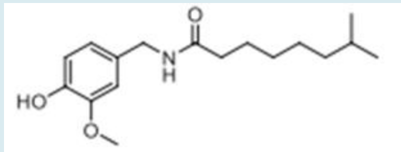
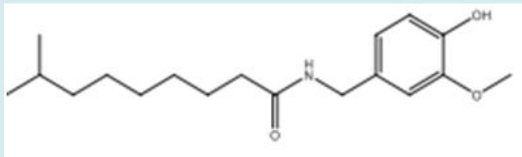
Components	Hot green chilli (Raw)	Green sweet chilli (Raw)	Hot red chilli
Carbohydrate (g)	9.46	4.64	56.63
Protein (g)	2.0	0.86	12.01
Fat (g)	0.20	0.17	17.27
Energy (kcal)	40.0	20.0	318.0
Iron (mg)	1.20	0.34	7.80
Calcium (mg)	18.0	10.0	148.0
Sodium (mg)	7.0	3.0	30.0
Potassium (mg)	340	175	214
Phosphorus (mg)	46.0	20.0	293.0
Copper (mg)	0.30	0.66	0.373
Selenium (mg)	0.50	0	8.80

3. Chemical constituents

3.1 Capsaicinoids

The intense and spicy flavour of chilli fruit which is attributed to their pungency is due to the presence of secondary metabolites called capsaicinoids. The biosynthesis of capsaicinoids is highly controlled at a molecular level (Sun *et al*., 2022). Capsicums possess defense against herbivores and phytopathogens. The capsaicinoids have a lengthy hydrocarbon chain, an amide group, a vanilloid group an aromatic ring with a hydroxyl and a methyl group as its structural foundation (Batiha *et al*., 2020). They also exhibit low polarity. Both the placental tissue and the interlocular septum synthesizes a particular class of alkaloids. Capsaicin and dihydrocapsaicin, which can reach concentrations of over 90% which are the two primary capsaicinoids found in the fruit pericarp, placenta and seed tissues of all peppers. Homocapsaicin, homodihydrocapsaicin and nordihydrocapsaicin are present in lesser proportions than 20% of the total (Delgado-Vargas *et al.,* 2000; Giuffrida *et al.,* 2013; Oleszek, 2000). Their biosynthesis is a genetically controlled trait and it also depends on the genotype. The environment can also have a significant impact (Aza-GonZalez *et al.,* 2011; Uarrota *et al.,* 2021). The chemical structures of the several capsaicinoids found in capsicum are listed in Table 2.

Table 2: Various structure of capsaicinoids (Rastogi *et al.*, 2024)

S.No.	Capsaicinoids	Formula	Structure
1	Capsaicin	$C_{18}H_{27}NO_3$	
2	Homocapsaicin	$C_{19}H_{29}NO_3$	
3	Homodihydrocapsaicin	$C_{19}H_{31}NO_3$	
4	Nordihydrocapsaicin	$C_{17}H_{27}NO_3$	
5	Dihydrocapsaicin	$C_{18}H_{27}NO_3$	

The Scoville Heat Unit (SHU) is a pungency metric created by Scoville and capsaicinoid concentration is a crucial indicator of the pungency. Chilli consumption per capita is 15.5 g/person in Saudi Arabia, 2.5 g/person in India, 20.0 g/person in Mexico and 5.0 g/person in Thailand. The total capsaicinoids ranged from 0.22 to 20 mg/g dry weight in chilli species, *viz., C. annuum*, *C. frutescens* and *C. chinense*. The placenta of chilli fruits spontaneously produces capsaicinoids through the enzymatic condensation of vanillyl amine and variously sized fatty acid chains that are lengthened by fatty acid synthase. There are numerous research on the chemical, enzymatic and tissue culture synthesis of chilli (Bai *et al*., 2011). Capsaicinoids are biologically and physiologically active compounds that can carry out a range of tasks, including those of antioxidants, anticarcinogens, energy metabolism promoters, fat accumulation suppressors and anti-inflammatory agents (Macho *et al*., 2003). The use of these compounds is restricted because of the irritation. Capsaicinoids are very important to the pharmaceutical and nutraceutical sectors because of all these health benefits. Purified or concentrated versions of capsaicinoids must be manufactured in bigger quantities in a very cost effective manner in order to develop capsaicinoid based products that potentially offer health advantages.

3.1.1 Capsaicin

The primary ingredient in many spices, including red chilli, hot peppers, etc., is capsaicin, also known by its chemical name, trans-8-methyl-N-vanillyl-6-nonenamide (Mehrotra *et al*., 2021) and it is the reddish hot chemical. This volatile, hydrophobic substance has antibacterial properties against a range of microbes. Extracts from chilli and its bioactive ingredients are said to have a range of pharmacological actions, including antimicrobial, anti-inflammatory, pain relieving and antioxidant effects (Bharathi *et al*., 2024). It is utilized in skin treatments, nasal showers and dermal patches to relieve pain. The primary flavour attribute of organic products, chilli's sharpness is impossible in the capsicum types and is produced by the synthetic alkaloid known as capsaicinoids. The five capsaicinoids are often referred to as capsaicin since it is the most persistent followed by dihydrocapsaicin. The extra five synthetic alkaloids are capsaicin, homocapsaicin, homodihydrocapsaicin, nordihydro-capsaicin and dihydrocapsaicin are minor capsaicinoids. The active ingredients, capsaicin contained antibacterial, anticarcinogenic and other healing properties. Capsaicin is becoming a more important component in the pharmaceutical industry due to its neuroprotective properties, discernible decreases in serum, myocardial, and aortic total cholesterol levels and capacity to alleviate pain (Baenas *et al*., 2019; Fattori *et al*., 2016). Therefore, it is advised to use it in the treatment of gastrointestinal issues, skin conditions and arthritis as well as for the healing of wounds and blood purification. In addition to its flavour and physiological effects, it has strong antibacterial and antioxidant properties against viruses and other foodborne pathogens. In food compositions, capsaicin is frequently employed as a condiment and preservative. It is also utilized as an active ingredient in functional foods. The benefits of preclinical and clinical studies of capsaicin have been detailed in Table 3.

Table 3: Benefits of preclinical and clinical studies of capsaicin (Yain *et al.*, 2023)

Model	Dosage	Outcomes
Preclinical studies		
High-fat diet induced obese mice	0.075% capsaicin	Decreased lipid accumulation in mesenteric and epididymal tissue
Mice	Oral administration of capsaicin	Prevention of obesity in male wild-type mice
Guinea pigs (high fat diet)	Capsaicin (doses 2.5, 5, 10 mg/kg)	Reduce oxidative stress and endothelial dysfunction
Human lung carcinoma cells	Erlotinib combined with 90% capsaicin (1:5 and 1:20)	Enhancement of cytotoxicity and inhibition of cell growth of erlotinib
Osteosarcoma cells	Capsaicin (100 µM) with cisplatin (16.7 µM)	Inhibitory effects on osteosarcoma cells, (apoptosis induction, cell cycle arrest and cell invasion inhibition
Clinical studies		
Male/Female (18-56 years)	Capsaicinoids supplements (12 weeks)	Reduced appetite, improved body composition (waist: hip ratio)
Male/Female (18-60 years)	135 mg capsaicin/day (3 months)	Increased fat oxidation during weight regain
Healthy young men	150 mg capsaicin 1 hour before exercise	Enhanced the activity of fat oxidation during low-intensity exercise

3.2 Carotenoids

Carotenoids are used as feed additives and for food colouring on a commercial scale, they are also a great natural source of colour. Because of their nutritional qualities coupled with protective effects against light and oxygen and involvement in preventing degenerative diseases, they are also essential for the health of plants and animals. Pharmaceutical, nutraceutical and cosmetic goods all includes carotenoids (del Rocio Gomez-Garcia; Ochoa-Alejo, 2013; Giuffrida *et al*., 2013; Materska and Perucka, 2005). As a carotenogenic fruit, chilli undergoes a transformation from chloroplast to chromoplast as it ripens. New carotenoids are also generated and chlorophylls vanish. Giuffrida *et al*. (2013) found that 12 distinct cultivars of capsicum showed a significant difference in the content of 52 different carotenoids. Carotenoids provide physiological advantages and serves a number of vital roles in human body. They exhibit provitamin A activity, function as antioxidants, lessen oxidative stress, guard against cardiovascular illnesses, stop cancerous cells from proliferating, slow down the aging process of the eyes and prevent cataracts (Arimboor *et al*., 2015; Giuffrida *et al*., 2013). It has been considered in nutraceutical interest against complications associated with oxidative stress (Saini *et al*., 2022). It is advised to use it for industrial purposes and to consume it for maximum nutraceutical effects because mature chilli has more antioxidants and has accumulated some carotenoids (Pola *et al*., 2022).

3.3 Phenolic compounds

Phenolic compounds provide health benefits because of their ability to scavenge free radicals in both *in vitro* and *in vivo* biological systems (Bogusz Jr *et al*., 2018; Perez-Jimenez *et al*., 2010). According to research findings, it was found that, variations in the phenolic content of capsicum are influenced by the cultivars. In this regard, Hallmann and Rembialkowsha (2012) noted that the bioactive compounds may be influenced by the developing system. Maturation-related phytochemical changes alter the antioxidant activity and the composition of chilli which may have an impact on how much of it is to be consumed (Howard *et al*., 2000). Shaha *et al*. (2013) investigated the bioactive components of chilli (*C. annuum*) at three different phases of ripening. While the total phenolic content was measured at full maturity of fruit, the bell pepper sample had the highest flavonoid concentration and antioxidant activity of all the samples at an intermediate ripening stage. Flavonoids are specialized metabolites that possess biofunctional and antioxidant capabilities due to its various chemical substitutions made to their flavone skeleton, a 15-carbon structural core. In the food, cosmetics and pharmaceutical industries they are indispensable. Since flavonoids can accumulate in specific organs or tissues in significant proportions, it is possible to identify abundant natural sources of these compounds (Moreno-Ramirez *et al*., 2019). It also impede viral cell entry and replication in human body (Banu *et al*., 2024). Numerous reports have indicated that the chilli contains flavonoids, indicating its potential as a phytochemical from organic origin (Dias *et al*., 2021)

4. Medicinal properties

4.1 Antioxidant properties

As per research findings, chilli contains moderate to high concentrations of phytochemicals, such as flavonoids and neutral phenolics which are crucial antioxidants in a plant-based diet and offer healthy advantages above and beyond basic nutrition. These substances have anti-inflammatory, antiallergy and antioxidant properties in their biochemical and pharmacological actions. They may also lower the risk of degenerative disorder (Azlan *et al*., 2022). Furthermore, antioxidants are linked to lower the death rate from heart disease (Hong *et al*., 2015), lower incidence of cancer in the mouth, throat, oesophagus, stomach, colon and lungs as well as lower the risk of premature aging (Hertog *et al*., 1992). Hossain *et al*. (2008) found that capsaicin suppresses oxidation of proteins and peroxidation of lipids caused by radiation induced metabolic changes. This research indicates that the compound capsaicin, which is present in chilli may have antioxidant and radioprotective properties for biological systems. Both pure and microemulsified capsaicin shows greater inhibitory capabilities in intervention trials compared to the synthetic antioxidant BHT (butylated hydroxyl toluene). In recipes for animal products, this mixture can serve as a natural preservative (Kang *et al*., 2011). The antioxidant properties of capsaicin found in chilli peppers have been demonstrated by Hossain *et al*. (2008) to be on par with those of synthetic antioxidants like butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT). Additionally, taking capsaicin along with other prescription drugs has a synergistic effect. For instance, by inhibiting the proliferation of the cancer cells, the combination of 5-fluorouracil (5-FU) and capsaicin improves the medication sensitivity of cholamgiocarcinoma (CCA), a kind of cancer that is resistant to multiple drugs (Mori *et al*., 2006). There is evidence that capsaicin functions as a potent antioxidant, surpassing even melatonin and caffeine in its ability to scavenge (Duranova *et al*., 2022). Capsaicin, which inhibits reactive oxygen species from oxidizing glutathione which is present in food and can reduce oxidative stress and boost antioxidant capacity in cells (Zhang *et al*., 2024). The potential of high blood cholesterol levels to suppress the antioxidant enzymes superoxide dismutase, glutathione reductase and glutathione transferase can be reversed by capsaicin.

4.2 Antiobesity properties

Research is being done on the possibility of using natural products to cure obesity. Natural goods are fantastic substitutes for conventional methods in the development of secure and efficient antiobesity medications (Wu *et al*., 2022). Many natural products, including separated pure natural components and crude extracts that can reduce body weight and prevent diet induced obesity, have been utilized extensively in the treatment of obesity (Ibrahim *et al*., 2014). Chillies are thermogenic agents that generate heat. It speeds up the process of producing heat. Eating chilli peppers also increases the intake of oxygen. Metabolic dysregulation, insulin resistant diabetes, hyperglycemia, hyperlipidemia and fatty liver diseases are all brought by obesity (Khang *et al*., 2011). An iron-rich diet dramatically reduces the quantity of insulin needed to bring blood sugar levels down in obese individuals. It also helps in weight loss by lowering LDL (Low density lipoprotein) cholesterol levels. Because capsaicin has an antiobesity impact, it has been shown to significantly change proteins associated with thermogenesis and lipid metabolism. Consuming the mild spicy sweet pepper, CH-19 can help reduce body weight. Research indicates that a solitary dosage of CH-19 sweet pepper raises body temperature and oxygen consumption, consistent ingestion of this chilli can facilitate weight loss and the combustion of stored fat (Arora *et al*., 2011). An important contributing element to the development of obesity is chronic low-grade inflammation (CLGI). The systemic knockdown of gluten produces glucose intolerance in obese individuals, destroys pancreatic β-cells and impairs insulin function. A study by Kang *et al*. (2011) found that the dietary capsaicin dramatically decreased the number of families that produce liposaccharides (LPS) and decreased high-fat diet induced CLGI linked to antiobesity characteristics. Moreover, it has been discovered that capsaicin suppresses hunger. In fact, there is evidence to support the beneficial effects of capsaicin on metabolism and weight control (Zhang *et al*., 2023). Due to their antiobesity properties, pigments like β-carotene and β-cryptoxanthin have been extensively studied; they have been linked to decreases in body weight, adipose tissue mass, adipocyte hypertrophy, blood lipid concentrations and the suppression of adipogenesis (Bonet *et al*., 2016). By encouraging the oxidation of fatty acids in adipocytes and other tissues, β-carotene appears to reduce obesity. According to reports, the anti-obesity action of β-carotene is only observed when it is transformed into vitamin A (Villa-Rivera *et al*., 2020). Research has shown that capsaicin can improve fat oxidation and raise the rate at which energy is expended. The bioactive ingredients in capsicum may aid in maintaining weight after a hypocaloric diet. For those with hyperlipidemia and/or obesity, taking capsaicin one hour before low-intensity exercise is advantageous since it stimulates lipolysis (Hernandez Perez *et al*., 2020). Capsaicin may help to burn stored fat by promoting thermogenesis which may support weight loss attempts. It might lessen cravings and calorie consumption which would aid in achieving weight control objectives. Furthermore, studies have indicated that capsaicin may lessen appetites for meals that are fatty, sweet or salty, which may lead to a general decrease in food intake (Rastogi *et al*., 2024). It is crucial to remember that although capsaicin may help to regulate appetite and metabolism, it should not be viewed as a miracle cure for weight loss. It can be seen as a single part of an all encompassing weight loss plan that also consists of a healthy diet and frequent exercise.

4.3 Anti-inflammatory agent

Among the many phytochemicals found in chilli, capsaicin exhibits anti-inflammatory properties. Additionally, anthocyanin, a pigment has anti-inflammatory properties. Capsaicin can both stop the spread of pro-inflammatory cytokines and lessen the inflammatory reactions that antigens elicit (Spiller *et al*., 2008). The neuropeptide substance P, which is linked to inflammatory processes, is strongly inhibited by capsaicin. It reduces inflammation because it increases blood flow to that location (Zayachkivska *et al*., 2005). Capsaicin delayed the onset of arthritis and decreased paw inflammation in animals. The anti-inflammatory properties of chilli shield lung tissues as well. The antioxidant properties of chilli may be associated with the flavonoid and total phenolic component concentrations. Thus, potential anti-inflammatory chemicals found in capsicum may serve as models for new developments in medicinal chemistry (Chakrabarty *et al*., 2017). When combined with other spices, capsaicin's anti-inflammatory properties could be amplified. This outcome emphasizes the possible advantages of mixing spices. It would be interesting to discover if the combination of spices in chilli powder produces better outcomes than the dried, ground chilli pepper alone. According to Vasanthkumar *et al*. (2018), pre-treating mice with a mixture of capsaicin and curcumin (primary active component of turmeric) provided superior protection against Lipopolysaccharide (LPS)-induced inflammation than did by capsaicin alone. This outcome emphasizes how mixing spices may have positive effects (Garnier and Shahidi, 2021). Carotenoids present in chilli have anti-inflammatory properties through downregulating pro-inflammatory chemicals, shielding membranes from oxidative damage, and increasing the activity of antioxidant enzymes (Honarvar *et al*., 2017). A carotenoid extract from chilli, which contains violaxanthin, β-cryptoxanthin and β-carotene has been found to have analgesic and anti-inflammatory activity. This effect is likely due to the inhibition of local prostaglandins (Villa-Rivera *et al*., 2020).

4.4 Anticancer properties

Capsaicin exhibits anticancer action, just like many other dietary phytochemicals. It modifies the expression of many genes that cause tumor cells to stop growing and encourage apoptosis. These benefits have been shown in a variety of cancer types, including prostate, breast, pancreatic, hepatic, colon and many others, without causing harm to healthy cells. Though, the exact processes by which capsaicin achieves these effects are still being investigated, they seem to include intracellular Ca^{2+} build-up, the production of reactive oxygen species and alteration of the potential of the mitochondrial membrane (Zhang *et al*., 2024). The significant antiproliferative impact of capsaicin on cultured human prostate cancer cells and the fundamental process by which chillies have an anticancer impact seems to be connected to: i) Triggered suicide of primary cell lines of prostate cancer, ii) Prostate-specific antigen (PSA) expression is delayed and iii) PSA transcription is inhibited causing a rapid decline in PSA levels (Mori *et al*., 2006). Certain compounds such as aflatoxin, vinyl carbonate, benzopyrine, various nitrosamine enzymes and aflatoxin may become more carcinogenic due to the presence of cytochromes which are live enzymes. These enzymes (cytochromes) are inhibited by capsaicin which protects against cancer (Surh and Lee, 1995). Additionally, it has been discovered that capsaicin can destroy prostate cancer cells and prevent the migration of Breast cancer cells (Oh *et al*., 2010). Even the DNA can be attacked by capsaicin metabolites such as reactive phenoxy radicals which can cause mutagenicity and malignant transformation (Arora *et al*., 2011). The variety of actions that capsaicin has on cancer cells including its ability to cause programmed cell death, impede cell division, block the development of new blood vessels and potentially stop the cancer from spreading to other areas of the body, offer a promising foundation for additional research. Recent decades have seen the development of new data confirming capsaicin's anticancer effects in particular carcinogenic compounds. Based on numerous studies, it has been established that pigments like β-cryptoxanthin, neoxanthin, zeaxanthin, capsanthin, capsorubin, and lutein can reduce oncogene signaling which cause cancer cells to undergo apoptosis, control the progression of the cell cycle, dynamically adjust the redox balance, prevent tumor-specific angiogenesis, manage tissue invasion and metastasis, alter gap junction intercellular communications, and alter medication resistance (Shin *et al*., 2020). The synergistic effect of capsaicin with other active components reduces its anticancer efficacy compared to extracts from chilli plants (Zheng *et al*., 2016). Potential application of capsaicin in cancer therapy with other chemotherapeutic medications is enhanced by its interactions with other cancer-preventive substances (Hernandez Perez *et al*., 2020). Capsaicin is a good option for specifically identifying and eradicating aberrant cells, which is a crucial component of cancer treatment since it can trigger pathways that lead to programmed cell death. Potential of it for cancer treatment agent is further enhanced by its inhibitory effects on cell proliferation (Radhakrishna *et al*., 2024).

Table 4: The antitumorigenic properties of capsaicin in a variety of cancer cell or cell lines

S.No.	Type of cancer	Cell line utilized	Impact	Reference
1.	Gastric cancer	AGS, HGC-27, SNU-668	Apoptosis, inhibition of cell proliferation	Park *et al*., 2014
2.	Breast cancer	T47D, MCF-7, SKBR-3, MDA- BT-474, MCF10A, BT-20, MB231	Decreased mitochondrial membrane potential, cell-cycle arrest, apoptosis	De-Sa-Junior *et al*., 2013
3.	Pancreatic cancer	AsPC-1, BxPC-3, PANC-1	Apoptosis	Zhang *et al*., 2013
4.	Colon cancer	SW480, CT-26, Lo Vo, HT-29, CoLo320, Colo205, HCT-116	Cell cycle arrest, apoptosis, changes in cell morphology, DNA fragmentation	Yang *et al*., 2013
5.	Prostate cancer	DU-145, LNCaP, PC-3	Apoptosis, dissipation of mitochondrial inner transmembrane potential	Wang *et al*., 2015

4.5 Analgesic activity

Capsaicin is approved as a remedy for osteoarthritis pain. Back pain can be lessened with the application of capsaicin cream or plaster. Additionally, capsaicin is beneficial for headaches, including migraine headaches. It is also effective in treating the discomfort brought on by cancer. The pharmaceutical industry produces capsaicin because research has shown it to be an effective pain reliever for a variety of pain conditions. Additionally, capsaicin is employed in neuropharmacological research on the management of pain and thermoregulation, particularly in cases where the illness or failure of the nervous system results in a patient's being bedridden (Patowary *et al*., 2017). The active component of many painkillers, capsaicin, is a naturally occurring analgesic that relieves joint and headache pain as well as pain from diabetes and arthritis. Substance P, a component of the body's pain-and-inflammatory chemistry, is blocked by capsaicin. Our brain releases endorphins in reaction to the burn, which are uplifting chemicals and the body's natural analgesics (their effects are comparable to those of morphine). In terms of medicine, it's one of the most effective local painkillers on the market and is frequently used to treat the discomfort associated with shingles, arthritis, toothaches and surgical scars. Capsaicin-containing ointments and lotions are also applied externally to relieve itching and nerve discomfort. Although, a single application of capsaicin may not lessen pain, several applications cause analgesia. The skin absorbs topical capsaicin quickly and efficiently. It is available in many formulations (creams, gels, and patches) and in doses between 0.025% and 0.15% (Chung and Campbell, 2016). Numerous clinical studies demonstrate the effectiveness of capsaicin in treating neuropathic and musculoskeletal pain with or without inflammatory components. It was determined that the effectiveness of the capsicum therapy over the place was statistically and clinically significant. For example, when capsaicin was given topically for one month to individuals with postherpetic neuralgia, some of them experienced pain relief with no serious side effects, with the exception of a few instances where they experienced an irregular, localized burning sensation. The women who undergo a mastectomy were treated with topical capsaicin (0.025%), following a four week course of treatment reported significant pain alleviation. Despite its irritability, it also reduced surgical pain and has adjuvant properties (Aitken *et al*., 2017). Considering all the available data, capsaicin may establish itself as a primary pain reliever and be used in conjunction with other pain management strategies.

4.6 Gastroprotective agent

The consumption of chilli kills microorganisms in the stomach, preventing the development of ulcers. Chilli causes the stomach to secrete more mucus and a buffering protective solution (Zayachkivska *et al*., 2005). Capsaicin has antibacterial properties, especially against *Helicobacter pyroli* bacterium, which is the cause of stomach ulcers (Lanker *et al*., 2011). It has been demonstrated by research that, a local defensive mechanism against stomach ulcers involves capsaicin-sensitive sensory nerves. In order to maintain the integrity of the gastrointestinal mucosa against harmful interventions, the gastrointestinal system also contains capsaicin-sensitive sensory nerves. Low concentrations of chillies stimulate the sensitive sensory nerves associated with capsaicin (Yeoh *et al*., 1995). The effects of capsaicinoids on the mucosa of the gastrointestinal tract can vary based on the dosage and length of time taken for therapy (Arora *et al*., 2011). Certain species of capsicum have been shown to facilitate the breakdown of starchy foods by increasing salivary amylase activity and the release of digestive enzymes from the liver, pancreas and small intestine. Chilli has been used in traditional medicine to treat a variety of gastrointestinal issues, including gastric ulcers, dyspepsia, loss of appetite and gastroesophageal reflux disease. More than 200 constituents have been found in chilli and some of its active constituents have been shown to have a number of positive effects on a variety of gastrointestinal disorders, including decreasing symptoms of gastroesophageal reflux disease (GERD), promoting digestion and gastric mucosal defense, inhibiting gastrointestinal pathogens, ulceration and cancer and regulating gastrointestinal secretions and absorptions (Maji and Banerji, 2016). Several investigations have revealed that the gastrointestinal system may suffer from extended exposure to high dosages of capsaicin. Enhancing the clinical efficacy of capsaicin based treatments thus requires investigating the minimal effective doses needed to achieve the intended therapeutic effects and limiting the potential side effects (Zhang *et al*., 2024).

4.7 Effects on cardiovascular diseases

Capsicum extract is used as a cardiotonic in southern and central Italy to enhance heart muscle contraction and blood pressure maintenance (Meghvansi *et al*., 2010). It has been discovered that capsaicin possesses characteristics that may reduce the risk of cardiovascular diseases. It might inhibit the functions of clotting factors VIII and IX and platelet aggregation, both of which are involved in the formation of blood clots. Capsaicin alters the fluidity of platelets by penetrating their plasma membrane and influencing platelet function. Research indicates that capsaicinoids, which includes capsaicin itself, may be helpful to heart health and may present new therapeutic possibilities for diseases like atherosclerosis, myocardial infarction, hypertension and coronary heart disease (Rastogi *et al*., 2024). Enhancing low density lipoprotein (LDL) resistance to oxidation is one of capsaicin's unique effects (Baruah *et al*., 2014). An essential stage in the development of atherosclerosis is LDL oxidation. Capsaicin has been shown to both delay and slow down LDL oxidation. Chipotle eating on a regular basis for four weeks was found to lower blood lipoprotein resistance to breakdown in both men and women. These results imply that capsaicin may benefit cardiovascular health by increasing LDL particle stability and possibly lowering the incidence of problems associated with atherosclerosis. By lowering the body's levels of free radicals and chelating peroxidation processes, vitamins C and E have strong antioxidant activity and lower the risk of cardiovascular illnesses (Hernandez Perez *et al*., 2020).

4.8 Inhibition of bacterial growth

It was discovered that capsaicin inhibited the growth of MtzR and MtzS strains *in vitro*. For people who refuse to take synthetic antibiotics and for strains of bacteria resistant to antibiotics, capsaicin may be a helpful treatment (Zeyrek and Oguz, 2005). The U.S. Food and Drug Administration (FDA) reports that a number of food-borne diseases are dangerous to the general public and especially dangerous to expectant mothers. According to Argaez *et al*. (2009), the well-known foodborne pathogens are *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Bacillus cereus* and *Enterobacter aerogenes*. These food borne pathogens can be killed by capsaicin.

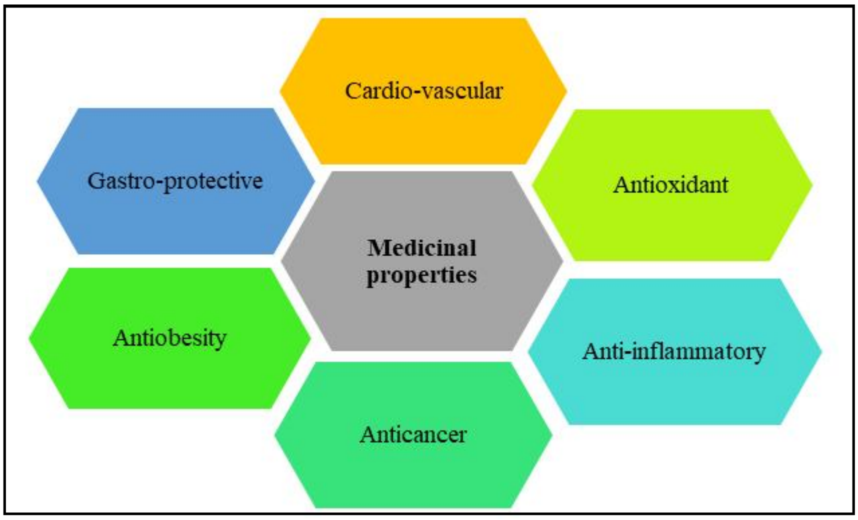


Figure 1: Medicinal properties of chilli.

Table 5: Pharmacological applications of different parts of chilli

Part used	Chemical compound	Effects	Reference
Fruit	Vitamins A, C and E	● Decline the health problems caused by free radicals. ● Helps in synthesis of red blood cells. ● Inhibits early senescence of skin and used for producing some natural skin oils. ● Lowering the risk of lung cancer, stomach cancer and prostate cancer.	Diaz-Laviada, 2010
	Capsaicin	● Declines the abdominal acid output and intestinal mucosal inflammation. ● Has anti-inflammatory, antiobesity and pain-relieving properties	Kwon *et al*., 2013
Seeds	Capsaicin	● Essential oil is effective pain reliever in joint and muscle aches. ● Increases hair growth. ● Accelerates blood circulation. ● Helps in wound healing.	Jarret *et al*., 2013
Leaves	Capsaicin	● Decreases the risk of cancer, cataracts, cardiovascular problems and macular degeneration.	Chakrabarty *et al*., 2017

5. Health risks

While chilli and its constituents have been found to be safe in most investigations, there have been reports suggesting that chilli may increase the risk of cancer. Capsaicin may be related to skin cancer according to Hwang *et al*. (2010). There is a correlation between excessive use of red chilli and high incidence rates of gallbladder cancer (GBC) in Bolivia, Peru, and Chile (Asai *et al*., 2012; Tsuchiya *et al*., 2011). The mutagenesis effects of capsaicin on microbes and other species have yielded conflicting results. On the other hand, capsaicin was thought to be either mildly mutagenic or non-mutagenic. Additionally, research on probe organisms has revealed that chilli consumption may have a carcinogenic or carcinogenic effect (Szallasi and Blumberg, 1999). Furthermore, there is no proof that capsaicin or other synthetic substances in chilli are responsible for the cancer-causing effects. Similarly, SCF36 observed that upper digestive tract cancer was linked to increased chilli consumption (25-200 mg/day) in Mexico and India. In contrast, the maximum daily consumption of paprika and mild chillies in Europe was calculated to be 1.5 mg and the risk of stomach cancer was not affected by this modest intake of chilli.

On the other hand, aflatoxin contamination rather than the capsaicin action may be the cause of the dangers. When Tssuchiya *et al.* (2011) investigated the effects of red chilli and pure capsaicin as mutagens and they discovered that capsaicin did not induce mutagenesis. They came to the conclusion that the aflatoxin contamination of the red chillies rather than the chemical in the chilli, may have been the cause of the mutagenesis. Aflatoxin is a highly carcinogenic chemical that is often produced in trace amounts. Aflatoxin exposure results in a variety of problems in both humans and animals. It results in kwashiorkor which slows down the digestion of micronutrients, immunodeficiency and immunosuppression in children, liver illness in those with hepatitis B or C and liver disease. In some countries, aflatoxin contamination of dry chilli has been observed. In 50% of the samples examined in Nigeria, aflatoxin levels were judged to be 50% greater than is reasonably achievable (Dhwaj and Singh, 2011).

6. Conclusion

The chilli is a crucial component in Indian cuisine. A tiny chilli fruit is a great source of minerals and vitamins A, C, B_2, B_6 and E. The only crop that produces the alkaloid component that gives anything its heat is capsicum. Capsaicinoids are a vital component that the pharmaceutical business use and is beneficial for neurology. Pharmacological characteristics of chilli includes anticancer, anti-inflammatory, antioxidant, antihemorrhoidal, antiobesity, gastroprotective, antipyretic, analgesic and relief from diabetes, arthritis, sinusitis, rhinitis and migraines to name a few. There are several health advantages to include even a modest amount of chilli in our daily diet. The most used flavour and sauce in the world, chilli is highly valued for its sharpness and ability to add a unique flavour to a variety of cooking methods. Despite the lack of evidence supporting its use as a medicinal spice, chilli has a long history of production and use in Eritrea. People all throughout the world have come to agree that chilli has medicinal and wellness effects. Chilli's medical applications and health advantages are also widely known. Research is still necessary, nevertheless, on matters pertaining to development, efficacy, safety and possible hazards, particularly those involving aflatoxin exposure. On the other side, by eliminating discoloured fruits and enhancing drying techniques, farmers can help lower aflatoxin contamination at the farm level.

A lot of attention has been paid to capsaicin in recent decades because of its biological and functional characteristics. Capsaicin showed promise as an antioxidant that might be employed to scavenge free radicals like DPPH and ABTS. Numerous research findings have demonstrated capsaicin's antibacterial action against a range of foodborne pathogens and bacteria that cause food deterioration, particularly *Staphylococcus aureus* and *Escherichia coli*. Furthermore, several investigations have documented capsaicin's inhibitory action on the synthesis of mycotoxins like aflatoxin and ochratoxin. However, this substance is susceptible to a variety of environmental factors, including light, heat and ultraviolet light. In conclusion, in addition to culinary uses and as food ingredient of the capsicum goods at the global level, a considerable number of nutraceutical and medicinal products based on the components generated from the fruits of this highly valued crop will be accessible shortly.

Conflict of interest

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

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Citation S. Devi Esakkiammal, R. Balakumbahan, K. Nageswari, G. Anand, S. Rajesh and S. Santha (2024). A comprehensive insights on pharmacological and nutritional benefits of Chilli (*Capsicum annuum* L). Ann. Phytomed., 13(2):206-217. http://dx.doi.org/10.54085/ap.2024.13.2.20.