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BHUT JOLOKIA (*CAPSICUM CHINENSE* JAQC): A REVIEW

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ABSTRACT: The northeast region of India, considered as 'hot spot' of biodiversity, having unique ecological environment with hot and high-humidity conditions, has given rise to the world's hottest chilli, 'Bhut jolokia or Bih jolokia', which is at least two times hotter than Red Savina Habanero in terms of Scoville heat units (SHU). The Assamese word "bhut" refers to the typical large pod size of the plant, while the term "bih" means "poison" indicating the high hotness in the fruits of the plant. It is extensively grown in North Eastern region of India, predominantly in the states of Assam, Nagaland, Manipur and Mizoram since ancient time. The main pungency principle of Bhut jolokia (*Capsicum chinense* Jacq.) is capsaicin (8-methyl-N-vanillyl-6-nonenamide) and its analogs collectively known as capsaicinoids synthesized in the epidermal cells of placenta of the fruit, and possesses anti-inflammatory and antioxidant activities. This review gives an update mainly on the pharmacological activities of Bhut jolokia (*Capsicum Chinense* Jacq.), benefits and toxicity of capsaicin.

INTRODUCTION: *Capsicum* is a herbaceous plant belonging to the family Solanaceae. The genus *Capsicum* comprises over 200 species among which five common cultivated species include *Capsicum annum* L., *Capsicum frutescens* L., *Capsicum chinense* Jacq., *Capsicum baccatum* L., and *Capsicum pubescens* L. These are indigenous and well distributed in Mexico, Australia, Britain, America, Sri Lanka, Bangladesh and India¹.

Bhut jolokia mainly belongs to the species *Capsicum Chinense* Jacq. *Bhut jolokia* placed among hottest chillis with '*Trinidad Moruga Scorpion*' is an indigenous cultivar growing in Brahmaputra flood plain of Assam, Nagaland, Manipur and other part of Northeast India.

The '*Bhoot Jolokia*' came in highlight when Tezpur (Assam) based Defense Research Laboratory declared it is as hottest chilli of the world which replaced the world famous Red Savina Habanera (scientifically *Capsicum chinense*). The traditional '*Bhoot Jolokia*' or '*Naga king*' chilli has several vernacular names like '*Naga Jolokia*', '*Bih Jolokia*', '*Dorset Naga*', '*Raja Mirchi*', '*Borbih Jolokia*', '*Nagahari*', '*Ghost chilli*', '*Naga Viper chilli*', '*Poison chilli*' etc². It was earlier thought to be a hybrid of *Capsicum frutescens* and *Capsicum chinense* on the basis of randomly amplified polymorphic DNA (RAPD) analysis³. However, it has recently been described as a distinct species (*Capsicum assamicum*) on the basis of morphological properties, molecular phylogeny of the internal transcribed spacer (ITS) region and differential proteomic analysis⁴.

In 2007, Guinness World Records certified that the *Bhut jolokia* or ghost pepper was the world's hottest chilli pepper, 401.5 times hotter than Tabasco sauce; the ghost chilli is rated at more than 1 million Scoville heat units (SHUs). Classic

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Tabasco sauce ranges from 2,500 to 5,000 SHUs. However, the bhut jolokia was shortly superseded by the infinity chilli in early 2011, followed by the Naga Viper, then later the trinidad moruga scorpion in 2012, and finally the "Carolina Reaper" on August 7, 2013⁵.

In 1902, Wilbur Scoville had developed this method and so the heat value was expressed as Scoville Units. The hot sensation of *Bhut jolokia* is caused by a compound 'capsaicin' localized mainly in the placenta and the flesh of a chilli fruit⁵. In Scoville's method, a measured amount of alcohol extract of the capsaicin oil of the dried pepper is produced, after which a solution of sugar and water is added incrementally until the "heat" is just barely detectable by a panel of (usually five) tasters; the degree of dilution gives its measure on the Scoville scale.

A sweet pepper or a bell pepper, containing no capsaicin at all which has a Scoville rating of zero, meaning no heat detectable. The heat of chilli is tested using spectrometer or HPLC (High Pressure Liquid Chromatography) to rate the chillies in Scoville units which indicate parts per million of capsaicin. The Scoville units of pure capsaicin are between 150,00,000-160,00,000⁶.

Plant description:

Capsicum chinense Jacq. is a self pollinated plant (**Fig.1.a**), however, considerable cross pollination (up to 10%) may occur when insect population is high. It behaves as a semi-perennial herb if grown under optimal condition. The plant grows to a height of 57-129cm at 6 months. Under semi perennial situation it may grow even taller. The stem is green with anthocyanin (dark color pigments) pigmentation on the nodes. Leaves are ovate in shape and the surface has the characteristic crinkle look. It has pendant, with creamy white corollas, often with a touch of light green and has clustering flowering habit with 2-3 flowers per node but at maturity there are rarely more than two fruits per node. The panthers are blue while the filaments are purple. The elongated fruits are 5 to 7 cm in length, 2.5 to 3.0 cm in diameter, with an undulating surface¹ (**Fig.1.b**). There are at least three distinct colours found in *Bhut jolokia* like light red, dark red and orange.

The following trends have been recorded such as⁷:

- Young light green coloured fruits turn orange at maturity⁷.
- Young dark green coloured fruits turn dark red at maturity⁷.
- Young green coloured fruits turn light red at maturity⁷.
- Young dark green coloured fruits turn dark chocolate at maturity⁷.

The fruit possess 4-5 hollow locules and bears about condition, in a single season a plant produces around 15-20 full sized fruits and 10-14 smaller fruits¹.



FIG. 1: (A) PICTURE OF BHUT JOLOKIA PLANT
(B) PICTURE OF BHUT JOLOKIA FRUIT

Traditional medicinal use:

Traditionally the fruits are mostly used for curing many human ailments. It is consumed as green or fully ripe fruits, either raw or cooked with vegetables ⁷.

- **Asthma:**

The hot principal of bhut jolokia, Capsaicin can reduce asthma. Clinically it has already been proved that capsaicin has the ability to dilate blood vessels thus giving relief in chronic congestions. But it should be consumed regular in low quantities ⁷.

- **Gastro-intestinal abnormalities:**

Capsaicin stimulates the secretion of saliva and gastric juice and also protect the mucous membrane from the mechanical and chemical damage. Here also regular consumption, but in small quantity is practiced ⁷.

- **Toothache and muscle pain:**

Hot infusions of the fruits are used for toothache and muscle pain as the hot principal of capsicum has the ability to alleviate the external pain in muscle. But the infusion should never be applied on injured tissues ⁷.

- **Removal of puss from boils:**

The tender leaves are ground to a fine paste and applied as thin coat over boils. This helps in easy removal of puss from boils ⁷. The leaves of *Capsicum chinense* also use for the ailments like headache and night blindness.

- **Arthritis:**

Paste of leaves are applied locally for the treatment of arthritis ⁶.

Besides having medicinal uses the fruits are sliced and made into pickles and preserved easily for months. It is also used as a remedy to summer heat, presumably by inducing perspiration.

Chemical composition:

Several extensive studies have been carried out to identify the various chemical constituents of

Capsicum chinense fruit. Compounds known as capsaicinoids cause the spicy flavor (pungency) of chilli pepper fruit.

The primary capsaicinoid in chilli pepper is capsaicin, followed by dihydrocapsaicin, nordihydrocapsaicin, homodihydrocapsaicin and homocapsaicin (**Fig.2**). Capsaicin and dihydrocapsaicin account for approximately 90% of capsaicinoids in chilli pepper fruit, are the two most potent capsaicinoids and their molecules differ only in the saturation of the acyl group ^{8, 9, 10}. The gland on the placenta of the fruit produces capsaicinoids ¹¹.

Liu and Nair (2010) quantified the concentration of capsaicin and dihydrocapsaicin in *Bhut jolokia* is 5.36%, which is about 338 and 18 times greater than in Scotch Bonnet and Jalapeno respectively ¹². The fruit is a good source of various natural colorants such as anthocyanins, carotenoids; and nutrients like ascorbic acid and minerals etc. ¹³.

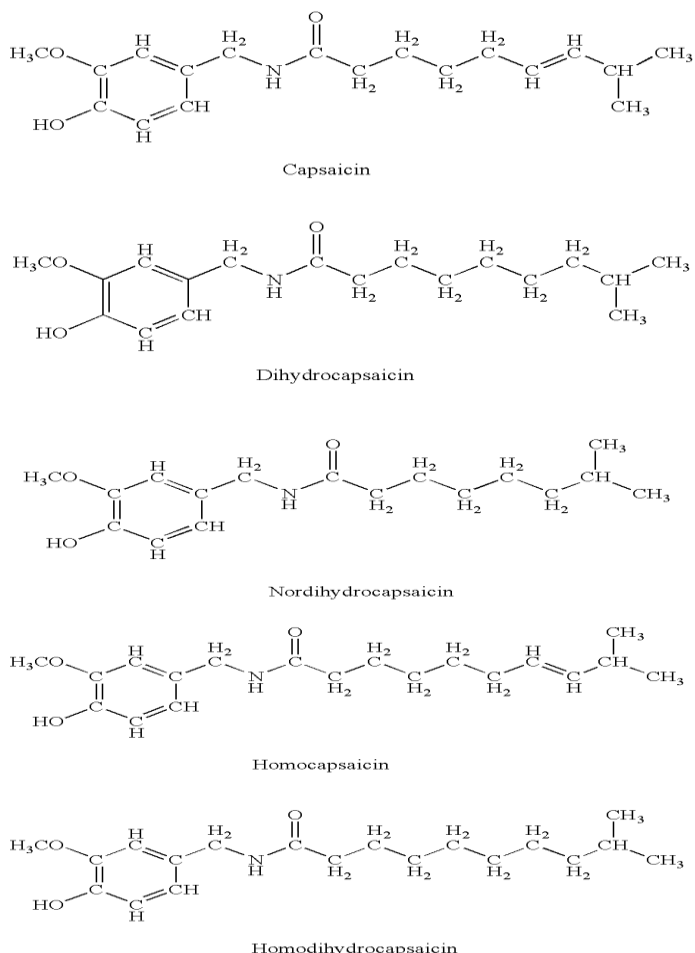


FIG.2: CHEMICAL STRUCTURE OF DIFFERENT CAPSAICINOIDS

Pungent principle of *Bhut Jolokia*:

The hotness or pungency of *bhut jolokia* is caused by a compound 'capsaicin' localized mainly in the placenta and the flesh of a chilli fruit⁶. Chemically it is a fat soluble phenolic compound which imparts pungent taste even if it is diluted to one part in eleven million parts of water¹⁴. Composition of capsaicin may vary among different varieties of same species and with fruit of a single variety. The pungency is influenced with the weather conditions such as heat wave and it increases with the growth of the maturity of fruit¹¹.

When placed in oral cavity, capsaicin diffuses across the lingual epithelium and selectively binds to transient receptor potential vanilloid 1 (TRPV1), previously known as the vanilloid receptor, which is mainly expressed on heat and pain sensitive sensory neurons. This receptor is a nonspecific calcium channel and when capsaicin binds to it, the channel opens¹⁵. The initial influx of calcium leads to neurotransmitter release and sensations of warmth with low concentrations of capsaicin and burning pain with higher concentrations. Prolonged activation results in depletion of the presynaptic neurotransmitter, substance P, and desensitization causes reduced responsiveness to capsaicin¹⁶. Although the precise mechanisms are unknown, somatosensory experiences following ingestion of capsaicin vary between individuals¹⁷.

Benefits of Capsaicin:

The capsaicin found in capsicum species has been reported to have various pharmacological activities and some of the clinical applications are as follows:

Pain relief:

Topical capsaicin has been suggested as an effective pain management adjunct for rheumatoid arthritis, osteoarthritis, neuralgias, diabetic neuropathy, and other conditions including neural dysfunction, inflammation, and painful or itching cutaneous disorders resulting from surgery, injury, or tumors¹⁸.

Anti-inflammatory property:

Jolayemi and Ojewole in their recent study concluded that capsaicin possesses a dose dependent anti-inflammatory effect, which is

comparable to inhibition of inflammation produced by diclofenac¹⁹.

Anticancer activity:

Capsaicin has been reported to be effective, both in vitro and in vivo against the growth of prostate cancer cells²⁰.

In the cultured cells, capsaicin was able to block breast cancer cell migration and kill prostate cancer cells, and dihydrocapsaicin was reported to induce the autophagy in HCT116 human colon cancer cells^{21, 22, 23}. Natural capsaicin also shows inhibition of the growth of leukemic cells²⁴. Capsaicin represses the growth of various immortalized or malignant cell lines by induction of cycle arrest, apoptosis, autophagy, and also by the inhibition of cellular metabolic activation^{25-28, 21, 22}.

Weight reduction:

Shin and Moritani, have reported that consuming capsaicin 1h before low intensity exercise improved lipolysis and may therefore be a valuable supplement in the treatment of individuals with hyperlipidemia and/or obesity²⁹. The non-pungent CH-19 sweet pepper (the major source of natural capsinoids), showed an attractive option for weight loss. It has been shown that a single dose of CH-19 sweet pepper could increase the body temperature and oxygen consumption while repeated CH-19 sweet pepper intake could reduce the body weight and promote the fat oxidation³⁰. Recently, another study reported that topical application of capsaicin to obese mice limits fat accumulation in adipose tissues and may reduce inflammation and increase insulin sensitivity³¹.

Hepatoprotective effects:

The potential hepatoprotective utility of capsaicin was studied against carbon tetrachloride (CCl₄)-induced liver injury in rats by disturbing the antioxidant system, generation of lipid peroxidation (LPOs) and activation of caspase-3 where capsaicin has shown hepatoprotective activity against CCl₄-induced liver toxicity³².

Gastrointestinal benefits:

Capsaicin in the gastrointestinal tract have produced controversial results and clearly indicates

the need for further clinical trials to better define effective dosages. At low concentrations (0.13–160 μM) in rats, capsaicin is reported to protect the gastric mucous against ulceration by ethanol³³, whereas when administered at high concentrations (1 or 2 mg/mL) in rat stomachs it is reported to worsen damage to the gastric mucous caused by ethanol or aspirin³⁴.

In a study involving 84 healthy human subjects, capsaicin was found to have protective properties against ethanol- and indomethacine-associated gastropathy, with a dose dependent decrease in base gastric acid output (ED50 for 400 μg capsaicin) and increased gastric emptying³⁵. A possible explanation is that capsaicin mediates the antiulcerous effect by vasodilation and increasing gastric mucous blood flow (GMBF) and this is mediated by nitric oxide and CGRP release by these TRPV1 bearing cells³⁵.

Bactericidal effect:

F.yildiz zeyrek et al. studied the *in vitro* activity of capsaicin on metronidazole-susceptible and resistant *Helicobacter pylori*. Here, capsaicin showed bactericidal effect even at lowest prepared concentration (25 $\mu\text{g}/\text{ml}$) and the best effect was seen at concentration of 50 $\mu\text{g}/\text{ml}$. Thus treatment with capsaicin may be a useful treatment for antibiotic resistant strains and for patients who do not wish to take synthetic antibiotics³⁶.

Recently, the antibacterial activity of capsaicin and capsaicin microemulsions were evaluated using Kirby-Bauer disk diffusion susceptibility tests against three common bacteria: *Staphylococcus aureus*, *Salmonella enterica*, and *Escherichia coli*. Both the pure capsaicin and capsaicin microemulsions are found to be active towards the three bacteria³⁷.

Cardiovascular activity:

Capsaicin can reduce the incidence of cardiovascular diseases by inhibition of platelet aggregation and the activity of clotting factors VIII and IX. Capsaicin can pass through plasma membrane of platelets and thus alter membrane fluidity. It has been reported that capsaicinoids have potential beneficial effects on the cardiovascular system to treat various

cardiovascular threats in human beings that include coronary heart disease, myocardial infarction, hypertension and atherosclerosis. Studies reveal that capsaicin has been able to increase the resistance of LDL to oxidation by delaying the initiation of oxidation and slowing the rate of oxidation. Consumption of chilli regularly for 4 weeks can increase the resistance of serum lipoproteins to oxidation in adult men and women⁶.

In a study of cardiovascular and metabolic effects of orally administered capsaicin in rats with the metabolic syndrome (MetS), reported that capsaicin did not improve lipid and glucose abnormalities in rats with the MetS. However, beneficial cardiovascular effects were observed³⁸.

Antioxidant effects of Capsaicin:

The antioxidant property of capsaicin in terms of inhibiting lipid peroxidation in rat liver³⁹ and in soybean phosphatidylcholine liposomal biomembrane has been reported⁴⁰. Capsaicin is observed to inhibit copper ion-induced lipid peroxidation of human LDL⁴¹. The data suggested that capsaicin is an effective antioxidant and offer protection against oxidation of human LDL.

In a study, Wistar rats administered capsaicin (3 mg/kg body weight) for 3 consecutive days showed a reduction of oxidative stress measured as malondialdehyde in the liver, lung, kidney and muscle and it is hypothesized that capsaicin can be a potent antioxidant even when consumed for a short period⁴².

Antidiabetic activity:

Capsaicin is also reported to have antidiabetic activity. Substance P, a neuropeptide released by capsaicin, has been shown to reverse diabetes in mice, but the effects to insulin secretion seem to be species dependent⁴³. Antidiabetic effect of caffeine and capsaicin on the blood glucose level of obese/diabetic model mice was found to decrease the blood glucose level of KK-A(y) obese/diabetic mice⁶.

New evidence supporting the use of capsaicin in a variety of clinical situations such as asthma, labor pains and delivery, Alzheimer's disease, promoting

skeletal muscle hypertrophy, Fibromyalgia, Reduced minimum inhibitory concentration (MIC) of ciprofloxacin has been identified. But these applications of capsaicin have not been well researched. Effectiveness of capsaicin in these conditions will form the areas of future research⁴⁴.

Toxicological aspects of capsaicin:

In contrast to the results of cellular and animal studies, several epidemiologic studies seem to indicate that consumption of hot peppers, which contain various levels of capsaicin, might be associated with an increased risk of cancer, and especially gastric cancer⁴⁵, skin cancer⁴⁶, colorectal cancer⁴⁷.

However, evidence for the effectiveness or safety of capsaicin use in pain relief is also controversial. Application of capsaicin to the skin causes an enhanced sensitivity to noxious stimuli, followed by a period with reduced sensitivity and, after repeated applications, persistent desensitization⁴⁸.

In a study of dermatological conditions Gooding et al. found no benefit in hemo dialysis induced pruritis, and idiopathic pruritis⁴⁹. Similarly, Li et al. found Capsaicin to be irritant when instilled intravesically⁵⁰.

Other unclear properties of capsaicin in different physiological systems are TRPV1 mediates the inflammation of the GI tract⁵¹, Platelet pro-aggregating effects⁵², No effect on energy expenditure or lipid oxidation seen^{53,54}.

Pharmacological action of *Bhut jolokia*:

Antioxidant and Anti-inflammatory activities:

Hot peppers are known for medicinally important capsaicinoids. Capsaicin (C) and dihydrocapsaicin (DHC) found in Bhut Jolokia, are compared with the commonly consumed hot peppers, Jalapeno (*Capsicum annum*) and Scotch Bonnet (*Capsicum chinense*). The concentration of C and DHC in Bhut Jolokia was 5.36%, which is about 338 and 18 times greater than in Scotch Bonnet and Jalapeno, respectively. In the same study, they have also isolated capsaicin (C) and dihydrocapsaicin (DHC) in pure form and determined lipid peroxidation (LPO) and cyclooxygenase (COX-1 and -2) enzymes

inhibitory concentrations. For the first time report of the quantification of capsaicin and DHC in *Bhut jolokia* was done, also comparison of capsaicinoids content in Bhut Jolokia with Jalapeno and Scotch Bonnet hot peppers and the COX and LPO inhibitory activities of C and DHC has been done¹².

Recently, Hazarika et al. isolated Capsaicinoid from *Capsicum chinense* and concluded that these compounds could have a better possibility as an antioxidant drug by inhibiting inducible nitric oxide synthase (iNOS) activity⁵⁵.

Antibacterial activities:

In a recent study, the acetonitrile extracts of *Capsicum chinense* fruits showed wide antibacterial activities against the human pathogens⁵⁶.

Anticancer activity:

Lebel et al. recently studied the antitumor potential of capsaicinoids extracted from Bhut Jolokia (*Capsicum chinense*) and found that exposure of HepG2 cells to acetonitrile extract, reduces cell viability. The capsaicinoids in the extract also suppressed the release of Lactate dehydrogenase (LDH), Nitric oxide (NO) and Lipid peroxidation (LPO) production at dose dependant manner. Thus, the study confirmed the anticancer property of the capsaicinoids in acetonitrile extract, through modulating the free radicals release and also established anti-inflammatory potential⁵⁷.

Gastric ulcer protective activity:

Evaluation on the ulcer protective activity of the ethanolic extract of *Capsicum chinense* Jacq and Ranitidine on aspirin induced gastric ulcer on albino mice were performed. The study showed *Capsicum chinense* Jacq has an ulcer protective effect similar to that of Ranitidine⁶.

Anti-arthritic activity:

A nanovesicle topical formulation prepared with the semipurified capsaicinoids extract of *Bhut Jolokia* demonstrated good anti-arthritic activity in rat model, superior to *Thermagel* (a marketed formulation of capsaicin) in the reduction of joint swelling and pain throughout the observation period. The nanovesicle formulation showed better

tolerability and acceptance on both animal and human models. This significant positive result with reduced irritant effect, suggest that it could be one of the choices for formulation development in anti-arthritic medicine⁵⁸.

CONCLUSION: Considering the importance of capsaicin in health and disease, and its commercial implications in the pharmaceutical and food industry, *Bhut jolokia* (*Capsicum Chinense* Jacq) offers great potential for future exploitation due to its high capsaicinoid content. So, further studies are needed to evaluate the toxicity of this fruit and its application in the field of medicine.

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