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The Medical Power of Capsaicin: Mechanisms, Applications, and Innovations

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Abstract

Introduction and Purpose: Capsaicin is an active alkaloid found in chili peppers (Capsicum spp.), exhibiting a wide range of biological effects. Its mechanism of action is primarily based on the activation of the TRPV1 receptor, which regulates processes related to pain, inflammation, metabolism, as well as the functioning of the cardiovascular and nervous systems. The aim is to review the current knowledge on capsaicin, with a particular focus on its mechanisms of action, current and potential medical applications, as well as to discuss the possibilities and challenges associated with its therapeutic use.

Materials and Methods: This article was developed based on a review of current scientific literature, including publications from databases such as PubMed and the results of clinical studies. Particular attention was given to the mechanism of action of capsaicin and its applications in various fields of medicine.

Results: Capsaicin has a wide range of applications in medicine, primarily as an analgesic in the treatment of neuropathic pain. In dermatology, it is used for treating psoriasis and chronic pruritus. In gastroenterology, its gastroprotective properties and effects on gut microbiota are being studied. In cardiology, it shows potential in regulating blood pressure and lipid metabolism, while in oncology, it is investigated for its role in inhibiting tumor growth and angiogenesis. Its neuroprotective properties in neurodegenerative diseases are also increasingly being explored.

Conclusion: Capsaicin exhibits tremendous therapeutic potential in various fields of medicine, ranging from pain management, skin diseases, and metabolic disorders to potential applications in oncology and neurology. Despite its many benefits, its use requires further clinical research to determine optimal dosages, efficacy, and long-term safety.

Keywords: Capsaicin; TRPV1 receptor; analgesic effect; anticancer effect; chili peppers; thermogenesis; neurodegeneration inhibition

Introduction

Capsaicin is an organic alkaloid belonging to the class of capsaicinoids, which are responsible for the characteristic hot, pungent, and sharp taste of chili peppers (Capsicum spp.). It is a lipophilic compound, soluble in organic solvents, alcohol, and oils, with a molecular formula of $C_{18}H_{27}NO_3$ and a melting point of 62°C. As the primary component responsible for the irritating effect of chili peppers, capsaicin interacts with pain and heat receptors, inducing a burning sensation and skin irritation without causing tissue necrosis.

The mechanism of action of capsaicin is based on its ability to bind to the TRPV1 (transient receptor

potential vanilloid 1) receptor, which plays a key role in the transmission of pain and thermal signals. The initial activation of this receptor leads to intense neuronal stimulation, followed by a prolonged refractory period that results in the desensitization of pain receptors. This effect is widely utilized in pain therapy, particularly in the treatment of neuropathic pain and chronic inflammatory conditions.

In addition to its analgesic properties, capsaicin exhibits a range of beneficial biological effects, including antioxidant, cardioprotective, anticancer, and thermogenic activities. Research suggests that it may also play a role in regulating metabolism and reducing body weight by influencing thermogenesis processes. Furthermore, there is evidence indicating that capsaicin can inhibit the activity of STAT3 (signal transducer and activator of transcription 3)[1], making it a potential candidate for further studies in anticancer therapies [2].

The first reports of the use of dried and ground chili peppers date back as far as 4000 BCE. In ancient times, they were used as a disinfectant-rubbed onto the skin after insect and rodent bites due to their antiseptic properties. In the northeastern regions of India, chili peppers were consumed in small amounts to alleviate digestive discomfort. Additionally, they were widely used as a natural pain reliever, particularly for treating tooth and gum pain.

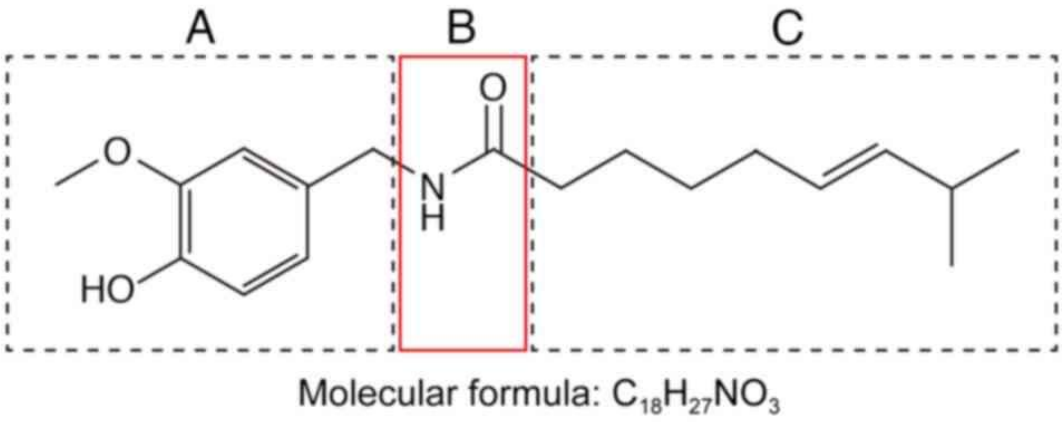
Over time, capsaicin found applications beyond traditional medicine. Its strong irritating properties were utilized in the defense industry for the production of pepper sprays, as well as in plant protection products and animal repellents. This compound was first isolated in 1816 by Christian Bucholz. Since its discovery, it has become an important component of homeopathic medicine, used in the treatment of severe pain and for soothing irritations.

Due to its wide range of biological effects, capsaicin has been the subject of extensive scientific research aimed at fully understanding its mechanisms of action and potential clinical applications. This article aims to present current data on the properties of capsaicin, its mechanisms of action, and its possible uses in medicine and pharmacotherapy.

Chemical Structure and Mechanism of Action of Capsaicin

Capsaicin ($C_{18}H_{27}NO_3$) is a hydrophobic, low-molecular-weight molecule composed of three main structural elements:

- **Vanilloid group** – responsible for interaction with the TRPV1 receptor,
- **Amide chain** – linking the vanilloid group to the hydrophobic segment,
- **Long-chain aliphatic fragment** – determining lipid solubility and permeability through cell



membranes (Figure 1).

Figure 1. Functionally important subdivisions of the capsaicin structure: (A) Aromatic ring, (B) amide bond and (C) hydrophobic side chain. [3]

It is a colorless, odorless substance that is soluble in organic solvents, alcohol, and fats. Due to its hydrophobic properties, it easily penetrates cell membranes, allowing it to interact with TRPV1 receptors present in the membranes of sensory neurons.

The TRPV1 receptor, belonging to the transient receptor potential (TRP) ion channel family, serves as a molecular sensor for various stimuli, such as:

- Capsaicin,
- Temperature changes (above 43°C),
- Lowered pH (< 6.5),
- Endogenous lipids and inflammatory factors.

Capsaicin acts as a selective agonist of TRPV1, leading to the activation of this ion channel. Upon binding, the channel opens, allowing the influx of calcium (Ca^{2+}) and sodium (Na^{+}) ions into the cell.

The sudden increase in intracellular calcium concentration initiates the depolarization of sensory neurons and the induction of action potentials, which are transmitted to the central nervous system. This mechanism is responsible for the sensation of intense burning and stinging at the site of capsaicin application.

The increased influx of Ca^{2+} into the cell also leads to the release of calcium from the endoplasmic reticulum and the activation of proteolytic enzymes. Prolonged activation of TRPV1 by capsaicin results in desensitization of the channel, leading to its long-term inactivity. This process occurs through:

1. **Inhibition of TRPV1 reactivation** – due to excessive calcium ion influx,
2. **Reduction of substance P** – a neuropeptide responsible for transmitting pain signals,
3. **Destruction of nerve endings** – leading to their temporary inability to conduct pain impulses.

This effect is therapeutically utilized in the treatment of neuropathic pain, arthritis, and postherpetic neuralgia-related pain.

Apart from its action on TRPV1 receptors, capsaicin exhibits several other biological effects:

- Capsaicin **modulates the inflammatory response** by inhibiting the production of pro-inflammatory cytokines such as IL-6, TNF-α, and PGE_2.
- It **reduces nitric oxide (NO) production**, thereby limiting the progression of inflammatory processes.
- Studies on animal models have shown that **low doses of capsaicin** may exert an **immunomodulatory effect** by increasing levels of the anti-inflammatory cytokine IL-10[4].

Capsaicin exhibits strong antioxidant activity, surpassing even melatonin. *Ex vivo* studies have demonstrated its ability to neutralize reactive oxygen species (ROS) and reduce the levels of lipid peroxidation products, such as malondialdehyde (MDA)[5].

Studies indicate that capsaicin may play a role in the treatment of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Stroke, Epilepsy, Depression.

Capsaicin affects neurons and glial cells, modulating both TRPV1-dependent and TRPV1-independent pathways.

Due to its ability to defunctionalize nociceptors, capsaicin has been applied in the treatment of chronic pain. The topical use of high concentrations of capsaicin effectively reduces hyperalgesia and allodynia in conditions such as: Postherpetic neuralgia, Neuropathic pain, Osteoarthritis, Migraines.

Medical Applications of Capsaicin

Pain Management

In recent years, capsaicin has gained recognition as a therapeutic agent in the form of creams, ointments, and high-concentration patches, which have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of neuropathic pain. Clinical studies have shown that applying an 8% capsaicin patch to the skin for 30–60 minutes leads to significant pain reduction for up to three months. After this period, nerve endings may regenerate, potentially causing pain recurrence and necessitating reapplication[6].

The use of 8% capsaicin patches is recommended for the treatment of:

- **Postherpetic neuralgia (PHN)** – significant pain reduction within 1–2 weeks after application,

- **Diabetic neuropathy** – effective in reducing foot pain and improving sleep quality,
- **HIV-induced neuropathic pain**,
- **Postoperative and post-traumatic neuropathy**,
- **Chemotherapy-induced peripheral neuropathy (CIPN)**[7].

There is evidence suggesting that capsaicin may be effective in the treatment of cluster headaches. Its mechanism of action involves reducing the release of substance P and desensitizing TRPV1 in nerve endings around the head and neck. Capsaicin patches offer an advantage over traditional pain medications due to their lack of significant systemic effects and prolonged action after a single application.
Despite its effectiveness, capsaicin creams require regular use, and common side effects such as erythema and skin burning may limit their long-term application.

Metabolic Disorders and Effects on Obesity

Studies have shown that capsaicin may promote weight loss by stimulating lipolysis in adipocytes, increasing energy expenditure, reducing appetite, and improving glucose tolerance[8].Due to its metabolic properties, capsaicin is being studied as a potential adjunct in the treatment of obesity and metabolic disorders, such as insulin resistance and type 2 diabetes. Its effects are based on the modulation of metabolic pathways, including the activation of brown adipose tissue, increased thermogenesis, and influence on the gut microbiome.[9] .Capsaicin activates TRPV1 receptors present in catecholaminergic neurons of the medulla oblongata, leading to the release of catecholamines such as adrenaline and noradrenaline. The stimulation of the sympathetic nervous system promotes:

- **Activation of brown adipose tissue (BAT)**, which is responsible for energy expenditure through heat production,
- **Increased lipolysis in white adipose tissue (WAT)**, contributing to the reduction of accumulated fat,
- **Elevation of metabolic rate**, resulting in increased calorie burning and weight loss.

Animal experiments have shown that a long-term diet enriched with capsaicin can lead to significant upregulation of TRPV1 expression in adipose tissue, enhancing its metabolic function and reducing adipogenesis[10].
Capsaicin may reduce hunger and regulate food intake through several mechanisms:

- Stimulation of satiety hormone secretion, such as glucagon-like peptide-1 (GLP-1), which suppresses appetite,
- Modulation of the gut microbiome, which influences nutrient absorption and lipid metabolism,
- Increased intestinal permeability, which may affect the interaction between gut microbiota and energy metabolism[11].

Capsaicin influences fat metabolism by:

- Inhibiting adipogenesis – limiting the differentiation of preadipocytes into mature fat cells,
- Increasing fatty acid oxidation – accelerating lipid metabolism in adipose tissue and the liver,
- Reducing plasma triglyceride levels, which may lower the risk of obesity-related cardiovascular diseases.

Research findings suggest that capsaicin may improve lipid profiles, providing additional support for

its use in the treatment of metabolic disorders. Capsaicin is efficiently absorbed in the stomach and small intestine, where it activates local TRPV1 receptors. Stimulation of these receptors leads to increased intestinal blood flow, which may enhance digestive processes.
Studies have shown that capsaicin lowers fasting glucose levels, increases insulin sensitivity, enhances the expression of glycolytic enzymes in liver cells, promoting better glucose utilization by the body. In C2C12 muscle cells, capsaicin increased glucose uptake through TRPV1-dependent calcium signaling activation[12].Similar effects were observed in HepG2 liver cells, where capsaicin increased the expression of genes involved in glucose metabolism, indicating its potential anti-insulin resistance effects[13]. Clinical studies have shown that capsaicin may lead to a reduction in Body Mass Index (BMI), Body Weight (BW), Waist Circumference (WC)- suggesting its potential application in obesity treatment.
Despite numerous evidence supporting capsaicin's beneficial effects on weight regulation and glucose metabolism, some studies indicate that capsaicin supplementation has no significant long-term impact on energy intake and appetite in humans. Further analysis is required to assess the long-term effects of capsaicin usage and determine its optimal therapeutic dosages.

Potential side effects of excessive capsaicin consumption should also be considered, including:
• Gastrointestinal irritation,
• Risk of intestinal mucosal inflammation,
• Hyperalgesia and increased pain sensitivity,
• Potential risk of gastric ulcers with prolonged use of high doses.

Capsaicin and Cancer

Studies have demonstrated that capsaicin can inhibit cancer cell proliferation, induce apoptosis, arrest the cell cycle, and limit angiogenesis and the metastatic potential of cancer cells. Capsaicin's ability to selectively eliminate cancer cells while having a minimal impact on healthy cells makes it a promising candidate for cancer therapy. The molecular mechanisms underlying this effect involve the activation of both TRPV1-dependent and TRPV1-independent signaling pathways, regulation of calcium homeostasis, and modulation of gene expression related to cell proliferation and survival.

One of the key mechanisms of capsaicin's action is its ability to induce apoptosis in cancer cells through several molecular pathways:
• **Accumulation of calcium ions (Ca^{2+}) in the cytoplasm**, leading to cellular homeostasis destabilization,
• **Generation of reactive oxygen species (ROS)**, which damage the DNA of cancer cells,
• **Disruption of mitochondrial membrane potential**, resulting in the release of cytochrome c and activation of caspases,
• **Upregulation of pro-apoptotic proteins** such as **Bax and caspase-3**, along with the **inhibition of anti-apoptotic proteins** like **Bcl-2**.

Studies have shown that capsaicin is effective in inducing apoptosis in various types of cancer, including colorectal, pancreatic, liver, prostate, and breast cancer[14].

Capsaicin can arrest the cell cycle of cancer cells at different phases, thereby inhibiting their proliferation. This mechanism involves:
• **Regulation of cell cycle gene expression**, including **p21 and p27**,
• **Inhibition of cyclin-dependent kinases (CDKs)**, preventing cells from transitioning from one phase

of the cell cycle to the next,
• **Suppression of transcription factors** such as **NF-κB and STAT3**, which play a key role in cancer cell proliferation.

Capsaicin has the ability to limit angiogenesis by:
• Reducing the expression of pro-angiogenic factors, such as vascular endothelial growth factor (VEGF),
• Inhibiting the migration and proliferation of endothelial cells, preventing the formation of new blood vessels,
• Disrupting paracrine signaling between cancer cells and vascular endothelial cells, leading to reduced nutrient supply to the tumor.

Capsaicin exhibits antimetastatic properties, restricting cancer cells' ability to invade and colonize distant tissues through:
• **Reducing the activity of extracellular matrix metalloproteinases (MMPs)**, particularly **MMP-9**, which are crucial for basement membrane degradation and cancer cell invasion,
• **Regulating E-cadherin expression**, a protein responsible for maintaining cell-cell adhesion and inhibiting tumor cell migration,
• **Inhibiting signaling pathways that promote tumor invasion**, such as **PI3K/Akt and MAPK**[15].

Studies have shown that capsaicin may increase the effectiveness of traditional cancer treatments, such as chemotherapy and radiotherapy. These mechanisms include:
•Enhancing the sensitivity of cancer cells to chemotherapeutic agents, such as cisplatin and doxorubicin,
• Reducing cancer cell resistance to radiotherapy by modulating apoptotic pathways,
• Inhibiting DNA repair mechanisms, making cancer cells more susceptible to therapy-induced damage[16].

Despite promising research on the anticancer properties of capsaicin, there are also controversies regarding its potential side effects. Some studies suggest that high capsaicin intake may increase the risk of gastric cancer, particularly when combined with Helicobacter pylori infection. Excessive TRPV1 activation may stimulate cancer cell proliferation in certain types of tumors and the effects of capsaicin may be dose- and context-dependent, requiring further clinical research to determine its safety and efficacy.

Despite these challenges, capsaicin remains one of the most promising natural bioactive compounds with potential applications in oncology, offering new opportunities in the fight against various types of cancer.

Application in Gastroenterology

Although capsaicin is commonly associated with an irritating effect on the digestive system, growing research suggests that it may have both beneficial and potentially harmful effects on the gastrointestinal tract.

On the one hand, capsaicin supports digestive health by improving mucosal microcirculation, stimulating the production of gastroprotective neuropeptides, enhancing nutrient absorption, and

modulating gut microbiota. On the other hand, excessive exposure to capsaicin may cause irritation, inflammation, and increased gut sensitivity, which is particularly relevant in conditions such as irritable bowel syndrome (IBS) and gastroesophageal reflux disease (GERD).

The transient receptor potential vanilloid 1 (TRPV1) receptor plays a key role in mediating the effects of capsaicin in the gastrointestinal tract. Its activation leads to the release of neuropeptides, including:
• Calcitonin gene-related peptide (CGRP) – improves microcirculation and supports mucosal repair,
• Substance P – regulates inflammatory responses and gut motility,
• Nitric oxide (NO) – increases gastric mucosal blood flow, contributing to its protection.

Contrary to popular belief, capsaicin is not ulcerogenic; instead, it exhibits protective effects on the gastric mucosa. These mechanisms include inhibition of gastric acid secretion, stimulation of mucus and bicarbonate secretion, which neutralizes gastric acidity, improvement of microcirculation, promoting the healing of mucosal injuries.

Epidemiological studies have shown that populations consuming high amounts of chili have a lower risk of gastric ulcers compared to groups that avoid spicy foods.

In individuals with GERD (gastroesophageal reflux disease), capsaicin administration can have both beneficial and negative effects:
• Short-term administration of capsaicin may exacerbate heartburn symptoms,
• Long-term use may lead to TRPV1 desensitization, reducing sensitivity to reflux stimuli and alleviating symptoms.

Studies have shown that patients who consumed chili for several weeks experienced a decrease in heartburn frequency, suggesting that capsaicin may have therapeutic potential in GERD treatment through pain receptor desensitization[17].

Capsaicin can modulate the gut microbiome both directly and indirectly through:
• Antibacterial activity – inhibiting the growth of harmful Gram-negative bacteria, including lipopolysaccharide (LPS)-producing bacteria[18],
• Stimulating the growth of beneficial bacteria, such as Akkermansia muciniphila, which is associated with metabolic improvement,
• Altering the Firmicutes/Bacteroidetes ratio, which may influence lipid metabolism and body weight regulation.

Some studies suggest that a diet rich in capsaicin may promote better metabolic and immune regulation in the intestines [19].

In patients with IBS (Irritable Bowel Syndrome), capsaicin may have both beneficial and adverse effects:

- High TRPV1 expression in the intestine may contribute to visceral hypersensitivity and pain.
- Desensitization of TRPV1 receptors through chronic capsaicin use may lead to a reduction in pain symptoms.
- Long-term capsaicin use may influence the gut microbiota, potentially improving digestive functions.

Capsaicin shows potential therapeutic effects in the treatment of functional dyspepsia (FD) by desensitizing nerve fibers and reducing visceral hypersensitivity, regulating neurotransmitter levels, such as substance P, reducing inflammation in the gastrointestinal tract, inhibiting gastric acid secretion and oxidative stress.

Research suggests that capsaicin may be an effective adjunct therapy for FD, but further clinical studies are needed to determine the optimal dosage[20].

Despite its numerous benefits, capsaicin can cause adverse effects, especially when consumed in high amounts. These include irritation of the gastric and intestinal mucosa, exacerbation of reflux symptoms in some individuals, increased peristalsis and diarrhea, potential risk of visceral hypersensitivity in patients with IBS[21].
For this reason, the therapeutic use of capsaicin should be individually tailored to each patient.

Neuroprotective Effects

In recent years, increasing research has highlighted the potential application of capsaicin in the treatment of neurodegenerative diseases, such as Alzheimer's disease (AD) and Parkinson's disease (PD). These mechanisms include reducing oxidative stress, decreasing neuroinflammation, stimulating autophagy, and improving cognitive function. As a result, capsaicin may serve as a potential candidate for adjunctive therapy in neurological disorders.

Neuroinflammation is one of the key factors in the pathogenesis of neurodegenerative diseases.

Capsaicin may alleviate inflammation by:

- Reducing the production of pro-inflammatory cytokines, such as IL-6, TNF-α, and NF-κB.
- Regulating microglia, thereby reducing excessive activation of glial cells.
- Enhancing antioxidant activity, reducing reactive oxygen species (ROS), and improving mitochondrial function.

Disruptions in autophagy and the accumulation of abnormal proteins—such as beta-amyloid and tau protein in Alzheimer’s disease and alpha-synuclein in Parkinson’s disease—contribute to the progression of neurodegeneration. Research has shown that capsaicin induces autophagy in microglia, enhancing their ability to clear beta-amyloid, reduces tau protein hyperphosphorylation, which may slow down neuronal degeneration, increases alpha-secretase activity, reducing the production of toxic beta-amyloid plaques.

In transgenic mice with AD, capsaicin administration resulted in improved learning ability and reduced synaptic damage. It is suggested that capsaicin may act as a neuroprotective agent by enhancing calcium homeostasis and reducing amyloid toxicity.

Parkinson’s disease is characterized by the degeneration of dopaminergic neurons in the substantia nigra and the accumulation of pathological alpha-synuclein deposits. Capsaicin administration in mice with PD alleviated symptoms of the disease and increased dopaminergic neuron survival, suggesting its potential as a neuroprotective agent.

Application in Dermatology and Skin Diseases

The mechanism of action of capsaicin in the skin is closely linked to the activation of TRPV1 receptors (transient receptor potential vanilloid 1), which are present in keratinocytes and nerve endings. Prolonged use of capsaicin leads to desensitization of these receptors, resulting in reduced inflammation and decreased perception of pain and itching.

Itching is a common symptom in dermatological diseases, and its mechanisms involve histamine, substance P, and protease-activated receptors (PAR-2).
Capsaicin exhibits anti-inflammatory effects by blocking the signaling pathways of pro-inflammatory cytokines, including IL-23/IL-17, IL-22, TNF-α, IL-6. This mechanism is particularly relevant for the treatment of inflammatory skin diseases, such as psoriasis and atopic dermatitis (AD). However, in atopic dermatitis, the use of capsaicin requires caution due to the potential for burning sensations and skin irritation.
Mechanisms of Action of Capsaicin in Psoriasis

- Reduction of keratinocyte proliferation – capsaicin lowers the levels of hypoxia-inducible factor-1α (HIF-1α), slowing down excessive epidermal cell proliferation.
- Inhibition of the IL-23/IL-17 pathway, which plays a key role in the pathogenesis of psoriasis.
- Reduction of inflammation, through the downregulation of TNF-α, IL-6, and IL-22.
- Relief of itching, which is a significant symptom associated with psoriasis.

Bernstein demonstrated that the use of a capsaicin-containing cream led to a significant reduction in psoriasis severity and skin redness. Ellis showed that applying 0.025% capsaicin cream significantly reduced itching and improved psoriasis severity scores after 4 and 6 weeks of therapy.

Skin irritation and burning sensations after using capsaicin are reported in 55% of patients. Respiratory discomfort, including coughing, sneezing, and watery eyes, observed in 6% of patients, indicating potential airway irritation following topical use.

Effects on the Cardiovascular System

Numerous studies suggest that capsaicin may influence heart and blood vessel function by acting on the vascular endothelium, inflammatory processes, lipid metabolism, and glucose homeostasis. Due to these properties, capsaicin is being investigated as a potential adjunct in the prevention and treatment of cardiovascular diseases, including atherosclerosis, hypertension, and myocardial infarction.

The TRPV1 receptor is expressed in sensory nerves of cardiac structures (near the epicardium), endothelial cells of blood vessels, cardiac muscle tissue. During myocardial ischemia (e.g., in a heart attack), reactive oxygen species (ROS) are produced, which activate TRPV1. Additionally, under oxidative stress, the levels of 12-hydroperoxyeicosatetraenoic acid (a metabolite of arachidonic acid) increase, further stimulating TRPV1 and leading to cardioprotective effects, such as reduction in infarct size, milder ischemia/reperfusion injury, protection of the vascular endothelium from damage.

Research has shown that capsaicin may protect the heart during myocardial infarction by:

- Reducing cardiac tissue damage,
- Lowering oxidative stress and inflammation,
- Preserving mitochondrial function.

Clinical studies have shown that capsaicin patches improved ischemic thresholds in patients with angina pectoris. However, one case of acute myocardial infarction was reported, highlighting the need for further research on the safety of this approach.
Capsaicin's effects on blood vessels are complex and can lead to either vasodilation (blood vessel widening) or vasoconstriction (blood vessel narrowing), depending on physiological conditions.

Vasodilation (Blood Vessel Expansion):

- TRPV1 activation stimulates the release of calcitonin gene-related peptide (CGRP), a potent vasodilator.
- Induction of endothelial nitric oxide synthase (eNOS) leads to the production of nitric oxide (NO), which promotes vascular relaxation and improves blood flow.

Vasoconstriction (Blood Vessel Narrowing):

- TRPV1 activation can trigger the release of substance P, a neuropeptide that modulates vascular tone.
- Substance P binds to neurokinin-1 receptors, which may lead to vasoconstriction in certain vascular regions.

The overall vascular response to capsaicin depends on tissue location and physiological conditions. In some cases, capsaicin may enhance tissue perfusion, while in others, it could increase blood pressure, which may explain variations in patient responses regarding blood pressure control.

Studies suggest that capsaicin may reduce the risk of atherosclerosis through multiple mechanisms, including lowering total cholesterol and triglyceride levels, reducing atherosclerotic plaque formation, activating the PPARγ/LXRα pathway, which prevents lipid accumulation in arterial walls, enhancing nitric oxide (NO) production, improving endothelial function.

Animal studies have demonstrated that capsaicin supplementation reduced atherosclerotic plaque area by 18% compared to control groups.

While capsaicin offers several cardioprotective benefits, it may also induce vasoconstriction in some patients, increase the risk of arrhythmias, potentially trigger acute cardiovascular events in individuals with pre-existing heart conditions.
Given these dual effects, the use of capsaicin in cardiovascular disease management requires further research and caution—particularly in patients with hypertension and coronary artery disease[22].

Conclusion

Capsaicin is a promising compound with a broad spectrum of therapeutic effects, finding applications in various fields of medicine, ranging from neuropathic pain relief and dermatological treatments to supporting metabolic, neurological, and oncological therapies. Its unique properties, derived from its interaction with the TRPV1 receptor, enable analgesic and anti-inflammatory effects, as well as potential roles in modulating lipid and glucose metabolism. Additionally, studies suggest that capsaicin may influence neuroprotective and immunomodulatory processes, opening new possibilities for its use in the prevention and treatment of neurodegenerative and autoimmune diseases.

However, despite its numerous therapeutic benefits, the full implementation of capsaicin as a medication requires further, well-controlled clinical studies. Key aspects that need to be addressed include:

- Determining optimal therapeutic dosages,
- Assessing long-term safety,
- Minimizing side effects, such as mucosal irritation and cardiovascular impact.

Another significant challenge is enhancing the bioavailability of capsaicin, which may be achieved through advanced drug delivery systems.

In the future, cutting-edge technologies such as nanotechnology and modern transdermal and oral formulations could significantly improve the efficacy and safety of capsaicin therapy. The development of capsaicin analogs with improved pharmacokinetic profiles could also lead to more selective actions with fewer adverse effects.

Moreover, the growing interest in capsaicin in oncological research suggests that it may be used as an adjuvant in cancer treatment, promoting apoptosis of cancer cells, inhibition of angiogenesis, enhancement of cancer cell sensitivity to conventional therapies.

At the same time, ongoing research is exploring capsaicin's potential in neurodegenerative diseases, where its neuroprotective mechanisms could help slow pathological processes in Alzheimer's and Parkinson's disease.

Capsaicin represents a highly intriguing research direction in medicine, with future applications spanning pain management, metabolic therapy, cardiology, neurology, and oncology. However, the key challenge remains a deeper understanding of its mechanisms of action and developing strategies to minimize potential side effects. Achieving these goals could pave the way for broader clinical applications of capsaicin in modern medical practice.

Disclosures

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