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Review Article

Dentistry Section

A Narrative Review on Capsaicin: A Multifaceted Herbal Agent

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ABSTRACT

Capsaicin, the fiery compound found in chilli peppers, has attracted significant attention recently, with extensive interest in its diverse pharmacological properties, including analgesic, anti-inflammatory, anti-cancer potential and antimicrobial effects. In recent years, research has extended into its dental applications, particularly its role as an alternative or adjunctive anaesthetic and anti-inflammatory agent. The present narrative review presents an in-depth examination of all medical and dental research on capsaicin to date, highlighting its mechanism of action, systemic effects and clinical relevance in dentistry, including its potential utility as a topical anaesthetic, its role in oral mucosal conditions and implications for minimally invasive procedures.

Keywords: Analgesic, Anti-inflammatory, Bioactive compound

INTRODUCTION

Capsaicin (8-methyl-N-vanillyl-6-nonenamide) is the active component in chilli peppers of the genus *Capsicum*. It exhibits high affinity for the Transient Receptor Potential Vanilloid-1 (TRPV1) receptor expressed on nociceptive neurons. This receptor plays a critical role in pain and inflammation modulation. By activating TRPV1, capsaicin leads to a cascade of depolarisation followed by desensitisation of sensory neurons, which underlies its analgesic action [1].

Traditionally used in topical ointments for arthritis and neuralgia, capsaicin is gaining attention for its potential role in oral medicine and dentistry. Its non opioid, non steroidal mechanism offers promising avenues for pain control in a field increasingly seeking safer anaesthetic alternatives. In light of emerging evidence, capsaicin has demonstrated applications in treating Burning Mouth Syndrome (BMS), Temporomandibular Joint Disorders (TMD), postoperative dental pain and inflammatory gingival conditions [2].

Mechanism of Action

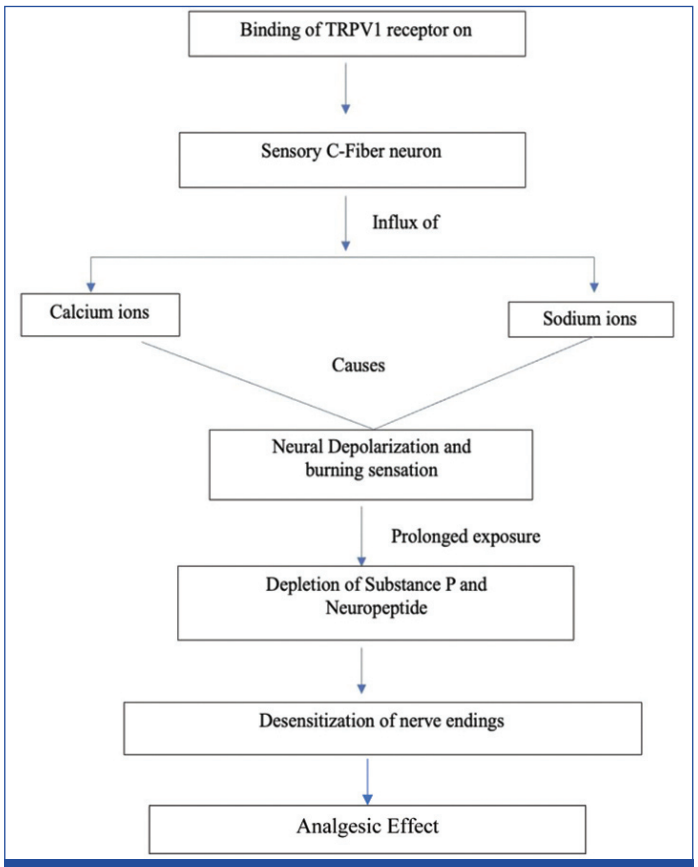
The desensitisation process forms a therapeutic basis for its use in chronic pain management [Table/Fig-1] [3]. It also causes reversible degeneration of epidermal nerve fibres, thereby reducing pain perception temporarily [4]. This makes capsaicin a potential candidate for temporary topical anaesthesia in dental procedures.

At the molecular level, it suppresses activation of NF-κB and reduces proinflammatory cytokines {Interleukin-1 beta ((IL-1β) Interleukin-6 (IL-6) Tumour Necrosis Factor-alpha (TNF-α)}, which leads to decreased vascular permeability and reduced inflammatory cell migration. These are pathways commonly involved in periodontal inflammation and oral mucositis [5]. In addition, capsaicin exhibits antimicrobial properties against oral pathogens, including *Porphyromonas gingivalis*, *Streptococcus mutans* and *Candida albicans*, making it a promising adjunctive agent for oral hygiene formulations [5].

CAPSAICIN'S ROLE IN HEALTHCARE

Pain Management

Chronic neuropathic pain: The Food and Drug Administration (FDA)-approved capsaicin 8% patch (Qutenza®) is indicated for Postherpetic Neuralgia (PHN) and diabetic neuropathy [6]. Malmberg AB et al., reported that a single one-hour application of a high-concentration patch can replicate the effects produced by prolonged exposure to low-concentration capsaicin creams, suggesting a new approach in chronic pain syndromes [7].



[Table/Fig-1]: Mechanism of action [3].

Nolano M et al., stated that degeneration of epidermal nerve fibres is the main reason for the analgesic effect of capsaicin [8]. Peripheral nociceptors that contain TRPV1 ion channels—those involved in pain signal transduction (a ligand-gated, non selective cation channel, expressed preferentially on small-diameter afferent neurons tuned to the detection of noxious stimuli)—are hypersensitive in many patients with PHN. Therefore, targeting TRPV1 is a logical approach for neuropathic pain management. By activating TRPV1-expressing nociceptors, capsaicin initially induces a burning sensation, allodynia, hyperalgesia and erythema, but after continued exposure, TRPV1-containing sensory axons become defunctionalised, thus inhibiting the initiation of pain transmission [9].

In the management of cancer: Capsaicin, the active compound found in chili peppers, has emerged as a promising agent in the fight against cancer due to its ability to influence critical signalling pathways, notably Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB), Cyclooxygenase-2 (COX-2) and Epidermal Growth Factor Receptor (EGFR). This bioactive compound, which is a derivative of homovanillic acid, also plays a significant role in altering the expression of various genes that govern essential processes such as cancer cell survival, growth arrest, angiogenesis and metastasis [10].

In experimental studies, capsaicin effectively promotes programmed cell death (apoptosis) while simultaneously inhibiting the proliferation of malignant cells, notably in Oral Squamous Cell Carcinoma (OSCC) [11]. Further investigations by Lu HF et al., revealed that capsaicin not only induces cell death but also elevates levels of Reactive Oxygen Species (ROS) and enhances the presence of pro-apoptotic proteins in colorectal cancer, highlighting its potential as a therapeutic agent against this malignancy [12]. In human breast cancer, capsaicin has been shown to amplify the apoptotic effects of trial by activating the calcium-CaMKII-Sp1 signalling pathway, illustrating its multifaceted role in managing cancer cell dynamics [13]. Moreover, a study by Bhutani M et al., revealed that capsaicin significantly inhibits cell proliferation and leads to a notable accumulation of cells in the G1 phase of the cell cycle, suggesting its potent influence on cancer cell cycle regulation [14].

Overall, these findings underscore capsaicin's potential as a valuable component in cancer prevention and treatment strategies.

Dermatology and Gastroenterology

Low-dose capsaicin creams (0.025-0.1%) are used for pruritus, psoriasis and Irritable Bowel Syndrome (IBS). In gastroenterology, oral capsaicin is paradoxically useful in functional dyspepsia by desensitising the gastric mucosa, mainly by desensitising C nociceptive fibres, modulating neurotransmitters and by reducing inflammation. It also balances the gut microbiota, limits the secretion of gastric acid and reduces oxidative stress damage [15]. Capsaicin leads to selective injury to nociceptive C fibres, which transmit pain information to the Central Nervous System (CNS) and has been reported to help relieve pain of cutaneous and mucosal origin [16].

DENTAL APPLICATIONS

Burning Mouth Syndrome (BMS)

Individuals affected by BMS often experience changes in taste perception, resembling parageusia. This condition predominantly affects women, especially those in the perimenopausal and postmenopausal stages of life [17]. Diagnosis of BMS is primarily clinical and involves ruling out other potential causes of oral discomfort and taste disturbances. Research has indicated that BMS is associated with both Axis I and Axis II psychiatric conditions, alongside structural and functional changes in the nervous system. These neurological alterations, coupled with circadian rhythm disruptions, can influence pain sensitivity and emotional state, potentially disturbing the Hypothalamic-Pituitary-Adrenal (HPA) axis [17].

Topical capsaicin, at concentrations of 0.02% and 0.05%, has shown promising results in treating BMS. In a double-blinded study conducted by Femiano F et al., over 60% of participants experienced a pain reduction exceeding 60% following four weeks of treatment with topical capsaicin [18]. The analgesic effect is thought to arise from the selective and temporary desensitisation of afferent sensory C-fibres. Notably, unmyelinated C-fibres in the oral mucosa have been implicated as key mediators of the burning sensations observed in BMS [19].

Topical Anaesthetic Use

Research has investigated capsaicin as a potential alternative to lidocaine. In a randomised, placebo-controlled clinical trial conducted by Hussain N et al., an 8% capsaicin patch was compared with a 5% lidocaine patch in patients suffering from diabetic peripheral neuropathic pain. The results indicated that capsaicin was effective and well tolerated by patients [20].

Topical formulations of capsaicin have demonstrated localised analgesic effects when applied to mucosal surfaces, with fewer systemic side-effects. A study by Kandasamy S et al., found that a 0.05% capsaicin gel produced a level of mucosal desensitisation comparable to that of benzocaine in dental extraction cases [21].

Gingivitis and Periodontal Inflammation

Capsaicin has anti-inflammatory properties that work by inhibiting the synthesis of prostaglandins and the expression of COX-2. It also modulates cytokines, including TNF-α and IL-6, which helps reduce inflammation in gingival tissues. Animal studies have demonstrated that the topical application of capsaicin leads to decreased gingival edema and improved periodontal health indicators [22].

In a study conducted by Wang W et al., on mouse periodontal tissue, it was found that capsaicin enhances the osteogenesis of Periodontal Ligament Stem Cells (PDLSCs) even in the presence of inflammation, while also reducing alveolar bone resorption in mice [23]. Additionally, an in-vitro study by Zhou Y et al., showed that capsaicin inhibits the growth of *P. gingivalis* and the expression of NF-κB p65, indicating its potential to prevent alveolar bone resorption [24].

The ability of capsaicin to inhibit *P. gingivalis* may be attributed to its role as a porin and efflux pump inhibitor. This action could enhance the effectiveness of other antibacterial agents by preventing biofilm formation and compromising the structural integrity of bacterial cells [25].

Oral Lichen Planus and Mucosal Ulcers

Capsaicin is not a first-line treatment, but it has shown promise for symptomatic relief in cases of erosive oral lichen planus and mucosal ulcers due to its desensitising effects [26]. Its use remains experimental and further trials are needed for validation.

In a study conducted by Berger A et al., involving 11 patients undergoing chemotherapy or radiotherapy, capsaicin administered orally demonstrated a significant analgesic effect on pain associated with oral mucositis; however, this effect was temporary for most patients [27].

Pharmacological Safety

Capsaicin is a liposoluble compound that is easily absorbed when taken orally, making it well tolerated in the digestive tract. When administered systemically, it reaches the entire body. It may be used in conjunction with anti-inflammatory drugs, potentially enhancing their effectiveness and allowing for lower doses, which can reduce systemic side-effects. Additionally, capsaicin has been linked to benefits in glucose homeostasis, possibly by altering certain gut bacteria at the genus level. These dietary changes can enhance glucose management by promoting the production of short-chain fatty acids and gut hormones while suppressing proinflammatory cytokines [25,28].

Adverse Effects

Capsaicin, though naturally derived, can cause side-effects. Common adverse effects include local irritation, burning sensation and erythema when used topically. In oral applications, particularly in mucosal tissues, a burning discomfort is the primary limiting factor in patient compliance [23,29]. This can be addressed by limiting the dosage for better tolerance, applying an adjunctive anaesthetic

before application and using palate cleansers such as milk, which can help dissolve capsaicin due to its fat content [23].

Oral administration of capsaicin is associated with gastrointestinal disturbances in some cases. In high doses, animal studies have suggested potential genotoxicity, but these findings have not been conclusively replicated in humans [30]. Importantly, capsaicin's application in dentistry requires careful control of dosage and formulation to prevent mucosal damage.

Formulations and Delivery Systems in Dentistry

Research has explored several delivery systems for capsaicin to enhance efficacy and minimise irritation:

Hydrogel formulations: These allow prolonged contact time with the mucosa and reduce irritation. The findings of this double-blinded randomised controlled trial suggest that both the capsaicin 0.1% hydrogel patch and the placebo patch led to significant improvements in pain intensity and related functional and psychological measures among patients with chronic myofascial neck pain. These results underscore the potential influence of placebo responses and patient expectations in pain management and highlight the need for further research to clarify the specific role of capsaicin in topical therapies [31].

Mouthwashes and rinses: A study showed good results with low-dose capsaicin rinses (0.02%) for managing BMS and postoperative inflammation with positive outcomes and minimal side-effects [19]. A case report by Dinan JE stated that a patient complaining of a burning sensation on the dorsum of the tongue for over a year was advised to use capsaicin mouthrinse three times daily and after a month the patient reported a substantial decrease in pain [32].

Capsule microparticles: Vesicle-based technologies offer enhanced drug bioavailability, minimised toxicity and precise delivery to targeted tissues or cells, making them a promising approach for pain management. Novel formulations using liposomal encapsulation or polymeric carriers for controlled release have been explored, particularly in topical delivery for inflammatory oral conditions and minor surgical sites [33].

Nanolipoidal Carriers (NLC) for topical application: Given the potent pungency and high oil-water partition coefficient of capsaicin, capsaicin-loaded NLCs were developed to increase permeation and achieve the analgesic, anti-inflammatory effect while minimising skin irritation. Capsaicin-loaded NLCs and their gel formulations demonstrated sustained release and showed no signs of cytotoxicity. Additionally, the use of NLCs significantly improved capsaicin's penetration, permeation flux and skin retention [34].

Recent Clinical Studies and Trials

Recent clinical studies propose that capsaicin may slow the progression of vascular aging and could constitute a new strategy to treat vascular aging-related diseases, since vascular aging is associated with chronic inflammation and metabolic disorders. Capsaicin works by activating TRPV1 and inhibiting the molecular pathways and signaling channels responsible for vascular cellular aging, thus reducing migration, proliferation and inflammation of vascular cells and mitigating vascular aging phenotypes such as endothelial dysfunction and atherosclerosis [35].

Ongoing trials are assessing capsaicin's role in alleviating oral mucositis in cancer patients receiving radiotherapy, where conventional analgesics often prove insufficient or cause systemic side-effects [36].

With growing interest in natural alternatives and the need to reduce reliance on opioids and synthetic anaesthetics, capsaicin offers a compelling area of exploration in dentistry.

Future research should focus on establishing standardised concentrations and suitable delivery vehicles for the oral use of capsaicin, ensuring both safety and therapeutic effectiveness. To strengthen clinical applications, long-term safety profiles should be assessed through robust multicentre randomised trials. Additionally, formulating combination therapies that incorporate capsaicin alongside anti-inflammatory and antimicrobial agents may enhance its clinical utility and broaden treatment potential. The development of sustained-release delivery systems would be particularly valuable for managing chronic conditions or supporting longer procedures, allowing for consistent therapeutic effects. Notably, the advent of TRPV1 receptor modulators presents a promising opportunity to create novel capsaicin analogs with increased efficacy and reduced irritation, paving the way for more tolerable and targeted pain management options [36].

CONCLUSION(S)

Capsaicin is a multifaceted compound with a well-documented pharmacological profile and an expanding role in both medicine and dentistry. In dental practice, its utility as a topical anaesthetic, anti-inflammatory and adjunct to conventional therapies holds significant promise. While its burning sensation poses a limitation, advances in formulation science are enabling better-tolerated applications. Current evidence supports its role in managing pain-related oral conditions such as BMS, minor surgeries and inflammatory periodontal diseases. However, standardised guidelines, dosage protocols and robust clinical data are necessary before routine use in dental offices can be endorsed. Continued research and improved formulation strategies could establish capsaicin as a beneficial natural alternative in comprehensive pain management and dental care protocols.

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