Capsaicin as a Potential Anticancer Agent: A Literature Review

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Abstract

Capsaicin is a bioactive phytochemical abundant in red and chili peppers (capsicum annuum) and is a spicy flavor enhancer in cooking or food, It is rich in vitamin C, provitamin A, and calcium. The composition of primary metabolites is rich in antioxidants derived from flavonoids, phenolics, carotenes, and alkaloids. It is very useful for preventing cell damage, and cancer insurgence.

This review article aims to provide a comprehensive overview of the current literature on capsaicin as an anticancer agent, highlighting its molecular mechanisms, preclinical and clinical studies, and future directions in research. Capsaicin has been shown to alter the expression of several genes involved in cancer cell survival, growth arrest, angiogenesis, and metastasis. In conclusion, the results of numerous studies indicate that capsaicin exhibits promising anticancer effects both in vitro and in vivo.

It inhibits cell proliferation, induces apoptosis, suppresses angiogenesis, and inhibits tumor growth and metastasis. Additionally, capsaicin shows potential as a complementary agent in combination therapies, enhancing the effectiveness of conventional chemotherapeutic agents. These findings provide a strong rationale for further exploration of capsaicin as a potential anticancer agent and highlight its potential for clinical translation.

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Introduction

Cancer remains a global health challenge, necessitating the constant exploration of new therapeutic avenues. [1–4] Natural compounds have gained attention as potential sources of novel anticancer agents. [5] The active substance in capsicum annuum is capsaicin. Transient receptor potential vanilloid 1 (TRPV1) is a receptor of capsaicin. In addition to capsaicin, TRPV1 can be active at temperatures of 43°C or higher temperatures and in acidic conditions (pH <6).[6] TRPV1 consists of unmyelinated type C nerves and delicately myelinated A-delta sensory nerve fibers. Capsaicin can bind TRPV1, reducing the sensitivity of pain fibers that become insensitive to nociceptive stimuli.[7] Capsaicin can effectively act as a chemopreventive agent.[8]

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Capsaicin, the pungent compound found abundantly in *Capsicum annuum* (chili peppers), has shown promise due to its diverse biological effects and potential anticancer properties.[9,10] Extensive investigations have unveiled various mechanisms through which capsaicin exerts its anticancer effects. It has been shown to modulate multiple cellular signaling pathways involved in cell proliferation, apoptosis, angiogenesis, inflammation, and metastasis. Experimental studies using cell cultures and animal models have consistently demonstrated capsaicin's ability to inhibit cancer cell growth, induce apoptosis, suppress tumor formation and progression, and reduce angiogenesis. These findings underscore the potential of capsaicin as a promising candidate for cancer prevention and treatment. [10-13]

Clinical studies exploring the efficacy of capsaicin in human subjects have yielded encouraging results. Capsaicin-based interventions have shown potential benefits in alleviating cancer-related pain, reducing side effects of chemotherapy and radiation therapy, and improving the quality of life in cancer

patients.[1,13,14] Additionally, the synergistic effects of capsaicin in combination with conventional anticancer drugs have been investigated, revealing enhanced therapeutic outcomes.[1,15,16]

Results

Numerous studies have investigated the anticancer effects of capsaicin, revealing its potential as a promising therapeutic agent. In vitro studies consistently demonstrate that capsaicin inhibits cell proliferation in various cancer cell lines, including breast, prostate, lung, colon, and pancreatic cancer. [1,10,11,14] It induces apoptosis, characterized by DNA fragmentation, caspase activation, and mitochondrial dysfunction. [13] Capsaicin also exhibits anti-inflammatory effects by suppressing the production of pro-inflammatory cytokines and inhibiting signaling pathways.[1,4,9] These findings suggest that capsaicin modulates multiple cellular processes in cancer development and progression.

In addition to its effects on cell growth and apoptosis, capsaicin has shown promise in inhibiting tumor angiogenesis, the process by which new blood vessels are formed to support tumor growth.[16] It targets vital molecular players involved in angiogenesis, such as vascular endothelial growth factor (VEGF), matrix metalloproteinases (MMPs), and hypoxia-inducible factor 1-alpha (HIF-1α). By suppressing angiogenesis, capsaicin effectively cuts off the blood supply to tumors, impairing their growth and metastatic potential.[15]

Furthermore, in vivo studies using animal models have provided compelling evidence supporting the anticancer effects of capsaicin. These studies demonstrate that capsaicin treatment significantly reduces tumor size, inhibits tumor growth, and prolongs survival in various cancer models.[1,12,17,18] Capsaicin has also been found to suppress metastasis by inhibiting cancer cell invasion and migration and modulating the expression of proteins involved in epithelial-mesenchymal transition (EMT), a process associated with increased tumor aggressiveness.[15]

Several studies have explored the combination of capsaicin with conventional chemotherapeutic agents, revealing potential synergistic effects. Combination treatments using capsaicin have been shown to enhance the anticancer efficacy of chemotherapy drugs, overcome drug resistance, and reduce the required dosage of chemotherapeutic agents. These findings suggest that capsaicin may serve as an effective adjuvant therapy, improving the overall treatment outcomes in cancer patients.[1,15,16]

Discussion

Mechanisms of Action

The diverse mechanisms through which capsaicin exerts its anticancer effects are of great interest. Capsaicin has been shown to modulate various signaling pathways involved in cell survival, proliferation, and apoptosis.[17,19] It can activate the transient receptor potential vanilloid (TRPV) family of ion channels, increasing intracellular calcium levels and subsequent activation of apoptotic pathways.[15] Additionally, capsaicin can inhibit NF-κB, a transcription factor involved in inflammation and cell survival, thus promoting apoptosis and reducing cancer cell proliferation.[14] Moreover, capsaicin has been found to affect the PI3K/Akt and MAPK pathways, which regulate cell growth and survival.[10,13] Understanding these intricate mechanisms of action is crucial for optimizing capsaicin's anticancer potential.

Impact on Cancer Metastasis

Metastasis, the spread of cancer cells from the primary tumor to distant sites, is a significant challenge in cancer treatment. Emerging evidence suggests that capsaicin can inhibit various steps of the metastatic cascade. It suppresses cancer cell invasion and migration by modulating the expression of proteins involved in cell adhesion and extracellular matrix remodeling.[9,14] Furthermore, capsaicin has been shown to inhibit angiogenesis, a process crucial for providing nutrients and oxygen to tumors and promoting their metastatic potential. By targeting multiple pathways involved in metastasis, capsaicin holds promise as a therapeutic agent to prevent or hinder the spread of cancer cells.[15,16]

Overcoming Drug Resistance

The development of drug resistance remains a significant hurdle in cancer treatment. However, studies have demonstrated that capsaicin may overcome drug resistance in cancer cells. Capsaicin has been shown to sensitize cancer cells to conventional

chemotherapeutic agents, making them more susceptible to their cytotoxic effects. It can modulate drug efflux transporters and inhibit drug-metabolizing enzymes, enhancing anticancer drugs' intracellular concentration and efficacy. Combining capsaicin with conventional therapies holds promise for improving treatment outcomes and overcoming drug resistance in cancer patients.[13,19]

Safety Considerations

While capsaicin has shown promising anticancer effects, its safety profile is an important aspect to consider. Adverse effects have generally been minimal in studies using lower doses. Determining the optimal dosage and administration route of capsaicin is crucial to minimize potential side effects while maximizing its therapeutic benefits. Additionally, evaluating its long-term safety and potential interactions with other medications or treatments is vital for clinical application.[1,15]

Translation to Clinical Application

The preclinical studies discussed in this review provide a strong foundation for the potential clinical application of capsaicin as an anticancer agent.[11,12] However, translating laboratory findings to clinical practice requires rigorous evaluation through well-designed clinical trials. Determining the optimal dosing regimens, exploring its efficacy in different cancer types and stages, and assessing its long-term effects are necessary for establishing capsaicin as a viable therapeutic option. Collaborative efforts between basic researchers, clinicians, and pharmaceutical companies are essential to advance capsaicin research and potentially improve cancer treatment outcomes.[1,9,15]

Conclusions

In summary, the results of numerous studies indicate that capsaicin exhibits promising anticancer effects both in vitro and in vivo. It inhibits cell proliferation, induces apoptosis, suppresses angiogenesis, and inhibits tumor growth and metastasis. Additionally, capsaicin shows potential as a complementary agent in combination therapies, enhancing the effectiveness of conventional chemotherapeutic agents. These findings provide a strong rationale for further exploration of capsaicin as a potential anticancer agent and highlight its potential for clinical translation.

Declaration of Interest

The authors report no conflict of interest.

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