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Unlocking the Potential of Propolis in the Battle Against Cancer: A Mini Comprehensive Exploration.

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Abstract

Cancer remains a formidable global health challenge, standing as the second leading cause of death worldwide. Despite significant advancements in treatment modalities, the limitations and side effects associated with conventional therapies underscore the urgent need for a product that is natural and innovative . This manuscript delves into the potential of propolis, a natural bee hive extract, as a promising alternative for cancer treatment, with a focus on its application in combating oral cancers.

Introduction:

In the year 2020, approximately 19.3 million new cancer cases were diagnosed, leading to over 10 million deaths globally.[1] Conventional cancer treatments, including radiation, chemotherapy, immunotherapy, targeted therapy, and hormone therapy, exhibit limitations and undesirable side effects, necessitating exploration into natural compounds. Propolis, historically used for various diseases, emerges as a natural product with promising anti-cancer properties.[2]

Propolis Composition and Biological Properties:

Propolis contains various components, with about 24 to 26% being fatty acids, 18 to 20% flavonoids, 0.5 to 2% microelements, 15 to 18% sugars, 5 to 10% aromatic acids, 2–6% esters, 2 to 3.3% alcohol and terpenes, and 2 to 4% vitamins. The main parts of raw propolis are resins and balms (50–60%), waxes (30–40%), essential oils (5–10%), pollen (5%), and vitamins (5%).[3,4]
Phytochemicals like polyphenols, flavonoids, phenolic acids, phenolic aldehydes, and ketones, gives propolis it biological properties. These properties include being an antioxidant, anti-inflammatory, and having potential against cancer. Propolis comes in different types, classified by origin, color, and texture. Generally, people in Asia and Europe use propolis for managing various diseases.[5]

Clinical Trials and Mechanisms of Action:

A study by Ebeid et al. explored propolis' potential preventive effect in breast cancer patients undergoing chemotherapy and radiation.[6] In a clinical trial with 135 participants, propolis capsules reduced harmful radiation effects, maintaining antioxidant levels and improving patients' disease-free lifetime without adverse effects.

Another clinical experiment tested propolis safety, toxicity, and efficacy in preventing oral mucositis (OM) in breast cancer patients undergoing doxorubicin and cyclophosphamide. Sixty patients using propolis with bicarbonate mouth rinses showed safety, tolerance, and effectiveness in preventing OM compared to sodium bicarbonate alone.

Chemotherapy side effects impact patients' nutritional health and quality of life. Propolis, known for antitumoral and immune-stimulating properties, is suggested as a nutritional supplement. A double-blind clinical trial on breast cancer patients after chemotherapy revealed propolis as a safe option to improve nutritional status and quality of life.

Understanding Propolis' Impact at the Molecular Level:

Previous studies have consistently found that propolis and its components trigger two main pathways leading to cell death in different cancer cells. The first pathway is the death ligand-mediated or extrinsic apoptotic pathway, while the second is the mitochondrial-mediated or intrinsic apoptotic pathway. Propolis achieves this by influencing various signaling molecules related to apoptosis in cancer cells.[7]

In specific terms, propolis and its constituents modulate several key molecules involved in apoptosis-related signaling. These include TRAIL, FasL, TNF-α/DR, p53, Bax, Bcl-2, Bcl-xL, caspases, and PARP.[8] These molecules play crucial roles in regulating the apoptotic process. Propolis appears to affect these signaling components, ultimately promoting pathways that lead to the programmed cell death of cancer cells. This suggests a potential mechanism by which propolis exerts its anti-cancer effects by orchestrating the intricate network of apoptosis-related molecules in various cancer cell types.

Literature review shows that propolis and its components can stop cells from moving, prevent a process called epithelial-to-mesenchymal transition, and hinder the spread of tumors. This is achieved by controlling important signaling molecules involved in these actions. Propolis influences molecules like growth factors (EGF, VEGF, PDGF, HIF-1, and FGF), markers for epithelial-to-mesenchymal transition (vimentin, E-cadherin, β-catenin, and Snail), and proteins related to tumor spread (MMPs, uPA, and interleukin).[9] This suggests that propolis has the potential to slow down or prevent the movement and spreading of cancer cells.

High-performance liquid chromatography-mass spectrometry (HPLC-MS) and ultra-performance liquid chromatography-mass spectrometry (ultra-PLC-MS) analyses have identified key bioactive components in propolis, such as chrysin, **Caffic acid prenylated ehtylalcohol(CAPE)**, artepillin C, nemorosone, galangin, cardanol, cardol, quercetin, kaempferol, and p-coumaric acid in Brazilian green propolis.[10]

CAPE in Oral Cancer Treatment:

Caffeic acid prenylated ethyl alcohol (CAPE), a key component of propolis, shows promise in treating oral squamous cell carcinoma (OSCC). Using CAPE alongside standard treatment could be beneficial for people with oral squamous cell carcinoma (OSCC). CAPE treatment slows down the growth of TW2.6 human OSCC cells by blocking Akt signaling. It changes the cell cycle by reducing the number of cells in the G1 phase, increasing those in the G2/M phase, and triggering cell death in TW2.6 cells. When CAPE is combined with 5-fluorouracil (5-FU), a common oral cancer drug, it further slows down cell growth. This suggests that patients undergoing chemotherapy may benefit from both CAPE and 5-FU, potentially allowing for lower 5-FU doses and reducing side effects.[11,12]

CAPE treatment has stopped the growth of Japanese squamous cell carcinoma SAS cells and Taiwanese oral epidermoid carcinoma OEC-M1 cells by causing G2/M arrest.[13] Importantly, it doesn't affect the normal human oral fibroblast (NHOF) cells at concentrations below 100 μM, indicating its specific impact on oral cancer cells. CAPE has been found to make cancer cells more responsive to chemotherapy and radiation in animal studies by blocking resistance pathways. Additionally, it helps protect tissues and organs from the harmful effects of chemotherapy.[14] This suggests that using CAPE alongside chemotherapy could benefit oral cancer patients by enhancing tumour regression and safeguarding their tissues and organs.clinical trials are necessary to isolate the individual components responsible for its beneficial effects. Combining CAPE with standard treatment, especially with 5-fluorouracil (5-FU), exhibits potential benefits for OSCC patients,

slowing down cell growth and potentially reducing side effects. CAPE's specific impact on oral cancer cells, without affecting normal cells, highlights its potential as an adjunct therapy.[15]

Quality Control, Metabolomics, and Geographical Variations:

Creating effective cancer treatments necessitates precise quality control and well-designed clinical trials. Metabolomics emerges as a valuable tool to meet these standards. The geographical variation in propolis composition underscores the importance of understanding chemo preventive doses for its safe use. Addressing potential side effects, particularly allergies, requires careful removal of responsible constituents.[16,17,18]

Conclusion:

This manuscript underscores the potential of propolis and its active component, CAPE, in the realm of cancer treatment, particularly oral cancers. By comprehensively exploring its mechanisms of action and synergies with conventional therapies, this study aims to contribute valuable insights to the development of targeted and effective anti-cancer treatments. Continued research into propolis' bioactive compounds and specific target molecules is essential for addressing the persistent challenge of chemotherapy resistance and paving the way for safer and more impactful cancer therapies.

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