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Mini Review

Synergistic Power of Phytochemicals and Nanotechnology in Cancer Treatment

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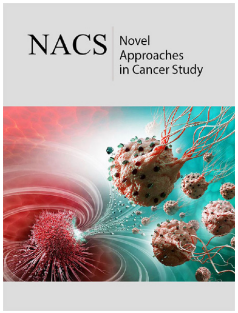

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Abstract

Bioactive Phytocompounds (BPCs) naturally found in plants, hold immense potential for cancer treatment. However, their limitations like poor solubility, bioavailability and stability hinder their effectiveness. This review explores how nanotechnology can overcome these limitations and empower phytochemicals in the fight against drug-resistant cancer. Despite advancements, conventional therapies (surgery, radiation, chemotherapy) often suffer from side effects and drug resistance. Understanding the complex signaling pathways involved in cancer development is crucial for designing targeted therapies. Phytochemicals offer diverse biological activities against cancer, but their inherent limitations restrict their use. They can induce apoptosis, inhibit growth, modulate inflammation, and bolster the immune response. Nanocarriers encapsulating phytochemicals enhance their solubility, stability, and bioavailability, enabling targeted delivery to cancer cells while minimizing harm to healthy tissues. Intricate nanocarriers are programmed for controlled release and specific targeting based on cancer cell markers. Although phytochemicals exhibit diverse anti-cancer activities, their limitations restrict their use. Nanotechnology offers a game-changer, enhancing solubility, and stability, and enabling targeted delivery to cancer cells, minimizing harm to healthy tissues. Exciting future advancements include intricate nanocarriers programmed for controlled release and personalized therapy tailored to individual patients. This intersection of phytochemicals, cancer research, and nanotechnology offers a beacon of hope, paving the way for personalized, safe, and effective therapies, bringing us closer to a world free from the devastating effects of drug-resistant cancer.

Keywords: Bioactive phytocompounds; Nanoformulation; Cancer; Targeted drug-delivery

Introduction

Cancer is a major public health concern, with approximately 19.3 million new cancer cases diagnosed and 10 million cancer-related deaths in 2020 worldwide [1]. The number of new cases is expected to rise to 28.6 million by 2040 [1]. Traditional cancer treatments such as surgery, radiation therapy, and chemotherapy have shown efficacy, but they may also have significant side effects [1]. Complex signaling pathways formed due to interconnected cellular pathways govern and coordinate cellular activities [2]. Several genes are involved in controlling these cellular activities, including cell growth control, cell cycle progression, and cell death [3]. Mutations in these genes can lead to uncontrolled cell division and the formation of tumors, which can be benign or malignant [1]. Cancer arises from mutations in Cancer Driver Genes (CDGs), impacting their ability to control cell growth and repair. These mutations, affecting genes like p53 and those in the Phosphatidylinositol-3-Kinase (PI3K) pathway, can disrupt crucial checks and balances, leading to uncontrolled cell proliferation. Mutations in tumor suppressor genes like p53, which normally halt cell division under stress, are particularly concerning. Unlike other such genes, p53 often undergoes missense mutations, causing dysregulation and even promoting cancer-promoting genes [4-6]. Understanding these specific mechanisms behind CDG mutations holds immense potential for developing targeted therapies against various cancers. For millennia, humankind has sought remedies from nature, utilizing bioactive compounds derived from plants, known as Bioactive

Phytocompounds (BPCs). Today, BPCs continue to offer immense potential in modern drug discovery, demonstrating promising biological activities against numerous diseases [7]. However, a major hurdle in translating their potential into actual therapies lies in their inherent limitations: low solubility, instability, short half-life, poor bioavailability, and non-specific targeting. Fortunately, the burgeoning field of Nanoformulation (NF) technologies offers a beacon of hope for overcoming these limitations. Nanotechnology emerges as a revolutionary solution, wielding tiny nanoscale carriers to unlock the true potential of BPCs [8].

Discussion

Phytochemicals in combating cancer

Emerging as a promising alternative, phytochemicals present a natural approach to combatting resistance [9,10]. Unlike conventional drugs that typically target single pathways, phytochemicals often exhibit multi-targeted activities, disrupting various cancer cell functions [11]. However, their inherent limitations, like poor solubility, short half-life, and vulnerability to degradation, hinder their full potential. Nanotechnology has emerged as a savior, encapsulating phytochemicals within tiny carriers for enhanced solubility and efficient delivery to cancer cells. Stability yet remains a major concern, as some phytochemicals succumb to degradation by environmental factors [12]. Nanocarriers act as protective shields, safeguarding these delicate compounds and ensuring their potency throughout their journey. However, the multi-targeted nature of phytochemicals can lead to collateral damage on healthy tissues. Fortunately, targeted delivery systems are being developed [13]. These systems, utilizing specific cancer cell markers, direct phytocompounds precisely to their targets, minimizing undesired side effects. Finally, the complexity of plant extracts, containing a mixture of active compounds with varying effects, poses a challenge. By focusing on specific key phytocompounds with desired pharmacological properties, researchers can streamline efficacy and safety profiles. By addressing these limitations through innovative approaches like targeted delivery and targeted isolation, we can utilize the true potential of phytochemicals. This opens doors to safe, effective and personalized therapies, utilizing BPCs to combat cancer.

Nanotechnology-a game-changer in phytocompound delivery

Nanotechnology presents a revolutionary solution by encapsulating BPCs within tiny nanoscale carriers. These nano-carriers effectively address the limitations of phytocompounds, enhancing their solubility, stability, and bioavailability [14]. Moreover, they act as shields, protecting these natural remedies from degradation. By designing these carriers to specifically target cancer cells, nanotechnology minimizes side effects on healthy tissues [15]. Key advantages with nanocarriers include enhanced solubility and bioavailability. Many BPCs are hydrophobic, limiting their absorption and transport within the body. Nanocarriers, crafted from various materials like lipids or polymers, make them highly soluble in the bloodstream. This allows them to navigate the watery terrain of the human body with ease, reaching target cancer cells in significant concentrations. Another major advantage entails the extended half-life and stability. Several stimuli like light, heat, or enzymes can degrade the BPCs. But nanocarriers offer a protective shield, acting as barriers against degradation. This extends the half-life of BPCs and ensures they remain potent throughout their journey. Incorporation of specific cancer cell markers onto their surface, these nano-warriors can recognize and specifically target cancer cells, delivering the BPC payload directly to the target cells. Further, these nanocarriers are designed to release their cargo in response to specific triggers, like changes in the tumor microenvironment, ensuring precise release at the optimal time and location. Others might carry additional therapeutic agents, creating a synergistic effect for even more potent cancer cellcombat. Thus, nanotechnology holds immense promise in overcoming the limitations of BPCs, transforming them into potent and targeted weapons.

Nanoparticle (NP) design plays a pivotal role in BPC delivery, aiming to achieve a delicate balance between therapeutic efficacy and minimal immune response. Ideally, NPs should be fabricated from biocompatible and biodegradable materials with well-defined degradation profiles, such as next-generation Poly Lactic-Co-Glycolic Acid (PLGA) copolymers or stimuli-responsive polymers. This facilitates the controlled release of encapsulated BPCs and subsequent clearance by the Mononuclear Phagocyte System (MPS), minimizing potential immune stimulation. However, extended in vivo half-life (weeks/months) due to physicochemical properties like irregular morphology, large size (>200nm), or a highly positive or negative zeta potential can lead to chronic immune cell activation and inflammation upon prolonged tissue persistence [16,17]. This risk is further amplified by the formation of a dynamic protein corona on the Nanoparticle (NP) surface in the bloodstream. Specific proteins within this corona, particularly opsonins, can trigger pro-inflammatory pathways via complement activation or macrophage recognition. Therefore, to mitigate these challenges, researchers are actively exploring advanced design strategies. Utilizing biocompatible and biodegradable materials with well-defined degradation kinetics minimizes long-term persistence and reduces the likelihood of chronic inflammation. Optimizing NP design parameters like size (ideally <200nm for optimal MPS clearance), shape (spherical for improved circulation), and surface charge (neutral or slightly negative for reduced protein adsorption) can further minimize immune recognition and the subsequent inflammatory cascade. Additionally, surface functionalization with zwitterionic polymers or targeted ligands can further enhance biocompatibility, reduce protein corona formation, and promote specific delivery to target tissues, minimizing off-target effects and inflammation. By carefully considering these factors during NP design and development, researchers can create safe, biocompatible, and targeted carriers for BPC delivery, maximizing therapeutic efficacy while minimizing the potential for inflammatory side effects.

Conclusion

Phytochemicals may help prevent chronic diseases, including cancer, but their inherent limitations have hampered their

effectiveness. Nanotechnology is a revolutionary game-changer armed with tiny nanoscale carriers that unlock the true potential of phytochemicals by enhancing their solubility, and stability, and delivering them with laser-like precision directly to their targets, minimizing harm to healthy tissues. The future holds even greater promise showing intricate nanocarriers programmed for controlled release, unleashing their therapeutic cargo at the optimal time and location. Ultimately, the goal is to personalize these nano-formulations, tailoring them to each unique cancer profile of a patient. This opens the door to a new era of targeted, effective, and accessible cancer therapies, offers a potential strategy in the fight against this global health challenge.

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