

Nanoparticles in the Treatment of Oral Cancer – An Updated Review

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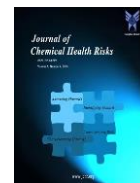
ABSTRACT:

Over the last ten years, nanomaterials (NMs) have been employed in the detection and therapy of head and neck cancers (HNCs). Given the tendency of HNCs to invade nearby tissues and create distant metastases, a significant number of HNC patients are typically diagnosed in advanced stages, resulting in unfavorable prognoses. Nanomaterials, owing to their ability to transport a diverse range of agents such as imaging substances, drugs, genes, vaccines, radiosensitizers, and photosensitizers, play a pivotal role in advancing innovative technologies for diagnosing and treating HNCs. Nanoparticles (NPs) have emerged as promising systems for targeted and regulated release of drugs. These NPs can accommodate various drugs, facilitating precision in drug delivery. The utilization of nanomaterials (NMs) has been documented to enhance the efficacy of drug delivery, ultimately improving the outlook for individuals with head and neck cancers (HNCs). This improvement is attributed to the NMs' ability to enable targeted delivery, controlled release, responsiveness to stimuli, and the conveyance of multiple agents. This review explores the state of the art progress in Nanoparticle technology, aiming to enhance the diagnosis, treatment, and prognosis of HNC patients, while also considering potential avenues for future research.

1. Introduction

Head and neck cancers (HNCs), with squamous cell carcinomas accounting for over 90%, encompass tumors developing in various areas such as the oral cavity, lips, larynx, pharynx, paranasal sinuses, and salivary glands. They stand as the sixth most prevalent form of malignant tumors globally^[1]. Diagnosis in the intermediate and advanced stages frequently reveals sizable tumors, making surgical intervention a potential cause of substantial structural deficiencies in the maxillofacial region. This can detrimentally impact patients' appearance, as well as impair their abilities to chew and swallow, ultimately influencing their future quality of life^[2]. Therefore, it is essential to improve the efficiency of both diagnosing and treating head and neck cancers (HNC). Traditional methods employed in cancer treatment encompass surgery, chemotherapy, radiation therapy, targeted therapy, immunotherapy, and hormone therapy^[3]. Recent initiatives have aimed to overcome

the constraints of current therapeutic methods through the utilization of nanoparticles. Systems for drug delivery based on nanoparticles have shown advantages in the treatment and control of cancer, showcasing favorable pharmacokinetics, accurate targeting, minimized side effects, and mitigation of drug resistance^[4]. Nanoparticles (NPs) are colloidal drug carrier systems that fall within the size range of 10 to 100 nm, comprising natural or synthetic polymers^[5]. The utilization of nanomaterials (NMs) is intricately linked to their size. For example, diminutive NMs (<20 nm) are commonly employed in detection and imaging due to their ability to traverse the blood-brain barrier and undergo rapid clearance via extravasation or the kidneys. On the other hand, larger NMs (>20 nm) are frequently utilized as delivery carriers because they can navigate physiological barriers and circulate for extended durations. Nanomaterials (NMs) are frequently employed as conveyors for transporting drugs, genes,



vaccines, radiosensitizers, and photosensitizers. They enhance the efficiency of drug delivery by utilizing both passive and active targeted delivery mechanisms^[6].

2. Pro's Of Nanoparticle^[6]

- Optimize tumor eradication,
- Minimize side effects dependent on dosage,
- Decrease the occurrence of severe complications,
- Improve the effectiveness of traditional chemotherapy and radiotherapy for cure,
- Lower the risk of recurrence.
- Nanomaterials (NMs) can react to various stimuli, enabling enhanced tumor diagnosis.
- Applied in combined therapies such as photodynamic therapy (PDT) and photothermal therapy.

3. Characteristics Of Nanocarriers^[7]:

- Capability to maintain stability within the vascular system (blood) until they reach their intended destination, the tumor microenvironment (TME).
- Evading clearance by the reticuloendothelial system (RES).
- Avoiding recognition by the mononuclear phagocyte system (MPS).
- Gathering in the tumor microenvironment through the tumor vasculature.
- Achieving deep penetration into the tumor fluid under high pressure.
- Effectively reaching the target and selectively engaging with cancer cells.

4. Factors That Permit The Entry Of Nanoparticles Within The Tumor Cell^[4]:

- In conditions of hypoxia or inflammation, the endothelial layer of blood vessels experiences increased permeability
- Neovascularization: The formation of new blood vessels, results in leaky vessels with large pores, reducing the perm-selectivity of tumor blood vessels compared to normal ones. This faulty angiogenesis, characterized by rapid and defective vessel formation, offers little resistance to the extravasation of nanoparticles (NPs), allowing them to diffuse from these vessels and accumulate within cancer cells.

- Impaired lymphatic drainage: Additionally, impaired lymphatic drainage in tumor formation disrupts normal fluid uptake, leading to minimal clearance of NPs, causing them to accumulate in the tumor interstitium

5. Mechanism Of Action Of Nanoparticle Within The Tumor Cell:

A limited set of techniques is commonly employed to target tumors and their cells, given the diverse phenotypes of cancer cells and tumors. Targeting mechanisms can be broadly categorized into two groups: passive targeting and active targeting. The more extensively investigated approach has been passive drug targeting, particularly with nanoparticles. This is facilitated by the distinctive characteristics of solid tumors, such as leaky vasculature and impaired lymphatic drainage, allowing nanoparticles to accumulate within the tumor^[8]. Passive targeting is ascribed to the presence of openings in the compromised blood vessels of the tumor and the inadequate drainage by the lymphatic system, collectively referred to as the "enhanced permeation and retention effect."^[8] as shown in figure 1a.

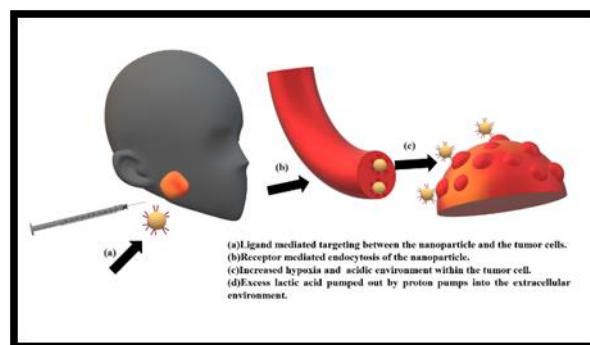


Figure 1a: Passive targeting (*Copyrights under process)

This form of tumor targeting lacks a particular ligand for specific types of tumor cells. The effectiveness of the EPR effect is heavily dependent on key aspects of tumor biology, including: 1) The level of angiogenesis and lymphangiogenesis, 2) The degree of perivascular invasion by the tumor, and 3) The pressure within the tumor^[8].

Active targeting involves the use of specific ligands or molecules, such as transferrin and folate, which can



attach to receptors that are either specifically expressed or overexpressed on the target cells. This targeting method is known as ligand-mediated targeting, as shown in figure 1b. To enhance affinity, nanoparticles (NPs) with ligands having particular functions like retention and uptake must be in close contact with the target. By employing this strategy, the proximity of NPs to cancer cells is increased, leading to improved drug penetration^[8].

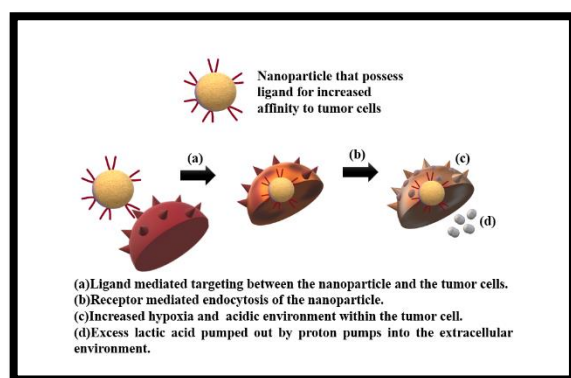


Figure 1b: Active targeting (*Copyrights under process)

6. Types of nanoparticles^[9]:

- ✓ Carbon-based nanoparticles exhibit a high degree of cell penetration.
- ✓ Ceramic-based nanoparticles demonstrate excellent biocompatibility.
- ✓ Metallic-based nanoparticles, particularly magnetic ones, are employed in the detection of metastatic breast carcinoma.
- ✓ Polymeric-based nanoparticles utilize a polymeric shell for the specific targeting of tumor cells.
- ✓ Lipid-based nanoparticles offer superior biocompatibility and lower toxicity compared to inorganic counterparts.

7. Limitations:

Medications transported by nanomaterials (NMs) may be swiftly removed by the reticuloendothelial system. In contrast, the nanomaterials themselves are not efficiently excreted and might persist in the body, heightening the risk of potential toxicity^[10].

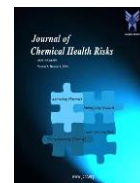
8. Conclusion:

To address the harmful nature of certain nanoparticles (NPs), green nanotechnology has emerged as a favorable alternative. It is characterized by its avoidance of harsh

methods involving high pressure, elevated temperatures, and harmful chemicals, as well as the exclusion of foreign stabilizing or coating agents. In this method, numerous microorganisms and plants are integrated into the synthesis of nanoparticles, resulting in the production of highly efficient, environmentally friendly particles with minimal toxicity, ensuring safety for both humans and the ecosystem. In general, the recent advancements in the realm of nanomaterials (NMs) have opened up numerous possibilities for diagnosing and treating Head and Neck Cancer (HNC). Nevertheless, additional research is necessary to refine raw materials into fully developed drugs suitable for clinical application. The heightened collaboration across disciplines has facilitated swift progress in tumor research and nanotechnology. This collaboration has led to the creation of nanomaterials that leverage the advantages of nanotechnology while aligning with the biological features of HNC. Consequently, it is anticipated that the utilization of nanomaterials will contribute to enhancing the prognosis for patients with Head and Neck Cancer.

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