

Nano-materials in Drug Delivery Systems for Oral Cancer Treatment: A Review

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Abstract

Oral cancer is a serious health concern requiring target-specific treatment strategies due to its high rates of morbidity and mortality. Early detection of cancer cells considerably improves prognosis and treatment outcomes. Recently, nanomaterials have opened a world of intriguing new possibilities for cancer diagnosis and therapy by providing creative ways to enhance patients' quality of life. Furthermore, modified nanoparticles use specially designed moieties to target cancer cells more precisely. Drug delivery methods could reduce side effects and significantly improve oral cancer treatment efficacy. In addition, polymer-based drug delivery methods are designed to release drugs gradually and in a controlled way. In addition, the combination therapy with a drug delivery system leads to a synergetic effect are also discussed.

Keywords: Chemotherapy, Drug delivery, Nanomaterials, Oral cancer.

Introduction

Oral cancer arises from tissues found in the mouth or throat. It can affect the lips, tongue, gums, cheeks, floor of the mouth, roof of the mouth, and tonsils, among other areas of the oral cavity. Oral cancer may present as an unhealing growth or sore, ongoing mouth pain, dysphagia, or voice abnormalities. Even though one-third of cases occur in India [1], this cancer type is the sixth most common

globally [2]. Numerous factors, including chewing areca nuts or beetle nuts, consuming alcohol, smoking, and having chronic inflammation, can lead to oral cancer (Fig. 1) [3]. Moreover, viral infections resulting from the human papillomavirus (HPV) and Epstein-Barr virus can also induce oral cancer [4]. In 2020, sources stated that there were 2,19,732 new cases of oral cancer in India, with 1,21,096 deaths.

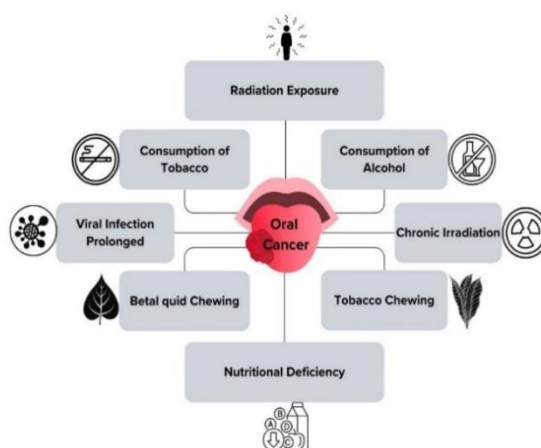


Figure 1. Illustration of Oral Cancer Triggers.

Early detection of cancer cells improves prognosis and treatment outcomes considerably. It's also critical to examine any changes in the texture of the lips, tongue, cheeks, roof, and floor of the mouth. Novel technologies, like tissue fluorescence visualization and salivary diagnostics, are being researched to aid in early detection. These technologies can help detect irregularities that might not be visible to the human eye. There are several therapeutic options available for oral cancer, including immunotherapy, hormone therapy, chemotherapy, radiation therapy, and surgery [5,6]. Because of its efficacy, chemotherapy is one of the most used methods for treating anticancer diseases, including oral cancer. Nevertheless, it causes numerous allergic reactions to infected tissues, damages the skin, and makes it challenging to identify and eliminate just tumor cells [7]. As a result, different strategies are needed to treat cancer.

Nanomaterials for Drug Delivery

Nano-materials like nanoparticles, nanotubes, nanowires, and nanorods have recently made a range of exciting cancer diagnosis and treatment methods feasible by offering innovative solutions to improve patients' quality of life. The diameters of these nanoparticles range from 1 to 100 nm. They can be used in many different fields because of their small size, superior surface area-to-

volume ratios, and tunable surface chemistry, making them an ideal candidate for targeted delivery, imaging and diagnosis, immunotherapy, and many more. Likewise, when used *in vivo*, these nano-based materials improve the stability, solubility, and bioavailability of therapeutic moieties. When encapsulated in various nanocarriers, such as polymers, liposomes, and dendrimers, the medicine can be transported more efficiently to the tumor site and released in a regulated and maintained manner [8-10].

In recent advancements in oral cancer treatment, nanoparticle encapsulation provides a precise method of getting chemotherapy medications into the malignant cells. This technique protects healthy tissues from harm, ensuring tailored therapy. Moreover, it can also be utilized to lengthen the drug's duration, boost cellular absorption, and stabilize its half-life. According to Dang and Guan [11], using nanoparticles in drug administration has several benefits over conventional methods, such as extended half-lives for drugs that are prone to degradation, better drug solubility for hydrophobic compounds, a reduction in systemic toxicity and the ability to release therapeutic drugs precisely and purposefully at the tumor site. The nanomaterials can easily be synthesized using biological and chemical processes along with tunable surface functionalization methods. The objective of

the drug delivery strategy for oral cancer is to maximize therapeutic efficacy while reducing systemic side effects. Serum glycoproteins, including transferrin, are essential for supplying iron to cells, which permits the targeting of cancer cells. While they are rarely present in normal cells, transferrin receptors are expressed in cancer cells. Transferrin molecules, as a result, attach to nanoparticles and are used in active targeting to provide therapeutic drugs to treat cancer (Fig. 2). Numerous studies have demonstrated the useful advantages that biopolymers such as proteins, lipids, gelatin, and chitosan offer for the encapsulating of drugs. These biopolymers are effective at encasing hydrophobic drugs and have biodegradable qualities.

Additionally, they allow for the precise and regulated release of medications into the desired tumor cells [12]. Polymer-based drug delivery method is designed to release drugs gradually and in a controlled way [13]. Biodegradable polymers can be manufactured into hydrogels, nanoparticles, or microspheres containing medication for extended-release within the oral cavity. Furthermore, the system of targeted drug delivery transports appropriate medications to the site of cancer. Recently, liposomes have emerged as a promising method of targeted drug delivery in oral cancer due to their ability to encapsulate and deliver drugs (doxorubicin, cisplatin) to specific cancer cells [14-16].

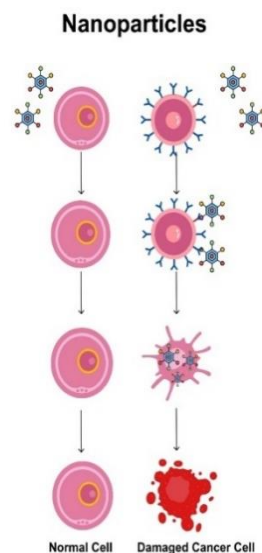


Figure 2. Nanoparticle Dynamics: Normal Cell vs Cancer Cell Reactions

Furthermore, many therapeutic medications can be administered simultaneously in combination therapy with a drug delivery system, leading to synergistic effects and improved treatment outcomes. The synergistic effect has multiple benefits, such as increasing drug effectiveness while lowering toxicity. Additionally, by altering the surface of the nanoparticles, systemic adverse effects can be greatly reduced by facilitating targeted distribution to tumor cells [17]. Additionally, these nanoparticles are regulated, and slow

drug release can maintain therapeutic concentrations inside the tumor for an extended time. By functionalizing them with specific ligands, nanoparticles become more selective against cancer cells while causing the least amount of damage to healthy cells. This focused technique is a promising approach in cancer therapy since it maximizes beneficial benefits while improving treatment efficacy [18]. The therapeutic medications that were encapsulated in these nanoparticles prevented them from degrading, boosting the drug's

stability and guaranteeing its efficient distribution to the intended spot. Furthermore, it increases permeability because tumor cells with leaky blood vessels preferentially accumulate nanoparticles [19]. Specifically targeting malignant cells in the oral cavity while minimizing the negative effects on healthy tissues is the goal of targeted medication delivery for oral cancer.

The varying responses of different tumors to therapy necessitate the development of tailored treatment approaches to optimize efficacy and outcomes. Hence, devising a method for administering suitable medications becomes imperative. Factors such as tumor type, stage, and genetic makeup influence the effectiveness of treatment, highlighting the importance of personalized medicine in oncology [20]. Additionally, considering individual patient factors such as age, overall health, and treatment tolerance is vital for achieving optimal therapeutic results. Thus, the ability to customize treatment strategies based on comprehensive patient and tumor characteristics is essential for improving patient outcomes in cancer care. Treatments for oral cancer vary in their effectiveness and responsiveness, which can lead to advanced stages of the disease and delayed identification, complicate biopsies by making tumors harder to access, spread to surrounding structures, and cause severe problems with eating, speaking, and facial appearance, among other things. In addition, the course of treatment involves invasive operations and strenuous therapies that negatively impact the quality of human life. There are obstacles to overcome, such as perfecting the formulation to guarantee that both medications are released in the proper way and the right amounts. Furthermore, a detailed assessment of the nanoparticles' safety and biocompatibility is required.

Conclusion

If cancer is identified early enough, contemporary technology can help cure almost any kind of cancer. Preventive measures are crucial in reducing the incidence of oral cancer, including avoiding all types of tobacco, drinking less alcohol, practicing good dental hygiene, protecting the lips from the sun, and receiving the HPV vaccine. Many kinds of nanomaterials have been used recently to fight various types of cancer. Significant advances have been made in delivery methods based on nanoparticles. For example, hybrid nanoparticles have recently become available for use in a variety of cancer treatments. Moreover, engineered nanoparticles employ tailored moieties to target cancer cells more accurately. Drug delivery systems have the potential to minimize adverse effects and greatly increase the effectiveness of oral cancer therapy. Enhancing therapeutic medicine's effectiveness while lowering its negative effects is the goal of the nanotechnology-based drug delivery system. Furthermore, nanoparticles are designed to identify cancer-related biomarkers (e.g., DNA mutations). By selectively binding to the biomarkers, these functionalized nanoparticles can alter their optical, electrical, and magnetic characteristics. These changes can be readily identified and measured, facilitating early diagnosis and individualized treatment plans. More research and development in these areas is required to provide patients with oral cancer with state-of-the-art personalized and targeted treatment.

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References

- [1]. Borse, V., Konwar, A.N., Buragohain, P., 2020. Oral cancer diagnosis and perspectives in India. *Sens Int.* 1, 100046.
- [2]. Liang, K.H., Lin, Y.Y., Chiang, S.H., Tsai, E.T., Lo, W.L., Wang, C.L., Wang, T.Y., Sun, Y.C., Kao, S.Y., Wu, C.H., Hung, K.F., 2021. Recent progress of biomarkers in oral cancers. *J Chinese Med Assoc.* 84, 987-992.
- [3]. Alam, M.K., Alqhtani, N.R., Alnufaiy, B., *et al.* 2024. A systematic review and meta-analysis of the impact of resveratrol on oral cancer: potential therapeutic implications. *BMC Oral Health.* 24, 412.
- [4]. Satapathy, P., Khatib, M.N., Gaidhane, S., Zahiruddin, Q.S., *et al.* 2024. Prevalence of human papillomavirus in head and neck cancer patients in India: a systematic review and meta-analysis. *BMC Infect Dis.* 24, 516.
- [5]. Arshad, S., Hussain, S.F.J., Jayaram, S., Veeraraghavan, V.P., Karobari, M.I., 2024. Perspective on enhancing quality of life in oral cancer patients: Integrative approaches and comprehensive care. *Oral Oncol Report.* 11, 100633.
- [6]. Mustafa, A., Indiran, M.A., Ramalingam, K., Perumal, E., Shanmugham, R., Karobari, M.I., 2024. Anticancer potential of thiocolchicoside and lauric acid loaded chitosan nanogel against oral cancer cell lines: a comprehensive study. *Sci Rep.* 14, 9270.
- [7]. Hosomi, Y., Morita, S., Sugawara, S., Kato, T., Fukuhara, T., Gemma, A., Takahashi, K., Fujita, Y., Harada, T., Minato, K., Takamura, K., Hagiwara, K., Kobayashi, K., Nukiwa, T., Inoue, A., 2020. North-East japan study group. gefitinib alone versus gefitinib plus chemotherapy for non-small-cell lung cancer with mutated epidermal growth factor receptor: NEJ009 Study. *J Clin Oncol.* 38, 115-123.
- [8]. Dristant, U., Mukherjee, K., Saha, S., Maity, D., 2023. An overview of polymeric nanoparticles-based drug delivery system in cancer treatment. *Technol. Cancer Res Treatment.* 22:1-23.
- [9]. Salari, N., Faraji, F., Torghabeh, F.M., Faraji, F., Mansouri, K., Abam, F., Shohaimi, S., Akbari, H., Mohammadi, M., 2022. Polymer-based drug delivery systems for anticancer drugs: A systematic review. *Cancer Treatment and Res Communication.* 32, 100605.
- [10]. Beaux, M.F., McIlroy, D.N., Gustin, K.E., 2008. Utilization of solid nanomaterials for drug delivery. *Expert Opinion Drug Deliv.* 5, 725-735.
- [11]. Dang, Y., Guan, J., 2020. Nanoparticle-based drug delivery systems for cancer therapy. *Smart Mat Med.* 1, 10-19.
- [12]. Saha, C., Kaushik, A., Das, A., Pal, S., Majumder, D., 2016. Anthracycline drugs on modified surface of quercetin-loaded polymer nanoparticles: A dual drug delivery model for cancer treatment. *PLoS One* 2016;11:e0155710.
- [13]. Beach, M.A., Nayanathara, U., Gao, Y., Zhang, C., Xiong, Y., Wang, Y., Such, G.K., 2024. Polymeric nanoparticles for drug delivery. *Chem Rev.* 124, 5505-5616.
- [14]. Gu, Z., Da Silva, C.G., Van der Maaden, K., Ossendorp, F., Cruz, L.J., 2020. Liposome-Based Drug Delivery Systems in Cancer Immunotherapy. *Pharmaceutics.* 12, 1054.
- [15]. Ghanbarikondori, P., Aliakbari, R.B.S., Saberian, E. *et al.* 2024. Enhancing Cisplatin Delivery via Liposomal Nanoparticles for Oral Cancer Treatment. *Ind J Clin Biochem.*
- [16]. Wang, J., Gong, J., Wei, Z., 2022. Strategies for Liposome Drug Delivery Systems to Improve Tumor Treatment Efficacy. *AAPS PharmSciTech* 23, 27.
- [17]. Duarte, D., Vale, N., 2022. Evaluation of synergism in drug combinations and reference models for future orientations in oncology. *Curr Res Pharmacol Drug Discov.* 3, 100110.

Conflict of Interest

The authors hereby declare that there is no conflict of interest in this study.

[18]. Gavas, S., Quazi, S., Karpiński, T.M., 2021. Nanoparticles for Cancer Therapy: Current Progress and Challenges. *Nanoscale Res Lett.* 16, 173.

[19]. Cheng, X., Xie, Q., Sun, Y., 2023. Advances in nanomaterial-based targeted drug delivery systems. *Front Bioeng Biotechnol.* 11, 1177151.

[20]. Krzyszczyk, P., Acevedo, A., Davidoff E.J., Timmins, L.M., Marrero-Berrios, I., Patel, M., White, C., Lowe, C., Sherba, J.J., Hartmanshenn, C., O'Neill, K.M., Balter, M.L., Fritz, Z.R., Androulakis, I.P., Schloss, R.S., Yarmush, M.L., 2018. The growing role of precision and personalized medicine for cancer treatment. *Technology (Singap World Sci)*, 6, 79-100.