Nano-Drug Delivery Systems in Oral Cancer Therapy

Subjects: Dentistry, Oral Surgery & Medicine

Contributor: Yun Zhang , Yongjia Wu , Hongjiang Du , Zhiyong Li , Xiaofeng Bai , Yange Wu , Huimin Li , Mengqi Zhou , Yifeng Cao , Xuepeng Chen

Oral cancer (OC), characterized by malignant tumors in the mouth, is one of the most prevalent malignancies worldwide. Chemotherapy is a commonly used treatment for OC; however, it often leads to severe side effects on human bodies. Nanotechnology has emerged as a promising solution for managing OC using nanomaterials and nanoparticles (NPs). Nano-drug delivery systems (nano-DDSs) that employ various NPs as nanocarriers have been extensively developed to enhance current OC therapies by achieving controlled drug release and targeted drug delivery.

oral cancer nanomaterial nanoparticle nano-drug delivery system targeting

1. Introduction

Oral cancer (OC), explicitly affecting the oral cavity and oropharynx, is classified as a subtype of head and neck cancer. It is characterized by the presence of malignant tumors in various tissues, including the lips, tongue, palate, floor of the mouth, hypopharynx, oropharynx, larynx, alveolar mucosa, buccal mucosa, gingiva, or a combination of these [1][2][3][4][5][6]. The most frequently occurring OC cases are lip and oral cavity cancers. Oral squamous cell carcinoma (OSCC) is the predominant type of OC, accounting for 90% of OC cases and ranking among the 15 most common cancers worldwide. OSCC is highly dangerous, with a high morbidity rate, malignancy, and poor prognosis. Treating OSCC is challenging due to its high recurrence rate and tendency for lymph node metastasis [3].

Excessive alcohol and tobacco use, biological factors such as human papillomavirus (HPV), syphilis, oro-dental factors, betel chewing, nutritional deficits, and viruses are potential risk factors for OC. Patients with OC may experience early symptoms such as non-healing ulcers, intraoral bleeding, leukoplakia, erythroplakia, oral submucous fibrosis, and abnormal lumps in the mouth [4]. However, during the early stages of OC, many patients may not experience noticeable symptoms or signs of deterioration. This can lead to a delayed diagnosis and, in some cases, may result in the cancer progressing to an advanced, incurable stage, ultimately leading to increased medical expenses for the patient [5][6]. Globally, the survival rates for OC patients over five years range from 45% to 72% [1][2]. The survival rates gradually decrease with the delay of disease detection, with the five-year survival rate approaching 80% when OC is detected at an early stage but dropping to less than 20% when it is diagnosed at a late stage [7].

For several decades, the primary treatments for OC have been surgery, chemotherapy, radiation therapy (RT), and combination therapy. However, these treatments often have severe side effects and toxicity [8][9][10]. OC surgery can result in impairment or changes in breathing, swallowing, speaking, and other functions due to the removal of some oral tissues. It can also cause pain, swelling, bruising, xerostomia, infection, and bumps or scars on the face or neck [11]. RT can lead to side effects, such as oral mucosal inflammation, hypofunction of salivary glands, dysphagia, oral infections, nausea, vomiting, and skin reaction [12]. Chemotherapy involves the use of highly toxic drugs like cisplatin (CDDP), paclitaxel (PTX), 5-fluorouracil (5-FU), doxorubicin (DOX), methotrexate, cetuximab, and docetaxel (DTX), which can cause ulcers, mucositis, xerostomia, and damage to the skin, hair, blood, and kidneys [13][14][15][16][17][18][19]. Although low-toxic therapies, such as light stimulus-responsive therapies, including photodynamic therapy (PDT) and photothermal therapy (PTT) [20][21], as well as immunotherapy [22][23], have been studied for OC treatment, they have not been mature in clinical practice.

The clinical manifestations and treatment effects on OC patients can cause severe impacts on their lives, including adverse psychosocial effects from various aspects, the decline and loss of aesthetic and oral function, and the ensuing physical changes. Moreover, the economic cost of cancer treatment can increase the burden of OC patients and significantly impact their quality of life [24]. Therefore, there is an urgent need for innovative therapeutic strategies that prioritize bioavailability and precise drug delivery while minimizing harm to healthy cells or tissues [25].

In recent years, nanotechnology has played a crucial role in this regard. Various nanoparticles (NPs) have been developed to detect, diagnose, and treat OC [26][27] while minimizing damage to healthy cells during treatment [1][28][29][30]. Nanomaterials have emerged as vital tools in the development of new and effective therapies for OC [29] since they can be directly used as antitumor drugs [3][31][32][33][34][35][36][37] or utilized to form nano-drug delivery systems (nano-DDSs) for the administration of antitumor drugs.

DDSs are commonly used to address issues such as low solubility, poor absorption, poor permeability, inappropriate size, instability, and first-pass metabolism of chemotherapy drugs. Conventional DDSs like oral tablets, capsules, and injections, have been widely used in clinical settings to control drug release and ensure targeted delivery, resulting in improved pharmacokinetics, sustained bioavailability, and enhanced distribution at the primary tumor site [1][5][38][39][40]. In addition, the manufacturing process for conventional DDSs is well-established and cost-effective. However, many conventional DDSs lack the ability to specifically target diseased cells or tissues, leading to potential off-target effects and low accumulation at the desired sites. Individual differences in absorption and metabolism can also affect the bioavailability of drugs in conventional DDSs, resulting in inconsistent treatment outcomes. Additionally, the poor solubility of certain drugs poses challenges in formulating them into effective conventional DDSs. In contrast, nano-DDSs offer various advantages over conventional DDSs. They can be designed to target specific cells or tissues, increase drug delivery efficiency, minimize off-target effects, and can also improve the solubility of poorly water-soluble drugs, enabling the delivery of a wider range of therapeutic compounds [30][41][42]. In addition, due to the high permeability of micro-vessels in tumor tissues and the poor lymphatic drainage, NPs can take advantage of the enhanced permeability and retention (EPR) effects, swiftly entering tumor tissues and accumulating at tumor sites, allowing for sustained and controlled release [43]. Despite

their benefits, some nanomaterials used in nano-DDSs may have toxicity issues, and their effective clearance and biodegradation in the body may present challenges, potentially leading to long-term accumulation and effects. Therefore, a comprehensive safety assessment is required. Furthermore, the manufacturing and scaling of nano-DDSs are technically challenging and require specialized equipment and expertise. So far, many NPs have been utilized as carriers for antitumor chemotherapy drugs and other therapeutic agents.

Targeted nano-drug delivery systems (nano-DDS) is a technology that allows drugs to be delivered precisely to the targeted organs, cells, or molecules [44], thereby safeguarding healthy cells and minimizing the side effects of loaded drugs, making it a practical approach for treating OC. Targeted drug delivery can be categorized as passive, active, immune, and magnetic targeting based on the targeting methods.

2. Passive Targeting

Passive targeting relies on the EPR effect of tumor tissue. The neovascularization in tumor tissue allows small-diameter nanocarriers to easily pass through the blood vessel wall and reach the tumor tissue with higher permeability compared to normal tissue. Nanocarriers are modified and assembled with drugs to increase their stability in plasma and extend their circulation time in the blood. This increases the chances of the nanocarriers aggregating in tumor tissues. The drugs are then delivered to the tumor cells through extracellular diffusion, which enhances the distribution and retention time of the drugs [44].

To achieve a better EPR effect, the nano-DDS must maintain stability in plasma without leakage and have a long blood circulation time to increase the chance of aggregation in tumor tissues [45] while also being able to penetrate deeply into the tumor. However, achieving long blood circulation and deep penetration into the tumor can be challenging, as these requirements may contradict each other. To achieve long circulation in the blood, the nano-DDS must possess a slightly larger particle size (such as 50~200 nm, preferably ca. 100 nm) [46] with a hydrophilic modification on the surface and be negatively charged [47]. On the other hand, for optimal uptake by tumor cells and deep penetration into the tumor tissue, nano-DDS should have a smaller size (such as <50 nm) and a positively charged surface after diffusion from capillaries to the tumor site [48]. In addition, the shape of the nano-DDS also plays a role in enhancing the EPR effect. By rationally designing the nano-DDS through size variation [49] [50], shape modification [51], surface charge reversion [52], and other factors, the EPR effect can be improved.

3. Active Targeting

For active targeting, the surface of nanocarriers is typically modified with specific ligands, such as aptamers, peptide chains, and antibodies. By recognizing and binding to receptors on tumor cells and in the tumor microenvironment (TME), the nanocarriers deliver drugs to the intended sites, effectively enhancing the precision and efficacy of drugs and minimizing toxic side effects of drugs on normal tissues [44][53][54].

In targeted tumor therapy for OC, various sites such as tumor vessels, interstitial fluid and extracellular matrix, tumor matrix cells, tumor cells, related dendritic synaptic cells, and tumor stem cells can be targeted using nano-

DDSs [28]. Depending on the characteristics of the tumors, different target sites can be selected in clinical treatment and nanocarriers can be modified accordingly. The identified overexpressed receptors in OC cells are listed in **Table 1**.

Table 1. Summary of ligands and targeted receptors overexpressed in OC cells.

Ligand	Target Receptor	Ref.
Folic acid (FA)	FA receptor	[55][56][57][58][59][60][61]
Protein corona-modulating Tf2 peptide	Transferrin receptor (TfR)	[62]
HN-1, a 12-amino acid peptide	HN-1 receptor	[63][64]
Anti Programmed death-ligand 1 (PD-L1) antibody	PD-L1	[65][66]
α-tocopherol	α-tocopherol receptor	[67]
Fucoidan	Scavenger-A receptors (SR-A), L-selectin, Toll-like receptors, and PD-L1	[68]
Antibodies specific for matrix metalloproteinase-1 (MMP-1)	MMP-1	[69]
pH-sensitive H-peptide	Epidermal growth factor receptor (EGFR)	[70]
Anti-Her-2 (human epidermal growth factor receptor 2) nanobody	Her-2	[71]
Dental pulp mesenchymal stem cell (DPSC), which expresses the CXCL8 binding receptor, CXCR2	Chemokine CXCL8	[72]
Chemokine SDF-1	CXC chemokine receptor 4 (CXCR4)	[73]
Shiga Toxin-B	Globotriaosylceramide receptor (GB3)	[74]
Fibroblast activation protein (FAP)-targeted peptide chains	FAP	[75]
AE105 (H-Asp-Cha-Phe-(d)Ser-(d)Arg-Tyr-Leu-Trp-SerOH) peptide	Urokinase plasminogen activator receptor (uPAR)	[76]

4. Immune Targeting

Cancer cells have developed various strategies to evade the immune system, such as reducing the expression of cell surface antigens, secreting antigens that inactivate the immune system, and stimulating the TME to release immune-suppressing chemicals that promote tumor growth. Cancer immune targeting is a treatment method that aims to activate the host's immune system using foreign materials, including both active and passive immunity approaches. Active immunotherapy involves stimulating the production of antibodies that specifically target and eliminate tumor cells by administering vaccines containing tumor antigens into the patient's body. On the other

hand, passive immunity involves using highly specific antibodies as carriers to introduce foreign substances with antitumor effects into the body. These antibodies target specific receptors on the surface of tumor cells, thereby enhancing the immune response. Nano-DDSs offer a promising approach in the field of OC immunotherapy, directly targeting cancer cells and helping facilitate the intracellular penetration of therapeutic agents, potentially minimizing autoimmune side effects and reducing treatment costs [77][78][79].

5. Magnetic Targeting

Magnetic NPs are inorganic materials that can be easily manipulated using external magnetic field gradients, allowing for precise targeting of desired sites [80][81]. Magnetic targeting is a technique used in cancer therapy where magnetic NPs are delivered to tumor cells and concentrated in the lesion area using external magnets. This method enhances the effectiveness of chemotherapy drugs that are administered along with magnetic NPs. Furthermore, magnetic NPs also possess magnetic hyperthermia properties, which can be utilized in an alternating magnetic field (AMF) to kill tumor cells.

References

1. Sachdeva, A.; Dhawan, D.; Jain, G.K.; Yerer, M.B.; Collignon, T.E.; Tewari, D.; Bishayee, A. Novel Strategies for the Bioavailability Augmentation and Efficacy Improvement of Natural Products in Oral Cancer. Cancers 2022, 15, 268.
2. Nor, J.E.; Gutkind, J.S. Head and Neck Cancer in the New Era of Precision Medicine. J. Dent. Res. 2018, 97, 601–602.
3. Yang, C.M.; Chu, T.H.; Tsai, K.W.; Hsieh, S.; Kung, M.L. Phytochemically Derived Zingerone Nanoparticles Inhibit Cell Proliferation, Invasion and Metastasis in Human Oral Squamous Cell Carcinoma. Biomedicines 2022, 10, 320.
4. Cardona-Mendoza, A.; Olivares-Nino, G.; Diaz-Baez, D.; Lafaurie, G.I.; Perdomo, S.J. Chemopreventive and Anti-tumor Potential of Natural Products in Oral Cancer. Nutr. Cancer 2022, 74, 779–795.
5. Vyas, K.; Rathod, M.; Patel, M.M. Insight on nano drug delivery systems with targeted therapy in treatment of oral cancer. Nanomedicine 2023, 49, 102662.
6. Mummudi, N.; Agarwal, J.P.; Chatterjee, S.; Mallick, I.; Ghosh-Laskar, S. Oral Cavity Cancer in the Indian Subcontinent—Challenges and Opportunities. Clin. Oncol. R. Coll. Radiol. 2019, 31, 520–528.
7. Peacock, Z.S.; Pogrel, M.A.; Schmidt, B.L. Exploring the reasons for delay in treatment of oral cancer. J. Am. Dent. Assoc. 2008, 139, 1346–1352.

8. Wessels, R.; De Roose, S.; De Bruyckere, T.; Eghbali, A.; Jacquet, W.; De Rouck, T.; Cosyn, J. The Mucosal Scarring Index: Reliability of a new composite index for assessing scarring following oral surgery. Clin. Oral. Investig. 2019, 23, 1209–1215.
9. Desai, K. Polymeric drug delivery systems for intraoral site-specific chemoprevention of oral cancer. J. Biomed. Mater. Res. B Appl. Biomater. 2018, 106, 1383–1413.
10. Furness, S.; Glenny, A.M.; Worthington, H.V.; Pavitt, S.; Oliver, R.; Clarkson, J.E.; Macluskey, M.; Chan, K.K.; Conway, D.I. Interventions for the treatment of oral cavity and oropharyngeal cancer: Chemotherapy. Cochrane Database Syst. Rev. 2010, 12, CD006386.
11. Nandini, D.B.; Rao, R.S.; Hosmani, J.; Khan, S.; Patil, S.; Awan, K.H. Novel therapies in the management of oral cancer: An update. Dis. Mon. 2020, 66, 101036.
12. Lin, A. Radiation Therapy for Oral Cavity and Oropharyngeal Cancers. Dent. Clin. N. Am. 2018, 62, 99–109.
13. Subramaniam, N.; Muthukrishnan, A. Oral mucositis and microbial colonization in oral cancer patients undergoing radiotherapy and chemotherapy: A prospective analysis in a tertiary care dental hospital. J. Investig. Clin. Dent. 2019, 10, e12454.
14. Mannelli, G.; Arcuri, F.; Agostini, T.; Innocenti, M.; Raffaini, M.; Spinelli, G. Classification of tongue cancer resection and treatment algorithm. J. Surg. Oncol. 2018, 117, 1092–1099.
15. Fang, L.; Zhou, H.; Cheng, L.; Wang, Y.; Liu, F.; Wang, S. The application of mesoporous silica nanoparticles as a drug delivery vehicle in oral disease treatment. Front. Cell Infect. Microbiol. 2023, 13, 1124411.
16. Hartner, L. Chemotherapy for Oral Cancer. Dent. Clin. N. Am. 2018, 62, 87–97.
17. Tewari, D.; Rawat, P.; Singh, P.K. Adverse drug reactions of anticancer drugs derived from natural sources. Food Chem. Toxicol. 2019, 123, 522–535.
18. Mitra, A.K.; Agrahari, V.; Mandal, A.; Cholkar, K.; Natarajan, C.; Shah, S.; Joseph, M.; Trinh, H.M.; Vaishya, R.; Yang, X.; et al. Novel delivery approaches for cancer therapeutics. J. Control Release 2015, 219, 248–268.
19. Calixto, G.; Bernegossi, J.; Fonseca-Santos, B.; Chorilli, M. Nanotechnology-based drug delivery systems for treatment of oral cancer: A review. Int. J. Nanomed. 2014, 9, 3719–3735.
20. Fan, H.Y.; Zhu, Z.L.; Zhang, W.L.; Yin, Y.J.; Tang, Y.L.; Liang, X.H.; Zhang, L. Light stimulus responsive nanomedicine in the treatment of oral squamous cell carcinoma. Eur. J. Med. Chem. 2020, 199, 112394.
21. Fan, H.Y.; Yu, X.H.; Wang, K.; Yin, Y.J.; Tang, Y.J.; Tang, Y.L.; Liang, X.H. Graphene quantum dots (GQDs)-based nanomaterials for improving photodynamic therapy in cancer treatment. Eur. J. Med. Chem. 2019, 182, 111620.

22. Mittal, D.; Gubin, M.M.; Schreiber, R.D.; Smyth, M.J. New insights into cancer immunoediting and its three component phases--elimination, equilibrium and escape. Curr. Opin. Immunol. 2014, 27, 16–25.
23. Moskovitz, J.; Moy, J.; Ferris, R.L. Immunotherapy for Head and Neck Squamous Cell Carcinoma. Curr. Oncol. Rep. 2018, 20, 22.
24. Valdez, J.A.; Brennan, M.T. Impact of Oral Cancer on Quality of Life. Dent. Clin. N. Am. 2018, 62, 143–154.
25. Perez-Herrero, E.; Fernandez-Medarde, A. Advanced targeted therapies in cancer: Drug nanocarriers, the future of chemotherapy. Eur. J. Pharm. Biopharm. 2015, 93, 52–79.
26. Chen, X.J.; Zhang, X.Q.; Liu, Q.; Zhang, J.; Zhou, G. Nanotechnology: A promising method for oral cancer detection and diagnosis. J. Nanobiotechnol. 2018, 16, 52.
27. Marcazzan, S.; Varoni, E.M.; Blanco, E.; Lodi, G.; Ferrari, M. Nanomedicine, an emerging therapeutic strategy for oral cancer therapy. Oral. Oncol. 2018, 76, 1–7.
28. Zhu, Y.; Wen, L.M.; Li, R.; Dong, W.; Jia, S.Y.; Qi, M.C. Recent advances of nano-drug delivery system in oral squamous cell carcinoma treatment. Eur. Rev. Med. Pharmacol. Sci. 2019, 23, 9445–9453.
29. Yu, C.; Li, L.; Wang, S.; Xu, Y.; Wang, L.; Huang, Y.; Hieawy, A.; Liu, H.; Ma, J. Advances in nanomaterials for the diagnosis and treatment of head and neck cancers: A review. Bioact. Mater. 2023, 25, 430–444.
30. Ding, Z.; Sigdel, K.; Yang, L.; Liu, Y.; Xuan, M.; Wang, X.; Gu, Z.; Wu, J.; Xie, H. Nanotechnology-based drug delivery systems for enhanced diagnosis and therapy of oral cancer. J. Mater. Chem. B 2020, 8, 8781–8793.
31. Essawy, M.M.; Mohamed, M.M.; Raslan, H.S.; Rafik, S.T.; Awaad, A.K.; Ramadan, O.R. The theranostic potentialities of bioavailable nanocurcumin in oral cancer management. BMC Complement. Med. Ther. 2022, 22, 309.
32. Subramanyam, G.K.; Gaddam, S.A.; Kotakadi, V.S.; Gunti, H.; Palithya, S.; Penchalaneni, J.; Challagundla, V.N. Green Fabrication of silver nanoparticles by leaf extract of Byttneria Herbacea Roxb and their promising therapeutic applications and its interesting insightful observations in oral cancer. Artif. Cells Nanomed. Biotechnol. 2023, 51, 83–94.
33. Halkai, K.R.; Halkai, R.; Patil, S.; Alawadi, J.; Alawadhi, W.S.; Marukala, N.R.; Mohammad, A.N.; Indi, S. Evaluation of cytotoxic effects of fungal origin nanosilver particles on oral cancer cell lines: An in vitro study. J. Cancer Res. Ther. 2022, 18, 240–244.
34. Wang, S.W.; Lee, C.H.; Lin, M.S.; Chi, C.W.; Chen, Y.J.; Wang, G.S.; Liao, K.W.; Chiu, L.P.; Wu, S.H.; Huang, D.M.; et al. ZnO Nanoparticles Induced Caspase-Dependent Apoptosis in Gingival

Squamous Cell Carcinoma through Mitochondrial Dysfunction and p70S6K Signaling Pathway. Int. J. Mol. Sci. 2020, 21, 1612.

35. Jing, D.; Jiang, N.; Wang, F.; Mao, C.; Han, S.; Ho, P.Y.; Xiao, W.; Li, Y.; Li, J.J.; Zhang, L.; et al. Nanoradiosensitizer with good tissue penetration and enhances oral cancer radiotherapeutic effect. Biomaterials 2022, 289, 121769.
36. Chen, M.H.; Chen, M.H.; Li, C.Y.; Tung, F.I.; Chen, S.Y.; Liu, T.Y. Using Gold-Nanorod-Filled Mesoporous Silica Nanobeads for Enhanced Radiotherapy of Oral Squamous Carcinoma. Nanomaterials 2021, 11, 2235.
37. Chen, L.; Kong, Q.; Tian, M.; Zhang, Q.; Xia, C.; Deng, C. Zn0.4Mg0.6Fe2O4 nanoenzyme: A novel chemo-sensitizer for the chemotherapy treatment of oral squamous cell carcinoma. Nanoscale Adv. 2023, 5, 851–860.
38. Masood, F. Polymeric nanoparticles for targeted drug delivery system for cancer therapy. Mater. Sci. Eng. C Mater. Biol. Appl. 2016, 60, 569–578.
39. Makvandi, P.; Josic, U.; Delfi, M.; Pinelli, F.; Jahed, V.; Kaya, E.; Ashrafizadeh, M.; Zarepour, A.; Rossi, F.; Zarrabi, A.; et al. Drug Delivery (Nano)Platforms for Oral and Dental Applications: Tissue Regeneration, Infection Control, and Cancer Management. Adv. Sci. 2021, 8, 2004014.
40. Zhang, M.; Liang, J.; Yang, Y.; Liang, H.; Jia, H.; Li, D. Current Trends of Targeted Drug Delivery for Oral Cancer Therapy. Front. Bioeng. Biotechnol. 2020, 8, 618931.
41. Ortega, A.; Da, S.A.; Da, C.L.; Zatta, K.C.; Onzi, G.R.; Da, F.F.; Guterres, S.S.; Paese, K. Thermosensitive and mucoadhesive hydrogel containing curcumin-loaded lipid-core nanocapsules coated with chitosan for the treatment of oral squamous cell carcinoma. Drug Deliv. Transl. Res. 2023, 13, 642–657.
42. Ying, N.; Liu, S.; Zhang, M.; Cheng, J.; Luo, L.; Jiang, J.; Shi, G.; Wu, S.; Ji, J.; Su, H.; et al. Nano delivery system for paclitaxel: Recent advances in cancer theranostics. Colloids Surf. B Biointerfaces 2023, 228, 113419.
43. Albanese, A.; Tang, P.S.; Chan, W.C. The effect of nanoparticle size, shape, and surface chemistry on biological systems. Annu. Rev. Biomed. Eng. 2012, 14, 1–16.
44. Witkowska, M.; Golusinska-Kardach, E.; Golusinski, W.; Florek, E. Polydopamine-Based Material and Their Potential in Head and Neck Cancer Therapy-Current State of Knowledge. Int. J. Mol. Sci. 2023, 24, 4890.
45. Kang, H.; Rho, S.; Stiles, W.R.; Hu, S.; Baek, Y.; Hwang, D.W.; Kashiwagi, S.; Kim, M.S.; Choi, H.S. Size-Dependent EPR Effect of Polymeric Nanoparticles on Tumor Targeting. Adv. Healthc. Mater. 2020, 9, e1901223.
46. Pastore, C. Size-dependent nano-bio interactions. Nat. Nanotechnol. 2021, 16, 1052.

47. Pattipeiluhu, R.; Arias-Alpizar, G.; Basha, G.; Chan, K.; Bussmann, J.; Sharp, T.H.; Moradi, M.A.; Sommerdijk, N.; Harris, E.N.; Cullis, P.R.; et al. Anionic Lipid Nanoparticles Preferentially Deliver mRNA to the Hepatic Reticuloendothelial System. Adv. Mater. 2022, 34, e2201095.
48. Yang, Z.Z.; Li, J.Q.; Wang, Z.Z.; Dong, D.W.; Qi, X.R. Tumor-targeting dual peptides-modified cationic liposomes for delivery of siRNA and docetaxel to gliomas. Biomaterials 2014, 35, 5226–5239.
49. Zhou, Y.; Liu, R.; Shevtsov, M.; Gao, H. When imaging meets size-transformable nanosystems. Adv. Drug Deliv. Rev. 2022, 183, 114176.
50. Cheng, X.; Li, H.; Ge, X.; Chen, L.; Liu, Y.; Mao, W.; Zhao, B.; Yuan, W.E. Tumor-Microenvironment- Responsive Size-Shrinkable Drug-Delivery Nanosystems for Deepened Penetration Into Tumors. Front. Mol. Biosci. 2020, 7, 576420.
51. Das, R.P.; Gandhi, V.V.; Singh, B.G.; Kunwar, A. Passive and Active Drug Targeting: Role of Nanocarriers in Rational Design of Anticancer Formulations. Curr. Pharm. Des. 2019, 25, 3034–3056.
52. Gou, J.; Liang, Y.; Miao, L.; Guo, W.; Chao, Y.; He, H.; Zhang, Y.; Yang, J.; Wu, C.; Yin, T.; et al. Improved tumor tissue penetration and tumor cell uptake achieved by delayed charge reversal nanoparticles. Acta Biomater. 2017, 62, 157–166.
53. Li, H.; Zhang, Y.; Xu, M.; Yang, D. Current trends of targeted therapy for oral squamous cell carcinoma. J. Cancer Res. Clin. Oncol. 2022, 148, 2169–2186.
54. Yan, S.; Huang, Q.; Chen, J.; Song, X.; Chen, Z.; Huang, M.; Xu, P.; Zhang, J. Tumor-targeting photodynamic therapy based on folate-modified polydopamine nanoparticles. Int. J. Nanomed. 2019, 14, 6799–6812.
55. Wang, F.; Wang, M.; Zhao, L.; Li, Q. A new biosafe reactive oxygen species responsive nanoplatform for targeted oral squamous cell carcinoma therapy. Mater. Express 2019, 9, 1076–1081.
56. Yin, H.; Wang, H.; Li, Z.; Shu, D.; Guo, P. RNA Micelles for the Systemic Delivery of Anti-miRNA for Cancer Targeting and Inhibition without Ligand. ACS Nano 2019, 13, 706–717.
57. Bharadwaj, R.; Medhi, S. Effectual nanotherapy against oral squamous cell carcinoma. Drug Dev. Ind. Pharm. 2021, 47, 711–724.
58. Rathinaraj, P.; Muthusamy, G.; Prasad, N.R.; Gunaseelan, S.; Kim, B.; Zhu, S. Folate-Gold-Bilirubin Nanoconjugate Induces Apoptotic Death in Multidrug-Resistant Oral Carcinoma Cells. Eur. J. Drug Metab. Pharmacokinet. 2020, 45, 285–296.
59. Cui, J.; Li, W.; Bu, W.; Liu, J.; Chen, X.; Li, X.; Liu, C.; Meng, L.; Chen, M.; Sun, H.; et al. Folic acid-modified disulfiram/Zn-IRMOF3 nanoparticles for oral cancer therapy by inhibiting

ALDH1A1+ cancer stem cells. Biomater. Adv. 2022, 139, 213038.

60. Cheng, X.Y.; Zhang, L.; Liu, X.Q.; Xu, L.P.; Liu, J.J. Folic acid mediated cisplatin magnetic nanodrug targeting in the treatment of oral squamous cell carcinoma. Mater. Express 2021, 11, 1299–1305.
61. Yin, X.; Li, Z.; Zhang, Y.; Zeng, X.; Wang, Q.; Liang, Z. Polydopamine surface-modified hyperbranched polymeric nanoparticles for synergistic chemo/photothermal therapy of oral cancer. Front. Bioeng. Biotechnol. 2023, 11, 1174014.
62. Mapanao, A.K.; Sarogni, P.; Santi, M.; Menicagli, M.; Gonnelli, A.; Zamborlin, A.; Ermini, M.L.; Voliani, V. Pro-apoptotic and size-reducing effects of protein corona-modulating nano-architectures enclosing platinum prodrug in in vivo oral carcinoma. Biomater. Sci. 2022, 10, 6135–6145.
63. Wang, Y.; Wan, G.; Li, Z.; Shi, S.; Chen, B.; Li, C.; Zhang, L.; Wang, Y. PEGylated doxorubicin nanoparticles mediated by HN-1 peptide for targeted treatment of oral squamous cell carcinoma. Int. J. Pharm. 2017, 525, 21–31.
64. Li, R.; Wang, Y.; Du, J.; Wang, X.; Duan, A.; Gao, R.; Liu, J.; Li, B. Graphene oxide loaded with tumor-targeted peptide and anti-cancer drugs for cancer target therapy. Sci. Rep. 2021, 11, 1725.
65. Chen, X.J.; Zhang, X.Q.; Tang, M.X.; Liu, Q.; Zhou, G. Anti-PD-L1-modified and ATRA-loaded nanoparticles for immuno-treatment of oral dysplasia and oral squamous cell carcinoma. Nanomedicine 2020, 15, 951–968.
66. Choi, B.; Choi, J.H.; Kim, U.K.; Hwang, D.S.; Kim, G.C. Gold nanoparticles conjugated with programmed death-ligand 1 antibodies induce apoptosis of SCC-25 oral squamous cell carcinoma cells via programmed death-ligand 1/signal transducer and transcription 3 pathway. Arch. Oral. Biol. 2021, 125, 105085.
67. Srivastava, S.; Gupta, S.; Mohammad, S.; Ahmad, I. Development of alpha-tocopherol surface-modified targeted delivery of 5-fluorouracil-loaded poly-D, L-lactic-co-glycolic acid nanoparticles against oral squamous cell carcinoma. J. Cancer Res. Ther. 2019, 15, 480–490.
68. Moustafa, M.A.; El-Refaie, W.M.; Elnaggar, Y.; El-Mezayen, N.S.; Awaad, A.K.; Abdallah, O.Y. Fucoidan/hyaluronic acid cross-linked zein nanoparticles loaded with fisetin as a novel targeted nanotherapy for oral cancer. Int. J. Biol. Macromol. 2023, 241, 124528.
69. Tsai, M.T.; Sun, Y.S.; Keerthi, M.; Panda, A.K.; Dhawan, U.; Chang, Y.H.; Lai, C.F.; Hsiao, M.; Wang, H.Y.; Chung, R.J. Oral Cancer Theranostic Application of FeAu Bimetallic Nanoparticles Conjugated with MMP-1 Antibody. Nanomaterials 2021, 12, 61.
70. Wang, C.S.; Chang, C.H.; Tzeng, T.Y.; Lin, A.M.; Lo, Y.L. Gene-editing by CRISPR-Cas9 in combination with anthracycline therapy via tumor microenvironment-switchable, EGFR-targeted,

and nucleus-directed nanoparticles for head and neck cancer suppression. Nanoscale Horiz. 2021, 6, 729–743.

71. Wu, W.; Shi, L.; Duan, Y.; Xu, S.; Shen, L.; Zhu, T.; Hou, L.; Meng, X.; Liu, B. Nanobody modified high-performance AIE photosensitizer nanoparticles for precise photodynamic oral cancer therapy of patient-derived tumor xenograft. Biomaterials 2021, 274, 120870.
72. Zhou, D.; Chen, Y.; Bu, W.; Meng, L.; Wang, C.; Jin, N.; Chen, Y.; Ren, C.; Zhang, K.; Sun, H. Modification of Metal-Organic Framework Nanoparticles Using Dental Pulp Mesenchymal Stem Cell Membranes to Target Oral Squamous Cell Carcinoma. J. Colloid. Interface Sci. 2021, 601, 650–660.
73. Xiong, J.; Feng, J.; Qiu, L.; Gao, Z.; Li, P.; Pang, L.; Zhang, Z. SDF-1-loaded PLGA nanoparticles for the targeted photoacoustic imaging and photothermal therapy of metastatic lymph nodes in tongue squamous cell carcinoma. Int. J. Pharm. 2019, 554, 93–104.
74. Navarro-Palomares, E.; Garcia-Hevia, L.; Galan-Vidal, J.; Gandarillas, A.; Garcia-Reija, F.; Sanchez-Iglesias, A.; Liz-Marzan, L.M.; Valiente, R.; Fanarraga, M.L. Shiga Toxin-B Targeted Gold Nanorods for Local Photothermal Treatment in Oral Cancer Clinical Samples. Int. J. Nanomed. 2022, 17, 5747–5760.
75. Li, R.; Liu, C.; Wan, C.; Liu, T.; Zhang, R.; Du, J.; Wang, X.; Jiao, X.; Gao, R.; Li, B. A Targeted and pH-Responsive Nano-Graphene Oxide Nanoparticle Loaded with Doxorubicin for Synergetic Chemo-Photothermal Therapy of Oral Squamous Cell Carcinoma. Int. J. Nanomed. 2023, 18, 3309–3324.
76. Zuo, J.; Huo, M.; Wang, L.; Li, J.; Chen, Y.; Xiong, P. Photonic hyperthermal and sonodynamic nanotherapy targeting oral squamous cell carcinoma. J. Mater. Chem. B 2020, 8, 9084–9093.
77. Yang, M.; Li, J.; Gu, P.; Fan, X. The application of nanoparticles in cancer immunotherapy: Targeting tumor microenvironment. Bioact. Mater. 2021, 6, 1973–1987.
78. Xie, X.; Feng, Y.; Zhang, H.; Su, Q.; Song, T.; Yang, G.; Li, N.; Wei, X.; Li, T.; Qin, X.; et al. Remodeling tumor immunosuppressive microenvironment via a novel bioactive nanovaccines potentiates the efficacy of cancer immunotherapy. Bioact. Mater. 2022, 16, 107–119.
79. Lubek, J.E. Head and Neck Cancer Research and Support Foundations. Oral. Maxillofac. Surg. Clin. N. Am. 2018, 30, 459–469.
80. Park, J.H.; Saravanakumar, G.; Kim, K.; Kwon, I.C. Targeted delivery of low molecular drugs using chitosan and its derivatives. Adv. Drug Deliv. Rev. 2010, 62, 28–41.
81. Grillone, A.; Ciofani, G. Magnetic Nanotransducers in Biomedicine. Chemistry 2017, 23, 16109–16114.

Retrieved from https://encyclopedia.pub/entry/history/show/120643