

ORAL CANCER: NOVEL TREATMENTS AND APPROACHES

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ABSTRACT

The aggressive tumour known as oral cancer can metastasize, produce a high fatality rate, and infect nearby tissue. Surgery, chemotherapy, and radiation therapy, for example, are common treatment options that, when used in clinical settings, have both minimal drawbacks and major side effects. Currently, oral therapeutic medication delivery using targeted drug administration is proving to be effective. In recent years, an effective alternative therapy known as "nanomedicine," or using nanoplateforms to deliver drugs for the treatment of cancer, has evolved. Thanks to the use of nanoplateforms, drug delivery to the tumour site can be done precisely and with minimal drug degradation in the body. As a result, the drug's toxicity is diminished, its concentration at the tumour site is elevated, and its distribution to other organs is kept to minimum. We present a contemporary review of the development medication delivery targeted for the treatment of oral cancer in this article different oral delivery systems, including as cyclodextrins, liposomes, hydrogel-based forms, and nanolipids are highlighted and explored. Biomimetic systems, such as therapeutic vitamins, proteins, exosomes, and virus-like particles, with a focus on cancer treatment, are also described. The study concludes with a brief analysis of future applications for nanoplateforms in the treatment of oral cancer.

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INTRODUCTION

Tumors are referred regarded as having "oral cancer." that develop in the mouth. Oral squamous cell carcinoma (OSCC), which has a survival rate of less than 50% and is the sixth most frequent cancer worldwide, develops from the mucosal epithelium in further 90% of cases of oral cancer (1). Lip and oral cavity cancer claimed the lives of 177,384 people in 2018, with 354,864 new cases being reported (2). Environmental variables, particularly excessive alcohol and tobacco use, are crucial in the multifactorial illness and carcinogenesis in as well as genetic and epigenetic pathways for the OSCC (3). Additionally, the Along with other factors, oesophageal squamous cell carcinoma is linked to the human papillomavirus (HPV) greatly influence the start and development of OSCC treatment (4).

The three main treatments for oral cancer in conventional therapeutic regimens are surgeries, chemotherapy, and radiation therapy. Although these techniques have achieved great advancements in the treatment of oral cancer, they are not without serious downsides and side effects. In contrast, radiation therapy patients may face temporary or permanent damage to

healthy tissues, which has a significant influence on their health and quality of life. For example, chemotherapy patients may experience nausea, vomiting, hair loss, infections, and diarrhoea (5).

The pathogenesis of oral cancer, which involves the genetic pathway, merits in-depth study. The expression of proteins, chemical mediators, and enzymes is impacted by changes to the DNA in OSCC. The continual activation of additional genetic defects and clonal expansion characterize the multi-step process of carcinogenesis. Because the tumour suppressor gene was inactivated and the oncogene activated in OSCC, abnormal cell proliferation and death resulted. The most frequent genetic changes that result in a gene's inactivation include gene amplification, oncogene overexpression, mutation, deletion, and hypermethylation (e.g, p53 tumour suppressor genes) (6).

Chemotherapy has been utilized to treat oral cancer. In modern regimens, anticancer medicines may be combined or used alone. They can, however, damage healthy tissues more severely due to their intravenously given nature and non-specific tissue dispersion throughout the body. Oral chemotherapy is also recognized to have difficulties due to the restricted

solubility, permeability, and absorption of these anticancer drugs in physiological fluids. Therefore, it is essential to develop new treatment regimens or modify existing strategies in order to improve human health and longevity against oral cancer and tissues (7).

The scientific community has resorted to nanotechnology to create new and more potent nanotechnology-based drug carrier systems to enhance oral, buccal, and intravenous delivery modalities in order to address the drawbacks of present therapeutic procedures. Targeted drug delivery systems hold promise for overcoming the limitations of conventional anticancer medications and enhancing treatment efficacy by potentially greatly increasing medication bioavailability and bio-distribution at the site of the primary tumour (8). To improve individual oral cancer health outcomes, customized medication delivery devices can release a bioactive chemical at a precise location (9). The two most frequently employed candidates for delivering chemotherapy medications into the tumour site are both synthetic and naturally produced polymers. Therefore, it is exciting that customized drug delivery systems have the potential to reduce the severity or scope of some chemotherapy drugs' side effects. It has special applications in the treatment of patients with oral, head, and neck cancer as well as other cancers (10).

Causes

"Snuff smoke is clearly carcinogenic, as evidenced by the fact that it can lead to pancreatic and mouth cancer, among other cancers," the IARC stated in its 2007 study (11). Smokers have a three times greater chance of acquiring mouth cancer than nonsmokers (12). Additionally, compared to people who still smoke, people who stopped smoking four years ago had a 35% lower risk of developing oral cancer, while people who haven't smoked in more than 20 years don't have a higher risk. People who never smoked but were involuntarily exposed to cigarette smoke have an 87% higher risk of acquiring oral cancer than those who never smoked but were not exposed (13). Smoking lowers oral immunity through promoting oral cancer, periodontitis, and gingivitis (14).

Carriers Using Nanotechnology to Treat Oral Cancer

Increased pharmaceutical efficacy and decreased potential toxicity are urgently required in order to solve the issues with current chemotherapeutic drugs. Due to the drug-loaded nanoparticles of the perfect size and innovative controlled nanodelivery systems can express the imaginative alteration of drug release behaviors when the microenvironment is slightly adjusted. This is used for specialized treatment, medication based on nanotechnology delivery systems

have made some OSCC treatments possible (15). Due to their advanced benefits in terms of better therapeutic impact and lower unwanted effects, specific drug delivery systems are frequently used for the controlled release of drugs in place of chemotherapeutic agents. The fundamental characteristics of a bioactive substance are metabolism, distribution, and excretion can be considerably improved by these systems (16). This review describes a variety of nanotechnology-based carriers with their qualities, such as those based on hydrogel, cyclodextrins, nanolipids, nanoparticles, and liposomes. Additionally, the potential use of biomimetic nanoparticles as chemotherapeutic drug carriers for the treatment of oral cancer has been explored. These nanoparticles include vitamins, exosomes, peptides/proteins, and virus-like particles.

Treatment via Immunotherapy

Immune checkpoint inhibitors are among the most important medications that have been created to address numerous conditions of malignancies, including OSCC (immunotherapy medicines). By focusing on immunological PD-L1, PD-1, and CTLA4 are examples of checkpoint molecules, Immunosuppressant has been demonstrated to play an important part in the aetiology of OSCC. Finding new immunotherapy targets is critical because immune checkpoint inhibitors only effectively treat about 30% of cancer patients (16). According to other research, work demonstrates how addressing the underlying facts of how common environmental pollutants depress the immune system might result in a hugely useful new technique to cancer prevention and immunotherapy (17).

Oral cancer treatment Polymeric and nanoparticles-based

Nanoparticles are used more frequently in Oral cancer treatment requires tailored drug delivery systems with improved bioactivity and effective treatments that reduce systemic toxicity. This is due to their flexible chemical and physical properties. These carriers, which are mostly made of organic and synthetic nanoparticles, can be used to load, stabilize, and transport chemotherapeutic medications in a variety of launching release profiles and loading content. A drug carrier should have favorable biodegradability, biocompatibility and localized, regulated drug release behaviors (18-19). The malignant development of oral epithelial dysplasia into frank carcinoma can be stopped by modifying them to act as chemo-preventive medications and administering them directly to the affected parts of the mouth cavity. PEG-poly (glutamic acid) block copolymer-based polymeric nanoparticles were created by Endo et al. to lessen the toxicity of cisplatin and enhance OSCC therapy (20). The routes for caspase-3 and caspase-7 may be activated by

these cisplatin-loaded nanoparticles, causing apoptosis to occur and the destruction of the oral cancers. Comparing controlled release of cisplatin from nanoparticles to oral cisplatin in solution, nephrotoxicity and neurotoxicity could be greatly reduced in vitro and in vivo (21).

Oral cancer is treated with both inorganic nanoparticles and polymeric-inorganic hybrid nanoparticles

Clinical studies have demonstrated that anti-EGFR/Au conjugates may be efficiently transported into cancer cells with deep penetration using near-infrared (NIR) laser light, Surface Au NPs can absorb the NIR with ease, resulting in the greatest therapeutic effects, making this practicable. In vitro experiments shown that anti-EGFR/Au conjugates might be destroyed by photothermal means by OSCC cells without expending a lot of energy (22). To specifically target OSCC cells surface-mounted EGFRs and limit tumour development, Lucky et al. developed a form of biodegradable up-conversion nanoparticles with PEGylated titanium dioxide encapsulated in it (TiO₂) (23). This photodynamic treatment (PDT) technique for inorganic nanoparticles systems was useful for treating oral cancer, which needed anticancer medications to penetrate deeply into the body (24).

The precise distribution of drugs method that enables the reduction of toxicity and improvement of therapeutic efficacy is acknowledged as one of the advanced therapeutic benefits of combination medication therapy. Phytochemical anticancer vincristine (VCR) and photothermal agents' plasmonic gold nanorods (GNRs), were combined to create a chemo-photothermal therapy by Darwish et al. for OSCC therapy (25). The use of chem-covalent assembly to wrap gold nanorods with silica coating, VCR was physically enclosed inside the Amphiphilic PEG polymers that self-assemble to form a polymeric corona (GNRs), Under acidic intracellular conditions, the breakage of amide bonds resulted in the sustained VCR release, making the created combinational therapeutic nanoprobe suitable candidates for application in clinical trials in the future (26).

Treatment of Oral Cancer with Liposomes

Phospholipids, cholesterol, and a lipid that resembles a membrane are the main components of liposomes, which are a collection of microscopic particles that are single or multilayered. Liposomes, which are not hazardous to the most often used method of drug delivery to promote drug accumulation is through healthy tissues or cells at target areas. This technique has received a lot of attention because it combines highly effective therapy with the distribution of medication distribution and release (27). For instance, Employing

Swiss mice and photodynamic therapy, it was possible to demonstrate the efficacy of the treatment for oral cancer by creating a liposome type that might control the release of aluminium phthalocyanine chloride (28). Another study showed targeted drug delivery by using mixed lipid vesicles (LVs) made of different ratios of 1,2-distearoyl-sn-glycero-3-phosphocholine and 1,2-dioleoyl-sn-glycero-3-phosphocholine (29). Future in-depth studies regarding PDT's intracellular mechanism for the treatment of oral cancer may use these interactions as a roadmap.

Treatment of Oral Cancer with Cyclodextrins

The cisplatin, Docetaxel, methotrexate, and paclitaxel are anticancer medications are examples of hydrophobic guest molecules that can connect with the host through interactions with cyclodextrins, a type of cyclic oligosaccharides (30).

While the external polar surface encourages solubilizing activities, the inside lipophilic chamber inhibits the hydrophobic molecules from solvating in aqueous solutions. Due to their significant pharmacological activity and great therapeutic efficacy, cyclodextrins in this class and its derivatives are frequently utilized as flexible, excipients that can be customized for specific drug delivery (31). Wang et al. utilizing phospholipids compound technology we identified a family of hydrophilic supramolecular complexes and HP, CD insertion method that ostensibly increased two curcuminoids' oral bioavailability and solubility (32). The complexes of these supramolecular had considerable potential for oral cargo delivery since they were easy to make and had improved gastrointestinal absorption capability.

Treatment of oral cancer by nanolipids

Despite the fact that nanoparticles are frequently used to treat oral cancer, their effectiveness is diminished by their potential cytotoxicity and the restricted uptake by malignant cells (33). Easily made and frequently used are nanolipids-based carriers utilized to get over this restriction in the treatment of oral cancer. The deformed crystalline structures of these lipid carriers with a core matrix and a nanostructure made of both liquid and solid lipids can accommodate these amorphous clusters of local chemopreventive drugs. For medicinal OSCC applications, nanolipids can enhance the bioavailability, absorption, and durability of drug carriers based on these benefits (34).

Utilizing hydrogel and biomimetic nanoparticles for the treatment of oral cancer

Drugs that are both other biomolecules, including those that are hydrophilic and hydrophobic, can be delivered in a sustained or triggered way using

hydrogel, which are nanoparticles based carriers. Additionally, the administration of several drugs simultaneously with hydrogel carriers' results in medication resistance is decreased while there are synergistic anti-cancer benefits (35-36). The ineffectiveness of natural or artificial materials used as targeted drug carriers due to their poor drug doses, oral absorption, and transport efficiency for therapies are still significant concerns that need to be solved.

Nanoparticles with vitamin coatings for the treatment of oral cancer

Vitamin B12 (VB12) can interact with an intrinsic factor to form a complex in the stomach because of the receptor-mediated endocytosis absorption pathway. This complex is easily transformed into nanoparticles to improve oral administration. Trimethyl-chitosan or calcium phosphate nanoparticles modified by VB12 increase in oral insulin absorption (37). Another research developed a targeted a biotin-coated liposome to dispense sublingual insulin that greatly enhanced the drug's bioavailability by promoting favorable cellular absorption and fast digestive transportation (38). The amount of folate that is absorbed by cells is increased by folic acid (FA), a form of vitamin B9. FA has the capacity to bind to the folate receptor with high affinity and specificity (39).

Exosome, Proteins and Peptides in the Treatment of Oral Cancer

Exosomes are significant because they have the ability to transport for the intercellular exchange, different biomolecules or chemotherapeutics. This suggests that they could function as a unique medication delivery method for certain purposes (40).

The studies identified intestinal goblet cells as the target of the Chitosan NPs coated with CSK peptide, which successfully enhanced various peptides' oral bioavailability, small medications by promoting intestinal cellular absorption for oral distribution (41). Functional peptide-conjugated transferrin receptor-specific nanocarriers improved transcytosis, altered intracellular trafficking, and increased intracellular absorption in polarized cells for targeted oral drug administration (42).

Treatment of Oral Cancer with Virus-Like Particles (VLPs)

Regulating VLPs and providing their multifunction is made simple by genetically and chemically engineering the VLP proteins (43). The effectiveness of VLPs as oral antigen carriers for immunization has been well investigated however it is still unclear whether they offer superior delivery capabilities for alternative treatments for oral cancer (44).

Conclusion and future aspects

Nanotechnology-based treatments for oral cancer have encountered a variety of issues and advancements. Based on these targeted drugs delivery systems, which have specific designs and a variety of physicochemical features, these components can be loaded with anticancer payloads to target the malignant cells with high efficiency and minimal harm to the healthy cells. This particular location delivery behavior is made possible by these carriers. Numerous drug delivery techniques, including hydrogel, liposomes, cyclodextrins, nanolipids, polymeric/inorganic nanoparticles, and numerous biomimetic forms, have been thoroughly studied as potential treatments for oral cancer. By utilizing their delicate regulators of the structure-property link, the majority of these carriers demonstrated a significant viable substitute to overcome the drawbacks of oral medicines and standard formulations. The specialized drug delivery techniques currently in use have received very few in-depth clinical evaluations, which have demonstrated that it is challenging to increase clinical effectiveness, regulate drug release, and reduce adverse effects.

The relatively intricate designs of most drug carriers are a major impediment to commercialization, resulting in serious problems like labor-intensive production. Due to the complexity of the cellular mechanisms involved in OSCC, elevated dosages of medicine and optimal certain medication release profiles devices are still key goals in order to treat oral cancer. It is important to make available additional nanotechnologies for the therapy for oral cancer, including ultrasonography, PTT OR PTD. The ability of ultrasonic technology to deliver payloads to the targeted areas with great precision has been shown to make it a promising tool for treating tumours. It is easy to use, non-invasive, widely accessible, and capable of doing so. Such payloads may respond to ultrasound through its thermal, mechanical, or a mix of the two effects. Another critical issue that must be taken into consideration in all cancer types is the clinic trials, including oral cancer. Studies conducted in vivo or in vitro still make up the majority of research. It is vital to remind physicians and scientists to fully appreciate all the relevant elements affecting the novel strategy and to utilize this knowledge to inform the design of appropriate clinical trials. The application of nanotechnology concepts in practical, interdisciplinary settings to treat oral cancer as well as needs further study. To give one example, the introduction of targeted therapies in the near future will result in more effective treatment, reduced costs, and increased survival rates, which will be advantageous to both oncologists and patients.

REFERENCES

- Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J. Clin.* 2018; 68: 394-424.
- Dissanayaka WL, Pitiyage G, Kumarasiri PV, et al. Clinical and histopathologic parameters in survival of oral squamous cell carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2012; 113: 518-525.
- Ali J, Sabiha B, Jan HU, et al. Genetic etiology of oral cancer. *Oral oncology.* 2017; 70: 23-28.
- Chaturvedi AS, Engels E, Pfeiffer R, et al. Human papillomavirus (HPV) and rising oropharyngeal cancer incidence and survival in the United States. *Journal of Clinical Oncology.* 2011; 29(15): 5529-5532.
- Catimel G, Verweij J, Mattijssen V, et al. Docetaxel (Taxotere®): an active drug for the treatment of patients with advanced squamous cell carcinoma of the head and neck. *Annals of Oncology.* 1994; 5(6): 533-537.
- Chen J, Ding J, Wang Y, et al. Sequentially responsive Shell-stacked nanoparticles for deep penetration into solid tumors. *Advanced Materials.* 2017; 29(32): 1701170
- Dissanayaka WL, Pitiyage G, Kumarasiri PV, et al. Clinical and histopathologic parameters in survival of oral squamous cell carcinoma. *Oral surgery, oral medicine, oral pathology and oral radiology.* 2012; 113(4): 518-525.
- Calixto G., Bernegossi J., Fonseca-Santos B., et al. Nanotechnology-based drug delivery systems for treatment of oral cancer: a review. *Int. J. Nanomed.* 2014; 9: 3719-3735.
- Barnes L, Eveson JW, Sidransky D, et al. Pathology and genetics of head and neck tumours. *IARC.* 2005; 25: 10-12.
- Catimel G., Verweij J., Mattijssen V., et al. Docetaxel (Taxotere): an active drug for the treatment of patients with advanced squamous cell carcinoma of the head and neck. *EORTC early clinical trials group. Ann Oncol.* 1994; 5: 533-537.
- IWGotEoCRt H. Organization WH, Cancer IAfRo: Smokeless tobacco and some tobacco-specific N-nitrosamines, vol. 89. Lyon, France: World Health Organization. 2007; 11(6): e896.
- Marron M, Boffetta P, Zhang ZF, et al. Cessation of alcohol drinking, tobacco smoking and the reversal of head and neck cancer risk. *International journal of epidemiology.* 2010 Feb 1; 39(1): 182-96.
- Lee YC, Marron M, Benhamou S, et al. Active and involuntary tobacco smoking and upper aerodigestive tract cancer risks in a multicenter case-control study. *Cancer epidemiology, biomarkers & prevention.* 2009; 18(12): 3353-3361.
- Lee J, Taneja V, Vassallo R. Cigarette smoking and inflammation: cellular and molecular mechanisms. *Journal of dental research.* 2012; 91(2): 142-149.
- Beloqui A., Solinís M. Á., Rodríguez-Gascón A., et al. Nanostructured lipid carriers: promising drug delivery systems for future clinics. *Nanomed. Nanotechnol. Biol. Med.* 2016; 12: 143-161.
- Mei Z, Huang J, Qiao B, et al. Immune checkpoint pathways in immunotherapy for head and neck squamous cell carcinoma. *International journal of oral science.* 2020; 12(1): 1-9.
- Slavich GM, Irwin MR. From stress to inflammation and major depressive disorder: a social signal transduction theory of depression. *Psychological bulletin.* 2014; 140(3): 774.
- Calori IR, Braga G, de Jesus PD, et al. Polymer scaffolds as drug delivery systems. *European Polymer Journal.* 2020; 129: 109621.
- Yang J, Wang H, Liu J, et al. Recent advances in nanosized metal organic frameworks for drug delivery and tumor therapy. *RSC advances.* 2021; 11(6): 3241-3263.
- Endo K, Ueno T, Kondo S, et al. Tumor-targeted chemotherapy with the nanopolymer-based drug NC-6004 for oral squamous cell carcinoma. *Cancer science.* 2013; 104(3): 369-374.
- Bhatnagar S, Shinagawa K, Castellino FJ, et al. Exosomes released from macrophages infected with intracellular pathogens stimulate a pro inflammatory response in vitro and in vivo. *Blood. The Journal of the American Society of Hematology.* 2007; 110(9): 3234-3244.
- Biscaglia F, Rajendran S, Conflitti P, et al. Enhanced EGFR targeting activity of plasmonic nanostructures with engineered GE11 peptide. *Advanced health care materials.* 2017; 6(23): 1700596.
- Lucky S. S., Idris N. M., Huang K., et al. In vivo biocompatibility, biodistribution and therapeutic efficiency of titania coated upconversion nanoparticles for photodynamic therapy of solid oral cancers. *Theranostics.* 2016; 6: 1844-1865.
- Chen J, Ding J, Wang Y, et al. Sequentially responsive Shell-stacked nanoparticles for deep penetration into solid tumors. *Advanced Materials.* 2017; 29(32): 1701170.
- Darwish W. M., Abdoon A. S., Shata M. S., et al.

- Vincristine-loaded polymeric corona around gold nanorods for combination (chemo-photothermal) therapy of oral squamous carcinoma. *Reactive Funct. Polymers*. 2020; 151: 104575.
26. Yang K, Zhang S, He J, et al. Polymers and inorganic nanoparticles: A winning combination towards assembled nanostructures for cancer imaging and therapy. *Nano Today*. 2021; 36: 101046.
 27. RJY LT, Lian T, and Ho RJY. Trends and developments in liposome drug delivery systems. *J Pharm Sci*. 2001; 90: 667-680.
 28. Josefsen LB, Boyle RW. Unique diagnostic and therapeutic roles of porphyrins and phthalocyanines in photodynamic therapy, imaging and theranostics. *Theranostics*. 2012; 2(9): 916.
 29. Bilginer R, Arslan Yildiz A. Biomimetic model membranes as drug screening platform. In *Biomimetic Lipid Membranes: Fundamentals, Applications, and Commercialization*. Springer; 2019.
 30. Agüeros M, Ruiz-Gatón L, Vauthier C, et al. Combined hydroxypropyl- β -cyclodextrin and poly (anhydride) nanoparticles improve the oral permeability of paclitaxel. *European Journal of Pharmaceutical Sciences*. 2009; 38(4): 405-413.
 31. Anirudhan TS, Divya PL, Nima J. Synthesis and characterization of silane coated magnetic nanoparticles/glycidylmethacrylate-grafted-maleated cyclodextrin composite hydrogel as a drug carrier for the controlled delivery of 5-fluorouracil. *Materials Science and Engineering: C*. 2015; 55: 471-481.
 32. Wang H., Luo J. C., Zhang Y. H., et al. Phospholipid/ hydroxypropyl-beta-cyclodextrin supramolecular complexes are promising candidates for efficient oral delivery of curcuminoids. *Int. J. Pharm*. 2020; 582: 119301.
 33. Pérez-Herrero E, Fernández-Medarde A. Advanced targeted therapies in cancer: Drug nanocarriers, the future of chemotherapy. *European journal of pharmaceuticals and biopharmaceutics*. 2015; 93: 52-79.
 34. Liang XJ, Chen C, Zhao Y, et al. Circumventing tumor resistance to chemotherapy by nanotechnology. In *Multi-drug resistance in cancer*. 2010; 66: 467-488).
 35. Arruebo M. Drug delivery from structured porous inorganic materials. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*. 2012; 4(1): 16-30.
 36. Zamani M, Prabhakaran MP, Ramakrishna S. Advances in drug delivery via electrospun and electrosprayed nanomaterials. *International journal of nanomedicine*. 2013; 8: 2997.
 37. Verma A, Sharma S, Gupta PK, et al. Vitamin B12 functionalized layer by layer calcium phosphate nanoparticles: A mucoadhesive and pH responsive carrier for improved oral delivery of insulin. *Acta biomaterialia*. 2016; 31: 288-300.
 38. Zhang L, Petit T, Peyer KE, et al. *Nanomed.: Nanotechnol. Biol. Med*. 2012; 8: 1074-1080.
 39. Shakeri-Zadeh A, Rezaeyan A, Sarikhani A, et al. Folate receptor-targeted nanoprobe for molecular imaging of cancer: Friend or foe?. *Nano Today*. 2021; 39: 101173.
 40. Batrakova EV, Kim MS. Using exosomes, naturally-equipped nanocarriers, for drug delivery. *Journal of Controlled Release*. 2015; 219: 396-405.
 41. Zhang X, Wu W. Ligand-mediated active targeting for enhanced oral absorption. *Drug discovery today*. 2014; 19(7): 898-904.
 42. Agrawal U, Sharma R, Gupta M, et al. Is nanotechnology a boon for oral drug delivery?. *Drug discovery today*. 2014; 19(10): 1530-1546.
 43. Yang G., Chen S., and Zhang J. Bioinspired and biomimetic nanotherapies for the treatment of infectious diseases. *Front. Pharmacol*. 2019; 10: 751.
 44. Chien M. H., Wu S. Y., and Lin C. H. Oral immunization with cell-free self-assembly virus-like particles against orange-spotted grouper nervous necrosis virus in grouper larvae, *Epinephelus coioides*. *Vet. Immunol. Immunopathol*. 2018; 197: 69-75.

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