Review Article

Nanotechnology applications in oral pathology: A scoping review

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Abstract

Developments in tissue engineering, diagnosis, and therapy of oral diseases can be made possible by nanotechnology. The purpose of this scoping review was to assess the state of nanotechnology applications in oral pathology at the moment. A thorough search for research published between 2000 and 2024 was done using various online data bases. Relevant studies were identified, screened, and included in accordance with the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines standards as per the selection criterion. A total of 57 studies satisfied the requirements for inclusion. Significant findings show that in oral disease, nanotechnology greatly enhances treatment delivery, regeneration capacity, and diagnostic accuracy. Among the most promising tools identified were nanofibers, liposomes, quantum dots, and gold nanoparticles. In the field of oral pathology, nanotechnology has great potential for novel approaches to early diagnosis, targeted therapy, and tissue regeneration. However, additional investigation are needed to solve safety and biocompatibility challenges.

Keywords: Nanofibers, nanotechnology, oral cancer, regenerative dentistry, targeted drug delivery

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INTRODUCTION

Nanotechnology is defined as the manipulation of matter on an atomic or molecular size, usually between 1 and 100 nanometers. It has demonstrated tremendous potential in the field of medical sciences. The application of nanotechnology in the medical field can revolutionize diagnostics, therapeutics, and tissue engineering.[1] Oral and maxillofacial pathology is that branch of dentistry, which deals with the diagnosis of various diseases of the oral and maxillofacial regions, including cancers, infections, and inflammatory conditions.[2] Conventional approaches frequently fall short in terms of sensitivity, specificity, and patient outcomes. The special qualities of nanomaterials can overcome such limitations, resulting in major improvements in patient care related to pathologies in the oral cavity.[3]

A scoping review is the most suitable method for methodically mapping the available information, identifying current research gaps, and outlining possible routes for future investigations because of the continuously

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changing nature of nanotechnology and its wide range of applications.

By adopting a scoping review methodology, this study aims to list the current research on the use of nanotechnology in oral pathology, determine the primary concepts and new developments in the subject, and emphasize challenges and research gaps pertaining to safety, clinical translation, and regulatory issues and by identifying areas that require more research, thereby providing the groundwork for future studies.

MATERIALS AND METHODS

Literature search

This scoping review was conducted following preferred reporting items for systematic reviews and meta-analyses-scoping review (PRISMA-ScR) guidelines[4] between February 2024 and June 2024. We determined the study topic as the first stage in the framework with the aim of gathering information on the role of nanotechnology in oral pathology. Therefore, the research question was defined as "What is the current status of nanotechnology in oral pathology?" The review protocol of the present scoping review was not registered.

Selection criteria

Relevant studies were identified through a search conducted across the databases PubMed, Scopus, and Web of Science from January 2000 to January 2024. Studies examining the use of nanotechnology for the detection, use, and treatment of oral diseases were considered which included peer-reviewed articles, clinical trials, and *in vivo* studies. Articles not directly related to pathology, and studies in languages other than English were excluded.

A search strategy was developed using keywords, and medical subject headings (MeSH) terms were used such as:

- Nanotechnology OR Nanoparticles OR Nanomedicine OR Nanofibers
- Oral Pathology OR Oral Cancer OR Drug Delivery Systems.

Boolean operators (AND, OR) were used to refine the search results.

Information sources and search strategy

A systematic search was performed by one author (AS) across three electronic databases, i.e., Scopus, PubMed, and Web of Science, from October 2023 with the last search conducted in January 2024.

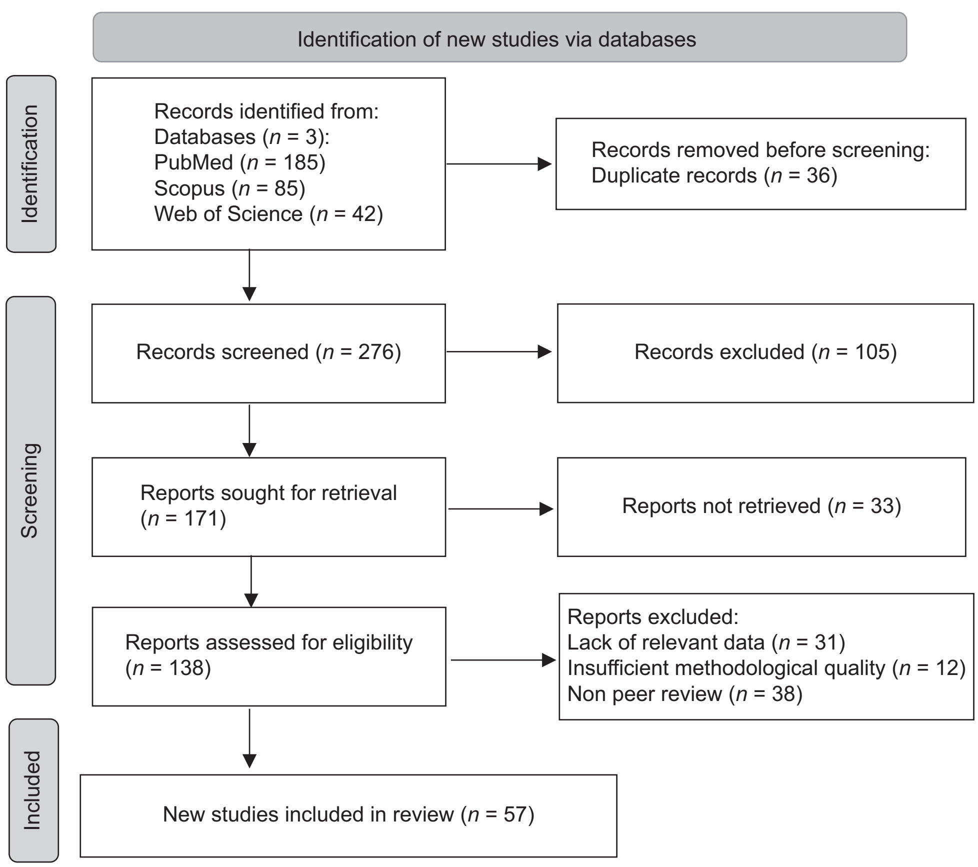

Figure 1: PRISMA flow diagram[4] depicting the process of article selection for the scoping review

Study selection

One author (AS) evaluated the first search results from all three databases for titles, and 312 articles were selected. Following the outlined selection criteria, these publications underwent independent full-text evaluation by two authors (AS and MS) after title and abstract screening. Any differences of opinion were settled through conversation and the assistance of a third author (VK). After a full-text assessment, 57 papers in total were chosen based on the qualifying criteria.

Charting the data

Two authors (AS and DN) independently plotted the data from the full-text publications that were chosen for the present scoping review using a pre-made format in Microsoft Excel software version 16.54. This format facilitated the collection of information such as author(s), year of publication, study location, type of study/article, study population, aim of the study, methods used, outcome measures, and significant findings. To provide a more comprehensive overview of the selected publications, the data extraction tables were subsequently jointly examined to find and fill in any missing evidence that was relevant to the review.

Critical appraisal of the selected articles

The main goal of this scoping review was to investigate and evaluate the forms of data that are currently available regarding the use of nanotechnology in oral pathology. An evaluation of the chosen sources of data was conducted to accurately determine the research gaps in the body of existing literature. The Crowe critical appraisal tool (CCAT) makes it easier to critically assess articles that cover a wide range of research methodologies.[5] Because there were no restrictions on research designs throughout the article selection process for this review, we decided to adopt CCAT for the present scoping review. Two writers (AK and MS) independently assessed the quality of the selected articles. Eight criteria are used by the CCAT to assess each paper: abstract, design, sample, data collecting, ethical issues, results/findings, and discussion. The highest possible score is 40, with each category receiving a separate score on a range of 0 to 5. If there were any ratings that disagreed, the two authors worked together with DN, the fourth author, before arriving at a conclusion.

Risk-of-bias assessment

Individual studies' risk of bias was determined using the Cochrane risk-of-bias tool for randomized trials and the ROBINS-I tool for non-randomized studies.

RESULTS

Study selection

The search performed resulted in 312 items. After deleting duplicates and screening titles and abstracts, 138 papers were selected for subjected to full-text review. Figure 1 displays the PRISMA flow diagram for this scoping review.[4] Among these, 57 studies met the inclusion criteria. [Table 1] Among the sources selected, the majority of the papers were cross-sectional studies (63%), followed by narrative reviews (24%). The three main areas of focus that were highlighted were diagnostics, medication delivery, and tissue engineering.

Risk of bias in included studies

The majority of studies showed a low to moderate bias risk. Incomplete outcome data and a lack of blinding were frequent issues. The overall data was analyzed, taking these considerations into account.

DISCUSSION

The purpose of this scoping review was to conduct a comprehensive study on how nanotechnology can revolutionize oral pathology. The goal was to establish a basic understanding of the use of nanotechnology so that budding oral pathologists and general dentists will be aware of the current and future aspects of its use in oral pathology.

Diagnostics

Gold nanoparticles

Gold nanoparticles (AuNPs) have peculiar optical characteristics, particularly potent surface plasmon resonance (SPR), which makes it a greatly enhanced diagnostic imaging approach in oral pathology. Due to this characteristic, AuNPs could enhance light scattering and absorption, which makes them highly beneficial for a variety of imaging modalities, including optical coherence tomography (OCT) and surface-enhanced Raman spectroscopy (SERS).[6-8] It was that El-Sayed *et al.*[9] in 2005, for the first time, introduced the the anti-epidermal growth factor receptor (anti-EGFR) antibody to a gold nanosurface to diagnose oral cancer. This technique allowed for a high degree of differentiation between tumour and normal cells. The capacity to target lesions using this imaging enables the early identification of malignant lesions and aids in the delineation of tumour margins, both of which are critical to optimal surgical procedures.[10]

Biomarker identification and quantification

Histopathology is one of the traditional diagnostic techniques that frequently depends on subjective interpretation and could overlook early-stage oral

Table 1: Articles selected for review

Title	Authors	Year
A novel intraarterial chemotherapy using paclitaxel in albumin nanoparticles to treat advanced squamous cell carcinoma of the tongue: Preliminary findings.	Damascelli B, Patelli GL, Lanocita R, Tolla GD, Frigerio LF, Marchianò A, Garbagnati F *et al*.	2003
Surface plasmon resonance scattering and absorption of anti-EGFR antibody conjugated gold nanoparticles in cancer diagnostics: Applications in oral cancer.	El-Sayed IH, Huang X, El-Sayed MA.	2005
Nanoshell-enabled photothermal cancer therapy: Impending clinical impact.	Lal S, Clare SE, Halas NJ.	2008
Nanotechnology: A promising method for oral cancer detection and diagnosis.	Chen XJ, Zhang XQ, Liu Q, Zhang J, Zhou G.	2008
Real-time optical imaging using quantum dot and related nanocrystals.	Kosaka N, McCann TE, Mitsunaga M, Choyke PL, Kobayashi H.	2010
Engineering hydrogels as extracellular matrix mimics.	Geckil H, Xu F, Zhang X, Moon S, Demirci U.	2010
Nano technology in cancer diagnosis and treatment: An overview. Oral Maxillofac Pathol J 2011;2:101–6	Ravindran R.	2011
Nanotechnology: A Revolution in cancer diagnosis. Indian J Clin Biochem 2012;27:214–20	Jaishree V, Gupta PD.	2012
Tumour-targeted chemotherapy with the nanopolymer-based drug NC-6004 for oral squamous cell carcinoma.	Endo K, Ueno T, Kondo S, Wakisaka N, Murono S, Ito M, Katoaka K, Kato Y, Yoshizaki T.	2013
Ellagic acid encapsulated chitosan nanoparticles for drug delivery system in human oral cancer cell line (KB).	Arulmozhi V, Pandian K, Mirunalini S.	2013
Polymeric-gold nanohybrids for combined imaging and cancer therapy.	Topete A, Alatorre-Meda M, Villar-Alvarez EM, Carregal-Romero S, Barbosa S, Parak WJ, *et al*.	2014
Oral and IV dosages of doxorubicin-methotrexate loaded- nanoparticles inhibit progression of oral cancer by down- regulation of matrix methaloproteinase 2 expression *in vivo*	Abbasi MM, Jahanban-Esfahlan R, Monfaredan A, Seidi K, Hamishehkar H, Khiavi MM, *et al*.	2014
Novel resveratrol and 5-fluorouracil coencapsulated in pegylated nanoliposomes improve chemotherapeutic efficacy of combination against head and neck squamous cell carcinoma.	Mohan A, Narayanan S, Sethuraman S, Krishnan UM.	2014
Nanotechnology-based drug delivery systems for treatment of oral cancer: A review.	Calixto G., Bernegossi J., Fonseca-Santos B., Chorilli M.	2014
A cell-targeted chemotherapeutic nanomedicine strategy for oral squamous cell carcinoma therapy	Wang ZQ, Liu K, Huo ZJ, Li XC, Wang M, Liu P, *et al*.	2015
Self-assembling monomeric nucleoside molecular nanoparticles loaded with 5-FU enhancing therapeutic efficacy against oral cancer	Zhao H, Feng H, Liu D, Liu J, Ji N, Chen F, *et al*.	2015
Biomarker quantification by multiplexed quantum dot technology for predicting lymph node metastasis and prognosis in head and neck cancer.	Hu Z, Qian G, Müller S, Xu J, Saba NF, Kim S, *et al*.	2016
Oral squamous cell carcinoma: Current treatment strategies and nanotechnology-based approaches for prevention and therapy.	Gharat SA, Momin M, Bhavsar C.	2016
In vivo biocompatibility, biodistribution and therapeutic efficiency of Titania coated upconversion nanoparticles for photodynamic therapy of solid oral cancers	Lucky SS, Idris NM, Huang K, Kim J, Li Z, Thong PS, *et al*.	2016
A chemopreventive nanodiamond platform for oral cancer treatment.	Yen A, Zhang K, Daneshgaran G, Kim HJ, Ho D.	2016
Comparative evaluation of PLGA nanoparticle delivery system for 5-fluorouracil and curcumin on squamous cell carcinoma.	Masloub SM, Elmalahy MH, Sabry D, Mohamed WS, Ahmed SH.	2016
Dual drug loaded nanoliposomal chemotherapy: A promising strategy for treatment of head and neck squamous cell carcinoma.	Mohan A, Narayanan S, Balasubramanian G, Sethuraman S, Krishnan UM.	2016
Buccal adhesive nanofibers containing human growth hormone for oral mucositis.	Choi J. S., Han S.-H., Hyun C., Yoo H. S.	2016
Nanotechnology in oral cancer: A comprehensive review.	Poonia, Monika; Ramalingam, Karthikeyan; Goyal, Sandeep; Sidhu, Supreet Kaur.	2017
Development and *in vitro* evaluation of mucoadhesive patches of methotrexate for targeted delivery in oral cancer.	Jin BZ, Dong XQ, Xu X, Zhang FH.	2018
Application of nanocarrier-based drug delivery system in treatment of oral cancer.	Sah AK, Vyas A, Suresh PK, Gidwani B.	2018
Codelivery of doxorubicin and MDR1-siRNA by mesoporous silica nanoparticles-polymerpolyethylenimine to improve oral squamous carcinoma treatment.	Wang D, Xu X, Zhang K, Sun B, Wang L, Meng L, Liu Q, Zheng C, Yang B, Sun H.	2018
Gold nanoparticles enhance X-ray irradiation-induced apoptosis in head and neck squamous cell carcinoma *in vitro*.	Teraoka S, Kakei Y, Akashi M, *et al*.	2018
Controlled drug delivery systems for oral cancer treatment−current status and future perspectives.	Ketabat F, Pundir M, Mohabatpour F, Lobanova L, Koutsopoulos S, Hadjiiski L, Chen X, Papagerakis S.	2019
AuNPs as an important inorganic nanoparticle applied in drug carrier systems. Artif Cells Nanomed Biotechnol 2019;47(1):4222–33.	Li W, Cao Z, Liu R, Liu L, Li H, Li X, Chen Y, Lu Cheng, Liu Y.	2019
Nanotechnology in cancer diagnosis: Progress, challenges and opportunities.	Zhang Y, Li M, Gao X, *et al*.	2019
Mineralized nanofiber segments coupled with calcium-binding BMP-2 peptides for alveolar bone regeneration.	Boda S. K., Almoshari Y., Wang H., Wang X., Reinhardt R. A., Duan B., *et al*.	2019
Nanotechnology in oral cavity carcinoma: Recent trends and treatment opportunities.	De Felice F., Cavallini C., Barlattani A., Tombolini M., Brugnoletti O., Tombolini V., *et al*.	2019
Effective combined photodynamic therapy with lipid platinum chloride nanoparticles therapies of oral squamous carcinoma tumor inhibition.	Gusti-Ngurah-Putu E. P., Huang L., Hsu Y. C.	2019
Phloretin loaded chitosan nanoparticles augments the pH-dependent mitochondrial-mediated intrinsic apoptosis in human oral cancer cells.	Mariadoss A. V. A., Vinayagam R., Senthilkumar V., Paulpandi M., Murugan K., Xu B., *et al*.	2019

Contd...

Table 1: Contd...

Title	Authors	Year
Host immune response triggered by graphene quantum-dot-mediated photodynamic therapy for oral squamous cell carcinoma.	Zhang X., Li H., Yi C., Chen G., Li Y., Zhou Y., *et al*.	2020
Glutathione-sensitive and folate-targeted nanoparticles loaded with paclitaxel to enhance oral squamous cell carcinoma therapy.	Fan L, Wang J, Xia C, Zhang Q, Pu Y, Chen L, Chen J, Wang Y.	2020
Anti-PD-L1-modified and ATRA-loaded nanoparticles for immuno-treatment of oral dysplasia and oral squamous cell carcinoma.	Chen XJ, Zhang XQ, Tang MX, Liu Q, Zhou G.	2020
Electrospun nanofibers of natural and synthetic polymers as artificial extracellular matrix for tissue engineering.	Keshvardoostchokami M, Majidi SS, Huo P, Ramachandran R, Chen M, Liu B.	2020
Electrospun nanofibrous materials for wound healing.	Dong Y., Zheng Y., Zhang K., Yao Y., Wang L., Li X., *et al*.	2020
Circumventing AKT-associated radioresistance in oral cancer by novel nanoparticle-encapsulated capivasertib.	Lang L., Lam T., Chen A., Jensen C., Duncan L., Kong F. C., *et al*.	2020
Antitumour effect of poly lactic acid nanoparticles loaded with cisplatin and chloroquine on the oral squamous cell carcinoma.	Li Q., Liu X., Yan W., Chen Y.	2020
Catechol-modified chitosan/hyaluronic acid nanoparticles as a new avenue for local delivery of doxorubicin to oral cancer cells.	Pornpitchanarong C., Rojanarata T., Opanasopit P., Ngawhirunpat T., Patrojanasophon P.	2020
Engineering electrospun nanofibers for the treatment of oral diseases.	Wang Y, Liu Y, Zhang X, Liu N, Yu X, Gao M, Wang W, Wu T.	2021
Nanotechnology-based biopolymeric oral delivery platforms for advanced cancer treatment.	Chivere VT, Kondiah PPD, Choonara YE, Pillay V.	2021
Function of gold nanoparticles in oral cancer beyond drug delivery: Implications in cell apoptosis.	Essawy M. M., El-Sheikh S. M., Raslan H. S., Ramadan H. S., Kang B., Talaat I. M., *et al*.	2021
Utilization of gold nanoparticles for the detection of squamous cell carcinoma of the tongue based on laser-induced fluorescence and diffuse reflectance characteristics: An *in vitro* study.	Nour M, Hamdy O, Faid AH, Eltayeb EA, Zaky AA.	2022
Gold nanomaterials for oral cancer diagnosis and therapy: Advances, challenges, and prospects.	Zhang Q, Hou D, Wen X, Xin M, Li Z, Wu L, Pathak JL.	2022
Nanomaterials in scaffolds for periodontal tissue engineering: Frontiers and prospects.	Chen S, Huang X.	2022
Tumour-targeted biomimetic nanoplatform precisely integrates photodynamic therapy and autophagy inhibition for collaborative treatment of oral cancer.	Dai H., Yan H., Dong F., Zhang L., Du N., Sun L., *et al*.	2022
Emerging applications of nanotechnology in healthcare and medicine: Molecules.	Malik S, Muhammad K, Waheed Y.	2023
What we need to know about liposomes as drug nanocarriers: An updated review.	Abbasi H, Kouchak M, Mirveis Z, Hajipour F, Khodarahmi M, Rahbar N, *et al*.	2023
Nanoparticles as drug delivery systems in the treatment of oral squamous cell carcinoma: Current status and recent progression.	Cui S, Liu H, Cui G.	2023
Nanoparticles as drug delivery systems: A review of the implication of nanoparticles' physicochemical properties on responses in biological systems.	Yusuf A, Almotairy ARZ, Henidi H, Alshehri OY, Aldughaim MS.	2023
Development of cellulose acetate/CuO/AgNP nanofibers based effective antimicrobial wound dressing.	Kumar, G., Khan, F. G., Abro, M. I., Aftab, U. and Jatoi, A. W.	2023
Thermosensitive and mucoadhesive hydrogel containing curcumin-loaded lipid-core nanocapsules coated with chitosan for the treatment of oral squamous cell carcinoma.	Ortega A., da Silva A. B., da Costa L. M., Zatta K. C., Onzi G. R., da Fonseca F. N., *et al*.	2023
Recent nanotheranostic approaches in cancer research.	Gupta D., Roy P., Sharma R., Kasana R., Rathore P., Gupta T.K.	2024

cancers and precancers.[11] The sensitivity and specificity of diagnostic examinations in oral pathology can be significantly increased by using AuNPs in biomarker detection.[12] In 2020, Seyyedi *et al*.[13] carried out a study in which human papillomavirus (HPV), a known risk factor for cervical cancer, was detected in cervical swab samples using AuNPs covered with a series of oligonucleotide probes that hybridized to particular DNA sequences of HR-HPV genotypes. According to this study, 733 out of 800 copies of type-specific HPV DNA were retrieved with complete specificity, enabling an accurate cervical cancer detection. Oral swabs containing HPV, which are essential for the early diagnosis and prompt treatment of HPV-induced oral cancer, might benefit from these developments in biomarker identification utilizing AuNPs, which will enhance patient outcomes.

Multiplexed detection and imaging capabilities

The potential of AuNPs to enable multiplexed detection and imaging is one of its most promising features in diagnostic applications. In challenging disorders like cancer, where numerous pathways and molecular alterations are involved, multiplexing, the simultaneous detection of several biomarkers or molecular targets, is very helpful. Multiple functional groups that each target, a distinct biomarker can be designed into AuNPs. Various studies were conducted using multiplexed SERS, where many cancer indicators may be detected concurrently on a single cell or tissue sample using AuNPs tagged with distinct Raman-active chemicals. This saves time and money by eliminating the need for multiple investigations and offers thorough diagnostic information.[14,15] Multiplexed detection in oral pathology with AuNPs can identify a range of biomarkers associated with infection, malignancy, and inflammation, giving a comprehensive picture of the disease state and providing individualized treatment plans.[12]

Quantum dots

Enhanced imaging with quantum dots

One of the quantum dots' (QD) greatest benefits for diagnostic applications are their multiplexed detection capacity, which is essential for extensive disease profiling. Multiplexing provides a thorough molecular characterisation of conditions like oral cancers by detecting numerous markers simultaneously.[16] Different-sized QDs may produce light at different wavelengths, making it possible to detect multiple targets in concurrently inside a single sample. This capability is particularly useful for diagnosing challenging diseases that include several signalling pathways.[17] Hu *et al*.[18] through his study in 2016, for instance, demonstrated a possible strategy for predicting lymph node metastasis, disease-free survival, and overall survival in head and neck squamous cell carcinoma (HNSCC) patients with multiplexed subcellular QD quantification of EGFR and E cadherin. In the long run, this multiplexed strategy may improve patient outcomes by resulting in earlier and more accurate diagnoses.

Real-time tracking and monitoring

Beyond their use in initial diagnosis, QDs are also invaluable for real-time tracking and monitoring of disease progression and treatment response in oral pathology. QDs are fluorescent substances with a high degree of sensitivity that are effective in labelling tissues and cells. Due to the low copy counts and/or concentrations of many cancer indicators, this is particularly crucial for cancer detection.[19] QDs also exhibit remarkable photostability; they are at times several thousand times more resistant to photobleaching than organic dyes. This feature makes it possible to monitor biological processes in real-time, which is essential for *in vivo* imaging and cancer biomarker studies where extended times are required. The ability to track these processes in real-time represents a significant advancement in the management and treatment of pathologies, contributing to more effective and personalized care.[20]

Drug delivery

Liposomes

Liposomes, spherical vesicles composed of phospholipid bilayers, have emerged as a promising drug delivery system, particularly for targeting cancers. Their ability to encapsulate both hydrophilic and hydrophobic drugs allows for versatile drug formulations tailored to specific therapeutic needs.[21] In the treatment of oral squamous cell carcinoma (OSCC), liposomal formulations can enhance the delivery and efficacy of chemotherapeutic agents while minimizing systemic toxicity. For example, using the thin film hydration process, Jin *et al*.[22] created methotrexate (MTX)-loaded liposomes, which were then cast in an optimal mucoadhesive film to create a mucoadhesive patch for the treatment of oral cancers. The half-maximal inhibitory concentration of MTX in human oral squamous carcinoma cell line (HSC-3) cells treated with MTX-loaded liposomes was significantly lower, according to the 3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide (MTT) assay. Furthermore, the MTX-loaded liposomes nearly tripled the apoptotic rate in HSC-3 cells. This targeted approach not only improves therapeutic outcomes but also enhances patient compliance and quality of life by reducing the incidence of side effects.

Liposomes in antimicrobial therapy for oral infections

Liposomes have also been effectively utilized in antimicrobial therapy to combat oral infections, which often involve bacterial biofilms that are resistant to conventional treatments. The encapsulation of antibiotics within liposomes enhances their delivery to the site of infection, improving penetration and efficacy against biofilms. Studies were conducted in 2001 by Jones *et al*.[23] and in 2003 by Catuogno and Jones[24] on the use of cationic liposomes (which contain phosphatidylcholine (DMPC), cholesterol, and dimethyldioctadecylammonium bromide (DDAB)) and anionic liposomes (which contain phosphatidylinositol [PI] and DMPC). These liposomes were used to deliver hydrophobic triclosan, hydrophilic benzylpenicillin, and zinc citrate particles to *in vitro* models of oral biofilms that contain a variety of Gram-positive microbes, including *Streptococcus salivarius* (S. *salivarius*), *Streptococcus sanguis* (S *sanguis*), and *Streptococcus oralis* (*S. oralis*). These studies showed that the antimicrobial-loaded liposomes had superior biofilm eradication effects than naked drugs, according to the results. The cationic liposomes only interacted with the biofilms through attractive electrostatic forces, whereas the anionic liposomes involved attractive hydroxy interactions (hydrogen bonding) and repulsive electrostatic interactions. Thus, liposomal drug delivery systems are a potential strategy for treating chronic oral infections and eliminating implications such as dental caries by enhancing the duration and efficacy of antibacterial activity.

Regenerative applications of liposomes

Beyond its application in antimicrobial therapy and cancer therapy, liposomes have great promise in tissue engineering and regenerative dentistry. Growth factors and other bioactive substances that support tissue regeneration and repair can be delivered using them. Liposomes can be added to scaffolds for tissue engineering, enabling the regulated and targeted release of these therapeutic compounds.[25] For example, a study conducted on rat models by Ferreira *et al*.[26] had shown that liposome-borne growth factors such as bone morphogenic protein (BMP4), transforming growth factor–beta 1 (TGFβ1), and BMP4/TGFβ1 combined were effective in accelerating the healing process in rat tooth sockets. Improved bone formation and integration resulted from the continuous stimulation of osteogenesis brought about by the regulated release of growth factors from liposomal carriers. In addition, it was shown that during the initial stages of bone healing, the expression of collagen type III and fibronectin increased. This method offers novel possibilities for successful regenerative treatments that restore function and aesthetics to the oral cavity, which has substantial implications for the treatment of several oral pathologies involving tissue loss and injury.

Polymeric nanoparticles

When it comes to treating OSCC, polymeric nanoparticles have emerged as a key component of targeted drug delivery systems. These nanoparticles can encapsulate and carry chemotherapy medications directly to cancer cells, maximizing treatment efficacy while avoiding systemic adverse effects. They are produced from biocompatible and biodegradable polymers like poly (lactic-co-glycolic acid) (PLGA).[27] For instance, it has been shown that a drug delivery system based on folic acid (FA)-targeted and glutathione (GSH)-sensitive nanoparticles loaded with paclitaxel (FA-PEG-S-S-PCL@PTX, FA-NPs) has a good targeting effect and can precisely release and increase the antitumour effectiveness of several antitumour medicines.[28] Chen *et al*.[29] in 2020 studied CD8+ T cells surrounding PD-L1-positive cells in the tumour microenvironment to assess the possible impact of polymer NPs on immune checkpoint inhibitors in oral dysplasia and OSCC cells. Results *in vitro* and *in vivo* indicated that treatment with ATRA-PLGA-PEG-PD-L1 increased the stimulation of CD8+ T cells. This targeted approach not only maximizes the drug concentration at the tumour site but also reduces the exposure of healthy tissues to the toxic effects of chemotherapy, thus improving patient outcomes.

Metallic nanoparticles

Metallic nanoparticles, especially those of gold and silver, have demonstrated significant potential for use in pathology for both therapeutic and diagnostic purposes. For instance, gold nanoparticles (AuNPs) are used in drug delivery systems due to their unique optical properties, ease of synthesis, and quick functionalization. AuNPs can be used in conjunction with medications, antibodies, or peptides to enhance the targeted delivery of therapeutic compounds to specific oral cavity cells or tissues.[30] In the treatment of oral infections, silver nanoparticles (AgNPs) have been extensively studied for their potent antimicrobial properties. The ability of proteoglycans to function as binding sites for Ag NPs and Ag ions within bacterial cells and on their membrane explains various aspects of Ag NPs' antibacterial action. As a result, the Ag breaks down the bacterial cell membrane. Additionally, the Ag ions can interact with sulfuryl groups in protein synthesis, which can damage and interfere with the replication of bacterial DNA. Cell death follows after this. Ag NPs' antibacterial action has recently been linked to the production of free radicals, specifically bactericidal reactive oxygen species (ROS). Bacterial cell membrane damage is caused by the free radicals that Ag NPs release.[31,32]

Synergistic use of polymeric and metallic nanopraticles

When used in drug delivery systems for pathology, metallic and polymeric nanoparticles can work in conjunction to provide beneficial outcomes. Metallic nanoparticles can improve targeting and imaging capabilities, whereas polymeric nanoparticles can deliver controlled and sustained medication release. For instance, hybrid nanoparticles with a gold shell and PLGA core have been created for dual medicinal and diagnostic uses. Topete *et al.* (2014) in their study used targeted multimodal chemotherapy and photothermal therapy in conjunction with optical and magnetic resonance imaging (MRI) in carcinoma with the use of FA-functionalized, doxorubicin (DOXO)/superparamagnetic iron oxide nanoparticles (SPION)-loaded PLGA-Au porous shell nanoparticles (NPs) as possible nanoplatforms. The targeting ligand FA functionalization of the PGNH NPs was found to increase the internalization efficiency and specificity of the NPs. This combination not only enhances the therapeutic efficacy but also enables real-time monitoring of the treatment progress through imaging techniques.[33] Such multifunctional nanoparticles can provide comprehensive solutions for the diagnosis, treatment, and monitoring of oral pathologies, paving the way for more effective and personalized therapeutic strategies.

Tissue engineering

Nanofibers

Nanofiber, a material with unique morphologies, significant surface area, and biomolecular compatibility have demonstrated their promise as an important tool in tissue engineering.[12]

Nanofibers for bone regeneration

Nanofibers have become one of the most promising materials for scaffold construction in oral tissue engineering because of their high surface area-to-volume ratio and structural similarity to the extracellular matrix (ECM). The ability of these nanostructures to resemble the natural ECM creates an environment that is favourable for cell adhesion, proliferation, and differentiation—all processes that are essential for tissue regeneration.[34] A popular method for creating nanofibers from biocompatible polymers, including collagen, PLGA, and polycaprolactone (PCL), is electrospinning. For example, PCL nanofibers have been utilized to fabricate scaffolds which promote the regeneration of periodontal tissues and assist the proliferation of gingival fibroblasts. For oral tissue engineering, these scaffolds can be further functionalized with growth factors, bioactive compounds, or antimicrobial agents to increase their potential for regeneration and efficacy in treatment.[35]

Nanofibers for soft tissue regeneration

Nanofibers serve as vital role in facilitating the oral cavity's soft tissue regeneration.[36] Nanofiber scaffold's adaptable characteristics and flexibility make them perfect for promoting soft tissue regeneration and repair. Scaffolds that encourage the migration and proliferation of epithelial and connective tissue cells have been produced using electrospun nanofibers derived from natural polymers such as collagen and silk fibroin. For effective tissue regeneration, these scaffolds may be made to wear down at a monitored rate that corresponds to the rate at which new tissue forms.[35,37] Moreover, antimicrobial agents added to nanofiber scaffolds may inhibit infections at the location of the wound, allowing for faster and more efficient healing.[38]

Hydrogels

Due to their high water content, biocompatibility, and customizable physical characteristics, hydrogels have attracted a lot of attention in the field of oral tissue engineering. These characteristics make them perfect for scaffold construction and cell distribution. These networks of hydrophilic polymers can simulate the ECM seen in biological terms, which creates a favourable environment for the growth and development of cells.[39] In case of oral cavity, hydrogels have been utilized to create scaffolds for periodontal regeneration. In a swine periodontal defect model, Fawzy El-Sayed *et al*.[40] investigated the effects of a hyaluronic acid hydrogel loaded with gingival mesenchymal stem cell (MSC) and interleukin 1 receptor antagonist (IL-1ra). In addition to a decreased junctional epithelium, both IL-1ra-loaded and unloaded constructions exhibited their ability for periodontal regeneration, producing a greater clinical attachment level, probing depth, periodontal attachment level, cementum regeneration, and bone regeneration. Additionally, the injectable nature of many hydrogels allows for minimally invasive application, conforming to irregularly shaped defects and ensuring a close interaction with surrounding tissues.[41] This characteristic is particularly advantageous in the oral cavity, where accessibility and anatomical complexity can pose significant challenges.

Hydrogels for drug and growth factor delivery

The ability of hydrogels to encapsulate and release bioactive molecules in a controlled manner is crucial for their application in oral tissue engineering. Hydrogels can be engineered to deliver therapeutic agents, such as antibiotics, anti-inflammatory drugs, or growth factors, directly to the site of injury or disease. For instance, a hydrogel layer and two aligned nanofiber layers were combined to create a sandwich-like composite scaffold for wound healing by Nur Adila Mohd Razali *et al*.[42] The centre hydrogel layer contained gentamicin, which releases its antibacterial properties naturally. Furthermore, the outer layers of nanofiber within the hydrogel act as diffusion barriers, lowering the initial burst release of gentamicin. Hydrogels containing growth factors like vascular endothelial growth factor (VEGF) and BMPs can encourage the development of new blood vessels and bone during periodontal regeneration, improving tissue integration and repair. Hydrogels' controlled release properties ensure the prolonged and localized delivery of these bioactive compounds, enhancing their effectiveness and mitigating systemic negative effects.[43]

Hydrogels in regenerative dentistry

Hydrogels are also essential in regenerative dentistry, where they are used to reactivate and repair dentin and tooth pulp. For the treatment of endodontic conditions like as pulpitis, dental pulp regeneration is essential. Stem cells or progenitor cells can be introduced into the pulp chamber using hydrogels, which will create an environment that is favourable for cell proliferation and differentiation. For instance, pulp tissue regeneration and the formation of new dentin have been demonstrated by gelatin-based hydrogels loaded with dental pulp stem cells. By designing these hydrogels to break down at a pace that corresponds with the growth of new tissue, it is possible to guarantee that the scaffold will continue to assist the regeneration process.[44] Additionally, hydrogels can be combined with bioactive materials such as calcium phosphates to enhance their osteoinductive properties, further promoting the regeneration of dentin and other dental structures.[45] The versatility and functionality of hydrogels make them a powerful tool in the development of advanced therapies for oral pathology and regenerative dentistry.

Research gaps

Notable research gaps still exist despite significant progress in the use of nanotechnology in oral pathology. The creation of nanoparticles for drug delivery systems, dental composites, and antimicrobial uses has been the main focus of recent research. Comprehensive assessments of these nanomaterials' long-term safety and biocompatibility profiles are still few, nevertheless. Furthermore, there are few large-scale, randomized controlled studies evaluating the therapeutic effectiveness of nanotechnology-based therapies in oral disease, despite promising preliminary results. Furthermore, not enough research has been conducted on the possible systemic and environmental effects of the increasing use of nanomaterials in dentistry. For the safe and successful incorporation of nanotechnology into oral healthcare methods, these gaps must be filled.

Strengths and limitations

An extensive examination of the literature on the application of nanotechnology in oral pathology has been made possible by this scoping review. The fact that the data came from only three electronic databases is one of the constraints, but even so, it was enough to determine the body of current evidence. Moreover, the analysis contained a few articles with low quality ratings from the critical assessment. This choice was taken to guarantee that all pertinent research was included and to provide a more thorough summary of nanotechnology applications. Despite the diverse study designs of the included articles, the utilization of a systematic framework facilitated the identification of the numerous nanotechnological breakthroughs that have the potential to significantly enhance oral pathology.

CONCLUSION

Significant advances in oral pathology can be achieved by using nanotechnology, especially in the areas of tissue engineering, medication administration, and diagnostics. Although the present research shows promise, the effective clinical adoption of nanotechnology-based therapies depends on overcoming biocompatibility, toxicity, and regulatory issues. Future research should concentrate on long-term safety and effectiveness, in addition to methods for removing current barriers to clinical implementation.

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Conflicts of interest

There are no conflicts of interest.

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