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Review Article

Nanomedicine in oral cancer

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ABSTRACT

Navigating the intersection of nanomedicine and oral cancer, this review surveys recent breakthroughs in leveraging nanotechnological approaches for enhanced therapeutic outcomes. Spotlighting the dynamic landscape of nanoparticle applications, particularly in targeted drug delivery, the article explores their potential to minimize systemic side effects and optimize treatment efficacy. Insightful analysis of diverse nanocarrier systems provides a nuanced understanding of their mechanisms and promising outcomes. Additionally, the review examines the diagnostic role of nanotechnology, emphasizing its contributions to early detection through advanced imaging modalities. By synthesizing current research, this article illuminates the transformative potential of nanomedicine in reshaping oral cancer treatment paradigms, offering a holistic perspective on the field's progress and future directions.

1. Introduction

Richard P. Feynman developed the idea of nanotechnology in 1959.[1] Tokyo Science University's Norio Taniguchi gave the following definition of the term: "Nanotechnology" consists of processing, separation, consolidation, and deformation of materials by one atom or one molecule. It was made popular by K. Eric Drexler. One billionth of a meter, or 10^9, is equal to one nanometer.

Oral cancer is a prevalent cancer that often recurs, with high rates of both death and morbidity.[2] The sixth most frequent type of cancer worldwide is head and neck squamous cell carcinoma. People inevitably have major adverse effects during therapy, thus it's critical to create safer and more efficient methods. Currently, nanomedicines that are utilized for effective treatment include biometric nanoparticles and extracellular vesicles (EVs).

In the cutting-edge field of nanotechnology, matter is manipulated at the atomic and molecular levels of physics. It is regarded as an interdisciplinary topic of scientific study concerning various kinds of nanoparticles and the use of novel nanomaterials and nano devices in various scientific domains.[1] In the realm of nanotechnology, we explore methods to employ minuscule devices in performing tasks currently done manually or with conventional equipment. Fundamentally, nanotechnology encompasses the manipulation, segregation, amalgamation, and generation of materials at the scale of individual atoms or molecules. Nano assemblers are tiny devices that may be programmed by a computer to carry out specific tasks. In order to fit into spaces that are difficult to access with the human hand or other forms of technology, the Nano assemblers that may be lesser in size than the nucleus of a cell may be used.

In single dimension, nanomaterials are called sheets; in dual dimensions, they are called nanowires and nanotubes; and in 3-D, they are called quantum dots. Two factors—the

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increase in surface area and quantum effects—make the properties of these particles different from those of other materials. When compared to larger particles, nanomaterials have a significantly higher surface area per unit mass because of their small size.

Nanaodiagnostics can be defined as the use of nanotechnology for clinical diagnostic purposes developed to meet the demands for increased sensitivity and early detection of disease.[1] By enabling new forms of drug delivery, the tissue molecules' synthesis, biomaterials development and improving the surfaces of medical gadgets, in vitro-in vitro methods, systems for biofiltration, and assembly of robots, nanotechnology's various applications are revolutionizing the field of biomedical engineering. Additionally, studying the dental structures from a nanoscale perspective would result in a better comprehension of the function, structure and physiological relationship of the tooth surfaces. Nanomedicine has the capacity to greatly improve diagnosis, management, and follow-up of many oral diseases such as oral carcinoma, dental caries, and dentin hypersensitivity can be quantified based on properties of tooth surface such as biophysical, morphological, and biochemical. Nano medicine uses equipment such as:

2. Nano Vectors

In the future, nano vectors might prove to be an effective means of delivering anti-cancer drugs.[3] They usually consist of three parts- a core material, a therapeutic and imaging, and biological surface modifiers which improve the nanoparticles' bio distribution and tumour targeting. Nano vectors can potentially deliver vast amounts of a therapeutic or imaging substance to a tumor during the targeted bio recognition process.[4]

3. Nanoscale Cantilevers

The cantilevers provide for molecular detection of carcinogens rapidly and selectively and are hence constructed as part of a larger diagnostic device.[3,5] Cancer specific molecules bind to molecules that act as sensors which results in change in conformation of the sensor. Since the sensor acts as a single lever cantilever, this movement is exaggerated. Gold nanoparticles coated with DNA from the basis of a system (in which magnetic micro particles – MMP are also used) that detects serum proteins' femtomolar concentration. In this instance, the MMP is coupled to a monoclonal antibody against the prostate specific antigen (PSA), which forms a free agent capable of capturing free PSA. A second antibody to PSA is added to the NP to create a sandwich of the trapped protein that can be readily separated using a magnetic field. PCR can then be used to amplify the barcode. By this method, an antigen may be quantified at concentrations that are not achievable using an enzyme-linked immunosorbent test.

4. Quantum Dots

Quantum dots are nano particles with unique electronic and optical properties, such as bright and intensive fluorescence.[6] Several research groups have concentrated on combining diagnostic and treatment capabilities into a nanoparticle-based agent. Quantum dots emerge as promising in theranostic platforms, serving either as the primary nano carrier or as integral components within a more intricate architecture, functioning as fluorescent labels.

5. Brachytherapy

Brachytherapy, also known as internal radiation, involves the insertion of a radioactive implant inside or near the tumor. The placement of the implant is typically a painless procedure. Depending on the specific cancer type and treatment strategy, the patient may receive either a temporary or a permanent implant.[7]

6. Nanoknife

The nano knife system employs electrical currents for tumor treatment. Delicate needles are strategically positioned around the tumor, and the system initiates currents between the needles through a process known as irreversible electroporation, aiding in the destruction of the tumor.[8]

7. Hazards of Nano Medicines

Nano particles, sharing dimensions akin to biological molecules like proteins within living systems, can promptly adsorb onto their surface.[9] Upon entering the tissues and fluids of the body, they encounter large molecules, with their ability to have molecules adhere to the surface contingent on the surface characteristics of the particles. This interaction holds significance not only for drug delivery applications but is also influenced by the dimensions of the nano particles. For example, nano particles with dimensions no larger than a few nanometers can penetrate well inside biomolecules, a feat unattainable for larger counterparts. Furthermore, nano particles can traverse cell membranes. Studies have indicated that inhaled nano particles can access the bloodstream, reaching target sites such as the liver, heart, or blood cells. Notably, nano particles exhibit limited degradation or dissolution, instead accumulating in biological systems and persisting for extended periods, raising concerns about their long-term impact. Hence, we are still in a stage of advancement towards the further development of these nanoparticles so that we can have minimum to negligible impact to the normal and healthy tissues and have the maximum impact on the targeted tissue.

8. Nanomaterials for Cancer Diagnosis

Cancer prevention stands as the most effective strategy, emphasizing the importance of early detection for improved survival rates.[3] Tumors detected in situ are more manageable than those that have metastasized. Various types of nanoparticles (NPs) find application in drug and gene delivery, DNA structure probing, and more. A study by Kah et al., the potential of antibody-conjugated gold NPs was demonstrated. These nanoparticles were shown to target the cancer cells and illuminate them using an optical imaging system based on reflectance. Notably, gold NPs were found to offer optical contrast, facilitating the discrimination between cancerous and non-cancerous cells. Additionally, conjugation of these with antibodies enabled the mapping of relevant bio markers required for molecular imaging.

9. Treatment of Oral Cancer

Nanomaterials play a crucial role in various aspects of medical applications, including brachytherapy and gene therapy. BrachySil^{TM} Nano vectors are designed for gene therapy, and nanotechnology serves as a key method for achieving site-specific action without harming normal cells, making it distinct in its ability to minimize side effects.[1]

In the realm of cancer therapy, nanotechnology represents a cutting-edge approach. This burgeoning field holds significant promise for enhancing cancer treatments on two primary fronts: enhancing the properties of pharmaceutical agents and precisely targeting these agents to the tumor site.

One effective strategy involves associating anticancer drugs with colloidal nanoparticles (NPs). This approach aims to work against resistance mechanisms, both noncellular and cellular-based, while concurrently enhancing drug selectivity towards oncogenic cells and diminishing their effect on normal tissues. The utilization of nanotechnology in cancer treatment thus stands as a beacon of hope for advancing therapeutic outcomes.

Nanoparticles (NPs) are able to function as customizable and targeted vehicles for delivery of drugs, transportingtherapeutic genes or chemotherapeutic agents specifically into cells which are malignant while minimizing the impact on cells which are healthy. This targeted delivery approach enables the administration of toxic substances in small doses directly to the intended tissue, enhancing the precision of treatment.

Various nano-delivery systems, such as dendrimers, micelles coated with silica, ceramic NPs, and liposomes that are cross-linked, can be tailored to target cancer cells. This heightened selectivity towards cancer cells contributes to a reduction in toxicity to normal tissues. Through monoclonal antibodies or cell surface receptor ligands getting attached, these nanoparticles bind specifically to cancer cells.

With sizes ranging from 5 nm to 200 nm, NPs engage in unique interactions with biological systems at the molecular level. Their composition allows for self-assembly, ensuring stability and specificity, which are pivotal for encapsulation of drug and biocompatibility.

10. Nanotechnology Based Drug Delivery Systems

Nanoparticles (NPs) have the capability to enhance drug stability and regulate targeted delivery, ensuring a consistent and unvarying concentration at the lesion site. This facilitates the extravasation of drugs into the tumor system, ultimately mitigating side effects.[3]

Polysaccharides, proteins, and biocompatible/biodegradable polymers like, poly-D, polylactic acid, poly (γ-benzyl l-glutamate), polylactide-co-glycolide, L-lactide,polyethylene glycol (PEG), L-glycolide, polycyanoacrylate, gelatin, chitosan, and sodium alginate have been employed in the fabrication of newer polymeric nanoparticles (PNPs). These particles exhibit physical stability, safeguard drugs which are labile from degradation, offer a release that is controlled, and demonstrate excellent tolerability. Consequently, they prove suitable for diverse methods of administration, including oral, parenteral, dermal, pulmonary, ocular and rectal delivery.

11. Liposomes

Liposomes have been extensively researched to enhance the delivery of chemotherapeutic drugs, that aim to upgrade therapeutic effectiveness while reducing toxicity to healthy cells.[1] These are a series of single- or multi-layer microscopic particles with the main constituent of a membrane-like lipid, phospholipids and cholesterol.[10,11] Formulations based on liposomes for gene therapy, like lipoplexes comprising synthetic cationic liposomal-DNA, show significant promise, especially in the context of treatment of oral carcinoma.

12. Hydrogels

This is a network of polymeric chains that are hydrophilic being dispersed in water, capable of swelling and releasing drugs as they dissolve and disintegrate through the gaps within their mesh.[3] Hydrogels hold appeal for administration by oral route due to the close interaction of their polymeric chains with saliva glycoproteins, resulting in a mucoadhesion phenomenon. A significant interest has been observed in employing hydrogels as a system for delivering various chemotherapeutic drugs, such as doxorubicin, paclitaxel, cisplatin and tamoxifen. It has been reported that the SAHA-cisplatin/PECE hydrogel system, administered through direct intratumoral injections, could serve as a valuable method for treatingvarious solid tumors and oral carcinomas.

13. Liquid Crystals

Liquid crystals (LCs) represent a substance in a distinct state, exhibiting characteristics that fall between those of a solid and a liquid.[1,12] This state is termed mesophase, where, "meso-" denotes an intermediate condition. Utilizing liquid crystal (LC) systems brings about substantial alterations in the drug release profile, leading to a reduction in drug toxicity and an enhancement in clinical efficiency. Liquid crystals hold promise as a potential strategy for treating various carcinomas, including oral cancer.

13.1. Layered nanoemulsions as mucoadhesive buccal systems

Oral squamous cell carcinoma (OSCC) three-dimensional outgrowth model treated topically with 5-fluorouracil matrix tablets demonstrated apoptotic effects on cancer cells. This suggests the potential effectiveness of locoregional chemotherapy for OSCC. Furthermore, effective experiments with modified chitosan nanoparticles containing 5-aminolevulinic acid have been conducted, showing that oral cancer cells absorb these particles via folate receptor-mediated endocytosis. When applied topically or locally to oral cancers, chitosan nanoparticles (NPs) have demonstrated promise as cancer medicine carriers. They can encapsulate anticancer medications such as ellagic acid,[13] glycyrrhetic acid,[14] cisplatin,[15] curcumin,[16] etc. and prevent biological deactivation. The capacity of chitosan's muco adhesive qualities to extend residence time at the delivery site can enhance the bioavailability of anticancer drugs.[17]

14. Conclusion

The impact of nanotechnology on dentistry, healthcare, and human life is poised to be more transformative than many previous developments. Undoubtedly, nanotechnology holds the potential to emerge as the most efficient and preferred approach for future cancer therapy and diagnosis. It is expected to be crucial in the upcoming years for the early identification of illness, diagnostic procedures, and therapeutic approaches, greatly improving oral health and human well-being in general.

15. Conflict of Interest

None.

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