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Review Article

Revolutionizing Nano-Pharmaceuticals for Dentistry and Maxillo-Facial Surgery: Intersection of Artificial Intelligence and Nanotechnology in Controlled Drug Delivery Systems

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Abstract

Graphical Abstract

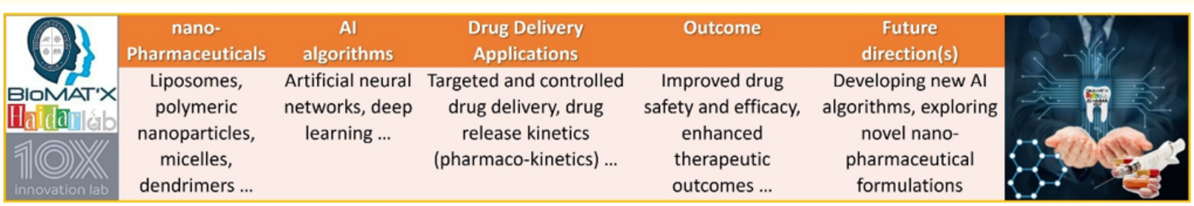

Figure 1

Keywords: *Nanopharmaceuticals; Artificial Intelligence; Drug Delivery; Oral Surgery; Dental Materials; Targeted Therapy; 3-D Printing; Machine Learning; Controlled Release; Nanoparticles*

Precis

Pharmaceuticals play a crucial role in modern or contemporary dentistry and oral surgery, helping to control and manage pain, reduce inflammation/edema, prevent infection, and facilitate oral and dental interventional procedures. Indeed, some common pharmaceuticals used in dentistry include local anesthetics, analgesics, anti-inflammatory drugs, antibiotics, and sedatives. Herein, nano-pharmaceutics is a rapidly developing sub-field of pharmacology, pharmaceuticals, and drug delivery systems that, basically, utilize nanoparticles (nanocapsules, nanospheres, amongst others) to target specific cells and/or tissues. They have shown promise in improving (controlled) drug delivery efficacy, reducing systemic toxicity, and increasing therapeutic outcomes. In dentistry and maxilla-facial surgery, nano-pharmaceuticals have been explored for a variety of bio-applications. AI (Artificial Intelligence) has the potential to revolutionize the pharmaceutical industry in several ways whether via improving the drug discovery process, speeding up clinical trials, and/or developing personalized medicine, to mention a few. Such combination is expected to improve patient clinical outcomes and reduce the overall cost of healthcare.

Introduction

Imagine a World where dental, oral and maxillo-facial surgeries are performed with minimal to no pain and discomfort? Well, cutting-edge localized and release-controlled drug delivery systems that precisely target the affected areas can make it a reality. Indeed, we are not far off, as the intersection of artificial intelligence and nanobiotechnology has been and continues to revolutionize the field of pharmacology, pharmaco-kinetics, pharmaco-dynamics, pharmaceutics, and pharmaceuticals. By leveraging the power of artificial intelligence to design and control drug delivery systems at the nano-scale, researchers are paving the way for more effective and personalized treatments for a range of dental and oral health conditions. In this article, we explore the exciting possibilities and opportunities of this evolving field and discuss all the challenges of bringing nano-pharmaceuticals to forefront of dentistry, oral and maxillo-facial surgery.

Dental pharmacology is the study of drugs used in dentistry [1]. It encompasses the scientific, technological, and clinical study of the properties, uses, and effects of drugs used in dentistry and oral surgery procedures, as well as the principles and practice(s) of drug therapy [2]. Herein, dental pharmaceuticals are the actual drugs or medications used to treat oro-dental diseases and conditions [3]. Hence, pharmacology and pharmaceuticals are related yet are also to be considered as distinct concepts in dentistry [4]. Indeed, both concepts are important in the field of oro-dental surgery, and dental healthcare professionals must have a good understanding of both to provide safe and effective patient care [1]. In addition, dental pharmacology plays a crucial role in the management of dental pain [5]. Understanding the mechanisms of action of analgesics and anesthetics can help clinicians select appropriate drugs and dosages for patients [5].

In general, local anesthetics continue to be commonly used to numb the nerves in the mouth and teeth/dentition of patients, making dental procedures more comfortable and reducing pain [6]. Herein, lidocaine, mepivacaine, and bupivacaine are examples of commonly used local anesthetics [7]. Analgesics such as acetaminophen and ibuprofen can also help to manage pain and discomfort following dental procedures [8], while anti-inflammatory drugs such as corticosteroids can help to reduce swelling and inflammation [9]. Chlorhexidine, a topical anti-septic, is used to control plaque and prevent the development of gum disease [10]. On the other hand, antibiotics [11] are often used to prevent or treat infections in the mouth, such as periodontal disease or abscesses. Commonly used antibiotics in dentistry include penicillin, amoxicillin, and metronidazole [11]. Further, sedatives such as nitrous oxide and oral sedatives can also be used to help patients relax and reduce anxiety during dental procedures [12]. Herein, it is important perhaps to note that any pharmaceuticals used in dentistry should only be prescribed and administered by a licensed dental professional [13]. Patients should also inform their dentist of any allergies or medical conditions that could affect their ability to safely take certain medications [14]. Overall, pharmaceuticals are an important tool in contemporary dentistry and oral surgery to help improve our patient comfort and clinical outcomes [15].

Nanotechnology has shown great promise in the field of controlled pharmaceutical delivery for dentistry and oral surgery [16]. It involves the use of nano-scale materials, formulations, and devices to deliver drugs to specific target sites in a controlled and sustained manner, improving the bio-distribution, residency, and effectiveness of drug (or multiple drugs) therapy while minimizing side effects [17]. Briefly, nano-pharmaceuticals are a class of drugs that are designed and engineered at the nano-scale level [18], typically ranging in size from 1 to 100 nanometers (some consider up to 999 nm) [19]. They are created using nanotechnology, which allows for precise control over the size, shape, and surface properties of the drug particles [20]. The small size of nano-pharmaceuticals provides several advantages over traditional drug delivery systems. For example, they can more easily penetrate biological barriers such as cell membranes, leading to improved drug efficacy and reduced side effects [21]. They can also be designed to selectively target specific cells or tissues, such as cancer cells, while leaving healthy cells unharmed [22]. Furthermore, nanoparticles tend to accumulate or amass (more than micro-scale, for example) at sites of inflammation, hence, amplifying therapeutic efficacy [23]. Further, nano-pharmaceuticals can be used to deliver a variety of therapeutic agents, including small molecules, proteins/cytokines, genes, and nucleic acids [24]. Some examples of nano-pharmaceuticals currently in development or already on the market include liposomes, polymeric nanocapsules, dendrimers, micelles, and metallic nanoparticles [25]. Nevertheless, there are also some challenges associated with the development and use of nano-pharmaceuticals, to date. For example, one concern is their potential toxicity, as the small size and unique surface properties of the particles can interact with biological systems in unexpected ways [26]. Regulatory agencies such as the FDA and EMA closely monitor the safety of nano-pharmaceuticals before they can be approved for clinical use [27]. In dentistry, nanotechnology-based drug delivery systems are being developed to treat a range of oral conditions such as periodontal disease, oral infections, and oral cancer, amongst others [28]. One example is the use of nano-carriers such as the afore-mentioned liposomes, dendrimers, and nanoparticles to deliver anti-microbial, -bacterial and/or -fungal agents directly to the site of infection in periodontal pockets [29]. In oral surgery, nanotechnology-based drug delivery systems are also being developed to improve the healing process and reduce pain and inflammation after surgical procedures (*in situ*). Herein, one example is perhaps the use of nanofibers and hydrogels to deliver growth factors, cytokines and other bioactive molecules designed and intended to stimulate tissue regeneration whilst reducing inflammation and pain [30].

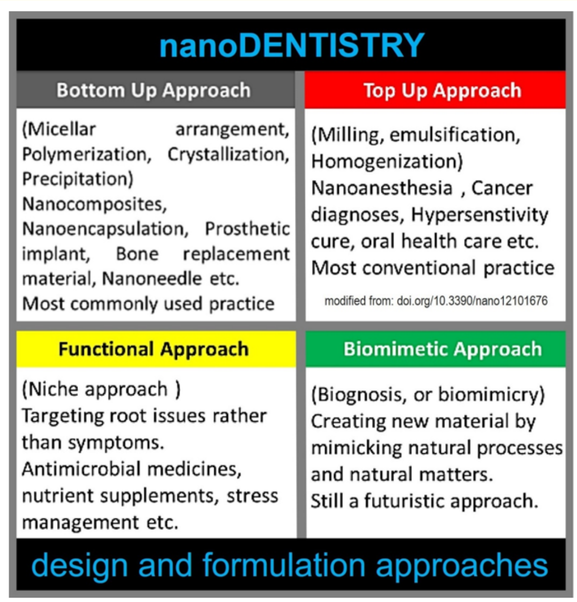

Figure 2

Nanodentistry: Another potential application of nanotechnology in dentistry and oral surgery is the use of nano-scale sensors to monitor and diagnose oral diseases. For example, nano-sensors could be used to detect early signs of oral cancer or to monitor the pH levels in dental plaque, which could help to prevent tooth decay [31]. Nanobiotechnology, drug delivery, and 3-D (three-dimensional/additive manufacturing) printing are all emerging technologies that are also being used in dentistry and oral surgery to improve patient outcomes and the delivery of dental care. Dental implants can be 3-D printed with nano-coatings that improve their durability and resistance to infection. These coatings can also be designed to release drugs over time, providing localized drug delivery to the surrounding tissues. Several examples of how nanotechnology, drug delivery, and 3-D printing (including hybrids) can be combined to improve oro-dental care.

3-D printed drug delivery devices: Researchers have developed 3-D printed drug delivery devices that can be customized to fit a patient's mouth and deliver medications to specific areas of the oral cavity [32]. These devices can be designed to control the release of drugs over a prolonged period, reducing the need for multiple treatment visits to the clinic.

3-D printed dental implants with nanoparticle coatings: Dental implants can be 3-D printed with nanoparticulate coatings that improve their durability and resistance of the treated surface to infection. These surface coatings can also be designed to release drug(s), controllably, over time, supplying localized drug delivery to the surrounding tissues [33].

3-D printed surgical guides with embedded nanoparticles: 3-D printed surgical guides can be embedded with nanoparticles that have antimicrobial properties, helping to prevent infections during dental procedures [34]. These guides can also be designed to release drugs to the surrounding tissues, promoting healing and reducing pain and inflammation.

Nanoparticle-reinforced dental materials: Researchers have developed dental materials, such as composites and cements, that are reinforced with nanoparticles to improve their strength, durability, and resistance to wear. These materials can also be designed to release drugs over time, providing localized drug delivery to the surrounding tissues [35].

Recently, hybrid printing has been increasingly used in dentistry and oral surgery to create custom-made dental implants, crowns, bridges, and other oral devices; useful for creating complex dental structures with intricate details [36]. With the ability to combine multiple 3-D printing techniques (and materials), hybrid printing can offer a range of benefits over traditional manufacturing methods [37]. Indeed, one of the key benefits of hybrid printing in dentistry is its precision. By combining different techniques such as Fused Deposition Modeling (FDM) and Stereolithography (SLA), hybrid printers can create dental devices with high accuracy and resolution, ensuring a precise fit and optimal function [38]. Another potential advantage of hybrid 3-D printing over traditional 3-D printing is its ability to create customized devices quickly and at a lower cost; time- and cost-effective [39]. Overall, the combination of nanobiotechnology, controlled drug delivery, and 3-D printing has the potential to revolutionize oral and dental healthcare, providing our patients with more customized, effective, and comfortable treatments; improving drug delivery and treatment outcomes in dentistry and oral surgery [40]. However, more research, development, and innovation (R&D&I) efforts and investments are needed to fully explore, understand and advance the safety and bio-efficacy of these new technologies, and to develop standardized protocols for use in clinical practice [40].

Artificial intelligence (AI): For dentistry, AI can be defined as the use of computer algorithms and machine learning techniques to perform tasks that typically require human intelligence, such as diagnosing oral diseases and conditions, predicting treatment outcomes, and improving patient care [41]. AI in dentistry involves the development and application of software and hardware technologies that can analyze and interpret large amounts of data, such as radiographs, photographs, and electronic health records, to provide dentists and oral healthcare professionals with insights and recommendations for patient care [42]. AI algorithms can be trained to recognize patterns and relationships in data that may be difficult for humans to identify, helping to improve accuracy and efficiency in diagnosis and treatment planning [43]. AI has the potential to revolutionize the innovation of dental and medical devices, products, solutions, and services, leading to improved patient outcomes and quality of life [44]. By leveraging machine learning algorithms, AI can analyze vast amounts of data and identify patterns and trends that can inform the design and development of new products and services [45]. For example, AI can be used to improve the accuracy of diagnosis and treatment planning, as well as to personalize treatment based on individual patient needs and characteristics [46]. Additionally, AI can be used to develop innovative dental and medical devices, such as smart prosthetics, remote patient monitoring systems, and surgical robots, which can improve the safety and effectiveness of medical procedures [47]. One of the key benefits of AI in dental and medical device innovation is that it can accelerate the development process, allowing new products and

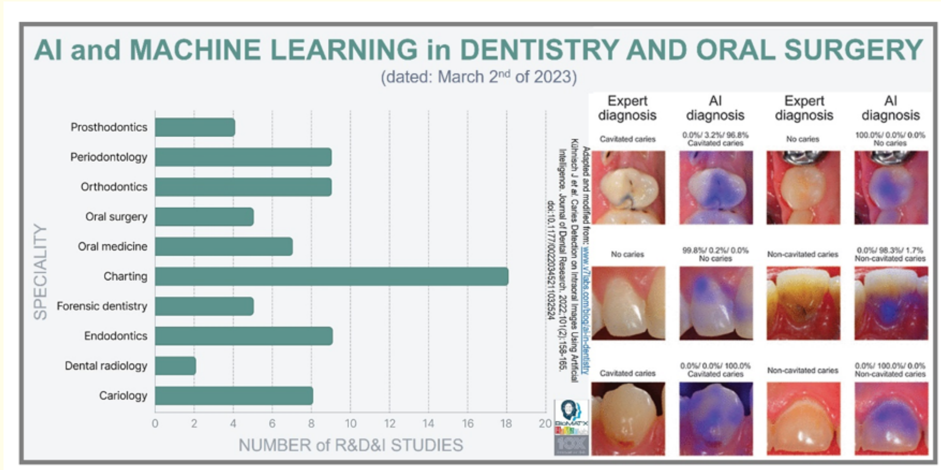

Figure 3

solutions to be brought to market more quickly [48]. AI can also help to reduce the cost of development by streamlining the research and development process and minimizing the need for expensive clinical trials [49]. Overall, the use of AI in dental and medical device innovation has the substantial potential to greatly improve patient outcomes and quality of life via enabling the development and optimization of more safe, effective, efficient, and customized products and solutions [50].

To summarize, AI can benefit and contribute to nanotechnology and drug delivery in dentistry and oral surgery (combinatorial approach and strategy) in several distinct ways.

Prediction, modeling, and characterization: AI can be used to predict and model the behavior of nanoscale materials and drug delivery systems, allowing researchers to optimize their designs and improve their performance [51]. AI can assist in the characterization of nanoparticles, which is important for determining their behavior *in vivo*. AI algorithms can analyze data from imaging and other sources to identify the size, shape, surface area, and other properties of nanoparticles [52]. AI can help us dentists and oral surgeons to predict and prevent oro-dental diseases and conditions by analyzing patient data to identify risk factors and potential health problems; leading to an earlier intervention and better outcomes for our patients, including for post-operative prognosis and care [53].

Drug discovery: AI can help to identify new drug candidates that are better suited for nanotechnology-based and release-controlled drug delivery systems, through analyzing very large datasets and identifying potential molecular targets and drug interactions [54].

Precision medicine: AI can help to personalize drug delivery (and vehicles/systems) based on a/the unique genetic, physiological characteristics and oral microbiome of an individual patient, via analyzing data from medical records, imaging, and other sources to identify optimal drug dosages, concentrations, delivery times (profiles) and methods. Thus, improves the effectiveness of drug therapy and reduce the risk of side effects [55].

Quality control: AI can be used to monitor and ensure the quality of nano-scale materials, nano-based release-controlled pharmaceuticals, and drug delivery systems, by analyzing data from bio-sensors and other sources to detect defects and anomalies in real-time. This can help to ensure the safety and effectiveness of these drug delivery systems [56].

Diagnostic tools: AI can be used to develop new diagnostic tools based on nano-bio-technology, by analyzing data from imaging and other sources to detect and classify oral diseases [57]. AI can analyze dental images, such as X-rays and CT scans, to help dentists and oral surgeons detect and diagnose oral diseases and conditions more accurately and efficiently [58]. AI algorithms can identify patterns, anomalies, and subtle variations *not* visible to the human eye, permitting earlier detection and intervention [59].

Treatment planning: AI can assist dentists and oral surgeons in treatment planning by analyzing patient data, such as medical history, dental records, and imaging results, to suggest the most effective treatment option [60]. AI can also help us to better personalize our treatment plans, based on the unique characteristics and needs of each patient [61].

Robotics: AI can be integrated with evolving dental robotics to perform dental procedures more accurately and efficiently. For example, AI-powered robots can assist dentists and oral surgeons in dental implant placement or even performing root canal treatments [62].

Patient communication: AI-powered chatbots and virtual assistants can help patients communicate with their dentists and oral surgeons more easily and efficiently. Patients can use such tools to ask questions, schedule appointments, and receive personalized treatment recommendations. Thus, AI can help us to improve our dental economics [63].

Overall, the combination of AI and nano-bio-technology (and all related sub-technologies, expanding to the emerging biomimetics and bio-inspired methods and techniques) can enable the development of more effective and efficient oral and dental nano-pharmaceuticals that would help to accelerate the development of new nano-scaled drug delivery systems and further improve, enhance and/or advance their bio-performance, while also enabling more personalized and precise treatments for our patients in complex dental and oro-maxillo-facial surgical applications [64,65]. AI is and will be providing dentists and oral surgeons with new powerful tools for improving patient care, boosting efficiency, and evolving medical/dental research, development, innovation, education, and training; an open call for our dental schools to quickly adapt and adopt to such shifts.

"The intersection of technology and healthcare will create an unprecedented opportunity for innovation that will transform the way we deliver care to patients." - Daniel Kraft, a physician-scientist, inventor, entrepreneur, and innovator. He is the founder and chair of Exponential Medicine, a program that explores the convergence of technology and medicine, and the executive director of FutureMed, an executive education program that focuses on exponential technologies and their potential to transform healthcare. Kraft is also an advisor at Singularity University, an interdisciplinary university (only by trade-name), headquartered in Santa Clara, California - United States (with other offices and locations around the world, including in Canada, Brazil, Australia, Europe, Latin America, and Asia), focused on technology translation and its potential to solve global challenges.

Conflict of Interest

The author of this article declares having no conflict of interest of any form or nature with any platelet concentrate product, protocol, technique, or company.

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