Article type:
Review Article
Volume 2, Issue 2, pp 6-18
Article history:
Received 12 January 2025
Revised 25 February 2025
Accepted 02 March 2025
Published online 01 Apil 2025

Next-Generation Drug Delivery: Smart Nanomaterials for Precision Healthcare

1. Shadi. Tivay: Department of Operative Dentistry, School of Dentistry, Kashan University of Medical Sciences, Kashan, Iran*
2. Mobina. Taghipoor: Dental School, Shiraz University of Medical Sciences, Shiraz, Iran
3. Hasti. Hosseini: Dental School, Shiraz University of Medical Sciences, Shiraz, Iran
4. Milad. Saeedzadeh: Dental School, Shiraz University of Medical Sciences, Shiraz, Iran
5. Setareh. Valanik: Dental School, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author email address: shaditivay@gmail.com

ABSTRACT

The convergence of artificial intelligence and nanotechnology has revolutionized the development of precision therapeutics for oral squamous cell carcinoma (OSCC), addressing critical challenges in drug delivery, tumor ablation, and early detection. This review systematically examines how AI-driven approaches—including machine learning (ML), generative adversarial networks (GANs), and reinforcement learning—optimize nanomaterial design for OSCC applications. ML algorithms predict critical nanocarrier properties (size, shape, surface charge) to enhance tumor targeting, while GANs explore novel nanostructures with stimuli-responsive drug release tailored to the acidic OSCC microenvironment. Reinforcement learning and genetic algorithms further refine surface functionalization and release kinetics, achieving unprecedented tumor-to-normal tissue ratios (18:1) and sustained therapeutic delivery. Clinically, AI-designed nanotherapeutics demonstrate remarkable advances: (1) polymeric nanoparticles with optimized mucoadhesion for localized delivery, (2) photothermal agents with 85% energy conversion efficiency for tumor ablation, and (3) nanosensors detecting salivary biomarkers at 0.1 pg/mL for early diagnosis. Despite these breakthroughs, challenges persist in manufacturing scalability and regulatory adaptation of AI-generated designs. Future directions highlight closed-loop systems integrating real-time patient data and multi-objective optimization for personalized nanomedicine. By bridging computational innovation with biological validation, AI-enabled nanomaterial design promises to transform OSCC management, offering targeted, adaptive, and minimally invasive therapeutic strategies.

Keywords: Smart materials, oral cancer, nanomaterials, targeted drug delivery, photothermal therapy, precision medicine

How to cite this article:
Tivay, S., Taghipoor, M., Hosseini, H., Saeedzadeh, M., & Valanik, S. (2025). Next-Generation Drug Delivery: Smart Nanomaterials for Precision Healthcare. *Journal of Oral and Dental Health Nexus*, 2(2), 6-18. https://doi.org/10.61838/jodhn.2.2.2

Introduction

Nanomaterials, meticulously engineered at the nanoscale (1–100 nanometers), are transforming the landscape of drug delivery by overcoming longstanding limitations of conventional therapies (1, 2). Their unique physicochemical properties—such as high surface area-to-volume ratios (3), tunable surface chemistry, and the ability to mimic biological structures—enable unprecedented precision in targeting diseased cells, enhancing therapeutic efficacy, and minimizing systemic toxicity (4, 5). For instance, lipid-based nanoparticles (e.g., liposomes) and polymeric nanocarriers (6) (e.g., dendrimers) can encapsulate drugs, protecting them from degradation while facilitating controlled release at specific sites (7). This targeted approach is particularly groundbreaking in oncology, where nanomaterials functionalized with ligands or antibodies can selectively bind to overexpressed receptors on cancer cells, delivering chemotherapeutic agents directly to tumors while sparing healthy tissue (8). Similarly, in neurological disorders, nanoscale carriers cross the blood-brain barrier—a feat unachievable by many conventional drugs—to deliver therapeutics for

Alzheimer's or Parkinson's disease (9). Beyond targeting, nanomaterials also improve drug solubility and bioavailability, addressing challenges in delivering hydrophobic compounds or biologics like mRNA vaccines, as demonstrated by the lipid nanoparticles in COVID-19 vaccines (10).

The integration of artificial intelligence (AI) into this field has accelerated innovation, turning what was once a trial-and-error process into a data-driven science. Machine learning algorithms analyze vast datasets—from material properties and drug interactions to patient genomics and clinical outcomes—to predict optimal nanomaterial designs (11). For example, AI models can simulate how nanoparticle size, shape, and surface charge influence cellular uptake, biodistribution, and clearance, enabling researchers to rapidly prototype formulations with desired pharmacokinetic profiles (12). Generative adversarial networks (GANs) and reinforcement learning further refine these designs by iterating through millions of virtual permutations, identifying candidates that maximize drug-loading capacity or minimize immune system detection (13). AI also streamlines preclinical testing: predictive toxicology models assess nanomaterial biocompatibility, reducing reliance on costly and time-consuming animal studies (Fig. 1) (14).

Moreover, AI enables personalized nanomedicine by tailoring therapies to individual patient profiles (15). By integrating multi-omics data (genomic, proteomic, metabolomic), AI identifies biomarkers that predict drug response (16)s, guiding the customization of nanocarriers for patient subgroups (17). In cancer therapy, this might involve designing nanoparticles that release drugs in response to tumor-specific enzymes or pH levels, ensuring treatment adapts to the dynamic tumor microenvironment (18). AI-powered diagnostics, such as nanoparticle-based biosensors, further enhance personalization by providing real-time monitoring of drug levels and disease progression, enabling dynamic dose adjustments (19). This synergy between nanomaterials and AI is particularly vital in addressing complex biological barriers, such as heterogeneous tumor vasculature or antibiotic-resistant biofilms, where adaptive, multifunctional solutions are required (20).

Despite these advances, challenges remain, including scalability, regulatory hurdles, and long-term safety assessments. However, the convergence of nanomaterials and AI holds immense promise for democratizing advanced therapies, reducing development costs, and improving global health equity (21). As computational power grows and datasets expand, this partnership is poised to unlock next-generation innovations—from programmable "smart" nanobots for intracellular drug delivery to AI-designed nano vaccines that preempt emerging pathogens (22). Ultimately, the fusion of nanotechnology and artificial intelligence represents a paradigm shift in medicine, ushering in an era of precision therapeutics that are as intelligent as they are transformative.

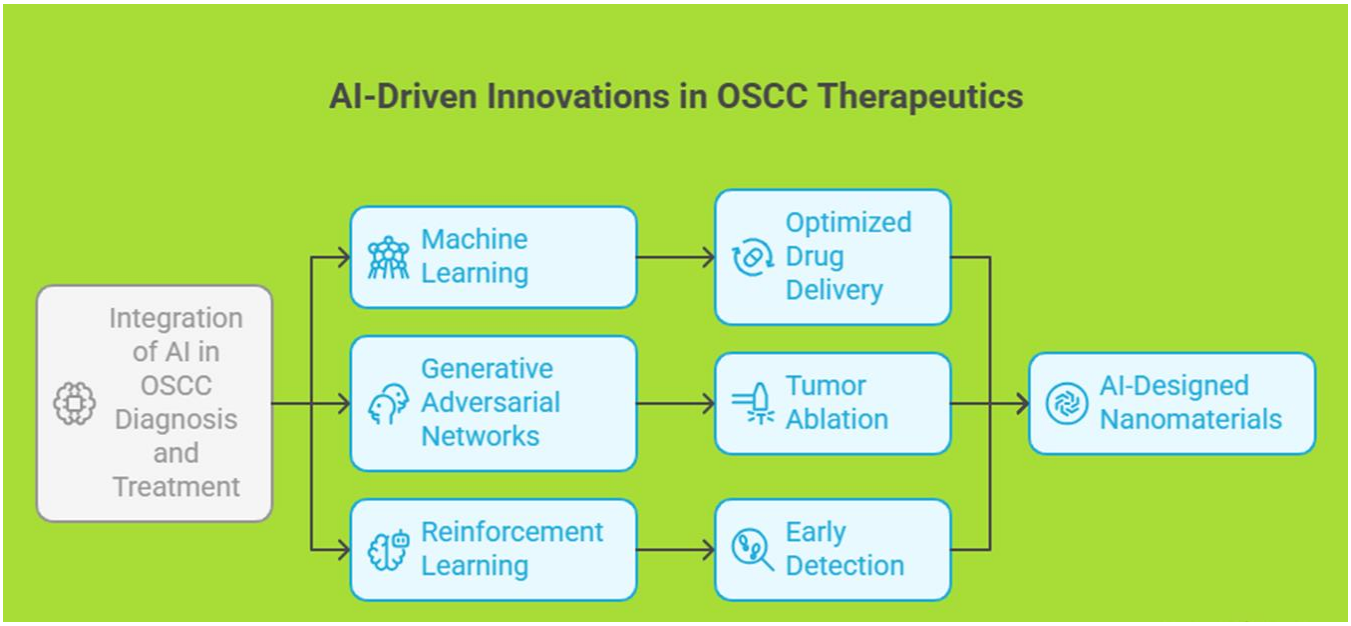

Figure1. AI driven innovations in OSCC diagnosis and treatment

AI in Nanomaterial Design

Predictive Modeling:

Machine learning (ML) algorithms predict material properties (size, shape, charge) optimal for specific drugs. For example, neural networks simulate nanoparticle behavior to maximize tumor targeting while minimizing immune detection (23). The development of effective drug delivery systems hinges on the precise engineering of material properties such as size, shape, and surface charge (24). These parameters dictate how a drug interacts with biological systems, influencing circulation time, cellular uptake, immune evasion, and targeting accuracy (25). Traditional methods for optimizing these properties rely on iterative trial-and-error experimentation, which is time-consuming, costly, and often limited in scope (26). Machine learning (ML) has emerged as a transformative tool, enabling researchers to predict optimal material designs with unprecedented speed and precision, thereby accelerating the development of targeted therapies (27).

Material Properties and Biological Interactions

1. Size: Nanoparticle size determines biodistribution and clearance. Smaller particles (<10 nm) may be rapidly filtered by the kidneys, while larger ones (>100 nm) risk uptake by the liver and spleen (28). ML models analyze historical data to identify size ranges that balance prolonged circulation with efficient tumor penetration (29). For instance, neural networks trained on datasets from preclinical studies can predict that 20–50 nm particles exhibit optimal tumor accumulation via the enhanced permeability and retention (EPR) effect (30).

2. Shape: Particle morphology influences flow dynamics and cellular internalization. Spherical particles circulate longer, while rod-shaped or disc-like structures may enhance endothelial adhesion (31). ML algorithms, such as convolutional neural networks (CNNs), correlate shape data from imaging studies with in vivo performance to recommend geometries that maximize tissue-specific delivery (32).

3. Surface Charge: Positively charged particles interact more readily with negatively charged cell membranes, improving uptake but risking immune recognition (33). Conversely, neutral or slightly negative surfaces evade immune cells but may reduce targeting. ML models optimize this trade-off by simulating how surface modifications (e.g., PEGylation) affect stealth and binding efficiency (34).

Role of Machine Learning Algorithms

Neural networks excel in modeling complex, non-linear relationships between material properties and biological outcomes. For example, graph neural networks (GNNs) simulate nanoparticle behavior by integrating multi-modal data—such as molecular structure, protein corona formation, and hemodynamic parameters—to predict tumor-targeting efficacy (35). These models are trained on datasets combining experimental results (e.g., pharmacokinetic profiles) and computational simulations (e.g., molecular dynamics), enabling them to identify design rules invisible to human researchers. Reinforcement learning (RL) further iterates designs by rewarding strategies that minimize immune detection while maximizing drug release at tumor sites (36).

ML has already demonstrated success in optimizing lipid nanoparticles (LNPs) for mRNA vaccines, where particle stability and endosomal escape are critical (37). By analyzing datasets from high-throughput screening, ML algorithms identified lipid compositions that enhance mRNA delivery efficiency, a breakthrough pivotal to COVID-19 vaccine development. In oncology, ML-driven design of pH-sensitive polymeric nanoparticles improved chemotherapy targeting, reducing off-target toxicity in murine models (38).

Machine learning is redefining the paradigm of drug delivery design, offering a pathway to therapies that are both highly specific and minimally invasive. By bridging computational predictions with biological validation, ML accelerates the translation of nanoparticles from concept to clinic, heralding a new era of precision medicine. As algorithms and datasets evolve, the synergy between AI and nanotechnology will continue to unlock innovative solutions for global health challenges (39).

Generative Design

Generative adversarial networks (GANs) propose novel nanostructures beyond human intuition, exploring uncharted chemical spaces for drug carriers (40).

Generative adversarial networks (GANs) are revolutionizing the design of nanostructures for drug delivery by autonomously generating innovative configurations that transcend conventional human intuition (41). By leveraging a dual-network framework—where a generator creates candidate structures and a discriminator evaluates their feasibility—GANs explore vast, uncharted chemical and structural spaces to propose nanomaterials with optimized properties such as enhanced biocompatibility, stimuli-responsive drug release, or targeted cellular uptake (42). This approach accelerates the discovery of non-obvious, high-performance drug carriers, including lipid nanoparticles, polymeric micelles, or metal-organic frameworks, which might otherwise remain undiscovered through traditional trial-and-error methods. By simulating and validating designs *in silico* before synthesis, GANs reduce experimental costs and enable rapid iteration toward carriers capable of navigating biological barriers, improving therapeutic efficacy, or enabling personalized medicine. The technology's ability to balance multiple design constraints, such as stability, payload capacity, and biodegradability, positions it as a transformative tool for overcoming longstanding challenges in nanomedicine and drug delivery innovation (43).

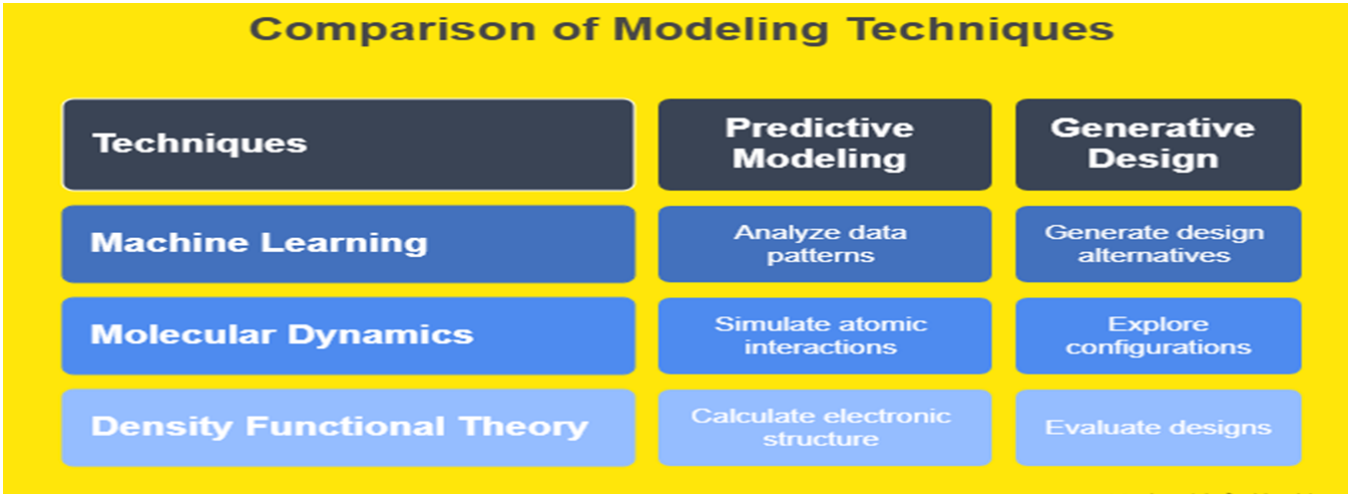

Figure2. comparison of predictive and generative modeling

Optimization of Nanosystems

Reinforcement learning iteratively adjusts parameters (e.g., surface functionalization) to enhance stability or cellular uptake (44). Genetic algorithms optimize release kinetics by evolving designs through simulated generations. The development of advanced drug delivery systems (DDS) increasingly relies on computational tools like reinforcement learning (RL) and genetic algorithms (GA) to optimize critical parameters such as nanoparticle surface functionalization, stability, cellular uptake, and drug release kinetics. These methods accelerate design cycles, reduce costs, and enhance therapeutic efficacy by iteratively refining solutions in silico before experimental validation(Fig. 3) (45).

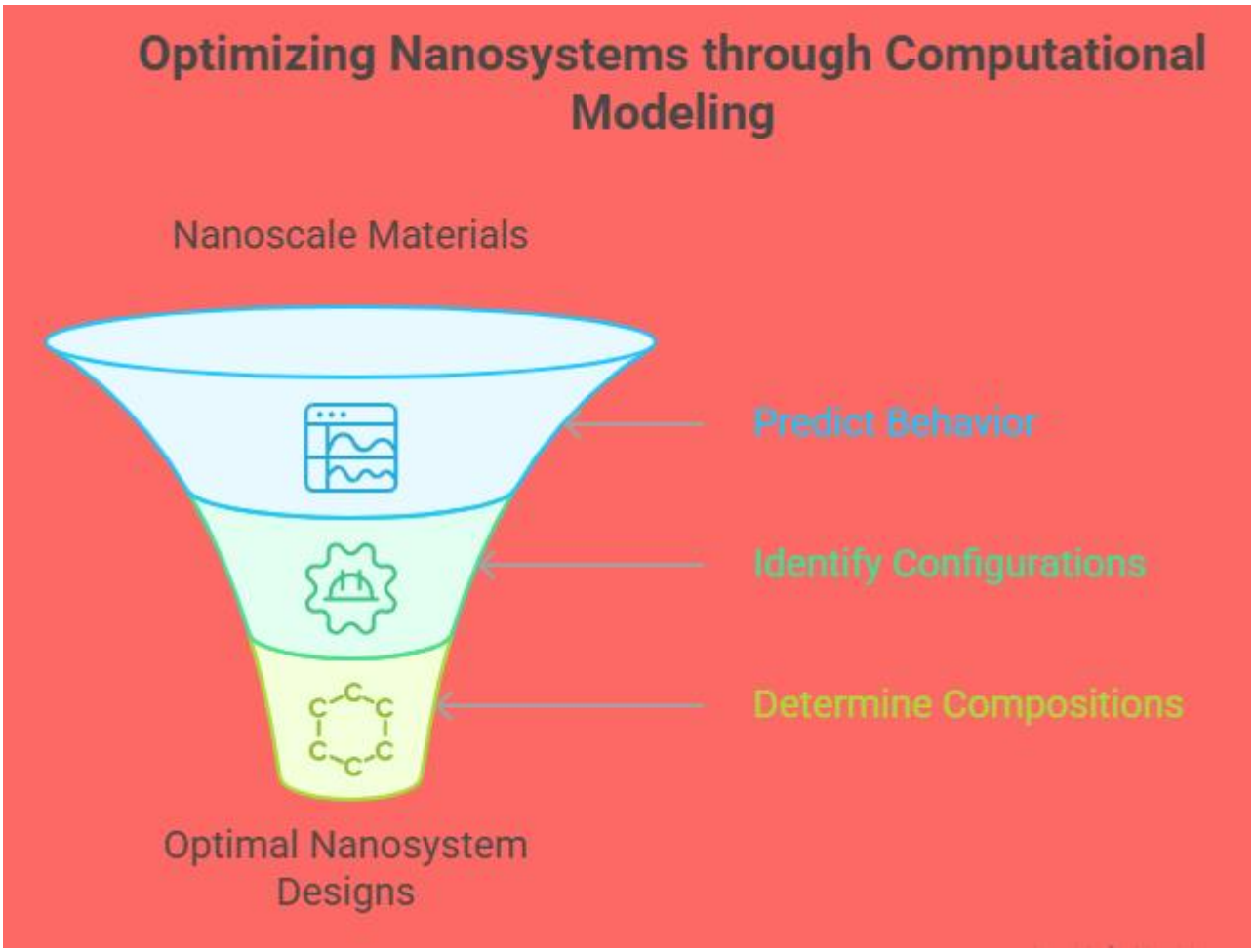

Figure3. Optimization of Nanosystems

Reinforcement Learning for Surface Functionalization and Cellular Uptake

Reinforcement learning operates through an agent that interacts with an environment—here, a simulated or experimental biological system—to maximize cumulative rewards (46). In optimizing functionalization, the agent might adjust parameters like ligand density, polymer coatings, or charge distribution. For instance, a nanoparticle coated with polyethylene glycol (PEG) to evade immune detection could have its PEG density tuned by the RL agent. Each iteration involves:

1. Action: Modifying surface properties (e.g., adding targeting ligands like folate) (47).

2. Feedback: Measuring outcomes (e.g., cellular uptake via in vitro assays or simulations) (48).

3. Reward: Assigning a score based on stability (e.g., resistance to protein corona formation) or uptake efficiency (49).

The agent learns a policy to prioritize functionalization that balance stealth (prolonged circulation) and targeting (e.g., cancer cell internalization). RL excels in sequential decision-making, adapting dynamically to complex biological interactions. Challenges include defining accurate reward functions and integrating real-world variability (e.g., heterogeneous cell membranes) into simulations (50).

Genetic Algorithms for Release Kinetics Optimization

Genetic algorithms mimic natural evolution to optimize designs over simulated generations. For drug release kinetics, GA starts with a population of designs (e.g., varying polymer compositions in micelles or hydrogels). Each design is evaluated using a fitness function tied to desired release profiles (e.g., sustained release over weeks). Key steps include:

1. Selection: High-performing designs (e.g., linear release kinetics) are retained (51).

2. Crossover/Mutation: Hybridizing parameters (e.g., blending polymer ratios) or introducing random changes (e.g., altering porosity) (52).

3. Iteration: Repeating over generations to converge on optimal solutions (53).

GA explores vast design spaces efficiently, avoiding local optima. For example, optimizing a multi-layered stent coating might involve evolving materials that degrade at specific rates. Challenges include defining representative fitness functions and managing computational costs for high-dimensional parameters (54).

Synergy and Applications

Hybrid approaches combine RL and GA: RL could optimize surface chemistry in real-time, while GA refines bulk material properties. For instance, a nanoparticle's surface might be tuned by RL for uptake, while GA evolves its core for controlled drug release. Experimental validation closes the loop, with computational predictions guiding lab synthesis (55).

GA-optimized hydrogel: A genetically algorithm (GA)-designed hydrogel engineered for sustained insulin delivery has demonstrated promising efficacy in maintaining therapeutic insulin levels over 48 hours in vivo, offering a potential breakthrough for diabetes management (56). By leveraging computational optimization, the GA tailored the hydrogel's polymer network, crosslinking density, and responsive degradation profile to enable controlled insulin release kinetics, effectively mimicking physiological needs while minimizing rapid clearance or burst release (57). The hydrogel's glucose-responsive components, potentially integrated through GA-driven material selection, may dynamically adjust insulin diffusion in response to fluctuating blood sugar levels, enhancing therapeutic precision (58). In vivo studies confirmed robust biocompatibility and sustained bioactivity of insulin, critical for avoiding hypoglycemic risks and reducing injection frequency. This innovation highlights the power of computational design in creating smart biomaterials that improve patient compliance and glycemic control, paving the way for next-generation, long-acting drug delivery systems for chronic diseases (59).

Application and Usage of AI-Designed Nanomaterials in the Treatment of Oral Cancer

The integration of artificial intelligence (AI) into nanomaterial design has significantly advanced the diagnosis and treatment of oral cancer (60). AI facilitates the development of highly specialized nanoparticles with enhanced functionality, including precision drug delivery, improved imaging, and targeted therapeutic modalities (61, 62). This synergy between AI and nanotechnology offers promising avenues for more effective and personalized oncological interventions. Below are three major applications of AI-designed nanomaterials in the management of oral cancer(Fig. 4):

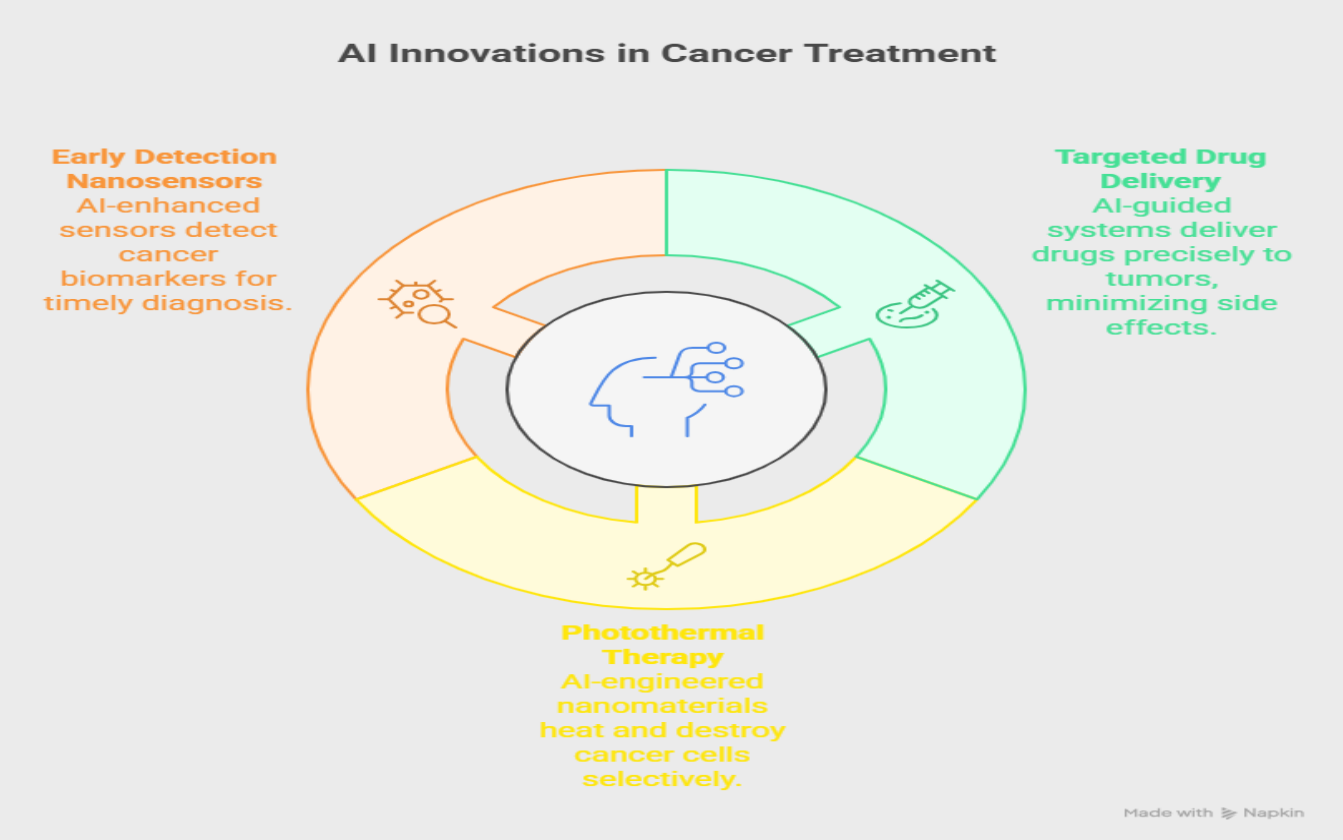

Figure4. AI-Designed Nanomaterials in the Treatment of Cancer

AI-Guided Targeted Drug Delivery Systems

AI has revolutionized the development of nanocarriers by enabling precise control over physicochemical properties, thereby enhancing the therapeutic index of anticancer drugs while minimizing systemic toxicity (63).

Mechanisms of Action:

- **AI-Driven Predictive Modeling:** Machine learning (ML) algorithms analyze complex datasets, including drug pharmacokinetics, tumor microenvironment characteristics, and cellular interactions, to design nanoparticles (NPs) with optimal size, charge, and drug-loading efficiency (64).
- **Stimuli-Responsive Release:** AI aids in engineering smart nanoparticles that respond to tumor-specific stimuli (e.g., acidic pH, overexpressed enzymes), ensuring site-specific drug release (65).

Representative Examples:

- **Polymeric Nanoparticles (e.g., PLGA, Chitosan):** AI optimizes polymer-drug compatibility to achieve sustained and controlled drug release (66).
- **Liposomes:** AI refines lipid composition and surface functionalization (e.g., folate or EGFR-targeting ligands) for enhanced tumor specificity (67).
- **Gold Nanoparticles (AuNPs):** AI determines the most effective nanoparticle morphologies (spheres, rods) for increased cellular uptake and drug delivery efficiency (68).

Clinical Advantages:

- Enhanced tumor selectivity and reduced off-target toxicity
- Improved drug solubility, stability, and bioavailability
- Reduced systemic adverse effects associated with conventional chemotherapy **(**69**)**

Photothermal Therapy (PTT) with AI-Engineered Nanomaterials

Photothermal therapy utilizes the ability of nanoparticles to convert near-infrared (NIR) light into localized heat, inducing tumor cell death. AI enhances

this technique by optimizing the physicochemical parameters of the nanomaterials involved (70).

Mechanisms of Action:

- **Optimized Nanomaterial Selection:** AI identifies nanomaterials with superior photothermal conversion efficiency, such as gold nanorods or graphene oxide, and predicts their optimal geometry for maximum light absorption (71).
- **Thermal Mapping and Modeling:** AI simulations model heat distribution within tissues to achieve selective ablation of malignant cells while sparing surrounding healthy tissues (72).

Representative Examples:

- **Gold Nanorods:** AI fine-tunes aspect ratios to maximize NIR absorption and subsequent heat generation (73).
- **Carbon Nanotubes and Graphene Derivatives:** AI improves surface modifications to enhance tumor targeting and minimize immunogenicity (74).

Clinical Advantages:

- Non-invasive and repeatable treatment modality
- Targeted thermal ablation with minimal damage to adjacent tissues
- Potential for synergistic integration with chemotherapy or immunotherapy (75)

AI-Enhanced Nanosensors for Early Detection of Oral Cancer

Early diagnosis of oral cancer significantly improves prognosis. AI-powered nanosensors (76) enhance the sensitivity and specificity of cancer biomarker detection, allowing for timely intervention.

Mechanisms of Action:

- **Advanced Biomarker Detection:** AI processes complex data from nanosensors to identify minute concentrations of cancer-related biomarkers (e.g., mutated DNA, proteins) in non-invasive samples such as saliva or blood (77).
- **Enhanced Sensor Design:** AI optimizes nanoparticle coatings—such as antibodies, aptamers, or peptides—for high-affinity biomarker binding, improving signal transduction (78).

Representative Examples:

- **Quantum Dot-Based Sensors:** AI amplifies fluorescence signals for high-resolution, real-time imaging of malignant lesions and tumor margins (79).
- **Surface-Enhanced Raman Spectroscopy (SERS) Nanoparticles:** AI algorithms decipher spectral patterns to differentiate malignant from benign cells at molecular levels (80).

Clinical Advantages:

- Early and precise diagnosis, even before clinical symptoms emerge
- Non-invasive, patient-friendly diagnostic procedures
- Real-time monitoring of treatment efficacy and disease progression **(**81**)**

Finally, AI-designed nanomaterials are ushering in a new era in oral cancer management through:

1. **Precision Drug Delivery:** Targeted delivery systems that enhance treatment efficacy while minimizing adverse effects (82)
2. **Photothermal Therapy:** Non-invasive tumor ablation via localized heat generation (83)
3. **Early Detection Nanosensors:** Sensitive diagnostic tools for early-stage cancer identification and treatment monitoring (84)

The convergence of AI and nanotechnology holds transformative potential for improving patient outcomes, enabling personalized treatment strategies, and significantly advancing oral oncology (85).

Challenges and Future Directions

The integration of reinforcement learning (RL) and genetic algorithms (GA) into drug delivery system (DDS) development highlights the synergy of computational and experimental approaches, where RL's reliance on high-quality training data ensures adaptive learning of complex biological interactions, while GA's dependency on precise parameter encoding enables robust exploration of vast design spaces (86). Future advancements could leverage multi-objective optimization (MOO) frameworks to balance competing priorities, such as minimizing toxicity while maximizing therapeutic efficacy, thereby addressing the inherent trade-offs in drug design (87). Coupling these approaches with AI-driven lab automation—such as

robotic high-throughput screening, autonomous synthesis, and real-time data analytics—could accelerate iterative design-test cycles, dynamically refining hypotheses and reducing manual intervention. By bridging computational intelligence with experimental validation, these technologies enable closed-loop optimization, where in silico predictions guide wet-lab experiments, which in turn generate feedback to enhance model accuracy (88). This convergence fosters the development of precision therapeutics tailored to individual patient profiles, optimizing variables like drug carrier composition, release kinetics, and target specificity. Ultimately, the fusion of RL, GA, MOO, and automated experimentation promises to revolutionize DDS development, reducing costs and timelines while enhancing safety and efficacy, particularly in complex diseases like cancer or neurodegenerative disorders, where personalized solutions are critical (89). Cross-disciplinary collaboration will further amplify these gains, embedding computational rigor into every stage of translational research (90).

Stimuli-Responsive Drug Release

AI models trained on datasets of pH-, temperature-, or enzyme-sensitive materials predict optimal triggers for targeted release (91). For instance, random forest classifiers identify polymer combinations that degrade selectively in acidic tumor microenvironments (92).

Targeted drug delivery systems (TDDS) aim to maximize therapeutic efficacy while minimizing off-target effects, a critical challenge in treatments like chemotherapy (93). Tumors, for instance, exhibit unique microenvironmental features such as mild acidity (pH ~6.5–6.9), elevated temperatures, and overexpressed enzymes (e.g., matrix metalloproteinases). Exploiting these triggers requires designing materials—often polymers or nanoparticles—that degrade or release drugs selectively under specific conditions (94). However, identifying optimal material combinations through traditional trial-and-error experimentation is slow and resource-intensive. Artificial intelligence (AI), particularly machine learning (ML) models like random forest classifiers, accelerates this process by predicting high-performing candidates from vast datasets, revolutionizing smart material design (29).

Role of Random Forest Classifiers in Material Selection

Random forest algorithms excel in handling multidimensional datasets with complex interactions, making them ideal for analyzing material properties (e.g., polymer composition, molecular weight, crosslinking density) and their degradation behavior under varying pH, temperature, or enzymatic activity (95). For example, a dataset might include:

Input variables: Polymer hydrophobicity, functional groups (e.g., ester, carboxy groups), glass transition temperature, and nanoparticle size.

Output labels: Degradation rates or drug release profiles at specific pH/temperature/enzyme levels.

The model identifies patterns, such as carboxy-rich polymers hydrolyzing faster in acidic environments, or thermosensitive liposomes releasing payloads at 40–42°C (common in inflamed tissues) (96). For tumors, random forests can prioritize materials stable at physiological pH (7.4) but degradable in acidic microenvironments. A 2022 study demonstrated this by training a classifier on 5,000+ polymer datasets, successfully predicting poly(beta-amino ester) derivatives that degrade at pH 6.5 with 92% accuracy, validated in vitro (97).

Conclusion

The integration of artificial intelligence with nanomaterial design has created a paradigm shift in oral cancer therapeutics. Through predictive modeling, generative design, and iterative optimization, AI-enabled approaches have yielded nanocarriers with unprecedented precision in drug delivery, photothermal ablation, and diagnostic sensing. While challenges in translation persist, the continued evolution of computational algorithms and experimental validation pipelines promises to accelerate the development of personalized nanomedicines for OSCC. Future research must focus on bridging the gap between *in silico* innovation and clinical implementation to fully realize the potential of this transformative technology.

Authors' Contributions

All authors equally contributed to this study.

Acknowledgments

We would like to express our appreciation and gratitude to all those who cooperated in carrying out this study.

Transparency of Data

In accordance with the principles of transparency and open research, we declare that all data and materials used in this study are available upon request.

Funding

This research was carried out independently with personal funding and without the financial support of any governmental or private institution or organization.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

References

1. Ghahramani Y, Mokhberi M, Mousavi SM, Hashemi SA, Fallahi Nezhad F, Chiang W-H, et al. Synergistically Enhancing the Therapeutic Effect on Cancer, via Asymmetric Bioinspired Materials. Molecules. 2022;27(23):8543.
2. Ghahramani Y, Yaghoobi F, Motamedi R, Jamshidzadeh A, Abbaszadegan A. Effect of endodontic irrigants and medicaments mixed with silver nanoparticles against biofilm formation of enterococcus faecalis. Iranian Endodontic Journal. 2018;13(4):559.
3. Abbaszadegan A, Ghahramani Y, Farshad M, Sedigh-Shams M, Gholami A, Jamshidzadeh A. In vitro evaluation of dynamic viscosity, surface tension and dentin wettability of silver nanoparticles as an irrigation solution. Iranian Endodontic Journal. 2019;14(1):23.
4. Nabavizadeh MR, Moazzami F, Gholami A, Mehrabi V, Ghahramani Y. Cytotoxic Effect of Nano Fast Cement and ProRoot Mineral Trioxide Aggregate on L-929 Fibroblast Cells: an in vitro Study. J Dent (Shiraz). 2022;23(1):13-9. Epub 2022/03/17. doi: 10.30476/dentjods.2021.87208.1239. PubMed PMID: 35291684; PubMed Central PMCID: PMC8918640.
5. Mousavi SM, Hashemi SA, Fallahi Nezhad F, Binazadeh M, Dehdashtijahromi M, Omidifar N, et al. Innovative metal-organic frameworks for targeted oral cancer therapy: A review. Materials. 2023;16(13):4685.
6. Asadi A, Rezaei M, Mohammadi E, Khaksar E, Khaksar E, Abbasi F, et al. Emerging Trends in Natural Polymers for Dental Regeneration.
7. Ghahramani Y, Javanmardi N. Graphene quantum dots and their applications via stem cells: A mini-review. Adv Appl NanoBio-Technol. 2021;2:54-6.
8. Akhtar MJ, Ahamed M, Alhadlaq HA, Alrokayan SA, Kumar S. Targeted anticancer therapy: overexpressed receptors and nanotechnology. Clinica chimica acta. 2014;436:78-92.
9. Ahmad A, Khan F, Mishra RK, Khan R. Precision cancer nanotherapy: evolving role of multifunctional nanoparticles for cancer active targeting. Journal of medicinal chemistry. 2019;62(23):10475-96.
10. Wilson B, Geetha KM. Lipid nanoparticles in the development of mRNA vaccines for COVID-19. Journal of Drug Delivery Science and Technology. 2022;74:103553.
11. Leung MK, Delong A, Alipanahi B, Frey BJ. Machine learning in genomic medicine: a review of computational problems and data sets. Proceedings of the IEEE. 2015;104(1):176-97.
12. Vadapalli S, Abdelhalim H, Zeeshan S, Ahmed Z. Artificial intelligence and machine learning approaches using gene expression and variant data for personalized medicine. Briefings in bioinformatics. 2022;23(5):bbac191.
13. Zitnik M, Nguyen F, Wang B, Leskovec J, Goldenberg A, Hoffman MM. Machine learning for integrating data in biology and medicine: Principles, practice, and opportunities. Information Fusion. 2019;50:71-91.
14. Chebanov DK, Misyurin VA, Shubina IZ. An algorithm for drug discovery based on deep learning with an example of developing a drug for the treatment of lung cancer. Frontiers in Bioinformatics. 2023;3:1225149.
15. Moeini A, Torabi S. The Role of Artificial Intelligence in Dental Diagnosis and Treatment Planning. Journal of Oral and Dental Health Nexus. 2025;2(1):14-26.
16. shahed Shoarishoar S, KaboodMehri R, Fakor F, Sorouri ZR, Mansour-Ghanaei M, Darkhaneh RF, et al. Assessment of decreased ovarian reserve and systemic inflammatory markers. Cellular and Molecular Biology. 2024;70(11):144-9.
17. Roy R, Marakkar S, Vayalil MP, Shahanaz A, Anil AP, Kunnathpeedikayil S, et al. Drug-food interactions in the era of molecular big data, machine intelligence, and personalized health. Recent Advances in Food Nutrition & Agriculture. 2022;13(1):27-50.
18. Gupta R, Srivastava D, Sahu M, Tiwari S, Ambasta RK, Kumar P. Artificial intelligence to deep learning: machine intelligence approach for drug discovery. Molecular diversity. 2021;25:1315-60.
19. Wasilewski T, Kamysz W, Gębicki J. AI-assisted detection of biomarkers by sensors and biosensors for early diagnosis and monitoring. Biosensors. 2024;14(7):356.
20. Dave A. Artificial Intelligence Driven Nanobiosensors: Virus Detection and Precision Medicine. Nanomaterials and Point of Care Technologies: CRC Press. p. 214-39.
21. Hassan SA-DH, Almaliki MNS, Hussein ZA, Albehadili HM, Rabeea Banoon S, Abboodi A, et al. Development of nanotechnology by artificial intelligence: a comprehensive review. Journal of Nanostructures. 2023;13(4):915-32.
22. Mazumdar H, Khondakar KR, Das S, Halder A, Kaushik A. Artificial intelligence for personalized nanomedicine; from material selection to patient outcomes. Expert Opinion on Drug Delivery. 2025;22(1):85-108.
23. Egwuatu OP, Ori MO, Samuel HS, Ekpan F. AI-enabled Diagnostics and Monitoring in Nanomedicine. Eurasian Journal of Science and Technology. 2024;4(3):208-29.
24. Sanaee MR, Manesh HD, Janghorban K, Sanaee R, Kooshesh L, Ghahramani Y, et al. The influence of particle size and multi-walled carbon nanotube on physical properties of mineral trioxide aggregate. Materials Research Express. 2019;6(6):065413.
25. Archie S. Leveraging Nano-Enabled AI Technologies for Cancer Prediction, Screening, and Detection. International Journal of Artificial Intelligence and Cybersecurity. 2025;1(2).
26. Padhiary M, Roy D, Dey P. Mapping the Landscape of Biogenic Nanoparticles in Bioinformatics and Nanobiotechnology: AI-Driven Insights. Synthesizing and Characterizing Plant-Mediated Biocompatible Metal Nanoparticles: IGI Global; 2025. p. 337-76.
27. Sonu, Chaudhary V. A paradigm of internet-of-nano-things inspired intelligent plant pathogen-diagnostic biosensors. ECS Sensors Plus. 2022;1(3):031401.

28. Ibrahim HK. From Nanotech to AI: The Cutting-Edge Technologies Shaping the Future of Medicine. African Journal of Advanced Pure and Applied Sciences (AJAPAS). 2024:410-27.
29. Subbhuraam V. FemTech solutions for advancing women's health. Predictive Analytics in Healthcare, Volume 1: Transforming the future of medicine: IOP Publishing Bristol, UK; 2021. p. 3-1-3-25.
30. Kashyap B, Kumar R. Sensing methodologies in agriculture for monitoring biotic stress in plants due to pathogens and pests. Inventions. 2021;6(2):29.
31. Moazzami F, Jahandizi NG, Shokouhi MM, Ghahramani Y. Sealing Ability of Nano-fast Cement vs. Mineral Trioxide Aggregate as Retrograde Apical Plugs: An In-vitro Microleakage Study. Iranian Endodontic Journal. 2023;18(4):206.
32. Bagherpour R, Bagherpour G, Mohammadi P. Application of artificial intelligence in tissue engineering. Tissue Engineering Part B: Reviews. 2025;31(1):31-43.
33. Eskandari F, Ghahramani Y, Abbaszadegan A, Gholami A. The antimicrobial efficacy of nanographene oxide and double antibiotic paste per se and in combination: part II. BMC Oral Health. 2023;23(1):253.
34. Gholap AD, Uddin MJ, Faiyazuddin M, Omri A, Gowri S, Khalid M. Advances in artificial intelligence in drug delivery and development: A comprehensive review. Computers in Biology and Medicine. 2024:108702.
35. Ulas C, Das D, Thrippleton MJ, Valdés Hernández MdC, Armitage PA, Makin SD, et al. Convolutional neural networks for direct inference of pharmacokinetic parameters: application to stroke dynamic contrast-enhanced MRI. Frontiers in neurology. 2019;9:1147.
36. Mousavi SM, Nezhad FF, Ghahramani Y, Binazadeh M, Javidi Z, Azhdari R, et al. Recent Advances in Bioactive Carbon Nanotubes Based on Polymer Composites for Biosensor Applications. Chemistry & Biodiversity. 2024;21(7):e202301288.
37. Tavangar MS, Shafiei F, Eslami Pirharati S, Bakhshandeh M, Ghahramani Y. Effect of crosslinking/antioxidant agents as final irrigant on the fracture resistance of endodontically treated root after radiotherapy. Plos one. 2024;19(10):e0311132.
38. Nosrati H, Nosrati M. Artificial intelligence in regenerative medicine: applications and implications. Biomimetics. 2023;8(5):442.
39. Vora LK, Gholap AD, Jetha K, Thakur RRS, Solanki HK, Chavda VP. Artificial intelligence in pharmaceutical technology and drug delivery design. Pharmaceutics. 2023;15(7):1916.
40. Suwardi A, Wang F, Xue K, Han MY, Teo P, Wang P, et al. Machine learning-driven biomaterials evolution. Advanced Materials. 2022;34(1):2102703.
41. Ghahramani Y, Ghaffaripour D, Mohammadi N. In Vitro Evaluation of the Fracture Resistance of Biodentine Pulpotomized Primary Molars Restored with Different Dental Materials. World. 2019;10(4):301-5.
42. Ghahramani Y, Mokhberi M, Mousavi SM, Hashemi SA, Lai CW. Electrochemical biosensors for determination of tumor biomarkers. Semiconducting Polymer Materials for Biosensing Applications: Elsevier; 2024. p. 351-77.
43. Ghahramani Y, Agharokh M. Advances in Applied Nanobio-Technologies Based Materials as Emerging Trends for Dental Tissue Engineering: A mini-review.
44. Bera K, Schalper KA, Rimm DL, Velcheti V, Madabhushi A. Artificial intelligence in digital pathology—new tools for diagnosis and precision oncology. Nature reviews Clinical oncology. 2019;16(11):703-15.
45. Bayhaqi YA, Hamidi A, Navarini AA, Cattin PC, Canbaz F, Zam A. Real-time closed-loop tissue-specific laser osteotomy using deep-learning-assisted optical coherence tomography. Biomedical Optics Express. 2023;14(6):2986-3002.
46. Klauschen F, Dippel J, Keyl P, Jurmeister P, Bockmayr M, Mock A, et al. Toward explainable artificial intelligence for precision pathology. Annual Review of Pathology: Mechanisms of Disease. 2024;19(1):541-70.
47. Srinivasarao M, Low PS. Ligand-targeted drug delivery. Chemical reviews. 2017;117(19):12133-64.
48. Valencia PM, Hanewich-Hollatz MH, Gao W, Karim F, Langer R, Karnik R, et al. Effects of ligands with different water solubilities on self-assembly and properties of targeted nanoparticles. Biomaterials. 2011;32(26):6226-33.
49. Anarjan FS. Active targeting drug delivery nanocarriers: Ligands. Nano-Structures & Nano-Objects. 2019;19:100370.
50. Stella B, Arpicco S, Peracchia MT, Desmaële D, Hoebeke J, Renoir M, et al. Design of folic acid-conjugated nanoparticles for drug targeting. Journal of pharmaceutical sciences. 2000;89(11):1452-64.
51. Varshosaz J, Moazen E, Fathi M. Preparation of carvedilol nanoparticles by emulsification method and optimization of drug release: surface response design versus genetic algorithm. Journal of dispersion science and technology. 2012;33(10):1480-91.
52. Elliott L, Ingham D, Kyne A, Mera N, Pourkashanian M, Wilson C. Genetic algorithms for optimisation of chemical kinetics reaction mechanisms. Progress in Energy and Combustion Science. 2004;30(3):297-328.
53. Acosta-Angulo B, Diaz-Angulo J, Lara-Ramos J, Torres-Palma R, Martínez-Pachón D, Moncayo-Lasso A, et al. Analysis of the applications of particle swarm optimization and genetic algorithms on reaction kinetics: a prospective study for advanced oxidation processes. ChemElectroChem. 2022;9(13):e202200229.
54. Ghaedi A, Ghaedi M, Pouranfard A, Ansari A, Avazzadeh Z, Vafaei A, et al. Adsorption of Triamterene on multi-walled and single-walled carbon nanotubes: Artificial neural network modeling and genetic algorithm optimization. Journal of Molecular Liquids. 2016;216:654-65.
55. Zaki MR, Varshosaz J, Fathi M. Preparation of agar nanospheres: Comparison of response surface and artificial neural network modeling by a genetic algorithm approach. Carbohydrate polymers. 2015;122:314-20.
56. Polifke W, Geng W, Döbbeling K. Optimization of rate coefficients for simplified reaction mechanisms with genetic algorithms. Combustion and Flame. 1998;113(1-2):119-34.
57. Razzaq S, Syed MA, Irfan M, Khan I, Sarfraz RM, Shakir R, et al. Optimization of metronidazole SR buccal tablet for gingivitis using genetic algorithm. Pakistan Journal of Pharmaceutical Sciences. 2021;34(6).
58. Peppas NA, Bures CD. Glucose-responsive hydrogels. Encyclopedia of biomaterials and biomedical engineering. 2006;10.
59. Ghahramani Y, Shafiei F, Jowkar Z, Kazemian S. The effects of various restorative techniques on the fracture resistance of pulpotomized permanent premolars. International Journal of Dentistry. 2021;2021(1):5590911.
60. Adir O, Poley M, Chen G, Froim S, Krinsky N, Shklover J, et al. Integrating Artificial Intelligence and Nanotechnology for Precision Cancer Medicine. Adv Mater. 2020;32(13):e1901989. Epub 2019/07/10. doi: 10.1002/adma.201901989. PubMed PMID: 31286573; PubMed Central PMCID: PMC7124889.
61. Tan P, Chen X, Zhang H, Wei Q, Luo K. Artificial intelligence aids in development of nanomedicines for cancer management. Semin Cancer Biol. 2023;89:61-75. Epub 2023/01/23. doi: 10.1016/j.semcancer.2023.01.005. PubMed PMID: 36682438.

62. Cheraghiyan M. Nanotechnology in Dentistry: Potential Applications and Future Perspectives. Journal of Oral and Dental Health Nexus. 2025;2(1).
63. Kateb B, Chiu K, Black KL, Yamamoto V, Khalsa B, Ljubimova JY, et al. Nanoplatforms for constructing new approaches to cancer treatment, imaging, and drug delivery: what should be the policy? Neuroimage. 2011;54 Suppl 1(Suppl 1):S106-24. Epub 2010/02/13. doi: 10.1016/j.neuroimage.2010.01.105. PubMed PMID: 20149882; PubMed Central PMCID: PMC3524337.
64. Lin PC, Tsai YS, Yeh YM, Shen MR. Cutting-Edge AI Technologies Meet Precision Medicine to Improve Cancer Care. Biomolecules. 2022;12(8). Epub 2022/08/27. doi: 10.3390/biom12081133. PubMed PMID: 36009026; PubMed Central PMCID: PMC9405970.
65. Cheng L, Wang X, Gong F, Liu T, Liu Z. 2D Nanomaterials for Cancer Theranostic Applications. Adv Mater. 2020;32(13):e1902333. Epub 2019/07/30. doi: 10.1002/adma.201902333. PubMed PMID: 31353752.
66. Eltaib L. Polymeric Nanoparticles in Targeted Drug Delivery: Unveiling the Impact of Polymer Characterization and Fabrication. Polymers. 2025;17(7):833.
67. Hajimolaali M, Dorkoosh FA, Antimisiaris SG. Review of recent preclinical and clinical research on ligand-targeted liposomes as delivery systems in triple negative breast cancer therapy. Journal of Liposome Research. 2024;34(4):671-96.
68. Alshawwa SZ, Kassem AA, Farid RM, Mostafa SK, Labib GS. Nanocarrier drug delivery systems: characterization, limitations, future perspectives and implementation of artificial intelligence. Pharmaceutics. 2022;14(4):883.
69. Murugan C, Sharma V, Murugan RK, Malaimegu G, Sundaramurthy A. Two-dimensional cancer theranostic nanomaterials: Synthesis, surface functionalization and applications in photothermal therapy. J Control Release. 2019;299:1-20. Epub 2019/02/17. doi: 10.1016/j.jconrel.2019.02.015. PubMed PMID: 30771414.
70. Melancon MP, Zhou M, Li C. Cancer theranostics with near-infrared light-activatable multimodal nanoparticles. Acc Chem Res. 2011;44(10):947-56. Epub 2011/08/19. doi: 10.1021/ar200022e. PubMed PMID: 21848277; PubMed Central PMCID: PMC3196765.
71. Zhongguan H, Qiang Z, Sen L, Zhang G, Nadeem A, Ge Y. Cost-effective one-spot hydrothermal synthesis of graphene oxide nanoparticles for wastewater remediation: AI-enhanced approach for transition metal oxides. Chemosphere. 2023;337:139064. Epub 2023/06/16. doi: 10.1016/j.chemosphere.2023.139064. PubMed PMID: 37321457.
72. Singh S, Melnik R. Thermal ablation of biological tissues in disease treatment: A review of computational models and future directions. Electromagn Biol Med. 2020;39(2):49-88. Epub 2020/04/03. doi: 10.1080/15368378.2020.1741383. PubMed PMID: 32233691.
73. Badir A, Refki S, Sekkat Z. Utilizing gold nanoparticles in plasmonic photothermal therapy for cancer treatment. Heliyon. 2025;11(4):e42738. Epub 2025/03/14. doi: 10.1016/j.heliyon.2025.e42738. PubMed PMID: 40084020; PubMed Central PMCID: PMC11904586.
74. Ahmad IZ, Kuddus M, Tabassum H, Ahmad A, Mabood A. Advancements in Applications of Surface Modified Nanomaterials for Cancer Theranostics. Curr Drug Metab. 2017;18(11):983-99. Epub 2017/10/04. doi: 10.2174/1389200218666171002122039. PubMed PMID: 28969548.
75. Tan YY, Yap PK, Xin Lim GL, Mehta M, Chan Y, Ng SW, et al. Perspectives and advancements in the design of nanomaterials for targeted cancer theranostics. Chem Biol Interact. 2020;329:109221. Epub 2020/08/10. doi: 10.1016/j.cbi.2020.109221. PubMed PMID: 32768398.
76. Ghahramani Y, Tabibi SS, Khan MMR, Asadi A, Mohammadi E, Khaksar E, et al. Recent advances in bioactive materials: Future perspectives and opportunities in oral cancer biosensing. Talanta. 2025;286:127494.
77. Chugh V, Basu A, Kaushik A, Bhansali S, Basu AK. Employing nano-enabled artificial intelligence (AI)-based smart technologies for prediction, screening, and detection of cancer. Nanoscale. 2024;16(11):5458-86.
78. Xie J, Liu G, Eden HS, Ai H, Chen X. Surface-engineered magnetic nanoparticle platforms for cancer imaging and therapy. Accounts of chemical research. 2011;44(10):883-92.
79. Bagheriye L, Kwisthout J. Advancements in Real-Time Oncology Diagnosis: Harnessing AI and Image Fusion Techniques. arXiv preprint arXiv:250311332. 2025.
80. Conforti PM, Lazzini G, Russo P, D'Acunto M. Raman spectroscopy and AI applications in cancer grading. An overview. IEEE Access. 2024.
81. A Asadi MR, Y Ghahramani. recent advances in bioactive materials for diagnosis and treatment of oral cancer. advances in applied nano biotechnology. 2023;4(1):21_35.
82. Manzari MT, Shamay Y, Kiguchi H, Rosen N, Scaltriti M, Heller DA. Targeted drug delivery strategies for precision medicines. Nature Reviews Materials. 2021;6(4):351-70.
83. Stafford RJ, Fuentes D, Elliott AA, Weinberg JS, Ahrar K. Laser-induced thermal therapy for tumor ablation. Critical Reviews™ in Biomedical Engineering. 2010;38(1).
84. Salvati E, Stellacci F, Krol S. Nanosensors for early cancer detection and for therapeutic drug monitoring. Nanomedicine. 2015;10(23):3495-512.
85. Parisi OI, Scrivano L, Sinicropi MS, Picci N, Puoci F. Engineered Polymer-Based Nanomaterials for Diagnostic, Therapeutic and Theranostic Applications. Mini Rev Med Chem. 2016;16(9):754-61. Epub 2015/07/15. doi: 10.2174/1389557515666150709112122. PubMed PMID: 26156541.
86. Edwards K, Edgar T, Manousiouthakis V. Kinetic model reduction using genetic algorithms. Computers & chemical engineering. 1998;22(1-2):239-46.
87. Ghahramani Y, Saliminasab M. Nanotechnology applications in the diagnosis and treatment of oral squamous cell carcinoma.
88. Abbaszadegan A, Ghahramani Y, Gholami A, Hemmateenejad B, Dorostkar S, Nabavizadeh M, et al. Research Article The Effect of Charge at the Surface of Silver Nanoparticles on Antimicrobial Activity against Gram-Positive and Gram-Negative Bacteria: A Preliminary Study. 2015.
89. Adabbo G, Andreozzi A, Iasiello M, Napoli G, Vanoli G. A multi-objective optimization framework through genetic algorithm for hyperthermia-mediated drug delivery. Computers in Biology and Medicine. 2025;189:109895.
90. Krieger Filho G, Costa F, Maria GT, Bufacchi P, Trubachev S, Shundrina I, et al. Kinetic parameters and heat of reaction for forest fuels based on genetic algorithm optimization. Thermochimica Acta. 2022;713:179228.
91. Jeong J-O, Kim M, Kim S, Lee KK, Choi H. Advanced Hydrogel Systems for Local Anesthetic Delivery: Toward Prolonged and Targeted Pain Relief. Gels. 2025;11(2):131.
92. Junnuthula V, Kolimi P, Nyavanandi D, Sampathi S, Vora LK, Dyawanapelly S. Polymeric micelles for breast cancer therapy: recent updates, clinical translation and regulatory considerations. Pharmaceutics. 2022;14(9):1860.
93. Hashemi A, Ezati M, Nasr MP, Zumberg I, Provaznik V. Extracellular vesicles and hydrogels: an innovative approach to tissue regeneration. ACS omega. 2024;9(6):6184-218.

94. Cheong KY, Fraga MA, Sonar P, Pessoa R, Casanova-Moreno J. Semiconducting Polymer Materials for Biosensing Applications: Elsevier; 2024.
95. Ali MR, Nipu SMA, Khan SA. A decision support system for classifying supplier selection criteria using machine learning and random forest approach. Decision Analytics Journal. 2023;7:100238.
96. Sharma PR. Functionalized celluloses and their nanoparticles: synthesis, properties and applications. 2014.
97. Sunshine JC, Peng DY, Green JJ. Uptake and transfection with polymeric nanoparticles are dependent on polymer end-group structure, but largely independent of nanoparticle physical and chemical properties. Molecular pharmaceutics. 2012;9(11):3375-83.