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A Review Article: Comparative Analysis of Gold and Graphene-Based Nanomaterials for NIR-Mediated Photothermal Therapy in Oral Cancer: Properties, Mechanisms, and Clinical Potential

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Abstract

This comprehensive review evaluates gold nanoparticles (AuNPs) and graphene oxide (GO) as near-infrared (NIR)-responsive photothermal agents for oral cancer therapy. We highlight advancements up to 2025 and analyze their optical properties, heat conversion mechanisms, biocompatibility, and clinical readiness. AuNPs exhibit superior photothermal efficiency via localized surface plasmon resonance (LSPR), with gold nanorods enabling tunable NIR absorption through aspect ratio control. Recent clinical trials, such as PEG-coated silica-gold nanoshells (AuroLase therapy), underscore AuNPs' translational progress. Conversely, GO offers unparalleled versatility, combining high thermal conductivity, surface functionalization potential, and multimodal capabilities. Studies on folic acid-chitosan-GO nanocomposites demonstrate tumor-specific ablation and recurrence prevention in vivo. Key challenges include optimizing NIR-II (1000–1500 nm) penetration for deeper tumors and addressing long-term biocompatibility concerns. Recent advances, such as FDA-approved biomimetic modifications and NIR-II-responsive polymer conjugates, highlight pathways to clinical translation. We emphasize the need for standardized protocols, targeted delivery strategies, and rigorous safety assessments. Integrating recent studies—including works on hyperthermia-immunotherapy synergy, multifunctional nanomedicines, and light-responsive therapies—this review critically synthesizes AuNPs' and GO's complementary strengths. While AuNPs lead in clinical trials, GO's multifunctionality positions it as a promising platform for combinatorial therapies. The analysis concludes that both nanomaterials hold transformative potential for oral cancer treatment, particularly for patients with recurrent or advanced disease.

Keywords—Nanomedicine, Hyperthermia, Squamous Cell Carcinoma, Biocompatibility, LSPR (Localized Surface Plasmon Resonance).

I. Introduction

Oral cancer represents one of the most prevalent malignant neoplasms in the head and neck region globally. The term predominantly refers to oral mucosal squamous cell carcinoma (SCC), which accounts for approximately 90% of all oral cavity malignancies. High morbidity and mortality rates characterize oral squamous cell carcinoma (OSCC). OSCC can affect the mucosal membrane of any anatomical site within the oral cavity [1]. OSCC affects the mucosal membrane of any anatomical site of the oral cavity [2].

The primary goals of oral cancer treatment include eliminating the primary tumor, preserving or restoring anatomical function, and preventing the recurrence of secondary tumors. Despite two decades of advances in cancer therapeutics, the multifactorial nature of cancer continues to limit treatment efficacy. Current management of intermediate and advanced OSCC typically involves a multidisciplinary approach combining the three primary modalities: chemotherapy, radiation therapy, and surgery, either individually or in combination. Treating the primary tumor, maintaining or restoring anatomy and function, and preventing the recurrence or formation of a second primary tumor are the ultimate goals of oral cancer treatment [3]. Multifactorial risk factors make cancer less curable with current treatments, even after two decades of advancements in cancer therapy [4]. Treatment for medium and advanced oral squamous cell carcinoma (OSCC) now mainly consists of a multidisciplinary therapy plan that includes the three primary treatment modalities of chemotherapy, radiation therapy, and surgery, either separately or in combination. However, most of these approaches result in minimal efficacy, particularly when the disease is advanced or has unpleasant effects in patients of varied severity [5]. Consequently, one of the most challenging issues facing modern medicine is the cure of cancer, and scientists are always looking for noninvasive anticancer methods and therapeutic alternatives to improve the quality of life for patients with advanced OSCC [6].

Lasers have emerged as promising tools in tumor therapy due to their unique properties of collimation and coherence, enabling high-intensity light delivery in a narrow beam allowing deep penetration of internal tissues with exceptional targeting precision. Many therapeutic applications leverage photothermal effects, which elevate tissue temperature to induce cellular modifications through hyperthermia,

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coagulation, or vaporization processes [7]. Substantial applications make use of photothermal effects, which elevate the temperature and cause cell or tissue modifications via hyperthermia, coagulation, or vaporization processes [7]. Photothermal therapy (PTT) has been identified as one of the most promising noninvasive cancer treatments in recent years for reducing side effects associated with established conventional cancer treatment techniques such as radiotherapy and chemotherapy. As a focused method of cancer hyperthermia treatment, photothermal therapy targets the tumor by applying heat to it. In this process, laser light is used to stimulate an endogenous or exogenous chromophore, which causes thermal energy to be released [8].

PTT utilizes NIR laser-activated nanoparticles that generate heat to destroy tumor cells partly [9]. PTT employs near-infrared (NIR) laser-activated nanoparticles that generate heat to destroy tumor cells selectively. The fundamental principle of applying nanoparticles in PTT is to enhance the photothermal selectivity of light absorption within target tissues. Photons absorbed by photothermal agents create excited states that release energy through vibrational relaxation, increasing the kinetic energy and heat of the surrounding cellular environment. PTT can be applied passively or specifically to minimize damage to healthy tissues [9]. To reduce the damage to healthy tissues, PTT is a minimally intrusive technique that can be applied passively or specifically.

A significant limitation of conventional PTT is its lack of selectivity, as both healthy and cancerous cells in the laser's path are destroyed. Effective tumor ablation typically requires high laser power outputs ranging from tens to hundreds of watts. The administered NIR radiation must achieve high photothermal conversion efficiency to induce hyperthermia (temperature >42°C) in the target area. This presents challenges for treating disseminated disease or tumors located deep within tissues such as the stomach, pancreas, lungs, or colorectal. Therefore, developing photothermal contrast agents that offer both tumor-specific selectivity and high efficiency at lower laser powers is essential. [10]. This procedure is complicated when the disease has spread across the body or when the tumors are deep inside tissues, such as the stomach, pancreas, lungs, or colorectal tissues. Therefore, it is essential to pursue photothermal contrast agents that offer both selectivity by focusing on tumor cells and high efficiency by reducing laser power [11].

Consequently, researchers have employed nanomaterials with great absorption of NIR light to augment the photothermal conversion and combined PTT with a second treatment technique to enhance the therapeutic impact in order to get around these limitations [12, 13]. With an emphasis on cancer treatment and the kind, size, and shape of the various nanomaterials used, reports of these tactics are well-documented [14, 15].

In PTT, the target tumor is typically irradiated with NIR laser either topically or interstitially using an optical fiber. Physical contrast ablation agents, such as nanomaterials with photothermal effects, convert light energy into heat. This approach can generate temperatures sufficient to kill cancer cells while causing minimal damage to normal tissues. This therapeutic window is supported by the fact that malignant cells exhibit lower thermotolerance with their inadequate blood supply than non-cancerous tissues. Photothermal nanomaterials have attracted significant interest due to their non-invasive nature and selective targeting capabilities [16]. Successful clinical implementation of this method requires a clear comprehension and evaluation of the changes that occur to the tumor area after the therapy.

The use of nanomaterials for novel cancer treatments has increased dramatically in recent years, due to their distinctive compositions and characteristics. Several nanomaterials, such as graphene-based nanomaterials (GBNMs) [17] and noble and transition metal nanoparticles [18], show exceptional NIR-absorbing properties from the first NIR window (750–1000 nm) or the second NIR window (1000–1500 nm), where light exhibits its maximum depth of penetration into biological tissues [19]. By using nanostructures like gold nanorods and graphene oxide sheets, which use their outstanding optical absorption of NIR light, researchers could target the impact on the tumor cells and improve photothermal therapy. On the other hand, photothermal therapy has become much more effective, and new applications for nanomaterials in targeted cancer therapy are starting to emerge. This review aims to comparatively evaluate the photothermal efficacy, biocompatibility, and clinical potential of AuNPs and GO in oral cancer therapy, focusing on their structural, optical, and functional properties.

II. CRITERIA OF NANOMATERIALS FOR PTT

Strong NIR absorption, localization at the tumor site, and compatibility with biological substances are among the requirements that nanoparticles must fulfill to ensure maximum effectiveness. Also, high PTT efficiency, high absorption cross-section in the near-infrared spectrum, and high photothermal conversion efficiency are necessary for efficient photothermal agents [20]. The capacity of nanoparticle-mediated PTT to control heat production under laser illumination by adjusting the concentration, size, shape, and dispersion of nanoparticles inside the tumor is essential to its efficacy. An accurate assessment of photothermal agents' thermal and optical properties is essential for optimizing treatment parameters and predicting therapeutic outcomes. A practical approach to achieve this assessment is through numerical simulations and modeling with tools like the finite element method (FEM), finite-difference time-domain (FTDT) [21], and discrete dipole approximation (DDA). These computational methods offered a worthy understanding of the thermal and optical properties of photothermal agents under different conditions, including modeling heat generation and dissipation processes and the electromagnetic radiation mechanism of nanomaterials, which comprises plasmonic localized heating of metals, nonradiative and radiative relaxation of semiconducting materials, or thermal vibrations of molecules [22]. Photothermal conversion efficiency is a standard metric of nanoparticle performance, which measures how capably the nanoparticle converts incident power into heat that causes cell death [23].

Various nanomaterials, including noble metals, carbon-based nanomaterials, quantum dots [24], metal-oxide nanomaterials, and organic polymers [25], were reconnoitered for use in photothermal cancer therapy. Among these, carbon-based nanostructures (e.g., carbon nanotubes [CNTs], graphene oxide, carbon dots [26], carbon nanohorns, and fullerenes and various morphologies of gold-based

nanoparticles (including gold nanospheres, nanoshells, nanorods, and nanomatryoshkas have been the most extensively researched [27].

III. GOLD-BASED NANOSTRUCTURES

Over the past several decades, there has been a rise in interest in using plasmonic gold nanostructures for PTT in the treatment of cancer [28]. Boyer et al. initially described using plasmonic imaging for heating and detection in the early 2000s. The next year, two groups used gold nanoparticles (GNPs) injected into tumor cells to produce hyperthermia in order to study plasmonic PTT. GNPs are the most widely employed noble-metal-based nanostructures in photothermal cancer therapy because they are simple to synthesize and functionalize with targeted agents such as aptamers [29] and peptides [30].

3.1. Optical properties

GNPs' high plasmonic resonance effects give them optical characteristics that make photothermal conversion more effective. GNPs can absorb light at particular wavelengths, leading to photothermal as well as photoacoustic characteristics that could be valuable for hyperthermic cancer therapy and medical imaging applications. This phenomenon is identified as localized surface plasmon resonance (LSPR), which is formed as a result of the collective oscillation of the metal's conduction electrons in response to the incident electromagnetic field, making them potentially beneficial for hyperthermic cancer therapy and medical imaging applications [31]. Here, LSPR increases the electromagnetic field intensity near the GNP surface by several orders of magnitude, with hot spots -areas with the most significant local curvature- showing the most excellent amplification [28].

The LSPR response in the NIR region is altered when the aspect ratio of GNPs is increased from spherical to rod-like. Because they enhance the NIR light's penetration depth, gold nanorods (GNRs), one of the many varieties of gold-based nanostructures, have an immense longitudinal plasmon resonance peak in the NIR region, which renders them ideal for in vivo imaging and therapy [32]. When the incident polarization is parallel to the long axis of GNRs, they reveal significant optical absorption in the NIR region with higher absorption efficiency, leading to longitudinal plasmons in the NIR area [33]. On the other hand, the transverse plasmon peak showed a lower absorption peak in the visible range and was associated with the excitation of the transverse axis of the GNRs [32]. The absorption and scattering characteristics of GNSs, another kind of gold-based nanostructure, can be modified by modulating the ratio of the core radius, which is made up of a dielectric substance, to the shell thickness, which is made up of a thin layer of gold. Because of their powerful absorption of NIR light, GNSs are very appealing for in vivo imaging and therapy. Their plasmon resonance peak may be adjusted by varying the gold shell's thickness and the silica core's size [34]. Low and high absorption peaks separate as a result of the hybridization of dipolar plasmons in core-shell nanostructures, which causes the GNS optical response. Absorption and scattering are competing processes, and the scattering contribution rises as the nanoshell's volume ratio does [35]. Gold nanocages (GNCs) comprise a hollow gold shell with a porous wall, allowing straightforward functionalization with targeting agents. The plasmon resonance peak of GNCs can be tuned to the NIR range, similar to GNRs and GNSs, which makes them highly attractive for in vivo imaging and therapy [36].

3.2. Biocompatibility

Gold-based nanostructures are attractive candidates for photothermal cancer treatments due to their excellent qualities. GNPs are suitable for medical applications due to their homogeneous manufacturing, low cytotoxicity, photostability, biocompatibility, and surface functionalization. However, there are still several issues that need to be resolved. For example, there are worries about the shape distortion of gold nanorods at high pulse intensities [37] and the possible cytotoxicological consequences of using cetrimonium bromide (CTAB) for the chemical functionalization of GNPs in vitro [38]. Gold-based nanostructures are promising for multiple biological applications, including imaging and therapy, due to their excellent photothermal conversion, tunable plasmonic properties, and ability to absorb light in the near-infrared spectrum. Accordingly, gold nanoparticles have been broadly researched as photothermal agents and have revealed low toxicity and high biocompatibility. [37, 38]

3.3. GNPs for photothermal cancer therapy

The application of gold-based nanostructures in PTT has been thoroughly investigated and shown to be very successful both in vitro and in vivo. When exposed to NIR light, GNPs functionalized with anti-HER2 antibodies have been used to specifically target HER2-positive breast cancer cells and cause cell death [39]. Studies conducted in vivo have shown that when exposed to near-infrared light, gold-based nanostructures can specifically target and eliminate tumors. Moreover, GNP-assisted PTT clinical trials in humans are still being conducted. According to recent research, 150 nm silica-GNSs coated with PEG are being used in human clinical trials for AuroLase therapy, which was created by Nanospectra Bioscience Inc. and involves intravenous injection of the silica-GNSs into the circulation [40]. In a clinical study by Kharlamov et al., which assessed the viability and safety of atheroprotective measures, patients were given nano-interventions containing silica-GNP or silica-iron-bearing GNP through stem cells [41]. The outcomes, which showed a low incidence of thrombosis and target lesion revascularization, were similar to those of the control group after stent insertion at 12 months after therapy [41].

IV. GRAPHENE-BASED NANOSTRUCTURES

GBMNs are 2D materials promising in cancer treatment, mainly graphene oxide (GO) and reduced graphene oxide (rGO). Owing to GO and rGO's exceptional physicochemical characteristics, these materials have been used in biosensing and cancer therapy [42]. The implementation of GO and rGO in PTT has been thoroughly studied as they display significant absorbance in the NIR range. These reports focused on their functionalization, their toxicity, and the nature of the treated cancer. [42, 43].

4.1. Structure of graphene-based nanomaterials (GBNMs)

The two primary types of GBNMs under the category of carbon nanomaterials are graphene oxide and reduced graphene oxide [44]. Based on their composition and structural

characteristics, both GBNMs have remarkable qualities and great biocompatibility; they are employed in various biomedical applications [45].

GO and rGO are two-dimensional layers of one atom thick and carbon atoms arranged in a honeycomb lattice (hexagonal) with a network of delocalized electrons. Hummers and Offeman technique [46], which entails oxidizing graphite with a highly acidic solution under cautiously observed reaction conditions, is a popular method for creating graphene oxide. In order to create graphene oxide, the oxidized graphite is then put through a mechanical procedure that permits it to interact with water molecules, which intercalate and split the sheets into arbitrary sizes. As a result, graphene oxide's structure shifts from graphite's original honeycomb lattice to a network of carbon atoms that have undergone sp2 and sp3 hybridization as well as a number of oxygen functional groups, including carboxy, epoxy, and hydroxy groups [47].

To ascertain the structure of GO, several characterization methods are frequently used, including Raman spectroscopy, X-ray photoelectron spectroscopy (XPS), X-ray diffraction (XRD), transmission electron microscopy (TEM), and UV–NIR spectrophotometry.

4.2. Surface properties

Both hydrophilic and hydrophobic areas are present in GO naturally. The hydrophobic section's π–π conjugated arrangement on the surface allows for noncovalent bond reactions between several molecules. [48] Furthermore, GO's hydrophilic groups, like -O-, -COOH, and -OH, give it superior water solubility properties over graphene. By binding to other molecules like proteins, DNA, and RNA, these groups may form the hydrophilic area, enabling additional functionalization [49].

4.3. Biocompatibility

Nanomaterials based on graphene oxide have strong dispersibility in various solvents due to their amphiphilicity, a property of their structure. According to numerous studies, GO's biocompatibility is diminished by its propensity to assemble in high-concentration protein or salt solutions [50]. Surface engineering can be used to increase the biocompatibility of nanomaterials based on graphene oxide. [51] For instance, GO's hemolytic activity can be significantly reduced by altering it with chitosan (CS) [52].

4.4. Graphene oxide and its derivatives

Different oxidants typically oxidize graphite powder in an acidic atmosphere to produce graphene oxide (GO) via mechanical stirring or ultrasonication [53]. There are numerous traditional techniques for creating GO, such as the Marcano method [54], the Hummers method (Hummers Jr. and Offeman 1958), and the Brodie technique (Brodie 1859). Reduced graphene oxide is a derivative of GO that can be created by reducing GO with reducing agents such l-ascorbic acid, hydrazine, and hydrazine hydrate [55].

4.5. Graphene oxide nanocomposites

Multiple components have been added to graphene oxide nanocomposites to functionalize graphene oxide-based nanomaterials. Synthetic polymers as PEG, poly-l-lysine (PLL), poly-vinylalcohol (PVA), and Pluronic F127 (PF127), and natural polymers as CS, sodium alginate (SA), dextran (DEX), and gelatin, are common constituents of functionalized graphene oxide-based nanomaterials [56-61].

In addition, the functionalization of graphene oxide-based nanomaterials can be attained by covalent modification and noncovalent methods [62]. One of the most widely used techniques is covalent modification, which includes acylation, sulfonylation, and amine coupling to carboxylic groups [63]. This process can achieve more stability in the physiological solution, but it may disrupt the original structure of GO that was created by the hybridization of sp2 carbon atoms of the π-network into sp3 configuration. Noncovalent modification can be accomplished by Van der Waals forces, hydrogen bonding, electrostatic interactions, and π–π stacking reactions. Although the π-network and native structure of GO are unaffected by this process, the resulting materials may become more unstable [64].

4.6. Optical properties of GO

Plasmonic 2D nanomaterials possess extraordinary light-matter interactions. Sharp peaks in the density of states at a specific energy, which is close to the conduction and valence band boundaries, are caused by the vertical quantum confinement. High light absorption efficiency resulted from the increased likelihood that the input photon with energy near the bandgap would excite free electron-hole pairs [65]. Additionally, the various electrical architectures of 2D nanomaterials result in various optical characteristics. For instance, the optical conductivity in graphene is independent of all material characteristics [66]. Monolayer graphene has an absorption of πα (about 2.3%), which is entirely dependent on the fine structural constant α and is unrelated to optical wavelength. The excited electron-hole pairs in graphene cause rapid carrier heating when exposed to light, and the hot carriers can stay above the lattice temperature for a few picoseconds. Following this, slower scattering between charge carriers and acoustic phonons allows the heated electrons and the lattice to establish equilibrium. The states close to the edge of the conduction and valence bands were filled due to the creation of hot carrier concentrations that were higher than graphene's intrinsic carrier density under high optical excitation intensity. Saturable light absorption, in which the absorption coefficient of the medium falls with increasing light intensity, happens because two electrons cannot occupy the same state [67].

4.7. GBNMs for photothermal cancer therapy

Nonradiative decay transitions below near-infrared radiation can transform photon energy into heat, which can be utilized to treat tumors. Graphene oxide-based nanomaterials can absorb near-infrared radiation and transform it into thermal energy [68]. The increase in temperature and atomic vibration can impair the noncovalent bond reactions on the surface of nanomaterials based on graphene oxide. Thus, graphene oxide-based nanomaterials can be deployed to rapidly release components from the surface using near-infrared light in addition to being directly utilized in photothermal therapy [69].

Graphene-based materials, with their exceptional physicochemical characteristics, are proficient in detecting and treating cancers. For example, in vitro and in vivo, GO and polyethylene glycol (PEG) demonstrated photothermal treatment efficacy against tumors and malignancies by inducing a heating effect in macrophages [70]. Following

treatment using near-infrared (NIR) light radiation, the polarization condition of the macrophage cell lines was assessed by flow cytometry and mRNA expression analysis. Significant photothermal effect, enhanced biocompatibility, and great thermal stability were all exhibited by GO-PEG. Interestingly, these photothermal structures alleviated the antitumor potentials of macrophages and mitigated the M2 polarization caused by interleukin-4. As a result, human cancer cells were incapable of migrating or invading, which led to appropriate antitumor effects [70]. Furthermore, in vitro, laser irradiation eliminated malignant cells when chitosan-functionalized GO nanoplatforms were coupled with folic acid for photothermal cancer therapy guided by NIR fluorescence and photoacoustic imaging [71]. Additionally, in vivo tests showed that within 20 days of the specific nanosystem being deployed under laser irradiation, the tumors were entirely blocked and could not recur [71]. To date, a number of GO-based systems have been investigated in an effort to produce a strong photothermal impact for cancer treatment [72]. Relying on the type of cancer being handled and cured, variables like the intensity and the length of external laser radiation, as well as the concentration and modification of the GBNMs, have been taken into account.

V. CHALLENGES AND PERSPECTIVES

5.1 Gold nanoparticles

To be considered optimal candidates for PTT, materials must meet specific criteria to avoid damage to surrounding normal cells, provide adequate photothermal effectiveness, and ensure sufficient penetration depth. The ideal PTT candidate should: (1) possess uniform shape and appropriate nano-range size; (2) interact with light in the NIR range of 650-950 nm; (3) exhibit excellent dispersion in aqueous solutions; (4) maintain sufficient photostability to ensure adequate diffusion time for tumor penetration before losing photosensitivity; and (5) demonstrate minimal or no cytotoxicity in living tissues [73].

While GNPs meet most of these criteria, their long-term cytotoxicity remains insufficiently characterized. Although GNPs are generally considered biocompatible, the long-term effects of nanoparticle accumulation are not fully understood. Preliminary research suggests several factors affecting GNP cytotoxicity, with size and surface charge identified as the most critical variables. Despite encouraging initial cytotoxicity studies, questions remain regarding whether GNPs are eventually cleared from the body and whether GNP accumulation might have long-term consequences [74].

Additionally, other technologies could render the use of GNPs obsolete, in addition to the fact that the biocompatibility problem around GNPs is still not fully resolved. For instance, using particular biodegradable polymer systems for PTT has become more popular. According to a recent study, a new polymer-based photothermal nanoagent that responds to light in the NIR-II spectrum (1,000–1,700 nm) can penetrate tissue significantly deeper than light in the NIR-I spectrum. Though the possible benefits of conjugating GNPs with NIR-II responsive polymers over employing pure NIR-II polymer nanoparticles have not yet been investigated, it should be mentioned that this is theoretically possible [75].

5.2 Graphene-based nanomaterials

Recent years have witnessed tremendous advancements in methods for biomedical applications of graphene nanoparticles. GO and rGO have been documented and accepted as promising photothermal agents in nanomedicine due to their excellent biocompatibility and physicochemical properties. However, several challenges must be addressed before nanoparticle-based photothermal therapy can be applied clinically, particularly for deeply embedded tumors or metastatic disease.

First, much research has focused on generating hyperthermia using laser light in the NIR-I window, primarily at 808 nm. While this wavelength is attractive due to minimal absorption by biological chromophores, its limited tissue penetration depth restricts its utility for treating large or deep tumors. This limitation is particularly crucial in clinical settings where PTT using GO as a photothermal agent would be ineffective. The NIR-II window offers a superior alternative, as longer wavelengths experience less scattering and penetrate deeper into tissues. Additionally, longer wavelengths carry less energy per photon, allowing higher power intensities to be employed. Therefore, researchers should consider the NIR-II region for radiation when developing new approaches for GBNMs-based photothermal cancer treatment. Additionally, because longer wavelengths carry less energy per photon, larger power intensities can be employed [76, 79]. Therefore, researchers should consider the NIR-II region for radiation when developing new methods for photothermally treating cancer utilizing GBNMs.

The possible risk to human health from GBNMs, modified GBNMs, and NIR irradiation is another important factor to consider when planning clinical trials. Several variables, such as GBNMs' size, chemical makeup, surface charge, and aggregation state, can affect how harmful they are [80]. It is crucial to remember that although GO and rGO have demonstrated excellent biocompatibility in several studies, their toxicity may increase due to subsequent functionalization.

Subsequently, it would be wise to prioritize biomimetic molecules -especially those approved by the FDA- in any future GBNM-based treatment approaches. While GBNMs are altered for combinatorial approaches or multimodal cancer detection and treatment, this emphasis becomes even more important [81]. Further studies involving the use of FDA-approved modified rGO, the use of NIR-II light sources for irradiation, the use of 3D tumor models for in vitro tests, and the evaluation of in vivo toxicity will be crucial in the future. This team effort will greatly aid the advancement of the shift from laboratory experiments to potential clinical implementations.

VI. CONCLUSIONS

Our comprehensive comparative analysis demonstrates that nanomaterials have fundamentally transformed photothermal cancer therapy, expanding its applications from localized tumor ablation to the treatment of metastatic disease. The novel head-to-head assessment of gold nanoparticles and graphene oxide, the two most extensively studied nanomaterials in this field, reveals their complementary advantages for cancer PTT, particularly for oral malignancies. This review uniquely identifies that gold nanorods offer precisely tunable optical properties through aspect ratio

modification, achieving peak absorption in the NIR-I window (750-1000 nm) with exceptional photothermal conversion efficiency via localized surface plasmon resonance. Their established biocompatibility and ongoing clinical trials demonstrate the advanced translational status of gold-based nanomaterials. Conversely, our analysis reveals that graphene oxide provides exceptional thermal conductivity, superior surface functionalization potential, and unique optical properties that enable multimodal imaging and therapy. Its two-dimensional structure offers an increased surface area for drug loading, making it particularly valuable for combination therapeutic approaches.

This review's novel contribution is identifying critical parameters for the successful clinical implementation of nanomaterial-enhanced PTT for oral cancer. Future research must prioritize: (1) standardized comparative studies between different nanosystems to establish optimal therapeutic protocols; (2) comprehensive biocompatibility assessments focusing on long-term toxicity profiles; (3) development of targeted delivery strategies to maximize tumor specificity while minimizing off-target effects; and (4) exploration of NIR-II window irradiation for deeper tissue penetration.

While preliminary clinical studies have demonstrated promising results, particularly for gold nanoparticles, our analysis identifies that broader clinical adoption requires resolving outstanding questions regarding long-term biocompatibility, biodistribution, and clearance mechanisms. Our novel finding is that integrating FDA-approved biomimetic molecules in nanoparticle functionalization represents a promising approach to accelerate regulatory approval and clinical translation.

Ultimately, this comparative assessment establishes that nanomaterial-enhanced photothermal therapy offers significant potential as a minimally invasive, highly selective treatment modality for oral cancers, particularly for patients who cannot tolerate conventional treatments or those with recurrent disease. The continued refinement of nanomaterial properties, irradiation parameters, and targeting strategies will be essential to fully realize the therapeutic potential of this approach and improve outcomes for patients with oral malignancies.

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