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REVIEW

Nanomedicine-Integrated Phototherapy for Cancer Theranostics: A Systematic Review of Photoresponsive Materials, Mechanisms, and Clinical Translation

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Background: Cancer remains a principal cause of mortality worldwide, and conventional treatments are constrained by non-specific cytotoxicity, therapeutic resistance, and incomplete tumor eradication. Nanomedicine-integrated phototherapy, encompassing photodynamic therapy (PDT) and photothermal therapy (PTT), has emerged as a spatiotemporally controlled theranostic modality with demonstrated preclinical promise.

Objective: This systematic review synthesizes current evidence on nanomedicine-based phototherapeutic agents across four research dimensions: nanotechnology design, phototherapeutic mechanisms, photoresponsive materials, and clinical translation.

Methods: A systematic literature search was conducted across PubMed, Scopus, Web of Science, and Embase (2000–2024) using predefined search terms related to nanomedicine, PDT, PTT, and cancer theranostics. Studies were screened according to PRISMA-aligned inclusion and exclusion criteria. A total of 1847 records were identified; following deduplication and full-text review, 78 studies met eligibility criteria and were included in the narrative synthesis.

Results: Nanocarrier design has advanced substantially, with enhanced permeability and retention (EPR)-mediated and active-targeted platforms achieving 10–50-fold tumor-to-tissue concentration ratios in preclinical models. Photoresponsive nanomaterials (including gold nanostructures with PCE 50–99%, carbon-based nanomaterials with PCE 40–80%, and hybrid metal-organic frameworks) demonstrate tunable optical properties suitable for NIR-activated therapy. Multifunctional theranostic platforms combining PDT or PTT with chemotherapy, immunotherapy, and multimodal imaging show synergistic efficacy. Clinical translation remains limited, with gold nanoshells (AuroLase Therapy, Nanospectra Biosciences) in Phase I evaluation for prostate cancer and several PDT photosensitizer formulations carrying regulatory approval.

Conclusion: Nanomedicine-integrated phototherapy addresses fundamental limitations of conventional oncology. Realizing its clinical potential requires development of biodegradable nanocarriers, standardized characterization protocols, companion diagnostics for patient stratification, and coordinated regulatory pathways. EPR variability in human tumors and the predominance of preclinical data necessitate a calibrated assessment of translational feasibility.

Keywords: nanomedicine, photodynamic therapy, photothermal therapy, cancer theranostics, photoresponsive nanomaterials, clinical translation

Introduction

Cancer is among the most pressing health challenges globally and a leading cause of premature death across diverse sociodemographic contexts.[1] Despite meaningful advances in oncology, conventional treatment modalities (including surgical resection, systemic chemotherapy, radiotherapy, and hormonal therapy) share inherent limitations that compromise treatment outcomes. These include limited tumor selectivity, dose-limiting off-target cytotoxicity, and susceptibility

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to therapeutic resistance mechanisms, most notably multidrug resistance (MDR), which substantially reduces the durability of treatment responses.[2,3]

The rise of nanomedicine has introduced transformative possibilities for cancer diagnosis and treatment.[3,4] Among the most clinically relevant applications is cancer theranostics, an integrative paradigm that unifies diagnostic imaging with therapeutic intervention within a single nanoplatform system.[5,6] Such multifunctional nanocarriers can simultaneously deliver diagnostic agents and therapeutic payloads to tumor sites, enabling real-time monitoring of treatment response. Critically, they can be engineered to respond to endogenous stimuli (such as tumor microenvironmental pH gradients, redox imbalances, and enzyme overexpression) or exogenous stimuli including light irradiation, ultrasound, and magnetic fields.[6,7]

Among phototherapy-based strategies, photodynamic therapy (PDT) and photothermal therapy (PTT) have attracted sustained attention as minimally invasive modalities with spatiotemporal precision.[8–11] PDT employs photosensitizers that, upon activation at specific wavelengths, generate cytotoxic reactive oxygen species (ROS) capable of selectively killing tumor cells through oxidative damage, vascular disruption, and immune stimulation (Figure 1A).[12,13] PTT, by

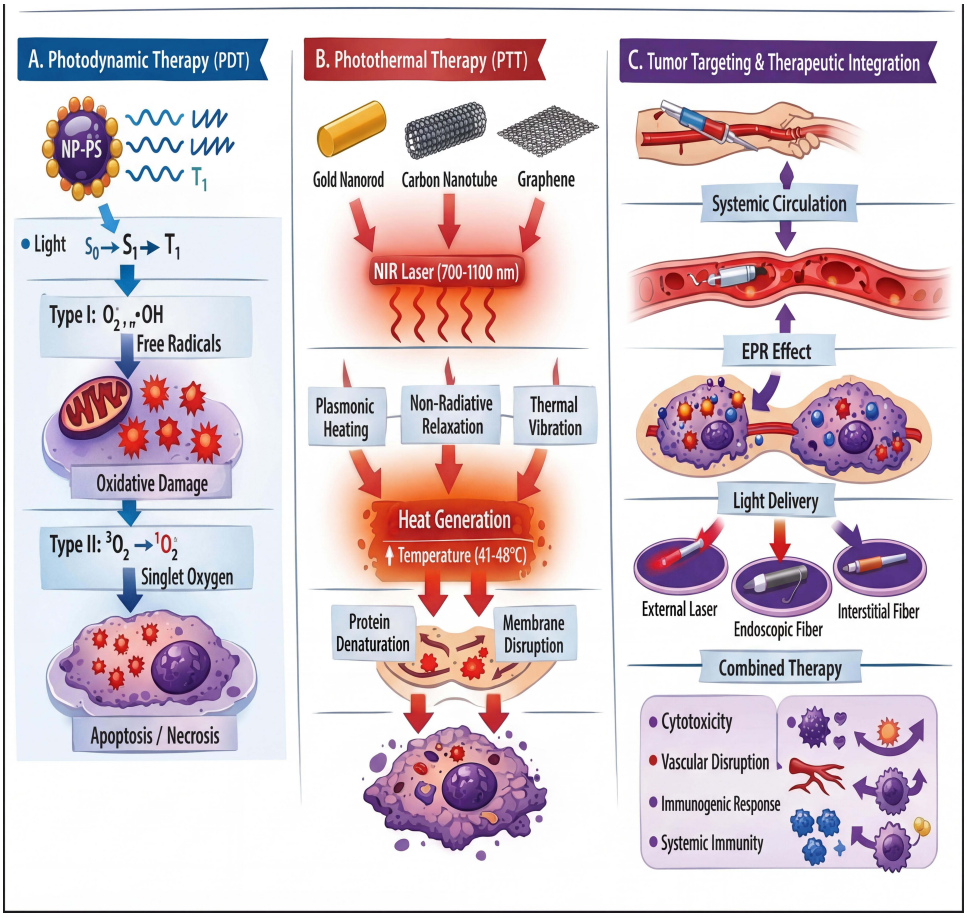

Figure 1 Mechanisms of nanomedicine-integrated phototherapy for cancer treatment. Panel A (Photodynamic therapy, PDT): A nanoparticle-bound photosensitizer (NP-PS) absorbs photons of the appropriate wavelength, undergoing electronic excitation from the ground singlet state (S_0) to the first excited singlet state (S_1), followed by intersystem crossing (right arrows indicating sequential state transitions) to the long-lived triplet state (T_1). From T_1, Type I reactions generate free radical species (including superoxide anion, $O_2^{\bullet-}$, and hydroxyl radical, $^{\bullet}OH$) via electron transfer, inducing oxidative damage to cellular macromolecules. Type II reactions transfer energy to molecular triplet oxygen ($^3O_2$), generating highly cytotoxic singlet oxygen ($^1O_2$; upward arrow denotes energy transfer from ground-state oxygen). Both pathways converge on apoptosis or necrosis. Panel B (Photothermal therapy, PTT): Noble metal photothermal agents (including gold nanorods, carbon nanotubes, and graphene nanosheets) absorb near-infrared (NIR) light in the 700–1100 nm range. Absorbed photon energy is converted to local heat through plasmonic heating, non-radiative relaxation, or thermal vibration mechanisms (upward arrow denotes temperature elevation above physiological baseline). Tumor temperatures of 41–48°C promote protein denaturation and membrane disruption, resulting in apoptotic or necrotic cell death. Panel C (Tumor targeting and therapeutic integration): Following intravenous administration, nanoparticles circulate systemically and preferentially accumulate in tumor tissue via the EPR effect, arising from aberrant tumor vasculature with enlarged fenestrations and impaired lymphatic drainage. Spatiotemporal control of therapeutic activation is achieved through light delivery using external lasers, endoscopic fibers, or interstitial fibers. Combined phototherapy simultaneously activates multiple cytotoxic mechanisms, including direct cytotoxicity, vascular disruption, immunogenic cell death with dendritic cell activation, and systemic anti-tumor immune responses. Created with DALL-E3.

contrast, relies on photothermal conversion agents that transform absorbed light energy into localized hyperthermia, causing thermal ablation of malignant tissue through protein denaturation and membrane disruption (Figure 1B).[12,14] The mechanistic distinctions between PDT and PTT (including differences in oxygen dependency, light wavelength requirements, and clinical applicability) are compared in Table 1.

The convergence of nanotechnology with phototherapy has substantially improved the potency and selectivity of both modalities.[14,17] Nanocarriers preferentially accumulate in tumors through the EPR effect, a consequence of aberrant tumor vasculature and impaired lymphatic drainage (Figure 1C).[18,19] This passive targeting mechanism can be augmented by surface conjugation of tumor-specific ligands, further concentrating therapeutic agents at disease sites while limiting systemic exposure.[20] Additionally, nanoplatforms can integrate multimodal imaging capabilities (including fluorescence, photoacoustic, and magnetic resonance imaging) enabling image-guided therapy and real-time response monitoring.[12,21]

Despite these advances, several barriers continue to limit the clinical translation of nanomedicine-integrated phototherapeutic agents (PTAs). Variability in EPR effect magnitude across tumor types and individual patients, concerns about long-term biocompatibility of non-biodegradable nanomaterials, manufacturing scalability, and inadequately defined regulatory pathways each present distinct challenges.[22] Light penetration depth remains a fundamental physical constraint, particularly for deep-seated tumors requiring interstitial or endoscopic light delivery.[8,23]

The present systematic review aims to synthesize current evidence on nanomedicine-based PTAs for cancer theranostics across four interrelated research dimensions: (1) nanotechnology-driven innovations in nanocarrier design; (2) phototherapeutic agent development and mechanistic optimization; (3) engineering of photoresponsive nanomaterials;

Table 1 Mechanistic and Clinical Comparison of Photodynamic Therapy (PDT) and Photothermal Therapy (PTT) in Nanomedicine-Integrated Cancer Treatment

Parameter	Photodynamic Therapy (PDT)	Photothermal Therapy (PTT)
Mechanism	Light-activated photosensitizers generate reactive oxygen species (ROS)—including singlet oxygen ($^1O_2$), superoxide anion radicals ($O_2^{\bullet -}$), and hydroxyl radicals (•OH)—that induce oxidative damage to cellular macromolecules, triggering apoptosis, necrosis, and vascular disruption.	Light-absorbing nanoparticles convert absorbed photon energy into localized hyperthermia via plasmonic heating, non-radiative relaxation, or thermal vibration, causing irreversible protein denaturation and membrane disruption.
Primary Therapeutic Agents	Porphyrins, chlorins (eg., Foscan/temoporfin), phthalocyanines, cyanine dyes, aggregation-induced emission (AIE) photosensitizers, two-photon photosensitizers	Gold nanostructures (nanorods, nanoshells, nanostars, nanocages), carbon nanomaterials (SWCNTs, graphene oxide, reduced GO), copper sulfide nanoparticles, semiconducting polymers
Activation Wavelength	400–700 nm (visible) or 650–900 nm (NIR-I window); determined by the photosensitizer absorption spectrum	700–1350 nm (NIR-I and NIR-II windows); tunable through nanoparticle size, shape, and elemental composition
Oxygen Dependency	Type II PDT strictly requires molecular oxygen for $^1O_2$ generation; Type I PDT is less oxygen-dependent but still benefits from aerobic conditions	Oxygen-independent; therapeutic efficacy is unaffected by tumor hypoxia
Key Advantages	Minimally invasive; repeatable treatment cycles; dual mechanism (direct cytotoxicity and vascular disruption); activates anti-tumor immune responses (immunogenic cell death); compatible with fluorescence imaging	Oxygen-independent (effective in hypoxic tumors); rapid therapeutic effect; deep-tissue access with NIR-II light; compatible with photoacoustic and thermal imaging modalities
Primary Limitations	Oxygen dependency limits efficacy in hypoxic tumors (Type II); restricted tissue penetration of visible-range light; photosensitizer photobleaching over repeated cycles; transient skin photosensitivity with some agents	Risk of collateral thermal injury to adjacent normal tissues; heat-sink effect near large blood vessels; biodistribution and long-term retention concerns for non-biodegradable photothermal agents
Clinical Translation Status[a]	Multiple FDA-approved formulations: Photofrin (porfimer sodium) for esophageal, pulmonary, and bladder cancers (1995); Levulan (aminolevulinic acid) for actinic keratosis (1999); Foscan (temoporfin) for head and neck malignancies (EU approval)	Limited approved applications to date; AuroShell (silica–gold nanoshells) has completed Phase I evaluation for focal prostate cancer ablation (NCT02680535); further agents remain investigational

Notes: [a]FDA approval data sourced from Gunaydin et al (2021)[15] and Alsaab et al (2020).[16]

Abbreviations: PDT, photodynamic therapy; PTT, photothermal therapy; ROS, reactive oxygen species; $^1O_2$, singlet oxygen; $O_2^{\bullet -}$, superoxide anion radical; •OH, hydroxyl radical; NIR, near-infrared; NIR-I, 700–900 nm; NIR-II, 1000–1350 nm; SWCNT, single-walled carbon nanotube; GO, graphene oxide; FDA, U.S. Food and Drug Administration; PCE, photothermal conversion efficiency.

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and (4) advances toward clinical translation. By critically evaluating research trends, persistent knowledge gaps, and emerging opportunities, this review provides a coherent framework for advancing nanomedicine-based phototherapy from preclinical proof-of-concept to clinical application.

Methodology

Review Protocol and Design

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, adapted for preclinical and translational research in nanomedicine. Although the protocol was not prospectively registered in PROSPERO or equivalent registries, methodological decisions regarding database selection, search terms, inclusion and exclusion criteria, and data extraction were defined a priori and applied consistently throughout the review process. The review was structured to synthesize evidence across four predetermined dimensions of nanomedicine-integrated phototherapy in cancer theranostics.

Research Dimensions Framework

Four interrelated research dimensions were defined to capture the breadth of nanomedicine-integrated phototherapy:

Dimension 1 (Nanotechnology Advancements): Innovations in nanocarrier design, surface functionalization, physicochemical characterization, and targeting strategies for enhanced tumor delivery.[3,21]

Dimension 2 (Phototherapeutic Agents): Development and optimization of photosensitizers for PDT and photothermal conversion agents for PTT, including molecular design principles, ROS generation mechanisms, and photothermal conversion efficiencies.[12,13]

Dimension 3 (Photoresponsive Materials): Integration of diverse photoresponsive nanomaterials (noble metals, carbon-based structures, metal oxides, semiconductors, and hybrid composites) with emphasis on structure-property relationships and material selection criteria.[24,25]

Dimension 4 (Clinical Translation): Synthesis of translational progress including preclinical validation, multifunctional platform development, combination therapy strategies, and barriers to clinical implementation.[22,26]

Literature Search Strategy

A comprehensive electronic literature search was conducted in PubMed/MEDLINE, Scopus, Web of Science, and Embase, covering publications from January 2000 through December 2024. The search strategy employed Boolean combinations of controlled vocabulary (MeSH terms) and free-text keywords, including: (“nanomedicine” OR “nanoparticle” OR “nanocarrier”) AND (“photodynamic therapy” OR “PDT” OR “photothermal therapy” OR “PTT”) AND (“cancer” OR “tumor” OR “neoplasm”) AND (“theranostic” OR “photosensitizer” OR “photothermal agent”). The search was limited to English-language, peer-reviewed publications. Conference abstracts, editorials, letters, and grey literature were excluded to maintain evidence quality.

Study Selection and Eligibility Criteria

Inclusion criteria were: (1) investigation of nanomedicine-based phototherapeutic strategies for cancer; (2) coverage of at least one of the four research dimensions; (3) reporting of original experimental data from in vitro, in vivo, or clinical studies; (4) provision of mechanistic information on phototherapy or nanoparticle design; and (5) publication in peer-reviewed English-language journals.

Exclusion criteria were: (1) purely theoretical or computational studies without experimental validation; (2) non-cancer phototherapy applications; (3) phototherapy without nanomedicine integration; (4) review articles, meta-analyses, or letters without original data; (5) inadequate methodological reporting; and (6) duplicate publications or redundant datasets.

Records were screened by title and abstract, followed by full-text review of potentially eligible studies. Disagreements were resolved by discussion among authors.

Data Extraction and Synthesis

Data were extracted systematically for each included study, covering: nanoparticle composition and physicochemical properties; phototherapeutic modality (PDT, PTT, or combined); light activation parameters (wavelength, power density, irradiation duration); experimental cancer model; efficacy metrics; mechanistic findings; and translational considerations. Given the substantial heterogeneity in experimental designs, nanomaterial compositions, cancer models, and outcome measures across included studies, quantitative meta-analysis was not feasible. A narrative synthesis approach was therefore adopted, organizing findings by research dimension and identifying cross-cutting themes, emerging trends, and knowledge gaps.

Quality Assessment and Heterogeneity

In the absence of a universally validated tool for preclinical nanomedicine studies, quality was assessed using the following indicators: rigor of nanoparticle physicochemical characterization; appropriateness of experimental models; inclusion of relevant controls and statistical analyses; transparency of limitations reporting; and biocompatibility assessment. Study heterogeneity (spanning in vitro cell culture systems, subcutaneous xenograft models, orthotopic animal models, and early-phase clinical investigations) was recognized as a primary constraint on data synthesis. Therapeutic outcomes reported across these different experimental contexts were interpreted accordingly, with particular caution applied to extrapolating preclinical efficacy data to human translational potential.

Results

Study Selection and Research Trends

From the initial database searches, 1847 records were retrieved. After removing 312 duplicates, 1535 records were screened by title and abstract, resulting in the exclusion of 1127 records that did not satisfy eligibility criteria. Full-text assessment of the remaining 408 records led to the exclusion of a further 330 studies (reasons: reviews without original data, n=154; non-cancer applications, n=89; insufficient methodology, n=87). A total of 78 studies met all eligibility criteria and were included in the final synthesis.

Analysis of publication trends across the included literature reveals three discernible phases of development in nanomedicine-integrated phototherapy. An exploratory phase (2000–2010) established foundational mechanisms and proof-of-concept studies. An acceleration phase (2011–2018) saw rapid diversification of nanomaterial classes and expansion of preclinical validation work. A translation-focused phase (2019–2024) has been characterized by increasing emphasis on multifunctional platform development, combination therapy strategies, and early-phase clinical evaluation. The proportional growth of clinical translation-focused publications during this final phase suggests progressive field maturation, though the absolute number of clinical studies remains small relative to the preclinical literature. Geographic contributions span Asia (China, South Korea, Japan), North America, and Europe, with increasing interdisciplinary collaboration across materials science, pharmaceutical sciences, and oncology.

Dimension 1: Nanotechnology Advancements in Cancer Diagnosis and Treatment

Contemporary nanomedicine platforms incorporate sophisticated design principles to address fundamental limitations in drug delivery. Nanocarrier size optimization within the 20–200 nm range has been established as critical for tumor targeting efficiency: particles smaller than 20 nm undergo rapid renal clearance, while those exceeding 200 nm demonstrate impaired tumor extravasation. Surface modification through PEGylation significantly extends circulatory half-life from minutes to hours or days by reducing opsonin binding and macrophage recognition. Emerging alternatives (including zwitterionic polymer coatings and biomimetic cell membrane camouflage) offer additional strategies to circumvent the limitations of PEGylation, such as the accelerated blood clearance (ABC) phenomenon.[19,27]

Distinct nanocarrier architectures offer complementary advantages. Lipid-based nanoparticles afford excellent biocompatibility, though photosensitizer loading capacity can be constrained. Polymeric nanoparticles provide tunable degradation kinetics and high drug loading. Inorganic nanoplatforms (particularly mesoporous silica nanoparticles and metal-organic frameworks, MOFs) offer exceptional surface areas and inherent therapeutic or imaging properties.[12]

The EPR effect, arising from abnormal tumor vasculature with fenestrations of 100–780 nm and impaired lymphatic drainage, enables passive nanoparticle accumulation at tumor sites, with preclinical models demonstrating tumor-to-normal tissue concentration ratios of 10–50-fold.[18,19] However, human tumor studies reveal substantially greater EPR variability than animal models, with elevated interstitial fluid pressure and dense extracellular matrix further limiting tumor penetration. Active targeting through surface-conjugated ligands (including antibodies, peptides, and aptamers directed against tumor-overexpressed receptors) augments passive accumulation and improves binding specificity. Dual and multi-receptor targeting strategies have been explored to address tumor heterogeneity and enhance binding avidity.[28,29]

Theranostic nanomedicines integrate real-time diagnostic functionality alongside therapeutic payload delivery, enabling personalized treatment monitoring. Multimodal imaging modalities provide complementary information: fluorescence imaging (FLI) offers high sensitivity for superficial lesions (1–2 cm depth); photoacoustic imaging (PAI) achieves optical contrast with ultrasonic detection depth (3–5 cm); magnetic resonance imaging (MRI) provides unlimited penetration depth with high anatomical resolution; and computed tomography (CT) enables rapid whole-body assessment.[12,21,30–32,77–79]

Dimension 2: Phototherapeutic Agents and Mechanisms

PDT and PTT operate through mechanistically distinct pathways, each with unique dependencies on tumor physiology and distinct clinical applicability profiles, as summarized in Table 1 and illustrated in Figure 1A and B.

PDT exploits photosensitizer molecules that, upon irradiation at specific wavelengths, undergo electronic excitation from the ground singlet state (S_0) through the excited singlet state (S_1) to the long-lived triplet state (T_1) via intersystem crossing. From the triplet state, two mechanistic pathways operate. Type I reactions involve electron or hydrogen transfer to substrate molecules, generating superoxide anion radicals ($O_2^{\bullet -}$), hydroxyl radicals ($^{\bullet}OH$), and hydrogen peroxide (H_2O_2). Type II reactions involve direct energy transfer to molecular oxygen, generating highly cytotoxic singlet oxygen ($^1O_2$) as the predominant cytotoxic species. Both reaction types culminate in oxidative damage to cellular macromolecules, initiating apoptosis or necrosis, and also elicit vascular disruption and immunogenic responses.[33,34]

First-generation photosensitizers, exemplified by Photofrin (porfimer sodium), demonstrated clinical utility but were limited by poor NIR absorption and prolonged cutaneous photosensitivity (4–6 weeks). Second-generation agents overcame many of these drawbacks: chlorins (eg., Foscan) offer red-shifted absorption spectra and reduced photosensitivity; phthalocyanines exhibit strong NIR absorption; and bacteriochlorins enable deeper tissue penetration. Third-generation photosensitizers incorporate advanced functionalization strategies, including antibody conjugation for active targeting, nanoparticle encapsulation to improve aqueous solubility and tumor accumulation, and activatable designs that remain quenched until triggered by tumor-specific microenvironmental stimuli. Emerging photosensitizer classes include aggregation-induced emission (AIE) photosensitizers with enhanced ROS generation in the aggregated state, and two-photon photosensitizers that enable NIR-activated treatment of deeper tissue volumes.[15]

PTT converts absorbed NIR light into localized hyperthermia through plasmonic heating, non-radiative relaxation, or thermal vibration mechanisms (Figure 1B). Tumor temperatures of 41–48°C sustained over 5–30 minutes promote apoptotic cell death, while temperatures exceeding 48°C induce immediate necrosis through protein denaturation. A key advantage of PTT is its oxygen-independence: tumor hypoxia, a common feature of solid tumors that limits PDT efficacy, does not impair photothermal ablation. Photothermal conversion efficiency (PCE) represents the primary performance metric, with leading agents achieving values of 50–99%.[12,35]

Gold nanoparticles represent the most clinically advanced photothermal agents, combining tunable localized surface plasmon resonance (LSPR), high PCE (50–90%), favorable biocompatibility, and versatile surface functionalization.[24,36] Nanoparticle morphology critically determines optical properties: spherical nanoparticles exhibit LSPR at 520–550 nm; nanorods with varying aspect ratios enable LSPR tuning across 600–1100 nm; nanoshells shift resonance into the NIR window; nanostars concentrate electromagnetic fields at sharp tips; and nanocages integrate drug-loading capacity with photothermal function.[37]

Carbon-based nanomaterials offer broad NIR absorption, high surface area for drug loading, and emerging biodegradability. Single-walled carbon nanotubes (SWCNTs) display diameter-dependent optical properties with PCE values of 50–80%, though biocompatibility concerns necessitate careful surface functionalization, typically through PEGylation. Graphene oxide (GO) provides improved aqueous dispersibility, while reduced graphene oxide (rGO) exhibits superior

photothermal properties (PCE 40–70%). Size-optimized graphene quantum dots (less than 10 nm) address biodegradability concerns through enzyme-mediated degradation pathways.[25,27,38,39]

Dimension 3: Photoresponsive Nanomaterials – Inorganic and Organic Classes

The landscape of photoresponsive nanomaterials encompasses a diverse array of material classes, each with distinct physicochemical properties, optical behaviors, and therapeutic applications, as systematically summarized in Table 2.

Noble metal nanoparticles, particularly gold nanostructures, derive their distinctive optical properties from collective electron oscillations that produce localized surface plasmon resonance.[48] Gold nanoparticles have emerged as the most translationally mature photothermal platform owing to their biocompatibility, surface functionalization versatility, and tunable plasmonic characteristics. Gold nanoshells have advanced furthest toward clinical application; the AuroLase Therapy system (Nanospectra Biosciences), comprising silica-gold nanoshells, has demonstrated technical feasibility, safety, and preliminary focal ablation efficacy in a Phase I clinical evaluation for prostate cancer.[49] Bimetallic nanostructures incorporating silver, copper, or platinum with gold offer expanded optical tuning and potentially synergistic therapeutic effects.[37,50]

Carbon nanotubes (diameters 1–100 nm) exhibit strong NIR absorption with PCE values of 50–80%. SWCNTs possess diameter-dependent optical properties, whereas multi-walled CNTs (MWCNTs) offer superior mechanical stability. Surface PEGylation substantially improves colloidal stability, aqueous dispersibility, and systemic clearance profiles.[38] Graphene and its derivatives benefit from exceptional specific surface area (theoretical maximum 2,630 m^2/g), broad NIR absorption, and rich surface chemistry for functionalization. Graphene quantum dots (less than 10 nm) additionally offer photoluminescence properties and enzyme-mediated biodegradability.[27,40]

Metal oxide nanoparticles provide unique combinations of optical, electronic, magnetic, and catalytic properties. Copper sulfide nanoparticles (CuS, Cu_2S) exhibit strong NIR absorption in the 900–1100 nm range with PCE values of 40–60% and offer a pathway to biodegradability through controlled copper ion release.[41] Iron oxide nanoparticles combine superparamagnetic behavior (enabling MRI contrast and magnetic hyperthermia) with moderate photothermal activity.[42] Transition metal dichalcogenides (MoS_2, WS_2) display layer-dependent bandgap tunability, NIR absorption, PCE values comparable to graphene (35–65%), and amenability to biodegradation through oxidative dissolution.[44] Black

Table 2 Classification and Comparative Profile of Photoresponsive Nanomaterials for Cancer Phototherapy

Material Category	Representative Examples	PCE[a] Range	Key Therapeutic Applications	Selected References
Noble Metals – Gold Nanoparticles	Nanospheres, nanorods, nanoshells, nanostars, nanocages	50–99%	PTT; photoacoustic imaging; theranostic combination platforms	Dreaden et al (2012);[36] Bai et al (2020);[24] Vines et al (2019)[37]
Carbon – Nanotubes	Single-walled CNTs (SWCNTs), multi-walled CNTs (MWCNTs)	50–80%	PTT; drug/gene delivery; photoacoustic imaging	Hwang et al (2017);[38] Qi et al (2023);[39] Cha et al (2013)[25]
Carbon – Graphene Derivatives	Graphene oxide (GO), reduced GO (rGO), graphene quantum dots (GQDs)	40–70%	PDT/PTT; drug/gene delivery; bioimaging; photoluminescence sensing	Tabish et al (2018);[27] Karami et al (2024)[40]
Metal Oxides/Sulfides	Copper sulfide (CuS, Cu_2S), iron oxide (Fe_3O_4), zinc oxide (ZnO)	40–60%	PTT; photoacoustic imaging; MRI contrast enhancement	Wang et al (2021);[41] Jiao et al (2018)[42]
Transition Metal Dichalcogenides (TMDs)	Molybdenum disulfide (MoS_2), tungsten disulfide (WS_2), black phosphorus (BP)	30–65%	PTT; photoacoustic imaging; biodegradable therapeutic platforms	Li et al (2021);[43] Zheng et al (2021)[44]
Hybrid/Composite Systems	Metal–organic frameworks (MOFs), core–shell nanoparticles, upconversion nanoparticles (UCNPs)	20–80%	Combined PDT/PTT; stimulus-responsive drug delivery; multimodal imaging	Cai et al (2019);[45] Xiao et al (2011);[46] Xie et al (2023)[47]

Notes: [a]PCE values represent typical ranges reported across peer-reviewed literature; specific values depend on nanoparticle size, morphology, and surface chemistry. [b]Representative citations only; comprehensive reference list available in the main text.

Abbreviations: PCE, photothermal conversion efficiency; PDT, photodynamic therapy; PTT, photothermal therapy; CNT, carbon nanotube; SWCNT, single-walled carbon nanotube; MWCNT, multi-walled carbon nanotube; GO, graphene oxide; rGO, reduced graphene oxide; GQD, graphene quantum dot; CuS, copper sulfide; Cu_2S, cuprous sulfide; Fe_3O_4, iron oxide; MoS_2, molybdenum disulfide; WS_2, tungsten disulfide; MOF, metal–organic framework; UCNP, upconversion nanoparticle; NIR, near-infrared.

phosphorus demonstrates promising photothermal performance (PCE 30–50%), layer-dependent bandgap tunability, and potential biodegradability through conversion to non-toxic phosphate species.[43]

Hybrid nanoplatforms integrate complementary materials to achieve synergistic therapeutic effects that exceed those of single-component systems. MOFs with exceptionally high surface areas (1,000–10,000 m^2/g) and tunable porosity provide unprecedented photosensitizer loading capacities; porphyrin-based MOFs incorporating photosensitizer molecules as structural linkers maximize loading while avoiding aggregation-caused quenching.[45] Core-shell architectures, such as Fe_3O_4@Au nanoparticles combining a magnetic core (MRI contrast, magnetic targeting) with a gold shell (PTT functionality, biocompatibility), exemplify the rational integration of diagnostic and therapeutic functions within a single nanoplatform.[46,47]

Recent investigations have also explored the potential of naturally derived and biocompatible photoresponsive materials. Plasmonic silver nanoparticles continue to attract attention for their versatile optical tunability in biological applications.[51] Carbon quantum dot hybrid systems demonstrate high photocatalytic efficiency under visible-light activation, offering potential as scaffolds for next-generation photoresponsive nanocarriers.[52] Moreover, plant-derived phytochemical compounds (including phenolic antioxidants and bioactive secondary metabolites from sources such as *Myrtus communis*) are increasingly investigated as biosynthesis templates for organic photosensitizers and photothermal agents with improved biocompatibility and reduced long-term toxicity.[53]

Dimension 4: Multifunctional Platforms and Clinical Translation

Contemporary nanomedicine increasingly emphasizes multifunctional platform engineering that integrates multiple treatment modalities with diagnostic functionality, as summarized for clinically advanced platforms in Table 3. Such

Table 3 Clinical Translation Status of Nanomedicine-Based Phototherapy Platforms

Nanoplatform	Cancer Type	Clinical Phase	Key Findings/Reference
Photofrin® (Porfimer sodium)	Esophageal, pulmonary, bladder cancer	FDA Approved (1995)	First-generation photosensitizer; established clinical efficacy across multiple malignancies; prolonged cutaneous photosensitivity (4–6 weeks) is the primary limiting adverse effect. Gunaydin et al (2021)[15]
Levulan® (5-Aminolevulinic acid)	Actinic keratosis, basal cell carcinoma	FDA Approved (1999)	Prodrug metabolized to protoporphyrin IX in situ; topical formulation; favorable local tolerability. Alsaab et al (2020)[16]
Foscan® (Temoporfin)	Head and neck squamous cell carcinoma	EMA Approved (2001)	Second-generation photosensitizer; red-shifted absorption (652 nm) and reduced photosensitivity duration relative to Photofrin. Benov (2014)[54]
AuroShell® (Silica–gold nanoshells)	Prostate cancer (focal ablation)	Phase I/Pilot (NCT02680535)	Safety and feasibility demonstrated in 16-patient pilot study (Rastinehad et al, 2019);[49] >100 patients treated in subsequent trials (NCT04240639); no dose-limiting toxicities reported
CYT-6091 (PEGylated colloidal gold–TNF)	Advanced solid tumors	Phase I	Safety profile established; selective tumor-targeted TNF delivery confirmed by tumor biopsy. Libutti et al (2010)
NK105 (Paclitaxel-loaded polymeric micelles)	Gastric cancer, breast cancer	Phase II/III	Improved pharmacokinetic profile versus solvent-based paclitaxel; significantly reduced peripheral neuropathy incidence. Kato et al (2012)
Gold nanorods (Investigational)	Various solid tumors	Preclinical	High PCE (>80%) with tunable NIR-I/II absorption via aspect-ratio engineering; surface functionalization strategies under active optimization. Dreaden et al (2012);[36] Bai et al (2020)[24]
Graphene oxide nanoplatforms (Investigational)	Glioblastoma, breast cancer	Preclinical	Exceptionally high drug-loading capacity; combined chemo-PTT efficacy demonstrated in orthotopic models; biocompatibility and immune response profiling ongoing. Tabish et al (2018)[27]
Black phosphorus nanosheets (Investigational)	Breast cancer, cervical cancer	Preclinical	Biodegradable platform converting to non-toxic phosphate species; broad NIR absorption; promising in vivo PTT efficacy in subcutaneous tumor models. Li et al (2021)[43]

Notes: Approval dates and clinical trial registrations verified against publicly available regulatory and registry databases. Preclinical entries represent platforms with published in vivo proof-of-concept data but without active clinical trials as of the search cutoff (December 2024).

Abbreviations: FD A, U.S. Food and Drug Administration; EMA, European Medicines Agency; PDT, photodynamic therapy; PTT, photothermal therapy; PCE, photothermal conversion efficiency; PEG, polyethylene glycol; TNF, tumor necrosis factor; NIR, near-infrared; NCT, ClinicalTrials.gov registration number.

approaches aim to address tumor heterogeneity and resistance mechanisms through simultaneous multi-target engagement, with treatment response monitored in real time.[3,12]

Phototherapy-chemotherapy combinations constitute the most extensively studied multimodal strategy, capitalizing on complementary mechanisms: phototherapy provides immediate local ablation and vascular disruption, while chemotherapy extends systemic coverage. Photothermal heating from PTT enhances drug release from thermosensitive nanocarriers and increases vascular permeability, potentially reversing MDR phenotypes. Preclinical studies consistently report superior therapeutic efficacy for co-loaded nanoplatforms relative to either monotherapy alone.

PDT-PTT combination strategies exploit mechanistic synergism: PDT-generated ROS augment photothermal agent efficacy, while hyperthermia from PTT increases tumor oxygenation and enhances PDT activity. Dual-wavelength irradiation protocols that co-activate both modalities achieve more complete tumor eradication at lower individual doses, potentially reducing systemic toxicity profiles.

The integration of phototherapy with immunotherapy represents an increasingly productive frontier. Phototherapy-induced immunogenic cell death (ICD) releases damage-associated molecular patterns (DAMPs) (including calreticulin, HMGB1, and ATP) that act as in situ vaccination signals, promoting dendritic cell maturation and cytotoxic T-lymphocyte priming. Combination with immune checkpoint inhibitors or immunostimulatory adjuvants amplifies systemic anti-tumor immunity, offering potential activity against distant metastases beyond the irradiated field.[14,17]

Despite extensive preclinical validation, clinical translation remains restricted to a small number of platforms (Table 3). Manufacturing scalability and batch-to-batch reproducibility present formidable challenges for complex multifunctional nanoplatforms, requiring GMP-compliant synthesis with stringent physicochemical quality control. Regulatory pathways for nanomedicine-based phototherapy are incompletely defined, with uncertainty regarding characterization requirements, toxicological evaluation protocols, and clinical trial design considerations for nanoparticle-based therapeutics.[26,55]

EPR variability in human tumors constitutes a particularly significant translational barrier. Preclinical xenograft models may substantially overestimate EPR-mediated nanoparticle accumulation achievable in human patients with diverse tumor types, prior treatment histories, and variable tumor microenvironments. This recognition has stimulated companion diagnostic development aimed at prospectively stratifying patients most likely to achieve adequate nanoparticle tumor accumulation.[22,56]

Despite these challenges, the AuroLase photothermal therapy system (AuroShell gold nanoshells, Nanospectra Biosciences) has demonstrated clinical feasibility for focal prostate cancer ablation. The 2019 PNAS pilot study in 16 patients demonstrated technical safety, precise thermal ablation of targeted tumor foci, and minimal collateral damage to surrounding urological structures. Subsequent trials (NCT02680535, NCT04240639) have collectively treated more than 100 patients as of 2023–2024, providing expanding evidence of clinical translatability.[49] In PDT, multiple photosensitizer formulations carry regulatory approval: Photofrin (porfimer sodium) for esophageal, pulmonary, and bladder cancers; Levulan (aminolevulinic acid) for actinic keratosis; and Foscan (temoporfin) for head and neck malignancies, establishing important clinical and regulatory precedents.[15,16]

Discussion

Synthesis of Key Findings

This systematic review has delineated the current state of nanomedicine-integrated phototherapy for cancer theranostics across four research dimensions, revealing substantial advances alongside persistent translational barriers. The overall trajectory of the field reflects a progression from foundational photochemistry and proof-of-concept nanocarrier designs toward increasingly sophisticated multifunctional platforms with expanding clinical evidence bases.

The evolution of nanocarrier design from passive EPR-dependent strategies to active multi-receptor targeting and stimuli-responsive release systems represents a pivotal conceptual advance.[28,29] Nonetheless, the magnitude of EPR-mediated tumor accumulation is substantially more variable in human tumors than in standardized preclinical animal models, reflecting differences in tumor vascularity, interstitial fluid pressure, and microenvironmental composition. This

variability challenges the assumption that EPR-mediated passive targeting is universally sufficient as a therapeutic delivery mechanism.[18,19]

The mechanistic characterization of PDT and PTT pathways has reached considerable depth at the molecular and cellular levels, elucidating how light-activated nanomaterial systems generate cytotoxic ROS or localized hyperthermia.[34,35] A particularly important insight has been the recognition that PDT efficacy is critically oxygen-dependent, motivating strategies to overcome tumor hypoxia through oxygen delivery systems or Type I photosensitizers capable of producing cytotoxic radicals via oxygen-independent radical transfer mechanisms.[57,58] Similarly, the discovery that PTT-induced ICD can elicit systemic anti-tumor immunity has opened the concept of photoimmunotherapy, in which localized photothermal ablation serves as a tumor antigen release mechanism to prime immune responses against distant disease.[14,17]

The material diversity of photoresponsive nanomaterials (from noble metals to carbon allotropes, semiconductors, and hybrid composites) provides a versatile toolkit for matching optical properties, biocompatibility, and functional capabilities to specific clinical scenarios.[24,42] Gold nanoplatforms retain an overall translational advantage owing to their biocompatibility and established surface chemistry, though concerns about long-term accumulation in reticuloendothelial organs continue to motivate parallel development of biodegradable alternatives.[59] The classification and comparative performance data provided in Table 2 facilitate rational material selection for specific therapeutic goals.

Study Heterogeneity and Limitations of Evidence

A critical interpretive challenge throughout this synthesis is the profound heterogeneity of included studies. Experimental systems range from two-dimensional cell culture models to subcutaneous xenografts, orthotopic tumor models, and early-phase human trials. These contexts differ fundamentally in their ability to recapitulate the complexity of human tumor biology, including stromal interactions, immune infiltration, heterogeneous vascularity, and three-dimensional architecture.[22] Subcutaneous xenografts, which constitute the majority of in vivo evidence, are acknowledged to overestimate EPR accumulation and therapeutic response relative to human tumors.

This heterogeneity has a direct bearing on data interpretation within this review. Findings from cell culture and animal studies cannot be directly extrapolated to predict human clinical efficacy. Therapeutic outcomes were accordingly contextualized within their respective experimental models, and translational claims were assessed conservatively. The preponderance of preclinical evidence relative to human data reflects the early developmental stage of many nanomedicine platforms rather than established clinical efficacy, and this distinction is important for calibrating expectations about near-term clinical impact.

Additional methodological variability exists in the reporting of nanoparticle characterization parameters, light delivery protocols, irradiation conditions, and efficacy endpoints across studies. This lack of standardization limits direct inter-study comparisons and highlights an important unmet need for consensus reporting frameworks in nanomedicine phototherapy research.

Theoretical and Clinical Implications

Theoretical Contributions

This review contributes to the theoretical understanding of cancer nanomedicine by assembling mechanistic insights across scales: from photochemical reactions at the molecular level, through cellular signaling cascades, to tissue-level therapeutic outcomes. The elucidation of structure-function relationships governing nanoparticle physicochemical properties and their consequences for biodistribution, cellular uptake, and therapeutic efficacy provides a rational framework for prospective platform design.[60,61]

The recognition that tumor microenvironmental characteristics (acidic pH, elevated glutathione, enzyme overexpression, and hypoxia) can serve as endogenous triggers for stimuli-responsive therapeutic activation represents a conceptual shift from systemic chemotherapy toward precision oncology.[6,7] This framework extends beyond phototherapy to inform nanomedicine design more broadly. Furthermore, the emerging evidence that phototherapy-induced ICD can convert immunologically cold tumors into hot tumors susceptible to immune checkpoint blockade provides mechanistic rationale for rational combination immunotherapy strategies.[14,17]

Clinical Practice Implications

From a practical perspective, spatiotemporal light activation allows selective tumor destruction while sparing adjacent normal tissues, potentially reducing treatment-related morbidity compared with systemic chemotherapy or external beam radiotherapy.[15,62] The minimally invasive nature of phototherapy (which can be delivered endoscopically or via percutaneous interstitial fiber placement) is particularly advantageous for tumors of the bladder, esophagus, airway, and prostate, and may enable outpatient delivery in appropriately selected patients.[23,54]

The theranostic paradigm (integrating real-time imaging feedback with therapeutic delivery) aligns with precision medicine principles by enabling individualized treatment monitoring and early identification of non-responders.[63,64] This capacity for adaptive therapeutic management represents a meaningful advance over conventional modalities for which early response assessment is often limited.

However, practical implementation challenges remain substantial. Manufacturing complex multifunctional nanoplatforms with consistent batch-to-batch characteristics at clinical scale is technically demanding.[55,65] Regulatory agencies have begun to develop frameworks for nanomedicine-specific evaluation, but standards for nanoparticle characterization, safety assessment, and clinical trial design remain incompletely harmonized across jurisdictions.[66,67]

Translational Barriers

Biocompatibility and long-term safety evaluation are prerequisite for clinical advancement, particularly for non-biodegradable inorganic materials with potential for hepatic and splenic accumulation.[59] Comprehensive toxicological programs (encompassing acute toxicity, chronic exposure, immunogenicity, and delayed adverse effects) are resource-intensive but essential. The strategic development of biodegradable nanocarriers that degrade predictably after therapeutic action represents a priority direction to mitigate long-term accumulation concerns.[41]

EPR variability in human patients represents perhaps the most fundamental challenge to passive targeting strategies. Tumor vascular permeability varies considerably across cancer types and individual patients; certain human malignancies exhibit minimal EPR effect. Companion diagnostic tools that prospectively assess tumor vascular permeability or nanoparticle accumulation capacity could enable patient stratification, potentially improving clinical trial success rates by enriching study populations for predicted responders.[22,56]

Light penetration depth remains a physical constraint for PTT and PDT in deep-seated tumors. NIR wavelengths penetrate several centimeters of tissue and substantially expand the accessible treatment volume relative to visible light. Emerging solutions including X-ray-activated phototherapy, upconversion nanoparticles that translate NIR excitation to UV-visible photosensitizer activation, and radioluminescent nanoparticles may extend applicability to previously inaccessible tumor locations.[68,69]

Manufacturing complexity and associated cost considerations are barriers to commercialization. Multifunctional nanoplatforms incorporating therapeutic agents, targeting ligands, and imaging components require sophisticated synthesis protocols that may be difficult to scale while maintaining quality standards. Cost-effectiveness analyses comparing nanomedicine-based phototherapy with established treatments are notably absent from the current literature but will be essential for reimbursement decisions.[66]

Future Research Directions

Material Innovation

Priority research directions include the development of biodegradable nanocarriers maintaining robust phototherapeutic performance with predictable elimination after therapeutic action.[59] Organic semiconducting polymer nanoparticles, MOFs with hydrolytically labile coordination bonds, and biomimetic nanocarriers incorporating natural cellular membranes represent promising approaches.[44,47]

Photosensitizer engineering should target further red-shifting of absorption spectra into the NIR window, increased singlet oxygen quantum yields, and improved photostability to expand applicability to deeper tumors.[70,71] Development of Type I photosensitizers generating cytotoxic radicals through oxygen-independent pathways can circumvent hypoxia-related limitations of Type II PDT.[72] Photothermal agent development should emphasize high PCE in the second NIR window (1000–1350 nm), which provides superior tissue penetration relative to NIR-I, alongside biodegradability.[73,74]

Mechanistic Understanding and Predictive Modeling

Advanced mechanistic investigation using single-cell analysis, spatial transcriptomics, and computational modeling would clarify relationships between nanoparticle properties, biodistribution, cellular uptake pathways, and therapeutic outcomes.[6] Quantitative structure-activity relationship models could reduce empirical optimization burden and guide rational nanoplatform design. Investigation of tumor microenvironment remodeling induced by phototherapy (including effects on vasculature, extracellular matrix, stromal cell populations, and immune infiltration) would provide mechanistic insights to guide combination regimen design.[20]

Clinical Translation Strategies

Establishing consensus standards for nanoparticle characterization, toxicological evaluation protocols, and clinical trial design in nanomedicine-based phototherapy would substantially streamline regulatory review and accelerate translational pathways.[66,67] International consensus efforts engaging researchers, clinicians, regulators, and industry partners are needed to harmonize these standards.

Companion diagnostic development to enable patient stratification based on predicted therapeutic benefit is a high-priority need.[22] Imaging biomarkers of tumor vascular permeability, hypoxia status, or nanoparticle accumulation could prospectively identify patient subpopulations most likely to benefit from EPR-dependent nanomedicine interventions. Adaptive clinical trial designs incorporating biomarker-driven patient selection, real-time imaging endpoints, and pharmacokinetic-pharmacodynamic modeling would generate robust efficacy evidence while conserving resources.[16]

Integration with Emerging Technologies

Convergence of nanomedicine-based phototherapy with artificial intelligence for treatment planning, precision robotics for light delivery, and advanced imaging for real-time response assessment offers pathways to enhanced treatment precision.[75] Machine learning applied to nanoparticle characterization datasets may identify non-obvious structure-function relationships that are difficult to discern through conventional experimental approaches.

Integration with immunotherapy (combining phototherapy-induced ICD with immune checkpoint inhibitors, adoptive cell therapies, or cancer vaccines) represents a particularly high-priority strategy for extending benefit to patients with metastatic disease.[14,17] Biological targeting innovations, including tumor-homing cell-based nanoparticle carriers, pH-responsive and enzyme-responsive delivery systems, and biomimetic nanoparticles camouflaged with cellular membranes, may further enhance tumor selectivity and reduce off-target accumulation.[6,76]

Conclusion

This systematic review has synthesized evidence on nanomedicine-integrated phototherapy for cancer theranostics across four dimensions: nanotechnology advances, phototherapeutic mechanisms, photoresponsive nanomaterials, and clinical translation. The findings demonstrate that nanotechnology has fundamentally transformed phototherapeutic approaches by improving tumor targeting specificity, photosensitizer and photothermal agent delivery, and multimodal therapeutic-diagnostic integration.[24,29]

The mechanistic basis of PDT and PTT is well characterized: light-activated nanomaterials generate cytotoxic ROS or localized hyperthermia through distinct but complementary pathways, with substantial potential for synergistic combination.[34,35] The diversity of photoresponsive nanomaterials (from gold nanostructures and carbon allotropes to biodegradable organic semiconductors) offers a broad toolkit for matching optical properties and functional capabilities to specific clinical contexts (Table 2). Multifunctional theranostic platforms integrating phototherapy with chemotherapy, immunotherapy, and multimodal imaging demonstrate synergistic efficacy in preclinical models and support real-time treatment monitoring.[14,77]

Despite significant preclinical advances, clinical translation remains limited by enduring barriers: EPR variability in human tumors, long-term biocompatibility uncertainties, manufacturing scalability demands, and incomplete regulatory frameworks.[78,79] The clinical evaluation of gold nanoshell-mediated photothermal ablation (AuroLase Therapy) and the regulatory approval of multiple PDT photosensitizer formulations validate the translational feasibility of the nanomedicine phototherapy approach, while identifying clear opportunities for further optimization.

Future directions should prioritize biodegradable nanocarrier development, mechanistic characterization using advanced single-cell and computational methods, systematic integration with immunotherapy to leverage phototherapy-induced ICD, and AI-assisted treatment optimization.[17,47] International collaborative networks supporting standardized evaluation protocols and multicenter clinical trials will be essential for accelerating knowledge generation and clinical implementation.

Nanomedicine-integrated phototherapy offers spatiotemporal control, tumor selectivity, and theranostic capability that address fundamental limitations of conventional cancer treatment. Realizing this clinical potential demands continued interdisciplinary innovation, rigorous translational validation, and strategic engagement with regulatory processes. The ongoing convergence of nanotechnology, photochemistry, tumor biology, and immunology constitutes a productive and evolving frontier in cancer therapeutics, provided that translational ambitions are grounded in realistic assessment of the gap between preclinical promise and clinical evidence.

Data Sharing Statement

Data sharing is not applicable to this article as no new data were created or analyzed. All data analyzed are from previously published sources cited in the reference list.

Ethics Approval

Ethics approval was not required for this systematic review, which analyzed previously published literature.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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References

1. Wang H, Naghavi M, Allen C. et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016;388:1459–1544.
2. Saeed M, Shoaib A, Kandimalla R, et al. Microbe-based therapies for colorectal cancer: advantages and limitations. *Semin Cancer Biol*. 2022;86:652–665. doi:10.1016/j.semcancer.2021.05.018
3. Nirmala MJ, Kizhuveetil U, Johnson A, et al. Cancer nanomedicine: a review of nano-therapeutics and challenges ahead. *RSC Adv*. 2023;13 (13):8606–8629. doi:10.1039/D2RA07863E
4. Shoaib A, Tabish M, Ali S, et al. Dietary phytochemicals in cancer signalling pathways: role of miRNA targeting. *Curr Med Chem*. 2021;28 (39):8036–8067. doi:10.2174/0929867328666210420101605
5. Bhushan A, Gonsalves A, Menon JU. Current state of breast cancer diagnosis, treatment, and theranostics. *Pharmaceutics*. 2021;13(5):723. doi:10.3390/pharmaceutics13050723
6. Cook AB, Decuzzi P. Harnessing endogenous stimuli for responsive materials in theranostics. *ACS Nano*. 2021;15(2):2068–2098. doi:10.1021/acsnano.0c09115
7. Mohapatra A, Uthaman S, Park IK. External and internal stimuli-responsive metallic nanotherapeutics for enhanced anticancer therapy. *Front Mol Biosci*. 2021;7:597634. doi:10.3389/fmolb.2020.597634
8. Paszko E, Ehrhardt C, Senge MO, et al. Nanodrug applications in photodynamic therapy. *Photodiagn Photodyn Ther*. 2011;8(1):14–29. doi:10.1016/j.pdpdt.2010.12.001
9. Yoo SW, Oh G, Ahn JC, et al. Non-oncologic applications of nanomedicine-based phototherapy. *Biomedicines*. 2021;9(2):113. doi:10.3390/biomedicines9020113
10. Garg T, Jain NK, Rath G, Goyal A. Nanotechnology-based photodynamic therapy: concepts, advances, and perspectives. *Crit Rev Ther Drug Carrier Syst*. 2015;32(5):389–439. doi:10.1615/CritRevTherDrugCarrierSyst.2015011645
11. He X, Zhang S, Tian Y, et al. Research progress of nanomedicine-based mild photothermal therapy in tumors. *Int J Nanomed*. 2023;18:1433–1468. doi:10.2147/IJN.S405020

12. Li J, Wang S, Fontana F, et al. Nanoparticles-based phototherapy systems for cancer treatment: current status and clinical potential. *Bioact Mater*. 2023;23:471–507. doi:10.1016/j.bioactmat.2022.11.013
13. Ji B, Wei M, Yang B. Recent advances in nanomedicines for photodynamic therapy (PDT)-driven cancer immunotherapy. *Theranostics*. 2022;12 (1):1879–1909. doi:10.7150/thno.67300
14. Li Y, Li X, Zhou F, et al. Nanotechnology-based photoimmunological therapies for cancer. *Cancer Lett*. 2019;442:429–438. doi:10.1016/j.canlet.2018.10.044
15. Gunaydin G, Gedik ME, Ayan S. Photodynamic therapy for the treatment and diagnosis of cancer: a review of the current clinical status. *Front Chem*. 2021;9:686303. doi:10.3389/fchem.2021.686303
16. Alsaab HO, Alghamdi MS, Alotaibi AS, et al. Progress in clinical trials of photodynamic therapy for solid tumors and the role of nanomedicine. *Cancers*. 2020;12(10):2793. doi:10.3390/cancers12102793
17. Liu Z, Xie Z, Li W, et al. Photodynamic immunotherapy of cancers based on nanotechnology: recent advances and future challenges. *J Nanobiotechnology*. 2021;19(1):160. doi:10.1186/s12951-021-00903-7
18. Subhan MA, Yalamarky SSK, Filipczak N, et al. Recent advances in tumor targeting via EPR effect for cancer treatment. *J Pers Med*. 2021;11 (6):571. doi:10.3390/jpm11060571
19. Fang J, Islam W, Maeda H. Exploiting the dynamics of the EPR effect and strategies to improve the therapeutic effects of nanomedicines by using EPR effect enhancers. *Adv Drug Deliv Rev*. 2020;157:142–160. doi:10.1016/j.addr.2020.06.005
20. Zhang C, Wang X, Du J, et al. Reactive oxygen species-regulating strategies based on nanomaterials for disease treatment. *Adv Sci*. 2021;8 (3):2002797. doi:10.1002/advs.202002797
21. Wang C, Zhang S. Advantages of nanomedicine in cancer therapy: a review. *ACS Appl Nano Mater*. 2023;6(24):22594–22610. doi:10.1021/acsanm.3c04487
22. Bhatia SN, Chen X, Dobrovolskaia MA, Lammers T. Cancer nanomedicine. *Nat Rev Cancer*. 2022;22(10):550–556. doi:10.1038/s41568-022-00496-9
23. Yoon I, Li JZ, Shim YK. Advance in photosensitizers and light delivery for photodynamic therapy. *Clin Endosc*. 2013;46(1):7–23. doi:10.5946/ce.2013.46.1.7
24. Bai X, Wang Y, Song Z, et al. The basic properties of gold nanoparticles and their applications in tumor diagnosis and treatment. *Int J Mol Sci*. 2020;21(7):2480. doi:10.3390/ijms21072480
25. Cha C, Shin SR, Annabi N, et al. Carbon-based nanomaterials: multifunctional materials for biomedical engineering. *ACS Nano*. 2013;7 (4):2891–2897. doi:10.1021/nn401196a
26. Bhattacharyya S, Kudgus RA, Bhattacharya R, Mukherjee P. Inorganic nanoparticles in cancer therapy. *Pharm Res*. 2011;28(2):237–259. doi:10.1007/s11095-010-0318-0
27. Tabish TA, Zhang S, Winyard PG. Developing the next generation of graphene-based platforms for cancer therapeutics: the potential role of reactive oxygen species. *Redox Biol*. 2018;15:34–40. doi:10.1016/j.redox.2017.11.018
28. He J, Li C, Ding L, et al. Tumor targeting strategies of smart fluorescent nanoparticles and their applications in cancer diagnosis and treatment. *Adv Mater*. 2019;31(40):1902409. doi:10.1002/adma.201902409
29. Raj S, Khurana S, Choudhari R, et al. Specific targeting cancer cells with nanoparticles and drug delivery in cancer therapy. *Semin Cancer Biol*. 2021;69:166–177. doi:10.1016/j.semcancer.2019.11.002
30. Duong T, Li X, Yang B, et al. Phototheranostic nanoplatform based on a single cyanine dye for image-guided combinatorial phototherapy. *Nanomedicine*. 2017;13(3):955–963. doi:10.1016/j.nano.2016.11.005
31. Jokerst JV, Gambhir SS. Molecular imaging with theranostic nanoparticles. *Acc Chem Res*. 2011;44(10):1050–1060. doi:10.1021/ar200106e
32. Fu Q, Zhu R, Song J, et al. Photoacoustic imaging: contrast agents and their biomedical applications. *Adv Mater*. 2019;31(6):1805875. doi:10.1002/adma.201805875
33. Zhou Z, Song J, Nie L, Chen X. Reactive oxygen species generating systems meeting challenges of photodynamic cancer therapy. *Chem Soc Rev*. 2016;45(23):6597–6626. doi:10.1039/C6CS00271D
34. Agostinis P, Berg K, Cengel KA, et al. Photodynamic therapy of cancer: an update. *CA Cancer J Clin*. 2011;61(4):250–281. doi:10.3322/caac.20114
35. Yang B, Chen Y, Shi J. Reactive oxygen species (ROS)-based nanomedicine. *Chem Rev*. 2019;119(8):4881–4985. doi:10.1021/acs.chemrev.8b00626
36. Dreaden EC, Alkilany AM, Huang X, et al. The golden age: gold nanoparticles for biomedicine. *Chem Soc Rev*. 2012;41(7):2740–2779. doi:10.1039/c1cs15237h
37. Vines JB, Yoon JH, Ryu NE, et al. Gold nanoparticles for photothermal cancer therapy. *Front Chem*. 2019;7:167. doi:10.3389/fchem.2019.00167
38. Hwang Y, Park SH, Lee JW. Applications of functionalized carbon nanotubes for the therapy and diagnosis of cancer. *Polymers*. 2017;9(1):13. doi:10.3390/polym9010013
39. Qi K, Sun B, Liu SY, Zhang M. Research progress on carbon materials in tumor photothermal therapy. *Biomed Pharmacother*. 2023;165:115070. doi:10.1016/j.biopha.2023.115070
40. Karami MH, Abdouss M, Rahdar A, Pandey S. Graphene quantum dots: background, synthesis methods, and applications as nanocarriers in drug delivery and cancer treatment. *Inorg Chem Commun*. 2024;161:112032. doi:10.1016/j.inoche.2024.112032
41. Wang X, Zhong X, Li J, et al. Inorganic nanomaterials with rapid clearance for biomedical applications. *Chem Soc Rev*. 2021;50(15):8669–8742. doi:10.1039/d0cs00461h
42. Jiao M, Zhang P, Meng J, et al. Recent advancements in biocompatible inorganic nanoparticles towards biomedical applications. *Biomater Sci*. 2018;6(4):726–745. doi:10.1039/C7BM01020F
43. Li L, Han X, Wang M, et al. Recent advances in the development of near-infrared organic photothermal agents. *Chem Eng J*. 2021;417:128844. doi:10.1016/j.cej.2021.128844
44. Zheng Q, Liu X, Zheng Y, et al. The recent progress on metal-organic frameworks for phototherapy. *Chem Soc Rev*. 2021;50(8):5086–5125. doi:10.1039/D1CS00056J
45. Cai X, Xie Z, Ding B, et al. Monodispersed copper(I)-based nano metal-organic framework as a biodegradable drug carrier with enhanced photodynamic therapy efficacy. *Adv Sci*. 2019;6(15):1900848. doi:10.1002/advs.201900848
46. Xiao L, Gu L, Howell SB, Sailor MJ. Porous silicon nanoparticle photosensitizers for singlet oxygen and their phototoxicity against cancer cells. *ACS Nano*. 2011;5(5):3651–3659. doi:10.1021/nn1035262

47. Xie Q, Tang J, Guo S, et al. Recent progress of preparation strategies in organic nanoparticles for cancer phototherapeutics. *Molecules*. 2023;28 (16):6038. doi:10.3390/molecules28166038
48. Sarfraz N, Khan I. Plasmonic gold nanoparticles (AuNPs): properties, synthesis and their advanced energy, environmental and biomedical applications. *Chem Asian J*. 2021;16(7):720–742. doi:10.1002/asia.202001202
49. Rastinehad AR, Anastos H, Wajswol E, et al. Gold nanoshell-localized photothermal ablation of prostate tumors in a clinical pilot device study. *Proc Natl Acad Sci USA*. 2019;116(37):18590–18596. doi:10.1073/pnas.1906929116
50. Kennedy LC, Bickford LR, Lewinski NA, et al. A new era for cancer treatment: gold-nanoparticle-mediated thermal therapies. *Small*. 2011;7 (2):169–183. doi:10.1002/smll.201000134
51. Alkac OS, Tuncel ME, Saracoglu O, Belguzar S. Silver nanoparticle and cold storage improves postharvest quality of cut gerbera (Gerbera jamesonii L.). *ISPEC J Agric Sci*. 2025;9(2):434–446. doi:10.5281/zenodo.15010913
52. Oguz T. Efficient Congo red photodegradation via Fe-doped CdS@carbon quantum dots under visible light irradiation. *ISPEC J Agric Sci*. 2025;9 (1):704–716.
53. Alan FN, Colak AM. Phytochemical and antioxidant characterization of myrtle (*Myrtus communis* L.) fruit. *ISPEC J Agric Sci*. 2025;9 (4):1182–1193.
54. Benov L. Photodynamic therapy: current status and future directions. *Med Princ Pract*. 2014;24(Suppl. 1):14–28. doi:10.1159/000362416
55. Egusquiaguirre SP, Igartua M, Hernandez RM, Pedraz JL. Nanoparticle delivery systems for cancer therapy: advances in clinical and preclinical research. *Clin Transl Oncol*. 2012;14(2):83–93. doi:10.1007/s12094-012-0766-6
56. Liu WL, Zou MZ, Liu T, et al. Expandable immunotherapeutic nanoplatforms engineered from cytomembranes of hybrid cells derived from cancer and dendritic cells. *Adv Mater*. 2019;31(18):1900499. doi:10.1002/adma.201900499
57. Wan Y, Fu LH, Li C, et al. Conquering the hypoxia limitation for photodynamic therapy. *Adv Mater*. 2021;33(48):2103978. doi:10.1002/ adma.202103978
58. Fan W, Huang P, Chen X. Overcoming the Achilles heel of photodynamic therapy. *Chem Soc Rev*. 2016;45(23):6488–6519. doi:10.1039/ C6CS00616G
59. Mir SA, Hamid L, Bader GN, et al. Role of nanotechnology in overcoming multidrug resistance in cancer therapy: a review. *Molecules*. 2022;27 (19):6608. doi:10.3390/molecules27196608
60. Zhao Z, Ukidve A, Krishnan V, Mitragotri S. Effect of physicochemical and surface properties on in vivo fate of drug nanocarriers. *Adv Drug Deliv Rev*. 2019;143:3–21. doi:10.1016/j.addr.2019.01.002
61. Anastasiadis SH, Chrissopoulou K, Stratakis E, et al. How the physicochemical properties of manufactured nanomaterials affect their performance in dispersion and their applications in biomedicine: a review. *Nanomaterials*. 2022;12(3):552. doi:10.3390/nano12030552
62. Bhole R, Bonde C, Kadam P, Wavwale R. A comprehensive review on photodynamic therapy (PDT) and photothermal therapy (PTT) for cancer treatment. *Turk Onkoloji Dergisi*. 2021;36:125–132.
63. Zackrisson S, Van De Ven S, Gambhir S. Light in and sound out: emerging translational strategies for photoacoustic imaging. *Cancer Res*. 2014;74 (4):979–1004. doi:10.1158/0008-5472.CAN-13-2387
64. Upputuri PK, Pramanik M. Recent advances toward preclinical and clinical translation of photoacoustic tomography: a review. *J Biomed Opt*. 2017;22(4):041006. doi:10.1117/1.JBO.22.4.041006
65. Lytton-Jean AK, Kauffman KJ, Kaczmarek JC, Langer R. Cancer nanotherapeutics in clinical trials. In: *Nanotechnology-Based Precision Tools for the Detection and Treatment of Cancer*. 2015:293–322.
66. Khizar S, Alrushaid N, Khan FA, et al. Nanocarriers based novel and effective drug delivery system. *Int J Pharm*. 2023;632:122570. doi:10.1016/j. ijpharm.2022.122570
67. Adepu S, Ramakrishna S. Controlled drug delivery systems: current status and future directions. *Molecules*. 2021;26(19):5905. doi:10.3390/ molecules26195905
68. Bessiere A, Durand JO, Nous C. Persistent luminescence materials for deep photodynamic therapy. *Nanophotonics*. 2021;10(12):2999–3029. doi:10.1515/nanoph-2021-0254
69. Sun W, Zhou Z, Pratx G, et al. Nanoscintillator-mediated X-ray induced photodynamic therapy for deep-seated tumors: from concept to biomedical applications. *Theranostics*. 2020;10(3):1296–1314. doi:10.7150/thno.41578
70. Escudero A, Carrillo-Carrion C, Castillejos MC, et al. Photodynamic therapy: photosensitizers and nanostructures. *Mater Chem Front*. 2021;5 (10):3788–3812. doi:10.1039/D0QM00922A
71. Plekhova N, Shevchenko O, Korshunova O, et al. Development of novel tetrapyrrole structure photosensitizers for cancer photodynamic therapy. *Bioengineering*. 2022;9(2):82. doi:10.3390/bioengineering9020082
72. Das S, Tiwari M, Mondal D, et al. Growing tool-kit of photosensitizers for clinical and non-clinical applications. *J Mater Chem B*. 2020;8 (48):10897–10940. doi:10.1039/D0TB02085K
73. Li J, Zhang W, Ji W, et al. Near infrared photothermal conversion materials: mechanism, preparation, and photothermal cancer therapy applications. *J Mater Chem B*. 2021;9(38):7909–7926. doi:10.1039/D1TB01310F
74. Vankayala R, Hwang KC. Near-infrared-light-activatable nanomaterial-mediated phototheranostic nanomedicines: an emerging paradigm for cancer treatment. *Adv Mater*. 2018;30(23):1706320. doi:10.1002/adma.201706320
75. Yang M, Chen Y, Zhu L, et al. Harnessing nanotechnology: emerging strategies for multiple myeloma therapy. *Biomolecules*. 2024;14(1):83. doi:10.3390/biom14010083
76. Nahhas AF, Webster TJ. A review of treating viral outbreaks with self-assembled nanomaterial-like peptides: from Ebola to the Marburg virus. *OpenNano*. 2022;8:100094. doi:10.1016/j.onano.2022.100094
77. Gao D, Guo X, Zhang X, et al. Multifunctional phototheranostic nanomedicine for cancer imaging and treatment. *Mater Today Bio*. 2019;5:100035. doi:10.1016/j.mtbio.2019.100035
78. Mousavi-Kiasary SMS, Senabreh A, Zandi A, et al. Synergistic cancer therapies enhanced by nanoparticles: advancing nanomedicine through multimodal strategies. *Pharmaceutics*. 2025;17(6):682. doi:10.3390/pharmaceutics17060682
79. Zhou Y, Wang X, Zhang D, et al. Precision-guided stealth missiles in biomedicine: biological carrier-mediated nanomedicine hitchhiking strategy. *Adv Sci*. 2025;12(21):2504672. doi:10.1002/advs.202504672