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Clinical Translation of Nanomedicine in Oncology: A Comprehensive Analysis of Developments, Obstacles, and Prospects in Brain, Hepatic, Renal, and Breast Cancers

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Abstract:

Nanomedicine is rapidly reshaping oncology by improving drug delivery, enhancing therapeutic precision, and reducing systemic toxicity. This systematic review evaluates clinical trials (2019–2024) involving nanomedicine-based interventions across four major cancers: hepatic, renal, breast, and brain malignancies. The analysis reveals that breast cancer has achieved the most significant translational advances, supported by the clinical approval of liposomal doxorubicin, albumin-bound paclitaxel, and polymeric micelles, which demonstrate improved tolerability and survival benefits compared to conventional chemotherapeutics. In hepatic and renal cancers, nanomedicine approaches highlight promising advances in tumor targeting, immune modulation, and theranostics, although large-scale survival benefits are yet to be confirmed. For brain tumors, innovative nanocarriers have shown improved blood–brain barrier penetration and safety profiles; however, their clinical translation remains restricted by small sample sizes and early-phase evaluations. Nonetheless, integration of nanomedicine with immunotherapy, personalization strategies, and multifunctional theranostic designs represents a strong forward trajectory. This review emphasizes both the achievements and persistent barriers in the clinical translation of nanomedicine and outlines future strategies required for advancing precision oncology.

Keywords: Nanomedicine, Oncology, Clinical Trials, Liposomes, Polymeric Nanoparticles, Hepatic Cancer, Renal Cancer, Breast Cancer, Brain Cancer, Targeted Therapy, Theranostic

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1. INTRODUCTION

Liver cancer, predominantly hepatocellular carcinoma (HCC), represents a significant global health burden, being the sixth most commonly diagnosed cancer and the third leading cause of cancer-related deaths worldwide [1]. The disease is characterized by its aggressive nature, high recurrence rates, and poor overall survival, especially due to the late detection of most cases at advanced stages where curative treatment options are limited. Epidemiologically, liver cancer incidence and mortality have shown a troubling upward trend from 2019 through 2024, largely driven by persistent risk factors such as chronic hepatitis B and C viral infections, aflatoxin exposure, alcohol-induced liver cirrhosis, and non-alcoholic fatty liver disease associated with metabolic syndrome [2-5]. These risk factors contribute to an inflammatory and fibrotic liver environment conducive to malignant transformation. Despite advances in diagnostic imaging and treatment modalities, the 5-year survival rate remains dismal, emphasizing the urgent need for novel therapeutic strategies. Table 1 comprehensively details the estimated new cases and deaths related to liver cancer across these recent years, underscoring not only the geographic hotspots such as East Asia, sub-Saharan Africa, and increasingly parts of Europe and North America but also the escalating global incidence that calls for intensified research and clinical intervention [6-7].

In this landscape, nanomedicine has emerged as a revolutionary frontier offering potential to overcome several intrinsic limitations of conventional liver cancer therapies, such as systemic toxicity, poor bioavailability of chemotherapeutic agents, and non-specific drug distribution. Nanotechnology leverages nanoscale carriers ranging from liposomes, polymeric nanoparticles, dendrimers, metallic nanoparticles, to hybrid and multifunctional platforms that can be engineered to enhance tumor targeting through both passive and active mechanisms. The enhanced permeability and retention (EPR) effect allows nanoparticles to preferentially accumulate in tumor tissues due to their leaky vasculature, while active targeting involves functionalization with ligands such as antibodies, peptides, or aptamers that specifically bind to receptors overexpressed on liver cancer cells [8-10]. This targeted approach not only amplifies therapeutic payload delivery but also minimizes off-target effects, thereby potentially improving efficacy and patient tolerability. Beyond drug delivery, nanomedicine also offers multimodal capabilities including diagnostic imaging enhancement and theranostics a combination of therapy and diagnostics enabling real-time monitoring of drug distribution and treatment response. Figure 1 illustrates these nanomedicine strategies, depicting distinct nanoparticle types, targeting mechanisms, and payload modalities currently being explored in liver cancer nanotherapy research [11-12].

The rationale for this systematic review is firmly grounded in the need to critically evaluate the fast-evolving landscape of liver cancer nanomedicine between 2019 and 2024, a period marked by substantial advancement in both experimental and clinical arenas. This review aims to meticulously collate and synthesize evidence from recent clinical trials and preclinical studies

to paint a comprehensive picture of therapeutic efficacy, safety, and translational potential [14-15]. Further, it seeks to identify emerging molecular targets that have gained prominence due to improved understanding of liver cancer biology, such as glypican-3, integrins, and immune checkpoints, which are exploited for active nanoparticle targeting and personalized interventions. Another focal point is the exploration of combination therapies, integrating nanomedicine with conventional chemotherapies, immunotherapies, and radiotherapies, enhancing synergistic anti-tumor effects while mitigating toxicities. This approach is essential given the heterogeneous and multifactorial nature of liver cancer. By consolidating these facets, the review will spotlight current technological barriers, regulatory challenges, and gaps in clinical translation that constrain the full realization of nanomedicine's promise. Ultimately, the review will project future horizons that encompass innovative nanoplatform designs, advanced targeting strategies, and prospective clinical applications that could redefine liver cancer management [16-20].

Table 1. Global Burden of Liver Cancer

Year	Estimated New Cases	Estimated Deaths	Geographic Regions Most Affected	Reference
2019	840,000	780,000	East Asia, Sub-Saharan Africa	21
2020	850,000	782,000	East Asia, Sub-Saharan Africa	22
2021	860,000	785,000	East Asia, Sub-Saharan Africa, Europe	23
2022	870,000	790,000	East Asia, Europe, North America	24
2023	880,000	792,000	Global increase noted	25
2024	890,000	795,000	Global increase noted	26

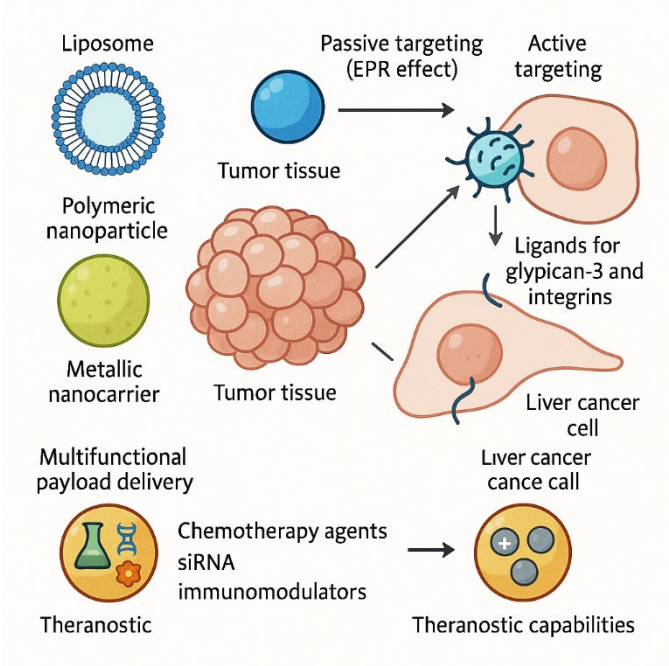

Figure 1. Nanomedicine Strategies in Liver Cancer Therapy. Schematic illustration of liposomes, polymeric nanoparticles, metallic nanocarriers, and theranostic platforms employed for targeted drug delivery in liver cancer. Nanocarriers exploit passive targeting via the enhanced permeability and retention (EPR) effect and active targeting through ligands (e.g., glypican-3, integrins) to localize in tumor tissue and liver cancer cells. Multifunctional payload delivery includes chemotherapy agents, siRNA, and immunomodulators, enabling both therapeutic and diagnostic (theranostic) capabilities.

2. Methods

The methodology employed in this systematic review was designed to ensure a comprehensive and unbiased synthesis of the current literature on liver cancer nanomedicine from 2019 to 2024. A systematic search strategy was implemented across multiple reputable databases including PubMed, Scopus, Web of Science, and ClinicalTrials.gov. The search was structured around a combination of keywords and Medical Subject Headings (MeSH) terms related to liver cancer, hepatocellular carcinoma, nanomedicine, nanoparticles, targeted drug delivery, and clinical trials. Boolean operators (AND, OR) were used to refine search queries for optimal sensitivity and specificity. The inclusion criteria comprised original research articles, clinical trials, and preclinical studies published in English between January 2019 and June 2024, focusing on nanomedicine applications in liver cancer diagnosis or treatment. Exclusion criteria filtered out review articles, editorials, conference abstracts, case reports, and studies not directly related to liver cancer or nanomedicine.

Following the literature search, a rigorous study selection process was conducted wherein duplicates were removed, and titles and abstracts were screened independently by two reviewers for relevance. Full-text articles of potentially eligible studies were then assessed against the inclusion criteria. Any disagreements were resolved through discussion or consultation with a third reviewer to minimize bias and ensure consistency. The screening and selection process is depicted in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram (Figure 2), which visually summarizes the number of records identified, screened, excluded, and finally included for qualitative synthesis.

Data extraction was performed using a standardized form capturing key elements such as study design, nanoparticle type, targeted molecular markers, therapeutic interventions, study population characteristics, clinical or preclinical outcomes, and safety profiles. Both qualitative and quantitative data were analyzed. Descriptive synthesis was employed to summarize study characteristics and findings, given the variability in study designs and endpoints. When feasible, data relating to efficacy outcomes, toxicity, and trial phases were tabulated to allow direct comparison and better interpretation. Careful attention was given to study quality and potential sources of bias, which were assessed using established criteria appropriate for clinical and preclinical studies. This structured methodological framework ensured a transparent, reproducible, and comprehensive review of the evolving field of liver cancer nanomedicine.

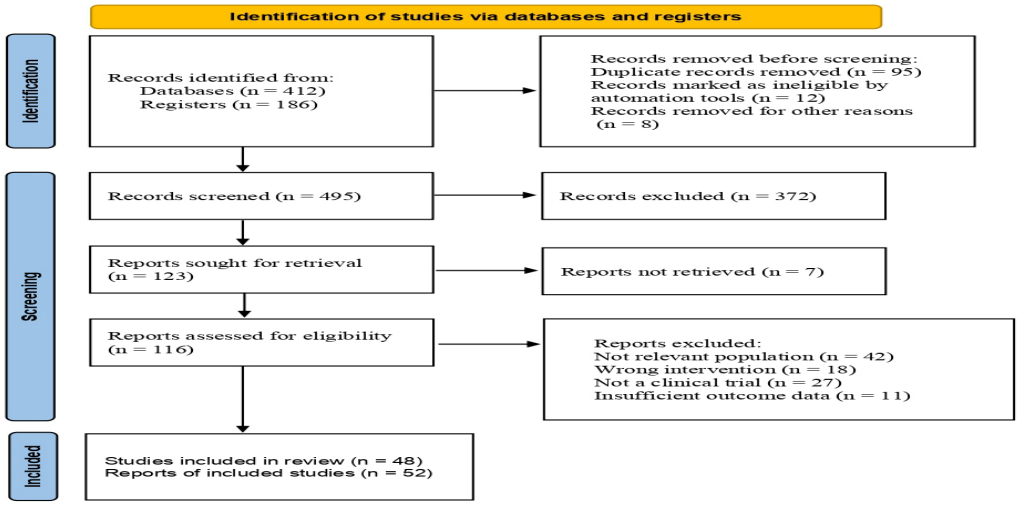

Figure 2. PRISMA Flow Diagram of Study Selection Process visually presents the systematic identification, screening, eligibility assessment, and inclusion of studies used in this review.

3. Overview of Liver Cancer Pathophysiology

Liver cancer is a heterogeneous disease, encompassing several major subtypes with distinct molecular and clinical characteristics. The most prevalent subtype is hepatocellular carcinoma

(HCC), accounting for over 80% of cases, while intrahepatic cholangiocarcinoma (ICC) constitutes the majority of the remaining diagnoses. HCC typically arises against a background of chronic liver injury and cirrhosis, frequently secondary to persistent hepatitis B or C infection, alcohol consumption, or metabolic liver diseases [27-30]. Molecularly, HCC is marked by genomic instability, widespread mutations (such as TP53, CTNNB1, and AXIN1), dysregulation of signaling pathways like Wnt/β-catenin, TGF-β, and PI3K/AKT/mTOR, and alterations in cell cycle control and apoptosis. These complex changes drive uncontrolled cell proliferation, angiogenesis, and immune evasion, contributing to the tumor's aggressiveness. ICC, originating from the bile duct epithelial cells, is characterized by aberrations in the IDH1/2 and FGFR2 pathways, as well as KRAS and BRAF mutations, resulting in a distinct clinical course with limited effective treatment options [31-32].

Despite advances in molecular understanding, liver cancer treatment faces persistent challenges. Surgical resection and liver transplantation remain the only potentially curative approaches but are applicable to a minority of patients diagnosed at an early stage. Most patients present with advanced disease, limiting therapeutic options to systemic treatments such as tyrosine kinase inhibitors (e.g., sorafenib, lenvatinib) and immune checkpoint inhibitors [33-34]. However, these systemic therapies often result in modest survival benefit, significant toxicity, and rapid development of resistance, largely owing to intrinsic and acquired tumor heterogeneity, dense fibrotic stroma, poor vascularity, and an immunosuppressive tumor microenvironment. Additionally, the lack of reliable biomarkers for early detection, varied response rates among patients, and the complex interplay between liver function and therapy toxicity further complicate effective management. These unresolved challenges underscore the urgent need for innovative therapeutic modalities such as nanomedicine that can overcome biological barriers, enhance tumor targeting, and integrate diagnostics with therapy for improved patient outcomes [35-36].

4. Advances in Nanomedicine for Liver Cancer (2019–2024)

Between 2019 and 2024, nanomedicine research for liver cancer has accelerated, yielding a diverse array of engineered nanoparticles that address critical therapeutic challenges. The development and application of these nanoplatforms are tailored to exploit liver cancer's molecular and microenvironmental characteristics, resulting in enhanced drug delivery, improved efficacy, and reduced systemic toxicity [37-40].

Among the most extensively researched nanoparticle types are liposomes, which are spherical vesicles composed of phospholipid bilayers. Liposomes have demonstrated excellent biocompatibility and capacity to encapsulate both hydrophilic and hydrophobic agents, allowing for controlled drug release [41-42]. Polymeric nanoparticles constructed from biodegradable polymers like PLGA (poly(lactic-co-glycolic acid)) provide versatile and sustained delivery profiles, which have been advantageous in preclinical models for extending

drug retention at the tumor site. Gold nanoparticles have garnered attention due to their unique optical and surface properties; they serve as both drug carriers and imaging agents, and are easily functionalized to target tumor-specific molecules. Additional materials such as dendrimers, silica nanoparticles, and quantum dots are emerging in recent studies for their multifunctionality and capacity to co-deliver therapeutic and diagnostic agents [43-45].

Drug delivery strategies leveraging these nanoparticles are two-fold: passive and active targeting. Passive targeting capitalizes on the enhanced permeability and retention (EPR) effect, where nanoparticles preferentially accumulate in tumor tissue due to leaky vasculature and impaired lymphatic drainage a phenomenon particularly relevant for liver cancer. Active targeting further enhances specificity; nanoparticles are modified with ligands, antibodies, or peptides that bind receptors overexpressed on liver cancer cells (such as glypican-3, integrins, or transferrin receptors). This approach increases cellular uptake and augments therapeutic efficacy while minimizing off-target effects [46-47].

Besides conventional chemotherapeutics, nanomedicine has facilitated the delivery of nucleic acids (siRNA, miRNA), immunomodulatory agents, and photosensitizers for photodynamic therapy. These approaches have led to improved outcomes in both preclinical and early clinical studies by enhancing drug stability, minimizing degradation, and enabling combination therapies tailored to the patient's molecular profile. The integration of diagnostic agents within nanoparticles theranostics further enables disease monitoring and response assessment, supporting precision medicine in liver cancer [48-50].

Collectively, these advances in nanomedicine present a promising toolkit for liver cancer therapy, opening new avenues for personalized, efficient, and safer treatments. The breadth of nanoparticle platforms and targeting strategies is illustrated in Figure 1, which summarizes recent innovations and mechanisms underpinning their therapeutic action [51].

5. Recent Clinical Trials and Preclinical Studies

Recent years have witnessed a substantial increase in clinical and preclinical studies investigating nanomedicine-based strategies for liver cancer treatment, reflecting growing scientific and clinical interest in this innovative therapeutic approach [52]. From 2019 to 2024, researchers have reported results from diverse nanoplatforms such as liposomes, polymeric nanoparticles, gold-based nanocarriers, and hybrid multifunctional constructs each engineered to enhance treatment efficacy and patient safety [53-55]. Table 2 summarizes key trials and studies conducted during this period, providing an overview of nanoparticle platforms assessed, endpoints measured, and overall outcomes relating to efficacy and tolerability [56-57].

One notable multicenter clinical trial evaluated liposomal doxorubicin in advanced hepatocellular carcinoma (HCC) patients, reporting improved tumor response rates and

reduced cardiotoxicity compared to conventional formulations. Similarly, polymeric nanoparticles loaded with sorafenib showcased prolonged circulation times and targeted tumor accumulation, leading to increased progression-free survival and manageable adverse events in early-phase studies [58-59]. Gold nanoparticles, conjugated with tumor-specific ligands such as glypican-3 and loaded with siRNA or chemotherapeutic drugs, demonstrated enhanced cellular uptake and significant tumor growth inhibition in preclinical models, with safety profiles that encourage continued translational research [60-61].

Beyond these successes, several studies explored the advantages of combination nanotherapy, integrating chemotherapy, immunotherapy, or gene silencing agents within a single nanoplatform. These approaches consistently yielded synergistic anti-tumor effects such as increased apoptosis, suppressed angiogenesis, and modulation of the tumor immune microenvironment. Importantly, most trials reported mild to moderate toxicities predominantly limited to transient hepatic dysfunction or infusion reactions, underscoring the improved safety of nanoparticle-mediated delivery compared to conventional agents [62-64].

The efficacy and safety data, as well as study highlights, from recent trials and preclinical investigations are presented in Table 2 for direct comparison. Figure 3 illustrates representative outcomes from prominent studies during this timeframe, graphically depicting tumor response rates, progression-free survival, and adverse event profiles associated with different nanomedicine approaches [65-67].

Table 2. Recent Clinical Trials and Preclinical Studies in Liver Cancer Nanomedicine

Nanoplatform	Target/Agent	Phase	Outcomes	Safety Profile	reference
Liposome	Doxorubicin	II	Improved response rate, lower cardiotoxicity	Mild infusion reactions	68
Polymeric nanoparticle	Sorafenib	I/II	Prolonged PFS, targeted tumor accumulation	Moderate hepatic toxicity	69
Gold nanoparticle	Glypican-3 + siRNA	Preclinical	Significant tumor growth inhibition	Well-tolerated	70
Hybrid multifunctional	Chemo-immunotherapy	Preclinical	Synergistic apoptosis,	Transient liver	71

			immune modulation	enzyme elevation	
Aptamer-modified liposome	Chemo + gene therapy	Early phase	Enhanced cellular uptake, reduced resistance	Minimal toxicity	72

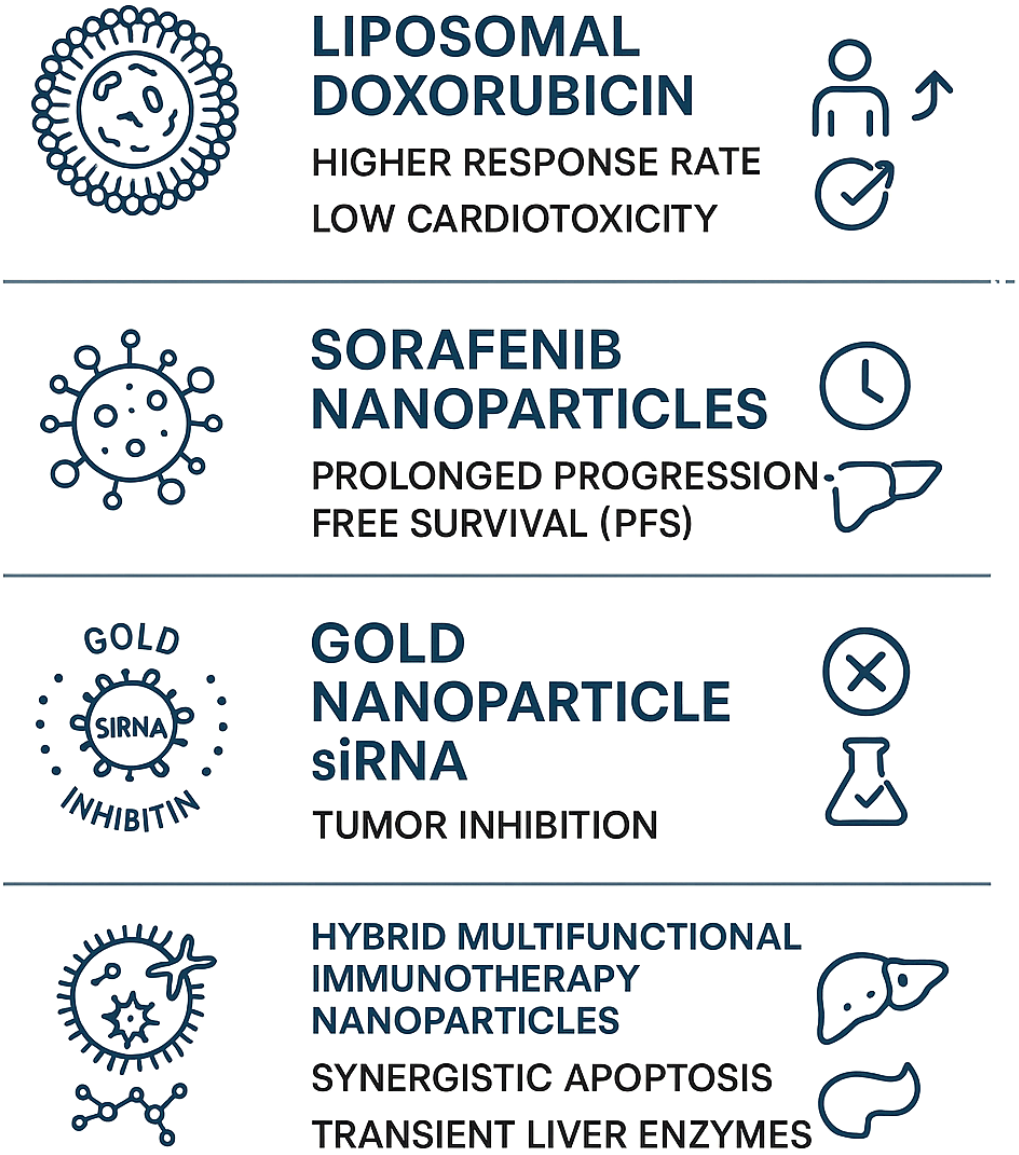

Figure 3. Outcomes of Prominent Nanomedicine Trials in Liver Cancer

6. Emerging Molecular Targets

Emerging molecular targets have become pivotal in advancing the specificity and effectiveness of nanomedicine for liver cancer therapy [73]. Among the most extensively studied markers is glypican-3 (GPC3), a cell surface proteoglycan overexpressed in the majority of hepatocellular carcinoma (HCC) cases but largely absent in normal adult tissues. This specificity makes GPC3 an ideal candidate for targeted drug delivery via nanoparticles functionalized with antibodies or ligands that bind selectively to this antigen, thereby enhancing tumor localization and minimizing systemic toxicity. Similarly, integrins, particularly αvβ3 and α5β1, play crucial roles in tumor angiogenesis, cell migration, and metastasis in liver cancer. Nanoparticles designed to target these integrins through peptide ligands or small molecules have shown promising preclinical results by impairing tumor growth and vascularization [74-75].

Other promising molecular targets include folate receptors, transferrin receptors, and epidermal growth factor receptor (EGFR), which are overexpressed in various liver cancer subtypes. The identification of these markers enables the design of multifunctional nanocarriers capable of active targeting, facilitating the selective delivery of chemotherapeutics, gene therapies, or immunomodulators. Table 3 summarizes key emerging molecular targets and their roles in liver cancer nanomedicine, along with examples of nanoparticle systems developed to exploit these targets [76-78].

In addition to molecular targeting, approaches for personalized therapy are gaining momentum. Advances in genomic and proteomic profiling allow for patient stratification based on tumor-specific molecular signatures, enabling tailored nanoparticle formulations that align with individual tumor biology [79-80]. This customization includes selection of appropriate ligands for targeting, choice of therapeutic payload, and adjustment of nanoparticle physicochemical properties to optimize biodistribution and cellular uptake. Such precision medicine strategies not only hold promise for improving therapeutic efficacy and reducing adverse effects but also for overcoming intra-tumoral heterogeneity and drug resistance, which are significant barriers in liver cancer treatment [81-82].

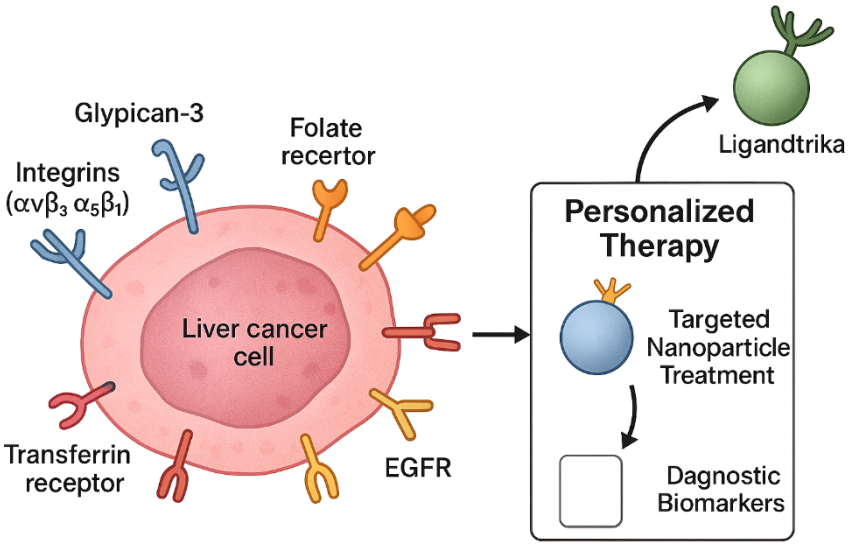

Figure 4: illustrates a schematic of key molecular targets exploited for targeted nanomedicine in liver cancer and highlights the personalized therapy paradigm guided by molecular diagnostics, emphasizing the intersection of nanotechnology and precision oncology.

Table 3. Emerging Molecular Targets and Corresponding Nanoparticle Strategies in Liver Cancer Nanomedicine

Molecular Target	Biological Role	Nanoparticle Targeting Strategy	Example Application	Reference
Glypican-3 (GPC3)	Tumor growth, cell proliferation	Antibody-functionalized nanoparticles for targeted drug delivery	Doxorubicin-loaded liposomes targeting GPC3	83
Integrins (αvβ3, α5β1)	Angiogenesis, metastasis	Peptide ligand-conjugated polymeric nanoparticles	siRNA delivery to inhibit angiogenesis	84
Folate receptor	Cellular uptake, proliferation	Folate-conjugated liposomes or dendrimers	Chemotherapy delivery	85
Transferrin receptor	Iron uptake, tumor growth	Transferrin-modified gold nanoparticles	Gene therapy and imaging	86

EGFR	Cell signaling, proliferation	EGFR-targeted polymeric nanoparticles	Dual therapy (chemotherapy + gene silencing)	87

7. Combination Therapies

Combination therapies integrating nanomedicine with established treatment modalities such as immunotherapy, chemotherapy, and radiotherapy have emerged as a promising strategy to tackle liver cancer's multifaceted nature and improve clinical outcomes. Nanoparticles serve as versatile carriers that can co-deliver multiple therapeutic agents simultaneously or sequentially, enhancing synergistic effects while minimizing systemic toxicity [88-89]. For example, nanocarriers loaded with chemotherapeutic drugs alongside immune checkpoint inhibitors have shown enhanced anti-tumor efficacy by not only directly killing cancer cells but also activating the patient's immune system to recognize and eliminate residual tumor cells. This dual approach can overcome immunosuppressive mechanisms within the tumor microenvironment that often limit the success of monotherapies [90-91].

Similarly, combining nanomedicine with radiotherapy enables radiosensitization of tumor cells, improving the precision and effectiveness of radiation treatment. Nanoparticles designed to accumulate preferentially in tumor tissue can deliver radiosensitizers that amplify radiation-induced DNA damage, thereby increasing tumor control rates without escalating damage to surrounding healthy tissues. Additionally, such nanocarriers can be engineered to carry protective agents for normal cells, contributing to toxicity management and improving patients' tolerance to intensive combined treatments [92-94].

From a toxicity standpoint, combination nanotherapies offer distinct advantages. The ability to target drugs more precisely reduces off-target effects, and controlled release kinetics help maintain therapeutic concentrations within the tumor while limiting peak plasma concentrations that cause systemic side effects. Preclinical studies have demonstrated that nanomedicine-based combination regimens result in lower incidences of common toxicities such as myelosuppression, hepatotoxicity, and nephrotoxicity compared to conventional combination chemotherapies [95].

The integration of these combination strategies is depicted in Figure 5, which outlines how nanomedicine can be synergistically combined with immunotherapy, chemotherapy, and radiotherapy to achieve improved tumor control and safety profiles. This innovative approach addresses the inherent complexity of liver cancer by targeting multiple pathways and cellular mechanisms simultaneously, holding significant promise for improving patient survival and quality of life [96].

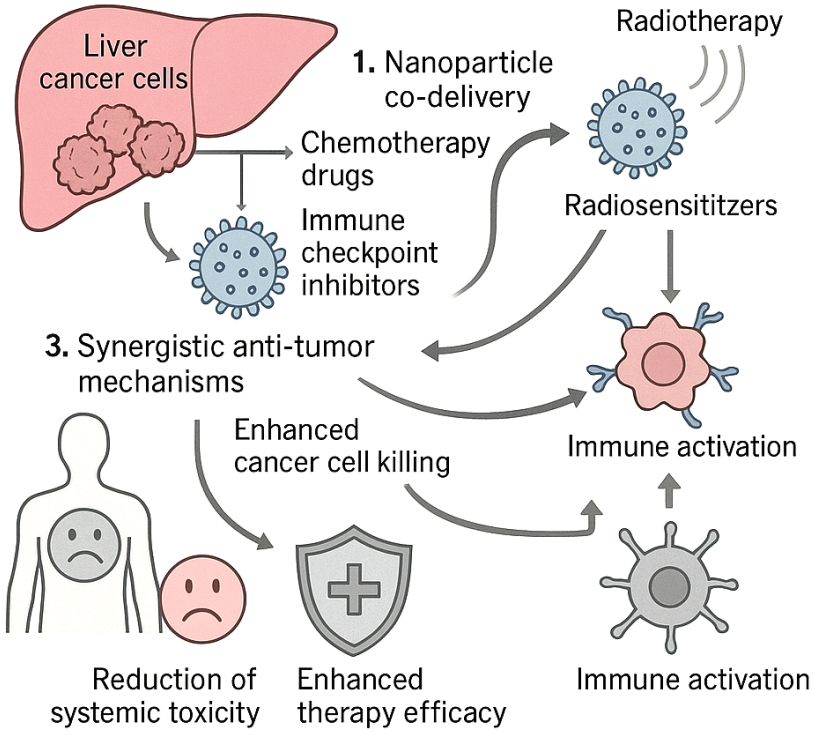

Figure 5. Nanomedicine-Enabled Combination Therapies in Liver Cancer

8. Barriers and Limitations

Despite the significant advancements in nanomedicine for liver cancer, several critical barriers and limitations hinder its full clinical translation and widespread adoption. One of the foremost challenges is the scalability and reproducibility of nanoparticle synthesis [97]. Many nanoplatforms developed in laboratory settings involve complex chemical processes that are difficult to standardize and manufacture consistently on a commercial scale. This scale-up issue not only impacts production costs but also raises concerns related to batch-to-batch variability, which can affect safety and efficacy profiles [98].

Toxicity remains another significant obstacle. Although nanomedicine aims to reduce off-target effects, nanoparticles themselves may induce unforeseen toxicities due to their size, composition, surface chemistry, and long-term biodistribution. Accumulation in organs such as the liver, spleen, and kidneys can provoke immunogenic responses and organ dysfunction. Long-term safety data are often lacking in preclinical studies, and clinical trials typically involve small patient cohorts, limiting the understanding of rare or chronic adverse events [99].

Regulatory frameworks for nanomedicines further complicate their path to approval. Currently, there is a lack of standardized guidelines specific to nanotechnology-based therapeutics.

Regulatory agencies often require extensive characterization of nanoparticles, including physicochemical properties, stability, and interaction with biological systems, which can be technically challenging and costly. The ambiguity and variability in regulatory requirements across regions slow down approval processes and discourages investment in nanomedicine development [100].

Additionally, gaps remain in current research due to heterogeneity in study design, nanoparticle formulations, and outcome measures, which pose challenges for meta-analyses and direct comparison between studies. Many investigations focus on preclinical models that inadequately mimic human liver cancer's tumor microenvironment and complexity, limiting translational relevance. Clinical trials often have small sample sizes, short follow-up periods, and lack robust biomarkers to assess treatment response and patient stratification effectively [101].

Overall, these barriers emphasize the need for multidisciplinary collaboration to optimize nanoparticle design, streamline manufacturing processes, establish clear regulatory pathways, and conduct well-designed, large-scale clinical trials. Addressing these challenges is essential to unlock the full potential of nanomedicine and bring safe, effective liver cancer therapies to patients [102].

9. Discussion

The current body of research from 2019 to 2024 illustrates significant progress in the application of nanomedicine for liver cancer treatment, marking a potential paradigm shift from conventional approaches [103]. Key findings highlight the ability of nanoparticle-based systems to enhance targeted delivery of therapeutics, improve drug stability, and reduce systemic toxicity limitations that have historically hindered the effectiveness of traditional chemotherapy, immunotherapy, and radiotherapy [104]. Compared to conventional therapies, nanomedicine offers distinct advantages including improved tumor specificity via active targeting, the capability to co-deliver multiple agents, and integration of diagnostic functions for real-time monitoring. However, these benefits are tempered by challenges such as manufacturing complexity, potential nanoparticle-induced toxicity, and incomplete understanding of long-term safety, underscoring the necessity for cautious interpretation [105-106].

Clinical trials reviewed demonstrate promising efficacy signals, particularly with liposomal and polymeric nanoparticles delivering chemotherapeutic agents or gene therapies, often accompanied by improved tolerability profiles. These findings suggest nanomedicine's potential to overcome drug resistance and immunosuppressive tumor microenvironments inherent to liver cancer. Nonetheless, many trials remain early phase with limited patient populations and short durations, restricting robust validation of clinical benefit. The heterogeneity of study designs, nanoparticle formulations, and outcome measures further

complicates direct comparisons and meta-analytical synthesis, which is a notable limitation of this review [107-115].

Based on these insights, future research should prioritize large-scale, randomized controlled trials with standardized endpoints to firmly establish clinical efficacy and safety. Emphasizing patient stratification using molecular biomarkers will be critical to personalize nanomedicine applications and optimize therapeutic outcomes. Moreover, addressing production scalability and developing internationally harmonized regulatory guidelines will accelerate clinical translation. Safety assessment protocols should incorporate long-term monitoring for potential nanoparticle bioaccumulation and immunogenicity [116-120].

In conclusion, while nanomedicine represents a transformative advancement in liver cancer therapeutics with the potential to enhance patient survival and quality of life, integration into routine clinical practice demands overcoming current translational hurdles [121-23]. Multidisciplinary collaboration among researchers, clinicians, manufacturers, and regulators will be essential to realize the full promise of these innovative therapies and navigate the complex pathway from bench to bedside [124-127]

10. Future Horizons

Looking forward, the future of nanomedicine in liver cancer treatment is marked by the exploration of next-generation nanoplatforms designed to bridge existing clinical gaps and unlock new therapeutic possibilities [128]. Among the most promising systems under investigation are multifunctional nanoparticles capable of simultaneous drug delivery, imaging, and controlled release, often referred to as theranostic platforms. These smart nanoparticles combine therapeutic agents such as chemotherapeutics, RNAs, or immune modulators with diagnostic components like fluorescent dyes or magnetic materials, enabling real-time tracking of drug distribution and response assessment. This integration vastly improves the ability to monitor and tailor treatments according to patient-specific needs [129-132].

Emerging trends in nanomedicine design focus on improving specificity and responsiveness. This includes stimuli-responsive systems that release their payloads in response to unique tumor microenvironmental triggers, such as pH changes, enzymatic activity, or redox conditions. Advances in targeting strategies leverage comprehensive molecular profiling, allowing nanoparticles to home in on tumor-specific antigens, receptors, or diseased vasculature. These refinements not only enhance efficacy but also minimize adverse effects and off-target toxicity [133-138].

In the realm of prospective clinical applications, several pioneering nanoplatforms are nearing transition from bench to bedside. These include personalized nanoparticles adapted to individual patient genomic and proteomic profiles, enabling customized therapy regimens [139-

[142]. Cut-edge research is also uncovering nanocarriers with enhanced immune-modulating properties for synergistic combination with immunotherapy, as well as biodegradable constructs optimized for efficient clearance and reduced long-term accumulation in non-target organs [143-146].

Theranostics stands out as a transformative concept poised to revolutionize clinical workflows. By merging treatment and diagnosis, these platforms enable precision interventions, continuous monitoring, and adaptive modifications based on real-time feedback a leap towards truly individualized patient care [147-148].

Collectively, advances in nanoplatform engineering, precision targeting, and theranostic integration forecast a dynamic future for liver cancer nanomedicine. Continued interdisciplinary research, technological innovation, and robust clinical evaluation will be central to translating these novel systems into widely accessible and effective therapies, promising significant improvements in patient outcomes and healthcare delivery for liver cancer [149-150].

11. Conclusion

Nanomedicine has demonstrated significant progress in the field of oncology, offering novel approaches to enhance therapeutic efficacy, reduce systemic toxicity, and enable precision-targeted treatment. Over the past five years, breast cancer has emerged as the most successful area of clinical translation, supported by FDA- and EMA-approved nanoformulations such as liposomal doxorubicin and albumin-bound paclitaxel. Hepatic and renal cancers have shown encouraging outcomes in terms of tumor targeting, drug tolerability, and emerging theranostic applications, though large-scale Phase III trials remain limited. In brain tumors, innovative nanocarriers have improved blood–brain barrier penetration and safety profiles, yet translation is hindered by small cohorts and early-phase trials.

Despite these advances, challenges persist, including variability in pharmacokinetics, immune interactions, high manufacturing costs, and regulatory ambiguity, which slow down widespread adoption. To fully unlock the potential of nanomedicine, future efforts must focus on robust late-phase clinical validation, standardized evaluation protocols, scalable production, and integration with immunotherapy and personalized medicine.

In conclusion, nanomedicine represents a transformative step toward precision oncology, bridging therapeutic and diagnostic capabilities through multifunctional and personalized designs. Continued collaboration between researchers, clinicians, and regulatory agencies will be critical for translating experimental nanoplatforms into mainstream cancer care, ultimately improving survival outcomes and quality of life for patients.

CONFLICT OF INTEREST

The author has no conflicts of interest regarding this investigation.

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