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Review Article

Berberine in Cancer Therapy: Emerging Role of Nanoparticle-Based Drug Delivery Systems

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ABSTRACT

Cancer remains one of the leading causes of morbidity and mortality worldwide, prompting the continuous search for more effective and safer therapeutic options. Berberine, a natural isoquinoline alkaloid extracted from various medicinal plants such as *Berberis* species, has garnered significant attention for its multifaceted anticancer properties. It exerts potent cytotoxic effects against a wide range of cancer types by inducing apoptosis, inhibiting cell proliferation, modulating key signaling pathways, and suppressing angiogenesis and metastasis. However, the clinical application of berberine is considerably limited due to its poor aqueous solubility, low oral bioavailability, and rapid systemic elimination. To overcome these challenges, nanotechnology-based drug delivery systems have emerged as a promising strategy to enhance the therapeutic potential of berberine. Various nanoparticle formulations—such as polymeric nanoparticles, liposomes, solid lipid nanoparticles, nanoemulsions, and metallic nanoparticles—have demonstrated improved solubility, enhanced cellular uptake, sustained release, and targeted delivery of berberine to tumor tissues. Preclinical studies have reported superior anticancer efficacy and reduced systemic toxicity of these nanoformulations compared to free berberine. This review comprehensively explores the anticancer potential of berberine, its underlying mechanisms of action, and the advances in nanoparticle-mediated delivery systems. Emphasis is placed on recent developments in berberine-loaded nanocarriers, their pharmacological performance, and translational prospects. While significant progress has been made, further research is warranted to address formulation challenges, scale-up processes, and clinical validation. The integration of nanotechnology with berberine-based therapy holds considerable promise for the future of targeted and effective cancer treatment.

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INTRODUCTION

Cancer continues to be a major public health concern worldwide, representing a leading cause of death and accounting for millions of new cases annually. According to global cancer statistics, the incidence and mortality rates of various cancer types—such as breast, lung, colorectal, and liver cancers—are steadily increasing. The complex and multifactorial nature of cancer, involving genetic mutations, aberrant signaling pathways, and uncontrolled cellular proliferation, makes it a challenging disease to treat. Despite advances in screening and diagnosis, the prognosis for many cancer patients remains poor, particularly in advanced stages. This growing burden underscores the urgent need for more effective, safe, and accessible therapeutic approaches.[1] Conventional chemotherapy remains one of the primary modalities for cancer treatment; however, it is often associated with significant limitations. The non-specific cytotoxicity of chemotherapeutic agents leads to collateral damage in healthy cells, resulting in severe side effects such as myelosuppression, gastrointestinal disturbances, and organ toxicity. Moreover, the development of multidrug resistance (MDR) in tumor cells severely hampers therapeutic efficacy, leading to treatment failure and disease relapse. The low selectivity of many chemotherapeutic drugs, along with their poor pharmacokinetic profiles and limited bioavailability, further restricts their clinical potential. These drawbacks have prompted the exploration of alternative strategies that can offer enhanced safety, targeted action, and improved patient outcomes.[2, 3] In recent years, there has been growing scientific interest in plant-derived phytochemicals for their anticancer properties. Among them, **berberine**, a naturally occurring isoquinoline alkaloid primarily found in plants such as *Berberis vulgaris*, has shown remarkable promise as a multi-targeted anticancer agent. Berberine exerts its therapeutic effects by modulating diverse molecular pathways involved in apoptosis, cell cycle regulation, inflammation, angiogenesis, and metastasis. It has demonstrated potent cytotoxic activity against various cancer cell lines including breast, lung, colon, and liver cancers. Despite its therapeutic potential, the clinical application of berberine is severely hampered by poor aqueous solubility, low gastrointestinal absorption, and rapid metabolism, leading to minimal systemic bioavailability.[4] To address these pharmacokinetic and delivery-related challenges, the integration of nanotechnology into drug delivery systems has emerged as a transformative approach. Nanoparticle-based formulations offer numerous advantages, including enhanced solubility, prolonged circulation time, targeted drug delivery, and controlled release profiles. By encapsulating berberine into various nanocarriers—such as polymeric nanoparticles, liposomes, solid lipid nanoparticles, and metallic nanoparticles—researchers have significantly improved its stability, cellular uptake, and antitumor efficacy. These innovative delivery systems not only overcome the inherent limitations of free berberine but also provide opportunities for combination therapy and tumor-specific targeting. This review aims to comprehensively examine the role of berberine in cancer therapy and highlight recent advancements in nanoparticle-based formulations that are paving the way for its clinical translation.[5]

Berberine: Source and Chemical Profile

Berberine is a naturally occurring isoquinoline alkaloid widely distributed in various medicinal plants, most notably in the *Berberis* genus, including *Berberis vulgaris* (barberry), *Berberis aristata*, and *Berberis aquifolium*. It is also found in other plant families such as *Ranunculaceae*

(e.g., *Coptis chinensis*), *Rutaceae* (e.g., *Zanthoxylum* species), and *Papaveraceae*. These plants have been traditionally used in Ayurveda, Chinese, and Unani medicine systems for treating infections, inflammation, and gastrointestinal disorders. The alkaloid berberine is primarily extracted from the roots, rhizomes, and stem bark of these plants, often isolated through solvent extraction and chromatographic purification.[6, 7] Chemically, berberine is classified as a quaternary benzylisoquinoline alkaloid with the molecular formula $C_{20}H_{18}NO_4^+$ and a molecular weight of approximately 336.36 g/mol. It exists as a yellow crystalline powder and possesses a planar structure that facilitates its interaction with various biological targets, including nucleic acids and proteins. The core structure comprises a tetrahydroisoquinoline ring fused with a dihydrodibenzoquinolizine moiety, responsible for its broad pharmacological activities. Berberine exhibits intrinsic fluorescence, which is advantageous in bioimaging and analytical applications. It is known for its strong binding affinity to DNA and its ability to intercalate into double-stranded nucleic acids, thereby interfering with replication and transcription processes in cancer cells.[8, 9, 10] Despite its potent biological properties, berberine faces significant challenges in terms of physicochemical characteristics that limit its clinical utility. It has **poor aqueous solubility** (approximately 1 mg/mL in water) and is sparingly soluble in organic solvents. Moreover, it is chemically unstable under light and oxidative conditions, which can lead to degradation and loss of activity. One of the major pharmacokinetic limitations of berberine is its **low oral bioavailability**, which is estimated to be less than 1%. This is primarily attributed to poor gastrointestinal absorption, P-glycoprotein-mediated efflux, extensive first-pass metabolism in the liver and intestines, and rapid systemic clearance.[11]

To overcome these limitations, various strategies have been explored to enhance the solubility, stability, and bioavailability of berberine. These include the use of bioenhancers, prodrug approaches, structural modifications, and more notably, incorporation into advanced drug delivery systems such as nanoparticles. Nanoformulations of berberine have shown significant promise in improving its pharmacokinetic profile, enabling better therapeutic outcomes in preclinical cancer models. Understanding its source, structure, and physicochemical limitations is essential for developing optimized formulations and realizing the full therapeutic potential of this phytochemical.[12]

Pharmacological Activities of Berberine

Berberine has emerged as a promising natural compound with broad-spectrum pharmacological activities, particularly its **anticancer potential**. Numerous in vitro and in vivo studies have demonstrated that berberine exerts potent cytotoxic effects on a wide variety of human cancer cell lines, including breast, colon, lung, liver, and prostate cancers. Unlike conventional chemotherapeutic agents, berberine targets multiple molecular mechanisms and cellular pathways, thereby minimizing the risk of drug resistance and enhancing therapeutic efficacy.[13] One of the most well-documented mechanisms underlying berberine's anticancer activity is its ability to **induce apoptosis**, or programmed cell death. Berberine activates both intrinsic (mitochondrial) and extrinsic (death receptor-mediated) apoptotic pathways. It promotes mitochondrial membrane depolarization, leading to the release of cytochrome c, activation of caspase-9 and caspase-3, and ultimately DNA fragmentation. Additionally, berberine upregulates pro-apoptotic proteins such as Bax and downregulates anti-apoptotic proteins like Bcl-2,

thereby tipping the balance toward cell death in cancer cells. In some studies, berberine has also been shown to enhance Fas receptor expression and activate caspase-8, contributing to extrinsic apoptosis.[14] Berberine also exerts antiproliferative effects by inducing **cell cycle arrest** at various checkpoints. It can cause G0/G1, S, or G2/M phase arrest depending on the cancer type and cellular context. This effect is mediated through the downregulation of cyclins (e.g., cyclin D1, cyclin B1) and cyclin-dependent kinases (CDKs), as well as the upregulation of CDK inhibitors such as p21^Cip1/Waf1 and p27^Kip1. These alterations prevent cancer cells from progressing through the cell cycle, thereby inhibiting uncontrolled proliferation—a hallmark of tumor growth. Additionally, berberine influences the expression of tumor suppressor proteins like p53, which plays a pivotal role in both apoptosis and cell cycle regulation.[15] Beyond apoptosis and proliferation control, berberine significantly inhibits **angiogenesis and metastasis**, two critical processes in cancer progression and recurrence. Berberine suppresses the expression of vascular endothelial growth factor (VEGF), hypoxia-inducible factor-1 alpha (HIF-1α), and matrix metalloproteinases (MMP-2 and MMP-9), which are key regulators of neovascularization and extracellular matrix degradation. By doing so, berberine impairs the formation of new blood vessels required for tumor nourishment and prevents the migration and invasion of cancer cells to distant organs. This anti-metastatic property is particularly valuable for controlling aggressive and treatment-resistant cancers.[16] At the molecular level, berberine's anticancer actions are largely mediated through the **modulation of multiple signaling pathways** involved in cell survival, inflammation, and metabolism. Notably, berberine activates **AMP-activated protein kinase (AMPK)**, a key regulator of cellular energy homeostasis, leading to the inhibition of mTOR signaling and suppression of tumor growth. It also interferes with the **MAPK pathway**, affecting downstream effectors like ERK1/2, JNK, and p38, which are involved in proliferation and apoptosis regulation. Furthermore, berberine exerts strong anti-inflammatory effects by inhibiting the **nuclear factor kappa B (NF-κB)** pathway, resulting in the downregulation of inflammatory cytokines, COX-2, and iNOS. These combined effects not only inhibit cancer cell survival but also modulate the tumor microenvironment to a less supportive state for cancer progression.[17, 18] Collectively, these multifaceted mechanisms make berberine a potent anticancer agent with the ability to interfere at various stages of cancer development and progression. Its pleiotropic actions underscore the importance of further exploring berberine as a candidate for cancer therapy, particularly in conjunction with modern drug delivery technologies.

Mechanism of Action in Cancer

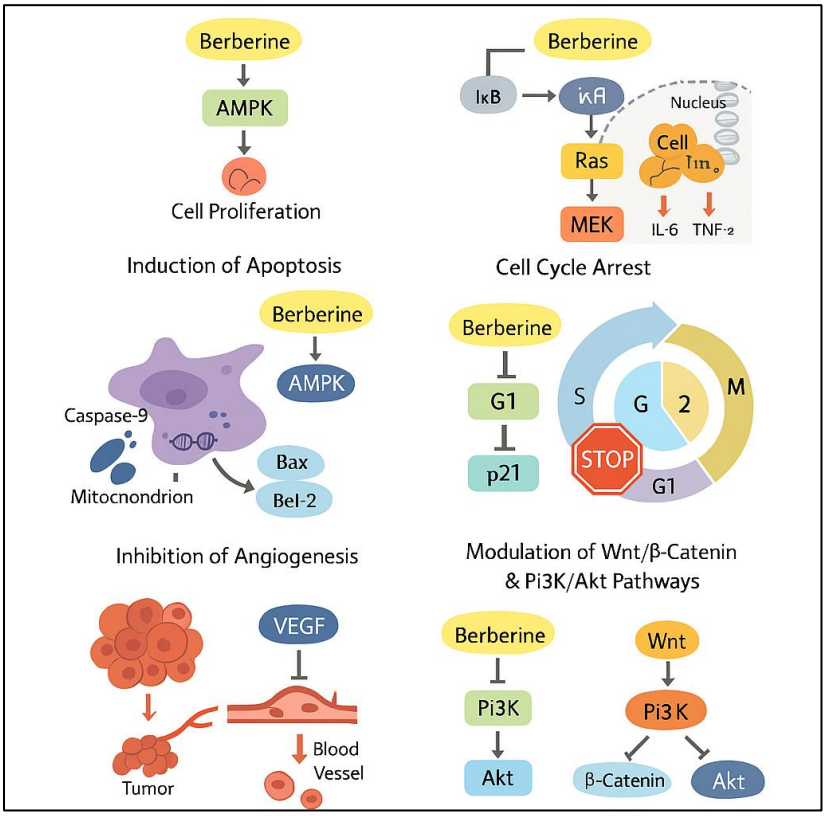

Figure 1: Berberine-Induced Modulation of Cellular Pathways in Cancer Cells

Berberine exerts its anticancer activity through multiple molecular mechanisms. It activates the AMP-activated protein kinase (AMPK) pathway, which subsequently inhibits mTOR signaling, leading to reduced cell proliferation and enhanced autophagy. Berberine also suppresses the nuclear factor-kappa B (NF-κB) pathway, resulting in decreased inflammatory responses and downregulation of anti-apoptotic genes. Inhibition of the mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK) signaling cascade further limits cancer cell survival and proliferation. Additionally, berberine induces apoptosis through caspase activation and disruption of mitochondrial membrane potential, while also causing cell cycle arrest by modulating cyclins and increasing the expression of tumor suppressor proteins such as p53 and p21. Its anti-angiogenic effects are mediated via downregulation of vascular endothelial growth factor (VEGF). Moreover, it inhibits the phosphoinositide 3-kinase/Akt (PI3K/Akt) pathway, promoting apoptotic signaling, and disrupts the Wnt/β-catenin signaling pathway, thereby inhibiting tumor progression and metastasis. Berberine exerts its anticancer activity through a variety of **molecular targets and cellular mechanisms**, allowing it to act as a multi-functional agent in the inhibition of tumor development and progression. Its ability to modulate numerous signaling cascades, affect gene expression, and interfere with the tumor microenvironment contributes to its promising therapeutic profile in oncology.[19, 20] Berberine's anticancer efficacy extends across various types of cancers, with evidence demonstrating its capability to intervene at multiple levels of cancer progression. In **breast cancer**, berberine has shown to downregulate estrogen receptor signaling and inhibit HER2 expression, thereby

suppressing proliferation and migration. Additionally, its anti-angiogenic effects are achieved through the downregulation of VEGF and HIF-1α, reducing tumor vascularization. In **colorectal cancer**, berberine disrupts the Wnt/β-catenin pathway, inhibits cyclin D1, and triggers mitochondrial-mediated apoptosis. These effects are further supported by the downregulation of COX-2 and survivin, which are commonly upregulated in colorectal malignancies.[21] In **lung cancer**, especially non-small cell lung cancer (NSCLC), berberine induces G2/M phase arrest and limits cellular migration through inhibition of matrix metalloproteinases (MMP-2 and MMP-9). Meanwhile, in **liver cancer**, it regulates cell metabolism by modulating AMPK activity and has shown to inhibit telomerase, thereby interfering with the unlimited replication potential of hepatocellular carcinoma cells. Other malignancies like **pancreatic, prostate**, and **gastric cancers** also respond to berberine through mechanisms tailored to their specific oncogenic pathways.[22] What sets berberine apart from many conventional agents is its **synergistic potential** with standard chemotherapy drugs. When combined with **doxorubicin**, berberine not only enhances cytotoxicity but also reduces cardiotoxic side effects by suppressing oxidative stress. Its co-administration with **cisplatin** results in amplified DNA damage and suppression of DNA repair pathways, making resistant tumors more susceptible. Berberine also improves the sensitivity of cancer cells to **5-fluorouracil (5-FU)** and **paclitaxel**, suggesting a promising role in overcoming multidrug resistance (MDR). These synergistic effects open avenues for reducing chemotherapy dosages, thus minimizing adverse effects without compromising efficacy.[23, 24] While berberine's mechanisms intersect with key signaling pathways such as **AMPK, NF-κB, MAPK, PI3K/Akt, and STAT3**, its ability to modulate these in a cancer-type specific manner underscores its multifaceted role in therapy. By targeting both tumor-intrinsic factors and the tumor microenvironment, berberine positions itself as a powerful agent in integrated cancer treatment regimens, especially when delivered through advanced platforms like nanoparticles.[25] In summary, berberine's anticancer action is mediated by its ability to target multiple signaling pathways, influence diverse cellular functions, and complement existing cancer therapies. These properties make it a strong candidate for inclusion in combinational and nanomedicine-based therapeutic strategies aimed at improving cancer treatment outcomes.

Limitations of Berberine in Clinical Use

Despite its promising anticancer potential, berberine faces several pharmacokinetic challenges that hinder its clinical application. One of the primary limitations is its **poor aqueous solubility**, which significantly affects its dissolution rate and absorption in the gastrointestinal tract. This, in turn, contributes to **low oral bioavailability**, with studies indicating that less than 1% of orally administered berberine reaches systemic circulation in its active form. Furthermore, berberine undergoes **extensive first-pass metabolism**, primarily in the liver and intestines, where it is rapidly converted into various metabolites, further reducing its therapeutic efficacy.[26] Another major drawback is berberine's **short biological half-life**, leading to **rapid elimination** from the body, which necessitates frequent dosing to maintain effective plasma concentrations. These pharmacokinetic barriers collectively limit its therapeutic utility, especially in cancer therapy where sustained and targeted drug delivery is essential. Therefore, there is a pressing **need for advanced drug delivery strategies**, such as nanoformulations, to enhance berberine's solubility, protect it from metabolic

degradation, prolong its circulation time, and ensure targeted delivery to tumor tissues.[27]

Nanoparticle-Based Drug Delivery Systems for Berberine

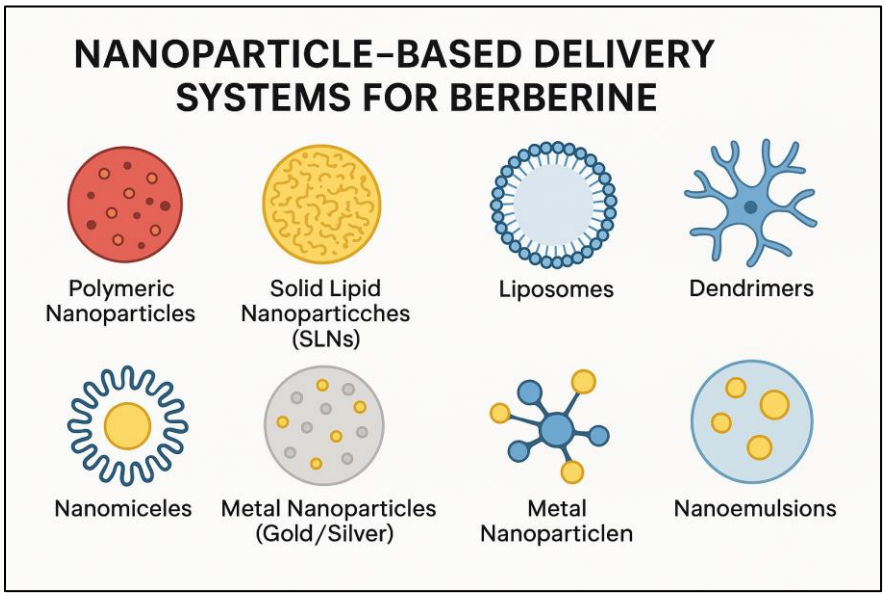

Figure 2: Types of Nanoparticle-Based Delivery Systems for Berberine

This schematic illustration represents various nanoparticle-based delivery systems explored for enhancing the therapeutic potential of berberine in cancer treatment. These include polymeric nanoparticles (e.g., PLGA, chitosan), solid lipid nanoparticles (SLNs), liposomes, dendrimers, nanomicelles, metal nanoparticles (gold and silver), and nanoemulsions. Each system offers distinct advantages such as improved solubility, stability, targeted delivery, and reduced toxicity, addressing the pharmacokinetic limitations of berberine and enabling more effective anticancer therapy. Nanotechnology has emerged as a transformative tool in cancer therapy, offering innovative solutions to long-standing challenges such as poor solubility, limited bioavailability, and non-specific toxicity of chemotherapeutic agents. In the case of berberine, nanoparticle-based delivery systems have shown immense potential in overcoming its pharmacokinetic limitations and enhancing its therapeutic efficacy. These nanocarriers not only improve berberine's solubility and stability but also provide targeted and sustained release profiles, allowing for efficient accumulation at tumor sites while minimizing systemic toxicity.[28, 29] A variety of nanoparticulate systems have been explored for delivering berberine in anticancer applications. **Polymeric nanoparticles**, particularly those made from biocompatible and biodegradable polymers such as **PLGA (poly(lactic-co-glycolic acid))** and **chitosan**, have demonstrated effective encapsulation of berberine, resulting in prolonged circulation time and controlled drug release. These carriers also offer the advantage of surface modification for active targeting to tumor cells.[30]

Solid lipid nanoparticles (SLNs) are another widely studied system for berberine delivery. They offer high biocompatibility and can improve berberine's stability by protecting it from degradation. SLNs also allow for controlled drug release and enhanced uptake by cancer cells. **Liposomes**, with their phospholipid bilayer structure, mimic biological membranes and can encapsulate both hydrophilic and hydrophobic

drugs. Berberine-loaded liposomes have been shown to enhance cellular uptake and reduce off-target toxicity.[31]

Dendrimers, with their highly branched and defined architecture, offer precise control over drug loading and release. Their modifiable surface enables conjugation with ligands for targeted therapy. Although still in early stages of application with berberine, dendrimers hold promise for precise and potent cancer targeting. **Nanomicelles**, composed of amphiphilic molecules, are particularly effective for solubilizing poorly water-soluble drugs like berberine. They enhance cellular internalization and can be engineered for stimulus-responsive drug release in the tumor microenvironment.[32] Inorganic nanocarriers such as **gold and silver nanoparticles** have also been employed for berberine delivery due to their unique optical properties and ease of surface functionalization. These systems offer the added advantage of enabling photothermal therapy in conjunction with chemotherapy. Lastly, **nanoemulsions**, which are fine oil-in-water or water-in-oil emulsions stabilized by surfactants, have been utilized to enhance berberine's solubility, absorption, and bioavailability through oral and parenteral routes.[33] Collectively, these nanoparticle systems not only improve berberine's pharmacokinetic profile but also facilitate **tumor-targeted delivery**, **enhanced cellular uptake**, and **reduced systemic toxicity**, making them ideal candidates for next-generation anticancer therapies.[34]

Berberine-Loaded Nanoparticles: Studies and Efficacy

Extensive **in vitro and in vivo** studies have demonstrated the promise of berberine-loaded nanoparticles in enhancing its pharmacological performance against various cancer types. These nanoformulations significantly address the inherent limitations of native berberine by improving its solubility, cellular uptake, and retention time, thereby enhancing therapeutic outcomes.[35] One of the key advantages observed in these studies is the **enhanced solubility and stability** of berberine when encapsulated in nanocarriers. Polymeric nanoparticles such as PLGA and chitosan have shown notable improvements in dispersibility and resistance to degradation, enabling sustained release profiles and better cellular uptake. Similarly, lipid-based systems like liposomes and solid lipid nanoparticles (SLNs) have provided a protective environment that prevents premature degradation of berberine, enhancing its overall stability in physiological conditions.[36]

Targeted delivery and increased bioavailability are other critical improvements observed with nanoparticle formulations. Functionalized nanoparticles have been designed to exploit the enhanced permeability and retention (EPR) effect in tumor tissues, leading to preferential accumulation at the tumor site. Additionally, surface modifications with ligands such as folic acid or peptides have enabled receptor-mediated targeting, further enhancing therapeutic specificity and minimizing off-target effects.[37] In terms of **antitumor efficacy**, nanoparticle formulations have consistently outperformed free berberine in various cancer models, including breast, lung, liver, colon, and ovarian cancers. These nanoformulations not only improved tumor suppression but also exhibited **reduced systemic toxicity** in animal models, confirming their safety and tolerability. Furthermore, co-delivery strategies combining berberine with other chemotherapeutic agents have revealed **synergistic effects**, leading to enhanced apoptosis and inhibition of tumor growth without increasing toxicity.[38]

Table 1: Summary of Berberine-Loaded Nanoparticle Formulations in Cancer Therapy

Nanoparticle Type	Targeted Cancer Type	Key Outcomes	Reference Highlights
PLGA Nanoparticles	Colon cancer	Improved bioavailability, sustained release, enhanced apoptosis	In vivo tumor regression observed
Chitosan Nanoparticles	Breast cancer	Enhanced cellular uptake, significant tumor size reduction	Receptor-mediated targeting successful
Liposomes	Lung cancer	Better solubility and stability, reduced inflammation	Lower toxicity in vivo
SLNs	Liver cancer	Improved pharmacokinetics, increased accumulation in liver tumor cells	Sustained cytotoxic effect
Nanomicelles	Ovarian cancer	Enhanced solubilization and mitochondrial targeting	High ROS generation and tumor inhibition
Gold NPs	Cervical cancer	Combined chemo-photothermal effect	Effective tumor ablation
Nanoemulsions	Prostate cancer	Improved absorption, better systemic availability	Enhanced therapeutic index

Challenges and Limitations of Nanoformulations

While nanoformulations of berberine have shown significant promise in enhancing its therapeutic profile, several challenges limit their widespread clinical application. One of the primary concerns is the **potential toxicity of nanocarriers** themselves. Although many nanoparticles are designed using biocompatible and biodegradable materials, some may induce unintended immunogenicity, oxidative stress, or organ accumulation, especially with prolonged use. Metallic nanoparticles, for instance, can trigger cytotoxic effects due to their reactive surfaces and potential to generate free radicals.[39]

Another considerable hurdle lies in the **manufacturing and scalability** of these formulations. Producing nanoparticles with uniform size, charge, and drug loading on a large scale remains a technical challenge. Batch-to-batch variability and the need for stringent control over physicochemical parameters often complicate the transition from lab-scale synthesis to industrial-scale production. Additionally, the requirement for sterile processing, advanced instrumentation, and sophisticated formulation techniques further adds to the complexity.[40]

Regulatory and safety concerns also pose a major barrier. Unlike conventional pharmaceuticals, nanomedicines must undergo rigorous preclinical and clinical testing to evaluate their biodistribution, metabolism, and long-term safety. Regulatory bodies like the FDA and EMA are still in the process of evolving standardized guidelines specific to nanoparticle-based drug delivery systems. The lack of universally accepted evaluation protocols complicates the approval

process and delays market entry.[41] Lastly, **cost-effectiveness** remains a pressing issue. Developing nanoformulations involves high research and development costs, specialized infrastructure, and complex quality control procedures. These factors can significantly increase the final product cost, potentially limiting accessibility, especially in low-resource settings. Hence, while nanoformulations offer a promising avenue for berberine delivery in cancer therapy, addressing these challenges is crucial for successful clinical translation and broader acceptance.[42, 43, 44]

Future Prospects and Research Gaps

The future of berberine-loaded nanoparticles in cancer therapy is promising, particularly with the integration of personalized medicine and theranostic approaches. By tailoring nanocarrier systems based on individual tumor profiles and incorporating imaging agents alongside therapeutic payloads, theranostic nanoparticles could allow real-time monitoring of drug delivery and response, enhancing treatment precision. Moreover, combining berberine with conventional chemotherapeutic or radiotherapeutic agents through co-loaded nanoparticles may offer synergistic benefits, overcoming drug resistance while minimizing toxicity. However, despite encouraging preclinical results, there remains a critical gap in clinical translation. Most studies are limited to in vitro or animal models, with a pressing need for well-designed human clinical trials to validate safety, efficacy, and pharmacokinetics. Additionally, regulatory challenges, including the lack of standardized evaluation protocols for nanomedicines, must be addressed to facilitate approval and clinical adoption. Another emerging focus is the green synthesis of nanoparticles using plant extracts or biological systems, which can enhance sustainability and biocompatibility while reducing environmental impact. Advancing research in these directions will not only expand the therapeutic utility of berberine in oncology but also align with the broader goals of safe, effective, and eco-friendly cancer treatments.[45, 46]

CONCLUSION

Berberine stands out as a promising natural compound in the realm of oncology, demonstrating potent anticancer effects through multiple mechanisms such as apoptosis induction, cell cycle arrest, and modulation of critical signaling pathways. However, its clinical potential has long been hampered by poor bioavailability, solubility, and rapid metabolism. The advent of nanotechnology offers a transformative solution to these challenges, significantly enhancing berberine's pharmacokinetic profile and therapeutic efficacy through targeted and controlled delivery systems. A variety of nanoparticle-based formulations have shown encouraging preclinical results, paving the way for more effective and safer cancer therapies. Nevertheless, translating these innovations from bench to bedside requires a concerted interdisciplinary effort involving pharmacologists, chemists, materials scientists, clinicians, and regulatory bodies. Future research should focus on optimizing formulations, ensuring safety, advancing clinical trials, and adopting sustainable nanotechnology practices. With such collaborative endeavors, berberine-loaded nanoformulations could become a vital component of next-generation cancer therapeutics.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this review article.

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