https://doi.org/10.33472/AFJBS.6.Si3.2024.712-726

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Convergence of Artificial Intelligence and Nanoparticle Delivery Systems: Enhancing Curcumin's Potential in Targeted Cancer Therapy

Surbhi Kamboj[1], Anil Kumar[2], Ankita Tripathi[3], L. Karpagavalli[4], Meenakshi Tyagi[5], Archana Sharma[6], Mathews T Thelly[7*], Pankaj Bhatt[8]

[1]KIET School of Pharmacy, KIET Group of Institutions, Ghaziabad
[2]Head & Assistant Professor, Department of Chemistry (PG), Sahibganj College Sahibganj, Jharkhand, India
[3]Associate Professor, IIMT College of Pharmacy, Greater Noida, U.P
[4]Professor, Department of Pharmaceutics, Saveetha College of Pharmacy, SIMATS, Chennai, India
[5]Associate Professor, Quantum University Roorkee-247667, India
[6]KIET Group of institutions, Ghaziabad
[7*]Associate Professor, Head and Research Guide, Department of Botany, Kuriakose Elias College Mannanam, Kottayam, Kerala, India
[8]Lloyd Institute of Management and Technology, Plot No. 11, Knowledge Park- II, Greater Noida, Uttar Pradesh 201308

Corresponding Author: Dr. Mathews T Thelly
Associate Professor, Head and Research Guide, Department of Botany, Kuriakose Elias College Mannanam, Kottayam, Kerala, India

Article Info

Volume 6, Issue Si3, June 2024

Received: 19 April 2024

Accepted: 25 May 2024

Published: 10 June 2024

doi: 10.33472/AFJBS.6.Si3.2024.712-726

ABSTRACT:

The convergence of artificial intelligence (AI) and nanoparticle delivery systems holds great promise in revolutionizing cancer therapy, particularly in enhancing the efficacy of curcumin-based treatments. This review explores the current challenges in cancer therapy, highlighting the resistance to traditional chemotherapy, lack of selectivity, and the need for innovative targeted therapies. We discuss curcumin's potential as an anti-cancer agent, its pharmacological properties, evidence of anticancer effects in preclinical studies, and limitations in bioavailability and delivery. Additionally, we delve into nanoparticle delivery systems, covering types of nanoparticles, advantages, and examples of formulations for curcumin delivery. Furthermore, we examine the integration of AI algorithms with nanoparticle design, predictive modeling for optimizing drug delivery parameters, and present case studies demonstrating AI-driven nanoparticle optimization for curcumin delivery. Finally, we discuss future perspectives, including opportunities for further research and development, regulatory considerations, and ethical implications of AI in cancer therapy. This comprehensive review underscores the transformative potential of AI-driven nanoparticle delivery systems in enhancing curcumin's efficacy for targeted cancer therapy, while also addressing the challenges and opportunities that lie ahead in this exciting field.

Keywords: artificial intelligence, nanoparticle delivery systems, curcumin, cancer therapy, drug delivery, targeted therapy, predictive modeling.

1. Introduction

Cancer therapy remains a formidable challenge in modern medicine due to its complexity, heterogeneity, and the limited efficacy of traditional treatment modalities[1]. Conventional chemotherapy often lacks specificity, resulting in off-target effects and systemic toxicity. Moreover, the development of drug resistance poses a significant obstacle to successful cancer treatment[2]. In this context, the exploration of novel therapeutic approaches is imperative to improve patient outcomes and address the shortcomings of current cancer therapies[3]. Curcumin, a natural polyphenol derived from the rhizome of Curcuma longa, has emerged as a promising candidate for cancer therapy[4]. Extensive preclinical studies have demonstrated its diverse pharmacological properties, including anti-inflammatory, antioxidant, and anticancer effects. Curcumin exhibits pleiotropic mechanisms of action, targeting multiple signaling pathways involved in cancer initiation, progression, and metastasis[5]. However, despite its remarkable therapeutic potential, the clinical translation of curcumin has been hindered by its poor aqueous solubility, low bioavailability, and rapid

metabolism. Nanoparticle delivery systems offer a promising solution to overcome the limitations of conventional curcumin formulations and enhance its therapeutic efficacy in cancer treatment[6]. Nanoparticles can encapsulate curcumin, protecting it from degradation and facilitating its targeted delivery to tumor sites. Various types of nanoparticles, including liposomes, polymeric nanoparticles, and solid lipid nanoparticles, have been explored for curcumin delivery, each offering unique advantages in terms of stability, biocompatibility, and controlled release properties[7]. By encapsulating curcumin within nanoparticles, researchers can achieve sustained drug release, improve cellular uptake, and enhance its pharmacokinetic profile, thereby maximizing its therapeutic potential against cancer[8]. Artificial intelligence (AI) has revolutionized healthcare by enabling data-driven decision-making, personalized treatment strategies, and predictive modeling for disease diagnosis and management[9]. In the context of cancer therapy, AI holds immense promise for optimizing treatment regimens, predicting therapeutic responses, and identifying novel drug targets. Machine learning algorithms can analyze vast datasets, including genomic, proteomic, and imaging data, to identify patterns and correlations that may elude human intuition[10]. By integrating AI-driven approaches with nanoparticle design and drug delivery optimization, researchers can expedite the development of innovative cancer therapeutics with enhanced efficacy and safety profiles. The convergence of artificial intelligence and nanoparticle delivery systems represents a paradigm shift in cancer therapy, offering a synergistic approach to overcome the inherent challenges associated with traditional treatment modalities[11]. AI algorithms can analyze patient-specific data to tailor nanoparticle formulations for optimal drug delivery, taking into account factors such as tumor characteristics, drug pharmacokinetics, and patient demographics[12]. Moreover, AI-driven predictive modeling can guide the rational design of nanoparticle carriers with improved physicochemical properties, targeting ligand specificity, and drug release kinetics, thereby enhancing the therapeutic index of encapsulated agents like curcumin[13].

Figure 1: Schematic representation of different types of nanoparticles

Current Challenges in Cancer Therapy

Cancer therapy continues to pose significant challenges despite advancements in medical

science and technology[14]. From resistance to traditional chemotherapy to the lack of selectivity and off-target effects, these challenges necessitate innovative approaches for effective treatment strategies[15].

A. Resistance to Traditional Chemotherapy

One of the foremost challenges in cancer therapy is the development of resistance to traditional chemotherapy agents. Cancer cells possess a remarkable ability to adapt and evolve, leading to the emergence of drug-resistant phenotypes[16]. This phenomenon, known as multidrug resistance (MDR), severely limits the efficacy of chemotherapy and contributes to treatment failure and disease progression[17]. The mechanisms underlying drug resistance are multifaceted and complex, involving alterations in drug transport, metabolism, and cellular signaling pathways. Efflux pumps, such as P-glycoprotein, actively pump chemotherapeutic agents out of cancer cells, reducing intracellular drug concentrations and rendering them ineffective[18]. Additionally, cancer cells can acquire mutations in genes encoding drug targets or downstream signaling molecules, thereby circumventing the cytotoxic effects of chemotherapy drugs[19]. Overcoming drug resistance represents a formidable challenge in cancer therapy, requiring innovative strategies to circumvent or reverse resistance mechanisms. Combination therapies that target multiple signaling pathways simultaneously may help overcome resistance and improve treatment outcomes. Furthermore, the development of targeted therapies directed against specific molecular alterations in drug-resistant tumors holds promise for personalized treatment approaches[20,21].

B. Lack of Selectivity and Off-Target Effects

Conventional chemotherapy suffers from a lack of selectivity, leading to off-target effects and systemic toxicity[22]. Chemotherapeutic agents often damage healthy tissues and organs, resulting in adverse side effects that impact patient quality of life and treatment adherence. The non-specific nature of chemotherapy also limits its therapeutic index, necessitating dose reductions or treatment interruptions to manage toxicity[23]. The lack of selectivity in chemotherapy is primarily attributed to the rapid proliferation of cancer cells compared to normal cells, making them more susceptible to cytotoxic agents. However, healthy tissues with high rates of cell turnover, such as the bone marrow and gastrointestinal tract, are also affected by chemotherapy-induced toxicity[24]. Additionally, chemotherapy drugs may exhibit off-target effects by interfering with essential cellular processes or disrupting physiological functions unrelated to cancer. Addressing the lack of selectivity and off-target effects in cancer therapy requires the development of targeted drug delivery strategies that selectively deliver therapeutic agents to tumor cells while minimizing systemic exposure[25]. Nanoparticle-based drug delivery systems offer a promising solution by encapsulating chemotherapy drugs within nanoparticles and functionalizing their surfaces with targeting ligands that recognize specific biomarkers expressed on cancer cells[26]. This targeted approach enhances drug accumulation at the tumor site while reducing exposure to healthy tissues, thereby improving therapeutic efficacy and minimizing toxicity[27].

C. Need for Innovative Targeted Therapies

The advent of targeted therapies has revolutionized cancer treatment by exploiting specific molecular alterations driving tumor growth and progression. Unlike traditional chemotherapy, which indiscriminately targets rapidly dividing cells, targeted therapies selectively inhibit key oncogenic pathways implicated in cancer pathogenesis[28]. This precision approach offers the potential for improved therapeutic outcomes with reduced systemic toxicity. Targeted therapies encompass various modalities, including small-molecule inhibitors, monoclonal

antibodies, and immune checkpoint inhibitors, each designed to interfere with specific molecular targets involved in tumor growth and survival[29]. For example, tyrosine kinase inhibitors (TKIs) block aberrant signaling pathways activated by mutant kinases, such as epidermal growth factor receptor (EGFR) or BRAF, in certain cancers. Similarly, monoclonal antibodies can selectively target cell surface receptors or ligands, inhibiting downstream signaling cascades and promoting immune-mediated tumor destruction[30]. Despite the clinical success of targeted therapies in certain cancer types, challenges remain, including the development of resistance, limited efficacy in some patients, and adverse effects associated with prolonged treatment[31]. Moreover, the heterogeneity of tumors and the dynamic nature of oncogenic signaling pathways pose significant obstacles to effective targeted therapy. Addressing these challenges requires innovative approaches that leverage emerging technologies, such as artificial intelligence (AI) and genomic profiling, to identify actionable molecular targets and predict therapeutic responses[32]. By integrating AI-driven algorithms with high-throughput screening assays and patient-derived data, researchers can accelerate the discovery and development of novel targeted therapies tailored to individual patient profiles[33].

Curcumin: A Potential Anti-Cancer Agent

Curcumin, a natural polyphenol derived from the rhizome of Curcuma longa, has garnered significant attention for its potential as an anti-cancer agent[34].

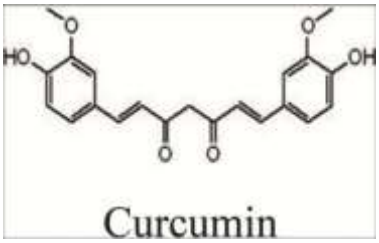

Figure 2: Structure of curcumin

A. Overview of Curcumin's Pharmacological Properties

Curcumin exhibits a diverse array of pharmacological properties that contribute to its potential as an anti-cancer agent. As a polyphenolic compound, curcumin possesses potent antioxidant and anti-inflammatory activities, which have been extensively studied in the context of cancer prevention and treatment[35]. Additionally, curcumin demonstrates the ability to modulate various cellular signaling pathways implicated in cancer pathogenesis, including nuclear factor-kappa B (NF-κB), signal transducer and activator of transcription 3 (STAT3), and phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT) pathways[36]. Furthermore, curcumin has been shown to induce apoptosis, inhibit angiogenesis, and suppress metastasis in cancer cells, highlighting its multifaceted mechanisms of action[37]. Its ability to target multiple hallmarks of cancer makes curcumin an attractive candidate for cancer therapy, offering the potential for synergistic effects when combined with conventional treatments[38].

B. Evidence of Curcumin's Anticancer Effects in Preclinical Studies

Preclinical studies have provided compelling evidence of curcumin's efficacy against various types of cancer, including breast, colorectal, prostate, lung, and pancreatic cancer, among others[39]. In vitro studies have demonstrated that curcumin inhibits cancer cell proliferation, induces cell cycle arrest, and promotes apoptosis through multiple mechanisms. Moreover, curcumin exhibits synergistic effects with conventional chemotherapy agents, enhancing their anticancer activity and overcoming drug resistance in cancer cells[40]. In animal models of

cancer, curcumin supplementation has been shown to suppress tumor growth, reduce tumor burden, and inhibit metastasis, underscoring its potential as a therapeutic agent. Additionally, curcumin has been found to modulate the tumor microenvironment, inhibiting inflammation and angiogenesis while promoting immune surveillance against cancer cells[41]. Despite the promising results observed in preclinical studies, the translation of curcumin's anticancer effects to clinical settings has been hindered by its poor aqueous solubility, low bioavailability, and rapid metabolism. These limitations pose significant challenges to the effective delivery of curcumin to tumor sites and limit its therapeutic efficacy in vivo[42].

C. Limitations of Curcumin's Bioavailability and Delivery

The bioavailability of curcumin is notoriously low due to its poor solubility in water and rapid metabolism and elimination in the body. After oral administration, curcumin undergoes extensive metabolism in the liver, leading to the formation of conjugated metabolites with reduced biological activity[43]. Additionally, curcumin is prone to degradation under physiological conditions, further compromising its bioavailability and therapeutic potential. To address the limitations of curcumin's bioavailability and delivery, various strategies have been explored, including the use of adjuvants, formulation of curcumin nanoparticles, and incorporation into lipid-based carriers[44]. Nanoparticle-based delivery systems offer a promising approach to enhance curcumin's stability, improve its solubility, and prolong its circulation time in the bloodstream, thereby increasing its accumulation at tumor sites[45]. Furthermore, the functionalization of nanoparticles with targeting ligands can facilitate site-specific delivery of curcumin to cancer cells, enhancing its therapeutic efficacy while minimizing off-target effects[46]. By overcoming the bioavailability barriers associated with conventional curcumin formulations, nanoparticle-based delivery systems hold the potential to unleash the full therapeutic benefits of curcumin in cancer therapy[47].

Nanoparticle Delivery Systems for Curcumin

Nanoparticle delivery systems represent a promising approach to enhance the therapeutic efficacy of curcumin in cancer therapy[48].

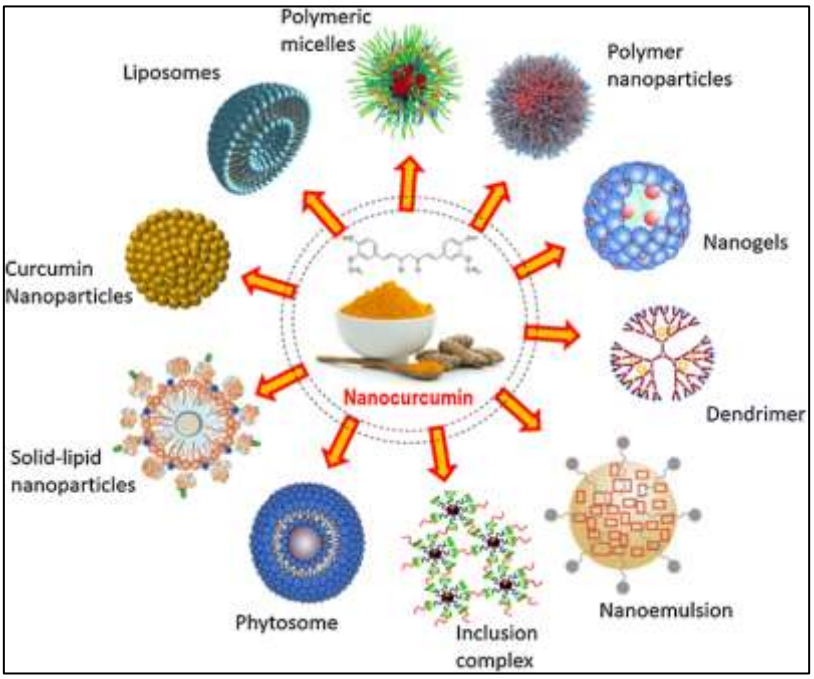

Figure 3: Different strategies of curcumin nano particles preparation

A. Types of Nanoparticle Delivery Systems

Nanoparticle delivery systems encompass a diverse range of formulations designed to encapsulate therapeutic agents, such as curcumin, and facilitate their targeted delivery to tumor sites. Some of the commonly used nanoparticle platforms include liposomes, polymeric nanoparticles, micelles, dendrimers, and solid lipid nanoparticles[49]. Liposomes are lipid-based vesicles composed of phospholipid bilayers that can encapsulate hydrophobic drugs like curcumin within their core or lipid membrane. Polymeric nanoparticles are synthetic or natural polymers, such as poly(lactic-co-glycolic acid) (PLGA) or chitosan, that form nanoparticles capable of entrapping curcumin through physical encapsulation or chemical conjugation[49]. Micelles are self-assembled structures composed of amphiphilic molecules that solubilize hydrophobic drugs like curcumin in their hydrophobic core[50]. Dendrimers are highly branched, tree-like molecules that can encapsulate curcumin within their interior void spaces. Solid lipid nanoparticles are colloidal particles composed of biocompatible lipids that encapsulate curcumin and provide sustained release upon administration[51]. Each type of nanoparticle delivery system offers unique advantages in terms of drug loading capacity, stability, biocompatibility, and controlled release properties, making them suitable for various applications in cancer therapy[52].

B. Advantages of Nanoparticle-Based Drug Delivery

Nanoparticle-based drug delivery systems offer several advantages over conventional formulations, particularly in the context of curcumin delivery for cancer therapy. First and foremost, nanoparticles can improve the solubility and stability of curcumin, overcoming its poor aqueous solubility and rapid degradation in physiological conditions[53]. By encapsulating curcumin within nanoparticles, researchers can protect it from enzymatic degradation and extend its circulation time in the bloodstream, thereby enhancing its bioavailability and therapeutic efficacy[54]. Moreover, nanoparticle delivery systems can facilitate targeted delivery of curcumin to tumor sites while minimizing exposure to healthy tissues, thereby reducing off-target effects and systemic toxicity[55]. Functionalization of nanoparticles with targeting ligands, such as antibodies or peptides, allows for site-specific accumulation of curcumin within cancer cells, enhancing its selective cytotoxicity and therapeutic index[56]. Furthermore, nanoparticle formulations can provide controlled release of curcumin over an extended period, ensuring sustained drug levels at the tumor site and minimizing fluctuations in plasma concentrations[57]. This prolonged exposure to curcumin may potentiate its anticancer effects and overcome drug resistance mechanisms in cancer cells.

C. Examples of Nanoparticle Formulations for Curcumin Delivery

Several nanoparticle formulations have been developed for curcumin delivery in cancer therapy, demonstrating the versatility and potential of this approach[58]. For example, liposomal formulations of curcumin have been shown to improve its solubility and stability, leading to enhanced anticancer activity in preclinical models of various cancer types, including breast, colorectal, and pancreatic cancer[59]. Polymeric nanoparticles have also been extensively investigated for curcumin delivery, with studies demonstrating their ability to encapsulate curcumin and achieve sustained release profiles[60]. PLGA nanoparticles loaded with curcumin have shown promising results in inhibiting tumor growth and metastasis in animal models of prostate and lung cancer[61]. Furthermore, solid lipid nanoparticles have emerged as a promising carrier for curcumin delivery, offering enhanced stability, biocompatibility, and controlled release properties[62]. Solid lipid nanoparticles loaded with curcumin have demonstrated superior anticancer activity compared to free curcumin in preclinical models of breast and colon cancer. These examples highlight the

potential of nanoparticle-based delivery systems to overcome the limitations of conventional curcumin formulations and enhance its therapeutic efficacy in cancer therapy[63,64].

Convergence of Artificial Intelligence and Nanoparticle Delivery Systems

The convergence of artificial intelligence (AI) and nanoparticle delivery systems represents a groundbreaking approach to optimize curcumin delivery for enhanced efficacy in cancer therapy[65].

A. Integration of AI Algorithms with Nanoparticle Design

The integration of AI algorithms with nanoparticle design offers a transformative approach to tailor nanoparticle properties for optimal curcumin delivery. Machine learning algorithms can analyze vast datasets encompassing physicochemical properties, drug release kinetics, and biological interactions to guide the rational design of nanoparticles with enhanced therapeutic performance[66,67]. AI-driven approaches enable the identification of key features influencing nanoparticle behavior, such as particle size, surface charge, and surface functionalization, thereby facilitating the optimization of nanoparticle formulations for specific applications. By leveraging computational modeling and predictive analytics, researchers can accelerate the development of nanoparticle carriers with tailored properties optimized for curcumin delivery, enhancing drug bioavailability and targeting efficiency[68,69].

B. Predictive Modeling for Optimizing Drug Delivery Parameters

Predictive modeling plays a pivotal role in optimizing drug delivery parameters to maximize curcumin's therapeutic efficacy and minimize adverse effects[70]. AI algorithms can predict drug release kinetics, biodistribution profiles, and pharmacokinetic parameters based on nanoparticle characteristics and physiological factors, enabling precise control over drug delivery parameters[71]. By integrating experimental data with computational simulations, researchers can iteratively refine nanoparticle formulations to achieve desired drug release profiles and optimize dosing regimens for optimal therapeutic outcomes[72]. Predictive modeling allows for the identification of optimal nanoparticle compositions, drug loading capacities, and release mechanisms, leading to the development of next-generation curcumin delivery systems with improved efficacy and safety profiles[73].

C. Case Studies Demonstrating AI-Driven Nanoparticle Optimization for Curcumin Delivery

Several case studies demonstrate the application of AI-driven approaches to optimize nanoparticle formulations for curcumin delivery, highlighting the potential of this synergistic approach in cancer therapy[23,1]. For instance, researchers have utilized machine learning algorithms to analyze high-throughput screening data and identify nanoparticle compositions that enhance curcumin solubility and stability[74]. In another study, predictive modeling techniques were employed to optimize the surface properties of polymeric nanoparticles for targeted curcumin delivery to tumor cells[75]. By integrating experimental data with computational simulations, researchers achieved precise control over nanoparticle surface modifications, resulting in enhanced cellular uptake and anticancer activity of curcumin in vitro and in vivo. Furthermore, AI-driven approaches have been employed to predict drug release kinetics and optimize formulation parameters for sustained curcumin delivery[76]. By leveraging advanced computational models, researchers can tailor nanoparticle formulations to achieve prolonged drug release profiles, thereby maximizing curcumin's therapeutic efficacy while minimizing systemic exposure and off-target effects[77]. These case studies

underscore the transformative potential of AI-driven nanoparticle optimization in revolutionizing curcumin delivery for cancer therapy[78]. By harnessing the power of artificial intelligence, researchers can overcome the inherent challenges associated with conventional drug delivery systems and unlock the full therapeutic potential of curcumin in the fight against cancer[79].

Future Perspectives and Challenges

As the convergence of artificial intelligence and nanoparticle delivery systems continues to advance, it presents exciting opportunities for further research and development, along with addressing regulatory considerations and ethical implications[80].

A. Opportunities for Further Research and Development

The intersection of artificial intelligence and nanoparticle delivery systems offers a multitude of avenues for future exploration and innovation. Research efforts can focus on refining AI algorithms to enhance predictive modeling of nanoparticle behavior and drug delivery kinetics, allowing for more precise control over therapeutic outcomes[81]. Additionally, there is a need for continued research into novel nanoparticle formulations and surface modifications that optimize curcumin delivery to tumor sites while minimizing off-target effects. Integration of AI-driven approaches with other emerging technologies, such as gene editing and immunotherapy, may also hold promise for synergistic therapeutic interventions in cancer treatment[82]. Furthermore, exploring the potential applications of AI in personalized medicine and treatment optimization could revolutionize cancer therapy by tailoring treatment regimens to individual patient characteristics and disease profiles. Collaborative efforts between researchers, clinicians, and industry stakeholders are essential to drive innovation and translate research findings into clinical practice[83,84].

B. Regulatory Considerations for AI-Driven Nanoparticle Delivery Systems

As AI-driven nanoparticle delivery systems move closer to clinical implementation, regulatory considerations become increasingly important to ensure patient safety and efficacy[85]. Regulatory agencies must establish clear guidelines for the evaluation and approval of AI-driven medical devices and drug delivery systems, taking into account the unique challenges posed by these technologies[86]. Key considerations include the validation of AI algorithms used in nanoparticle design and optimization, ensuring robustness, reliability, and generalizability across diverse patient populations and disease states[87]. Additionally, regulatory agencies must assess the safety and efficacy of nanoparticle formulations, including their biocompatibility, stability, and long-term effects on patient outcomes[88]. Collaboration between regulatory authorities, academic researchers, and industry stakeholders is essential to establish standardized protocols for the evaluation and approval of AI-driven nanoparticle delivery systems[54]. Clear communication and transparency are crucial to foster trust and confidence in these emerging technologies among healthcare professionals and patients[53,9].

C. Ethical Implications and Societal Impact of AI in Cancer Therapy

The integration of AI in cancer therapy raises important ethical considerations and societal implications that warrant careful examination[22]. Ethical concerns may arise regarding patient privacy, data security, and informed consent in the context of AI-driven decision-making and personalized treatment strategies[89]. Moreover, there is a need to address issues of equity and access to AI-driven cancer therapies, ensuring that these technologies benefit all patients, regardless of socioeconomic status or geographic location[32]. Transparency and accountability are essential to mitigate biases and ensure fair and equitable distribution of AI-

driven healthcare resources[5,18]. Furthermore, societal attitudes towards AI in healthcare, including cancer therapy, may influence acceptance and adoption of these technologies[55]. Public education and awareness campaigns are necessary to demystify AI and foster informed discussions about its potential benefits and risks in cancer treatment[90,67].

2. Conclusion

The convergence of artificial intelligence and nanoparticle delivery systems presents a groundbreaking opportunity to advance cancer therapy, particularly in enhancing the efficacy of curcumin-based treatments. Through the integration of AI algorithms, researchers can optimize nanoparticle design and predict drug delivery parameters, leading to personalized treatment strategies tailored to individual patient profiles. This synergy holds tremendous potential for improving therapeutic outcomes and patient quality of life. However, regulatory considerations, ethical implications, and societal impact must be carefully addressed to ensure responsible and equitable implementation of AI-driven healthcare solutions. Collaborative efforts between researchers, clinicians, regulatory agencies, and industry stakeholders are essential to overcome these challenges and realize the full potential of AI in cancer therapy. With continued research, innovation, and interdisciplinary collaboration, the integration of artificial intelligence and nanoparticle delivery systems will revolutionize cancer treatment, offering new hope to patients and transforming the landscape of oncology.

3. References

[1] Iriventi P., Gupta N.V., Osmani R.A.M., Balamuralidhara V. Design & development of nanosponge loaded topical gel of curcumin and caffeine mixture for augmented treatment of psoriasis. Daru. 2020;28:489–506. doi: 10.1007/s40199-020-00352-x.

[2] Kumar B., Sahoo P.K., Manchanda S. Curcumin Loaded Ethosomal Gel for Improved Topical Delivery: Formulation, Characterization and Ex-vivo Studies. Pharm. Nanotechnol. 2021;9:281–287. doi: 10.2174/2211738509666210208225826.

[3] Rachmawati H., Edityaningrum C.A., Mauludin R. Molecular inclusion complex of curcumin-beta-cyclodextrin nanoparticle to enhance curcumin skin permeability from hydrophilic matrix gel. AAPS PharmSciTech. 2013;14:1303–1312. doi: 10.1208/s12249-013-0023-5.

[4] Sana E., Zeeshan M., Ain Q.U., Khan A.U., Hussain I., Khan S., Lepeltier E., Ali H. Topical delivery of curcumin-loaded transfersomes gel ameliorated rheumatoid arthritis by inhibiting NF-kappabeta pathway. Nanomedicine. 2021;16:819–837. doi: 10.2217/nnm-2020-0316.

[5] Scomoroscenco C., Teodorescu M., Raducan A., Stan M., Voicu S.N., Trica B., Ninciuleanu C.M., Nistor C.L., Mihaescu C.I., Petcu C., et al. Novel Gel Microemulsion as Topical Drug Delivery System for Curcumin in Dermatocosmetics. Pharmaceutics. 2021;13:505. doi: 10.3390/pharmaceutics13040505.

[6] Deshmukh R.A., Bagewadi A.S. Comparison of effectiveness of curcumin with triamcinolone acetonide in the gel form in treatment of minor recurrent aphthous stomatitis: A randomized clinical trial. Int. J. Pharm. Investig. 2014;4:138–141. doi: 10.4103/2230-973X.138346.

[7] Nasra M.M.A., Khiri H.M., Hazzah H.A., Abdallah O.Y. Formulation, in-vitro characterization and clinical evaluation of curcumin in-situ gel for treatment of periodontitis. Drug Deliv. 2017;24:133–142. doi: 10.1080/10717544.2016.1233591.

[8] Fonseca-Santos B., Bonifacio B.V., Baub T.M., Gremiao M.P.D., Chorilli M. In-Situ Gelling Liquid Crystal Mucoadhesive Vehicle for Curcumin Buccal Administration and Its Potential Application in the Treatment of Oral Candidiasis. J. Biomed. Nanotechnol. 2019;15:1334–1344. doi: 10.1166/jbn.2019.2758.
[9] Chandrashekar A., Annigeri R.G., Va U., Thimmasetty J. A clinicobiochemical evaluation of curcumin as gel and as buccal mucoadhesive patches in the management of oral submucous fibrosis. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. 2021;131:428–434. doi: 10.1016/j.oooo.2020.12.020.
[10] Das R.P., Gandhi V.V., Verma G., Ajish J.K., Singh B.G., Kunwar A. Gelatin-lecithin-F127 gel mediated self-assembly of curcumin vesicles for enhanced wound healing. Int. J. Biol. Macromol. 2022;210:403–414. doi: 10.1016/j.ijbiomac.2022.04.134.
[11] El-Refaie W.M., Elnaggar Y.S.R., El-Massik M.A., Abdallah O.Y. Novel curcumin-loaded gel-core hyaluosomes with promising burn-wound healing potential: Development, in-vitro appraisal and in-vivo studies. Int. J. Pharm. 2015;486:88–98. doi: 10.1016/j.ijpharm.2015.03.052.
[12] Deepa D., Krishnamoorthy V., Balan S., Raja S. Comparative Evaluation of Topical Curcumin Gel and Clotrimazole Solution in the Management of Oral Candidiasis. Cureus. 2019;11:8. doi: 10.7759/cureus.5429.
[13] Gairola A., Kalra M., Raut R., Jaiswal R., Tiwari R., Sahu R. Efficacy of a new curcumin-gel in the treatment of oral lichen planus: A randomized controlled clinical trial. J. Oral Biol. Craniofac. Res. 2021;11:296–301. doi: 10.1016/j.jobcr.2020.12.004.
[14] Mahadik R.M., Ashtankar M.B. Formulation and Evaluation of Mouth Dissolving Film of Curcumin. Int. J. Pharm. Sci. Rev. Res. 2020;64:134–139.
[15] Mandal S., Basu S.K., Sa B. Design, development and characterization of microemulsion drug delivery system of acyclovir for improvement of oral bioavailability. AAPS PharmSciTech. 2009;10:917–923. doi: 10.1208/s12249-009-9288-9.
[16] Ahmed S.M., Samy W.M. Novel topically applied second generation non-ionic surfactant vesicles: Spanlastics for the enhanced delivery of fluconazole in an in vivo dermatophytosis model. Drug Deliv. 2014;21:120–130. doi: 10.3109/10717544.2013.840688.
[17] Bisht S., Maitra A. Systemic delivery of curcumin: 21st century solutions for an ancient conundrum. Curr. Drug Discov. Technol. 2009;6:192–199. doi: 10.2174/157016309789052125.
[18] Bhawana, Basniwal R.K., Buttar H.S., Jain V.K., Jain N. Curcumin nanoparticles: Preparation, characterization, and antimicrobial study. J. Agric. Food Chem. 2011;59:2056–2061. doi: 10.1021/jf104402t.
[19] Gupta S.C., Patchva S., Aggarwal B.B. Therapeutic roles of curcumin: Lessons learned from clinical trials. AAPS J. 2013;15:195–218. doi: 10.1208/s12248-012-9432-8.
[20] Lal J., Gupta S.K., Thavasu P.W., Sangar V., William P. Role of curcumin in cancer therapy: Insights into potential mechanisms of action and current status of clinical trials. J. Exp. Ther. Oncol. 2009;8:239–249.
[21] Koch M., Loffler S., Goette J., Maaser K. Topical use of curcumin for wound healing: Potential therapeutic implications and molecular mechanisms. Curr. Pharm. Biotechnol. 2012;13:1109–1116. doi: 10.2174/138920112800399002.
[22] Tsuda T., Horio F., Uchida K., Aoki H., Osawa T. Dietary curcumin and liver protection: Effects on lipid metabolism and gene expression. Faseb J. 2003;17:286–288. doi: 10.1096/fj.02-0337fje.
[23] Weiss B., deCory T.R. Dietary curcumin: Bioavailability, bioefficacy, and tolerance in

humans. Adv. Food Nutr. Res. 2007;52:161–220. doi: 10.1016/S1043-4526(06)52004-3.
[24] Heger M., van Golen R.F., Broekgaarden M., Michel M.C. The molecular basis for the pharmacokinetics and pharmacodynamics of curcumin and its metabolites in relation to cancer. Pharmacol. Rev. 2014;66:222–307. doi: 10.1124/pr.110.004044.
[25] Kunnumakkara A.B., Anand P., Aggarwal B.B. Curcumin inhibits proliferation, invasion, angiogenesis and metastasis of different cancers through interaction with multiple cell signaling proteins. Cancer Lett. 2008;269:199–225. doi: 10.1016/j.canlet.2008.03.009.
[26] Kocaadam B., Sanlier N. Curcumin, an active component of turmeric (Curcuma longa), and its effects on health. Crit. Rev. Food Sci. Nutr. 2017;57:2889–2895. doi: 10.1080/10408398.2015.1077195.
[27] Dende C., Meena J., Nagarajan P., Nagaraj V.A., Panda A.K., Padmanaban G. Nanocurcumin is superior to native curcumin in preventing degenerative changes in experimental cerebral malaria. Sci. Rep. 2015;5:10096. doi: 10.1038/srep10096.
[28] Kamal A., Srivastava A.K., Srivastava S., Agarwal A., Sinha S. Curcumin encapsulated pH-sensitive nanoparticles for effective delivery to colon cancer. Biomed. Pharmacother. 2020;129:110417. doi: 10.1016/j.biopha.2020.110417.
[29] Chattopadhyay I., Biswas K., Bandyopadhyay U., Banerjee R.K. Turmeric and curcumin: Biological actions and medicinal applications. Curr. Sci. 2004;87:44–53.
[30] Naksuriya O., Okonogi S., Schiffelers R.M., Hennink W.E. Curcumin nanoformulations: A review of pharmaceutical properties and preclinical studies and clinical data related to cancer treatment. Biomaterials. 2014;35:3365–3383. doi: 10.1016/j.biomaterials.2013.12.090.
[31] Dharmendra Bhati et al., “FUSED AND SUBSTITUTED PYRIMIDINE DERIVATIVES AS POTENT ANTICANCER AGENTS,” Biochemical and Cellular Archives/Biochemical and cellular archives, vol. 24, no. 1, Jan. 2024, doi: https://doi.org/10.51470/bca.2024.24.1.749.
[32] K. J. Mangala et al., “NANOCELLULOSE: A VERSATILE AND SUSTAINABLE CARRIER FOR DRUG AND BIOACTIVE COMPOUNDS,” Biochemical and Cellular Archives/Biochemical and cellular archives, vol. 24, no. 1, Jan. 2024, doi: https://doi.org/10.51470/bca.2024.24.1.553.
[33] Rohit Kumar Trivedi et al., “REVOLUTIONIZING DRUG DELIVERY THROUGH 3D PRINTING TECHNOLOGY: CURRENT ADVANCES AND FUTURE DIRECTIONS,” Biochemical and Cellular Archives/Biochemical and cellular archives, vol. 24, no. 1, Jan. 2024, doi: https://doi.org/10.51470/bca.2024.24.1.521.
[34] H. Rastogi, P. Bhatt, S. Garg, S. Kamboj, V. Deva, and R. Goel, “EXPLORING THE POTENTIAL OF QUANTUM DOTS AS LUMINOUS PROBES FOR TARGETED DRUG DELIVERY AND BIOIMAGING IN CLINICAL DIAGNOSTICS,” Biochemical and Cellular Archives/Biochemical and cellular archives, vol. 24, no. 1, Jan. 2024, doi: https://doi.org/10.51470/bca.2024.24.1.457.
[35] M. shama, “CRISPR-Cas9 gene editing in pharmaceuticals : Current applications and future prospects,” Biochemical and Cellular Archives/Biochemical and cellular archives, vol. 23, no. S1, Dec. 2023, doi: https://doi.org/10.51470/bca.2023.23.s1.1655.
[36] S. Arora, Saiphali, G. Dharmamoorthy Dharmendra Bhati, T. Gupta, and P. Bhatt, “Advancements in peptide-based therapeutics: Design, synthesis and clinical applications,” Biochemical and Cellular Archives/Biochemical and cellular archives, vol. 23, no. S1, Dec. 2023, doi: https://doi.org/10.51470/bca.2023.23.s1.1415.
[37] M. Singhal et al., "Formulation development and characterization of powder for oral suspension containing H2 blocker drug to combat GERD and peptic ulcer,"

NeuroQuantology, vol. 20, no. 11, pp. 1258, 2022.
[38] S. Ahamed, P. Bhatt, S. J. Sultanuddin, R. Walia, M. A. Haque, and S. B. InayathAhamed, "An Intelligent IoT enabled Health Care Surveillance using Machine Learning," in 2022 International Conference on Advances in Computing, Communication and Applied Informatics (ACCAI). IEEE, 2022.
[39] V. Ahmed, S. Sharma, and P. Bhatt, "Formulation and evaluation of sustained release tablet of diltiazem hydrochloride," International Journal of Pharmaceutical Sciences and Research, vol. 11, no. 5, pp. 2193–2198, 2020.

[40] A. E. Al-Snafi, S. Singh, P. Bhatt, and V. Kumar, "A review on prescription and non-prescription appetite suppressants and evidence-based method to treat overweight and obesity," GSC biol pharm sci, vol. 19, no. 3, pp. 148–155, 2022.
[41] B. Baskar, S. Ramakrishna, and A. Daniela La Rosa, Eds., Encyclopedia of green materials. Singapore: Springer Nature Singapore, 2022.
[42] P. Bhatt et al., "Nanorobots recent and future advances in cancer or dentistry therapy- A review," Am J PharmTech Res, vol. 9, no. 3, pp. 321–331, 2019.
[43] P. Bhatt et al., "Citrus Flavonoids: Recent Advances and Future Perspectives On Preventing Cardiovascular Diseases," in The Flavonoids, 2024, pp. 131-152.
[44] P. Bhatt et al., "Functional and tableting properties of alkali-isolated and phosphorylated barnyard millet (Echinochloa esculenta) starch," ACS Omega, vol. 8, no. 33, pp. 30294–305, 2023.
[45] P. Bhatt et al., "Plasma modification techniques for natural polymer-based drug delivery systems," Pharmaceutics, vol. 15, no. 8, p. 2066, 2023.
[46] P. Bhatt et al., "Comparative study and in vitro evaluation of sustained release marketed formulation of aceclofenac sustained release tablets," Pharma Science Monitor, vol. 9, no. 2, 2018.
[47] P. Bhatt et al., "Development and characterization of fast dissolving buccal strip of frovatriptan succinate monohydrate for buccal delivery," Int J Pharm Investig, vol. 11, no. 1, pp. 69–75, 2021.
[48] P. Bhatt et al., "Artificial intelligence in pharmaceutical industry: Revolutionizing drug development and delivery," The Chinese Journal of Artificial Intelligence, 2023.
[49] P. Bhatt et al., "Blockchain technology applications for improving quality of electronic healthcare system," in Blockchain for Healthcare Systems, 2021, pp. 97–113.
[50] P. Bhatt, "Mouth Dissolving Tablets Challenges, Preparation Strategies with a Special Emphasis on Losartan Potassium–A Review," World J. Pharm. Pharm. Sci, vol. 7, no. 9, pp. 271-287, 2018.
[51] C. Goyal et al., "Estimation of shelf-life of Balachaturbhadrika syrup containing different sweetening agents," Res J Pharm Technol, pp. 5078–5083, 2022.
[52] T. Kaur and S. Singh, "Controlled release of bi-layered malvidin tablets using 3D printing techniques," J Pharm Res Int, pp. 70–78, 2021.
[53] M. Kaurav et al., "In-depth analysis of the chemical composition, pharmacological effects, pharmacokinetics, and patent history of mangiferin," Phytomed Plus, vol. 3, no. 2, p. 100445, 2023.
[54] A. Kumar, P. Bhatt, and N. Mishra, "Irritable bowel Syndrome with reference of Alosetron Hydrochloride and Excipient profile used in the manufacturing of Alosetron tablet-A review," J Chem Pharm Sci, vol. 12, no. 03, pp. 71–78, 2019.
[55] M. K. Malik et al., "Significance of chemically derivatized starch as drug carrier in developing novel drug delivery devices," Nat Prod J, 2022.
[56] M. K. Malik et al., "Preclinical safety assessment of chemically cross-linked modified mandua starch: Acute and sub-acute oral toxicity studies in Swiss albino mice," ACS

Omega, vol. 7, no. 40, pp. 35506–35514, 2022.
[57] M. K. Malik et al., "Phosphorylation of alkali extracted mandua starch by STPP/STMP for improving digestion resistibility," ACS Omega, vol. 8, no. 13, pp. 11750–11767, 2023.
[58] Pankaj, "Anti-cancer cyclodextrin nanocapsules based formulation development for lung chemotherapy," J Pharm Res Int, pp. 54–63, 2021.
[59] Pankaj, "Cyclodextrin modified block polymer for oral chemotherapy," J Pharm Res Int, pp. 21–29, 2021.
[60] V. Raghuwanshi et al., "Recent Advances In Nanotechnology For Combating Against Corona Virus Infection," Journal of Pharmaceutical Negative Results, pp. 1811-1820, 2022.
[61] K. K. Sahu et al., "Utility of nanomaterials in wound management," in Nanotechnological Aspects for Next-Generation Wound Management, 2024, pp. 101–130.
[62] S. K. Sharma et al., "Combined therapy with ivermectin and doxycycline can effectively alleviate the cytokine storm of COVID-19 infection amid vaccination drive: A narrative review," J Infect Public Health, vol. 15, no. 5, pp. 566–572, 2022.
[63] S. K. Sharma and P. Bhatt, "Controlled release of bi-layered EGCG tablets using 3D printing techniques," J Pharm Res Int, pp. 5–13, 2021.
[64] S. K. Sharma and S. Singh, "Antimicrobial Herbal Soap Formulation," Journal of Pharmaceutical Research International, vol. 32, no. 36, pp. 82-88, 2022.
[65] S. Singh et al., "Cardiovascular comorbidity of COVID-19 disease: A review," WJPMR, vol. 8, no. 4, pp. 216–225, 2022.
[66] S. Singh et al., "Phytonutrients, Anthocyanidins, and Anthocyanins: Dietary and Medicinal Pigments with Possible Health Benefits," in Advances in Flavonoids for Human Health and Prevention of Diseases, 2024, pp. 23-46.
[67] S. Singh et al., "Digital Transformation in Healthcare: Innovation and Technologies," in Blockchain for Healthcare Systems, 2021, pp. 61–79.
[68] S. Singh et al., "Alginate based Nanoparticles and Its Application in Drug Delivery Systems," Journal of Pharmaceutical Negative Results, pp. 1463-1469, 2022.
[69] R. Johari et al., "Artificial Intelligence and Machine Learning in Drug Discovery and Development," in 2023 12th International Conference on System Modeling & Advancement in Research Trends (SMART), 2023, pp. 556-561.
[70] P. Bhatt et al., "Impact of Cross□Linking on the Physicochemical and Physiological Characteristics of Barnyard Millet (Echinochloa frumentacea) Grains Starch," Stärke/Starch, May 2024, doi: https://doi.org/10.1002/star.202300285.
[71] V. Kumar et al., "Ultrasound assisted techniques for starch modification to develop novel drug delivery systems: A comprehensive study," Journal of bioactive and compatible polymers, May 2024, doi: https://doi.org/10.1177/08839115241249143.
[72] Deepa D., Krishnamoorthy V., Balan S., Raja S. Comparative Evaluation of Topical Curcumin Gel and Clotrimazole Solution in the Management of Oral Candidiasis. Cureus. 2019;11:e5429. doi: 10.7759/cureus.5429.
[73] Mukerjee A., Vishwanatha J.K. Formulation, characterization and evaluation of curcumin-loaded PLGA nanospheres for cancer therapy. Anticancer Res. 2009;29:3867–3875.
[74] Huang Z., Thakkar A., Zha Z., Wu X., Zhang Z., Sumer B.D., Gao J., Li C., CuS nanoparticles conjugated with doxorubicin to enable synergistic photothermal-chemo therapy. Nanoscale. 2013;5:11562–11568. doi: 10.1039/c3nr03782b.
[75] Saptarini N.M., Ariyani S., Sari D.F., Rosidah R. Effect of chitosan gel on the skin penetration of nanoemulsion-based curcumin. Adv. Pharmacol. Sci.

2020;2020:9235104. doi: 10.1155/2020/9235104.
[76] Bucolo C., Drago F., Salomone S. Pharmacological management of diabetic retinopathy: Current and emerging treatments. Pharmacol. Ther. 2012;134:353–360. doi: 10.1016/j.pharmthera.2012.02.005.
[77] Tiwari S., Verma A., Agarwal A., Pawar P. Review on formulation and characterization of nanoemulsion. Int. J. Pharm. Sci. Res. 2012;3:4640–4648.
[78] Mahran R.I., Hagras M.M., Sun D., Brenner D.E., Ghosh A.K., Helmy M.W. Nano-encapsulation of curcumin in PLGA-PEG polymeric nanoparticles for breast cancer therapy. Colloids Surf. B Biointerfaces. 2017;123:823–830. doi: 10.1016/j.colsurfb.2014.09.033.
[79] Gupta M., Agrawal U., Vyas S.P. Nanocarrier-based topical drug delivery for the treatment of skin diseases. Expert Opin. Drug Deliv. 2012;9:783–804. doi: 10.1517/17425247.2012.682528.
[80] Upadhyay A., Dalvi R.S., Gupta R., Cowsik S.M., Ramanujam R.P. Fatty acid conjugation enhances the anti-cancer activity of curcumin in breast cancer cells. Life Sci. 2019;239:117028. doi: 10.1016/j.lfs.2019.117028.
[81] Nagpal M., Sood S., Goyal S., Jat R.K., Coumar M.S. Role of curcumin-loaded nanoparticles in cancer therapy. Biomed. Rep. 2013;1:155–161. doi: 10.3892/br.2012.29.
[82] Patel D., Shukla S., Gupta S. Apigenin and cancer chemoprevention: Progress, potential and promise (Review). Int. J. Oncol. 2007;30:233–245.
[83] Lall R., Ganapathy S., Asokkumar S., Kumar A., Kannappan R., Biswas G., Rajasekaran M. Preparation and characterization of curcumin nanoparticles using microemulsion phase transition method and their anticancer effect on human lung cancer cells. Pharmaceutics. 2020;12:119. doi: 10.3390/pharmaceutics12020119.
[84] Yallapu M.M., Jaggi M., Chauhan S.C. Curcumin nanoformulations: A future nanomedicine for cancer. Drug Discov. Today. 2012;17:71–80. doi: 10.1016/j.drudis.2011.09.009.
[85] Teow H.M., Zhou Z., Najlah M., Yusof S.R., Ahmed M.H., Abbott T., Greco F., Fang X. Delivery of curcumin by polymeric micelles for the treatment of colon cancer. Int. J. Pharm. 2013;449:42–50. doi: 10.1016/j.ijpharm.2013.03.034.
[86] Liu W., Zhai Y., Heng X., Che S., Zhai G. Oral bioavailability of curcumin: Problems and advancements. J. Drug Target. 2016;24:694–702. doi: 10.3109/1061186X.2016.1157886.
[87] Thangapazham R.L., Sharma A., Maheshwari R.K. Multiple molecular targets in cancer chemoprevention by curcumin. AAPS J. 2006;8:E443–E449. doi: 10.1208/aapsj080354.
[88] Tsuda T. Curcumin as a functional food-derived factor: Degradation products, metabolites, bioactivity, and future perspectives. Food Funct. 2018;9:705–714. doi: 10.1039/C7FO01242J.
[89] Xu Y., Ku B., Tie L., Yao H., Jiang W., Ma X., Li X. Curcumin reverses the effects of chronic stress on behavior, the HPA axis, BDNF expression, and phosphorylation of CREB. Brain Res. 2006;1122:56–64. doi: 10.1016/j.brainres.2006.08.009.
[90] Aggarwal B.B., Harikumar K.B. Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. Int. J. Biochem. Cell Biol. 2009;41:40–59. doi: 10.1016/j.biocel.2008.06.010.