



NANOTECHNOLOGY-BASED DRUG DELIVERY SYSTEMS FOR CANCER THERAPY: A COMPREHENSIVE REVIEW OF COLON, GASTRIC, HEPATOCELLULAR AND LUNG CANCERS

Deeksha Sharad Saini^{*1}, Sahil Ravindra Sadavarte², Reetesh Ajay Rout³, Rohini Manoj Verma⁴, Pratiksha Shivaji Bagal⁵, Dr. Mukund G. Tawar⁶

India.



***Corresponding Author: Deeksha Sharad Saini**

India.

DOI: <https://doi.org/10.5281/zenodo.23036762>

How to cite this Article: Deeksha Sharad Saini^{*1}, Sahil Ravindra Sadavarte², Reetesh Ajay Rout³, Rohini Manoj Verma⁴, Pratiksha Shivaji Bagal⁵, Dr. Mukund G. Tawar⁶. (2026). Nanotechnology-Based Drug Delivery Systems For Cancer Therapy: A Comprehensive Review Of Colon, Gastric, Hepatocellular And Lung Cancers. World Journal of Pharmaceutical and Life Sciences, 12(10), 39–86.

This work is licensed under Creative Commons Attribution 4.0 International license.



Article Received on 22/08/2026

Article Revised on 12/09/2026

Article Published on 01/10/2026

ABSTRACT

Many treatment shortcomings are attributed to a poor drug delivery strategy for the treatment of cancer: low drug bioavailability, lack of targeting to cancer tissue, systemic toxicity, emergence of multidrug resistance and metastasis. Here, nanotechnology has attracted attention and its application in chemotherapy with drugs like 5-fluorouracil, oxaliplatin, irinotecan, rapamycin and folinic acid as cargo molecule has been reported for targeting colon cancer with solid lipid nanoparticles, polymeric nanoparticles, liposomes and siRNA nanoparticles. They improved bioavailability and targeting of the drugs and showed increased anticancer efficiency, co-delivery showed enhanced prevention of both tumor growth and invasion with lower toxicity. In case of gastric cancer, nanotechnology drug delivery systems were utilized with 5-fluorouracil, docetaxel, LY294002, paclitaxel, epirubicin and platinum-based drugs through using chitosan, acid-conjugated chitosan, PLGA nanoparticles, ginsenoside liposomes, polymeric micelles and polydopamine nanoparticles. The nanocarriers have significantly enhanced cellular uptake, enhanced retention time, accumulation at the tumor site, and potency to kill tumors with fewer toxicities and significantly reduced peripheral neuropathy developed as a side effect of treatment. Nanocarriers loaded with lenvatinib, sorafenib and doxorubicin for hepatocellular carcinoma demonstrated enhanced clinical performance. Lenvatinib presented 23.3% response, 76.7% disease control, 14-months OS and so on, while sorafenib formulations showed great pharmacokinetic enhancement, tumor accumulation and high potent of therapeutic action with better encapsulation efficiency (87%) and doxorubicin nanoparticles showed 85.98% apoptosis rates, with non-hemolysis activity of merely 2.82% that represents higher antitumor efficacy and less toxicity. Starch nanoparticles, inhalable nanoliposomes, CSO-modified liposomes, PLGA nanoparticles and folate-targeted liposomal and albumin nanocarriers for lung cancer using gefitinib, osimertinib, paclitaxel, docetaxel, vinorelbine and doxorubicin exhibited enhanced cellular uptake, sustained release of drugs, strong tumor targeting action with better anti-tumorigenesis and tumor metastasis with improved outcomes of patients. Furthermore, some of them are also found effective in overcoming drug resistance of cisplatin for lung cancer treatment. Taken together, in all the applications mentioned above nanotechnology-drug delivery systems have showed the promise ability in addressing the issue of delivery, efficacy and security in the treatment of colon, gastric, liver and lung cancers.

KEYWORDS: Colon. Lungs, Cancer, Drugs, Therapy.

INTRODUCTION

Cancer is a worldwide health problem and a significant cause of morbidity and mortality, with many kinds of malignancies regarded as challenging to treat and deadly.

Despite the fact that various anticancer medications are used in clinical settings, the treatment has a significant number of restrictions, resulting in low efficacy. The key restrictions include low medication bioavailability,

targetability, and accumulation in tumor tissue, significant systemic toxicity, low controllable release, and multidrug resistance. This leads to the development of the new drug delivery systems which are capable of improving medication solubility and stability, promoting cellular internalization and tumor accumulation and targeting, controlled or pH-dependent release, and reduced toxicity, has been a promising direction for cancer therapy. Anticancer medications, including 5-Fluorouracil, oxaliplatin, irinotecan, FOLFOX combination chemotherapy, paclitaxel, docetaxel, epirubicin, doxorubicin, capecitabine, gefitinib, osimertinib, vinorelbine, cisplatin, sorafenib, lenvatinib these drugs are modified for the targeted and controlled delivery of treatment by developing solid lipid nanoparticles, magnetic polymeric nanoparticles, PLGA and starch nanoparticles, liposomes, chitosan and chitosan-modified liposomes, polymeric micelles, nano-emulsions, siRNA nanoparticles, EGFR-targeted liposomes, hyaluronic acid-conjugated nanoparticles, folic acid-targeted, ultrasound-triggered, and theranostic nanoparticles are nanocarriers investigated for anticancer drug delivery in colon, gastric, lung and hepatocellular carcinoma. These formulations improve tumor targeting and cellular internalization of pharmaceutical compounds, as well as overcoming multidrug resistance and reducing toxicity. The use of NDDS was suggested as a promising method for malignancy treatment because it can help overcome some of the limitations of current anticancer medications. For particular, non-small cell lung cancer (NSCLC) is regarded as one of the most lethal malignancies because of the high likelihood of developing brain secondaries, hepatocellular carcinoma (HCC) is usually diagnosed at advanced stages when limited treatment options are available. However, in some cases, liver resection, transplantation, or other locoregional treatments can be considered for the treatment of HCC in early stages. This study will discuss the anticancer medications used for the treatment of colon, gastric, lung, and hepatocellular carcinomas, their mechanism of action, NDDS for their delivery and preparation, and the importance of nanotechnology in pharmaceutical compounds for malignancy treatment.

COLON CANCER STUDY

Drug	Mechanism	NDDS	Target Site	Preparation Method	Evaluation Parameter	Final Result	Original Research Article
5-Fluorouracil (5-FU)	5-Fluorouracil (5-FU) is an inhibitor of thymidylate synthase that arrests DNA replication while its metabolites are incorporated into RNA and DNA to impair their functions, leading to programmed cell death in colorectal cancer cells. Entrapment in solid lipid nanoparticles (SLNs) improves tumor targeting, prolonged drug delivery, and reduced toxicity	Solid Lipid Nanoparticles	Colon carcinoma	Solvent evaporation method	Particle size	147.9 ± 1.48 nm	1
					Zeta potential	+14.7 mV	
					Entrapment efficiency	90.60 ± 0.01 %	
					Drug loading	3.40 ± 0.03 %	
					Drug release	85.16 ± 0.26 % in 24 h (sustained release)	
					FTIR	Drug successfully encapsulated; no significant chemical interaction; intermolecular hydrogen bonding observed	
					DSC	Reduced crystallinity with successful drug incorporation into SLNs	
					SEM	Smooth, spherical nanoparticles	
					TEM	Spherical nanoparticles with uniform morphology	
					In vitro cytotoxicity	Enhanced cytotoxicity against HCT-116 cells	
					In vivo efficacy	Reduced tumor incidence, multiplicity, aberrant crypt foci (ACF), and tumor size	
					Antioxidant activity	Significant increase in SOD,	

						CAT and GSH levels compared with DMH-treated group	
					Stability	Stable under ICH storage conditions (25 ± 2°C, 60 ± 5% RH)	
Drug	Mechanism	NDDS	Target Site	Preparation Method	Evaluation Parameter	Final Result	Original Research Article
5-Fluorouracil (5-FU)	The folic acid functionalized magnetic triblock copolymer nanoparticles act selectively on the folate receptors over-expressed by colon cancer cells. After the uptake of these particles by the cancerous cells, the drug 5-fluorouracil (5-FU) is released from these particles to inhibit thymidylate synthase, DNA synthesis, and apoptosis of the cancerous cells.	Magnetic Copolymers	Targeted tumor site	Copolymerization technique	Particle size (TEM)	Spherical nanoparticles with an average size of ~50 nm.	2
					Hydrodynamic particle size (DLS)	85 nm for drug-loaded nanoparticles; 37.2 nm for blank nanoparticles.	
					Morphology	Uniform, spherical nanoparticles confirmed by TEM.	
					Drug Loading Capacity (DLC)	5%.	
					Encapsulation Efficiency (EE)	56.5%.	
					In vitro drug release	pH-responsive sustained release; 20.05 ± 0.33% released in 8 h, 26.25 ± 0.78% in 48 h, and 77.23 ± 3.96% after 15 days. Drug release was higher under acidic pH.	
					Cytotoxicity (MTT assay)	5-FU-loaded nanoparticles showed significantly greater cytotoxicity than free 5-FU	

						against all colon cancer cell lines.	
					IC ₅₀ (HT29)	Free 5-FU: 46.1 ± 4.7 µM; Nanoparticles: 5.1 ± 0.88 µM.	
					IC ₅₀ (Caco-2)	Free 5-FU: 41.9 ± 1.5 µM; Nanoparticles: 4.8 ± 0.7 µM.	
					IC ₅₀ (SW480)	Free 5-FU: 12.0 ± 2.2 µM; Nanoparticles: 3.9 ± 0.4 µM.	
					IC ₅₀ (HCT116)	Free 5-FU: 6.5 ± 0.3 µM; Nanoparticles: 3.2 ± 0.2 µM.	
					IC ₅₀ (Normal HUVEC cells)	Free 5-FU: 5.2 ± 0.7 µM; Nanoparticles: 3.8 ± 0.1 µM, indicating relatively lower toxicity enhancement in normal cells.	
					Cellular uptake (ICP-OES)	HT29 cells: 12.65 ± 1.2 pg Fe/cell; HUVEC cells: 2.96 ± 0.27 pg Fe/cell, demonstrating enhanced folate receptor-mediated uptake.	
					Cellular uptake (Prussian blue staining)	Strong nanoparticle uptake in HT29 cancer cells; markedly lower uptake in HUVEC cells.	
					In vivo tumor targeting	Folic acid-conjugated nanoparticles accumulated more effectively in tumor tissue than non-targeted nanoparticles.	
					Tumor volume	Day 20 tumor volume: Saline 3898 mm ³ ; Blank NPs 3217 mm ³ ; Free 5-FU 1495 mm ³ ; 5-FU-loaded FA-NPs 613 mm ³ (greatest inhibition).	
					Survival study	Median survival: Saline 22 days; Blank NPs 27 days; Free 5-FU 33 days; 5-FU-loaded FA-NPs 48 days.	
					Western blot (Bax/Bcl-2)	Bax protein significantly increased; Bax/Bcl-2 ratio highest in the 5-FU-loaded nanoparticle group, indicating	

						enhanced apoptosis.	
					Overall conclusion	FA-conjugated PEG-PCL-PEG/SPION nanoparticles produced sustained, pH-responsive release, enhanced tumor targeting, greater cellular uptake, lower IC ₅₀ values, stronger tumor inhibition, prolonged survival, and increased apoptosis compared with free 5-FU.	
Drug	Mechanism	NDDS	Target Site	Preparation Method	Evaluation Parameter	Final Result	Original Research Article
Oxaliplatin and Rapamycin	The drug combination is simultaneously delivered to the cells of the colon through liposomal delivery. Rapamycin interferes with the mTOR pathway, and its activity retards the growth and multiplication of the cells, while oxaliplatin forms DNA crosslinks resulting in apoptosis of cancer cells.	Co-delivery Liposomes	Combination therapy targets	Thin film hydration	Particle size	134.1 ± 1.8 nm (FA@R/O Lps)	3
					Polydispersity Index (PDI)	0.14 ± 0.01	
					Zeta potential	-40.54 ± 2.26 mV	
					Drug Loading (Rapamycin)	2.38 ± 0.17%	
					Drug Loading (Oxaliplatin)	5.41 ± 0.29%	
					Encapsulation Efficiency (Rapamycin)	96.6 ± 0.8%	
					Encapsulation Efficiency (Oxaliplatin)	97.4 ± 0.6%	
					Liposome stability	Stable for 22 days at 4°C with no significant change in size, PDI, zeta potential, or drug content.	

					Cellular uptake	Folate-modified liposomes showed significantly higher uptake than non-targeted liposomes.	
					Cytotoxicity	FA@R/O Lps showed the lowest IC ₅₀ and highest cytotoxicity against CT26 and MC38 cells.	
					Colony formation assay	Strong inhibition of colony formation compared with free drugs and non-targeted liposomes.	
					Migration assay	Significant inhibition of CT26 cell migration (41.7 ± 2.9 migrated cells vs 354.3 ± 10.2 in control).	
					Apoptosis	Highest apoptosis observed with FA@R/O Lps ($23.2 \pm 1.7\%$), greater than free drug combination and non-targeted liposomes.	
					Immunogenic Cell Death (ICD)	Highest CRT exposure, HMGB1 release (1.37 ± 0.11 -fold), and ATP secretion (2.40 ± 0.18 -fold), indicating enhanced ICD.	
					Live/Dead assay	Maximum tumor cell death observed in FA@R/O Lps-treated cells.	
					Tumor inhibition (in vivo)	Tumor volume reduced to 282.7 ± 69.3 mm ³ with 81.2% tumor inhibition rate, the best among all treatment groups.	
					Ki-67 staining	Significant reduction in tumor cell proliferation.	
					TUNEL assay	Strong induction of apoptosis in tumor tissues.	
					Immune response	Increased CRT, HMGB1, CD4 ⁺ and CD8 ⁺ T-cell infiltration; decreased Foxp3 ⁺ regulatory T cells.	

					Liver metastasis	Nearly complete suppression of colorectal cancer liver metastasis with markedly reduced metastatic lesions.	
					Hemocompatibility	Negligible hemolysis across tested concentrations.	
					Systemic toxicity	No significant body-weight loss and no observable histopathological damage to major organs, indicating good biosafety.	
Drug	Mechanism	NDDS	Target Site	Preparation Method	Evaluation Parameter	Final Result	Original Research Article
Oxaliplatin	Colorectal cancer cells are targeted by nanoparticles that have siRNA molecules loaded into them to selectively target and kill those cancer cells that express resistance genes against oxaliplatin. As a result, tumor cells regain their sensitivity to the effects of oxaliplatin treatment.	siRNA Nanoparticles	Tumor microenvironment	Self-assembly method	Cell lines used	HCT116, LOVO colorectal cancer cells	4
					Animal model	HCT116 xenograft nude mice (6–8 weeks old)	
					Target gene	ATP7A (ATPase copper transporter A)	
					siRNA delivery system	DOTAP-assisted PEG-PLGA nanoparticles (DAN)	
					Nanoparticle size	101.4 ± 13.84 nm	
					Zeta potential	+21.77 ± 3.26 mV	
					Stability	Stable in RPMI-1640 containing 10% FBS for 48 h	
					Gene silencing efficiency	Significant ATP7A mRNA and protein knockdown both in vitro and in vivo (P < 0.001)	
					Cellular uptake	Efficient intracellular uptake confirmed by Cy5-labeled siRNA confocal microscopy	
					Cell viability	Significantly reduced after DAN-siATP7A + oxaliplatin	

						treatment (P < 0.001)	
					IC50 (HCT116)	Reduced from 8.407 mg/mL to 1.604 mg/mL after ATP7A knockdown	
					IC50 (LOVO)	Reduced from 5.439 mg/mL to 1.713 mg/mL after ATP7A knockdown	
					Apoptosis	Significantly increased with DAN-siATP7A + oxaliplatin (P < 0.001)	
					Colony formation	Significantly inhibited (P < 0.001)	
					Migration/Invasion	Significantly suppressed in wound healing and Transwell assays (P < 0.001)	
					Tumor volume	Significantly decreased in combination treatment (P < 0.001)	
					Tumor weight	Significantly reduced in DAN-siATP7A + oxaliplatin group	
					TUNEL assay	Highest apoptosis observed in combination therapy	
					Histology (H&E)	Greater tumor destruction in combination-treated mice	
					Body weight	No significant loss; treatment well tolerated	
					Organ toxicity	No pathological changes in heart, liver, spleen, lung, kidney, or brain	
					Blood biochemistry	ALT, AST, GGT, BUN, Creatinine, and Uric acid remained within normal range; no significant toxicity	
					Overall therapeutic outcome	DAN-mediated ATP7A siRNA delivery successfully reversed oxaliplatin resistance and enhanced antitumor efficacy with minimal systemic toxicity.	
Drug	Mechanism	NDDS	Target Site	Preparation Method	Evaluation Parameter	Final Result	Original Research Article

Irinotecan + Oxaliplatin	The combination of drugs is delivered simultaneously by a liposome, reaching the cancer cells of the colon. Oxaliplatin causes DNA cross-links, whereas irinotecan blocks the enzyme topoisomerase I that results in DNA damage and ultimately causes cell cycle arrest and apoptosis.	Combination Liposomes	Multidrug resistant cells	Lipid film hydration	Particle Size	194.63 ± 3.97 nm	5
					Polydispersity Index (PDI)	0.106 ± 0.027	
					Zeta Potential	−3.03 ± 0.13 mV	
					Encapsulation Efficiency (EE%)	Oxaliplatin: 13.44 ± 2.62%; Irinotecan: 87.80 ± 6.80%	
					Drug Loading (DL%)	Oxaliplatin: 2.10 ± 0.40%; Irinotecan: 5.09 ± 0.95%	
					Morphology	Spherical, uniform liposomes (TEM)	
					In vitro Stability	Stable in PBS (pH 7.4) and 10% plasma; less stable in RPMI-1640 medium	
					In vitro Drug Release	Biphasic release (initial burst followed by sustained release); synchronized release maintained OXA:IRI ratio around 1:1–1:1.5	
					Cellular Uptake	Higher uptake and co-delivery efficiency than mixture of single liposomes	
					In vitro Cytotoxicity	Co-loaded liposomes showed significantly greater cytotoxicity than free drug mixture and single-drug liposome mixture (CT-26 & HCT-116 cells)	
					In vivo Biodistribution	Higher tumor accumulation than free drug (~5.60% vs 0.94% for free DiR)	
					In vivo Antitumor Activity	Superior tumor inhibition compared with solution	

						mixture and single-loaded liposomes	
					Histopathology / Safety	Reduced systemic toxicity; no obvious tissue abnormalities; lower toxicity than free-drug formulations	
					Optimized Drug Ratio	Oxaliplatin : Irinotecan = 1 : 1.5 (molar ratio)	
					Overall Conclusion	Co-loaded liposomes provided synchronized drug delivery, enhanced antitumor efficacy, improved tumor targeting, and reduced toxicity.	
Drug	Mechanism	NDDS	Target Site	Preparation Method	Evaluation Parameter	Final Result	Original Research Article
Irinotecan	EGFR targeted liposome acts as an internalization vector to deliver Irinotecan. This drug releases the active moiety SN-38 by getting accumulated in the tumor cells with EGFR over expression and causes DNA damage by inhibiting topoisomerase I enzyme.	EGFR-targeted Liposomes	EGFR expressing cells	Post-insertion method	Particle size	84.6 ± 1.2 nm (CPT-11 liposome); 150.4 ± 0.8 nm (EGFR-targeted liposome)	6
					Morphology	Spherical/irregular nanoparticles	
					Physical stability	Stable for at least 14 days with no significant particle size change	
					Drug loading (Encapsulation)	0.5519	
					Drug release	Sustained release; ~35% released at 12 h, >95% released by 72 h	
					Cell viability	EGFR-Lipo-CPT-11 produced the lowest survival rate in SW620 cells compared with free CPT-11 and non-targeted liposome	
					IC50 (Free CPT-11)	55.45 µg/mL (SW620 cells)	

					Cellular targeting	Specific targeting toward EGFR-overexpressing SW620 cells	
					ROS generation	Approximately 1.5-fold higher intracellular ROS than free CPT-11	
					Apoptosis	Free CPT-11: 20.05%; Lipo-CPT-11: 34.64%; EGFR-Lipo-CPT-11: 42.45%	
					Caspase activation	Significant upregulation of cleaved caspase-3 and cleaved caspase-9	
					In vivo antitumor efficacy	EGFR-targeted liposome produced significantly greater tumor inhibition than free CPT-11 and non-targeted liposome	
					Overall conclusion	EGFR-targeted DSPE-PEG2000 liposomes improved targeting, sustained drug release, apoptosis, ROS production, and antitumor efficacy while enhancing irinotecan delivery	
Drug	Mechanism	NDDS	Target Site	Preparation Method	Evaluation Parameter	Final Result	Original Research Article
FOLFOX Regimen	Nanoconjugates are used to deliver oxaliplatin and folinic acid to the tumour cells, where 5-fluorouracil is administered as a follow-up. The folinic acid will inhibit thymidylate synthase, which will be enhanced by the effect of 5-fluorouracil on the other hand, while oxaliplatin will cause DNA damage and induce immunogenic cell death.	Advanced Nanoparticles	Metastatic colorectal cancer	Nanoprecipitation	Particle size	35 ± 3 nm	7
					Polydispersity	≈ 0.30	

					Index (PDI)		
					Zeta potential	≈ +2 mV	
					Morphology	Spherical nanoparticles (TEM)	
					Encapsulation Efficiency (EE%)	≈ 98%	
					Drug Loading Capacity (LC%)	≈ 38 wt%	
					In vitro drug release	>95% release at pH 5.5 within 24 h; significantly slower at pH 7.4	
					Serum stability	Stable up to 12 h in 10% serum; aggregation observed at 24 h	
					Cellular uptake/Targeting	AEAA-targeted nanoparticles showed significantly higher tumor uptake than non-targeted nanoparticles	
					Cytotoxicity (IC ₅₀)	Nano-FdUMP ≈ 20 μM; 5-FU ≈ 70 μM (24 h)	
					ROS generation	Significantly increased compared with free 5-FU	
					Apoptosis	Significantly enhanced; reduced after NAC treatment confirming ROS-mediated apoptosis	
					Immunogenic Cell Death (ICD)	Strong induction (CRT exposure, ATP secretion, HMGB1 release); highest with Nano-FdUMP + Nano-Folox	
					Pharmacokinetics	Half-life: Nano-FdUMP ≈ 1.6 h (CRC) and 1.4 h (HCC); free 5-FU ≈ 5–6 min	
					Biodistribution	Enhanced tumor accumulation and reduced liver accumulation compared with non-targeted formulation	
					In vivo antitumor efficacy	Marked tumor regression in orthotopic CRC and HCC models	
					Immune response	Increased CD8 ⁺ T cells, CD4 ⁺ T cells, memory T cells,	

						dendritic cells; decreased MDSCs, Tregs and M2 macrophages	
					Survival	Long-term survival in 5/6 CRC mice and 4/6 HCC mice after Nano-FdUMP + Nano-Folox treatment	
					Combination therapy	Nano-FdUMP + Nano-Folox + anti-PD-L1 produced the best therapeutic efficacy against CRC liver metastasis with long-term survival in 5/6 mice	
					Safety/Toxicity	No significant systemic toxicity at therapeutic doses; no significant changes in body weight, hematological, liver or kidney parameters	

Gastric Cancer Study

Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
5-Fluorouracil	Pyrimidine analogue; inhibits thymidylate synthase, blocking DNA synthesis	Chitosan nanoparticles	Gastric cancer SGC-7901 cells	Ionic gelation	Particle size	283.9 ± 5.25 nm	8
					Polydispersity Index (PDI)	0.243 ± 0.012	
					Zeta potential	+45.3 ± 3.23 mV	
					Entrapment Efficiency (EE)	44.28 ± 1.69 %	
					Drug Loading Capacity (LC)	20.13 ± 0.007 %	
					Morphology (TEM)	Spherical nanoparticles with smooth surface	
					In vitro Drug Release	Biphasic release (initial burst followed by sustained release); ~76% released at 0.7 h, sustained release continued up to 8 h	

					Release Kinetics	First-order kinetics ($r = 0.9273$)	
					Cytotoxicity (MTT assay)	5-FU nanoparticles showed cytotoxicity comparable to 5-FU injection; blank chitosan nanoparticles were non-toxic	
					Pharmacokinetic Study	AUC, MRT, and half-life significantly increased compared to free 5-FU, demonstrating sustained release	
					AUC (0–t)	1078.826 ± 307.302 mg/L/min	
					AUC (0– ∞)	1138.703 ± 307.836 mg/L/min	
					MRT (0–t)	81.226 ± 31.261 min	
					Half-life ($t_{1/2z}$)	84.636 ± 33.542 min	
					Stability	Good colloidal stability (zeta potential >30 mV)	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
5-Fluorouracil (5-FU)	CD44-mediated targeted delivery enhances cellular uptake, ROS generation, mitochondrial apoptosis, and antitumor activity	HA-coated Chitosan Nanoparticles	CD44-overexpressing tumor cells (A549); mitochondria	Ion gelation followed by HA surface coating	Evaluation Parameter	Final Result (from the paper)	9
					Particle size	118.9 ± 9.8 nm	
					Zeta potential	$+15.6 \pm 3.7$ mV	
					Polydispersity Index (PDI)	0.19 ± 0.05	
					Encapsulation Efficiency (EE)	$86.7 \pm 6.18\%$	
					Drug Loading / Loading Efficiency	Measured (LE evaluated), numerical value not reported in the paper	
					Morphology	Sub-spheroidal nanoparticles (TEM)	
					In vitro Drug Release	Sustained biphasic release;	

						>75% of 5-FU released within 48 h	
					FTIR	Confirmed successful HA coating on chitosan nanoparticles; no new chemical bond formed	
					Cytotoxicity (MTT)	HA-coated 5-FU NPs showed highest cytotoxicity against CD44-overexpressing A549 cells	
					IC50 (A549, 48 h)	8.0 µg/mL	
					IC50 (HepG2, 48 h)	6.7 µg/mL	
					Cellular Uptake	Significantly enhanced in CD44-overexpressing A549 cells	
					Mitochondrial Membrane Potential (JC-1)	Significant decrease, indicating mitochondrial damage	
					ROS Assay	ROS generation significantly increased (dose-dependent)	
					Apoptosis (Annexin V/PI)	64.3% apoptotic cells with HA-coated 5-FU NPs	
					Western Blot	↑ Cytochrome c, ↑ Caspase-9, ↑ Cleaved Caspase-3, ↓ Bcl-2	
					Targeting Efficiency	Improved CD44-mediated targeting and intracellular accumulation	
					Overall Antitumor Effect	HA-coated 5-FU nanoparticles exhibited superior antitumor efficacy compared with free 5-FU and uncoated nanoparticles	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Capecitabine	Oral prodrug converted to 5-FU by thymidine phosphorylase; inhibits DNA/RNA synthesis	Prebiotic xylan-stearic acid conjugate nanoparticles (SCXN)	Colorectal tumor tissue (gastrointestinal tract)	Self-assembly (nanoprecipitation)	Particle morphology	Spherical, homogeneous nanoparticles (TEM)	10
					Particle size	152.37 ± 1.88 nm	

					Zeta potential	-22.17 ± 0.69 mV	
					Drug loading (DL)	0.0949	
					Encapsulation efficiency (EE)	0.8759	
					In vitro drug release	<7% release in PBS (48 h); ~75% release in mouse caecal content (48 h)	
					Stability	Stable in artificial gastric juice for 8 h	
					Intestinal absorption	Sustained absorption; ~53.1% absorbed after 4 h (vs >80% for free Cap)	
					Biodistribution	Increased tumor accumulation; prolonged intestinal retention	
					Pharmacokinetics	AUC increased 2.31-fold; Half-life increased 2.73-fold; Plasma clearance reduced to 43.18% of free Cap	
					Biocompatibility	No significant body weight loss; normal blood biochemistry; minimal organ toxicity	
					Histopathology	Normal H&E of major organs; reduced intestinal mucosal damage compared with free Cap	
					Tumor inhibition rate (CT26 model)	0.7178	
					Tumor inhibition rate (MC38 model)	0.8733	
					Apoptosis (TUNEL)	Markedly increased tumor cell apoptosis	
					Survival study	Median survival increased from 14 days to 33.5 days	
					Immune response	Increased mature dendritic cells, increased CD8 ⁺ T-cell infiltration, reduced Treg cells	
					Gut microbiota	Increased Bifidobacterium, Roseburia, Akkermansia; decreased harmful bacteria	

					Short-chain fatty acids	≥37% increase in total SCFAs; butyrate increased 3.53-fold vs saline and 3.27-fold vs Cap	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Oxaliplatin (NC-4016)	DACH-Pt (active moiety of Oxaliplatin) forms DNA cross-links, inhibiting DNA replication and transcription, leading to apoptosis.	Polymeric micelle (NC-4016) composed of PEG–poly(glutamic acid) [PEG–P(Glu)] block copolymer (~40 nm).	Tumor tissue (KB xenograft) via the Enhanced Permeability and Retention (EPR) effect.	DACH-Pt was converted to an aqueous complex using AgNO ₃ , followed by polymer–metal complexation with PEG–P(Glu) in distilled water to form NC-4016 micelles.	In vitro cytotoxicity (MTS assay, IC ₅₀)	NC-4016 showed lower cytotoxicity than Oxaliplatin (higher IC ₅₀ values), indicating slower drug release.	11
					Tumor volume inhibition	NC-4016 significantly reduced tumor volume compared with control and showed better inhibition than Oxaliplatin.	
					Tumor weight	Tumour weight decreased by 74% with NC-4016 versus 33% with Oxaliplatin (P=0.009), demonstrating superior antitumor efficacy.	
					Body weight (toxicity)	No significant body-weight loss was observed in either treatment group.	
					Plasma platinum concentration	NC-4016 produced significantly higher and prolonged plasma platinum exposure than Oxaliplatin.	
					Tumor platinum accumulation	NC-4016 accumulated significantly more platinum in tumor tissue than Oxaliplatin, with peak accumulation at 48 h.	
					Cold allodynia (Acetone test)	NC-4016 did not induce cold hyperalgesia/allodynia, whereas Oxaliplatin caused significant cold	

						hypersensitivity from days 1–7.	
					Heat allodynia	No significant changes were observed in either group.	
					Mechanical allodynia (von Frey test)	No significant changes were observed in either group.	
					Overall conclusion	NC-4016 demonstrated superior in vivo antitumor efficacy, greater tumor targeting, and reduced acute peripheral neuropathy compared with conventional Oxaliplatin.	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Paclitaxel (PTX)	Paclitaxel inhibits cancer cell proliferation by stabilizing microtubules, resulting in G2/M phase cell-cycle arrest and apoptosis. In this formulation, PTX acts synergistically with ginsenosides (Rh2, Rg3, Rg5) to enhance anticancer activity.	Multifunctional Ginsenoside-based Liposomes (Rh2-lipo, Rg3-lipo, Rg5-lipo). Ginsenosides function as membrane stabilizers, chemotherapy adjuvants, and active targeting ligands.	Gastric cancer (BGC-823) tumor cells. Active targeting occurs through GLUT (glucose transporter)-mediated uptake, with prolonged circulation enhancing passive tumor accumulation via the EPR effect.	Thin-film hydration method. Lipids (EYPC + ginsenoside $\pm$ PTX) were dissolved in chloroform/ethanol (1:1), rotary-evaporated to form a thin lipid film, hydrated with 5% glucose solution at 50°C for 30 min, followed by probe sonication (300 W, 5 min) to obtain PTX-loaded liposomes.	Particle size	PTX-C-lipo: 125.76 $\pm$ 2.46 nm; PTX-Rh2-lipo: 77.71 $\pm$ 3.22 nm; PTX-Rg3-lipo: 60.11 $\pm$ 3.42 nm; PTX-Rg5-lipo: 112.5 $\pm$ 4.1 nm	12
					Polydispersity Index (PDI)	PTX-C-lipo: 0.26 $\pm$ 0.011; PTX-Rh2-lipo: 0.27 $\pm$ 0.014; PTX-Rg3-lipo: 0.17 $\pm$ 0.013; PTX-Rg5-lipo: 0.25 $\pm$ 0.009	
					Zeta potential	PTX-C-lipo: -21.86 $\pm$ 0.82 mV; PTX-Rh2-lipo: -39.21 $\pm$ 1.03 mV; PTX-Rg3-lipo: -29.32 $\pm$ 0.41 mV; PTX-Rg5-	

						lipo: -34.4 ± 0.8 mV	
					Encapsulation efficiency (EE)	PTX-C-lipo: $90.1 \pm 1.6\%$; PTX-Rh2-lipo: $91.3 \pm 2.1\%$; PTX-Rg3-lipo: $95.5 \pm 3.3\%$; PTX-Rg5-lipo: $82.8 \pm 1.6\%$	
					Drug loading (LE)	PTX-C-lipo: $6.4 \pm 0.2\%$; PTX-Rh2-lipo: $5.6 \pm 0.3\%$; PTX-Rg3-lipo: $7.3 \pm 0.4\%$; PTX-Rg5-lipo: $4.0 \pm 0.1\%$	
					Morphology	Spherical liposomes with smooth surface (TEM).	
					Stability	Stable particle size and PDI for 1 week at 4°C; PTX-Rh2-lipo and PTX-Rg3-lipo showed <25% drug leakage after 48 h, indicating better stability than conventional liposomes.	
					Cellular uptake	Rh2-lipo: 3.1-fold, Rg3-lipo: 2.5-fold, Rg5-lipo: 2.8-fold higher uptake than conventional liposomes.	
					Cytotoxicity (MTT assay)	PTX-loaded ginsenoside liposomes showed significantly higher cytotoxicity and lower IC ₅₀ than free PTX and PTX-C-lipo.	
					Cell cycle analysis	PTX-loaded liposomes induced significant G2/M phase arrest.	
					Apoptosis assay	PTX-loaded ginsenoside liposomes significantly increased apoptosis; PTX-Rh2-lipo induced 85.83% early apoptosis.	
					In vivo tumor targeting	Strong tumor accumulation via GLUT-mediated active targeting; targeting order: Rh2-lipo = Rg3-lipo > Rg5-lipo > C-lipo.	
					Pharmacokinetics	Rh2-lipo exhibited blood circulation comparable to PEGylated liposomes;	

						circulation order: Rh2-lipo > Rg5-lipo > Rg3-lipo.	
					In vivo antitumor efficacy	PTX-Rh2-lipo and PTX-Rg3-lipo produced the greatest tumor inhibition and outperformed Lipusu® and Abraxane®, with no significant systemic toxicity.	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Docetaxel (TXT) + LY294002	Docetaxel: Stabilizes microtubules, disrupts microtubule dynamics, and induces apoptosis. LY294002: Selective PI3K inhibitor that blocks the PI3K/AKT signaling pathway, suppressing proliferation and promoting apoptosis. The combination enhances antitumor activity through simultaneous chemotherapy and PI3K/AKT pathway inhibition.	PLGA (Poly(lactic-co-glycolic acid)) nanoparticles co-loaded with Docetaxel and LY294002 for controlled and tumor-targeted drug delivery.	Gastric cancer tumor tissue (MKN45 gastric cancer cells and gastric tumor site) via passive tumor targeting through the Enhanced Permeability and Retention (EPR) effect.	Emulsion–solvent evaporation method: PLGA (10 mg), Docetaxel (0.3 mg), and LY294002 (0.3 mg) were dissolved in dichloromethane, added dropwise into 1% polyvinyl alcohol (PVA) solution, probe-sonicated to form an emulsion, stirred to evaporate the solvent, centrifuged, washed, and redispersed to obtain PLGA nanoparticles.	Particle size	155.3 ± 3.5 nm	13
					Polydispersity Index (PDI)	0.146 ± 0.171	

					Zeta potential	-16.9 ± 1.6 mV	
					Encapsulation efficiency (Docetaxel)	$60.2 \pm 2.0\%$	
					Encapsulation efficiency (LY294002)	$34.2 \pm 1.3\%$	
					Drug loading (Docetaxel)	$1.70 \pm 0.06\%$	
					Drug loading (LY294002)	$1.00 \pm 0.04\%$	
					Morphology	Uniform spherical nanoparticles without aggregation (TEM)	
					In vitro drug release	Controlled release; Docetaxel: $52.33 \pm 3.21\%$ (48 h), $61.00 \pm 2.65\%$ (120 h); LY294002: $54.67 \pm 3.06\%$ (48 h), $67.67 \pm 3.51\%$ (120 h)	
					Cellular uptake	PLGA nanoparticles showed significantly enhanced intracellular uptake compared with free dye	
					Cytotoxicity	Bare PLGA was non-toxic; PLGA(TXT+LY294002) showed strong dose-dependent cytotoxicity	
					Cell apoptosis	PLGA(TXT+LY294002) produced significantly higher apoptosis than single-drug groups	
					Cell cycle	Induced G2/M and G1/S cell-cycle arrest	
					Biodistribution	Higher tumor accumulation, maximum fluorescence at 48 h	
					In vivo antitumor efficacy	Greatest inhibition of tumor growth among all treatment groups	
					Final tumor weight	73.82 ± 18.66 mg (PLGA(TXT+LY294002)); compared with 124.5 ± 25.68 mg (TXT+LY294002), 195.89 ± 36.8 mg (TXT), 734.7 ± 170.55 mg (saline)	
					Ki-67 staining	Lowest proliferation in	

						PLGA(TXT+LY294002) group	
					TUNEL assay	Highest apoptosis in PLGA(TXT+LY294002) group	
					Histopathology (H&E)	No significant toxicity in heart, liver, spleen, lung, or kidney	
					Overall conclusion	PLGA co-delivery system provided controlled release, tumor targeting, enhanced anticancer activity, and good biocompatibility.	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Doxorubicin (DOX)	DOX is loaded onto PDA-ICG-PEG nanoparticles by π - π stacking and hydrophobic interactions. After accumulation in the tumor, DOX is released preferentially under acidic pH (tumor/lysosomal environment) and is further enhanced by 808 nm NIR laser-triggered photothermal heating, producing a synergistic chemo-photothermal therapeutic effect.	Polydopamine (PDA)-ICG-PEG nanoparticles (PEGylated polydopamine nanoplatfrom) with Mn ²⁺ chelation for MR imaging (PDA-ICG-PEG/DOX(Mn)).	Tumor tissue (4T1 tumor model); intracellular tumor cells/lysosomes, where acidic pH and NIR irradiation promote DOX release. The nanoplatfrom is designed for MR imaging-guided chemo-photothermal therapy.	1. Synthesize PDA nanoparticles by oxidation-induced self-polymerization of dopamine under alkaline conditions. 2. Load ICG onto PDA. 3. PEGylate using C18PMH-PEG. 4. Incubate with DOX (pH 8.0, overnight) for drug loading via π - π stacking/hydrophobic interaction. 5. Chelate Mn ²⁺ ions to obtain PDA-ICG-PEG/DOX(Mn).	Particle size	PDA: ~112 nm; PDA-ICG-PEG: ~129 nm (DLS)	14
					Morphology	Uniform spherical	

						nanoparticles confirmed by TEM	
					UV-Vis spectroscopy	Red-shift of ICG absorption from 780 nm to 800 nm; DOX peak at 490 nm confirming drug loading	
					Drug loading capacity	≈150% (DOX/PDA, w/w)	
					Drug release	41.8% release at pH 5.0 vs 15.7% at pH 7.4 after 24 h; NIR laser further enhanced release	
					Photothermal performance	Temperature increase of 26°C for PDA-ICG-PEG vs 11°C for PDA alone under 808 nm laser (0.8 W/cm ² , 5 min)	
					Photostability	Stable after 5 laser irradiation cycles; free ICG rapidly photobleached	
					In vitro cytotoxicity	Measured by MTT assay; blank nanoparticles showed negligible toxicity; DOX-loaded nanoparticles showed effective cytotoxicity	
					Cellular uptake	Confocal microscopy and flow cytometry showed increased uptake after NIR irradiation	
					MRI evaluation	T ₁ /T ₂ -weighted MR imaging; r ₁ = 14.15 mM ⁻¹ s ⁻¹ , r ₂ = 39.2 mM ⁻¹ s ⁻¹	
					Blood circulation	Two-compartment half-life: t _{1/2α} = 0.55 ± 0.12 h, t _{1/2β} = 8.53 ± 0.77 h	
					In vivo antitumor efficacy	4/5 tumors completely eliminated in the PDA-ICG-PEG/DOX + laser group	
					Histopathology	H&E staining confirmed extensive tumor damage after combination therapy	
					Biocompatibility/Systemic toxicity	No significant body-weight loss; no obvious damage to major organs	

Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Epirubicin (NC-6300)	Topoisomerase II inhibitor (anthracycline). Causes DNA intercalation, inhibits DNA replication and repair, leading to cancer cell death. The study also states that the synergism with oxaliplatin results from inhibition of DNA repair after platinum-induced DNA damage.	Polymeric micelle (NC-6300)	Tumor tissue (gastric cancer xenograft). The micelles accumulate selectively in tumors through the Enhanced Permeability and Retention (EPR) effect and release epirubicin inside acidic lysosomes of cancer cells.	NC-6300 is synthesized by covalently conjugating epirubicin to PEG–poly(aspartate) block copolymer through an acid-labile hydrazone bond. The conjugate spontaneously self-assembles into polymeric micelles (60–70 nm) in aqueous media. Drug release is pH-dependent and accelerated under acidic conditions.	Particle size	NC-6300: 60–70 nm	15
					In vitro cytotoxicity (IC ₅₀)	NC-6300: 55 ± 2.3 nM; Free Epirubicin: 15 ± 1.3 nM	
					Combination Index (CI)	0.98–0.35, indicating synergistic effect	
					Tumor growth inhibition	NC-6300 + NC-4016 significantly inhibited tumor growth more than Epirubicin + Oxaliplatin (p < 0.001)	
					Orthotopic antitumor activity	Higher antitumor activity than free-drug combination (p = 0.016)	
					Survival study	Overall survival significantly improved (p = 0.015)	
					Pharmacokinetics	Higher tumor accumulation and prolonged retention of epirubicin; peak tumor concentration at 24 h; AUC in tumor increased 2.11-fold	
					Hematological toxicity	Less leukopenia and anemia than free-drug treatment	

					Hepatotoxicity	Only slight, transient elevation of AST/ALT	
					Nephrotoxicity	No nephrotoxicity observed	
					Cardiotoxicity	Markedly reduced; ejection fraction remained normal, significantly better than free Epirubicin ($p < 0.001$)	
					Overall conclusion	NC-6300-based micellar therapy showed stronger antitumor efficacy, higher tumor drug accumulation, prolonged survival, and lower systemic toxicity than conventional Epirubicin therapy.	

Hepatocellular Cancer Study

Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Lenvatinib	Blocks signal pathway of VEGFR/FGFR, and therefore stops angiogenesis and tumor development.	PLGA Nanoparticles	Hepatocellular carcinoma cells	Emulsion solvent evaporation	Particle size	100–250 nm	16
					Polydispersity Index (PDI)	<0.30	
					Zeta potential	± 20 to ± 40 Mv	
					Drug loading	5–15%	
					Entrapment efficiency	80–95%	
					In-vitro drug release	Sustained release over 24–72 hours	
					Stability studies	Stable for 1–3 months under storage conditions	
					MTT cytotoxicity assay	Higher cytotoxicity than free drug	
					Cellular uptake	Significantly increased	

						compared with free drug	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Sorafenib	multi -kinase blocker; the process involves inhibition of Raf-1 and B-Raf, both VEGFR and PDGFR in this case.	sorafenib-loaded nano-emulsion (Sor-NanoEm)	Liver/HCC tumor; nano-size may promote tumor accumulation through the EPR effect	Ultrasonication followed by homogenization-assisted nano-emulsification	Droplet size	121.75 ± 12 nm	17
					PDI	0.310	
					Zeta potential	-12.33+1.34mV	
					pH	4.83+ 0.3	
					Viscosity	34,776 ± 3,276 cP	
					TEM morphology	Spherical nano-droplets; no aggregation.	
					TEM droplet size range	60.9–102 nm	
					In-Vitro release method	Dialysis bag diffusion method.	
					Drug release	53% at 8 h; 87.93% at 10 h	
					Release kinetics	Zero-order kinetics; sustained release	
					Cytotoxicity method	MTT assay	
					Cell line	HepG2	
					IC ₅₀ – Sor-NanoEm	4.73 µg/mL	
					IC ₅₀ – Sorafenib suspension	11.14 µg/mL	
					In-vivo toxicity	Sor-NanoEm LD ₅₀ ≈ 48 mg/kg	
					NOAEL	30 mg/kg	
					Cmax	17.33 ± 0.24 µg/mL	

					AUC _{0-∞}	232.2 ± 0.21 µg·h/mL	
					Half-life (t _{1/2})	50.93 ± 0.174 h	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Doxorubicin	Dox is known to interfere with DNA replication and topoisomerase function, while inducing ROS creation and apoptosis process.	Doxorubicin-loaded folic acid-functionalized alginate-modified PLGA nanoparticle. (FA-PLGA-Dox-Alg)	Folate receptors on HepG2 and Huh7 liver cancer cells	Double Emulsion (Water-in-Oil-in-Water, W/O/W) Solvent Evaporation Method	Particle size	PLGA: 164 nm; PLGA-FA: 187 nm; FA-PLGA-Alg: 225 nm; FA-PLGA-Dox-Alg: 293 nm	18
					Particle morphology	Oval/semi-spherical morphology; 55–85 nm diameter.	
					Zeta potential	+4.3 mV, near-neutral surface charge	
					Thermal stability	Total weight loss: 96.82% for FA-PLGA-Alg and	
					Drug content/entrapment	Approximately 0.9% Dox entrapment/content	
					In-vitro drug release	pH-sensitive and controlled release	
					Release at pH 7.4 Release at pH 6.0 Release at pH 5.0	Release at pH 7.4 Approximately 29% release Approximately 41% release	
					Cytotoxicity	Strong cytotoxicity against HepG2 and Huh7	
					HepG2 viability	Approximately 12% viability	
					Huh7 viability	Approximately 10% viability	
					HepG2 free Dox comparison	~43% viability with free Dox vs 12% with nanocarrier	

					Normal HGF cell viability	Approximately 74% with FA-PLGA-Dox-Alg	
					IC50	FA-PLGA-Dox-Alg: 100 nM at 24 h and 50 nM at 48/72 h for HepG2 and Huh7	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Sorafenib	Sorafenib prevents the transmission of Raf/MEK/ERK pathway signals and tyrosine kinase receptors, so that formation of tumors is avoided.	Sorafenib-loaded PLGA–chitosan nanoparticles	HepG2 human hepatocellular carcinoma (HCC) cells	Emulsion-solvent evaporation technique	Particle size	200 ± 13.13 nm	19
					PDI	0.233 ± 0.01	
					Zeta potential	+32 ± 0.11 mV	
					Encapsulation efficiency	0.87	
					Drug loading	0.088	
					Surface morphology	Spherical nanoparticles	
					Drug-excipient compatibility	No significant incompatibility	
					Physical consistency	No significant change in color/texture	
					Crystalline nature	No significant characteristic peaks; effective encapsulation	
					In-vitro drug release	24.5 ± 0.12% at 24 h; 82 ± 0.05% at 240 h	
					Release kinetics	Higuchi model; R ² = 0.9947	
					Release mechanism	n = 0.61; non-Fickian diffusion	
					Cytotoxicity	IC ₅₀ = 3.9 ± 0.15	

						$\mu\text{g/mL}$	
					C _{max}	$4.3 \pm 0.048 \mu\text{g/mL}$	
					AUC _{0-t}	$140.3 \pm 1.94 \mu\text{g}\cdot\text{h/mL}$	
					MRT	$527.9 \pm 1.78 \text{ h}$	
					Half-life ($t_{1/2}$)	$374.09 \pm 3.34 \text{ h}$	
					Volume of distribution (V _d)	$14,288.2 \pm 0.52 \text{ mL}$	
					Clearance (Cl)	$26.469 \pm 0.014 \text{ mL/h/kg}$	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Doxorubicin (DOX) + miR-122	Combination of Fe-miR-122/DOX active nanoparticles provides delivery of both miR-122 and doxorubicin to cancer cells. Fe-miR-122 plays a role of P-gp inhibitor, thereby decreasing drug resistance. On the other hand, doxorubicin destroys DNA of the tumor cells.	Iron (Fe ²⁺)-Coordinated Self-Assembled Nanoparticles	Hepatocellular carcinoma (HCC) cells (HepG2) – with intracellular delivery to the cytoplasm and nucleus.	Fe ²⁺ Coordination-Driven Self-Assembly (One-Pot Synthesis)	Particle morphology	Uniform spherical nanoparticles with smooth surface.	20
					Particle size	Average diameter 155.6 nm.	
					Zeta potential	+3.79 mV, indicating positively charged nanoparticles.	
					Drug Loading Content (DLC)	DOX DLC increased up to 58.35 wt.% at 20:1 DOX: miR-122 ratio.	
					Drug Loading Efficiency (DLE)	At DOX: miR-122 ratio of 20:1, loading efficiencies were approximately 54.7% (DOX) and 55.5%	

						(miR-122). At ratios below 10:1, DLE exceeded 70% for both.	
					Colloidal stability	Stable for 24 h in water, HEPES, 10% FBS, and 20% FBS; partial degradation after 48 h.	
					Drug release study	In HEPES (24 h): DOX 7.6%, miR-122 3.5% released.	
					Cellular uptake	In cell lysate (24 h): DOX 70.3%, miR-122 51.4% released.	
					Lysosomal escape	Nanoparticles successfully escaped lysosomes after uptake, enabling cytoplasmic drug release.	
					Cell viability (Cytotoxicity)	Fe-miR-122/DOX showed significantly greater cytotoxicity than free DOX	
					Apoptosis assay	Apoptosis rates: PBS 11.14%, miR-122 13.13%, DOX 34.44%, Fe-miR-NC/DOX 49.04%, Fe-miR-122/DOX 85.98% (highest).	
					Western blot analysis	↓P-gp, ↓Bcl-2, ↓cIAP1, ↓PARP-1; ↑Caspase-3, confirming reduced drug resistance and enhanced apoptosis.	
					Hemocompatibility	Haemolysis rate 2.82%, below the acceptable 5% threshold,	

						indicating good biocompatibility	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Final Result	Specific Research Article (Reference)
Lenvatinib	All type of VEGFR, FGFR, PDGFR, RET and SCF receptors should be blocked in order to avoid angiogenesis	Ultrasound-triggered ROS-responsive polymeric nanoparticles. (Len-RNPs)	Hepatocellular carcinoma (HCC) tumor tissue	Thin Film Hydration Method	Particle Size	Len-RNPs: 121.37 nm; Len-NRNPs: 120.49 nm	21
					Polydispersity Index (PDI)	Len-RNPs: 0.142; Len-NRNPs: 0.144	
					Drug Loading Content (DLC)	Len-RNPs: 9.17%; Len-NRNPs: 9.21%	
					In vitro Drug Release	Without ultrasound: 28.17% released in 48 h. With 1 min ultrasound: 50.70%. With 3 min ultrasound: 76.70%..	
					Pharmacokinetics (Half-life)	Free Len: 4.10 ± 0.09 h; Len-RNPs: 8.86 ± 1.07 h.	
					AUC (0–24 h)	Free Len: 14.75 ± 1.46 $\mu\text{g/mL} \cdot \text{h}$; Len-RNPs: 101.00 ± 11.93 $\mu\text{g/mL} \cdot \text{h}$.	
					Biodistribution	Tumor accumulation increased 3.35-fold (6 h), 5.61-fold (24 h), and 7.25-fold (48 h) compared with free Len. Ultrasound further increased tumor concentration	

					In vivo Antitumor Activity	Tumor suppression rate (TSR): Free Len 29.94%; Ultrasound 22.45%; Len-NRNPs 43.90%; Len-RNPs 40.81%; Len-RNPs + Ultrasound: 95.71%, with 60% of mice cured.	
					Histopathology (H&E)	Extensive tumor necrosis observed in the Len-RNPs + Ultrasound group; no major organ damage detected.	
					Immune Cell Analysis	Increased CD4 ⁺ T cells, CD8 ⁺ T cells, NK cells, activated dendritic cells, M1 macrophages; decreased MDSCs and M2 macrophages.	
					Inflammatory Cytokines	Increased IFN- γ , IL-6, and TNF- α , indicating enhanced immune activation.	
					Safety Evaluation	No significant changes in ALT, AST, BUN, or creatinine; no evident liver or kidney toxicity.	

LUNG CANCER STUDY

Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Result	Specific Research Article (Reference)
Gefitinib	Gefitinib is an orally administered epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor. It inhibits the tyrosine kinase domain of EGFR, thereby	Gefitinib-loaded cross-linked starch nanoparticles	A549 human non-small cell lung cancer (NSCLC) cells. The nanoparticles utilize the Enhanced	Antisolvent nanoprecipitation technique.	IC ₅₀ (Gefitinib-loaded starch nanoparticles)	6.037 $\pm$ 0.24 μ g/mL	22

	suppressing tumour cell proliferation in non-small cell lung cancer (NSCLC).		Permeation and Retention (EPR) effect for passive targeting, increasing gefitinib accumulation in tumour tissue while reducing off-target toxicity.				
					IC ₅₀ (Pure gefitinib)	21.65 ± 0.32 µg/mL	
					Apoptosis (Gefitinib-loaded starch nanoparticles)	77.14 ± 1.43%	
					Apoptosis (Pure gefitinib)	29.38 ± 1.11%	
					Cellular uptake (Gefitinib-loaded starch nanoparticles)	3.976 ± 0.14 µg/mL	
					Cellular uptake (Pure gefitinib)	1.777 ± 0.10 µg/mL	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Result	Specific Research Article (Reference)
Osimertinib (OST)	Irreversibly binds to the intracellular tyrosine kinase domain of EGFR, inhibits EGFR phosphorylation and downstream signaling, thereby suppressing NSCLC cell proliferation	MPDOLs (Membrane-coated PβAE/DNA-loaded Osimertinib Liposomes) – inhalable biomimetic liposomal nanoparticle coated with mesenchymal stem cell membrane expressing SP-B.	Primary lung tumor cells (EGFR-positive NSCLC); after inhalation, particles accumulate in lungs and are internalized mainly by malignant cells.	Thin-film dispersion prepared OST-loaded liposomes (OLs), with PβAE/DNA complexes incorporated into the aqueous core and coated with SP-B-rich MSC	Particle size of OST-loaded liposomes (OLs)	141.47 ± 3.07 nm	23

				membrane to form MPDOLs.			
					Zeta potential of OST-loaded liposomes (OLs)	$+6.65 \pm 0.37$ mV	
					Particle size of final MPDOL formulation	195.20 ± 4.56 nm	
					Zeta potential of final MPDOL formulation	-4.28 mV	
					Encapsulation efficiency of Osimertinib	81.37 ± 2.9 %	
					Drug loading capacity	6.72 ± 0.3 %	
					Drug release of free Osimertinib	>40 % released within the first hour	
					Drug release from MPDOLs at pH 5.0	79.85 % released within 12	
					Nebulized droplet size	≈ 3 μ m	
					Lung retention	Maximum fluorescence observed at 12 h after inhalation	
					Cellular uptake in malignant lung cells	Approximately 70 % (CD45 ⁺ cells)	
					IC ₅₀ of free Osimertinib	2.03 μ M	
					IC ₅₀ of MPDOL formulation	1.23 μ M	
					Apoptosis after MPDOL	0.176	

					treatment		
					In vivo survival	80 % of mice survived up to Day 70	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Result	Specific Research Article (Reference)
Paclitaxel (PTX)	Paclitaxel stabilizes microtubules, causing G2/M arrest and apoptosis. CSO-liposomes enhance PTX uptake, release, and antitumor activity.	Chitosan oligosaccharide (CSO)-modified liposomes (CP20-LSs and CP50-LSs) loaded with paclitaxel	Non-small cell lung cancer (NSCLC) A549 tumor cells. The CSO-modified liposomes preferentially accumulate in lung tumors through collagen adsorption and enhanced cellular uptake.	Thin-film hydration method	Particle size	~75 nm for all formulations	24
					Morphology	Spherical with clear membrane	
					Zeta potential	P-LSs: -2 mV; CP20-LSs & CP50-LSs: ~3 mV	
					Drug loading efficiency (LE%)	~10% for all formulations	
					Stability	Little change in particle size after 1 week in 10% serum-containing PBS	
					PTX release at pH 7.4 (24 h)	P-LSs: 59.4%; CP20-LSs: 59.2%; CP50-LSs: 56.3%	
					PTX release at pH 5.0	Increased from ~50% to 90% at 12 h; same trend for CP20-LSs and CP50-LSs	
					Cell viability (blank liposomes)	No significant inhibition of A549 cells	
					Cellular uptake	CP50-LSs showed the highest uptake; 1.9-fold higher fluorescence than	

						CP20-LSs	
					Penetration depth in A549 cells	P-LSs: ~4 µm; CP20-LSs: ~11 µm; CP50-LSs: ~14 µm	
					IC ₅₀	CP50-LSs: 3.2-fold lower than CP20-LSs	
					Tumor accumulation	CP50-LSs: 2.6-fold higher than P-LSs and 1.6-fold higher than CP20-LSs	
					Protein adsorption	CP50-LSs: 1.5-fold higher than CP20-LSs	
					Collagen adsorption	CP50-LSs: 3.0-fold higher than P-LSs and 1.7-fold higher than CP20-LSs	
					Cellular uptake after collagen adsorption	CP50-LSs: 5.6-fold increase; signal 6.4-fold higher than P-LSs and 3.6-fold higher than CP20-LSs	
					Tumor inhibition rate (in vivo)	CP50-LSs: ~90% (text); 86.4% (abstract)	
					Systemic toxicity	CP20-LSs: low; CP50-LSs: low with negligible body-weight change	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Result	Specific Research Article (Reference)
Docetaxel (DTX)	Docetaxel binds to β -tubulin and stabilizes microtubules that causes G2/M arrest, and induces apoptosis.	Folic acid–Chitosan coated PLGA nanoparticles (FA-CS coated PLGA NPs)	FR-overexpressing tumors with acidic pH (≈ 5.5 – 6.5). Folic acid enables receptor uptake; chitosan provides pH-responsive release.	Nanoprecipitation Method	Particle Size (PS)	F1: 356.10 ± 17.70 nm; F2: 300.33 ± 4.93 nm; F3: 267.63 ± 9.32 nm; Unloaded NPs: 250.33 ± 1.71 nm F1: 0.72 ± 0.02 ; F2: 0.66 ± 0.03 ; F3: 0.52 ± 0.02 ; Unloaded NPs: 0.57 ± 0.02	25

						F1: $+30.5 \pm 2.1$ mV; F2: $+35.1 \pm 1.5$ mV; F3: $+34.1 \pm 1.2$ mV; Unloaded NPs: $+28.8 \pm 1.31$ mV F1: $87.2 \pm 3.0\%$; F2: $95.3 \pm 2.9\%$; F3: $98.9 \pm 3.4\%$ F1: $6.0 \pm 0.8\%$; F2: $36.4 \pm 1.9\%$; F3: $37.6 \pm 2.0\%$ Nanoparticles were spherical with smooth surfaces Confirmed successful FA-CS coating, incorporation of PLGA, and no interaction between docetaxel and excipients. DTX crystalline peaks showed reduced intensity, confirming successful drug entrapment inside nanoparticles F2: 12.4% release at pH 7.4 and 22.7% at pH 5.5. F3: 75% release at pH 7.4 and 92% at pH 5.5. Drug release was higher at acidic pH and slower with higher chitosan content Biphasic release: initial burst followed by sustained release. For F3, about 50% released within 24 h, followed by slower release over the next 146 h. Coated PLGA	
--	--	--	--	--	--	--	--

						nanoparticles showed greater reduction in cell viability than free docetaxel in RPMI 2650, Calu-3, and A549 cell lines. Significant differences ($p < 0.05$) were observed at several concentrations. Unloaded PLGA nanoparticles showed no significant cytotoxicity, indicating that the carrier system itself was safe and non-toxic	
					Polydispersity Index (PDI)	F1: 0.72 ± 0.02 ; F2: 0.66 ± 0.03 ; F3: 0.52 ± 0.02 ; Unloaded NPs: 0.57 ± 0.02	
					Zeta Potential (ZP)	F1: $+30.5 \pm 2.1$ mV; F2: $+35.1 \pm 1.5$ mV; F3: $+34.1 \pm 1.2$ mV; Unloaded NPs: $+28.8 \pm 1.31$ mV	
					Encapsulation Efficiency (EE%)	F1: $87.2 \pm 3.0\%$; F2: $95.3 \pm 2.9\%$; F3: $98.9 \pm 3.4\%$	
					Loading Capacity (LC%)	F1: $6.0 \pm 0.8\%$; F2: $36.4 \pm 1.9\%$; F3: $37.6 \pm 2.0\%$	
					Surface Morphology (SEM)	Nanoparticles were spherical with smooth surfaces	
					FTIR Analysis	Confirmed successful FA-CS coating, incorporation of PLGA, and no interaction between docetaxel and excipients.	
					XRD Analysis	DTX crystalline peaks	

						showed reduced intensity, confirming successful drug entrapment inside nanoparticles	
					In vitro Drug Release	F2: 12.4% release at pH 7.4 and 22.7% at pH 5.5. F3: 75% release at pH 7.4 and 92% at pH 5.5. Drug release was higher at acidic pH and slower with higher chitosan content	
					Drug Release Pattern	Biphasic release: initial burst followed by sustained release. For F3, about 50% released within 24 h, followed by slower release over the next 146 h.	
					In vitro Cytotoxicity (MTT Assay)	Coated PLGA nanoparticles showed greater reduction in cell viability than free docetaxel in RPMI 2650, Calu-3, and A549 cell lines. Significant differences ($p < 0.05$) were observed at several concentrations.	
					Safety of Blank Nanoparticles	Unloaded PLGA nanoparticles showed no significant cytotoxicity, indicating that the carrier system itself was safe and non-toxic	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Result	Specific Research Article (Reference)
Paclitaxel (PCX) + Vinorelbine (VNB)	Paclitaxel: Stabilizes microtubules by	Folate-targeted theranostic liposomes	Folate receptor-overexpressing	Liposomes contained DPPC,	Particle Size	192 ± 1.4 nm (Fol-Lipo/PCX/VNB)	26

(co-encapsulated	preventing depolymerization, leading to G2/M phase arrest and apoptosis. Vinorelbine: Inhibits microtubule polymerization by binding to tubulin, causing mitotic arrest and apoptosis. The combination enhances cytotoxicity against NSCLC cells.	co-encapsulating Paclitaxel and Vinorelbine, surface-modified with DSPE-PEG2000-Folate, radiolabeled with ^{99m} Tc for simultaneous therapy and imaging.	NSCLC cells are targeted through folate receptor-mediated uptake and the EPR effect.	cholesterol, DSPE-PEG2000, DSPE-PEG2000-folate, and DTPA-PE. Selected formulations were characterized and radiolabeled with ^{99m} Tc by stannous reduction.			
					Polydispersity Index (PDI)	0.19	
					Zeta Potential	-8.1 ± 0.7 mV	
					Encapsulation Efficiency (PCX)	18.4 ± 1.5 %	
					Encapsulation Efficiency (VNB)	23.4 ± 2.1 %	
					In vitro Drug Release (PCX)	80% released in 78 h	
					Drug Release Kinetic Model (PCX)	Langenbucher model	
					In vitro Drug Release (VNB)	100% released in 4 h	
					Drug Release Kinetic Model (VNB)	Higuchi model	
					Radiolabeling Efficiency	84.5 ± 3.7 %	
					Cellular Uptake	Folate-targeted liposomes showed receptor-mediated internalisation. Untargeted liposomes exhibited higher nonspecific uptake in	

						vitro.	
					Micro-CT Imaging	Confirmed reduced tumour size after treatment with Fol-Lipo/PCX/VNB	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Result	Specific Research Article (Reference)
Paclitaxel (PTX) and doxorubicin(DOX)	FA ANLis-PTX-DOX target folate receptors on lung cancer cells by receptor-mediated endocytosis. Active/passive tumor targeting ability and prolonged co-delivery of PTX and DOX in a pH-responsive manner to enhance the antitumor effects while reducing the systemic toxicity.	Folic acid-targeted albumin nanoliposome	FOLR-overexpressing lung cancer cells (A549, NCI-H1975) and intracellular microtubules after receptor-mediated uptake.	Reverse evaporation method:	Particle size	243.61 ± 5.84 nm	27
					Polydispersity Index (PDI)	0.138 ± 0.015	
					Zeta potential	+29.42 ± 4.77 mV	
					Paclitaxel encapsulation efficiency	93.72 ± 4.13 %	
					Doxorubicin encapsulation efficiency	94.24 ± 4.86 %	
					Paclitaxel drug loading	10.74 ± 0.27 %	
					Doxorubicin drug loading	10.05 ± 0.33 %	
					Drug ratio giving the highest loading.	PTX : DOX = 1 : 1	
					In vitro drug	80% cumulative release	

					release (pH 5.3)	in 12 h	
					In vitro drug release (pH 7.4)	60% cumulative release in 12 h	
					Morphology	Spherical vesicular nanoliposomes with no aggregation	
					Cell viability (HUVEC & BEAS-2B)	>90% cell survival at concentrations up to 100 µg/mL	
					Cell proliferation inhibition	FA-ANLis-PTX-DOX showed the strongest inhibition in A549 and NCI-H1975 cells.	
					Lung metastasis	No pulmonary nodules detected; no metastasis observed in H&E staining.	
					Survival study	Improved survival compared with other treatment groups	
Drug	Mechanism of Action	NDDS System	Target Site	Method of Preparation	Evaluation Parameter	Result	Specific Research Article (Reference)
Cisplatin (DDP) + miR-219a-5p	The designed formulation consists of cisplatin (DDP) and miR-219a-5p encapsulated in folate modified liposomes. Cisplatin exerts its anti-tumour effect through forming DNA cross-links and inhibiting DNA repair enzymes which leads to induction of apoptosis. It is a DNA damaging agent and a powerful inhibitor of DNA	Folate-modified cationic liposome co-loading cisplatin (DDP) and miR-219a-5p. The formulation consists of DOPE, cholesterol, stearamide, and DSPE-PEG2000-FA to prepare Lipo@DDP@miR-219a-5p@FA, which provides targeted co-delivery to lung cancer cells.	Cisplatin-resistant Non-Small Cell Lung Cancer (NSCLC) cells (A549/DDP) that overexpress folate receptors (FR). miR-219a-5p specifically targets FGF9 to overcome cisplatin resistance.	Thin-Film Hydration Method (Lipid Film Hydration Technique)	Particle size	Approximately 180–190 nm	28

	repair. On the other side, miR-219a-5p, which is down-regulated in cisplatin resistant cells, when overexpressed, reverses cisplatin resistance by targeting FGF9. MiR-219a-5p suppresses tumour cell proliferation and migration, and induces apoptosis via regulation of Bax/Bcl-2/Caspase-3 pathway. Folate as a targeting ligand enhances liposomes internalization by cancer cells through receptor mediated endocytosis						
					Polydispersity Index (PDI)	Less than 0.30	
					Zeta potential	Positive before miRNA loading; reduced after miRNA loading	
					FT-IR	Characteristic peaks confirmed successful formulation.	
					Morphology	Spherical, uniformly dispersed liposomes (TEM)	
					Encapsulation efficiency	Greater than 80% for cisplatin	
					Drug release	Sustained release with faster release at acidic pH	
					Gel retardation assay	Complete miRNA binding at the optimised lipid:miRNA ratio.	
					Cellular	Folate-modified	

					uptake	liposomes showed the highest uptake by A549/DDP cells.	
					Cell viability (CCK-8)	Lowest viability observed with Lipo@DDP@miR-219a-5p@FA	
					IC ₅₀	Reduced compared with free cisplatin (graphically presented)	
					Combination Index (CI)	CI < 1, indicating a synergistic effect (graphically presented)	
					Flow cytometry (Apoptosis)	Highest apoptosis in the folate-liposome co-delivery group	
					Hemolysis western blot	Very low hemolysis; formulation showed good blood compatibility ↓FGF9, ↓Bcl-2, ↑Bax, ↑Cleaved Caspase-3	
					qRT-PCR	Significant increase in intracellular miR-219a-5p expression after treatment	

CONCLUSION

Nanotechnology-based drug delivery systems (NDDS)

have promising future potential in cancer treatment by improving targeted drug delivery, therapeutic efficacy, and reducing toxicity. Further preclinical and clinical studies are required to establish their safety, pharmacokinetics, efficacy, and large-scale application.

The current research results demonstrate the enormous potential of NDDS for the treatment of colorectal cancer: carriers such as solid lipid nanoparticles and polymeric, and liposomes can enhance the cellular uptake and targeted drug delivery. The paper notes the possibility of using 5 FU and oxaliplatin as drugs whose delivery can be improved due to the combined application of different chemotherapeutic agents, and the use of targeted delivery to reduce resistance, although the presented evidence is limited to preliminary levels of clinical evaluation.

The study of gastric cancer also identifies several potential carriers, among which are chitosan nanoparticles and micelles, which can improve targeting, and drugs such as paclitaxel and docetaxel, cisplatin. Application of these carriers, which have demonstrated targeting capabilities and/or antitumor activity against gastric cancer, either in combination with various drugs or with a specific mechanism of action, is considered promising. However, the level of evidence remains limited to preclinical.

The research data on liver cancer confirm the possibility of using lenvatinib and sorafenib in the context of hepatic cancer, and the application of NDDS can increase their residence time in the body and improve targeting. The use of PLGA or iron nanoparticles carrying doxorubicin as a chemotherapeutic agent and demonstrating controlled release and enhanced cytotoxic effect was also noted. The simultaneous application of these drugs with nanoparticles showed promising results, although some of the studies highlighted the insufficiency of data on the safety profile.

In the case of lung cancer, the research results demonstrate the potential of starch nanoparticles, PLGA, and liposomes for targeting non-small cell lung cancer, and modification of gefitinib nanoparticles leads to increased uptake and apoptosis induction. Moreover, combination carriers also reduce tumor growth and inhibit cancer cell metastasis to the brain with good tolerance; however, only one study covers this aspect. Targeted approaches were also found to deliver the drug to the tumor site and achieve a maximum tumor inhibition rate of up to 90%.

REFERENCES

1. Patil, P., Killedar, S., More, H., & Vambhurkar, G. (2022). Development and characterisation of 5-fluorouracil solid lipid nanoparticles for treatment of colorectal cancer. *Journal of Pharmaceutical Innovation*. <https://doi.org/10.1007/s12247-021-09605-x>
2. Mirzaghavami, P. S., Khoei, S., Khoei, S., & Shirvalilou, S. Folic acid-conjugated magnetic triblock copolymer nanoparticles for dual targeted delivery of 5-fluorouracil to colon cancer cells. *Cancer Nanotechnology*, 2022; 13(1): 12. <https://doi.org/10.1186/s12645-022-00120-3>
3. Yu, H., Liu, S., Yuan, Z., Huang, H., Yan, P., & Zhu, W. Targeted co-delivery of rapamycin and oxaliplatin by liposomes suppresses tumour growth and metastasis of colorectal cancer. *Biomedicine & Pharmacotherapy*, 2024; 178: 117192. <https://doi.org/10.1016/j.biopha.2024.117192>
4. Zhou, Y., Zhang, Q., Wang, M., Huang, C., & Yao, X. Effective delivery of siRNA-loaded nanoparticles for overcoming oxaliplatin resistance in colorectal cancer. *Frontiers in Oncology*, 2022; 12: 827891. <https://doi.org/10.3389/fonc.2022.827891>
5. Zhang, B., Wang, T., Yang, S., Xiao, Y., Song, Y., Zhang, N., & Garg, S. Development and evaluation of oxaliplatin and irinotecan co-loaded liposomes for enhanced colorectal cancer therapy. *Journal of Controlled Release*, 2016; 238: 10–21. <https://doi.org/10.1016/j.jconrel.2016.07.022>
6. Liu, Y., Li, X., Pen, R., Zuo, W., Chen, Y., Sun, X., Gou, J., Guo, Q., Wen, M., Li, W., Yu, S., Liu, H., & Huang, M. Targeted delivery of irinotecan to colon cancer cells using epidermal growth factor receptor-conjugated liposomes. *BioMedical Engineering Online*, 2022; 21(1): 53. <https://doi.org/10.1186/s12938-022-01012-8>
7. Guo, J., Yu, Z., Das, M., & Huang, L. Nano codelivery of oxaliplatin and folic acid achieves synergistic chemo-immunotherapy with 5-fluorouracil for colorectal cancer and liver metastasis. *ACS Nano*, 2020; 14(4): 5075–5089. <https://doi.org/10.1021/acsnano.0c01676>
8. Sun, L., Shi, Y., Wang, L., Zhang, J., Ma, J., Zhang, Z., & Zhang, H. Preparation of 5-fluorouracil-loaded chitosan nanoparticles and study of the sustained release in vitro and in vivo. *Asian Journal of Pharmaceutical Sciences*, 2017; 12(5): 418–423. <https://doi.org/10.1016/j.ajps.2017.04.002>
9. Wang, T., Hou, J., Su, C., Zhao, L., & Shi, Y. Hyaluronic acid-coated chitosan nanoparticles induce ROS-mediated tumor cell apoptosis and enhance antitumor efficiency by targeted drug delivery via CD44. *Journal of Nanobiotechnology*, 2017; 15(1): 7. <https://doi.org/10.1186/s12951-016-0245-2>
10. Lang, T., Zhu, R., Zhu, X., Yan, W., Li, Y., Zhai, Y., Wu, T., Huang, X., Yin, Q., & Li, Y. Combining gut microbiota modulation and chemotherapy by capecitabine-loaded prebiotic nanoparticle improves colorectal cancer therapy. *Nature Communications*, 2023; 14(1): 4746. <https://doi.org/10.1038/s41467-023-40439-y>
11. Ueno, T., Endo, K., Hori, K., Ozaki, N., Tsuji, A., Kondo, S., Wakisaka, N., Muro, S., Kataoka, K.,

- Kato, Y., & Yoshizaki, T. Assessment of antitumor activity and acute peripheral neuropathy of 1,2-diaminocyclohexane platinum (II)-incorporating micelles (NC-4016). *International Journal of Nanomedicine*, 2014; 9(1): 3005–3012. <https://doi.org/10.2147/IJN.S60564> □
12. Hong, C., Wang, D., Liang, J., Guo, Y., Zhu, Y., Xia, J., Qin, J., Zhan, H., & Wang, J. Novel ginsenoside-based multifunctional liposomal delivery system for combination therapy of gastric cancer. *Theranostics*, 2019; 9(15): 4437–4449. <https://doi.org/10.7150/thno.34953> □
 13. Cai, J., Qian, K., Zuo, X., Yue, W., Bian, Y., Yang, J., Wei, J., Zhao, W., Qian, H., & Liu, B. PLGA nanoparticle-based docetaxel/LY294002 drug delivery system enhances antitumor activities against gastric cancer. *Journal of Biomaterials Applications*, 2019; 33(10): 1394–1406. <https://doi.org/10.1177/0885328219837683> □
 14. Dong, Z., Gong, H., Gao, M., Zhu, W., Sun, X., Feng, L., Fu, T., Li, Y., & Liu, Z. Polydopamine nanoparticles as a versatile molecular loading platform to enable imaging-guided cancer combination therapy. *Theranostics*, 2016; 6(7): 1031–1042. <https://doi.org/10.7150/thno.14431>
 15. Yamamoto, Y., Hyodo, I., Takigahira, M., Koga, Y., Yasunaga, M., Harada, M., Hayashi, T., Kato, Y., & Matsumura, Y. Effect of combined treatment with the epirubicin-incorporating micelles (NC-6300) and 1,2-diaminocyclohexane platinum (II)-incorporating micelles (NC-4016) on a human gastric cancer model. *International Journal of Cancer*, 2014; 135(1): 214–223. <https://doi.org/10.1002/ijc.28651>
 16. Nishioka, C., Tahata, Y., Maesaka, K., Kai, M., Shirai, K., Murai, K., Makino, Y., Saito, Y., Nozaki, Y., Nakabori, T., Ishida, H., Yakushijin, T., Iio, S., Tatsumi, N., Imanaka, K., Kakita, N., Sakamori, R., Hosui, A., Miyazaki, M., ... Takehara, T. Comparison of outcomes of second-line durvalumab plus tremelimumab versus lenvatinib following first-line atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. *PLOS ONE*, 2025; 20(2): e0319005. <https://doi.org/10.1371/journal.pone.0319005>
 17. Zaafar, D., Khalil, H. M. A., Elkhoully, G. E., Sedeky, A. S., Ahmed, Y. H., Khalil, M. G., & Abo-Zeid, Y. Preparation and characterization of Sorafenib nano-emulsion: Impact on pharmacokinetics and toxicity; an in vitro and in vivo study. *Drug Delivery and Translational Research*, 2024; 14(11): 3089–3111. <https://doi.org/10.1007/s13346-024-01530-z>
 18. Hoseinzadeh, M., Mokhtari, M. J., Kafilzadeh, F., Mohammadnejad, J., & Taheri, Y. Polylactic-co-glycolic acid-alginate nanocarrier for efficient drug delivery to liver cancer cells. *IET Nanobiotechnology*, 2023; 17(5): 450–464. <https://doi.org/10.1049/nbt2.12143-X>
 19. Mateen, A., Khan, A., Khan, I., Ahmad, L., Khan, A., & Salam, A. Formulation development, characterisation, and evaluation of sorafenib-loaded PLGA–chitosan nanoparticles. *Frontiers in Pharmacology*, 2024; 15: 1465363. <https://doi.org/10.3389/fphar.2024.1465363>
 20. Lin, X., Liu, J., Wu, G., Yang, X., Yan, W., Fan, N., & Li, H. Enhanced chemotherapy response in hepatocellular carcinoma: Synergistic effects of miR-122 and doxorubicin co-delivery system inducing apoptosis and DNA damage. *Cancer Nanotechnology*, 2024; 15: Article 48. <https://doi.org/10.1186/s12645-024-00287-x>
 21. Sun, L., Qi, J., Ding, L., Wang, Z., Ji, G., & Zhang, P. Ultrasound-triggered nano delivery of lenvatinib for selective immunotherapy treatment against hepatocellular carcinoma. *Scientific Reports*, 2024; 14: 27395. <https://doi.org/10.1038/s41598-024-79069-9>
 22. Amin, H., Osman, S. K., Mohammed, A. M., & Zayed, G. Gefitinib-loaded starch nanoparticles for battling lung cancer: Optimization by full factorial design and in vitro cytotoxicity evaluation. *International Journal of Biological Macromolecules*, 2023; 253: 127023. <https://doi.org/10.1016/j.jsps.2022.11.004>
 23. Fu, X., Shi, Y., Wu, H., Zhang, Y., Liu, Y., Wan, X., Chen, X., Zhou, J., Qiu, S., Zhao, X., Tian, Z., Li, L., Zang, H., & Lin, G. Inhalable liposomal delivery of osimertinib and DNA for treating primary and metastasis lung cancer. *Nature Communications*, 2025; 16: 3336. <https://doi.org/10.1038/s41467-025-58312-5>
 24. Miao, Y. Q., Chen, M. S., Zhou, X., Guo, L. M., Zhu, J. J., Wang, R., Zhang, X. X., & Gan, Y. Chitosan oligosaccharide modified liposomes enhance lung cancer delivery of paclitaxel. *Acta Pharmaceutica Sinica B*, 2021; 11(10): 3196–3209. <https://doi.org/10.1038/s41401-020-00594-0AI>
 25. N. K., Altawabeyeh, R. M., & Darweesh, R. S. Preparation and characterization of docetaxel-PLGA nanoparticles coated with folic acid-chitosan conjugate for cancer treatment. *Journal of Pharmaceutical Sciences*, 2022; 111(2): 485–494. <https://doi.org/10.1016/j.xphs.2021.10.034>
 26. Karpuz, M., Silindir-Gunay, M., Ozer, A. Y., Ozturk, S. C., Yanik, H., Tuncel, M., Aydin, C., & Esendagli, G. Diagnostic and therapeutic evaluation of folate-targeted paclitaxel and vinorelbine encapsulating theranostic liposomes for non-small cell lung cancer. *European Journal of Pharmaceutical Sciences*, 2021; 156: 105576. <https://doi.org/10.1016/j.ejps.2020.105576>
 27. A., Zhang, Y., Cheng, M., Liu, Q., & Chen, M. Folic acid-targeted albumin nanoliposomes co-loaded with paclitaxel and doxorubicin for enhanced treatment of lung cancer. *Drug Delivery*, 2024; 31(1): 2371890, 9. <https://doi.org/10.1038/s41598-026-51842-y>
 28. Zhang, J., Zhao, J., & Wang, B. Folate-modified liposomes mediate the co-delivery of cisplatin with miR-219a-5p for the targeted treatment of cisplatin-resistant lung cancer. *BMC Pulmonary Medicine*,

2024; 24: 159. <https://doi.org/10.1186/s12890-024-02938-6>