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NANOTECHNOLOGY-DRIVEN TARGETED THERAPIES FOR COLORECTAL CANCER: A NEW FRONTIER IN PRECISION ONCOLOGY

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Abbreviations: CRC- Colorectal Cancer, NP- Nanoparticles, IRN- irinotecan, 5- FU- 5-Fluorouracil, EGFR- Epidermal Growth Factor Receptor, PNP- Polymeric Nanoparticles, Rapa- Rapamycin, DPD- dihydropyrimidine dehydrogenase, hnRNP- heterogeneous nuclear ribonucleoprotein, CNT- Carbon nanotubes, MSNs- mesoporous silica nanoparticles, SWCNT - single-walled carbon nanotubes, MWCNT- Multi walled carbon nanotubes, Ag-NPs- silver nanoparticles, OXA- oxaliplatin, (AuNPs)- Gold nanoparticles, PDA- polymerized dopamine, TDP1- tyrosyl-DNA phosphodiesterase 1, MHC- molecular histocompatibility complex (MHC), MVBs- multivesicular bodies, UGT- UDP glucuronosyltransferases, GR- glutathione reductase, Rapa- Rapamycin, PAMAM- Poly(amidoamine).

ABSTRACT

One of the biggest causes of cancer-related morbidity and death globally is still colorectal cancer (CRC). Systemic toxicity and medication resistance are two drawbacks of conventional therapies such as radiation, chemotherapy, and surgery. Consequently, targeted therapies have emerged as promising alternatives aimed at improving treatment specificity and efficacy while minimizing side effects. This review highlights various targeted treatment modalities for CRC, with a particular emphasis on nanotechnology-based approaches. Because of their capacity to deliver therapeutic drugs directly to tumour locations, nanoparticles (NPs), such as liposomes and polymeric nanoparticles, have drawn a lot of attention. Liposomes, characterized by their biocompatibility and capacity to encapsulate both hydrophilic and hydrophobic drugs, enhance drug accumulation in cancerous tissues through passive and active targeting mechanisms. Additional benefits of polymeric nanoparticles include stability, controlled drug release, and the ability to modify their surface to increase targeted effectiveness. These nanoscale carriers can be engineered to recognize specific molecular markers overexpressed in CRC cells, thereby enabling precision medicine approaches. In addition to nanoparticles, monoclonal antibodies and small molecule inhibitors that block signalling pathways essential to tumour development and metastasis are also mentioned as targeted treatments. The review also addresses current advances in nano preparative techniques and the ongoing clinical trials that validate the potential of these novel therapies. By improving therapeutic results and lowering side effects, the combination of nanotechnology and molecular targeting techniques holds the potential to completely transform the treatment of colorectal cancer. Overall, targeted treatments, especially nanoparticle-based systems, represent a significant leap forward in the management of colorectal cancer.



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INTRODUCTION

One of the most dangerous types of the disease is colorectal cancer (CRC), which is the third most common type worldwide. CRC affects the epithelial cells lining the lumen of the colon and is categorized based on the extent of the original cancer's invasion, the presence of distant metastases, and the involvement of lymph node metastases. As a result, the characteristics of the tumour and the patient's reaction determine how CRC is treated and the associated therapeutic techniques.^[12]

People over 50 are more likely to get colorectal cancer (CRC) worldwide. Both hereditary and environmental risk factors have a major impact on the development of colorectal cancer. CRC is curable and prevented if caught early. Currently, modern screening tools and medicines for CRC therapy minimize the incidence rate among the population, however the micro metastasis of cancer may lead to recurrence. Consequently, the difficulty is in creating a substitute treatment to get over this issue. Because it allows for the direct and selective delivery of more potent, customized chemotherapy to cancer cells, nanotechnology is crucial to the treatment of cancer. Furthermore, compared to conventional chemotherapies, nanotechnology improves patient survival rates. It may be possible to use nanoparticles for both diagnostic and treatment simultaneously. Researchers from all over the world have been drawn to investigate the potential of nanoparticles for both effective therapy and early detection of colorectal cancer due to their intriguing features. Modern CRC screening techniques and treatment approaches are included in this review and the causes and stages of colorectal cancer are shown in figure-1.^[22]

Types:

Numerous studies have shown that the colon is a suitable site for medication absorption since it degrades less, increasing the drug's bioavailability. Special concerns are necessary while designing CTDD as the pharmaceuticals need to be protected from gastric pH and enzymes. The physiology of the colon and the remainder of the GIT is very different. The irregularities of colonic pH, transit time, and fluid volume—all of which vary greatly based on the colon portion, diet, and metabolic enzymes—have an impact on CTDD. The presence of microbial enzymes and the viscosity of colonic fluid are two more significant parameters influencing the effectiveness of CTDD.^[12]

Therapeutics have recently been delivered to the colon using a variety of nanoparticle-based DDSs, including liposomes, natural-derived nanoparticles, biodegradable polymeric nanoparticles, and dendrimers. originated metastases. Because they provide better safety and biocompatibility than other nanoparticles, liposomal nanoparticles were the first to be used in nano-DDSs for the treatment of cancer.

A range of nanoparticle types, generally categorized as organic, inorganic, and hybrid nanoparticles, are used in nanoparticle-based targeted medication delivery systems for colorectal cancer (CRC). Each kind is designed to lessen systemic toxicity, increase tumour targeting, and improve medication delivery. Based on current developments, the types of nanoparticles used to treat colorectal cancer are shown in figure-2:

1. Organic Nanoparticles

1.1 Liposomes:

The development of nanoparticles (NPs), particularly liposomes, is encouraging and may provide a less invasive method, particularly in chemotherapy, to deliver



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cancer treatments to tumour cells with precision and reduce off-target side effects. Liposomes have a wide range of applications as medication carriers since they are among the most biocompatible and safe NPs for human usage. Apart from that, their composition and functionalisation are highly tuneable hence providing a greater advantage for liposomes to be therapeutically beneficial in cancer treatment.^[47]

Alkaloid-derived camptothecins are effective antitumor agents that are members of the topoisomerase I interaction chemicals class. Two camptothecins, topotecan and irinotecan (IRN), were approved by the US FDA. A first-line medication called IRN (7-Ethyl-10-(4-[1-piperidino]-1-piperidino) carbonyloxycamptothecin) is authorized to treat several tumours, such as colorectal, lung, and gynaecological cancers. Although it can be used alone, it is typically utilized as a rescue treatment for 5-FU-refractory disease and in conjunction with cytotoxic drugs such as oxaliplatin and 5-fluorouracil (5-FU). Since Topo1, the main target, is widely expressed, the medication has been demonstrated to have significant adverse effects with significant inter-individual variability. Myelosuppression (neutropenia) and gastrointestinal issues (mostly diarrhoea) are among the toxicities linked to IRN and are known to be dose-limiting toxicity for this medication.

IRN is a prodrug that undergoes significant in vivo metabolism and has a complex pharmacologic profile. The conversion of water-soluble IRN into the powerful metabolite SN-38 (7-ethyl-10-hydroxycamptothecin) is the first of three main stages of metabolism in the gastrointestinal system. In the second stage, SN-38 is converted to a glucuronide that can be exported to the colon and reabsorbed by bacterial β -glucuronidase, which

reactivates it to its deadly form. The drug's local reactivation in the gastrointestinal tract is caused by its toxicity.

There has been no progress in finding biomarkers to identify which patient population will be most affected. Therefore, different delivery platforms are a good way to integrate precision medicine into the medication delivery system. The drug's complicated pharmacokinetic profile after intravenous administration lends more credence to this idea. Although SN-38 possesses anticancer effects that are 100–1000 times more powerful than those of free IRN, less than 5% of IRN is converted to SN-38 following intravenous treatment, primarily in the liver. An esterification event involving the enzyme carboxyl esterase results in the open lactone structure found in the most active form of camptothecin.^[48]

Chemotherapy medications based on 5-fluorouracil (5-FU) are the initial treatment for colorectal cancer. However, 5-FU is toxic to normal cells, and its effects have been restricted by the emergence of multidrug resistance. One Combining 5-FU treatments with additional medicines is now showing promise to enhance CRC treatment. Traditionally used as immunosuppressors, Rapamycin (Rapa) has been widely utilized to treat a variety of cancers, including skin, bladder, cervix, and osteosarcoma, according to new studies. Through several methods, such as cell proliferation, invasion, migration inhibition, apoptosis promotion, and anti-angiogenesis impact, Rapa exhibits anticancer activity. Furthermore, a growing body of research suggests that Rapa might be enhanced in effectiveness by combining it with modern chemotherapeutic medications like paclitaxel and cisplatin. For instance, rape and cisplatin work together to prevent endometrial cancer by

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enhancing the cytotoxicity of natural killer (NK) cells triggered by IL-27.7. Another study found that cyclic octapeptide liposomes loaded with doxorubicin and Rapa enhance the therapeutic results for triple-negative breast cancer.

Rapa's weak water solubility (2.6 µg/mL) limits the development of clinical uses. Everolimus, a macrolide derivative of Rapa, is a second-line treatment for advanced renal cell carcinoma, however it helps with low solubility. Therefore, increasing local medication concentration and bioavailability is a crucial tactic for enhancing the therapeutic efficacy. These days, anticancer medications are delivered to treat colorectal cancer using nanotechnology-based drug delivery systems. Additionally, several studies showed that Rapa's aqueous solubility, bioavailability, and anticancer activities are all improved by nanoscale delivery vehicles such as liposomes, micelles, and nanoparticles.^[10]

1.2 Nanoparticles:

Currently, CRC is treated with a variety of authorized medications. Chemotherapy's primary side effects include nausea, vomiting, diarrhoea, mouth sores, and neuropathy. Targeted therapy is a type of treatment that focuses on specific genes found in tumour cells or the tissue environment. While reducing the damage to healthy cells, this kind of treatment stops the growth and division of malignant cells. New techniques for the efficient identification of proteins, genes, and other components in a patient's cancer should be developed to determine an effective and dependable treatment for colorectal cancer. Anti-angiogenesis therapy and epidermal growth factor receptor (EGFR) inhibitor therapy are options for treating colorectal cancer.

The most frequent adverse effects of the targeted therapy are facial and upper body rashes. Poor drug response to chemotherapy during CRC treatment is commonly documented; this may be mainly because tumour cells have developed multidrug resistance. Numerous investigations have demonstrated how colorectal cancer cells develop treatment resistance. According to some research, the effects of cetuximab and panitumumab can be rendered ineffective by mutations in the BRAF or PIK3CA genes, or by amplification of the MET, KRAS, and ERBB2 genes, which prevents EGFR signalling. Resistance to 5-FU may result from overexpression of the dihydropyrimidine dehydrogenase (DPD) gene, as DPD may change 5-FU into an inert metabolite. Furthermore, the LV may be blocked by decreased expression of proton-coupled folate transporter and reduced folate transporter 1. The response of oxaliplatin may also be impacted by changes in glutathione reductase (GR) and metallothionein levels. Furthermore, the action of IRI may be limited by enhanced DNA damage repair mechanisms such as tyrosyl-DNA phosphodiesterase 1 or increased activity of UDPglucuronosyltransferases (UGT). Nanomedicine seems to be a new tactic to improve the prognosis for people with colorectal cancer by overcoming multidrug resistance.^[6]

Hydrophilic polymer-modified nanocarriers work as active targeting agents, delivering drugs to tissues or organs. To achieve selective medication concentrations in tumour tissue and cells, for instance, active targeting combines active recognition between molecules on the nano system's surface and particular molecules and proteins on the tumour site. This contrasts with passive drug targeting. Instead of boosting the overall



accumulation of tumours, most of the active drug targeting aims to improve target cell identification and uptake. By combining polymer nano-carriers with specific combinations of antigens or receptors on the tumour cell surface, targeted nano-drug preparations can be created that enable the active administration of medications. Drugs may be passively accumulated into tumours using pharmacological nanocarriers that may stay in the bloodstream for an extended length of time, such as liposomes, micelles, or polymeric nanoparticles. Long in-vivo half-lives are typical for nano drug carriers. Advances in targeted medication delivery have made it possible to target tumour cells without harming non-tumour cells. Instead of increasing the overall buildup of tumours, several nanoparticles are being developed and studied for the effective delivery of cytotoxic medications to the target site, improving target cell identification and absorption. By combining polymer nano-carriers with specific combinations of antigens or receptors on the tumour cell surface, targeted nano-drug preparations can be created that enable the active administration of medications. To improve therapeutic distribution and bioavailability while lowering side effects, several nanoparticles are being developed and studied for the effective delivery of cytotoxic medicines to the target site. Although few clinical trials have demonstrated that immunotherapy can treat individuals with colorectal cancer, it is still merely an experimental technique.^[27]

1.3 Polymeric Nanoparticles:

Small, polymeric nanoparticles typically range from 1 nm to 1000 nm. They can have two distinct structural shapes, nanospheres and nano capsules, depending on how they are made. In the first scenario, a polymer layer envelops the therapeutic material, which may or may not be the core itself. On

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the other hand, the medicine is put into nanospheres, which are made of a cross-linked polymer. In either scenario, the drug may potentially be absorbed onto the nanoparticle's surface.

The characteristics of a particular polymeric nanoparticle are essential for the controlled distribution of a medication for cancer treatment. The process used to create PNPs has a significant impact on their size, shape, molar mass, polymer molar ratio, or zeta potential, and stability in a biological system.

To work effectively and get beyond biological barriers, the nanoparticle's size should be appropriate for the application site; nevertheless, too-small nanoparticles could be destroyed by the phagocytic system. Because polymeric nanoparticles of this size can penetrate fenestrations in a blood vessel's endothelium, it is believed that a diameter of approximately 100 nm is the most effective for delivery to vascularized tumours. However, a study by Gao et al. found that smaller diameters of polymeric nanoparticles, about 70 nm, appear to be more beneficial in the case of malignant tumours in the brain's periphery in an animal model. Since the pharmacology and function of PNPs are primarily determined by their shape, it is ideal to obtain PNPs with a spherical structure since the target cells will better absorb a given nanoparticle. Polyethylene glycol (PEG) coating is used to increase the duration of PNPs' residence in the bloodstream and to stop unwanted interactions with plasma proteins. The improvement in the stability of the nanoparticles and the lengthening of their half-life in the bloodstream is directly linked to this alteration. PEG coating is used to encapsulate hydrophobic and hydrophilic medications to achieve regulated release, and it also increases the



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particles' hydrophilicity in addition to extending their residence time in the body.

PNPs are mostly made from biodegradable and biocompatible polymers. These consist of co-polymers like poly lactide-co-glycoside, which are presently approved by the Food and Drug Administration (FDA), and synthetic polymers like poly lactide or poly-caprolactone. Biopolymers, primarily collagen or chitosan, are also used in polymeric drug delivery systems because of their nonimmunogenic qualities. In this manner, the matrix is hydrolysed into innocuous products when the medication is released. Another significant benefit of PNPs is that they allow for the manipulation of a polymeric nanoparticle's properties through appropriate modification. This allows for the controlled release of the drug from the nanoparticle at a specific location within the body and the creation of a water-soluble drug. In vitro attempts have been made to use polymeric nanoparticles as carriers for genome-editing tools, and they are also being used to treat colorectal and female malignancies. Thus, this review's objective is to provide the most recent data regarding the application of polymeric nanoparticles as a drug delivery mechanism in certain gene therapy and cancer treatments.^[36]

1.4 Exosomes:

Exosomes are naturally occurring nanoscale (30–200 nm) membrane vesicles that are released by a variety of cell types because of the plasma membrane fusing with multi-vesicular structures. Compared to other carriers, exosomes are an appealing alternative for the delivery of cancer-like drugs because of their high stability, low toxicity or non-toxicity, low immunogenicity, biocompatibility, ability to cross biological barriers, and potential to be loaded with different drugs. Various

applications of exosomes are shown in figure-3

Exosome surface characterization has been altered by binding different ligands against markers through genetic and chemical modification, even though exosomes derived from different cells exhibit a variety of intrinsic cell targeting properties based on their specific surface structures. This is especially true in cancer therapy. Chemical modification functionalizes exosome surfaces with a variety of natural and synthetic ligands, in contrast to genetic manipulation, which is restricted to targeting genetically encodable patterns. AS1411, a stable G-quadruplex-forming DNA sequence, has a high affinity and specificity for nucleolin, its target protein. Nucleolin, a ubiquitous protein with carcinogenic qualities, is overexpressed in the cytoplasm and cell surface of many tumour cells in comparison to their normal counterparts.^[40]

Because of their tiny size (nano-scale dimension), exosomes can transport medications to the target cells, which is how they function in many cancer treatments. Exosomes can, in fact, transport active medicinal ingredients or interfering RNA (siRNA) to the intended cells or locations. For instance, exosomes carrying doxorubicin have occasionally been employed to transport the medications to the intended organs during the inhibition of colorectal cancer cell development. According to several studies, manipulating exosomes can help treat colorectal cancer by reducing the disease's rate of progression. It has been discovered that miR-379 inhibits CRC cell migration in CRC CDEs, and that recipient cells' migration is reduced when these modified exosomes overexpressing miR-379 are transferred to them. Additionally, exosomal miRNA-375 has been shown to stop tumour cell growth by inhibiting Bcl-2 in colorectal



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cancer (CRC), which raises the possibility that exosomal miRNA-375 could be a potential target for treatment.^[4]

1.5 Dendrimers:

The increased permeability and retention (EPR) effect is one of the most extensively researched aspects of polymeric drug delivery. The tendency of macromolecules to accumulate in solid tumours is referred to as the EPR effect. Tumours contain rich, leaky vasculature that facilitates facile molecular penetration due to the rapid angiogenesis linked to solid tumour growth. Delivered substances are retained and accumulate in a tumour due to microvasculature and a lack of lymphatic outflow. To reach its target via EPR targeting, the therapeutic substance is locally released and absorbed by tumour cells. Thus, passive targeting by the EPR effect allows drug accumulation at the tumour site and improves therapeutic index compared to the free drug.

The PAMAM dendrimers' intrinsic tertiary amines can be used for hydrogen bonds, acid-base interactions, and other non-covalent interactions. The polymers are efficient agents for solubilizing hydrophobic medicines because they include encapsulated guest molecules. Up till generation 4, PAMAM dendrimers have been demonstrated to have the least amount of cytotoxicity. Wiwattanapatapee initially reported on PAMAM dendrimers' potential as oral medication delivery vehicles in 2000.^[39]

For targeted CC chemotherapy, nanoparticles (NPs) are being studied therapeutically as smart nanocarriers that can reduce dosages and improve the drug's water solubility and bioavailability while reducing adverse effects. However, burst release, aggregation, and reduced stability are problems with biodegradable nanoparticles such micelles, nanogels,

liposomes, nano emulsions, and polymeric NPs. Conversely, inorganic NPs, like metal NPs, carbon-based NPs, and silica NPs, have a limited capacity to load drugs, a slow rate of clearance, and a smaller range of functionalization options. Compared to these drug carriers, dendrimers' distinct physicochemical characteristics and biodegradable backbones make them suitable for usage as carriers. Dendrimers are consistently hyperbranched, monomeric nanomaterials that start from a central core and have arms or branches that resemble trees. For a specific use on the outer surface of the dendrimer, the arms' various anionic, neutral, or cationic end groups can be further embellished with several functional groups. Monomeric branches that are added to the core during synthesis are known as a dendrimer generation. Dendritic macromolecules usually become larger and more spherical as their formation increases, providing a lot of vacuum area for encapsulation. Drug loading into dendrimer core cavities and conjugate targeting ligands onto the surface terminals can be accomplished by hydrogen bonds, chemical bonds, or hydrophobic interactions. The development of functionalized dendrimers for targeted therapy enhances the CC drug's chemotherapeutic effectiveness and lowers its systemic toxicity. The utilization of dendrimers as an intelligent nanocargory for the delivery of anticancer drugs against CC is the main topic of this review.^[45]

2. Inorganic Nanoparticles:

2.1 Mesoporous silica nanoparticles:

One of the most significant groups of inorganic nanomaterials that can be employed as an efficient drug delivery system (DDS) or nanocarrier is mesoporous silica nanoparticles (MSNs). MSN's special qualities—such as its porosity, dual or multiple drug loading capacity,



biodegradable and biocompatible qualities, controlled drug release, and incorporation with detectable agents—have drawn a lot of interest. By conjugating gatekeepers at pore entrances, which may be regulated by endogenous and/or external stimuli, intelligent drug release from MSNs at the desired location can be controlled. Functionalized MSNs with pH-responsive gatekeepers, like gold nanoparticles, can efficiently convert closed tunnels to an open state in response to an endogenous signal and control the release of guest molecules because the pH value of TME is typically a little lower than that of normal tissues. For the on-demand release of anti-cancer medications, several intelligent pH-responsive MSNs based on gold nanoparticles have been developed.

Many viral and nonviral vectors have recently been investigated by researchers to deliver miRNA mimics or anti-miRs to the target cells. Because of their special qualities, such as their wide surface area and pore volume, tuneable pore structure, favourable biocompatibility, thermal stability, and ease of surface modification, mesoporous silica nanoparticles (MSNs) have emerged as one of these vectors' most promising options. Several stimuli-responsive gatekeepers have been created that allow medications to be released from MSNs under controlled conditions. The catechol group of dopamine, when exposed to weak alkaline circumstances (pH 8.5), forms polymerized dopamine (PDA), which can spontaneously bond to any material surface through covalent and noncovalent interactions. MSNs' PDA film, which acts as a pH-sensitive gatekeeper to regulate drug release in the acidic tumour environment, can also interact with active targeting ligands that are amine- or thiol-terminated, such SH-aptamer. AS1411 aptamer, the first US Food and Drug Administration-approved aptamer, can

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precisely bind to nucleolin, which is overexpressed on the cell surface of several cancers including CRC.^[26]

2.2 Carbon Nanotubes:

Carbon graphitic nanomaterials (CNTs) are well-ordered, hollow, and possess a variety of characteristics. High surface area, high aspect ratio, and lightweight weight are a few of these. CNTs are often divided into two categories: single-walled (SWCNT) and multiwalled (MWCNT). Depending on the temperature at which they were created, SWCNTs are made up of a single cylindrical carbon layer that ranges in diameter from 0.4 to 2 nm. It has been noted that a greater diameter results from a higher growing temperature. MWCNTs, on the other hand, are typically composed of several cylindrical carbon layers, the outer tubes having a diameter of 2–100 nm and the interior tubes 1–3 nm.

It has been suggested that the fundamental carbon arrangement of SWCNTs differs from that of MWCNTs based on the structural differences between the two types of CNTs. SWCNTs can have chiral, helical, zigzag, or armchair configurations in their structure. However, based on the configurations of the graphite sheets, MWCNTs can be classified into two categories. There are two types of graphite structures: one that resembles a "Russian doll" with concentric layers of graphite sheets, and another that resembles parchment with a single graphite sheet wound around itself.

Carbon nanotubes (CNTs) are carbon nanocomposites made by sp² hybridization in three dimensions. Their unparalleled physicochemical qualities, including biocompatibility, non-immunogenicity, relatively noncytotoxic nature, structural flexibility, extremely high drug loading efficiency, greater aspect ratio, and biodegradability, have made them



appealing for biomedical applications. When CNTs are functionalized, their solubility, blood circulation time, selectivity, and tumour cell uptake are all improved. Researchers are currently investigating surface modifications of carbon nanotubes (CNTs) to provide regulated drug administration and to achieve biological targets with improved specificity. CNTs circumvent the limitations of cancer treatment, such as low permeability and non-specificity at the tumour location.^[35]

Because of their distinct catalysis and unusual electrical, magnetic, thermal, and optical characteristics, decorating carbon nanotubes (CNTs) with metal, metal oxide, or metal sulphide nanoparticles has garnered a lot of interest. CNTs adorned with silver nanoparticles are becoming more well-known due to their affordability, environmental friendliness, and wide range of potential uses in the biomedical sector. To fully utilize these kinds of nanomaterials, the special qualities of each material can be combined, and the interactions between the two elements may provide new capabilities. Because of this, carbon-based Ag composites have received a lot of interest and are currently a popular scientific issue. Several methods, such as molten salt sorptive techniques, in situ filling during the material's arc discharge growth, and other wet chemical approaches, can be used to fill carbon nanotubes with metal. The unique electrical, optical, and biological properties of silver nanoparticles are driving the rapid growth of this new class of nanomaterials. Ag-NPs often have a short half-life in solution because they easily combine in aqueous solution. To get over this problem, functionalized carbon nanotubes can affix nanoparticles. A range of chemical

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reagents, irradiations, and templates were used to create SFMWCNT nanohybrids.

Numerous research has demonstrated the applicability of CNT in a wide range of biomedical applications. To learn more about the development of CNTs as potential safe drug delivery vehicles in cancer treatment, various strategies have been investigated, including functionalization and their crucial roles in targeting specific intracellular regions and tumour microenvironments. Additionally, CNT has made significant strides recently in the identification and treatment of cancer.^[11]

2.3 Gold Nanoparticles:

Gold nanoparticles (AuNPs) are the most stable nanomaterial for creating a variety of nanostructures, including nano cubes, nanospheres, nanorods, nanoflowers, nano branches, nanowires, nano-bipyramids, nano shells, and nanocages. Recent technological developments have produced precise surface coatings of AuNPs with precise particle sizes and shapes. Gold nanostructures' specificities make them a safer and more effective anticancer and medication delivery agent. Furthermore, a study based on mathematical modelling and artificial intelligence showed that gold nanoparticles can modify their wavelengths, optical densities, and light absorbencies. Consequently, a larger level of light absorbance within the nanoparticle itself may be possible by altering the optimal wavelength with nanoparticle size, which would increase the effectiveness of gold nanoparticles against cancer cells. According to a recent study, gold nanoparticles (NPs) decompress CRC arteries, increasing the transport of cisplatin and enhancing chemotherapy. Nucleic acids and gold nanoparticles are employed as a molecular technique for cellular absorption.^[13]



Conclusion:

Targeted therapies have transformed the landscape of colorectal cancer treatment by offering more precise, effective and less toxic alternatives to conventional methods. Nanoparticles, especially liposomes and polymeric nanoparticles have emerged as promising platforms for targeted drug delivery due to their unique physicochemical properties, small size and ability to be engineered for selective tumour targeting. These nanocarriers enhance drug bioavailability and accumulation at the tumour site, potentially overcoming challenges such as systemic toxicity and drug resistance. Alongside nanoparticle-based systems, other targeted strategies including monoclonal antibodies and small molecule inhibitors play vital roles in disrupting key molecular pathways involved in CRC progression. Continued advances in nanotechnology and molecular targeting are expanding the therapeutic arsenal against CRC, supported by ongoing clinical trials and patents. Despite encouraging progress, further research is needed to optimize nanoparticle design, improve targeting specificity and ensure safety and efficacy in clinical settings. Ultimately, the integration of nanotechnology with personalized medicine holds great promise to improve patient outcomes and revolutionize colorectal cancer management.

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