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Recent Advances in Nanoformulation for Targeted Drug Delivery Systems

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Abstract: Intravascular medication delivery allows nanoparticles to enter the circulation via blood vessels and treat intravascular illnesses by acting at precise locations inside the blood vessels. Another method of drug delivery including nanoparticles is known as extravascular drug delivery, and it involves local administration (e.g., oral, inhalation, subcutaneous injection, etc.) to target tissues. Utilising the principles of nanotechnology, nano pharmaceuticals have completely transformed the way drugs are delivered and treatment approaches in contemporary medicine. Utilising nanoparticles (NPs) and nanocarriers (NCs), these state-of-the-art formulations overcome significant drawbacks of traditional treatments by providing better targeting, increased bioavailability, and less toxicity. Their revolutionary effect on healthcare is shown by the clinical success of several nano pharmaceuticals. By decreasing the negative effects induced by systemic medications by local targeting, nonmaterial may be employed as vascular-targeted carriers for intravascular drug delivery. Intravascular inflammation changes the local environment, which may inspire new nanoparticle designs. When inflammatory stimuli are high, nanoparticles may target immune cells and the receptors on their membranes. Nanoparticle formulation of α-mangostin for cancer drug delivery system and "α-mangostin nanoparticle for cancer drug delivery system" constitute the basis of the investigation. We spoke about the possibilities and difficulties of smart systems for the targeted treatment of various vascular and non-vascular illnesses.

Keywords: Nano formulation, targeted, drug, delivery, Systems

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INTRODUCTION

The most prevalent kind of cancer in the head and neck area is oral squamous cell carcinoma (OSCC), which is a persistent and crippling illness. To address the frequent adverse effects of traditional medications, such as a decrease in bone marrow function, kidney damage, ototoxicity, and inadequate systemic stability, several nano formulations have been developed. It was shown that a nanoparticle loaded with ligand-decorated CDDP–polylactic acid–polyethylene glycol (PLGA–PEG)–NR7 had a higher potential for drug penetration in OSCCs tissue and showed rapid intracellular infiltration.

Utilising the principles of nanotechnology, nano pharmaceuticals have completely transformed the way drugs are delivered and treatment approaches in contemporary medicine. Utilising nanoparticles (NPs) and nanocarriers (NCs), these state-of-the-art formulations overcome significant drawbacks of traditional treatments by providing better targeting, increased bioavailability, and less toxicity. Their revolutionary effect on healthcare is shown by the clinical success of several nano pharmaceuticals.

Achieving the targeted accumulation of therapeutic substances at the intended place is the goal of targeted medication delivery. An exciting new direction in targeted drug delivery is the combination of therapeutic medications with nanoparticles and the development of appropriate targeting routes, which have the potential to transport multiple molecules to precise anatomical sites. In order to achieve optimal targeting efficiency, it is crucial that the DDS remains in the physiological system for a sufficient duration to specifically target cells and tissues, releasing the delivery medication while evading the immune system. To enhance safety and efficacy, nanoparticles may make encapsulated cargo more stable and soluble, make transmembrane transport easier, and lengthen cycle durations. Intravascular medication delivery allows nanoparticles to enter the circulation via blood vessels and treat intravascular illnesses by acting at precise locations inside the blood vessels. Another method of drug delivery including nanoparticles is known as extravascular drug delivery, and it involves local administration (e.g., oral, inhalation, subcutaneous injection, etc.) to target tissues.

Intravascular targeting nanoparticles

Intravascular disease specific DDS has seen extensive application as a future therapeutic strategy for several illnesses and conditions in the last decade, including cancer and cardiovascular disorders. The total area of an adult's blood vessels ranges from 43,000 to 75,000 square feet. Nevertheless, vascular disease is limited to a little portion of this surface, indicating inflammation on a local level. It is common for pathogen infection to rise and tissue healing to be postponed when systemic pharmacological treatment is used to reduce vascular inflammation. In order to lessen the negative effects of systemic medications, nanomaterials may be used as vascular-targeted carriers for intravascular drug delivery. Intravascular inflammation changes the local environment, which may inspire new nanoparticle designs. When inflammatory stimuli are high, nanoparticles may target immune cells and the receptors on their membranes.

Surface modification and active targeting

In order to achieve local therapeutic effects, nanocarriers have their surfaces altered in a way that allows them to penetrate the circulatory system and bind to markers on the arterial wall. This method of medication delivery enhances therapeutic effectiveness while decreasing adverse effects associated with systemic dosing. According to reports, therapeutic genes and medicines may be made cell specific when ligands can be targeted to nanomaterials. The vascular endothelium is also a good place to focus vascular-targeted treatments. Endothelial cells and the vascular lumen make up the vascular endothelium, which plays an important role in maintaining the homeostasis of the blood vessels and the balance of tissue fluids.

Atherosclerosis, severe cardiovascular disorders (including PAD, CA, stroke, and MI), sepsis, acute respiratory distress syndrome, and COVID-19 respiratory distress all stem from endothelial dysfunction. An increase in vascular cell adhesion molecule 1 (VCAM-1) expression may be seen in areas where blood flow is locally impaired. Inflamed endothelium has clearly elevated VCAM-1 levels, whereas healthy endothelium has clearly decreased levels. An effective delivery of therapeutic nucleotides to inflammatory endothelial cells was achieved by Zhou et al. using a VCAM1-targeting polyelectrolyte complex micelle that targeted the inflammatory vascular endothelium.

Solid Lipid Nanoparticle

An effort was made by F. Bonafè and colleagues to create α-mangostin conjugated with CD44 Thio aptamer solid lipid nanoparticles that might be used by MCF-7 cells to target multicellular tumour spheroids (MCTSs). A method called nanoprecipitation was used to create lipid nanoparticles from PLGA, soybean lecithin, and DSPE-PEG2000-COOH. Then, two catalysts called 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide and N-hydroxy succinimide were used to attach the Thio aptamer to these nanoparticles.

Nanotechnology-Mediated Cancer Therapy

The use of nanotechnology in cancer treatment has shown impressive results. The magnetothermal and photothermal properties of certain nanomaterials have led to the development of novel therapeutics. Using superparamagnetic materials may provide very high sensitivity in imaging and diagnosing tumour lesions. Furthermore, in order to kill tumour cells, the temperature may be increased to 40–45 °C while an external magnetic field is applied. Applying nanomedical devices can efficiently perform complicated functions such as administering intracellular medication, producing power, and even detoxifying the blood vessels, allowing for more efficient biological therapy and medical cell functioning. Because each PDT NP may carry many photosensitive molecules, it is feasible to deliver a large number of these molecules to the tumour site. In photodynamic therapy (PDT), it may deliver a plethora of photosensitive chemicals directly to the tumour, where they kill cancer cells. Strong photocatalytic activity is shown by a number of nanomaterials, including semiconductor-related ones such nanoscale titanium dioxide (TiO2) and zinc oxide (ZnO). Nanomaterials outperform traditional photosensitisers in terms of stability, affordability, catalytic performance, and cytotoxicity. Most importantly, it has the potential to destroy the tumour while avoiding harming healthy tissue. PDT expands the photosensitizer's application possibilities and is an important component of combination treatment for malignancies.

Cancer Treatment Using Photodynamic Therapy-Based Nanotechnology

Semiconductor nanoparticles may be used as a photosensitiser in tumour photodynamic treatment (PDT) because of their usually strong photocatalytic activity. An increasingly important part of cancer treatment is photodynamic therapy (PDT). Utilising a photosensitiser, photodynamic therapy (PDT) may selectively destroy tumours and other local aberrant tissues by increasing ROS and ALA peptide synthesis via a photodynamic reaction. A single oxygen and oxygen-free radicals, as well as other reactive oxygen species (ROS), are released when the photosensitiser that is located on the targeted molecules is activated. The interaction of reactive oxygen species (ROS) with various biological chemicals found in tumour cells and tissues may lead to cytotoxicity, which in turn kills tumour cells and eliminates tumour tissues.

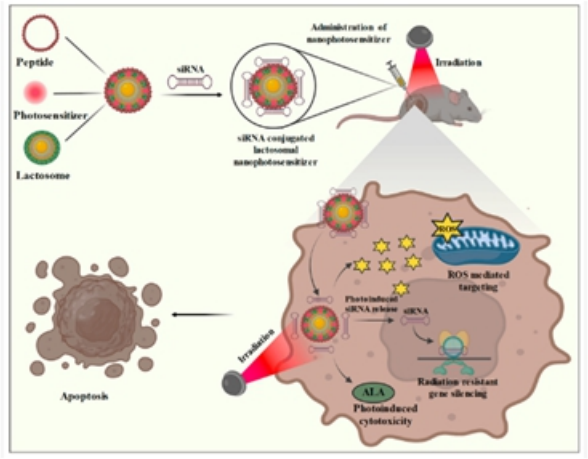

Figure 1. Photodynamic therapy assisted by lactosomal nano photosensitizers. The formulation of a lactosomal nano photosensitizer is achieved by combining a photosensitiser with siRNAs with a polypeptide. Radiation treatment of the administered lactosomal nano photosensitizer triggers the release of bound siRNAs, which in turn silence genes involved in radiation resistance. The production of reactive oxygen species (ROS), which facilitate cell death, is another function of the nano photosensitizer.

Role of Nanotechnology in Cancer Immunotherapy

Nanotechnology has not only improved immunotherapy but also chemotherapy, two mainstays in the fight against cancer. Evidence suggests that inorganic NPs such as acetylated dextran (AcDEX) and mesoporous silica might enhance the immune response when used as adjuvants in immunotherapy. When it comes to chemo-immunotherapy, nanotechnology has been a boon for breast cancer cells. On top of that, immunotherapy and chemotherapy together are thought to be the most effective and superior way to treat cancer.

Nanotechnology Mediated CRISPR/Cas9 Delivery for Cancer Therapy

While viral vectors have shown some promise in delivering nucleic acids and proteins, there is need for improvement in terms of toxicity, tissue targeting, and overall efficacy of gene delivery. Because of their safety and effectiveness in clinical settings, nano-vehicles may be used as a mechanism to overcome hurdles and as a potential tool for genome editing in cancer treatment. Such projected substitution may aid in the formulation of very successful therapeutic regimens that are applicable in clinical settings. In contrast to Bcl-2 inhibitors and RNAi technologies, CRISPR/Cas9 entirely inhibits the Bcl-2-mediated anti-oxidative stress pathway. In many cases, the CRISPR/Cas9 system is able to efficiently and safely reach the target tissues. Because of the CRISPR/Cas9 plasmid, the integration and distribution of vectors have become much more challenging. Consequently, developing a reliable and efficient vector is a significant challenge for deploying the CRISPR/Cas9 system. An engineered and built nano-domino-CRISPR (TAN) that is tumor-specific, in conjunction with the chlorins e6 (Ce6) photosensitiser and the CRISPR/Cas9 plasmid that encodes the Bcl-2 gene, is designed to give a personalised treatment by disrupting anti-oxidative stress and inducing apoptosis.

OBJECTIVES OF THE STUDY

1. To study on Role of Nanotechnology in Cancer Immunotherapy
2. To study on Cancer Treatment Using Photodynamic Therapy-Based Nanotechnology

RESEARCH METHOD

A literature review utilising the keywords "nano formulation of α-mangostin for cancer drug delivery system," "nanoparticle formulation of α-mangostin for cancer drug delivery system," and "α-mangostin nanoparticle for cancer drug delivery system" published within the past decade formed the basis of this review. The literature was sourced from Google Scholar, PubMed, but also Scopus. Exclusion criteria included subjective opinions, evaluations, and irrelevant topics including bioactivities and pharmaceutical features.

α-Mangostin

Mangosteen pericarps contain the metabolite α-mangostin, which is a 1,3,6,7-tetrahydroxy-2,8-di(3-methyl-2-butenyl) xanthone. The solubility of α-mangostin in water is 2.03 × 10−4 mg/L at 25 ◦C, and it is soluble in methanol as shown in Table 1. Because α-mangostin is little soluble in water, its bioavailability is also limited. Research on the pharmacokinetics of α-mangostin in mice after a single oral dosage of 20 mg/kg indicated a low bioavailability (F = 2.29%), which was believed to be caused by the drug's fast metabolism in the liver and small intestine, as well as its poor absorption in the gastrointestinal tract.

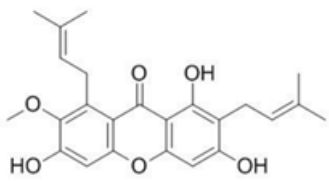

Figure 2. Chemical structure of α-mangostin.

The biological actions of α-mangostin are diverse and extensive, including hepatoprotective, cardioprotective, antimalarial, anti-obesity, and neuroprotective effects in Alzheimer's disease. According to earlier research, α-mangostin inhibits cancer cells via controlling the β-catenin gene, downregulating the PI3K/Akt pathway, and reducing fatty acid synthase. Its low oral bioavailability is the biggest limitation to its therapeutic potential, even if it has the aforementioned anticancer characteristics. The development of α-mangostin nano formulations has been driven by the need to address these difficulties and enhance the delivery of α-mangostin for improved therapeutic results.

DATA ANALYSIS

α-Mangostin Nano formulation

The creation of nanoparticle therapeutic carriers is a direct outcome of nanotechnology's use in the medical field. To minimise side effects, it is best to use particles between 10 and 200 nm in cancer treatments. This

size range permits the particles to readily penetrate tumour blood vessels, which may leak and accumulate in tumour tissue. The development of various nanoparticles as cancer drug delivery systems is ongoing. These include micelles, nano polymers, liposomes, lipid emulsions, lipid-drug conjugates, and ligand-targeted products like antibodies, folate, and transferrin conjugated molecules. At least one of the components of a nanoparticle is an active medicinal ingredient; often, there are two or more components. Nanoparticle size and form, active component physicochemical qualities, target delivery, stability, and safety are the primary considerations when choosing materials and procedures for nanoparticle assembly. The success of the planned administration strategy and the drug's targeting capabilities depend critically on the components and procedures chosen.

Table 1. Summary of α-mangostin nano formulations

Carrier	Cell Line	Outcome	References
Ethyl carbodiimide hydrochloride (EDC) and polyethyleneimide (a crosslinker) with silk fibroin	Caco-2 MCF-7	Indian indigenous biologics are priced much cheaper than their originators due to lenient regulatory criteria and minimal research and development expenditures.	
Acetobacter xylinum	B16F10; MCF-7; hGF; HaCaT	Much less harmful to healthy cells than malignant cells Mildly harmful to normal cells (HaCaT cells)	
DSPE-PEG2000-COOH Thioaptamer (ligand), soybean lecithin, and PLGA	MCF-7	With a size range of 150-300 nm The process of nanoparticle internalisation Spheroids of MCF-7 multicellular tumours strongly de-aggregate.	

Oleoyl chitosan (as a coating agent), miglyol 812, cetyl paomitate, and montanov 82	Caco-2 Hela	Ensuring a particle size below 200 nm Extremely steady bodily state Highly effective encapsulation (EE > 90%) Internalisation at the cellular level Enhancement of cytotoxicity Repression of the anti-apoptotic gene BCL2 and cyclin D1 (CCND1)	
PLGA	The AsPC-1, PANC-1, and Mia-Paca-2 pancreatic cancer cell lines are cancer stem cells.	Ensuring a particle size below 200 nm Amplifies access to cells Upregulation of E-cadherin and downregulation of pluripotency maintenance factors, Pancreatic cancer growth, progression, and metastasis are all hindered by induced apoptosis.	
PLGA	Normal epithelial cells (CRL-1831) in HCT116 and HT29	The process of nanoparticle internalisation Notch receptors and its ligands, γ-secretase complex protein, and downstream targets' expression is inhibited. Induced cancer cells and did not trigger apoptosis in normal cells	

ECH acts as a linker with α, β, and γ cyclodextrin (CD).	CT26WT	Complexation with βCD nanoparticles demonstrated the best solubility and complexation efficiency of α-mangostin. The loading ratio of the α-mangostin complexes was greater than that of the CDs themselves. Both quick and gradual release Reduced cell death	
β-cyclodextrin	A549	Large particles (< 50 nm) The nuclear morphology was altered when nanoparticles were internalised by cancer cells. Enhancement of cytotoxicity	
The crosslinker Genipin is composed of chitosan and alginate.	HT-29	Approximately 400–500 nanometres in size The loading capacity and effectiveness of the nanoparticles are both greatly enhanced by using genipin as a crosslinker. Enhancement of cytotoxicity	

Nanostructured Lipid Carriers

Novel therapeutic formulations known as nanostructured lipid carriers are made up of surfactants, co-surfactants, and physiological and biocompatible lipids. Being a lipid-based nanoparticle that is both biocompatible and biodegradable, NCL has the potential to greatly enhance the therapeutic capacity of chemotherapeutic medicines while maintaining low pharmacokinetic features. Its improved physical and

chemical stability further adds to its attractiveness as a carrier. The potential oral administration of α-mangostin prompted the development of the mucoadhesive NLC. The nanoparticles, which were made in a size range of 200 to 400 nm, exhibited low polydispersity, zeta potentials of 40.9 mV, and an outstanding encapsulation efficiency of more than 90%. They were coated with oleoyl-quaternized-chitosan using a high-pressure homogenisation process. The results showed that when tested against Hela and Caco-2 cells, the NLC-CS was more hazardous than the NLC.

Cyclodextrin Nanoparticles

When starch-modified products undergo cyclisation due to the action of cyclodextrin glycosyltransferase (CGTase), the resulting non-reducing oligosaccharides have a ring-shaped chemical structure and are known as cyclodextrins. Under the right circumstances, three primary classes of cyclodextrin will be formed: α-, β-, and γ-cyclodextrins, which contain 6, 7, and 8 units of (1,4) linked D(+)-glucopyranose, respectively. Water solubility is due to the presence of several hydroxyl groups at both ends of the molecule, but the presence of hydrophobic interior groups inside the cyclic structure creates a "molecular pocket" that may trap other molecules with similar properties. Cavity size is determined by the number of glucose units, and α-, β-, and γ-cyclodextrin have cavity diameters of 5.7, 7.8, and 9.5 Å, respectively. Without affecting their bioactivity, hydrophobic medications such as α-mangostin may be trapped in the cyclodextrins molecular pocket. The cytotoxicity of α-mangostin-encapsulated cyclodextrin nanoparticles (CDNP) was tested in CT26WT cancer cells after their development by a polyaddition procedure involving epichlorohydrin. This hyperbranched polymer, which contains cyclodextrin, was synthesised via a simple poly-addition process using epichlorohydrin (ECH) and cyclodextrin. The procedure successfully incorporates several cyclodextrins into the polymer.

Since their effects on people are largely unknown, nanoparticle toxicity is a major issue. Nanoparticles' remarkable physicochemical features may cause changes to pharmacokinetics and the capacity to bypass biological barriers, raising safety concerns despite the vast potential medical applications of these tiny particles. Translation has also been hindered by the chemicals' intrinsic toxicity and their ability to accumulate and remain in the human body. Because of their biodegradability, biocompatibility, and toxicity reduction capabilities, biological capping materials like chitosan are an obvious option for nanocarriers. Clinical translation success depends on these nanoparticles' stability, circulation time, accessibility, bioavailability, and safety profile to disease sites. Consequently, in order to comprehend the α-mangostin nano formulation’s in vivo behaviour, which might eventually result in the development of an appropriate formulation with better therapeutic effectiveness, clinical studies are required.

Table 2. Tumour treatment volume reduction with various α-mangostin nanoformulations.

Formulartion	Type of tumor	Reduction of tumor volume	References

PLGA	Pancreatic	At 20 mg/kg, tumours were reduced by almost 60%.	
Cyclodextrin nanoparticle	Colon	At a dose of 10 mg/kg, tumours are reduced by around 56%.	
Coated with the CREKA peptide, PEG-PLA nanomicelles	Pancreatic	At a dose of 20 mg/kg, tumours were reduced by more than 70%.	
MPEG-PCL nanomicelles	Melanoma	A dose of 50 mg/kg reduced tumour development by almost half.	
MPEG-PLA nanomicelles	Glioma	At 50 mg/kg, tumours are reduced by around 65%.	

Current Trends in Modern Nano pharmaceuticals´ Design

Current developments in the design of contemporary nano pharmaceuticals include nano-encapsulation, biomimetics and bioinspiration, green design, 3D printing, and nanosuspension technology.

Nanosuspension Technology

To increase the oral bioavailability and solubility of pharmaceuticals and plant extracts, nanosuspension technology is a promising nanotechnological strategy. A nanosuspension was successfully prepared using the nanoprecipitation technique. A plant-derived nanosuspension was prepared using the nanoprecipitation method, which entails dissolving the plant extract in an organic phase (ethanol) and then filtering the mixture. The final solution was slowly added to an aqueous phase that already included a stabiliser, such as a surfactant or polymer, while being constantly stirred.

Nano-Encapsulation

The use of nano capsules to transport bioactive substances such as medicines, nutraceuticals, and others has recently gained traction. Drug release kinetics, stability, and targeting may be precisely controlled by their unique structure, which is a core-shell design with a diameter usually ranging from 10 to 1000 nm. The many materials and formulation procedures used to create nano capsules are discussed in this

overview, along with their possible uses and where the field may go from here, particularly in the medication delivery industry and beyond.

Because of its mild gelation conditions, low immunogenicity, and biocompatibility, alginate—an anionic natural polysaccharide—is used in drug carrier nano formulations. In addition to its well-documented advantages, alginate is a polymer that responds to changes in pH, allowing it to protect payloads in acidic conditions while releasing medications in alkaline ones. A potential oral delivery system for medications to the intestines has been developed using nano capsules manufactured from alginate. The pharmaceutical industry often utilises dextran sulphate, a polyanionic polymer that is both biocompatible and biodegradable, for the administration of drugs. Electrostatic integration is often used to make multilayer nano capsules from a combination of dextran sulphate and CS. The CS and dextran sulphate nano capsules showed remarkable stability even without the inclusion of any further covalent agents. Changing the CS to dextran ratio changes the drug release behaviour. A higher concentration of carboxymethyl dextran in chitosan-extra nanoparticles may improve nanoparticle dissociation, leading to an increase in gene release in serum or cytoplasm.

Biomimetics and Bioinspiration in Nano pharmaceuticals/Nanomedicines

Nanotechnology has opened up new possibilities for the creation and development of novel treatment techniques, which has transformed several areas, including medicine. Drawing inspiration from the complex patterns and processes seen in nature, biomimetics and bioinspiration have become influential concepts in the field of nano pharmaceuticals and nanomedicines. This groundbreaking work delves into the ways in which nanotechnology, biomimetics, and bioinspiration are influencing one another to transform nanoscale medication delivery, diagnostics, and therapies.

Some of the medical and biotechnological innovations that have resulted from biomimetics include bio-inspired drug delivery systems, artificial organs that replicate the shape and function of real tissues and organs, and scaffolds made of synthetic tissues. By applying biological principles to medical technology, researchers hope to create therapies for a wide range of illnesses and injuries that are both effective and compatible with the body. By drawing inspiration from the vast array of solutions found in nature, biomimetics presents an exciting new direction for innovation. Biomimetic researchers seek to solve critical global issues with technologies that are both more sustainable and robust, by studying nature's designs.

Targeted Drug Delivery

Nature offers simple but effective ways to deliver therapeutic payloads to certain cells or tissues. Nanomedicines with a biological focus use this idea to their advantage by attaching to abnormally expressed molecular markers on sick cells using targeted ligands like antibodies or peptides.

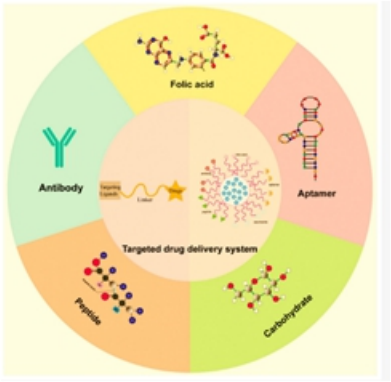

Figure 3. Various targeting ligands are employed in targeted medication delivery.

To maximise therapeutic effectiveness and minimise off-target effects, these nanocarriers may selectively transport medications to the site of action by imitating the specificity of biological recognition systems. By modelling its precise targeting mechanisms after those found in nature, bioinspiration has completely transformed targeted medication delivery in nanomedicines. To improve the precision and efficiency of delivering therapeutic payloads to sick cells or tissues while minimising off-target effects, bioinspired nanocarriers imitate biological recognition mechanisms. An exploration of bioinspired targeted drug delivery and its nanomedicine applications is presented here:

Biological Targeting Ligands: Proteins, antibodies, or aptamers are examples of targeting ligands used in bioinspired nanomedicines. These ligands bind to particular molecular markers that are overexpressed on sick cell surfaces. These nanocarriers may reduce systemic toxicity and save healthy tissues by selectively delivering medications to the site of action, much like biological recognition systems.

Cellular Membrane Camouflage: To imitate the surface characteristics of host cells, biomimetic nanocarriers may encase themselves in vesicles produced from cell membranes. Nanocarriers may promote connections with target cells while evading immune detection and clearance because to their camouflage. By capitalising on natural cellular absorption processes, these nanomedicines with a biomedical bent improve the effectiveness of targeted drug delivery across biological barriers.

Exosome-Mimetic Nanovesicles: Natural extracellular vesicles released by cells, exosomes facilitate cargo movement and intercellular communication. Nanomedicines that draw inspiration from nature aim to accomplish targeted drug delivery by modelling their structure and function after exosomes. Nanovesicles mimicking exosomes may target medication delivery to particular cells or tissues by taking use of endocytic pathways and cell-to-cell contacts.

Biological Barriers' Penetration: To reach their goals, nanomedicines inspired by nature must first cross biological barriers, such as the BBB or the tumour microenvironment. Successful medication distribution to otherwise inaccessible locations is made possible by nanocarriers that imitate the size, shape, and surface characteristics of biological entities. This allows them to more easily cross cellular membranes and penetrate tissue barriers.

Challenges and Limitations of Nanopharmaceuticals

Due to the unique properties of nanoparticles, investigations conducted on these tiny particles in both in vitro and animal models have shown encouraging findings. Nevertheless, the majority of studies are still in the early stages, and the advantages to patients are insufficient. Multiple targeting designs that account for physiological aspects like blood flow, illness condition, and tissue shape are required for the hard challenge of building a tailored nanomedicine delivery system. Research on the effects of nanodrugs on humans is still in its infancy due to the wide range of results shown in animal models. This restriction may render targeted nanoparticles distribution and function patient specific, which would be problematic owing to inter-patient variability and would likely limit their utility. One notable development that might pave the way for tailored drug delivery systems to become more relevant is the increasing interest in precision or personalised medicine. Nanoparticle buildup in tumours has been linked to the EPR phenomenon in several studies. On the other hand, there are stories that cast doubt on this finding. The EPR effect and passive transport account for a negligible portion of the nanoparticle accumulation in tumours, according to new imaging research that used a mouse tumour model. Nanoparticle buildup may also be facilitated by molecular processes, interactions between immune cells, and protein coatings. Quantitative evaluation of nanoparticle delivery and dispersion is therefore necessary with ongoing exploration of the EPR effect as a promoter of nanoparticle accumulation. At the same time, studying tumours and the biological barriers around them could be a very challenging task. The body's mucus membranes, particularly those in the lungs and gastrointestinal system, significantly impede the targeted nanoparticle delivery of medications. Nanoparticles encounter a more complicated barrier due to the fact that many circumstances, such as the patient's lifestyle and illness status, may cause the mucus to have varying characteristics.

CONCLUSION

To enhance bioavailability and efficacy in cancer therapy, many nano formulations of α-mangostin have been created in the last few years. α-mangostin has promising anticancer effects, however it is not practical to use it as a powerful cancer medication due to its low solubility, fast elimination, and poor pharmacokinetic features. The creation of nanosized delivery vehicles is one of the approaches taken to this problem. This change is much appreciated for α-mangostin in the form of nanoparticles as they may enhance the dispersion of α-mangostin in water and provide additional benefits that are not achieved with traditional methods of administration. Among these benefits are the ability to alter surface properties and particle size. As an example, cancer cells may be specifically targeted by combining α-mangostin nanoparticles with targeting ligands like peptides and aptamers. When it comes to individualised medicine, nanomedicine has tremendous potential to transform medication administration and treatment. Theranostic agents that may transport drugs and conduct diagnostic imaging at the same time are one example of a potential future trend in nanomedicine. Other potential developments include multifunctional nanoparticles and tailored drug carriers. Researchers may create patient-specific formulations with improved therapeutic effectiveness and less systemic toxicity by using nanoparticles' unique features, such as controlled drug release, surface functionalisation, and size-dependent pharmacokinetics. Wearable gear, health applications for smartphones, and remote monitoring systems are just a few examples of the digital health innovations that might revolutionise individualised healthcare. The use of these technologies allows for the optimisation of therapy, early illness identification, and patient involvement via the continuous monitoring of health markers, real-time data collecting, and personalised feedback. The advent of patient-specific formulations

and personalised medicine has the potential to revolutionise healthcare by providing individuals with more effective, more efficient, and safer therapies that also improve their quality of life. In order to realise personalised medicine's revolutionary promise in healthcare delivery, stakeholders must embrace new technology, advance regulatory frameworks, and address ethical concerns. This will speed the adoption of personalised medicine. Collaboration, innovation, and a dedication to patient-centered care will play a crucial role in moulding healthcare's future and bringing about a new age of precision medicine as we negotiate the intricate terrain of personalised medicine.

References

1. F. Bonafè et al., A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 2018, 68, 394–424.
2. Majolo, F.; de Oliveira Becker Delwing, L.K.; Marmitt, D.J.; Bustamante-Filho, I.C.; Goettert, M.I. Medicinal plants and bioactive natural compounds for cancer treatment: Important advances for drug discovery. Phytochem. Lett. 2019, 31, 196–207.
3. Pham, D.T.; Saelim, N.; Tiyaboonchai, W. Alpha mangostin loaded crosslinked silk fibroin-based nanoparticles for cancer chemotherapy. Colloids Surfaces B Biointerfaces 2019, 181, 705–713.
4. Sung, H.; Ferlay, J.; Siegel, R.L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J. Clin. 2021, 71, 209–249.
5. Baskar, R.; Lee, K.A.; Yeo, R.; Yeoh, K.W. Cancer and radiation therapy: Current advances and future directions. Int. J. Med. Sci. 2012, 9, 193–199.
6. Tohme, S.; Simmons, R.L.; Tsung, A. Surgery for Cancer: A Trigger for Metastases. Cancer Res. 2018, 77, 1548–1552.
7. Swain, S.M. Chemotherapy: Updates and New Perspectives. Oncologist 2011, 16, 30–39.
8. Pérez-Herrero, E.; Fernández-Medarde, A. Advanced targeted therapies in cancer: Drug nanocarriers, the future of chemotherapy. Eur. J. Pharm. Biopharm. 2015, 93, 52–79.
9. Huang, C.Y.; Ju, D.T.; Chang, C.F.; Muralidhar Reddy, P.; Velmurugan, B.K. A review on the effects of current chemotherapy drugs and natural agents in treating non-small cell lung cancer. Biomedicine 2017, 7, 12–23.
10. Lin, S.R.; Chang, C.H.; Hsu, C.F.; Tsai, M.J.; Cheng, H.; Leong, M.K.; Sung, P.J.; Chen, J.C.; Weng, C.F. Natural compounds as potential adjuvants to cancer therapy: Preclinical evidence. Br. J. Pharmacol. 2020, 177, 1409–1423.
11. Nirmala, M.J.; Samundeeswari, A.; Sankar, P.D. Natural plant resources in anti-cancer therapy—A review. Res. Plant Biol. 2011, 1, 1–14.
12. Khan, T.; Gurav, P. PhytoNanotechnology: Enhancing delivery of plant based anti-cancer drugs. Front.

Pharmacol. 2018, 8, 1002.

13. Subramaniam, S.; Selvaduray, K.R.; Radhakrishnan, A.K. Bioactive compounds: Natural defense against cancer? Biomolecules 2019, 9, 758.

14. Rejhová, A.; Opattová, A.; Cumov ˇ á, A.; Slíva, D.; Vodiˇcka, P. Natural compounds and combination therapy in colorectal cancer treatment. Eur. J. Med. Chem. 2018, 144, 582–594.

15. Bishayee, A.; Sethi, G. Bioactive natural products in cancer prevention and therapy: Progress and promise. Semin. Cancer Biol. 2016, 40–41, 1–3.

16. Davatgaran-Taghipour, Y.; Masoomzadeh, S.; Farzaei, M.H.; Bahramsoltani, R.; Karimi-Soureh, Z.; Rahimi, R.; Abdollahi, M. Polyphenol nanoformulations for cancer therapy: Experimental evidence and clinical perspective. Int. J. Nanomed. 2017, 12, 2689–2702.

17. Mary Lazer, L.; Sadhasivam, B.; Palaniyandi, K.; Muthuswamy, T.; Ramachandran, I.; Balakrishnan, A.; Pathak, S.; Narayan, S.; Ramalingam, S. Chitosan-based nano-formulation enhances the anticancer efficacy of hesperetin. Int. J. Biol. Macromol. 2018, 107, 1988–1998.

18. Cosco, D.; Mare, R.; Paolino, D.; Salvatici, M.C.; Cilurzo, F.; Fresta, M. Sclareol-loaded hyaluronan-coated PLGA nanoparticles: Physico-chemical properties and in vitro anticancer features. Int. J. Biol. Macromol. 2019, 132, 550–557.

19. Hamishehkar, H.; Bahadori, M.B.; Vandghanooni, S.; Eskandani, M.; Nakhlband, A.; Eskandani, M. Preparation, characterization and anti-proliferative effects of sclareol-loaded solid lipid nanoparticles on A549 human lung epithelial cancer cells. J. Drug Deliv. Sci. Technol. 2018, 45, 272–280.

20. Fang, R. H., Hu, C. M., Luk, B. T., Gao, W., Copp, J. A., Tai, Y., et al. (2014). Cancer cell membrane-coated nanoparticles for anticancer vaccination and drug delivery. Nano Lett. 14 (4), 2181–2188. doi:10.1021/nl500618u

21. Fang, J., Islam, W., and Maeda, H. (2020). Exploiting the dynamics of the EPR effect and strategies to improve the therapeutic effects of nanomedicines by using EPR effect enhancers. Adv. Drug Deliv. Rev. 157, 142–160. doi:10.1016/j.addr.2020.06.005

22. Fromen, C. A., Fish, M. B., Zimmerman, A., Adili, R., Holinstat, M., and Eniola-Adefeso, O. (2016). Evaluation of receptor-ligand mechanisms of dual-targeted particles to an inflamed endothelium. Bioeng. Transl. Med. 1 (1), 103–115. doi:10.1002/btm2.10008

23. Fu, J., Li, T., Yang, Y., Jiang, L., Wang, W., Fu, L., et al. (2021). Activatable nanomedicine for overcoming hypoxia-induced resistance to chemotherapy and inhibiting tumor growth by inducing collaborative apoptosis and ferroptosis in solid tumors. Biomaterials 268, 120537. doi:10.1016/j.biomaterials.2020.120537

24. Gabizon, A., Catane, R., Uziely, B., Kaufman, B., Safra, T., Cohen, R., et al. (1994). Prolonged circulation time and enhanced accumulation in malignant exudates of doxorubicin encapsulated in polyethylene-glycol coated liposomes. Cancer Res. 54 (4), 987–992.

25. Galstyan, A., Markman, J. L., Shatalova, E. S., Chiechi, A., Korman, A. J., Patil, R., et al. (2019). Blood-brain barrier permeable nano immunoconjugates induce local immune responses for glioma therapy. Nat. Commun. 10 (1), 3850. doi:10.1038/s41467-019-11719-3

26. Galvani, S., Sanson, M., Blaho, V. A., Swendeman, S. L., Obinata, H., Conger, H., et al. (2015). HDL-bound sphingosine 1-phosphate acts as a biased agonist for the endothelial cell receptor S1P1 to limit vascular inflammation. Sci. Signal 8 (389), ra79. doi:10.1126/scisignal.aaa2581

27. Gao, J., Chu, D., and Wang, Z. (2016). Cell membrane-formed nanovesicles for disease-targeted delivery. J. Control Release 224, 208–216. doi:10.1016/j.jconrel.2016.01.024

28. Gao, W., Li, S., Liu, Z., Sun, Y., Cao, W., Tong, L., et al. (2017). Targeting and destroying tumor vasculature with a near-infrared laser-activated "nanobomb" for efficient tumor ablation. Biomaterials 139, 1–11. doi:10.1016/j.biomaterials.2017.05.037

29. Gao, X., Zhang, J., Huang, Z., Zuo, T., Lu, Q., Wu, G., et al. (2017). Reducing interstitial fluid pressure and inhibiting pulmonary metastasis of breast cancer by gelatin modified cationic lipid nanoparticles. ACS Appl. Mater Interfaces 9 (35), 29457–29468. doi:10.1021/acsami.7b05119

30. Gao, W., Li, X., Liu, Z., Fu, W., Sun, Y., Cao, W., et al. (2019). A redox-responsive self-assembled nanoprobe for photoacoustic inflammation imaging to assess atherosclerotic plaque vulnerability. Anal. Chem. 91 (1), 1150–1156. doi:10.1021/acs.analchem.8b04912

31. Gao, C., Huang, Q., Liu, C., Kwong, C. H. T., Yue, L., Wan, J. B., et al. (2020). Treatment of atherosclerosis by macrophage-biomimetic nanoparticles via targeted pharmacotherapy and sequestration of proinflammatory cytokines. Nat. Commun. 11 (1), 2622. doi:10.1038/s41467-020-16439-7

32. Hasheminejad, N.; Khodaiyan, F.; Safari, M. Improving the antifungal activity of clove essential oil encapsulated by chitosan nanoparticules. Food Chem. 2019, 275, 113–122

33. Bussio, J.I.; Molina-Perea, C.; González-Aramundiz, J.V. Lower-Sized Chitosan Nanocapsules for Transcutaneous Antigen Delivery. Nanomaterials 2018, 8, 659.

34. Elbaz, N.M.; Owen, A.; Rannard, S.; McDonald, T.O. Controlled synthesis of calcium carbonate nanoparticles and stimuli-responsive multi-layered nanocapsules for oral drug delivery. Int. J. Pharm. 2020, 574, 118866.

35. Menard, M.; Meyer, F.; Parkhomenko, K.; Leuvrey, C.; Francius, G.; Begin-Colin, S.; Mertz, D. Mesoporous silica templated-albumin nanoparticles with high doxorubicin payload for drug delivery assessed with a 3-D tumor cell model. Biochim. Biophys. Acta Gen. Subj. 2019, 1863, 332–341.

36. Shang, B.; Zhang, X.; Ji, R.; Wang, Y.; Hu, H.; Peng, B.; Deng, Z. Preparation of colloidal polydopamine/Au hollow spheres for enhanced ultrasound contrast imaging and photothermal therapy. Mater. Sci. Eng. C 2020, 106, 110174.

37. Rata, D.M.; Cadinoiu, A.N.; Atanase, L.I.; Bacaita, S.E.; Mihalache, C.; Daraba, O.M.; Gherghel, D.;

Popa, M. "In vitro " behaviour of aptamer-functionalized polymeric nanocapsules loaded with 5-fluorouracil for targeted therapy. Mater. Sci. Eng. C 2019, 103, 109828.

38. Jafari, S.M. (Ed.) An overview of nanoencapsulation techniques and their classification. In Nanoencapsulation Technologies for the Food and Nutraceutical Industries; Academic Press: London, UK, 2017; pp. 1–34.

39. Human, C.; de Beer, D.; van der Rijst, M.; Aucamp, M.; Joubert, E. Electrospraying as a suitable method for nanoencapsulation of the hydrophilic bioactive dihydrochalcone, aspalathin. Food Chem. 2019, 276, 467–474.

40. Habib, S.; Singh, M. Recent Advances in Lipid-Based Nanosystems for Gemcitabine and Gemcitabine–Combination Therapy. Nanomaterials 2021, 11, 597.

41. Rodrigues, V.M.; Oliveira, W.N.; Pereira, D.T.; Alencar, É.N.; Porto, D.L.; Aragão, C.F.S.; Moreira, S.M.G.; Rocha, H.A.O.; Amaral-Machado, L.; Egito, E.S.T. Copaiba Oil-Loaded Polymeric Nanocapsules: Production and In Vitro Biosafety Evaluation on Lung Cells as a Pre-Formulation Step to Produce Phytotherapeutic Medicine. Pharmaceutics 2023, 15, 161.

42. Oliveira, A.C.S.; Oliveira, P.M.; Cunha-Filho, M.; Gratieri, T.; Gelfuso, G.M. Latanoprost loaded in polymeric nanocapsules for effective topical treatment of alopecia. AAPS PharmSciTech 2020, 21, 305.

43. Mora-Huertas, C.E.; Fessi, H.; Elaissari, A. Polymer-based drug-delivery nanocapsules. Int. J. Pharm. 2010, 385, 113–142.

44. Kothamasu, P.; Kanumur, H.; Ravur, N.; Maddu, C.; Parasuramrajam, R.; Thangavel, S. Nanocapsules: The weapons for novel drug delivery systems. Bioimpacts BI 2012, 2, 71–81.

45. Shastri, V.P. Non-degradable biocompatible polymers in medicine: Past, present and future. Curr. Pharm. Biotechnol. 2003, 4, 331–337.

46. Almeida, J.P.M.; Chen, A.L.; Foster, A.; Drezek, R.J.N. In vivo biodistribution of nanoparticles. Nanomedicine 2011, 6, 815–835.

47. Ventola, C.L. Medical Applications for 3D Printing: Current and Projected Uses. Pharm. Ther. 2014, 39, 704–711.

48. Goyanes, A.; Robles-Martinez, P.; Buanz, A.B.M.; Basit, A.W.; Gaisford, S. Effect of Geometry on Drug Release from 3D Printed Tablets. Int. J. Pharm. 2015, 494, 657–663.

49. Lim, S.H.; Kathuria, H.; Tan, J.J.Y. 3D Printing of Polymers for Biomedical Applications. Eur. Polym. J. 2020, 133, 109812.

50. Wang, H.; Zhou, L.; Liao, J.; Tan, W.; Liu, J.; Lin, H.; Liao, L. 3D Printing of Conductive Nanomaterials for Flexible Electronics and Energy Applications: A Review. Nanoscale 2019, 11, 19279–19304.

51. Zhang, B.; Li, S.; Hingorani, H.; Serjouei, A.; Larush, L.; Pawar, A.A.; Goh, W.H.; Sakhaei, A.H.;

Hashimoto, M.; Kowsari, K.; et al. Highly stretchable hydrogels for UV curing based high-resolution multimaterial 3D printing. J. Mater. Chem. B. 2018, 6, 3246–3253.

52. Choudhury, A.; Das, S.; Bahadur, S.; Saha, S.; Roy, A. Formulation and Evaluation of 3D Printed Omeprazole Tablets. Indian J. Pharm. Sci. 2010, 72, 491–494.

53. Cardoso, P.H.; Araújo, E.S. An Approach to 3D Printing Techniques, Polymer Materials, and Their Applications in the Production of Drug Delivery Systems. Compounds 2024, 4, 71–105.

54. Yu, L.X. Pharmaceutical quality by design: Product and process development, understanding, and control. Pharm. Res. 2008, 25, 781–791. [Google Scholar]

55. Martinez-Marquez, D.; Mirnajafizadeh, A.; Carty, C.P.; Stewart, R.A. Application of quality by design for 3D printed bone prostheses and scaffolds. PLoS ONE 2018, 13, e0195291.

56. Dou, H.; Sun, G.; Zhang, L. CA242 as a biomarker for pancreatic cancer and other diseases. Prog. Mol. Biol. Transl. Sci. 2019, 162, 229–239.

57. Utkarsh, K.; Kumar, A.; Khan, A.; Nayyar, A.; Haque, S.; Iqbal, S. Circulating and non-circulating proteins and nucleic acids as biomarkers and therapeutic molecules in ovarian cancer. Genes Dis. 2022, 10, 1005–1018.

58. Zhao, X.; Dai, X.; Zhao, S.; Cui, X.; Gong, T.; Song, Z.; Meng, H.; Zhang, X.; Yu, B. Aptamer-based fluorescent sensors for the detection of cancer biomarkers. Spectrochim. Acta Part A Mol. Biomol. Spectrosc. 2021, 247, 119038.

59. Li, Z.; Wang, L.; Li, Y.; Feng, Y.; Feng, W. Frontiers in carbon dots: Design, properties and applications. Mater. Chem. Front. 2019, 3, 2571–2601.

60. Chan, C.C.; Fan, C.W.; Kuo, Y.B.; Chen, Y.H.; Chang, P.Y.; Chen, K.T.; Hung, R.P.; Chan, E.C. Multiple serological biomarkers for colorectal cancer detection. Int. J. Cancer 2010, 126, 1683–1690

61. Kal-Koshvandi, A.T. Recent advances in optical biosensors for the detection of cancer biomarker α-fetoprotein (AFP). TrAC Trends Anal. Chem. 2020, 128, 115920.

62. Moradi, A.; Srinivasan, S.; Clements, J.; Batra, J. Beyond the biomarker role: Prostate-specific antigen (PSA) in the prostate cancer microenvironment. Cancer Metastasis Rev. 2019, 38, 333–346.

63. Zhang, M.; Cheng, S.; Jin, Y.; Zhao, Y.; Wang, Y. Roles of CA125 in diagnosis, prediction, and oncogenesis of ovarian cancer. Biochim. Biophys. Acta Rev. Cancer 2021, 1875, 188503.

64. Chinen, A.B.; Guan, C.M.; Ferrer, J.R.; Barnaby, S.N.; Merkel, T.J.; Mirkin, C.A. Nanoparticle probes for the detection of cancer biomarkers, cells, and tissues by fluorescence. Chem. Rev. 2015, 115, 10530–10574.

65. Gumus, E.; Bingol, H.; Zor, E. Lateral Flow Assays for Detection of Disease Biomarkers. J. Pharm. Biomed. Anal. 2022, 225, 115206.

66. Hasham, K.; Ahmed, N.; Zeshan, B. Circulating microRNAs in oncogenic viral infections: Potential diagnostic biomarkers. SN Appl. Sci. 2020, 2, 442.

67. Treerattrakoon, K.; Roeksrungruang, P.; Dharakul, T.; Japrung, D.; Faulds, K.; Graham, D.; Bamrungsap, S. Detection of a miRNA biomarker for cancer diagnosis using SERS tags and magnetic separation. Anal. Method. 2022, 14, 1938–1945.

68. Tabrizi, S.; Martin-Alonso, C.; Xiong, K.; Blewett, T.; Sridhar, S.; An, Z.; Patel, S.; Rodriguez-Aponte, S.; Naranjo, C.; Shea, D. A DNA-binding priming agent protects cell-free DNA and improves the sensitivity of liquid biopsies. Cancer Res. 2023, 83, 3371.

69. Lin, D.; Shen, L.; Luo, M.; Zhang, K.; Li, J.; Yang, Q.; Zhu, F.; Zhou, D.; Zheng, S.; Chen, Y. Circulating tumor cells: Biology and clinical significance. Signal Transduct. Target. Ther. 2021, 6, 404.

70. Guo, L.; Mu, Z.; Yan, B.; Wang, J.; Zhou, J.; Bai, L. A novel electrochemical biosensor for sensitive detection of non-small cell lung cancer ctDNA using NG-PEI-COFTAPB-TFPB as sensing platform and Fe-MOF for signal enhancement. Sens. Actuators B Chem. 2022, 350, 130874.

71. Proenca, C.A.; Baldo, T.A.; Freitas, T.A.; Materon, E.M.; Wong, A.; Duran, A.A.; Melendez, M.E.; Zambrano, G.; Faria, R.C. Novel enzyme-free immunomagnetic microfluidic device based on Co0.25Zn0.75Fe2O4 for cancer biomarker detection. Anal. Chim. Acta 2019, 1071, 59–69.

72. Wei, X.; Chen, K.; Guo, S.; Liu, W.; Zhao, X.-Z. Emerging microfluidic technologies for the detection of circulating tumor cells and fetal nucleated red blood cells. ACS Appl. Bio Mater. 2021, 4, 1140–1155.

73. Yin, B.; Qian, C.; Wang, S.; Wan, X.; Zhou, T. A microfluidic chip-based MRS immunosensor for biomarker detection via enzyme-mediated nanoparticle assembly. Front. Chem. 2021, 9, 688442.

74. Kulkarni, S.; Pandey, A.; Mutalik, S. Heterogeneous surface-modified nanoplatforms for the targeted therapy of haematological malignancies. Drug Discov. Today 2020, 25, 160–167.