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Review Article

Nanoparticulate System as a Promising Approach for Anticancer Drugs

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Abstract

In the beyond few years, there was a number of interests in and use of particulate delivery structures as immune providers each for small and large molecules withinside the area of drug administration. A form of drug molecule has pharmacokinetic and pharmacodynamic properties that adjust and enhance used inclusive of nanoparticles. In vivo, they were used to protect drug entities withinside the systemic circulation, restrict drug gets entry to sure areas, and distribute drugs at a regulated and constant price to the activity site. Various polymers are applied withinside the appearance of nanoparticles for drug delivery evaluation to increase healing benefit while decreasing side effects. This paper discusses an extensive variety of subjects associated with nanoparticle formulation, characterization, structural effects, and applications in drug delivery and therapeutic gene delivery. This study examines several themes relating to the formation of nanoparticles, characterisation, architectural impacts, and drug delivery and medicinal gene therapy application.

Keywords: Nanoparticles, drug delivery, targeting, drug release.

INTRODUCTION

Nanoparticles can be characterised as having a reach from 1,000-1000 NM that should be measured in a colloidal, solid state form. The measurement is constantly decreasing. The medicine is dissolved, trapped, encapsulated, or added to a gill their size inevitably decreases. A drug in one of several processes is broken down, entangled, shown or attached to a nanoparticles network. For nanoparticles the materials used should be non-toxic, biodegradable, sterilizable, etc. The article behind the nanoparticle's proposal. Made from advanced semi-synthetic polymers that transmit protein-like Stoops for drugs Current intake or any compound structure restricts the use of medicines in polymer grid particles, strong mode or perhaps bonded molecule surfaces [1]. The development of an ample range of nanoparticles containing lipids, polymers and inorganic components resulted in different physicochemical characteristics and hence applications of transportation systems [2-5] Nanoparticles with diameters smaller than 200 nm have a slower satisfaction rating and hence a longer circulation period compared with nanoparticles with a greater mass [6]. In order to distribute them in an ideal way, the medically optimum rates and dose rates are ensured by regulating the size of the particles, surface characteristics and pharmacologically active substances release. In the overall process, liposomes also play a critical role. They are utilised with possible benefits, in particular in safeguarding medicines from deterioration, reduce toxicity and play an important role throughout the whole process. They can also be used to protect pharmaceuticals against deterioration, reduced toxicity and adverse effects, target the site of action, etc. They have the positive effects. Liposomes have certain defects, such limited encapsulation effectiveness or fast leakage of water. In the existence of blood products and, last but not least, poor storage durability, the existence of polymer nanoparticles has eclipsed the presence of liposomes. Partly because of the many advantages that these systems offer in return for drugs, their appeal. These weapon systems could be immediately infused into the circulatory system due to the Nano size, hence reducing the risk of blocking blood vessels.

There are the following advantages of using nanoparticles as a drug delivery system:

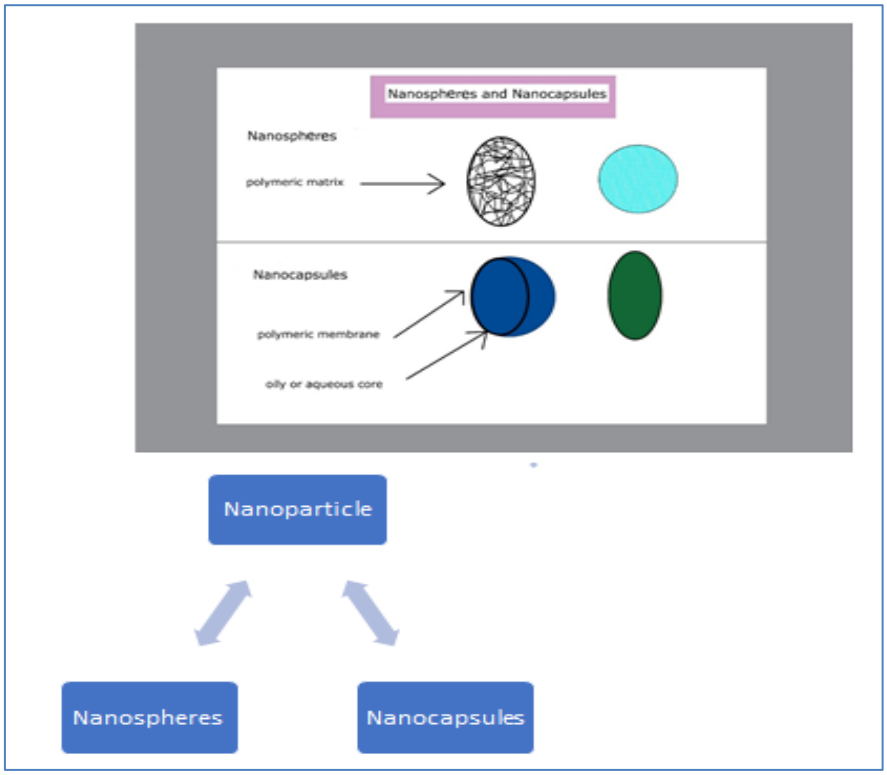
1. The particle size and surface properties of nanoparticles can be easily swayed following intravenous delivery to allow active and passive medication delivery.
2. Controlling and discharging the drug during transit at the site of location, while altering the organ

distribution of the drug and drug clearance, can result in clinical effects and decrease in shoulder.

3. A regulated releasing and particulate disintegration may be readily and cheaply modulated by using matrix components, by reducing chemical reaction while integrating pharmaceuticals in the system. In addition, drug loads usually plays an important function in maintaining gang activity on a greater side.
4. The targeting of the ligands on particle surfaces or employing magnetic guiding can achieve site-specific targets.
5. Medications can be administered in the body by numerous channels like orally, intranasal, injectable, ocular, etc. Both the volume surface area 3,4 and the surface energy ratio 5 will be increased. If the size of a material declines from bulk to nanoscale. This is because larger energies from nanoscales are freed because they do not remain in non-thermodynamic conditions when composed of bulk materials in comparison to a nanoscale item.

Temperatures in the usual room and pressure conditions. the nanomaterial phase should be metastable as such [7] Nanoparticles consist of three layers i.e.

a. The surface layer, which may be functionalized with a variety of small molecules, metal ions, surfactants, and polymers.
b. The shell layer, exhibiting dissimilarly from the core literally.
c. The core, forming is essentially the central portion of the Nanoparticle and usually refers to the Nanoparticle itself owing to such exceptional characteristics; these materials got the immense interest of researchers in multidisciplinary fields. Polymeric nanoparticles with a size in the nanometer range protect drugs against in vitro and in vivo degradation [8]. The use of a single thermodynamic descriptor as a proxy for reactants is an established strategy to estimate catalyst performance. In the instance of an ORR for example, the binding energy of an atomic oxygen on the metal surface can be a complex multistep reaction [9]. We examine three distinct nanoparticle morphologies to increased thrombin surface plasmon resonance SPR detection (nanocages, nanorods, and quasi-spherical nanoparticles). Besides the increase in nanoparticles, each kind employed here has at least one dimension at a distance of 40−50 nm,, Modifying the form also allows for the adjustment in a significantly greater range of sample lengths of localised surface plasmon features of the nanoparticle [10]. Polymer nanocomposites has recently received a lot of attention because of their potential to manufacture materials with novel mechanical, electrical and optical characteristics [11]. Certain techniques have been developed to measure the combination of micro and nanoparticles with cells.Rapid methods including Fluorescence Activation Cell Filtering, Depending on the process utilised for preparing nanoparticles, nanospheres or nanocapsules can be produced. Submicronic structures are nanoparticles that are usually but not always comprised of polymers (biodegradable or not). Nanospheres or nanocapsules can be formed according to the method employed for preparing the nanoparticles [12, 13] Contrary to nanospheres, that are outer body in which a drug is limited to an aqueous or oily cavity with only one lipid bilayer, nanocapsules are outer body in which a medicine is stored in a watery or oily cavity, and encircled by a single polymer membranes.). This allows the consideration of nanocapsules as a system "reservoir (Fig.1) [14]. Nanoparticles may be employed as a medication-supply system to target tumour cells or cells efficiently, while still safeguarding the medicine against premature inactivation when properly constructed in transport. The massive dissemination or convective action of both the iv administered nanoparticle build-up in tumour levels by the leaky hypermeable tumour vasculature is indeed due. Such substances could come in handy for drug administration via the membrane of this protein including such intestine epithelia, resistant to antibiotics cancers and the barriers of blood and brain [15]. Specific identification (active targeting) in ligand-decorated nanoparticles may also be activated. These devices may provide an extended exposure of the medicine at its site after it accumulates at its target. Aquatic solubility of various hydrophobic medications has been improved through solubilization in the hydrophilic head of nanoparticles with nanoparticles consisting of biocompatible materials [16].



Nanospheres

A medicine is scattered within a structure of the matrix. 2 categories of nano-particles are nanospheres with a homogeneous particles size, and nanocapsules with a conventional core-shelled structure. Nanospheres include microspheres with sizes of between 10 and 200 nanometres, which have new dimensional dependence compared to the large spheres of same substance. The medicine is absorbed, encased inside, or linked to the matrix of polymers. The medicine is disseminated throughout the polymer matrix system physically and consistently. Medications that may be amorphous can protect nanosphere against the degradation of [17-19] enzymes or chemical substances.

Benefits of Nanospheres drug delivery system

- Towards a small quantity in the nanosphere, even the tiniest capillary capillaries [20-21] can be readily passed.
- They can prevent phagocytes from being easily removed and they can remain in blood for a long time.
- Nanospheres can be easily transmitted to target organ potential as the heart, spleen, lung, backbone, and lymphatic system through cells and tissual hole.
- The substance emerges in sustained delivery.
- A location targeting permits binding the ligand to the surfaces of the spheres.
- A multitude of methods, such oral, nasal, injectable etc. could be used for these purposes.
- The toxicity decrease of both nanospheres also has a major benefit. Drawback of Nanospheres drug delivery system:
- Physical handling of Nanospheres in liquids and dry form is difficult.
- Nanospheres have a higher chance of particle aggregation due to their smaller size and larger surface area
- Because of the smaller size and larger surface area, drug loading and burst release are limited [23].

Nanocapsules

Drug-containing membrane wall structures with an oil core. Interfacial deposition of preformed polymers is the most common method of producing nanocapsules [24]. A solution of the medicine is developed in this technique, for example or without a lipophilic surfactant, in water-mixable organic liquid. To these solutions, a powder is applied that is soluble with both the solvent but miscibility in the combination and is disseminated throughout the aqueous phase often with a hydrophilic surfactant (often poloxamer). With modest motion, the solvents are diffused into the aqueous solution and the polymer adds around the oil droplet. Nanocapsules could also be produced by a version of solvent displacement techniques where oil is introduced to the organic phase [25]. Nanocapsules are akin to vesicular structures during which a medicine is housed in a hollow surrounding by a concrete object with a fluid internal nucleus. Based on the core & architecture of a surrounding polymer, two different modifications are available. The centre is often an oily

fluid, the polymer surrounding it is a polymer containing layer, and the vesicle is known to be a nanocapsule [26]. However, nano-vesicular systems can be classified as systems with a core spherical shell, which contain the medication in a reservoir or reservoir surrounding on a large level by a lipid bilayer or coating [27]. The active substance in the cavity may be liquid, solid or molecular in form [28]. Similarly, this reservoir may be lipophilic or hydrophobic depending on the technique of synthesis and the basic ingredients utilised. Nanocapsules may also transport the active ingredient on their surfaces or absorbed by a polymeric membrane [29], bearing in mind operational limits of the methods of preparation (Fig. 2b).

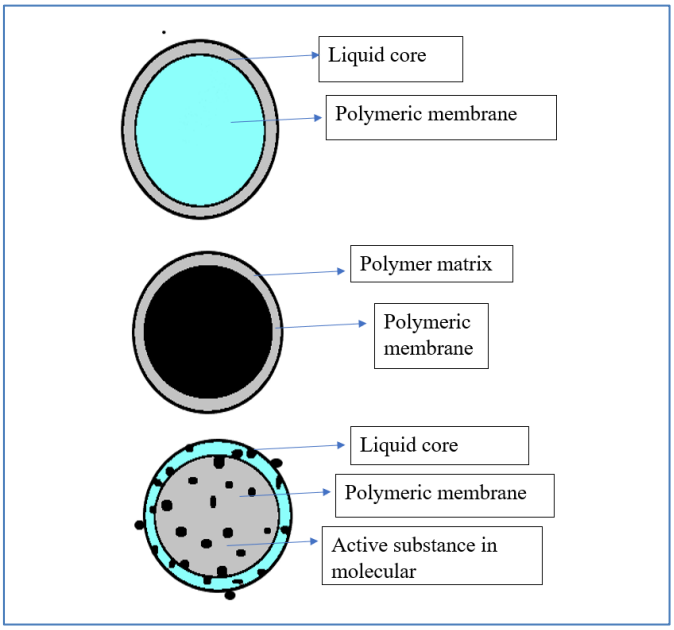
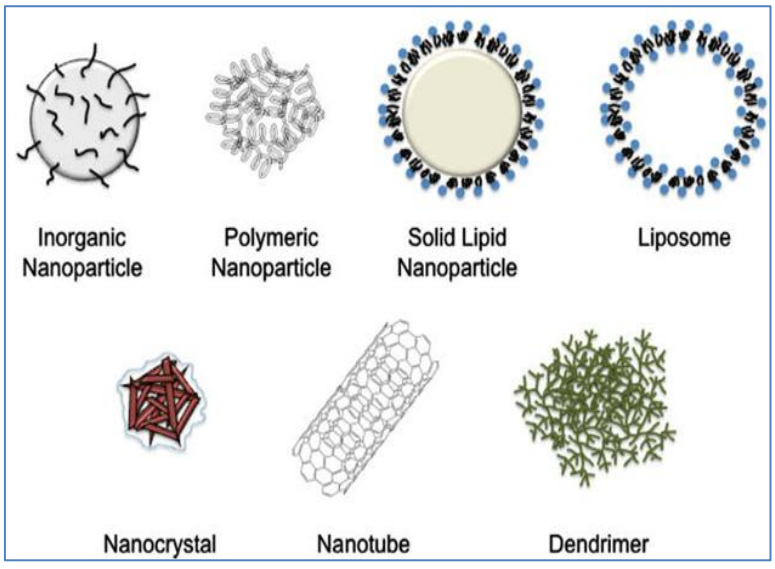


Fig-1: Different nanocapsular structures: (a) liquid core, (b) polymer matrix and (c) active substance in molecular dispersion

Types of Nanoparticles



Quantum Dot A blur reduction is a semiconductor nanostructure that contains electrons, valence band holes or free electrons in all different physical ways, such as conducting group couples and conductive band holes. Attributed to the prevalence of, or mixture, the semiconducting surface of, a semiconductor nanocrystal, the containment can be caused by electrostatic potentials (generate by external electrodes, doping, strain, impurities) because there is an interaction among different semiconductors (for instance, in the case of auto assembled quantum dots).

There is a discrete spectrum of amounts of a quantum point. A little quantum point is here. A blurring is an electron-conductor, valence ribbon holes or free electrons nanostructure in all physical ways, for instance conductivity of group pairs and conducting ribbon holes. Attributed to the prevalence of, or mixture, the semiconducting surface of, a semiconductor nanocrystal, the containment can be caused by electrostatic potentials (generate by external electrodes, doping, strain, impurities) because there is an interaction among different semiconductors (for instance, in the case of autoassembled quantum dots). The spectrum of quantities of a quantum dot is discrete.

There's a little quantum dot number (of the order of 1-100) of conduction band electrons, valence band holes, or excitons, i.e., an integer number of elementary electric charges. Tiny quantum dots could be of as small as two and 10 nanomets, equating to between 10 and 50 atoms in diameters, with a maximum of 100 to 100,000 inside the quantum dot volume such as colloidal semiconductor nanocrystals. Typically, personality quantum dots range from 10 to 50 nanometers.

Quantium points in semiconductor heterogeneic devices, which may have requirements. in addition, exceeding 100 nanometres, with lithographed patterning strategy which focuses or greffing of electron-dominated gases.

About three million Quantum dots with 10 nanometers in diameter might be placed in the human thumb's width to the end. In comparison with other nanostructures, quantum points could be compared to:

1) Quantum cables, confined in two spatial directions to electron or holes movement, provide the three-way free propagation.
2) Quantum wells, containing less in one axis electron motion, permit a free spread in two directions.

The shell fillings may be shown in quantiums with an almost inversion symmetry or with flat quantum points with near cylindrical symmetric, according the atome rules of the Hund. And sometimes those points are referred to as 'manufactured atoms. 'In controst to the atoms, by regulating geometry, form and strength of the confining potential, the spectral distribution of a solar cell may be designed.

Polymeric Nanoparticle

Speiser *et al*. created polymeric nanoparticles. As drug carriers for liposomes, they offer attractive possibilities. Normally, they have a lengthy shelf life and good barrier properties. Their adsorption and covering their surface with various chemicals are preferable than liposomes when targeted to particular organ or tissue. During polymerization of nanoparticles, like alkyl cyanoacrylates, it is possible to produce either premade polymers, including such polyesters (i.e. polylactic acid), or monomers. Most of the methods based on the polymerization of monomers consist of adding a monomer into the dispersed phase of an emulsion, an inverse microemulsion, or dissolved in a non-solvent of the polymer.

Solid Lipid Nanoparticle

As an alternate delivery mechanism to traditional polymeric nanoparticles, solid lipid nanoparticles have indeed been produced. SLNs are colloidal submicrons (50-1000nm) consisting of physiologic lipid, distributed into a surfactant, or watery in a solution. The benefits of polymer nanoparticles and fat emulsions and liposomes are combined in the SLNs, while avoiding certain downsides. Biodegradability, biocompatibility and non-toxicity.

Liposome

A liposome is a sphere vesicle containing a phospholipide bilayer wall used to transport into a cell medications or genetic information. Natural phospholipids having mix lipid chains (such as egg and sphingomyelin) or purified constituents, such as DOPE may be made of liposomes (dioleolylphosphatidylethanolamine).The lipid bilayer may merge with other bilayers (for example the plasma membrane) and thereby contain the liposome. If liposomes (which ordinarily would not diffuse through the membrane) are formed in a solution of DNA or medicines, they (indiscriminately) can be provided beyond the lipid bile-layer.

Nanocrystalline silico

The allotropic form of silicone is like semiconductor materials (a-Si), because of the amorphous phase of silicon nanocrystalline silicone (NC-Si). However, the difference is that in the amorphous phase NC-Si has minute grains of crystalline silicone. In contrast, polycrystalline (poly-Si) silicone is made up of crystalline silicon granules, which are separated by cereal bounds. No-Si is also sometimes referred to as silicone microcrystalline (µc-Si). The difference is based on the crystalline grain size alone. Many grain materials in the micrometre range are really polysilicon with fine grains; therefore nanocystalline silicon is a preferable name.

Photonic crystal

Photonical crystals consist of regular intervals insulator or nano-dielectro constructions, which, in accordance to the periodic potential in a semiconductor crystal, affect electron motion by trying to define permitted and strictly prohibited electronic energy levels, are designed to impact the electromagnetic radiation (EM).

The photonic physical structure has same length scale as half the wavelength of EM waves, which are ~300 nm in the case of photonic crystals in the visible part of the spectrum, because as underlying physical phenomenon is dependent on diffraction. This makes it complicated and complex to synthesise. To by-pass nanotechnology with their large and intricate process.

Effect of Characteristics of Nanoparticles on Drug Delivery

Particle size

The most important characteristics of nanoparticle systems are particle size and size distribution. They determine nanoparticle systems' in vivo distribution, biological fate, toxicity, and targeting ability. They may also affect drug loading, drug release, and nanoparticle stability. Many studies have shown that sub-micron nanoparticles have some benefits over microparticles about drug delivery [30]. Because of their small size and relative mobility, nanoparticles have a higher intracellular uptake than microparticles and are available to a wider range of biological targets. In a Caco-2 cell line [31**]**, Desai *et al*. found that 100 nm nanoparticles are 2.5 times greater than 1 m and 6 times greater than 10 m microparticles. Desai et colleagues discovered in a federal sample 31 that 100 nm of nanoparticles were 2.5 times more readily available and 6 times as high as 10 m of micropartments. In a federal test [32] Nanoparticles entered submucosal layers in a rat in situ intestinal using around whereas majority of the microparticles were all in the epithelial lining. Nanoparticles have also been observed to pass the blood-brain barrier whereas hyperosmotic mannitol opens up close connections.

Possibility for the provision of medicinal medicines for challenging conditions such as brain tumours for long periods of time [33]. The blood-brain barrier [34] was demonstrated to transport nanoparticles coated in Tween 80. Some cell lines efficiency only accept submicron nanoparticles, and not big microparticles [35]. The size of the particle affects the release of drugs. Since smaller particulate matter has a wider surface area, due to rapid release of drugs many medication materials are at or close to the surface. Heavier molecules have greater cores on both sides to encapsulate and gradually disseminate more medicines [36]. Smaller nanoparticles are more susceptible to aggregating over nanoparticles during stockage and transport. This is always a problem to formulate nanoparticles with the lowest dimension possible while maintaining optimum stability. The particle size can affect the breakdown of the polymer. In vitro, for example, the rate of degradation of PLGA polymers increased with an increase in particle diameter.

In former years PLGA breakdown products created in tiny particles could rapidly spread from the particulate, while larger particle degradation more likely remained inside the polymer matrix for a longer period leading to autocatalytic material deterioration [37]. This is supposed to accelerate the decomposition or release of polymers from bigger particles. Panyam *et al*., on the other hand, synthesised PLGA particles in different diameters and observed no material differences in the polymer degradation rates in vitro.

The simplest and most frequent approach to determine size of the particles is photon correlation spectroscopic and dynamical dispersion of light [38].

Rayleigh movement and optical dispersion characteristics determine the particle diameter in the spectroscopy of light correlation, including information of particulate carrier [39].

The results of the photon correlation spectroscopy are frequently checked by scanning or transmission of electron microscopy (SEM or TEM).Nanoparticles surface properties: As nanoparticles are delivered intravenously, the immune systems of the body are recognisable rapidly and are removed from circulation by phagocytes [40]. A hydrophobic part of nanoparticles, that is really independant of size, refers to the amount of the adsorption blood stuff, mostly proteins (opsonins). In turn, this determines the in vivo destiny of nanoparticles.

The channels for customer or link between nanoparticle and phagocyte of these opsonins with the particle surface [41, 42]. The biodistribution profile is improved when a medicine is attached to a typical carrier because it is usually supplied to the mononuclear phagocyte system. MPS affects the liver, spleen, lungs and bone marrow for just few reasons. [43] Interstitial fluid once they enter. IgG, complements to C3 components, often recognises foreign compounds, especially external macromollecules. In order to maximise the possibility of success with a nanoparticle drug targeting [44], it is necessary to reduce phagocytosis and extend nanoparticles circulating in vivo. It can be performed by (a) coating hydrophilic nanoparticles / substrates; (b) producing nanoparticles with detachable hydrophilic sections such as propylene glycol, Polyethylene Oxide, Polymers, Poloxamine and Polysorbate 80. 80 nanoparticles with biodeterminable segments. (Exchange of 80) [45]. It mirrors the potential difference of particles and is affected by both the structure of the particle and the medium it is distributed into. Nanoparticles of greater than or equal zeta potential of 30 mV are durable in suspension as the surfaces load does not permit the combination of particles. It is possible to use the zeta potentials to see if

an active substance charged on a nanocapsula surface is encapsulated or adsorbed [46].

Applications of Nanoparticulate Delivery Systems

Nanoparticle delivery methods for the targeting of tumours. It is acceptable to use nanoparticles to treat the tumour.

1) The concentrate dose of medication in nearby tumour target may be delivered by Nanoparticles due to higher permeability and/or active retention of the ligands at the surface of the particle;
2) Nanoparticles limit the distribution of drugs to the target organ and reduce the exposure of drugs to healthy tissues.

In Verdun *et al*., mice were observed to have greater concentrated doxorubicin in the liver, splesen and lungs of poly(isohexylcyanoacrylate) nanosphere than that of the free-doxorubicin mouse [47]. All nanoparts have a substantial impact on drug spatial distribution in vivo, as per studies, in polymeric material such as kind, surface charge and the polymer's biodegradation profile; the related molecular structure of the drug, nano location, and embodiment technique. The precise mechanism is unknown although biodiversity is rapidly distributed within 1/2 to 3 hours, and MPS and the endocytosis/phagocytoses procedure are expected to take part [48].

Bibby *et al*. [49] have recently described the blood distribution and pharmacokinetics of cyclic formulations RGD-doxorubicin-nanoparticle in tumor-bearing mice. The concentrations of drugs in heart, lungs, kidneys and plasma decline over time, but in their biodistribution studies the concentration of pharmaceutics in the liver, spleen and cancer is growing. The bulk of administered dose was found in the liver (56 percent) and in cancer only 1.6 percent 48 hours after eating, which shows a significant trend to collect nanoparticles. It shows that preventing the liver and spleen mononuclear phagocytosis system from absorbing particles is most difficult component of the use [50].

The capacity to provide therapeutic agents for these cells from the endocytosis/phagocytosis propensity of nanoparticles is one instance. Biodiversity can be useful in the treatment of clustered malignancies such hepatic carcinomas, hepato-cell carcinoma, hepatic or gynécological cancers, bronchopulmonary tumours, primordial and cell growth tumours, small cell cancers, myeloma and leuchemia, for MPS-rich organ/tissue treatment. A mouse hepatic metastasis model was demonstrated to be effective with the usage of standard doxorubicin-laden nanoparticles. The amount of metastasis was observed to have decreased further when the free medication was used. kupffer cells The histológica examination [51] could not clearly identify nanoparticles and nanoparticles in malignant cells. After a significant absorption of phagocytosis, kupffer cells were able to trigger doxorubicin release, leading to the gradient of the concentration of drugs favouring prolonged dissemination of the free and still active drug into nearby metastasic cells. [52] When utilised in chemotherapy as carriers of conventional nanopartics, certain cytotoxic effect is expected for Kupffer cells, which increases cell deficiency in Kupffer and hence reduces liver absorption and therapeutic effect at administration intervals of less than two weeks.

In addition, typical nanoparticles can reach the MPS, which is a critical yet undesirable site with most anticancer medicines because the immunosuppressive effect may be increased by chemotherapy from such carriers [53]. Therefore, traditional nanoparticles' potential to increase the effectiveness of anticancer medication is restricted to targeting cancer cells in MPS-rich organ levels. Moreover, it is unable to send anti-cancer-polluted nanoparticles to other locations if nanoparticles are efficiently cleansed following intravenous delivery.

Long circulating nanoparticles

Nanoparticles must be able to target cancers outside of MPS-rich organs, in addition, to be successful as a drug delivery system. In the last decade, a lot of effort has gone towards developing so-called "stealth" particles or PEGylated nanoparticles that are invisible to macrophages or phagocytes [54].

Reversion of multidrug resistance in tumor cells

Anticancer medications can work against one range of possible types of cancer since cancer cells can build their resilience, even while they're in the interstitial tumour. Elements of strength According to these methods, chemotherapy are avoided by cancers. Multidrug resistance is one of the biggest issues in chemotherapy (MDR). MDR is primarily the result of insufficient membrane lipid p-glycoprotein that can extrude a range of xenobiotics, including several anti-cancer medications, from hepatocytes [55].

A number of techniques have already been used, using polymeric nanoparticles, to increase the susceptibility of cancer cells to medicines, by overcoming MDR mediated by Pgp. It is based on Pgp's recognition that the medications are likely to be released from the cancer cells as a reason to mix medication with colloid transporters such as nanoparticles to prevent antibiotic resistance. Only if the medication is retained in the cell membrane, not until endocytosis in the cytoplasm or organelle [56].

Nanoparticles for oral delivery of peptides and proteins

A huge number of phytochemicals and immunizations, primarily on protein molecules, were found as a result of tremendous progress in biotech and biochemistry. Gastrointestinal cells are present also because bioavailability and susceptibility to GI breakdown is regulated by epithelial barriers to the digestive system [57]. Encapsulated bioactive modules protect them against enzyme and hydrolyte breakdown in polymeric nanoparticles. Insulin-laden nanoparticles were identified to conserve the activity of glucose and decreased blood glucose in treated patients for up to 14 days after oral injection [58-60].

Nanoparticles for gene delivery

Polynucleotide immunizations are used in transportation to host cells by means of the respective enzyme genes that produce antigenic peptide in the proximity of professional antigenic cells, causing an immune reaction [61]. Since intracellular protein synthesis is generated through humoral and tumour immunization rather than extrinsic accumulation, both neuronal and humoral immunity is produced by such vaccines [62].

Nanoparticles for drug delivery into the brain

The blood-brain barrier is by far the most important obstacle restricting the creation of effective treatment for the central nervous system .The relatively impermeable BBB consists of close connected endothelial cells, the participation of enzymes and processes of active efflux transport.In the main, it inhibits water-soluble molecules from entering the circulation of the Brains and decrease the size of water-soluble particles in the CNS. Enzymes or efflux govern the lipophilic compounds in the brain [63].

CONCLUSIONS

Because of its various advantages such as longer circulation, the passive targeting and the better solubilization of hydrophobic products, nanoparticulate drug delivery made of copolymer amphipylic blocks have been carefully examine. Micelles, nanosphers, nanocapsules and polymersoms are only few of the systems discovered, all of which has a unique set of physical and physical features. The composition, molecular geometry and proportional block lengths of component copolymers and platform comes also influence the morphology of these distinct particles.Studies have demonstrated that even small differences in these variables can lead to considerable differences in the overall and morphological characteristics of the final deliverable

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