REVIEW ARTICLE

ISSN:2394-2371
CODEN (USA):IJPTIL

Nano carriers as a promising agent for drug delivery system: A review report

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ABSTRACT

The use of Nano carriers as drug delivery systems for chemotherapeutic agents can improve the overall pharmacological properties of commonly used drugs in chemotherapy. The clinical success, as well as the ease with which surface modifications can be made to both liposomes and micelles to accommodate targeting ligands have made these Nano carriers in particular attractive candidates for future work involving targeted drug delivery. Although not targeted, there are clinically approved liposomal-based drugs that are currently used to treat various types of cancers. Furthermore, there are several other formulations involving both of these Nano carriers which are now in various stages of clinical trials. This review discusses the use of liposomes and micelles in cancer therapy and attempts to provide some current information regarding the clinical status of several of these Nano carrier-based drugs. In addition, recent work involving the incorporation of targeting ligands to systems such as these in order to improve colocalization between the drug and cancer cells is also addressed. Furthermore, while the use of these Nano carriers in particular is the primary focus here, this review also contains a discussion on other commonly used Nano carriers in cancer therapy to include various polymer-based and polymer-protein conjugates. Finally, the possibility of using combinatorial approaches involving multiple surface modifications made to both liposomes and micelle

Keywords: - Nanocarriers; Liposomes; Micelles; Drug delivery; Chemotherapy; Nanoparticles; Targeted drug delivery systems.

INTRODUCTION

Cancer treatment involving chemotherapy is typically accompanied by toxic side effects, thereby limiting the amount of the drug that can be given to a patient. As a result, all of the tumor tissue may not be exposed to a lethal dose of the drug. The use of nanocarriers such as liposomes and micelles can improve the pharmacological properties of traditional chemotherapeutics. Their small size (~100nm or less) allows them to readily extravagate from circulation through vascular defects typically present at tumour sites due to on going

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Article Received on: 08-06-2016
Published on: 30-07-2016

angiogenesis where they can then deliver encapsulated cytotoxic agents to tumour tissue. Liposomes and micelles in cancer therapy seems promising, obstacles associated with drug transfer from these nanocarriers to tumor cells within the tumor site remain particularly challenging**.** Fig.1. shows different types of nanocarriers.

CLASSIFICATION OF NANO CARRIERS FOR DRUG DELIVERY

1. Liposome:

Liposomes have been the first to be investigated as drug carriers. They are nano/micro-particular or colloidal carriers, usually with 80–300 nm size range. They are spherical vesicles composed of phospholipids and steroids (e.g., cholesterol), bilayers, or other surfactants and form spontaneously when certain lipids are dispersed in aqueous media where liposomes can be prepared, e.g., by sonication . Liposomes have been reported to increase the solubility of drugs and improve their pharmacokinetic properties, such as the therapeutic index of chemotherapeutic agents, rapid metabolism, reduction of harmful side effects and increase of in vitro and in vivo anticancer activity. A drug is incorporated in liposomes by the encapsulation process. The release of a drug from liposomes depends on the liposome composition, pH, osmotic gradient, and the surrounding environment. Additionally, a prolonged residence time increases the duration of action of such particles, but decreases their number. Interactions of liposomes with cells can be realized by: adsorption, fusion, endocytosis, and lipid transfer. There are a lot of drug examples in liposomal formulations, such as showed anticancer drugs, neurotransmitters (serotonin) antibiotics anti-inflammatory and ant rheumatic drugs. Recent studies have reported the clinical outcomes and side effects of photodynamic therapy (PDT) by means of intense pulsed light (IPL) and spray (liposome encapsulated 0.5% 5-aminolevulinic acid) which was used for the treatment of inflammatory facial acne. Turkovaet compared the efficacy and safety of deoxycholate and lipid (liposomal) amphotericin B formulations (AMBF) in the treatment of invasive fungal disease (IFD) in neonates. The authors of the study have reported that deoxycholate amphotericin B is cheap and effective in treating neonatal IFD. The therapy appears to be safe for use as a first-line therapy if the underlying risk for nephrotoxicity is low. Safdar and co-workers conducted a meta-analysis in order to evaluate nephrotoxicity associated with amphotericin B lipid complex (ABLC) and liposomal amphotericin B (L-AmB). The multifunctional liposomes,

containing the specific proteins, antigens, or other biological substances, can be used to design drugs which act selectively on a particular tissue. It is a promising approach for targeted delivery of therapeutics. Biswas et al.presented hydrazine-functionalized poly(ethylene glycol)-phosphatidylethanolamine (PEG-PE)based amphiphilic polymer which can conjugate a variety of ligands. The researchers investigated the reversible model ligands monoclonal antinucleosome antibody 2C5 and antimyosin antibody 2G4, as well as glycoproteins concanavalin A (Con-A).

The versible attachment of homing devices is useful especially in modified liposomal systems, where after they successfully perform the function of targeting at the specific site. Ligands, such as antibodies, are cleaved off in response to an environmental stimulus, e.g., pH. In addition, cationic liposomes (CLs) can be used as a gene delivery carrier. They are better than natural or anionic liposomes for gene transfer. Kim and co-workers studied modified cationic liposomes either by polyethylene glycol (PEG)-grafting or PEG-adding methods as transfection complexes of plasmid DNA. In a recent study, Biswasetal. have examined polyethylene glycol-phosphatidyl ethanolamine (PEG-PE) conjugate with the TPP group as drug carriers. They used paclitaxel (PTX) as a model drug and studied them for their toxicity, mitochondrial targeting, and efficacy in delivering. As a result, they suggested that TPPPEG-PE can be used as non-toxic, mitochondria targeted drug delivery systems.

SLN (solid lipid nanoparticles), NLC (nanostructured lipid carriers) and LDC (lipid drug conjugates) are types of carrier systems based on solid lipid matrix,

i.e., lipids solid at the body temperature. They have been exploited for the dermal, peroral, parenteral, ocular, plumonary, and rectal delivery. SLN are particles made of solid lipids, e.g., highly purified triglycerides, complex glyceride mixtures or waxes stabilized by various surfactants Three types of NLC have been introduced: imperfect type NLC (general imperfections in the matrix nanostructure form free spaces for the accommodation of the guest molecules), multiple type NLC (drugs are solved in oils and protected from degradation by the surrounding solid lipid) and amorphous type NLC (the crystallization that causes drug expulsion is avoided) exploited for dermal applications. LDC were developed in order to expand applicability of lipid based carriers to lipophobic drug molecules. These insoluble drug-lipid conjugates can be prepared by salt formation or by covalent linking followed by homogenization.

2. Polymeric nanoparticles

Polymeric nanoparticles (PNPs) are structures with a diameter ranging from 10 to 100 nm. The PNPs are obtained from synthetic polymers, such as polye-caprolactone , polyacrylamide and polyacrylate, or natural polymers, e.g., albumin , DNA chitosan [gelatin. Based on in vivo behavior, PNPs may be classified as biodegradable, i.e., poly(L-lactide) (PLA), polyglycolide (PGA) , and non-biodegradable, e.g., polyurethane .

PNPs are usually coated with nonionic surfactants in order to reduce immunological interactions (e.g., opsonisation or presentation PNPs to CD8 T-lymphocytes) as well as intermolecular interactions between the surface chemical groups of PNPs (e.g., van der Waals forces, hydrophobic interaction or hydrogen bonding) .Delivery of 5-fluorouracil to cancer cells. The hypothesized mechanism of 5-FU controlled release from this polymeric nanocarrier is swelling followed by conformational changes during a LCST able thermo-responsive chitosan-g-poly(N-vinylcaprolactam)-biopolymer used for the (lower critical solution temperature) transition. The high toxicity to cancer cells, comparatively lower to the normal ones, was observed. The application of biodegradable nanosystems for thedevelopment of nanomedicines is one of the most successful ideas. Nanocarriers composed of biodegradable polymers undergo hydrolysis in the body, producing biodegradable metabolite monomers, such as lactic acid and glycolic acid. Kumarietal. reported a minimal systemic toxicity associated with using of PLGA for drug delivery or biomaterial applications. Such nanoparticles are biocompatible with tissue and cells . Drug-biodegradable polymeric nanocarrier conjugates used for drug delivery are stable in blood, non-toxic, and non-thrombogenic. They are also non-immunogenic as well as non-proinflammatory, andthey neither activate neutrophils nor affect reticuloendothelialsystem.

3. Dendrimer nanocarriers

Dendrites are unique polymers with well-defined size and structure. Dendritic architecture is one of the most popular structures observed throughout all biological systems. Some of the examples of nanometric molecules possessing dendritic structure include: glycogen, amylopectin, and proteoglycans. In the structure of dendrimer, in contrast to the linear polymer, the following elements can be distinguished: a core, dendrons, and surface active groups.

Dendrites cytotoxicity depends on the core material and is strongly influenced by the nature of the dendrimers surface. For example, changing the surface amine groups into

hydroxyl ones may result in lower levels of cytotoxicity. The term polyvalence defines the number of active groups on a dendrimer surface. They observed no effect on other hematological (excluding red blood cells, hematocrit value and hemoglobin) and biochemical parameters (excluding the decrease of glucose levels in the high-NH2 dose) as well as on feed intake, body and organ weights. In addition, the histopathology showed a toxic effect on liver and kidneys. PEGylation of dendritic systems is a way of lowering general toxicity.

A modification of the synthesis conditions, such as the ratio of reagents, temperature, concentration of the catalyst, and pressure of drying, allows to alter properties of xerogels used in controlled drug release. Phenytoin , doxorubicin, cisplatin, metronidazole , nifedipine, diclofenac , and heparin are examples of drugs which have been loaded into xerogels using this technique. The MSNs, in comparison with xerogels, possess more homogenous structure, lower polydispersity and higher surface area for adsorption of therapeutic or diagnostic agents. The mechanism of drug loading into mesoporous silica material is a chemical or physical adsorption. By these processes, diverse types of drugs, including anticancer drugs , antibiotics, and heart disease drugs , have been embedded into MNSs.

However, recent studies have revealed in vitro and in vivo toxicity and certain hazards of using nanosilica. Most of the in vitro studies of silica nanoparticles show the adverse effect in investigated cells. The formation of nucleoplasmic aggregates impairs suchand excretionnuclear functions as inhibiting replication and transcription. Yang and coworkers implied that perturbation of intracellular free calcium homeostasis may be responsible for cytotoxic effect of silica nanoparticles.

4. Carbon nanocarriers

Carbon nanocarriers used in DDS are differentiated into nanotubes (CNTs) and nanohorns (CNH). CNTs are characterized by unique architecture formed by rolling of single (SWNCTs single walled carbon nanotubes) or multi (MWCNTs – multi walled carbon nanotubes) layers of graphite with an enormous surface area and an excellent electronic and thermal conductivity. Biocompatibility of nanotubes may be improved by chemical modification of their surface[11] . Such adjustment can be implemented by covalent anchoring of PAMAM dendrimers, amphiphilicdiblock copolymers.

Drug release from carbon nanotubes can be electrically or chemically controlled. To

prevent the unwanted release of the drug, the open ends of CNTs were sealed with polypyrrole (PPy) films. Homing devices, i.e., folic acid and epidermal growth factor , were attached to improve selectivity of such drug delivery systems. Nanohorns – a typeof the only single-wall nanotubes – exhibit similar properties to nanotubes. Their formation process does not require a metal catalyst, thus, they can be easily prepared with very low cost and are of high purity . The immobilization of drugs may rely on adsorption on nanohorns walls or nanoprecipitation of drugs with nanohorns.

A comparison of these two paths of cisplatin incorporation into nanohorns showed that nanoprecipitation is much more effective (almost 3-fold increase in the number of molecules entrapped in nanohorns) than adsorption[6]. The toxicity of carbonnanomaterials also depends on their unique well-defined geometric structure . The toxic potential of carbon nanotubes can result from the high length to diameter ratio and the toxicity of the sole material, which is graphite. In addition, some impurities, such as residual metal and amorphous carbon, contribute to the level increase of reactive oxygen species (ROS), thus, inducing the oxidative stress in cells. Recent studies have pointed out the similarity in carcinogenic potential between CNT and asbestos. Carbon nanotubes have been shown to cause necrosis or apoptosis of macrophage cell lines and changes in cellmorphology. Radomski et al. studied the effects of engineered carbon nanoparticles (MWCNT and SWCNT) on human platelet aggregation in vitro and rat vascular thrombosis in vivo. Incubation of platelets with carbon nanomaterials caused platelet aggregation with little or no granular release [13].

MWNTs multi walled nanotubes; f-CNTs functionalized carbon nanotubes; SWNTs-PL-PEG-NH2 amine-functionalized single-walled carbon nanotubes.

Unmodified MWCNT caused pro-inflammatory response in keratinocytes cell lines, e.g., release of cytokine interleukin 8 and formation of cytoplasmic vacuoles.

5. Magnetic nanoparticles

Magnetic nanoparticles exhibit a wide variety of attributes, which make them highly promising carriers for drug delivery. In particular, these are: easy handling with the aid of an external magnetic field, the possibility of using passive and active drug delivery strategies, the ability of visualization (MNPs are used in MRI), and enhanced uptake by the target tissue resulting in effective treatment at the therapeutically optimal doses [10]. However, in most of the cases where magnetic Nano carriers have been used, difficulties in

achieving these objectives appeared[8]. It is most likely associated with inappropriate features of magnetic nanoparticles or inadequate magnet system. Magnetic nanoparticles, for instance, tend to aggregate into larger clusters loosing the specific properties connected with their small dimensions and making physical handling difficult. In turn, magnetic force may not be strong enough to overcome the force of blood flow and to accumulate magnetic drugs only at target site.

Depending on magnetic properties, MNPs can be divided into pure metals (such as cobalt, nickel, manganese, and iron, their alloys and oxides. However, narrowing theMNPs applications only to biomedicine reduces significantly the choice of magnetic material. Such a restriction results from the lack of knowledge of the negative effects which the majority of these nanomaterial's have on the human body. Iron oxide nanoparticles, due to the favourable features they exhibit, are the only type of MNPs approved for clinical use by Food and Drug Administration. In addition, iron oxides – magnetite and maghemite occur naturally in human heart, spleen and liver [6], which indicates their biocompatibility and non-toxicity at a physiological concentration. It is essential to estimate a safe upper limit of MNPs for biomedical use.

Connecting a drug with MNP may be achieved by covalent binding [6], electrostatic interactions, adsorption, or encapsulation process . Targeting of drug-MNPs conjugates to diseased tissues (magnetic targeted drug delivery systems – MTDDS), depending on their size and surface chemistry, can be carried out by passive or active mechanism. Passive targeting is a result of enhanced vascular permeability and retention (EPR) of tumor tissues. Active strategy relies on the attraction of nanoparticle to the affected site by using recognition ligands (e.g., antibodies) attached to the surface of MNPs and by handling of an external magnetic field. Therapeutic activity of diverse drugs incorporated into iron oxide Nano carriers have been tested and reported. Concomitant use of magnetic resonance or magneto fluorescent imaging and targeted therapy (via conjugation of targeting moieties) can enhance effectiveness of cancer therapy [4].Magnetic nanoparticles can be quickly opsonized by plasma proteins, recognized and subsequently removed from the bloodstream by macrophages of the reticuloendothelialsystem. The greatest overall uptake of nanoparticles can be observed in liver and spleen[5]. Investigations concerning the deformation of cells upon their exposure to nanoparticles have revealed that the toxicity of MNPs (at the same molarity) increase.

APPLICATIONS OF MEDICAL NANOCARRIERS

Short segments of DNA can be used for detection of genetic sequence in a sample. With the help of nanotechnology, damaged tissue can be reproduced or repaired. These so called artificially stimulated cells are usedEven today various disease like diabetes, cancer, Parkinson's disease, Alzheimer's disease, cardiovascular diseases and multiple sclerosis as well as different kinds of serious inflammatory or infectious diseases (e.g. HIV) constitute a high number of serious and complex illnesses which are posing a major problem for the mankind. Nanomedicine is an application of nanotechnology which works in the field of health and medicine. Nano-medicine makes use of nano materials, and nano electronic biosensors. In the future, nano medicine will benefit molecular nanotechnology [11]. The medical area of nano science application has many projected benefits and is potentially valuable for all human races. With the help of nano medicine early detection and prevention, improved diagnosis, proper treatment and follow-up of diseases is possible. Nano particles were found useful in delivering the myelin antigens, which induce immune tolerance in a mouse model with relapsing multiple sclerosis. In this technique, biodegradable polystyrene micro particles coated with the myelin sheath peptides will reset the mouse's immune system and thus prevent the recurrence of disease and reduce the symptoms as the protective myelin sheath forms coating on the nerve fibers of the central nervous system [26]. This method of treatment can potentially be used in treatment of various other autoimmune diseases.

1. Application in cancer: Due to the small size of nano particles can be of great use in oncology, particularly in imaging. Nano particles, such as quantum dots, with quantum confinement properties, such as size-tunable light emission, can be used in conjunction with magnetic resonance imaging, to produce exceptional images of tumorsites[23]. As compared to organic dyes, nano particles are much brighter and need one light source for excitation. Thus the use of fluorescent quantum dots could produce a higher contrast image and at a lower cost than organic dyes used as contrast media. But quantum dots are usually made of quite toxic elements.

Nano particles have a special property of high surface area to volume ratio, which allows various functional groups to get attached to a nano particle and thus bind to certain tumorcells[28]. Furthermore, the 10 to 100 nm small size of nanoparticles, allows them to preferentially accumulate at tumor sites as tumors lack an effective lymphatic drainage

system. Multifunctional nano particles can be manufactured that would detect, image, and then treat a tumor in future cancer treatment [27]. Kanzius RF therapy attaches microscopic nano particles to cancer cells and then "cooks" tumors inside the body with radio waves that heat only the nanoparticles and the adjacent (cancerous) cells.

2. Applications in Ophthalmology:

The aim of nano medicine is the to monitor, control, construct, repair, defense, and improve human biological systems at the molecular level, with the help of nano devices and nanostructures that operate massively in parallel at the unit cell level, in order to achieve medical benefit. Principles of nanotechnology are applied to nano medicine such as bio mimicry and pseudo intelligence. Some applications of nanotechnology to ophthalmology are include treatment of oxidative stress; measurement of intraocular pressure; theragnostics; use of nano particles for treatment of choroidal new vessels, to prevent scars after glaucoma surgery, and for treatment of retinal degenerative disease using gene therapy; prosthetics; and regenerative nanomedicine[25]. The current therapeutic challenges in drug delivery, postoperative scarring will be revolutionized with the help of nanotechnology and will help in various unsolved problems such as sight-restoring therapy for patients with retinal degenerative disease [29]. Treatments for ophthalmic diseases are expected from this emerging field. A novel nanoscaledispersed eye ointment (NDEO) for the treatment of severe evaporative dry eye has been successfully developed [36]. The excipients used as semisolid lipids were petrolatum and lanolin, as used in conventional eye ointment, which were coupled with medium-chain triglycerides (MCT) as a liquid lipid; both phases were then dispersed in polyvinyl pyrrolidone solution to form nanodispersion. A transmission electron micrograph showed that the ointment matrix was entrapped in the nano emulsion of MCT[26], with a mean particle size of about 100 nm. The optimized formulation of NDEO was stabledelivery andwhen stored for six months at 4°C, and demonstrated no cytotoxicity to human corneal epithelial cells when compared with commercial polymer-based artificial tears (Tears Natural® Forte). The therapeutic effects of NDEO were evaluated and demonstrated therapeutic improvement, displaying a trend of positive correlation with higher concentrations of ointment matrix in the NDEO formulations compared to a marketed product. Histological evaluation demonstrated that the NDEO restored the normal corneal and conjunctival morphology and is safe for ophthalmic

application. Recent research [30] shows applications of various nanoparticulate systems like microemulsions, nanosuspensions, nanoparticles, liposomes, niosomes, dendrimers and cyclodextrins in the field of ocular drug delivery and also depicts how the various upcoming of nanotechnology like nanodiagnostics, nano imaging and nanomedicine can be utilized to explore the frontiers of ocular drug therapy.

3. Application of Nanotechnology in Modified Medicated Textiles

Using nanotechnology newer antibacterial cotton has been developed and used for antibacterial textiles [21]. Developmental works using nanotechnology, new modified antibacterial textiles have been developed. Application of conventional antimicrobial agents to textiles has been already reported. This technique has been advanced by and application of these materials to the textiles.[16]

4. Application of nanocarriers for the delivery of active ingredients and fractions

Applications of nano carriers via different administration routes are summarized in. Many nanocarriers were designed to orally administer drugs by altering the physicochemical properties of the drug,such as poor water solubility and stability [13], and overcoming the various barriers that hinder drug absorption, such as drug efflux [16] and low permeability through mucus membrane[16]. In case of parenteral administration, most of the investigations were focused on utilizing nanocarriers to enhance antitumor efficiency through passive targeting or active targeting [4,6,1], controlling drug release at the tumor site [7,16,18], or overcoming multidrug resistance [5]. In recent years ,topical drug delivery by nano carriers has also drawn great attention owing to its advantages over other administration routes and outstanding contribution in improving local action [16,18] or systemic absorption[13]. For example, Zhang et al. designed solid lipid nanoparticles(SLN) to achieve topical delivery of aconitine, an active ingredient extractedfrom *Aconitum carmichaelii Debeaux*[20]. This nanocarrier showed high transdermal permeability and desirable accumulation in epidermis. In addition, compared with tinctures, aconitine-loaded SLN. The enhanced anti-inflammatory and analgesic effects.In the past decade, nanocarriers have been mainly designed to deliver active ingredients and fractions that are regarded as important ingredients for therapeutic effects, and for which the absorption and metabolism mechanisms were clearly illustrated. Several attempts have also been made to formulate TCM formulas; however, their encapsulation

and drug release, as well as their in vivo pharmacological effects, are not satisfactory. The use of nanocarriers to deliver multicomponent systems of fractions and TCM formulas based on an understanding of the mechanisms underlying TCM needs further investigate onto improve therapeutic effects and decrease toxicity and side effect.

TOXICITY EVALUATION OF NANO CARRIERS FOR THE ORAL DELIVERY OF MACROMOLECULAR DRUGS

Oral administration is the most commonly use and accepted route for drug administration .However , two of the main concerns are the poor intestinal epithelium permeability and rapid degradation, which limit absorption of drug in this context , Nano carriers have shown great potential for oral drug delivery. The different physicochemical parameters influencing their properties and show their potential toxic effect. This review describes first some aspects related to behaviour of Nano system within the gastrointestinal tract and then some aspects of Nano toxicology .Oral drug delivery constitutes a great challenge. First, the lumen is a highly photolytic environment due to its different pH conditions and the presence of digestive enzymes (e.g. pepsin, try sin and hemotropism)[13]. Second, the intestinal epithelium, which is covered by the mucus layer, is permeable only to small molecules, which hinders the bioavailability of the large majority of biologically active macromolecules [14]. Nano particle-based systems have many advantageous features for oral drug delivery. Thus, once administered orally, NPs diffuse into the harsh environment, first to the acidic medium of the stomach and then to the intestinal milieu, protecting the cargo [13,15]. Nano particle-based systems have many advantageous features for oral drug delivery. Thus, once administered orally, NPs diffuse into the harsh environment, first to the acidic medium of the stomachand then to the intestinal milieu, protecting the cargo .

Nanotoxicology

Nanotechnology is one of the most innovative areas of research, which can find application in almost all essential aspects of our life.Thus, the development of new nanomaterials is growing dramatically and many products based on nanotechnology are already onthe market. However, the successes of nanotechnology have notbeen associated with a parallel development of adequate methodsto assess and manage the potential risks for humans. In this regard,it has been pointed out that ‘‘a new technology will only be successfulif those promoting it can show that it is safe, but historyis littered with examples of promising technologies that never fulfilledthe true potential and/or caused untold damage because

early warnings were ignored" [31].In the last decades, it has been widely demonstrated that through the application of nanotechnology in health care it is possible to improve conventional medical therapiesand diagnosis for many pathological conditions. However, the same properties determining their efficacy in the host (targeting and controlled release properties) and making NPs so attractivein medicine, may contribute to toxicological issues. Hence, to usethe full potential of NPs in nanomedicine, particular attention must be paid to safety and toxicological issue [32].

CONCLUSION AND DISCUSION

Material design, there is an opportunity to develop nanocarrier systems for target-specific drug and gene delivery that will respond to the local stimuli. Nanotechnology has moved into our present life with smart materials, nano scale bios tructure and drug delivery. Innovations in nanotechnology have already shown large medical applications. As With greater understanding of physiological differences between normal and disease tissues and advances in the field of drug delivery continues to move forward, it will be increasingly important to design drug nanocarriers with tailorable properties for efficient drug delivery and improved therapeutic efficacy. Surface engineering will continue to be key design parameters of drug nanocarriers. Bioinspired zwitterions, including phosphorylcholine (PC), carboxybetaine (CB) and sulfobetaine (SB), are very promising to play a role in the development of nanomedicine.

FUTURE PROSPECTS

Nanotechnology is one of the most innovative areas of research, which can find application in almost all essential aspects of our life. Thus, the development of new nonmaterial's is growing dramatically and many products based on nanotechnology are already on the market[22]. However, the successes of nanotechnology have not been associated with a parallel development of adequate methods to assess and manage the potential risks for humans. In this regard, it has been pointed out that ''a new technology will only be successful if those promoting it can show that it is safe, but history is littered with examples of promising technologies that never fulfilled the true potential and/or caused untold damage because early warnings were ignored" [12]. Applications of nanotechnology for treatment, diagnosis, monitoring, and control of biological systems has recently been referred to as "nanomedicine" by the National Institutes of Health. Research into the rational delivery and targeting of pharmaceutical, therapeutic, and diagnostic agents is at the forefront of projects in nanomedicine. These involve the identification of precise targets (cells and

receptors) related to specific clinical conditions and choice of the appropriate nanocarriers to achieve the required responses while minimizing the side effects. Mononuclear phagocytes, dendritic cells, endothelial cells, and cancers (tumor cells, as well as tumorneovasculature) are key targets. Today, nanotechnology and nanoscience approaches to particle design and formulation are beginning to expand the market for many drugs and are forming the basis for a highly profitable niche within the industry, but some predicted benefits are hyped.

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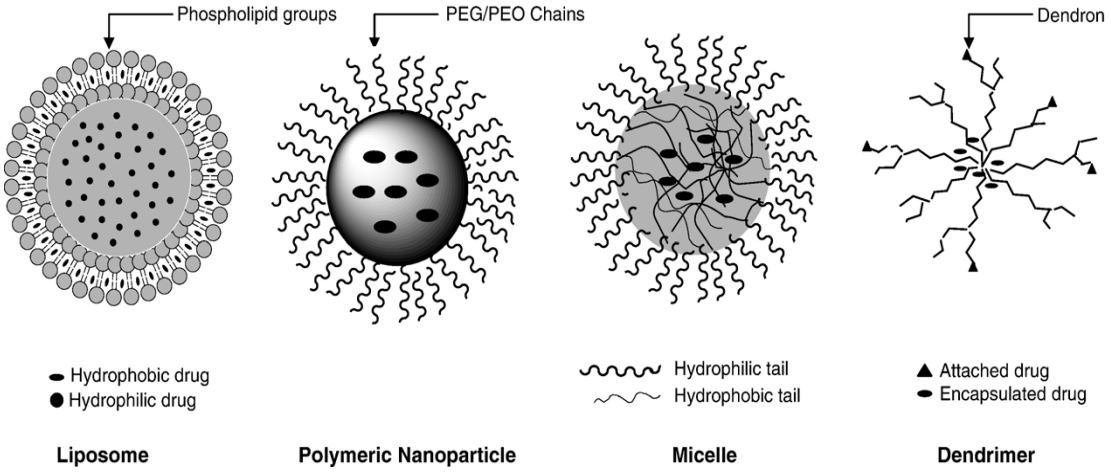

Fig.1. Different types of nanocarriers.