How to Cite:
Madhusudhanan, J., Gundu, S., Kavitha, K., Abirami, D., Manickam, R., & Ahamed, N. M. I. (2022). Role of nanomaterials with special reference to pharmaceutical technology. *International Journal of Health Sciences*, *6*(S3), 7210–7227. https://doi.org/10.53730/ijhs.v6nS3.7736

Role of nanomaterials with special reference to pharmaceutical technology

Madhusudhanan J.
Department of Biotechnology, Anand Institute of Higher Technology, Kazhipattur, Chennai, Tamilnadu
Email: jmadhuj2008@gmail.com

Shravanya Gundu
Department of Biomedical Engineering, University College of engineering, Hyderabad, Telangana
Email: shravanya.g@uceou.edu

Kavitha K.
Department of Biochemistry, Vivekanandha College of Arts and Science for Women (Autonomous), Tiruchengode, Namakkal, Tamilnadu
Email: kavithakbiochem@gmail.com

Abirami D.
Department of Zoology, Sri G.V.G.Visalakshi College for Women, Udumalpet, Tamilnadu
Email: sunabiphd@gmail.com

Rajalakshmi Manickam
Department of Microbiology, Rathinam College of Arts and Science, Eachanari, Coimbatore, Tamilnadu
Email: rajalakshmi.microbiology@rathinam.in

Niyas Ahamed M. I.
Department of Biochemistry, Sacred Heart College (Autonomous), Tirupattur, Tamilnadu
*Corresponding author email: driniyasahamed@shctpt.edu

***Abstract*---**Nanocarriers have emerged as a safe and effective method of medication administration and release during the past few years. When compared to their larger-scale counterparts, nanoparticles display amazing properties. The excellent biocompatibility of many of these carriers makes them more attractive, as does the fact that they provide better effectiveness, particularly in cancer therapies. Over the past half-century, nanocrystal, liposomal, and micelle nanocarriers for

drug administration and release have been widely studied. As a result of these successful uses, the pharmaceutical industry now has a whole new product to choose from. An overview of recent works on nanocarrier materials and designs to improve the efficacy of medications for illness treatment is provided below. As organic and inorganic nanocarrier materials that are highly biocompatible and easy to manipulate get the most interest, specific emphasis is paid to the design and implementation of novel nanocarrier materials such as nanohydrogels, chitins, graphene oxides, and solid lipoprotein nanoparticles. Each summary shows how far the project has progressed. In order to give better therapy to patients, there is a pressing demand in pharmaceutical technology for improved knowledge of the current condition of these nanomaterials.

***Keywords*---**nanocarrier, drug delivery, nanomaterials, controlled, drug release.

Introduction

Nanomaterials are defined as materials with one or more dimensions below 100 nm (1). According to the European Commission, a nanomaterial was defined as follows in 2011: Particles in an unbound condition, aggregates, or agglomerates, in which at least 50% of the particles in the number size distribution have an exterior dimension in the range of 1 nm-100 nm, in a natural, incidental, or produced substance (2). Nanomaterials offer considerable research and development/product\s development potential in medical applications. Some of these applications include DNA/ RNA nanotechnology, diagnostics by\s molecular imaging, biosensing, nanomedicine, and nanocarriers\s for medication delivery (3). Graphene (GR)/ GR oxide (GO) nanosheets, iron oxide nanoparticles, gold nanoparticles, ceria oxide nanoparticles, and carbon nanotube/nanoparticles are only a few examples of the numerous nanomaterials that have been created, manufactured, and used in various sectors.

Nanomaterials display exceptional optical, electrical, and/or\s mechanical characteristics when contrasted with their higher scaled\s forms. Their colour, conductivity and reactivity can be different from macro forms. Surface area to volume ratio can also differ. Surface tension can also differ. Due\s to this, nanomaterials have drawn the interest of scientists\s for their potential application in vaccinations, medicine development, and\s drug delivery (4). Over many years, several nanomaterials have been\s adopted as nanocarriers, i.e. nanohydrogels, oil-in-waters emulsions, liposomes, and nanoparticles based on synthetic\s polymers or natural macromolecules (5). In the late 1970s, Couvreur et al (6). and Kreuter and Speiser (7), used polymeric nanocapsules as lysosomotropic carriers and adjuvants in their initial research.

In most cases, drug nanocarriers are used for one of two purposes: controllable medication release and precise drug delivery to a specific organ, tissue, or cell type. Biocompatible nanoparticles or nanocapsule and targeting molecules are the building blocks of medication delivery. Hydrophobic carrier systems or

pharmaceuticals can be made more hydrophilic by including biocompatible components. Directly targeting tissues, organs, or cells with antibodies or avidin/biotin is the primary mode of action of targeting agents. The environmentally sensitive structure of the carrier provides the drug release characteristics found in nanocarrier systems. Preventing healthy tissue damage caused by some medications, such as chemotherapy treatments, is a major benefit of controlling drug release, which releases the drug with high efficiency in the desired location (8). Polymer-based nanoparticles, which are solid colloidal particles between 10 and 500 nanometers in diameter, have been used to develop nanocarriers (4). Dissolution, entrapment, adsorption, adhesion, or encapsulation are all techniques of drug integration into nanocarriers (9). Nanocarrier systems are reviewed in this section. Nanocarriers such as chitosan (CS) nanoparticles, graphene/graphene oxide nanoparticles (GR/GO), and solid lipid nanoparticle (SLN) have been widely used in recent years. The most strongly rotated amphiphilic nanocarrier materials are nanohydrogels and CS nanoparticle derivatives. A large variety of carrier designs may be achieved by using GR/GO nanomaterials. It's now the most promising and innovative lipophilic drug carrier is solid lipid nanocarriers (SLNs) (10).

Nanohydrogel Carriers

Starting with descriptions of macro-scale hydrogels, nanohydrogels may be described. A hydrogel is a network of hydrophilic polymer chains that is crosslinked in three dimensions. Natural or manmade polymers can be used to create network structures that expand when they come into contact with water or bodily fluids. It's also possible for them to return back to their original condition if they're not in contact with water or biological fluids. 11-13 Hydrogels have gotten a lot of interest and use in biological applications including drug transport, drug release, and vaccine creation because of their distinctive properties (14). The crosslink-controlled pore architectures of hydrogel drug delivery and release system designs have been and are still regarded appealing in medicine. Hydrogels, on the other hand, have a physiochemical similarity to the human body's extracellular matrix. Hydrogels are noted for their great biocompatibility because of their high-water content. Their viscosity was a major drawback, prompting the development of nanohydrogels as a workaround. A needle may readily be used to inject these submicron drug carriers. Further bioconjugation is made possible by reduced size and increased surface area (11), (15).

Systemic drug delivery is possible using nanogels in the 10-100 nm size range. Designing nanogel carriers with kidney filtration clearance in mind, the diameter must fall below 10 nm. In order to deliver drugs to cells and tissues, nanohydrogels, which are generally between 5 and 100 nm in diameter, are used (16). The crosslink bond concentration that develops or breaks changes the mesh size in stimuli-dependent designs, such as temperature- and pH-sensitive ones (15). Drug release acceleration can be controlled by regulating the breakages of crosslinking bonds that produce the initial mesh size of the carriers. The swelling capability of nanohydrogels can also be used in other designs (17). As the edoema progresses, the mesh size expands, allowing the medicine to be released over time (15). Environmentally responsive nanohydrogel carriers include designs that are sensitive to pH, temperature, electric field, light, enzyme, calcium, glucose, redox,

etc (18). Some of these designs are described in this study based on their sensitive qualities as seen in the following figure. According to this description, there are numerous common materials that stand out when compared to others as nanohydrogel carriers. Table 1 lists the materials that scientists are most interested in.

Temperature-sensitive nanohydrogel carriers

Temperature-sensitive nanohydrogel carriers are systems that\s exhibit swelling behaviour that is dependent on temperature\s changes and are a highly explored field (19). A temperature sensitive\s drug-release design was disclosed by Ichikawa and\s Fukumori (20), in 1999. The concept comprises of a water-soluble\s hemostatic drug core inside a thermosensitive poly [Nisopropylacrylamide\s (NIPAAm)] nanohydrogel comprising an\s ethyl cellulose shell. Ichikawa and Fukumori (20), indicated that the\s mentioned shell may vary and revert to its initial size with\s temperature variations between 30°C and 50°C in water and\s that nanohydrogels display positive thermosensitive swelling.

The drug release rate is found to be not only temperature\s dependent but also nanohydrogel concentration dependent (20). A fairly recent study presented thermosensitive 5-fluorouracil\s (5-FU; a chemotherapeutic medication utilised for solid tumor\s treatments) incorporating methyl cellulose (MC) nanohydrogels\s for minimised adverse effects of chemotherapy. In this 2018 study\s Dalwadi and Patel (21) created MC nanohydrogels via a tip probesonicator\s method from MC hydrogels. The release of 5-FU is temperature and biodegradability dependent. Conventional chemotherapy uses a significant number of cytotoxic drugs that explode in an area over a long period of time (21).

PH- and/or ionic-strength-sensitive nanohydrogel carriers

pH and/or ionic strength sensitivity permits nanocarriers' mesh\s size to be changed according to the ambient pH.Nanohydrogels were created by inverse microemulsion polymerization in 2010 by Elsaeed et al (22). On\s average, the diameter of these nanohydrogels is reported to\s range between 60 and 80 nm. When the pH is between 4.00 and 8.00, the poly (NIPA-co-AAC) nanohydrogel is characterised for its swelling behaviour between these two pH values, a feasible drug release technique is provided. Researchers found that the swelling capacity of nanohydrogels increased with the pH of their surroundings (22). Previous research has shown that pH-sensitive poly (N-isopropylacrylamide) derivative copolymers or poly(alkyl(meth)acrylate) diblock copolymers can be used as carriers for indomethacin (a nonsteroidal anti-inflammatory drug), fenofibrate (a drug for treating abnormal blood lipid levels), and doxorubicin (DOX) and aluminium chloride phthalocyanine (ACP). Free radical polymerization was said to be used to make PNIPAM copolymers, whereas atom transfer radical polymerization was said to be used to make poly[alkyl(meth)acrylate) diblock copolymers. A combination of in vitro and in vivo testing was used by the members of the team. An alternative to Cremophor®EL for weakly water-soluble medicines has been suggested by Dufresne and colleagues (23). The nanoparticles of polyethylene glycol (PEG) were also claimed to be effective transporters for hydrophobic medicines that may be taken orally, according to the study.

Increasing the pH causes dissociation in the carrier system, according to one investigation (23).

Chitosan nanocarriers

As the raw material for CS nanocarriers, chitin is a long-chain polymer derivative of glucose [poly (1-4)-Nacetyl-D-glucosamine)] (CSNs). A linear backbone connected by glycosidic linkages is formed when chitin is deacetylated to a level of around 50% (24), (25). CS's bio-adhesiveness and permeability make it a desirable nanocarrier material among hydrophilic polymers (26). As a nanocarrier, CS has a high rate of drug loading. C-2 NH2 protonation at the D-glucosamine repeat C-2 is one of the most essential properties of D-glucosamine, as seen in Figure 1 (24). CS nanocapsules, on the other hand, are an ideal delivery method for hydrophobic medicines (27). CS nanoparticles are an ideal nanocarrier material because of the above-mentioned characteristics.

It is also pH sensitive because of the acetylated monomers in the chains and their arrangement (28). Scientists use this characteristic to release regulated amounts of drugs. Because tumour cells have a pH that is lower than that of healthy cells, delivering drugs to them and regulating their release is a frequent example of this (29). Table 2 provides a historical overview of the research on CSNs as drug delivery methods. Ionotropic gelation, the most popular process for producing CS carriers, is predicated on the polyelectrolyte's capacity to crosslink in the presence of counter ions (30).

Fernández-Urrusuno et al (31). proposed the use of CS nanoparticles as possible drug carriers for transmucosal administration in 1999, according to Table 2. CS nanoparticles loaded with insulin were designed for nasal administration to conscious normoglycemic rabbits. The serum glucose levels are said to have dropped by 40% (31). PEG-grafted CS nanoparticles as peptide drug carriers were described by Aktaş et al (34). In an aqueous solution, they observed the production of nanoparticles via intermolecular hydrogen bonding. Insulin absorption and release were influenced by the degree of PEG chain incorporation on CS and the observed long-term release phenomena (52), (53). A study by Pérez-Alvarez et al. (51). one of the most current research projects in this sector, provides a clear picture of where things stand in 2019. Their work makes use of the CSN as a promising vehicle for delivering polyoxometalate to tumour cells. To make CSN, it is necessary to crosslink low molecular weight CS gel particles in an inverse microemulsion medium by dissolving them in 1 percent (v/v) acetic acid solutions. The team was able to limit the release of cytotoxic drugs using pH-sensitive features (51).

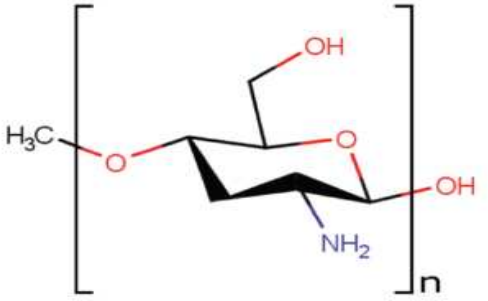


Figure 1. Chitosan monomer

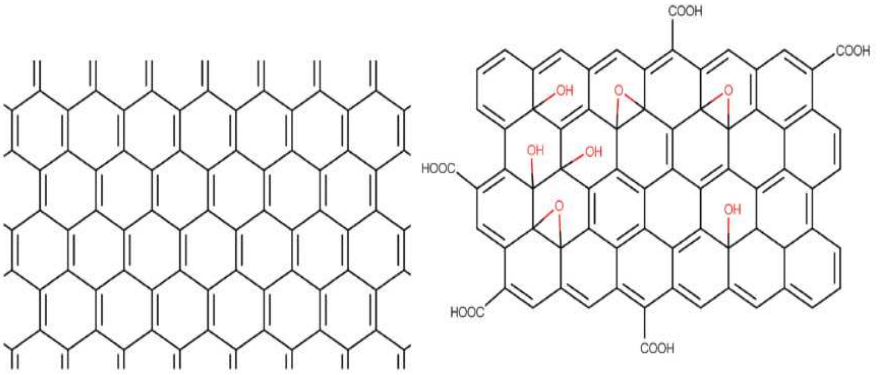


Figure 2. Molecular structure of graphene and graphene oxide

Graphene and graphene oxide Nanocarriers

GR production was eventually nailed down in 2004 by Professors Andre Geim and Kostya Novoselov, who produced a ground-breaking discovery. The discovery was noteworthy since it was previously impossible to make a single layer of graphite (carbon atoms with honeycomb-shaped sp2 links). One of the first graphitic materials to emerge was spherical GR, also known as 0D fullerenes, carbon nanotubes, and 3D graphite; later, it became regarded as the fundamental building block of graphitic materials (54-58). GR's submicron size and the - conjugation in its structure were the first things scientists noticed after its discovery. The thermal, mechanical, and electrical characteristics of GR have been discovered (57).

Research into the physical and chemical nature of GR's surface has generated interest in medical and pharmaceutical technologies and other sectors of study due to the new knowledge. Nanoscaffolds, chemical/biosensing, imaging, drug delivery, and controlled drug release are all possible applications for GR (59). GR and its composites have a key role in nanomedicine and nanocarriers because of their huge surface area (2600 m2 g-1), number of layers, lateral dimension, surface chemistry, and purity (60-62). By virtue of its above-mentioned properties, GR may be deemed a good candidate for a nanocarrier with a high drug load capacity (58).

It's common to see GR derivatives like GO, GR with oxygen-containing functions (such as epoxide, carbonyl, carboxyl, and hydroxyl groups). Because of this, the performance of nanocarriers GR and GO differs greatly from one another. When it comes to using GR in biological fluids, GO is very hydrophilic, but GR is hydrophobic, requiring surface modifications for utilisation. Thus, any nanocarrier design using GR must take into account the various contaminants and unfavourable consequences, such as cytotoxicity, that may arise (61, 63). As a result, scientists are turning away from GR nanocarrier designs in favour of those that incorporate GO.

Table 3 summarises the various GR/GO nanocarrier configurations. According to Hummer's technique of manufacture, graphite oxidative exfoliation with NaNO3 is the most prevalent way of production. Nanocarrier designs have evolved over time into more sophisticated systems that use chemotherapy and photothermal treatment to cure cancer, however Hummer's manufacturing process is commonly chosen rather than other difficult approaches.

A noncovalent physisorption chemotherapeutic drug delivery method utilising PEG-functionalized GO nanocarriers was demonstrated by Liu et al (87), in 2008. The researchers found that the nanocarriers were capable of cellular absorption in vitro (87). GO nanocarriers have been the subject of a recent investigation by Bullo and colleagues (88). Hummer's approach reportedly produces GO. Protocatechuic acid and chlorogenic acid are added to the GO to increase its biocompatibility and make it more effective in treating cancer. In order to target cancer cells, the carrier is coated with folic acid since tumour membranes contain a higher number of folate receptors, With a median size of 8 nm, the final size of the nanocarrier system is said to be 9-40 nm. To achieve a consistent therapeutic impact, the researchers found that medication release from this design required more than 100 hours (88).

Solid lipid nanoparticles

Nanocarriers based on polymers provide a distinct advantage in terms of chemical changes, including the creation of block and comb polymers. Combining and avoiding the shortcomings of SLNs is a benefit that may be used in (89) designs that employ SLNs.

Table 1. Popular nanohydrogel materials utilized as nanocarriers

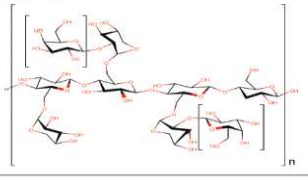
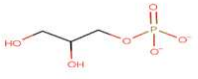
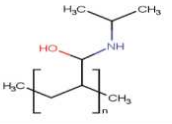
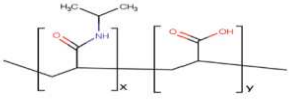
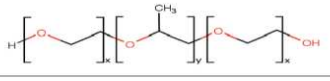
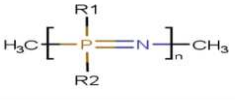
Nanohydrogel carrier material	Structure
Xyloglucan	
Glycerophosphate	
Poly (N-isopropylacrylamide)	
Poly (N-isopropylacrylamide-co-acrylic acid)	
Poloxamer (Pluronic)	
Poly (Organo phosphazene)	

Table 2. A literature summary of CSNs

Date	Drug	Nanocarrier design & advantages	CS nanoparticle production	Reference
1999	Insulin	Blood glucose control nasal absorption pH selective release	Ionotropic gelation with Penta-sodium tri-polyphosphate	31
2005	Epirubicin	Chemotherapy chitosan-bound magnetic nanocarrier	Carboxymethylated Chitosan covalently bound onto Fe3O4 nanoparticles	32
2005	BSA	Carboxymethyl konjac glucomannan–chitosan nanoparticles	Dropping method	33
2005	Z-DEVD-FMK	Cerebral Ischemia Therapy CS-PEG-BIO-SA/OX26	Chitosan acetylation 13.7%	34
2005	Insulin	Oral/Nasal Drug Carrier CS nanoparticles, CS nanocapsules and CS-coated lipid nanoparticles	Ionotropic gelation	35
2006	Triclosan Furoscmide	Higher solubility in water hydroxypropyl cyclodextrin containing chitosan nanocarrier	Ionotropic gelation	36
2006	Protein complex P1	Transmucosal drug carrier glucomannan-coated chitosan nanoparticles	Ionotropic gelation	37
2006	Salmon calcitonin	Oral drug carrier carrier for peptide drugs through the intestinal epithelium	Ionotropic gelation	38
2007	-	Transmucosal drug carrier hydrophilic cyclodextrin-chitosan core and chitosan coating	Ionotropic gelation	39
2008	Indomethacin	Ophthalmic Drug Delivery	Ionotropic gelation by addition of TPP anions	40
2009	HP-b-CD complex simvastatin	Oral delivery of drugs that are insoluble in water	Ionotropic gelation with Penta-sodium tri-polyphosphate	41
2010	Bleomycin	Chemotherapy Fe_3O_4 containing chitosan nanoparticles	Ionotropic gelation with Penta-sodium tri-polyphosphate	42
2010	siRNA	PEGylated Chitosan Nanocarriers Imidazole-modified chitosan-IAA nanoparticles	Complex coacervation of nonmodified chitosan or chitosan-IAA with siRNA	43
2010	Glutathione	Oral Drug Carrier Chitosan and Chitosan/cyclodextrin NPs	Ionotropic gelation	44
2010	Mesalazine	Colon Specific Drug Delivery Superparamagnetic chitosan–dextran sulfate NPs	Ionotropic gelation	45
2011	Silver NPs	Colon Cancer Apoptosis Chitosan-based nanocarrier of silver NPs	Ionotropic gelation with Penta-sodium tri-polyphosphate	46
2011	Curcumin	Hydrophobic drug delivery for cancer treatment Carboxymethyl chitosan nanocarriers	Ionic cross linking between carboxyl group	47
2014	100% iron saturated-bovine lactoferrin	Osteoarthritis treatment	-	48
2014	Rosmarinic acid	Antioxidant delivery	Ionotropic gelation with Penta-sodium tri-polyphosphate	49
2015	Paclitaxel	Chitosan based glycolipid-like nanocarrier		50
2019	Polyoxometalates	Breast cancer therapy pH selective release	Crosslinked in inverse microemulsion medium	51

CSN: Chitosan nanocarriers

Table 3. A literature summary of GR/GO nanocarriers

Date	Drug	Nanocarrier	Nanocarrier design & advantages	GR or go synthesis	Nanocarrier size on average	Reference
2010	Camptothecin (CPT) Doxorubicin (DOX)	FA-GONS-p-amino benzenesulfonic acid	Sulfonic acid groups render stability in physiological solutions Target: human breast cancer cells	Hummer's method	GONS (thickness) < 150 nm	64
2011	Ellagic acid (EA)	GONS-Pluronic F38(F38), GONS - Tween 80(T80), GONS–Maltodextrin (MD)	High drug loading (For GO-T80, 1.22 g per 1 g)	Hummer's method	GONS-F38 (thickness)=6-7 nm GONS-T80 (thickness)=7-8 nm GONS-MD (thickness) =5-6 nm	65
2011	Doxorubicin (DOX)	PEG-GONS	Both chemotherapy and near infrared (NIR) photothermal therapy Lower systematic toxicity	Hummer's method	-	66
2011	Tamoxifen Citrate (TmC)	Pyridinium bromide (PY+-Chol)-Graphene (GR)	Enhanced the apoptosis of cancer cells	-	PY+-Chol-GR (hydrodynamic diameter)=150-200 nm	67
2013	Doxorubicin (DOX)	Polyethylene Glycol-Branched Polyethyleneimine-Reduced GO (PEG-BPEI-rGO)	Photothermally controlled anti-cancer drug delivery Higher cancer cell death	Reduction by hydrazine monohydrate	100-200 nm	68
2013	5-fluorouracil (5-FU)	Fe_3O_4-GONS	pH dependent chemotherapy High drug loading capacity of up to 0.35 mg mg^{-1}	Hummer's method	-	69
2013	Doxorubicin (DOX)	PVP-GONS-FA	pH sensitive nanocarrier Both chemotherapy and near infrared (NIR) photothermal therapy	Hummer's method	GONS=100 nm	70
2013	Doxorubicin (DOX)	FA-GONS-Chitosan (CHI)	High drug loading efficiency (0.98 mg/mg) & prolonged drug release rate pH sensitive drug release	Hummer's method	-	71
2014	Doxorubicin (DOX)	GO/integrin aVb3 mono-antibody (Abs)/ polyethyleneimine (PEI)/citraconic anhydride functionalized poly(allylamine) (PAH-Cit)	Charge-reversal, target specific nanocarrier Drug release in acidic intracellular organelles	Hummer's method	GO/PEI/PAH-Cit/ DOX=20-200 nm	72
2014	Doxorubicin (DOX)	Hyaluronic acid (HA)-GONS	Targeted and pH sensitive drug delivery High loading efficiency of drug (42.9%)	Hummer's method	GONS (lateral)=10-200 nm	73

2014	Doxorubicin (DOX)	PEG-Poly (allylamine hydrochloride) (PAH)-2,3-dimethylmaleic anhydride (DA)-GONS	pH sensitive drug release Both chemotherapy and photothermal therapy	Hummer's method	PEG-PAH-DA-GONS=70 nm	74
2015	Paclitaxel (PTX)	PEG-GO	Nontoxic chemotherapy carrier Increased biocompatibility and physiological stability	Hummer's method	PEG-GO-PTX (lateral)=50-200 nm	75
2015	Irinotecan (IRI) Doxorubicin (DI)	Poloxamer 188-GONS	Photothermal therapy with dual chemotherapies in one system	Hummer's method	GONS=200 nm	76
2015	Indomethacin (IMC) Doxorubicin (DOX)	poly(N-isopropylacrylamide) (PNIPAM)-GO	Enhanced thermal stability Improved dispersibility in aqueous and cell medium	Hummer's method	GONS=0.85 nm NIPAM-GONS=3.2 nm	77
2016	Doxorubicin (DOX)	Gold Nanoparticle (AuNP) - Folic Acid - GONS	Targeted chemotherapy and photothermal ablation	-	AuNP-FA-GONS (Hydrodynamic size)=188.2±7.2 nm AuNP-GO (diagonal)=135 nm	78
2018	Doxorubicin (DOX) Camptothecin (CPT)	Folic acid (FA)-Graphene Oxide Nanosheet (GONS)	FA linked GONS for high affinity to folate receptor	Hummer's method	2.7 nm	79
2018	Tetracycline (TC)	Carboxymethylcellulose (CMC)-Zn-Based Metal-Organic Framework (MOF-5)-GO	Efficient oral drug delivery Effective protection against stomach pH	Hummer's method	CMC/MOF-5/GO (diameter)=344 nm	80
2018	Doxorubicin (DOX)	Carboxymethylcellulose (CMC)-Zn-Based Metal-Organic Framework (MOF-5)-GONS	Targeted delivery and controlled release of chemotherapy human blood cancer cell lines	Hummer's method	GONS (Thickness)=30 nm CMC/MOF-5/GONS=80 nm	81
2019	Quercetin (QSR) Gefitinib (GEF)	Polyvinylpyrrolidone (PVP)-GO	High biocompatibility Enhanced anticancer activity within a dosage range	Hummer's method	GO=166.5 nm PVP-GO=300-400 nm	82
2019	Cis-diamminedichloroplatinum (II) (CisPt)	Maghemiteγ-Fe_2O_3-GO	Efficient Malignant glioma chemotherapy GONP accumulates in U87 human glioblastoma subcutaneous tumor xenografts	Hummer's method	GO (width)=80-100 nm GO (thickness)=6.3 nm	83
2019	Methotrexate (MTX)	Polyethylene Glycol bis Amin (PEGA)- GO Magnetic NS (GOMNS)	Magnetic Iron NPs Increased efficacy in chemotherapy with pH dependent drug release and biocompatibility	Hummer's method	-	84
2019	5-Fluorouracil (5-FU) Curcumin (CUR)	Chitosan-rGO	Increased efficiency of chemotherapy against colon cancer	-	-	85
2019	Doxorubicin (DOX)	κ-Carrageenan (κ-Car)-GONS-biotin	Targeted therapy for cervical cancer pH-sensitive drug release	Hummer's method	κ-Car-GONS-biotin (thickness)=219 nm	86

Hydrophobic or hydrophilic molecules that are insoluble in water and soluble in organic solvents are called lipids (90). In 1995, the IUPAC provided the following additional definition: Soluble in nonpolar solvents, biologically derived compounds are referred to be "solubilized." Glycerides (fats and oils) and

phospholipids, as well as nonsaponifiable lipids, such as steroids, make up the majority of these lipids "(91). An alternative colloidal carrier for drug delivery and drug release has been discovered by researchers in the form of colloidal nanospheres (SLNs) (5). According to the surfactant employed during manufacture, SLNs have an average diameter of 150 to 300 nm, although they can be as large as 1000 nm, depending on the surfactant utilized (92). Smaller SLNs are more stable over time, have a higher drug loading capacity, and release more slowly than larger SLNs (93). Accordingly, SLNs offer a number of advantages, including the fact that they do not harm healthy tissue and are easy to produce in larger batches, the ability to load both lipophilic and hydrophilic therapeutic agents, and the capability to carry large amounts of drugs (5). Oral medication administration is the most prevalent use for SLN nanocarriers. SLNs have also been used to deliver doxorubicin, idarubicin, thymopentin, and camptothecin, among other medicines (96).

Discussion and Conclusion

Researchers may now use nanocarriers to deliver drugs to specific areas of the body while also controlling the rate at which the drugs are released. When compared to their larger-scale counterparts, nanocarriers offer a unique set of properties that have made them an important focus in pharmaceutical technology. Color, visible light, reactivity, surface area to volume ratio, conductivity, and surface tension are all used to describe these properties in this study. A variety of these carriers are increasingly common because to their high\s biocompatibility, assuring improved efficacy specifically in cancer\s treatments. One of the most important benefits of successful applications has been the creation of new pharmacological options. Among the nanocarrier materials discussed in this study are nanohydrogels, CSNs, GR/GO nanocarriers, and SLNs, which are referred to as nanohydrogels carriers. Besides these nanomaterials there are also a great\s number of alternative nanocarrier designs that are not included in\s this study, such as gold nanocarriers (97), starch and/or cellulose\s nanocarriers (98). cerium oxide nanocarriers (99), and carbon nanotube\s incorporated nanocarriers (100). It is apparent that, with further\s information obtained on nanocarriers for drug delivery and the\s current position in the development process of these nanomaterials there is a great chance to give better therapy to patients\s desperate in need of efficient treatment options.

References

1. Grimsdale AC, Müllen K. The chemistry of organic nanomaterials. Angew Chem Int Ed Engl. 2005;44:5592-5629.
2. EU Definition of a Nanomaterial https://www.safenano.org/knowledgebase/ regulation/substances/eu-definition-of-a-nanomaterial/
3. Nalwa HS. A special issue on reviews in nanomedicine, drug delivery and vaccine development. J Biomed Nanotechnol. 2014; 10:1635-1640.
4. Han J, Zhao D, Li D, Wang X, Jin Z, Zhao K. Polymer-based nanomaterials and applications for vaccines and drugs. Polymers (Basel). 2018;10(1).

5. Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery - a review of the state of the art. Eur J Pharm Biopharm. 2000; 50:161-177.
6. Couvreur P, Kante B, Roland M, Guiot P, Bauduin P, Speiser P. Polycyanoacrylatenanocapsules as potential lysosomotropic carriers: preparation, morphological and sorptive properties. J Pharm Pharmacol. 1979; 31:331-332.
7. Kreuter J, Speiser PP. *In vitro* studies of poly(methyl methacrylate) adjuvants. J Pharm Sci. 1976; 65:1624-1627.
8. De Jong WH, Borm PJ. Drug delivery and nanoparticles: applications and hazards. Int J Nanomedicine. 2008; 3:133-149.
9. Ochekpe NA, Olorunfemi PO, Ngwuluka NC. Nanotechnology and Drug Delivery Part 2: Nanostructures for Drug Delivery. Trop J Pharm Res. 2009; 8:275-287.
10. Lombardo D, Kiselev MA, Caccamo MT. Smart nanoparticles for drug delivery application: development of versatile nanocarrier platforms in biotechnology and nanomedicine. Journal of Nanomaterials. 2019; 2019:1-26.
11. Hoare TR, Kohane DS. Hydrogels in drug delivery: progress and challenges. Polymer. 2008; 49:1993-2007.
12. Choudhary B, Paul SR, Nayak SK, Qureshi D, Pal K. Synthesis and biomedical applications of filled hydrogels. In: Pal K, Banerjee I, eds. Polymeric Gels: Characterization, Properties and Biomedical Applications (1st ed). United Kingdom; Elsevier, 2018:283-302.
13. Klouda L, Mikos AG. Thermoresponsive hydrogels in biomedical applications. Eur J Pharm Biopharm. 2008; 68:34-45.
14. Wang ZG, Ding B. DNA-based self-assembly for functional nanomaterials. Adv Mater. 2013; 25:3905-3914.
15. Li J, Mooney DJ. Designing hydrogels for controlled drug delivery. Nat Rev Mater. 2016; 1:16071.
16. Lin CC, Metters AT. Hydrogels in controlled release formulations: network design and mathematical modeling. Adv Drug Deliv Rev. 2006; 58:1379-1408.
17. Brannon-Peppas L, Peppas NA. Equilibrium swelling behavior of pH-sensitive hydrogels. Chemical Engineering Science. 1991; 46:715-722.
18. Garg T, Singh S, Goyal AK. Stimuli-sensitive hydrogels: an excellent carrier for drug and cell delivery. Crit Rev Ther Drug Carrier Syst. 2013; 30:369-409.
19. Liu J, Yin Y. Temperature responsive hydrogels: construction and applications. Polym Sci. 2015; 1:1.
20. Ichikawa H, Fukumori Y. A novel positively thermosensitive controlled-release microcapsule with membrane of nano-sized poly(N-isopropylacrylamide) gel dispersed in ethylcellulose matrix. J Control Release. 2000; 63:107-119.
21. Dalwadi C, Patel G1. Thermosensitive nanohydrogel of 5-fluorouracil for head and neck cancer: preparation, characterization and cytotoxicity assay. Int J Nanomedicine. 2018;13(T-NANO 2014 Abstracts):31-33.
22. Elsaeed SM, Farag RK, Maysour NS. Synthesis and characterization of pH-sensitive crosslinked (NIPA-co-AAC) nanohydrogels copolymer. J Appl Polym Sci. 2012; 124:1947-1955.

23. Dufresne MH, Garrec DL, Sant V, Leroux JC, Ranger M. Preparation and characterization of water-soluble pH-sensitive nanocarriers for drug delivery. Int J Pharm. 2004; 277:81-90.
24. Rinaudo M. Chitin and chitosan: properties and applications. Progress in Polymer Science. 2006; 31:603-632.
25. Ravi Kumar MNV. A review of chitin and chitosan applications. React Funct Polym. 2000; 46:1-27.
26. de la Fuente M, Csaba N, Garcia-Fuentes M, Alonso MJ. Nanoparticles as protein and gene carriers to mucosal surfaces. Nanomedicine (Lond). 2008; 3:845-857.
27. Calvo P, Remuñán-López C, Vila-Jatu JL, Alonso MJ. Novel hydrophilic chitosan-polyethylene oxide nanoparticles as protein carriers. J. Appl. Polym. Sci. 1997; 63:125-132.
28. Csaba N, Garcia-Fuentes M, Alonso MJ. The performance of nanocarriers for transmucosal drug delivery. Expert Opin Drug Deliv. 2006; 3:463-478.
29. Zhang X, Lin Y, Gillies RJ. Tumor pH and its measurement. J Nucl Med. 2010; 51:1167-1170.
30. Giri TK. Alginate containing nanoarchitectonics for improved cancer therapy. In: Holban AM, Grumezescu AM, eds. Nanoarchitectonics for Smart Delivery and Drug Targeting. Elsevier, 2016;565-588.
31. Fernández-Urrusuno R, Calvo P, Remuñán-López C, Vila-Jato JL, Alonso MJ. Enhancement of nasal absorption of insulin using chitosan nanoparticles. Pharm Res. 1999; 16:1576-1581.
32. Chang YC, Shieh DB, Chang CH, Chen DH. Conjugation of monodisperse chitosan-bound magnetic nanocarrier with epirubicin for targeted cancer therapy. J Biomed Nanotechnol. 2005; 1:196-201.
33. Du J, Sun R, Zhang S, Zhang LF, Xiong CD, Peng YX. Novel polyelectrolyte carboxymethyl konjac glucomannan-chitosan nanoparticles for drug delivery. I. Physicochemical characterization of the carboxymethyl konjac glucomannan-chitosan nanoparticles. Biopolymers. 2005; 78:1-8.
34. Aktaş Y, Yemisci M, Andrieux K, Gürsoy RN, Alonso MJ, Fernandez- Megia E, Novoa-Carballal R, Quiñoá E, Riguera R, Sargon MF, Celik HH, Demir AS, Hincal AA, Dalkara T, Capan Y, Couvreur P. Development and brain delivery of chitosan−PEG nanoparticles functionalized with the monoclonal antibody OX26. Bioconjug Chem. 2005; 16:1503-1511.
35. Prego C, García M, Torres D, Alonso MJ. Transmucosal macromolecular drug delivery. J. Control. Release. 2005; 101:151-162.
36. Maestrelli F, Garcia-Fuentes M, Mura P, Alonso MJ. A new drug nanocarrier consisting of chitosan and hydoxypropylcyclodextrin. Eur J Pharm Biopharm. 2006; 63:79-86.
37. Cuña M, Alonso-Sandel M, Remuñán-López C, Pivel JP, Alonso- Lebrero JL, Alonso MJ. Development of phosphorylated glucomannan-coated chitosan nanoparticles as nanocarriers for protein delivery. J NanosciNanotechnol. 2006; 6:2887-2895.
38. Prego C, Fabre M, Torres D, Alonso MJ. Efficacy and mechanism of action of chitosan nanocapsules for oral peptide delivery. Pharm Res. 2006; 23:549-556.
39. Trapani A, Garcia-Fuentes M, Alonso MJ. Novel drug nanocarriers combining hydrophilic cyclodextrins and chitosan. Nanotechnology. 2008; 19:185101.

40. Badawi AA, El-Laithy HM, El Qidra RK, El Mofty H, El dally M. Chitosan based nanocarriers for indomethacin ocular delivery. Arch Pharm Res. 2008; 31:1040-1049.
41. Vyas A, Saraf S, Saraf S. Encapsulation of cyclodextrin complexed simvastatin in chitosan nanocarriers: a novel technique for oral delivery. J Incl Phenom. 2009; 66:251-259.
42. Kavaz D, Odabaş S, Güven E, Demirbilek M, Denkbaş EB. Bleomycin loaded magnetic chitosan nanoparticles as multifunctional nanocarriers. J. Bioact. Compat. Polym. 2010; 25:305-318.
43. Ghosn B, Singh A, Li M, Vlassov AV, Burnett C, Puri N, Roy K. Efficient gene silencing in lungs and liver using imidazolemodified chitosan as a nanocarrier for small interfering RNA. Oligonucleotides. 2010; 20:163-172.
44. Trapani A, Lopedota A, Franco M, Cioffi N, Ieva E, Garcia-Fuentes M, Alonso MJ. A comparative study of chitosan and chitosan/ cyclodextrin nanoparticles as potential carriers for the oral delivery of small peptides. Eur J Pharm Biopharm. 2010; 75:26-32.
45. Saboktakin MR, Tabatabaie R, Maharramov A, Ramazanov MA. Synthesis and characterization of superparamagnetic chitosandextran sulfate hydrogels as nano carriers for colon-specific drug delivery. Carbohydr. Polym. 2010; 81:372-376.
46. Sanpui P, Chattopadhyay A, Ghosh SS. Induction of apoptosis in cancer cells at low silver nanoparticle concentrations using chitosan nanocarrier. ACS Appl Mater Interfaces. 2011; 3:218-228.
47. Anitha A, Maya S, Deepa N, Chennazhi KP, Nair SV, Tamura H, Jayakumar R. Efficient water-soluble O-carboxymethyl chitosan nanocarrier for the delivery of curcumin to cancer cells. Carbohydr. Polym. 2011; 83:452-461.
48. Samarasinghe RM, Kanwar RK, Kanwar JR. The effect of oral administration of iron saturated-bovine lactoferrin encapsulated chitosan-nanocarriers on osteoarthritis. Biomaterials. 2014; 35:7522- 7534.
49. da Silva SB, Amorim M, Fonte P, Madureira R, Ferreira D, Pintado M, Sarmento B. Natural extracts into chitosan nanocarriers for rosmarinic acid drug delivery. Pharm Biol. 2015; 53:642-652.
50. Hu YW, Du YZ, Liu N, Liu X, Meng TT, Cheng BL, He JB, You J, Yuan H, Hu FQ. Selective redox-responsive drug release in tumor cells mediated by chitosan-based glycolipid-like nanocarrier. J Control Release. 2015; 206:91-100.
51. Pérez-Álvarez L, Ruiz-Rubio L, Artetxe B, Vivanco MD, Gutiérrez- Zorrilla JM, Vilas-Vilela JL. Chitosan nanogels as nanocarriers of polyoxometalates for breast cancer therapies. CarbohydrPolym. 2019; 213:159-167.
52. Kumar MN, Muzzarelli RA, Muzzarelli C, Sashiwa H, Domb AJ. Chitosan chemistry and pharmaceutical perspectives. Chem Rev. 2004; 104:6017-6084.
53. Ahmed TA, Aljaeid BM. Preparation, characterization, and potential application of chitosan, chitosan derivatives, and chitosan metal nanoparticles in pharmaceutical drug delivery. Drug Des DevelTher. 2016; 10:483-507.
54. Geim AK, Novoselov KS. The rise of graphene. Nat Mater. 2007; 6:183-191.
55. Geim AK. Graphene: status and prospects. Science. 2009; 324:1530-1534.

56. Stankovich S, Dikin DA, Dommett GH, Kohlhaas KM, Zimney EJ, Stach EA, Piner RD, Nguyen ST, Ruoff RS. Graphene-based composite materials. Nature. 2006; 442:282-286.
57. Allen MJ, Tung VC, Kaner RB. Honeycomb carbon: a review of graphene. Chem Rev. 2010; 110:132-145.
58. Liu J, Cui L, Losic D. Graphene and graphene oxide as new nanocarriers for drug delivery applications. Acta Biomater. 2013; 9:9243-9257.
59. Shao Y, Wang J, Wu H, Liu J, Aksay IA, Lin Y. Graphene based electrochemical sensors and biosensors: A review. Electroanalysis 2010; 22:1027-1036.
60. Shen H, Zhang L, Liu M, Zhang Z. Biomedical applications of graphene. Theranostics. 2012; 2:283-294.
61. Wang Y, Li Z, Wang J, Li J, Lin Y. Graphene and graphene oxide: biofunctionalization and applications in biotechnology. Trends Biotechnol. 2011; 29:205-212.
62. Liu Z, Sun X, Nakayama-Ratchford N, Dai H. Supramolecular chemistry on water-soluble carbon nanotubes for drug loading and delivery. ACS Nano. 2007; 1:50-56.
63. Pumera M. Nanotoxicology: the molecular science point of view. Chem Asian J. 2011; 6:340-348.
64. Zhang L, Xia J, Zhao Q, Liu L, Zhang Z. Functional graphene oxide as a nanocarrier for controlled loading and targeted delivery of mixed anticancer drugs. Small. 2010; 6:537-544.
65. Kakran M, Sahoo NG, Bao H, Pan Y, Li L. Functionalized grapheme oxide as nanocarrier for loading and delivery of ellagic acid. Curr Med Chem. 2011; 18:4503-4512.
66. Zhang W, Guo Z, Huang D, Liu Z, Guo X, Zhong H. Synergistic effect of chemo-photothermal therapy using PEGylated graphene oxide. Biomaterials. 2011; 32:8555-8561.
67. Misra SK, Kondaiah P, Bhattacharya S, Rao CN. Graphene as a nanocarrier for tamoxifen induces apoptosis in transformed cancer cell lines of different origins. Small. 2012; 8:131-143.
68. Kim H, Lee D, Kim J, Kim TI, Kim WJ. Photothermally triggered cytosolic drug delivery via endosome disruption using a functionalized reduced graphene oxide. ACS Nano. 2013; 7:6735- 6746.
69. F an X, Jiao G, Zhao W, Jin P, Li X. Magnetic Fe3O4-graphene composites as targeted drug nanocarriers for pH-activated release. Nanoscale. 2013; 5:1143-1152.
70. Qin XC, Guo ZY, Liu ZM, Zhang W, Wan MM, Yang BW. Folic acid-conjugated graphene oxide for cancer targeted chemophotothermal therapy. J PhotochemPhotobiol B. 2013; 120:156-162.
71. Wang Z, Zhou C, Xia J, Via B, Xia Y, Zhang F, Li Y, Xia L. Fabrication and characterization of a triple functionalization of grapheme oxide with Fe3O4, folic acid and doxorubicin as dual-targeted drug nanocarrier. Colloids Surf B Biointerfaces. 2013; 106:60-65.
72. Zhou T, Zhou X, Xing D. Controlled release of doxorubicin from graphene oxide based charge-reversal nanocarrier. Biomaterials. 2014; 35:4185-4194.
73. Song E, Han W, Li C, Cheng D, Li L, Liu L, Zhu G, Song Y, TanW. Hyaluronic acid-decorated graphene oxide nanohybrids asnanocarriers for

targeted and pH-responsive anticancer drugdelivery. ACS Appl Mater Interfaces. 2014; 6:11882-11890.
74. Feng L, Li K, Shi X, Gao M, Liu J, Liu Z. Smart pH-responsivenanocarriers based on nano-graphene oxide for combined chemoandphotothermal therapy overcoming drug resistance. Adv HealthcMater. 2014; 3:1261-1271.
75. Xu Z, Zhu S, Wang M, Li Y, Shi P, Huang X. Delivery of paclitaxelusing pegylated graphene oxide as a nanocarrier. ACS Appl MaterInterfaces. 2015; 7:1355-1363.
76. Tran TH, Nguyen HT, Pham TT, Choi JY, Choi HG, Yong CS, KimJO. Development of a graphene oxide nanocarrier for dual-drugchemo-phototherapy to overcome drug resistance in cancer. ACSAppl Mater Interfaces. 2015; 7:28647-28655.
77. Kundu A, Nandi S, Das P, Nandi AK. Fluorescent graphene oxide viapolymer grafting: an efficient nanocarrier for both hydrophilic andhydrophobic drugs. ACS Appl Mater Interfaces. 2015; 7:3512-3523.
78. Chauhan G, Chopra V, Tyagi A, Rath G, Sharma RK, Goyal AK. "Goldnanoparticles composite-folic acid conjugated graphene oxidenanohybrids" for targeted chemo-thermal cancer ablation: *in vitro*screening and *in vivo* studies. Eur J Pharm Sci. 2017; 96:351-361.
79. He H, Li S, Shi X, Wang X, Liu X, Wang Q, Guo A, Ge B, KhanNU, Huang F. Quantitative nanoscopy of small blinking grapheme nanocarriers in drug delivery. Bioconjug Chem. 2018; 29:3658-3666.
80. Karimzadeh Z, Javanbakht S, Namazi H. Carboxymethylcellulose/MOF-5/graphene oxide bio-nanocomposite as antibacterial drugnanocarrier agent. Bioimpacts. 2019; 9:5-13.
81. Javanbakht S, Pooresmaeil M, Namazi H. Green one-pot synthesisof carboxymethylcellulose/Zn-based metal-organic framework/graphene oxide bio-nanocomposite as a nanocarrier for drugdelivery system. CarbohydrPolym. 2019; 208:294-301.
82. Tiwari H, Karki N, Pal M, Basak S, Verma RK, Bal R, Kandpal ND,Bisht G, Sahoo NG. Functionalized graphene oxide as a nanocarrierfor dual drug delivery application: the synergistic effect ofquercetin and gefitinib against ovarian cancer cells. Colloids SurfB Biointerfaces. 2019; 178:452-459.
83. Makharza SA, Cirillo G, Vittorio O, Valli E, Voli F, Farfalla A, Curcio M,Iemma F, Nicoletta FP, El-Gendy AA, Goya GF, Hampel S. Magneticgraphene oxide nanocarrier for targeted delivery of cisplatin: aperspective for glioblastoma treatment. Pharmaceuticals (Basel).2019;12(2).
84. Abdollahi Z, Taheri-Kafrani A, Bahrani SA, Kajani AA. PEGAylatedgraphene oxide/superparamagnetic nanocomposite as ahigh-efficiency loading nanocarrier for controlled delivery ofmethotrexate. J Biotechnol. 2019; 298:88-97.
85. Dhanavel S, Revathy TA, Sivaranjani T, Sivakumar K, PalaniP, Narayanan V, Stephen A. 5-Fluorouracil and curcumin coencapsulatedchitosan/reduced graphene oxide nanocompositesagainst human colon cancer cell lines. Polym Bull. 2019 Mar 15.doi:10.1007/s00289-019-02734-x
86. Vinothini K, Rajendran NK, Munusamy MA, Alarfaj AA, Rajan M.Development of biotin molecule targeted cancer cell drug deliveryof

doxorubicin loaded κ-carrageenan grafted graphene oxidenanocarrier. Mater Sci Eng C Mater Biol Appl. 2019; 100:676-687.
87. Liu Z, Robinson JT, Sun X, Dai H. PEGylated nanographene oxidefor delivery of water-insoluble cancer drugs. J Am Chem Soc.2008; 130:10876-10877.
88. Bullo S, Buskaran K, Baby R, Dorniani D, Fakurazi S, Hussein MZ.Dual drugs anticancer nanoformulation using graphene oxide-PEG as nanocarrier for protocatechuic acid and chlorogenic acid.Pharm Res. 2019;36:91.
89. Mehnert W, Mäder K. Solid lipid nanoparticles. Advanced DrugDelivery Reviews. 2012; 64:83-101.
90. Gordillo-Galeano A, Mora-Huertas CE. Solid lipid nanoparticles andnanostructured lipid carriers: a review emphasizing on particlestructure and drug release. Eur J Pharm Biopharm. 2018; 133:285-308.
91. Moss GP, Smith PAS, Tavernier D. Glossary of class names oforganic compounds and reactivity intermediates based on structure (IUPAC Recommendations 1995). Pure &App Chem. 1995; 67:1307-1375.
92. Naseri N, Valizadeh H, Zakeri-Milani P. Solid lipid nanoparticlesand nanostructured lipid carriers: structure, preparation andapplication. Adv Pharm Bull. 2015; 5:305-313.
93. Yoon G, Park JW, Yoon IS. Solid lipid nanoparticles (SLNs) andnanostructured lipid carriers (NLCs): recent advances in drugdelivery. J Pharm Investig. 2013; 43:353-362.
94. Cavalli R, Caputo O, Gasco MR. Solid lipospheres of doxorubicinand idarubicin. Int J Pharm. 1993;89:R9-R12.
95. Morel S, Ugazio E, Cavalli R, Gasco MR. Thymopentin in solid lipidnanoparticles. Int J Pharm. 1996; 132:259-261.
96. Yang S, Zhu J, Lu Y, Liang B, Yang C. Body distribution ofcamptothecin solid lipid nanoparticles after oral administration. Pharm Res. 1999;16:751-757.
97. Choi WI, Kim JY, Kang C, Byeon CC, Kim YH, Tae G. Tumorregression *in vivo* by photothermal therapy based on gold-nanorodloaded, functional nanocarriers. ACS Nano. 2011; 5:1995-2003.
98. Kang B, Okwieka P, Schöttler S, Winzen S, Langhanki J, Mohr K,Opatz T, Mailänder V, Landfester K, Wurm FR. Carbohydrate-basednanocarriers exhibiting specific cell targeting with minimuminfluence from the protein corona. Angew Chem Int Ed Engl.2015; 54:7436-7440.
99. Sack M, Alili L, Karaman E, Das S, Gupta A, Seal S, Brenneisen P.Combination of conventional chemotherapeutics with redox-activecerium oxide nanoparticles—a novel aspect in cancer therapy. MolCancer Ther. 2014; 13:1740-1749.
100. Hampel S, Kunze D, Haase D, Krämer K, Rauschenbach M, RitschelM, Leonhardt A, Thomas J, Oswald S, Hoffmann V, BüchnerB. Carbon nanotubes filled with a chemotherapeutic agent: ananocarrier mediates inhibition of tumor cell growth. Nanomedicine (Lond). 2008; 3:175-182.