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REVIEW ARTICLE

Nanopharmaceuticals: A New Perspective of Drug Delivery System

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ABSTRACT

Nano-sized objects can be transformed in numerous ways to alter their characteristics. Drug molecules sized in nanometre range provide some unique features which can lead to prolonged circulation, improved drug localization, enhanced drug efficacy etc.; and these increased performance come through a variety of dosage forms. In fact, wide spectrum application of nanotechnology in pharmaceutical formulations is changing the scientific landscape of prevention, diagnosis and treatment of diseases. Various pharmaceutical nanotechnology based systems which can be termed as Nanopharmaceuticals like liposomes, carbon nanotubes, quantum dots, dendrimaers, polymeric nanoparticles, metallic nanoparticles etc. have brought about revolutionary changes in drug delivery as well as the total medical service system. The present review summarizes the most important applications of nanotechnology in drug delivery systems.

Keywords: Nanotechnology, Drug Delivery, Liposomes, Polymeric Nanoparticles, Dendrimers, Carbon Nanotubes, Quantum Dots.

INTRODUCTION

Nanotechnology can be defined as the science of material featuring between 10^{-9} and 10^{-7} of a meter. [1] To be more application oriented, Nanotechnology is circumscribed as the science of materials and devices whose structures and constituents demonstrate novel and considerably altered physical, chemical and biological phenomenon due to their nanoscale size. In a report by European Science Foundation (ESF), Nanomedicine was defined as 'the science and technology of diagnosing, treating and preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body.' [2] This resembles the definition given by the US NIH, 'Nanomedicine refers to highly specific medical intervention at the molecular scale for curing diseases or repairing damaged tissues, such as bone, muscle, or nerve.' The ESF specified five sub-disciplines [2] of nanomedicines, which in many ways are overlapping. These are Analytical tools, Nanoimaging tools, Nanomaterials and Nanodevices, Clinical and toxicological issues and Novel therapeutics and drug delivery systems. Here we are going to discuss specifically about drug delivery systems and novel therapeutics based on Nanotechnology. There are immense opportunity to get some novel drug delivery system by utilizing nanotechnology, because 'Nanosizing' of drugs-

- Increase drug targeting ability [3],[4],[5],[6],[7],[8]
- Reduce the dose needed [9],[10],[11]
- Enhance oral bioavailability [12]
- Decrease toxicity [12],[13],[14]
- Enhance solubility [15], [16]
- Increase the stability of drug and formulation [17],[18],[19]
- Increase surface area [20]
- Enhance rate of dissolution [20],[21]
- Decrease drug resistance [22],[23]
- Increase patient compliance [18]

CANRBON NANOTUBES

Carbon Nanotubes (CNTs) are hollow, well ordered, carbon nanomaterial with a variety of properties. These

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have high aspect ratio and surface area, and ultra-light weight. [23] Generally, CNTs are classified as single-walled (SW) or multi-walled (MW) carbon nanotubes. Where MWCNTs are made from a number of cylindrical carbon layers and are of diameter 2-100 nm, SWCMTs consists only one cylindrical layer and their diameter ranges from 0.4–2 nm. [25] As commercially available CNTs are heavily contaminated with amorphous carbons and metal catalysts, to make them less toxic and more biocompatible, some appropriate molecules are attached to their surface. This process is called as Functionalization. [26] Recent studies emphasize greatly on delivering chemotherapeutic agents to various cancer sites by means of CNTs. CNTs provide a greater targeting ability to the formulations and some examples of this are presented in Table-1.

Drug	Type of Disease	Type of CNTs	References
Daunorubicin	Leukemia	SWCNTs	3
Doxorubicin	Lymphoma	SWCNTs	4
	Breast cancer	MWCNTs	5
Methotrexate	Breast cancer	MWCNs	6
Paclitaxel	Breast cancer	SWCNTs	7
Gemcitabine	Ovarian cancer	SWCNTs	27
Amphotericin B	Leishmania donovani (parasite)	Not specified	28
Carboplatin	Bladder cancer	Not specified	29

Table-1: Drugs those can be delivered via Carbon Nanotubes

Along with delivering drugs for treatment of cancer, CNTs are also found effective in gene delivery. These are very good non-viral vector for gene therapy as they cross cell membrane by endocytosis process. Moreover, due to functionalization, DNA transfer takes place without any degradation. [17] Recent experiments indicated that siRNA delivered by MWCNTs can reduce tumour growth significantly. [30]

QUANTUM DOTS

Quantum dots (QDs) consist of a semiconductor core and are coated by a shell for improved optical properties. These also possess a cap which provides higher solubility in aqueous buffers. Functionalized QDs, conjugating them with targeting ligands, can be used to target specific tissues. Various colloidal core/shell usually synthesized are CdSe/ZnS, CdTe/CdSe, InP/ZnS and CdSe/CdS/ZnS. [31] QDs have a potential for improved treatment of cancer by targeted drug delivery systems. But before that, while preparing QD-drug formulations, some guidelines must be followed (a)Surface of nanoparticles must be functionalized (b)Nanoparticle size is to be minimized (c)To prevent detrimental effects, drug molecules should be kept within the nanoparticle (d)To avoid collapse, a biocompatible polymer must be attached to QD surface. Some of drugs successfully delivered by QDs are listed in Table-2

Drugs/ Therapeutics	Target cells/Diseases	Type of QDs	Efficacy	References
Saquinavir	HIV-1	Carboxyl-terminated QDs	High site-specificity and can cross BBB	8
Doxorubicin	Ovarian cancer	Mucin1- aptamer QD	Higher accumulation on target	32
5-Fluorouracil	Breast cancer	ZnS QDs	Targeting and controlled drug delivery to cancer cells.	33
Daunorubicin	Leukaemia	CdTe QDs	Enhanced drug uptake	9
Daunorubicin	Leukemia K562 cells	CdS QDs	Inhibit multidrug resistance	22

Table-2: Drugs those can be delivered via Quantum Dots.

Apart from targeting of anticancer drugs, QDs are also effective to deliver other biomolecules and drugs and through various routes of administration. QDs have shown high possibility for delivering siRNA molecules to block expression of disease causing genes. [34] Due to their ability to penetrate skin, which is dependent on the size and coating of QDs, they can also be effective in Transdermal delivery of drugs. [35] QDs can cross the BBB to reach brain parenchyma following intra-arterial administration and delivery of MMP 9-siRNA to brain microvascular endothelial cells was also reported, [36] so they can be operational in brain targeting. QDs and Doxorubicin (Dox) nanoconjugate were testified to target alveolar macrophages cells and has showed the potential of QDs for macrophage-selective therapy of pulmonary disease. [37]

DENDRIMERS

Dendrimers are a versatile class of well-defined and highly branched Nano-scale structure with several surface-active groups. Due to their smaller size (<100 nm), narrower molecular weight distribution, greater functionality, higher quantity of surface groups and relatively easier

incorporation of targeting ligands they are very good candidates for drug delivery. The main characteristics which make it special are three different topological sites (a) polyfunctional core (b) interior layers and (c) multivalent surface. [38] Several antiretrovirals, anticancer agents and brain specific drugs can be delivered by Dendrimers. Some of them are listed in Table-3.

Drugs/Therapeutics	Type of Dendrimers/Conjugates	Target cells/ Indications/ Functions	Advantages/ Features	References
Efavirenz	Tuftsin-conjugated PPE dendrimers	HIV	Targeted delivery to macrophages	39
Lamivudine	Mannose-capped PPE dendrimers	HIV	Increased cellular uptake, reduced cytotoxicity	10
siRNA	Amino-terminated carbosilane dendrimers	Lymphocytes	Reduced HIV infection, in-vitro	40
Sulphated oligosaccharides	Polylysine dendrimers	HIV	Higher activity due to dendrimer product	11
Galactosylceramide analogues	Multivalent phosphorus-containing catanionic dendrimers	HIV-1	Higher stability and anti-viral property, lower toxicity	13
Doxorubicin	2,2 bis(hydroxymethyl) propanoic acid-based dendrimers	Colon carcinoma cells of rat	In vitro and in vivo, dendrimer product was ten times less toxic	14
SN38	G3.5 PAMAM dendrimers	Hepatic colorectal cancer cells	Increase oral bioavailability and decrease gastrointestinal toxicity	12
Boron	EGF-carrying PAMAM dendrimers	Neuron capture technology	Intratumoral injection or CED	41
EGFR siRNA	Dendriworms	Knockdown EGFR expression	IV or CED	42
Plasmid pEGFP-N2	Angiopep-carrying PEGylated PAMAM dendrimer G5.0	Encode green fluorescence protein	IV	43

Table-3: Drugs those can be delivered via Dendrimers

PAMAM= Poly(amido amine), PPE= poly (propyleneimine)

The most widely explored and used dendrimers are Poly-AmidoAmine (PAMAM) dendrimers. PAMAM dendrimers can facilitate transport through epithelial barrier which show their potential as a carrier for oral delivery. [44] These are also efficient as gene delivery system and in fact they have at least equal efficacy as other cationic carriers like polylysine. [45] Cationic dedrimers (G2 PAMAM, G3 PAMAM, PEGylated G3) can also be used as pulmonary delivery carriers to administer large molecular weight anionic drug like low molecular weight heparin. [46] Pulmonary delivery of Plasmid DNA by G9 PAMAM dendrimers was also reported. [47] PAMAM dendrimers are also used for ocular insert or patches. [48] Commercial dendrimer products for biomedical applications has also been produced i.e. **VivaGel™**, for prevention of sexually transmitted diseases and **SuperFect®** for gene transfection.

Incorporation of large amount of drug is possible into dendrimers because of its structural configuration. Various techniques like (a) adsorption to the surface, (b) encapsulation in hydrophobic microcavities and (c) direct covalent conjugation with surface active groups can be employed to do so. And due to these properties dendrimer can be used as a carrier of water soluble and water insoluble drugs simultaneously. [49]

LIPOSOMES

Liposomes are lipid vesicular systems which are composed of an aqueous core enclosed by natural or synthetic phospholipid bilayers. The aqueous core can be used to encapsulate hydrophilic drugs, and on the other hand, hydrophobic and amphiphilic drugs can be solubilized within the phospholipid bilayers. Depending on the structure of the lipid bilayers liposomes can be classified as (a) small unilamellar vesicles (SUV) (b) large unilamellar vesicles and (LUV) (c) multilamellar vesicles (MLVs).

Liposomes were first introduced for drug delivery as early as in 1965. [50] And in recent studies, these are the most widely used Nano-pharmaceutical carriers. Usually, liposomes are rapidly cleared from blood by phagocytic cells and they possess a low transport rate. But these

disadvantages can be overcome by coating the surface with a biocompatible and inert polymer such as PEG or by incorporating targeting ligands. [51]

Liposomal formulations are well researched for delivering chemotherapeutic and anticancer agents. Successful delivery of Placitaxel can be done by conjugating liposome with poly (d, l-lactic acid) - polyethylene glycol [PLA-PEG]. [52] Epirubicin uptake at the folate receptors of human cervical carcinoma cell was also observed with increased antiproliferative ability. [53] But, the main impact of liposomal formulations on cancer chemotherapy was observed in the combination therapies. (Table-4) Some pharmaceutical products like CPX-351 [54] and CPX-1 [55] are currently under clinical trials.

As liposomes, in their natural form, can be taken up by reticuloendothelial system, they can serve for macrophage delivery of antiretrovirals. Phillips et al delivered Zidovudine to macrophages by liposomal system. [56] Incorporation of ethanol into liposome increases the transdermal flux to form ethosomes. Studies were conducted incorporating antiretroviral drugs like Acyclovir, Indinavir and Lamivudine into these modified liposomal systems. [57], [58] Through various mechanisms liposomes enter into skin and steady state flux of drug through the skin is maximum for cationic liposomes, followed by anionic and neutral liposomes. [58]

Prospect of receptor-mediated delivery of drug molecules and nucleic acids to the brain was investigated by Pardridge et al. [59] Recently, sodium borocaptate (BSH) is successfully delivered to glioma cells using anti EGFR antibody-carrying immunoliposomes. [60] PEGylated liposomes were also researched to encapsulate vector/DNA plasmid complexes e.g. Polyethylenimine/Oligodeoxynucleotides and as a result, Oligodeoxynucleotides accumulation in the brain was considerably increased when transferrin receptorspecific antibody 8D3 was non-covalently bound to PEGylated liposomes. [61] Simultaneous encapsulation of topotecan and gadodiamide can also be done employing non-PEGylated liposomes and this has a prospective use in therapy of glioblastoma multiforme. [62] To deliver Serotonin, liposome is used as a secondary vehicle to transport it across BBB. [63]

In radiation based therapies, photosensitizers can be delivered via Liposomes. [64] Liposomes and very widely explored for Pulmonary and Ocular delivery of drugs. (Table-4 and 5) Liposomal formulations are delivered to the lung in liquid state and nebulizers are used for the aerosol delivery of liposomes. Recently, dry powder formulations have also been studied for pulmonary liposomes delivery. [65] Cationic liposomes facilitate transcorneal drug delivery as well as the anionic and neutral liposomes. It can also be mentioned that some pharmaceutical liposomal products have been included in the market e.g.Doxil/caylex (a liposome-based formulation of an anticancer drug Doxorubicin, Ortho-Biotech) and Alveofact® (a synthetic lung surfactant for pulmonary instillation for the treatment of respiratory distress syndrome, Dr Karl Thomae GmbH, Biberach, Germany).

Therapeutics	Type of Liposome	Indications	References
Topotecan+Vincristine	PEG-Liposome	Brain cancer	66
Irinotecan + Cisplatin	Mixture of two Liposomes	Small-cell lung cancer	67
siRNA + Doxorubicin	PEG-Liposome	MDR-breast cancer	68
Doxorubicin+Verapamil	Transferrin- (Tf-) conjugated PEG-Liposome	MDR-leukemia	69
Budesonide	Small molecular liposome	Asthma	70
Ketotifen	Small molecular liposome	Asthma	71
VEGF gene	Gene liposme	Pulmonary hypertension	72
Amiloride hydrochloride	Small molecular liposome	Cystic fibrosis	73
Tobramycin	Small molecular liposome	Pulmonary Infections	74
Interleukin-2	Protein liposome	Lung cancers	75
Insulin	Protein liposome	Diabetes	76

VEGF=Vascular endothelial growth factor

Table-4: Drugs those can be delivered via Liposomes

Drug	Type of Liposome	Effects	References
Diclofenac	Coated with low-molecular weight chitosan	High corneal permeation, better sustained drug release	77
Ciprofloxacin	Liposomal hydrogel	Fivefold higher transcorneal permeation	78
Demeclocycline	Not available	Effect of drug lasts for longer period of time	79
Plasmid DNA	Cationic liposomes	Increased transfection efficiency of pDNA	80

Table-5: Ophthalmic drugs those can be delivered via Liposomes

POLYMERIC NANOPARTICLES

Synthetic and semisynthetic polymers are a very potential media for Nano-technology based drug delivery as they provide a plethora of advantages like increased efficacy, lower toxicity, controlled release rates, sustained bioactivity, manufacturing reproducibility, higher stability, lesser administration frequency and capability of co-delivering drugs resulting in synergistic effects. [18] Some common polymers used for manufacturing nanoparticles intended for drug delivery are poly (lactic acid) [PLA], poly (lactic-co-glycolic acid) [PLGA], poly (ethylene glycol- co-(lactic-glycolic acid)), poly (methyl) methacrylate, poly (caprolactone) and poly (alkyl) cyanoacrylates. PNPs are often produced by pairing with PEG to provide prolonged systemic circulation time. [81]

Processes of drug loading into PNPs include entrapment, encapsulation and dissolution or dispersion. A wide spectrum of hydrophobic and hydrophilic drugs can be incorporated into these nanoparticles for drug delivery, tissue engineering and various other biomedical applications. Table-6 enlists some antiretroviral, brain targeted and anticancer drugs, and corresponding PNPs for nanotechnology based drug delivery .

Therapeutics	Type of polymer/ Functionalization	Indication/ Activity	Effects	References
Paclitaxel	Aptamer- PEG-PLGA	Gliomas	Enhanced delivery	82
Cisplatin	Aptamer- PEG-PLGA	Prostate cancer	Higher efficiency	83
Vincristine + Verapamil	PLGA	Hepatocellular carcinoma	Reduced multidrug resistance	23
Doxorubicin+Cyclosporine A	PACA	Various cancers	Synergistic effect.	84
Zidovudine	Poly (isohexyl cyanate)	Targeting lymphoid tissue	Drug levels is four times higher	15
Zidovudine	Polyhexylcyano acrylate	Targeting lymphoid tissue	Higher Zidovudine levels in the body	16
Stavudine	Polybutylcyano acrylate (PBCA)	HIV/AIDS	8–20 times higher Permeability	85
Lamivudine	Methylmethacrylate-sulfopropylmethacrylate	HIV/AIDS	100% increased BBB permeability	85
Nerve growth factor (NGF)	Polysorbate 80 coated PBCA	Parkinsonism	Improved transport across the BBB	86
Amphotericin B	PLA-b-PEG	Neurodegenerative diseases	Improved transport across the BBB	87

Table-6: Drugs those can be delivered via Polymeric Nanoparticles

PACA= Polyalkylcyanoacrylate, PLA-b-PEG =Polysorbate 80 coated poly(lactic acid)-b-poly(ethylene glycol), PLGA= poly (lactide-co-glycolide)

PNPs are also found effective in ophthalmic delivery. Transcorneal permeability of Flurbiprofen was increased when nanoparticles formulation was prepared with PLGA and polyepsilon-caprolactone. [88] These are also studied extensively for pulmonary delivery of antiasthmatic, [89] antituberculosis, [90] pulmonary hypertension, [91] and anticancer drugs.[92] But, the biodegradability and toxicity of PNP pulmonary formulation still need further close examination to avoid accumulation of polymer carriers after repeated dosing.

SOLID-LIPID NANOPARTICLES

SLNs are lipid-based nanoparticles systems and these fatty acids are either solid or semisolid at room temperature. These preparations provide increased physical stability, reduced degradation of drug, lower toxicity and relative ease in the production. [19] Altering SLNs properties, for example, by changing their lipid composition, surface charge and size site specificity and sustained release of drug can be accomplished. These can also be programmed so that SLNs formulations will release the drug in response an external stimulus such as pH or temperature. Solid lipid preparations provide greater drug stability and better control over drug kinetics than the liquid lipid formulations.

SLNs loaded with Doxorubicin increased apoptotic cell death very efficiently by higher accumulation of doxorubicin in cancer cells. [19] Anticancer agent Curcumin was also incorporated within transferrin-mediated SLNs for targeted delivery to breast cancer cells. [93] The first antiviral loaded SLN preparation contained Zidovudine Palmitate in which Trilaurin was used as the lipid core. [94] In this study, it was also reported that higher lipid content can lead to higher incorporation of drug in SLNs. And in another study, it was reported that surface modification with PEG moieties increased the plasma circulation of the drug. [95]

Brain delivery via SLNs drug delivery was first exploited regarding two anticancer agents - Camptothecin and Doxorubicin and accumulation of drug in the brain was successful. [96], [97] Antiviral agents Stavudine, Delavirdine, and Saquinavir were independently evaluated and here also, the incorporation efficacy of the drugs increased with increasing lipophilicity. [98] Because of entrapment of drug in SLNs, permeability was enhanced 4-11 times than traditional delivery. Drugs like Indomethacin, Ketoprofen, Isoniazid and pyrazinamide was reported to be targeted to the pulmonary system. [99], [100] SLNs have some limitations such as uncontrolled drug expulsion and low capacity of drug loading. To address these problems Nanostructure Lipid Carriers (NLCs) have been developed which contains a mixture of solid lipids and liquid lipids. [101] In these, liquid lipids like medium chain triglycerides can be added.

MICELLAR NANOPARTICLES

Amphiphilic molecules are those which possess polar/hydrophilic groups as well as non-polar/hydrophobic groups. Micellar Nanoparticles (MNs) can be defined as nanoparticles formed by amphiphilic molecules and usually they have a hydrophobic core within an aqueous phase. For drug delivery, MNs are mainly used to deliver poorly soluble drugs as micellar formulations increase their solubility and so, bioavailability as well. Moreover, hydrophobic compounds which have limitations in crossing BBB can be entrapped in MNs to avoid rapid blood clearance and degradation. Cholesterol-terminated PEG was modified with TAT peptide for transporting nanoparticles, loaded with Ciprofloxacin, to brain. [102] N-hexylcarbamoyl-5-fluorouracil (HCFU) is poorly water soluble drug. Nanogels of HCFU have been formulated by cross-linked polymeric micelles of Nisopropylacrylamide and N-vinylpyrrolidone and higher accumulation of HCFU in brain was reported. [20]

Lidocaine, a local anesthetic drug, can be encapsulated in MNs using PEG to form unimolecular micelles and a sustained release up to 50 hours can be achieved. [103] Prodrug of anticancer agent Placitaxel was prepared in MNs formulation using PEG-Polycaprolactone polymer and sustained release of as long as 14 days has been achieved. [104] Nanomicelles of copolymers have also been found effective for conjugating anti-cancer drugs. Combination of Placitaxel and siRNA is successfully developed; in which Placitaxel is encapsulated in the inner hydrophobic core and siRNA was complexed within outer hydrophobic shell. [105]

MISCELLANEOUS

There is several other nano-particulate and nano-structured systems available for drug delivery. There usability, though explored to a lower extent, is also very beneficial in novel drug delivery systems. Nanodiamonds (NDs) are effective agents in biomedical applications because of higher biocompatibility, minimum cytotoxicity, commercial availability and ease of purification. Functionalized NDs can serve as a delivery method for increased solubility and better targeting ability of drugs. [21] Various virus-based nano-carriers have also been documented for drug delivery in scientific literatures; Cowpea and Red clover mosaic viruses have been researched as successful viral nano-carrier.[106] Multifunctional Gold Nanoparticles, nanometre sized colloidal suspensions, demonstrated very stable and multipurpose platforms for drug delivery. [107] Nanoparticles of inorganic materials such as titanium, silicon dioxide, gold, and silver, copper have been found useful for numerous pharmaceutical applications and especially in cancer therapeutics. [108] Magnetic Nanoparticles is very effective in cell targeting and cell labelling of skin and have been proved to be beneficial for transdermal delivery. [109] Various lipid vesicles other than liposomes such as Transferosomes, Niosomes, Ethosomes and Bicelles have been developed and found efficient in treansdermal delivery. [110]

CONCLUSION

Richard Feynman rightly said that there is plenty of room at the bottom. And as our review presents the most important uses of nanotechnology in drug delivery, we

understand the wide spread applications of nanotechnology for betterment of human life. Numerous problems related to drug delivery, especially in cancer therapy, has been addressed successfully by nanotechnology; which engenders new hope within us. But, more studies on toxicology and immune systems induction should be carried out for implementation of these new technologies into mainstream health services.

REFERENCES

1. W.H. Fissell, H.D. Humes, A.J. Fleischman, S. Roy, Dialysis and Nanotechnology: Now, 10 Years, or Never, Blood Purification, 2007, 25(1), 12-17. http://www.ncbi.nlm.nih.gov/pubmed/17170531
2. C.R. Martin, Welcome to nanomedicine, Nanomedicine, 2006, 1(1), 5-5.
3. Taghdisi SM, Lavaee P, Ramezani M, Abnous K. Reversible targeting and controlled release delivery of daunorubicin to cancer cells by aptamer wrapped carbon nanotubes. Eur J Pharm Biopharm. 2011; 77:200–206. http://www.ncbi.nlm.nih.gov/pubmed/21168488
4. Liu Z, Fan AC, Rakhra K, Supramolecular stacking of doxorubicin on carbon nanotubes for in vivo cancer therapy. Angew Chem Int Ed Eng. 2009; 48:7668–7672. http://www.ncbi.nlm.nih.gov/pubmed/19760685
5. Ali-Boucetta H, Al-Jamal KT, McCarthy D, Prato M, Bianco A, Kostarelos K. Multiwalled carbon nanotube-doxorubicin supramolecular complexes for cancer therapeutics. Chem Commun (Camb). 2008; 4:459–461. http://www.ncbi.nlm.nih.gov/pubmed/18188467
6. Samori C, Ii-Boucetta H, Sainz R. Enhanced anticancer activity of multi-walled carbon nanotube-methotrexate conjugates using cleavable linkers. Chem Commun (Camb). 2010; 46:1494–1496. http://www.ncbi.nlm.nih.gov/pubmed/20162159
7. Liu Z, Chen K, Davis C. Drug delivery with carbon nanotubes for in vivo cancer treatment. Cancer Res. 2008; 68:6652–6660. http://www.ncbi.nlm.nih.gov/pubmed/18701489
8. Mahajan SD, Roy I, Xu G, Yong K-T, Ding H, Aalinkeel R. Enhancing the Delivery of Anti-Retroviral Drug "Saquinavir" Across the Blood Brain Barrier Using Nanoparticles. Current HIV Research. 2010; 9: 396-404. http://www.ncbi.nlm.nih.gov/pubmed/20426757
9. Zhao Y, Lin K, Zhang W, Liu L. Quantum dots enhance Cu2+-induced hepatic L02 cells toxicity. Journal of Environmental Sciences. 2010; 22: 1987-92. http://www.ncbi.nlm.nih.gov/pubmed/21462720
10. Dutta T, Jain NK. Targeting potential and anti-HIV activity of lamivudine loaded mannosylated poly(propyleneimine) dendrimer. Biochim Biophys Acta. 2007;1770(4):681–6. http://www.ncbi.nlm.nih.gov/pubmed/17276009
11. Roy R, Zanini D, Meunier SJ, Romanowska A. Solid-phase synthesis of dendritic sialoside inhibitors of influenza A virus haemagglutinin. J Chem Soc, Chem Commun. 1993; 24:1869–1872.
12. Goldberg DS, Vijayalakshmi N, Swaan PW, Ghandehari H.. G3.5 PAMAM Dendrimers Enhance Transepithelial Transport of SN38 while minimizing Gastrointestinal Toxicity. J Control Release. 201; 150(3): 318–325. http://www.ncbi.nlm.nih.gov/pubmed/21115079
13. Blanzat M, Turrin CO, Perez E, Rico-Lattes I, Caminade AM, Majoral JP. Phosphorus-containing dendrimers bearing galactosylceramide analogs: Self-assembly properties. Chem Commun (Camb). 2002; 17:1864–5. http://www.ncbi.nlm.nih.gov/pubmed/12271647
14. Lee CC, Gillies ER, Fox ME, Guillaudeu SJ, Fréchet JM, Dy EE, Szoka FC. A single dose of doxorubicin-functionalized bow-tie dendrimer cures mice bearing C-26 colon carcinomas. Proc Natl Acad Sci USA.2006;103:16649–54. http://www.ncbi.nlm.nih.gov/pubmed/17075050
15. Dembri A, Montisci M-J, Gantier JC, Chacun H, Ponchel G. Targeting of 3′-azido 3′-deoxythymidine (AZT)-loaded poly(isohexylcyanoacrylate) nanospheres to the gastrointestinal mucosa and associated lymphoid tissues. Pharm Res. 2001; 18(4):467–73. http://www.ncbi.nlm.nih.gov/pubmed/11451033
16. Lobenberg R, Maas J, Kreuter J. Improved body distribution of 14Clabelled AZT bound to Mataraza nanoparticles in rats determined by radioluminography. J Drug Target. 1998; 5(3):171–79. http://www.ncbi.nlm.nih.gov/pubmed/9606007
17. Cai D, Qin ZH. Highly efficient molecular delivery into mammalian cells using carbon nanotube spearing.Nat Methods. 2005; 2: 449–54. http://www.ncbi.nlm.nih.gov/pubmed/15908924
18. Brewer E, Coleman J, Lowman A. Emerging technologies of polymeric nanoparticles in cancer drug delivery. J Nanomater. 2011; 2011:1–10.
19. Kang KW, Chun MK, Kim O. Doxorubicin-loaded solid lipid nanoparticles to overcome multidrug resistance in cancer therapy. Nanomedicine. 2010; 6(2):210–13. http://www.ncbi.nlm.nih.gov/pubmed/20060074
20. Soni S, Babbar AK, Sharma RK, Maitra A. Delivery of hydrophobised 5-fluorouracil derivative to brain tissue through intravenous route using surface modified nanogels. J Drug Target 2006; 14:87– 95. http://www.ncbi.nlm.nih.gov/pubmed/16608735
21. Krueger A. New carbon materials: biological applications of functionalized nanodiamond materials. Chemistry. 2008; 14(5):1382–90. http://www.ncbi.nlm.nih.gov/pubmed/18033700
22. Li J, Wu C, Gao F, Zhang R, Lv G, Fu D. In vitro study of drug accumulation in cancer cells via specific association with CdS nanoparticles. Bioorganic & Medicinal Chemistry Letters. 2006; 16: 4808-12. http://www.ncbi.nlm.nih.gov/pubmed/16844372
23. X. R. Song, Y. Zheng, G. He. Development of PLGA nanoparticles simultaneously loaded with vincristine and verapamil for treatment of hepatocellular carcinoma," Journal of Pharmaceutical Sciences. 2010; 99(12): 4874– 79.
24. Sahoo NG, Bao H, Pan Y. Functionalized carbon nanomaterials as nanocarriers for loading and delivery of a poorly water-soluble anticancer drug: A comparative study. Chem Commun (Camb). 2011; 47: 5235–7. http://www.ncbi.nlm.nih.gov/pubmed/21451845
25. Bekyarova E, Ni Y, Malarkey EB. Applications of carbon nanotubes in biotechnology and biomedicine. J Biomed Nanotechnol. 2005; 1:3–17. http://www.ncbi.nlm.nih.gov/pubmed/19763242
26. Prato M, Kostarelos K, Bianco A. Functionalized carbon nanotubes in drug design and discovery. Acc Chem Res. 2008; 41:60–8. http://www.ncbi.nlm.nih.gov/pubmed/17867649
27. Kam NW, Dai H. Carbon nanotubes as intracellular protein transporters: Generality and biological functionality. J Am Chem Soc. 2005; 127:6021–6. http://www.ncbi.nlm.nih.gov/pubmed/15839702

28. Prajapati VK, Awasthi K, Gautam S. Targeted killing of Leishmania donovani in vivo and in vitro with amphotericin B attached to functionalized carbon nanotubes. J Antimicrob Chemother. 2011; 66:874–9. http://www.ncbi.nlm.nih.gov/pubmed/21393222
29. Hampel S, Kunze D, Haase D. Carbon nanotubes filled with a chemotherapeutic agent: A nanocarrier mediates inhibition of tumor cell growth. Nanomedicine. 2008; 3:175–182. http://www.ncbi.nlm.nih.gov/pubmed/18373424
30. Podesta JE, Al-Jamal KT, Herrero MA. Antitumor activity and prolonged survival by carbon-nanotube-mediated therapeutic siRNA silencingin a human lung xenograft model. Small. 2009; 5:1176–1185. http://www.ncbi.nlm.nih.gov/pubmed/19306454
31. Cai W, Shin DW, Chen K, Gheysens O, Cao Q, Wang SX. Peptide-Labeled Near-Infrared Quantum Dots for Imaging Tumor Vasculature in Living Subjects. Nano Lett. 2006;6:669-76. http://www.ncbi.nlm.nih.gov/pubmed/16608262
32. Savla R, Taratula O, Garbuzenko O, Minko T. Tumor targeted quantum dot-mucin 1 aptamer-doxorubicin conjugate for imaging and treatment of cancer. Journal of Controlled Release. 2011; 153 (1): 16-22. http://www.ncbi.nlm.nih.gov/pubmed/21342659
33. Mathew ME, Mohan JC, Manzoor K, Nair SV, Tamura H, Jayakumar R. Folate conjugated carboxymethyl chitosan-manganese doped zinc sulphide nanoparticles for targeted drug delivery and imaging of cancer cells. Carbohydrate Polymers.2010;80:442-8.
34. Xu G, Yong K-T, Roy I, Mahajan SD, Ding H, Schwartz SA. Bioconjugated Quantum Rods as Targeted Probes for Efficient Transmigration Across an in Vitro Blood−Brain Barrier. Bioconjugate Chem. 2008; 19: 1179-85. http://www.ncbi.nlm.nih.gov/pubmed/18473444
35. Ryman-Rasmussen JP, Riviere JE, Monteiro-Riviere NA. Penetration of intact skin by quantum dots with diverse physicochemical properties. Toxicol Sci. 2006; 91:159–165. http://www.ncbi.nlm.nih.gov/pubmed/16443688
36. Bonoiu A, Mahajan SD, Ye L, Kumar R, Ding H, Yong KT. MMP-9 gene silencing by a quantum dot-siRNA nanoplex delivery to maintain the integrity of the blood brain barrier. Brain Res 2009; 1282:142–55. http://www.ncbi.nlm.nih.gov/pubmed/19477169
37. Chakravarthy KV, Davidson BA. Helinski JD, Hong Ding MS, Law WC, Yong KT. Doxorubicin conjugated quantum dots to target alveolar macrophages/inflammation. Nanomedicine. 2011; 7(1): 88–96. http://www.ncbi.nlm.nih.gov/pubmed/20887813
38. du-Toit LC, Pillay V, Choonara YE. Nano-microbicides: Challenges in drug delivery, patient ethics and intellectual property in the war against HIV/AIDS. Adv Drug Deliv Rev. 2010; 62(4–5):532–46. http://www.ncbi.nlm.nih.gov/pubmed/19922751
39. Dutta T, Garg M, Jain NK. Targeting of efavirenz loaded tuftsin conjugated poly(propyleneimine) dendrimers to HIV infected macrophages in vitro. Eur J Pharm Sci. 2008;34(2–3):181–189. http://www.ncbi.nlm.nih.gov/pubmed/18501568
40. Weber N, Ortega P, Clemente MI. Characterization of carbosilane dendrimers as effective carriers of siRNA to HIV-infected lymphocytes. J Control Release. 2008;132(1):55–64. http://www.ncbi.nlm.nih.gov/pubmed/18727943
41. Yang W, Barth RF, Wu G, Huo T, Tjarks W, Ciesielski M. Convection enhanced delivery of boronated EGF as a molecular targeting agent for neutron capture therapy of brain tumors. J Neurooncol 2009; 95:355–65. http://www.ncbi.nlm.nih.gov/pubmed/20848301
42. Agrawal A, Min DH, Singh N, Zhu H, Birjiniuk A, von Maltzahn G, Harris TJ, Xing D, Woolfenden SD, Sharp PA, Charest A, Bhatia S. Functional delivery of siRNA in mice using dendriworms. ACS Nano 2009; 3:2495–504. http://www.ncbi.nlm.nih.gov/pubmed/19673534
43. Ke W, Shao K, Huang R, Han L, Liu Y, Li J, Kuang Y. Gene delivery targeted to the brain using an Angiopep-conjugated polyethyleneglycol-modified polyamidoamine dendrimer. Biomaterials 2009; 30:6976–85. http://www.ncbi.nlm.nih.gov/pubmed/19765819
44. Kitchens KM, Kolhatkar RB, Swaan PW, Eddington ND. Transport of poly(amidoamine) dendrimers across Caco-2 cell monolayers: influence of size, charge and fluorescent labeling. Pharm Res. 2006; 23:2818–26. http://www.ncbi.nlm.nih.gov/pubmed/17094034
45. Qin L, Pahud DR, Ding Y, Bielinska AU, Kukowska-Latallo JF, Baker JR, Efficient transfer of genes into murine cardiac grafts by Starburst polyamidoamine dendrimers. Hum Gene Ther.1998; 9:553–60. http://www.ncbi.nlm.nih.gov/pubmed/9525316
46. Bai S, Thomas C, Ahsan F. Dendrimers as a carrier for pulmonary delivery of enoxaparin, a low-molecular weight heparin. J Pharm Sci. 2007; 96:2090–106. http://www.ncbi.nlm.nih.gov/pubmed/17286291
47. Ziady AG, Gedeon CR, Miller T. Transfection of airway epithelium by stable PEGylated poly-L-lysine DNA nanoparticles in vivo. Mol Ther. 2003; 8:936–947. http://www.ncbi.nlm.nih.gov/pubmed/14664796
48. Wagh VD, Inamdar B, Samanta MK. Polymers used in ocular dosage form and drug delivery systems. Asian J Pharmaceutics. 2008;2:12–7.
49. L. Zhang, F. X. Gu, J. M. Chan, A. Z.Wang, R. S. Langer, and O. C. Farokhzad, Nanoparticles in medicine: therapeutic applications and developments. Clinical Pharmacology and Therapeutics. 2008; 83(5): 761–9.
50. A.D. Bangham, M.M. Standish, and J. C. Watkins. Diffusion of univalent ions across the lamellae of swollen phospholipids, Journal ofMolecular Biology. 1965; 13(1): 238–252. http://www.ncbi.nlm.nih.gov/pubmed/5859039
51. M. C. Woodle, Controlling liposome blood clearance by surface-grafted polymers, Advanced Drug Delivery Reviews. 1998; 32(1-2):139–52. http://www.ncbi.nlm.nih.gov/pubmed/10837640
52. Puri A, Kramer-Marek G, Campbell-Massa R. HER2-specific affibody-conjugated thermosensitive liposomes (Affisomes) for improved delivery of anticancer agents. J Liposome Res. 2008; 18(4): 293–307. http://www.ncbi.nlm.nih.gov/pubmed/18937120
53. Canal F, Vicent MJ, Pasut G, Schiavon O. Relevance of folic acid/polymer ratio in targeted PEG-epirubicin conjugates. J Control Release. 2010; 146(3):388–99. http://www.ncbi.nlm.nih.gov/pubmed/20621587
54. E. J. Feldman, J. E. Lancet, J. E. Kolitz. First-in-man study of CPX-351: a liposomal carrier containing cytarabine and daunorubicin in a fixed 5:1 molar ratio for the treatment of relapsed and refractory acute myeloid leukemia. Journal of Clinical Oncology, 2011; 29(8)979–85.

55. G. Batist, K. A. Gelmon, K. N. Chi, Safety, pharmacokinetics, and efficacy of CPX-1 liposome injection in patients with advanced solid tumors, Clinical Cancer Research, 2009; 15(2): 692–700. http://www.ncbi.nlm.nih.gov/pubmed/19147776
56. Phillips NC, Skamene E, Tsoukas C. Liposomal encapsulation of 3'-azido-3'-deoxythymidine (AZT) results in decreased bone marrow toxicity and enhanced activity against murine AIDS-induced immunosuppression. J Acquir Immune Defic Syndr. 1991; 4(10):959–66. http://www.ncbi.nlm.nih.gov/pubmed/1890605
57. Jain S, Tiwary AK, Sapra B, Jain N. Formulation and evaluation of ethosomes for transdermal delivery of lamivudine. AAPS PharmSciTech. 2007; 8(4):249–57. http://www.ncbi.nlm.nih.gov/pubmed/18181532
58. Dubey V, Mishra D, Nahar M, Jain V, Jain NK. Enhanced transdermal delivery of an anti-HIV agent via ethanolic liposomes. Nanomedicine. 2010; 6(4): 590-6. http://www.ncbi.nlm.nih.gov/pubmed/20093197
59. Pardridge WM, Boado RJ, Kang YS. Vector-mediated delivery of a polyamide (peptide) nucleic acid analogue through the blood-brain barrier in vivo. Proc Natl Acad Sci U S A. 1995; 92:5592–6. http://www.ncbi.nlm.nih.gov/pubmed/7777554
60. Feng B, Tomizawa K, Michiue H, Miyatake S, Han XJ, Fujimura A. Delivery of sodium borocaptate to glioma cells using immunoliposome conjugated with anti-EGFR antibodies by ZZ-His. Biomaterials 2009; 30:1746–55. http://www.ncbi.nlm.nih.gov/pubmed/19121537
61. Ko YT, Bhattacharya R, Bickel U. Liposome encapsulated polyethylenimine/ODN polyplexes for brain targeting. J Control Release 2009; 133:230–7. http://www.ncbi.nlm.nih.gov/pubmed/19013203
62. Grahn AY, Bankiewicz KS, Dugich-Djordjevic M, Bringas JR, Hadaczek P, Johnson GA, Eastman S, Luz M. Non-PEGylated liposomes for convection-enhanced delivery of topotecan an gadodiamide in malignant glioma: initial experience. J Neurooncol 2009; 95:185–97. http://www.ncbi.nlm.nih.gov/pubmed/19466380
63. Afergan E, Epstein H, Dahan R, Koroukhov N, Rohekar K, Danenberg HD, Golomb G. Delivery of serotonin to the brain by monocytes following phagocytosis of liposomes. J Control Release 2008; 132:84–90. http://www.ncbi.nlm.nih.gov/pubmed/18805446
64. A. Yavlovich, B. Smith, K. Gupta, R. Blumenthal, A. Puri. Light-sensitive Lipid-based Nanoparticles for Drug Delivery: Design Principles and Future Considerations for Biological Applications. Mol Membr Biol. 2010; 27(7): 364–81. http://www.ncbi.nlm.nih.gov/pubmed/20939770
65. Joshi M, Misra AN. Pulmonary disposition of budesonide from liposomal dry powder inhaler. Methods Find Exp Clin Pharmacol. 2001; 23:531–6. http://www.ncbi.nlm.nih.gov/pubmed/11957743
66. S. M. Lee, T. V. O'Halloran, and S. T. Nguyen, Polymercaged nanobins for synergistic cisplatin-doxorubicin combination chemotherapy. J Am. Chem. Society. 2010; 132(48): 17130–8. http://www.ncbi.nlm.nih.gov/pubmed/21077673
67. P. G. Tardi, N. Dos Santos, T. O. Harasym. Drug ratio-dependent antitumor activity of irinotecan and cisplatin combinations in vitro and in vivo. Molecular Cancer Therapeutics, 2009; 8(8):2266–75. http://www.ncbi.nlm.nih.gov/pubmed/19671743
68. Y. Chen, S. R. Bathula, J. Li, and L. Huang, Multifunctional nanoparticles delivering small interfering RNA and doxorubicin overcome drug resistance in cancer. J of Bio. Chem.2010; 285(29): 22639–50. http://www.ncbi.nlm.nih.gov/pubmed/20460382
69. J. Wu, Y. Lu, A. Lee. Reversal of multidrug resistance by transferrin-conjugated liposomes co-encapsulating doxorubicin and verapamil. Journal of Pharmacy and Pharmaceutical Sciences, 2007; 10(3), 350–7. http://www.ncbi.nlm.nih.gov/pubmed/17727798
70. Patton JS, Byron PR. Inhaling medicines: delivering drugs to the body through the lungs. Nat Rev Drug Discov. 2007; 6:67–74; 10(3):350–7.http://www.ncbi.nlm.nih.gov/pubmed/17195033
71. Brigger I, Dubernet C, Couvreur P. Nanoparticles in cancer therapy and diagnosis. Adv Drug Deliv Rev. 2002; 54:631–51. http://www.ncbi.nlm.nih.gov/pubmed/12204596
72. Azarmi S, Roa WH, Lobenberg R. Targeted delivery of nanoparticles for the treatment of lung diseases. Adv Drug Deliv Rev. 2008; 60:863–75. http://www.ncbi.nlm.nih.gov/pubmed/18308418
73. Konduri KS, Nandedkar S, Duzgunes N, Efficacy of liposomal budesonide in experimental asthma. J Allergy Clin Immunol. 2003; 111:321–7. http://www.ncbi.nlm.nih.gov/pubmed/12589352
74. Joshi M, Misra A. Disposition kinetics of ketotifen from liposomal dry powder for inhalation in rat lung. Clin Exp Pharmacol Physiol. 2003; 30:153–6. http://www.ncbi.nlm.nih.gov/pubmed/12603343
75. Ohashi K, Kabasawa T, Ozeki T, Okada H. One-step preparation of rifampicin/poly(lactic-co-glycolic acid) nanoparticle-containing mannitol microspheres using a four-fluid nozzle spray drier for inhalation therapy of tuberculosis. J Control Release. 2009; 135: 19–24. http://www.ncbi.nlm.nih.gov/pubmed/19121349
76. Huang YY, Wang CH. Pulmonary delivery of insulin by liposomal carriers. J Control Release. 2006; 113:9–14. http://www.ncbi.nlm.nih.gov/pubmed/16730838
77. Li N, Zhuang C, Wang M, Sun X, Nie S, Pan W. Liposome coated with low molecular weight chitosan and its potential use in ocular drug delivery. Int J Pharm.2009; 379(1):131–8. http://www.ncbi.nlm.nih.gov/pubmed/19559775
78. K. M. Hosny, Ciprofloxacin as ocular liposomal hydrogel. AAPS PharmSciTech. 2010; 11(1): 241–6. http://www.ncbi.nlm.nih.gov/pubmed/20151337
79. Afouna MI, Khattab IS, Reddy IK. Preparation and characterization of demeclocycline liposomal formulations and assessment of their intraocular pressure-lowering effects. Cutan Ocul Toxicol. 2005; 24(2):111–24. http://www.ncbi.nlm.nih.gov/pubmed/17040889
80. S. Kawakami, A. Harada, K. Sakanaka. In vivo gene transfection via intravitreal injection of cationic liposome/plasmid DNA complexes in rabbits. Int J Pharm. 2004; 278(2): 255–62. http://www.ncbi.nlm.nih.gov/pubmed/15196630
81. Owens DE 3rd, Peppas NA. Opsonization, biodistribution, and pharmacokinetics of polymeric nanoparticles. Int J Pharm. 2006; 307(1):93–102. http://www.ncbi.nlm.nih.gov/pubmed/16303268
82. Guo J, Gao X, Su L. Aptamer-functionalized PEG-PLGA nanoparticles for enhanced anti-glioma drug delivery. Biomaterials. 2011; 32(31):8010–20. http://www.ncbi.nlm.nih.gov/pubmed/21788069
83. Dhar S, Gu FX, Langer R, Farokhzad OC, Lippard SJ. Targeted delivery of cisplatin to prostate cancer cells by aptamer functionalized Pt(IV) prodrug-PLGA-PEG nanoparticles. Proc Natl Acad Sci U S A. 2008; 105(45):17356–61. http://www.ncbi.nlm.nih.gov/pubmed/18978032

84. C. Emilienne Soma, C. Dubernet, D. Bentolila, S. Benita, and P. Couvreur. Reversion of multidrug resistance by coencapsulation of doxorubicin and cyclosporin A in polyalkylcyanoacrylate nanoparticles. Biomaterials, 2000; 21(1):1–7. http://www.ncbi.nlm.nih.gov/pubmed/10619673
85. Kuo Y-C, Chen H-H. Effect of nanoparticulate polybutylcyanoacrylate and methylmethacrylate-sulfopropylmethacrylate on the permeability of zidovudine and lamivudine across the in vitro blood-brain barrier. Int J Pharm. 2006; 327(1–2):160–9. http://www.ncbi.nlm.nih.gov/pubmed/16939704
86. Kurakhmaeva KB, Djindjikhashvili IA, Petrov VE, Balabanyan VU, Voronina TA, Trofimov SS, Kreuter J, Gelperina S, Begley D, Alyautdin RN. Brain targeting of nerve growth factor using poly (butyl cyanoacrylate) nanoparticles. J Drug Target 2009; 17:564–74. http://www.ncbi.nlm.nih.gov/pubmed/19694610
87. Ren T, Xu N, Cao C, Yuan W, Yu X, Chen J, Ren J. Preparation and therapeutic efficacy of polysorbate-80-coated amphotericin B/PLA-b-PEG nanoparticles. J Biomater Sci Polym Ed 2009; 20:1369–80. http://www.ncbi.nlm.nih.gov/pubmed/19622277
88. Valls R, Vega E, Garcia ML, Egea MA, Valls JO. Transcorneal permeation in a corneal device of non-steroidal anti-inflammatory drugs in drug delivery systems. Open Med Chem J. 2008; 2:66–71. http://www.ncbi.nlm.nih.gov/pubmed/19662145
89. Seong JH, Lee KM, Kim ST, Jin SE, Kim CK. Polyethyleniminebased antisense oligodeoxynucleotides of IL-4 suppresses the production of IL-4 in a murine model of airway inflammation. J Gene Med. 2006; 8:314–23. http://www.ncbi.nlm.nih.gov/pubmed/16292779
90. Pandey R, Sharma A, Zahoor A, Sharma S, Khuller GK, Prasad B. Poly(DL-lactide-co-glycolide) nanoparticle-based inhalable sustained drug delivery system for experimental tuberculosis. J Antimicrob Chemother. 2003; 52:981–6. http://www.ncbi.nlm.nih.gov/pubmed/14613962
91. Kimura S, Egashira K, Chen L. Nanoparticle-mediated delivery of nuclear factor {kappa}B decoy into lungs ameliorates monocrotaline-induced pulmonary arterial hypertension. Hypertension. 2009; 53(5):877-83. http://www.ncbi.nlm.nih.gov/pubmed/19307469
92. Azarmi S, Tao X, Chen H. Formulation and cytotoxicity of doxorubicin nanoparticles carried by dry powder aerosol particles. Int J Pharm. 2006; 319:155–61. http://www.ncbi.nlm.nih.gov/pubmed/16713150
93. Mulik RS, Mönkkönen J, Juvonen RO, Mahadik KR, Paradkar AR. Transferrin mediated solid lipid nanoparticles containing curcumin: enhanced in vitro anticancer activity by induction of apoptosis. Int J Pharm. 2010; 398(1–2):190–203. http://www.ncbi.nlm.nih.gov/pubmed/20655375
94. Heiati H, Tawashi R, Shivers RR, Phillips NC. Solid lipid nanoparticles as drug carriers. I. Incorporation and retention of the lipophilic prodrug 3'-azido-3'-deoxythymidine palmitate. Int J Pharm. 1997; 146(1):123–31.
95. Heiati H, Tawashi R, Phillips NC. Solid lipid nanoparticles as drug carriers: II. Plasma stability and biodistribution of solid lipid nanoparticles containing the lipophilic prodrug 3'-azido-3'-deoxythymidine palmitate in mice. Int J Pharm. 1998; 174(1–2):71–80.
96. Yang S, Zhu J, Lu Y, Liang B, Yang C. Body distribution of camptothecin solid lipid nanoparticles after oral administration. Pharm Res. 1999; 16(5):751–757. http://www.ncbi.nlm.nih.gov/pubmed/10350020
97. Zara GP, Cavalli R, FundarÒ A, Bargoni A, Caputo O, Gasco MR. Pharmacokinetics of doxorubicin incorporated in solid lipid nanospheres (SLN).Pharmacol Res.1999;40(3):281–6. http://www.ncbi.nlm.nih.gov/pubmed/10479474
98. Jin C, Bai L, Wu H, Liu J, Guo G, Chen J. Paclitaxel-loaded poly(D,L-lactide-co-glycolide) nanoparticles for radiotherapy in hypoxic human tumor cells in vitro. Cancer Biol Ther. 2008; 7(6):911–6. http://www.ncbi.nlm.nih.gov/pubmed/18367873
99. Schreier H, Gonzalez-Rothi RJ, Stecenko AA. Pulmonary delivery of liposomes. J Control Release. 1993; 24:209–23.
100. Beaulac C, Sachetelli S, Lagace J. Aerosolization of low phase transition temperature liposomal tobramycin as a dry powder in an animal model of chronic pulmonary infection caused by Pseudomonas aeruginosa. J Drug Target. 1999; 7:33–41. http://www.ncbi.nlm.nih.gov/pubmed/10614813
101. Patlolla RR, Chougule M, Patel AR, Jackson T, Tata PN, Singh M. Formulation, characterization and pulmonary deposition of nebulized celecoxib encapsulated nanostructured lipid carriers. J Control Release. 2010; 144:233–41. http://www.ncbi.nlm.nih.gov/pubmed/20153385
102. Liu L, Guo K, Lu J, Venkatraman SS, Luo D, Ng KC, Ling EA, Moochhala S, Yang YY. Biologically active core/shell nanoparticles self-assembled from cholesterol-terminated PEG-TAT for drug delivery across the blood-brain barrier. Biomaterials 2008; 29:1509–17. http://www.ncbi.nlm.nih.gov/pubmed/18155137
103. Yang X, Zhu B, Dong T, Pan P, Shuai X, Inoue Y. Interactions between an anticancer drug and polymeric micelles based on biodegradable polyesters. Macromol. Biosci 2008; 8(12):1116-25. http://www.ncbi.nlm.nih.gov/pubmed/18663739
104. Forrest ML, Yanez JA, Remsberg CM, Ohgami Y, Kwon GS, Davies NM. Paclitaxel prodrugs with sustained release and high solubility in poly (ethylene glycol)-b-poly (ε-caprolactone) micelle nanocarriers: pharmacokinetic disposition, tolerability, and cytotoxicity. Pharm. Res 2008; 25(1):194–206. http://www.ncbi.nlm.nih.gov/pubmed/17912488
105. C. Zhu, S. Jung, S. Luo. Co-delivery of siRNA and paclitaxel into cancer cells by biodegradable cationic micelles based on PDMAEMA-PCL-PDMAEMA triblock copolymers, Biomaterials, 2010; 31(8): 2408–16.
106. Sherman MB, Guenther RH, Tama F. Removal of divalent cations induces structural transitions in red clover necrotic mosaic virus, revealing a potential mechanism for RNA release. J Virol. 2006; 80(21):10395–406. http://www.ncbi.nlm.nih.gov/pubmed/16920821
107. Han G, Ghosh P, Rotello VM. Multi-functional gold nanoparticles for drug delivery. Adv Exp Med Biol. 2007; 620:48–56. http://www.ncbi.nlm.nih.gov/pubmed/18217334
108. Porcel E, Liehn S, Remita H. Platinum nanoparticles: A promising material for future cancer therapy. Nanotechnology. 2010; 21(8):85103. http://www.ncbi.nlm.nih.gov/pubmed/20101074
109. Baroli B, Ennas MG, Loffredo F, Isola M, Pinna R, López-Quintela MA. Penetration of metallic nanoparticles in human full-thickness skin. J Invest Dermatol. 2007; 127:1701–12.
110. Elsayed MM, Abdallah OY, Naggar VF, Khalafallah NM. Lipid vesicles for skin delivery of drugs: Reviewing three decades of research. Int J Pharm. 2007; 332:1–16. http://www.ncbi.nlm.nih.gov/pubmed/17222523.

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