BioImpacts, **2012**, 2(2), 71-81
doi: 10.5681/bi.2012.011
http://bi.tbzmed.ac.ir/

Nanocapsules: The Weapons for Novel Drug Delivery Systems

Pavankumar Kothamasu[1*], Hemanth Kanumur[2], Niranjan Ravur[2], Chiranjeevi Maddu[1], Radhika Parasuramrajam[2], Sivakumar Thangavel[1]

[1]*Department of Pharmacy, Nandha College of Pharmacy and Research Institute, Tamilnadu, India*
[2]*Department of Pharmaceutics, Nandha College of Pharmacy and Research Institute, Tamilnadu, India*

ARTICLE INFO

Article Type:
Review Article

Article History:
Received: 24 Aug 2011
Revised: 31 March 2012
Accepted: 04 April 2012
ePublished: 05 April 2012

Keywords:
Nanocapsules
Encapsulation
Drug Delivery Systems
Nanocapsule Bandages
Targeted Drug Release

ABSTRACT

Introduction: Nanocapsules, existing in miniscule size, range from 10 nm to 1000 nm. They consist of a liquid/solid core in which the drug is placed into a cavity, which is surrounded by a distinctive polymer membrane made up of natural or synthetic polymers. They have attracted great interest, because of the protective coating, which are usually pyrophoric and easily oxidized and delay the release of active ingredients. ***Methods:*** Various technical approaches are utilized for obtaining the nanocapsules; however, the methods of interfacial polymerization for monomer and the nano-deposition for preformed polymer are chiefly preferred. Most important characteristics in their preparation is particle size and size distribution which can be evaluated by using various techniques like X-ray diffraction, scanning electron microscopy, transmission electron microscopy, high-resolution transmission electron microscopy, X-ray photoelectron spectroscopy, superconducting quantum interference device, multi angle laser light scattering and other spectroscopic techniques. ***Results:*** Nanocapsules possessing extremely high reproducibility have a broad range of life science applications. They may be applied in agrochemicals, genetic engineering, cosmetics, cleansing products, wastewater treatments, adhesive component applications, strategic delivery of the drug in tumors, nanocapsule bandages to fight infection, in radiotherapy and as liposomal nanocapsules in food science and agriculture. In addition, they can act as self-healing materials. ***Conclusion:*** The enhanced delivery of bioactive molecules through the targeted delivery by means of a nanocapsule opens numerous challenges and opportunities for the research and future development of novel improved therapies.

Introduction

Nanocapsules, as characteristic class of nanoparticles, are made up of one or more active materials (core) and a protective matrix (shell) (Benita 1998) in which the therapeutic substance may be confined. The nanocapsules have attracted great interest because of their protective coating, which is usually pyrophoric and easily oxidized. Nanoparticles have also been extensively investigated as drug carriers and for the past five decades, many of such carriers in the nanometer range have been in development. Most of them are used in cancer therapy and diagnosis. Anticancer drugs are embedded in or conjugated with inert nanocarriers and are referred as nanomedicines. They are therapeutically more advantageous over free drugs; however, the inert carrier materials acting as major component (generally more than 90%) possess low drug loading contents and thus, necessitate excessive use of parenteral excipients (Shen *et al* 2010). Their main advantages are namely sustained release, incremental drug selectivity and effectiveness, improvement of drug bioavailability and alleviation of drug toxicity. Nanocapsules, which are submicron in size, when administered intravenously, reach to the target and release the encapsulated drug.

Polymeric nanoparticles are named nanocapsules (Jager *et al* 2007) when they contain a polymeric wall composed of non-ionic surfactants, macromolecules, phospholipids (Beduneau *et al* 2006, Mohanraj *et al* 2006) and an oil core (Adriana *et al* 2008). These are prepared mostly by two technologies: the interfacial polymerization and interfacial nano-deposition.

Nanocapsules, holds the biomedical interest because they can be used, for the controlled release and targeting of drugs against the protection of enzymes, proteins, and foreign cells, etc. (Diaspro *et al* 2002).

***Corresponding author:** Pavankumar Kothamasu (Master of Pharmacy), Tel./Fax: +91-9843510962, E-mail**:** kpk34field@gmail.com

The interest in research on magnetic nanocapsules has increased considerably because of their intermediate states between mass and atomic materials. These materials may present different magnetic behaviors from their corresponding counterparts. Researchers in China have succeeded in synthesizing a new type of inter-metallic nanocapsule that can be applied in cryogenic magnetic refrigerator devices (Berger 2006).

Some drugs find difficulty in marketing due to their unpleasant side effects. However, when they are placed inside the cavity of nanocapsule, they deliver drug directly to the target site in a reducible dosage (10,000 fold) and thus lead significantly to the removal of any side effects or at least an appropriate acceptable level (Radhika *et al* 2011).

Due to the miniscule size, nanocapsules possess greater capability to take on an extensive range of applications with extremely high efficient reproducibility. The production of nanocapsules depends on their application and pharmaceutical, biochemical, electrical, optical or magnetic characteristics. The enhanced delivery of bio-active molecules through the targeted delivery by means of a nanocapsule provides numerous challenges and opportunities for the research and future development of novel improved therapies.

Materials and methods

Polymers

Gum Arabica, Hydroxypropylmethylcellulose (HPMC), Hydroxypropoxymethylcellulose, Phthalate (HPMCP), semisynthetic polymers such as diacyl beta cyclodextrin and synthetic polymers such as poly (D, L lactide), poly (E-caprolactone), poly (alkylcyanoacrylate) and a broad range of oils used for the preparation of nanocapsules including vegetable or mineral oils and pure compounds such as ethyl oleate and benzyl benzoate (Bruce 1993, Wan *et al* 1992). The dispersion of preformed polymers is frequently utilized for the preparation of biodegradable nanoparticles from poly (lactic acid) (PLA), poly (D, L-glycolide), PLG, poly (D, L-lactide-co-glycolide) (PLGA) and poly (cyanoacrylate) (PCA) (Kompella *et al* 2003, Kumar *et al* 2004, Li *et al* 2001). Both hydrophilic and lipophilic surfactants can be used to stabilize the nanocapsules (Adriana *et al* 2007, Xinfei *et al* 2010). Generally, the lipophilic surfactant is a natural lecithin of relatively low phosphatidylcholine content whereas hydrophilic one is synthetic: anionic (laryl sulphate), cationic (quatery ammonium), or more commonly nonionic [poly (oxyethylene) – poly (propylene) glycol]. Nanocapsules can be prepared in the absence of surfactants; however, aggregation during storage limits this condition.

Preparation of nanocapsules

Nanocapsules composition

Nanocapsules comprise of an oily or an aqueous core, which is surrounded by a thin polymer membrane (Dongwoo *et al* 2010). Two technologies have been utilized for obtaining such nanocapsules: the interfacial polymerization for monomer and the interfacial nano-deposition method for preformed polymer. The development in technologies in pharmaceutical research field has been spread widely in designing of the tumor targeting nano-scale vectors, capable of delivering radionuclides. Among them, the lipid nanocapsules (LNCs) as a nanovector-based formulation with bio-mimetic properties (Heurtault *et al* 2002) shows to be an applicable therapeutic option for HCC (Hepatocellular carcinoma) treatment (Jason *et al* 2002, Cha *et al* 2010). It is composed of a liquid lipid core, which is surrounded by a shell of tensioactive. LNCs results in the encapsulation of a lipophilic composite of radioactive Rhenium-188 (Hsieh *et al* 1999).

The capsules are constructed in several steps layer by layer:

1. In capsule preparation, the positively or negatively surface charged polymer addition comprises the first actual step.

2. Second step utilizes layer by layer self-assembling to form an ultrathin polymer film. Each new layer has the opposite charge to that of previous layer. The polymer coating is thrown by electrostatic gravities. They create shells of well ordered polyelectrolyte complex layers. This will result in capsule walls with 4 to 20 layers with a thickness of 8-50 nm.

The completed capsules will possess precise properties. Additional functions are often taken on by their surfaces for instance to provide connections for antibodies to dock.

It is optional that in the case of demand, the core of the capsule can be removed or various substances can fill the empty capsule shells.

Researchers suggest a number of approaches for preparing nanocapsules, but mostly four different approaches are utilized, namely: methods of interfacial polymerization or interfacial precipitation or interfacial nano-deposition, and self-assembly methods. For designing the optimized drug carrier systems, each procedure

offers its advantages and disadvantages. Nanocapsules can also be prepared according to the nanoprecipitation method.

The preparation of nanocapsules involving the organic phase which constitutes solvent, polymer, oil, and drug is penetrated into the pores of an ultrafiltration membrane via the filtrate side and then it is pressed. The aqueous phase containing water and surfactant circulates inside the membrane module, and removes the nanocapsules forming at the pore outlets.

Methods of preparation

Polymerization method

The monomers are polymerized in an aqueous solution to form nanoparticles followed by placing the drug either by dissolving in the medium of polymerization or by the adsorption of nanoparticles. Ultracentrifugation method, which has been utilized for purifying the nanoparticle suspension, removes various stabilizers and surfactants employed for polymerization. The nanoparticles are then resuspended in an isotonic surfactant free medium. It has been suggested for making polybutylcyanoacrylate or polyalkylcyanoacrylate nanoparticles (Qiang *et al* 2001, Boudad *et al* 2001). The formation of nanocapsules and their particle size depends on the usage concentration levels of the surfactants and physical and chemical stabilizers (Puglisi *et al* 1995). Based on a phase-inversion process, the nanoparticles are formulated and the results suggest a mean diameter range of 20 nm-100 nm, depending on the excipients quantity.

Interfacial polymerization

Interfacial polymerization (Lambert *et al* 2000, Morgan 1987, Jang *et al* 2006) is an alternative to bulk polymerization of condensation polymers, which would require high temperatures. It comprises of two immiscible solvents, in which monomer in one solvent instantaneously reacting with monomer of the other solvent or it may depend on the time scale. Higher molecular weights of monomers are obtained since it is more likely to stumble upon a growing chain than the opposing monomer. For instance, the nanocapsules can be formulated by using the aqueous core containing oligonucleotides of isobutylcyanoacrylate in a W/O emulsion. The resultant nanocapsules are then purified by ultracentrifugation followed by resuspending in water to yield a dispersion of aqueous core nanocapsules.

Arc-discharge method

Arc-discharge (Song *et al* 2006) has rarely been employed in synthesizing aggregates of self-assembled nanocapsules. The method has been developed with modified strategies into a new way of synthesizing the aggregates (Yosida *et al* 1994, Ziyi *et al* 2000), for example by involving changes in the hydrogen pressure, introducing a gadolinium–aluminium alloy ($GdAl_2$) ingot as the anode, and adjusting the proportions of elements in the anode according to their evaporation pressures, to synthesize a new type of nanocapsule, with the intermetallic compound $GdAl_2$ as the core and amorphous Al_2O_3 as the shell, that enlarges the family of magnetic nanocapsules. At the same time, regularly aligned three-dimensional macroaggregates self-assembled by the nanocapsules without any template and catalyst were simultaneously synthesized in an arc-discharge process (Zhang *et al* 2004).

Emulsion polymerization

Pre-emulsion preparation (Yang *et al* 2008) for one of the nanocapsules (M-6) is provided as an example. The preemulsion was synthesized by blending two parts; Part I contained 40 g styrene, 0.8 g DVB (divinylbenzene) , 0.82 g AIBN (2,2′-azobisisobutyronitrile) and 40 g Desmodur BL3175A; and Part II contained 1.71 g SDS (sodium dodecyl sulfate), 1.63 g Igepal CO-887, and 220 g water. Parts I and II were magnetically blended in separate containers for 10 minutes. Part II was then added to Part I under mechanical agitation and the contents were stirred at 1,800 rpm for 30 minutes. The resulting preemulsion was cooled to <5°C before sonication using a Misonix sonicator 3000 (until a particle size <250 nm was achieved). The pre-emulsion (Jackson *et al* 1991) was transferred to a three-neck round bottom flask, which was equipped with a mechanical stirrer, reflux condenser, and a nitrogen inlet, and degassed for 30 minutes. The temperature was increased to 70°C and preserved for 8 hours to complete the polymerization. Other preparation methods for nanocapsules include electron irradiation deposition (Sung *et al* 2007), chemical vapor deposition (Kimberly *et al* 2004), laser vaporization-condensation (Samy *et al* 1996), charge transferring (Kensuke *et al* 2003), organic reagent assisted method (Qingyi *et al* 2002), solution-liquid-solid method (Boal *et al* 2000) and catalytic vapor-liquid-solid growth (Zhu *et al* 2001).

Encapsulation of nanocapsules

Recent advances in the encapsulation technology has been utilized to formulate micro/nanocapsules with their explicit application properties displayed in Table 1 used in food, (Stenekes *et al* 2001) biology, (Sarah *et al* 2009) and medicine (Sarah *et al* 2009).

Most encapsulation techniques employ isocyanates in either solvent or bulk to construct shell (or matrix) materials for the encapsulation of functional materials and releasable fill materials (Matkan *et al* 1987), or making pressure on sensitive copying paper (Irii *et al* 1987). Encapsulation delays the release of drug from nanocapsules, e.g., Xerogels and Aerosil 200 that are used as the encapsulated materials (Arenas *et al* 2006). The Aerosil 200 has the strong drawback as bursting the nanocapsule. To diminish the burst release of drugs from xerogel mesopores, different strategies have been

proposed (Slowing *et al* 2007). To avoid a high burst release, it has been suggested to use polymeric nanocapsules as coating material for the agglomerates of drug-loaded xerogel. This complex architecture considers that the polymeric nanocapsules are hydrophobic and, consequently, they could retard the contact of the microparticles with water (continuous phase), avoid a burst and delay the drug release. Although by the technique of fabrication which encapsulates the nanocapsule hydrophilic DNA in an oily core, it meets the criteria for blood injection (Vonarbourg *et al* 2009).

Characterization of nanocapsules

Particle size

Particle size and size distribution plays a crucial role in nanocapsule systems and it establishes the *in vivo* distribution, bioavailability, toxicity and the targeting capacity of nanoparticulate systems. It also quite often influences the capacity of drug loading, drug release and the stability of nanoparticulate systems. Depend on the particle size the effect of releasing dosage and the time lapse of pharmacological action is the basis. The smaller particles have greater surface area; therefore, most of the therapeutic agents associated at or near to the surface particle, lead to instant drug release, whereas, the larger particles having the large core surfaces gradually diffuse out (Redhead *et al* 2001). Particle size can also affect the polymer degradation. For example, the rate of poly (D, L-lactide-co-glycolide) (PLGA) polymer degradation revealed an enhancement with an increase in particle size *in vitro* (Dunne *et al* 2000). Photoncorrelation spectroscopy or dynamic light scattering are used to determine the particle size (Repka *et al* 2002).

Surface properties of the nanocapsules

In view of drug targeting by means of nanocapsules, it is necessary to diminish opsonization and lengthen their circulation *in vivo*, (Jang *et al* 2006) which is succeeded by (a) surface coating of nanocapsules with addition of hydrophilic polymers and/or hydrophilic surfactants, and (b) formulation of nanocapsules with their biodegradable copolymers of hydrophilic segments like poly-ethylene glycol (PEG), poly-ethylene oxide (PEO), poly-oxamer, polo-xamine and poly-sorbate 80 (Tween 80). The zeta potential of nanocapsule is efficiently used to characterize charge on the surface property of nanocapsule (Couvreur *et al* 2002).

Fluorescence quenching

Quenching of fluorescence (Lambert *et al* 2000) is mainly utilized to confirm the localization of nanocapsules, which contains the aqueous core containing oligonucleotides (Daniel *et al* 2010, Bingyun *et al* 2003).

Evaluation studies

X-Ray Diffraction (XRD) studies

Phase analysis of the products is performed by powder XRD on a Rigaku D/max-2000 diffractometer with graphite monochromatized CuKα ($\lambda = 0.154\ 056$ nm) at a voltage of 50 kV and a current of 250 mA. The XRD pattern shows the phase composition of prepared products (Aiyer *et al* 1995).

Table 1. Materials used for encapsulation of nanocapsules

Encapsulation Material	Application	References
Aqueous monomers (ethylene diamine, hexamethylene diamine, and 1,4-diaminobutane)	Profound effects on the drug (curcuminoid) loading capacity	Redhead *et al* 2001
Chitosan, gelatin, and alginate	Hydrophilicity of artemisinin (ART) crystals was improved after encapsulation.	Lboutounne *et al* 2004
Isocyanates have been successfully encapsulated into polystyrene, and hydroxyl and amine functionalized nanospheres using a commercially available blocked isocyanate.	The thermally dissociated isocyanate can be utilized as an active functional group in coatings and adhesive applications.	Haolong *et al* 2011
Poly (epsilon-caprolactone)	Reduces the percutaneous drug absorption through stripped skin	Salaun *et al* 2009
Poly (isobutylcyanoacrylate) (PIBCA)	Targeting action	Yang *et al* 2008
Spherical hybrid assemblies based on cationic surfactants and anionic porous polyoxometalate nanocapsules $[\{(Mo)Mo_5O_{21}(H_2O)_6\}_{12}\{Mo_2O_4(SO_4)\}_{30}]^{72-}$ (Mo_{132} for short) are fabricated by the method combining an electrostatic encapsulation process.	Not only presents a new route to assemble Mo_{132} nanocapsules but also demonstrates a new concept of using the microenvironment of supramolecular assemblies to adjust the ion-trapping properties of Mo_{132}	Youfang *et al* 2009, Ingersoll *et al* 2005
Xerogels	To diminish the burst release of drugs from xerogel mesopores instead to Aerosil 200	Adriana *et al* 2008

Scanning Electron Microscopy (SEM)

The architecture of the hierarchical branching aggregates, characterized from nanocapsules, may be of flocculent structure, small clusters, big clusters and big branches step by step at different scales, which confirms the self-similar attributes of the structure (Watnasirichaikul *et al* 2000). It is characterized by a Philips XL-30 scanning electron microscope (SEM) which shows at a high magnification the clear morphology of small clusters. The clusters are composed of flocculent structure formed by the small particles adhered together (Sung *et al* 2007). A low-magnification SEM image may reveal the coral-like architecture that contains hierarchical branching characteristics along the axial and lengthwise directions.

Differential Scanning Calorimetry (DSC)

DSC analysis is conducted in both open samples (no lid) and closed samples (pan capped possessing a small hole in the center). Both methods have similar thermal behavior as per the observations reported (Douglas *et al* 1999).

Transmission Electron Microscopy (TEM)

The transport of particularly insulin-loaded nanocapsules across the epithelium can be assessed by transmission electron microscopy after their oral administration to experimental rats when they are subjected to *in vitro* and *in vivo* studies (Kepczynski *et al* 2009, Huguette *et al* 2003). TEM observations indicate the intestinal absorption of biodegradable nanocapsules leading to the transport of insulin across the epithelium mucosa.

High-Resolution Transmission Electron Microscopy (HRTEM)

The detailed morphology of the corresponding nanocapsules examined by means of high-resolution transmission electron microscopy clearly shows the shell/core structure of the nanocapsules (Song *et al* 2006, Zhang *et al* 2001). The morphology of nanocapsules constructing the aggregates is tested from the low-magnification TEM images.

X-Ray Photoelectron Spectroscopy (XPS)

X-ray photoelectron spectroscopy measurements are performed on an ESCALAB-250 with a monochromatic x-ray source (an aluminium Kα line of 1486.6 eV energy and 150 W) to describe the valency of surface aluminium atoms present on the nanocapsules at a depth of 1.6 nm. The XPS technique is highly specific to the solid surface due to the narrow range of photoelectrons that are excited. The excited energy of the photoelectrons emitting from the sample is determined by using a concentric hemispherical analyzer (CHA) which demonstrates a spectrum with a serial levels of the photoelectron peaks. The binding energies of the peaks are characteristic to each element. The peak areas are utilized (with equivalent sensitivity factors) to demonstrate the composition of the surface materials. The shape of each peak and binding energy can be slightly varied by the emitting atom of chemical state. XPS technique provides the chemical bonding information as well (Pohlmann *et al* 2008).

Superconducting Quantum Interference Device (SQUID)

The magnetic properties of nanocapsules are measured by using Quantum Design MPMS-7s or MPMS-5s superconducting quantum interference device. SQUIDs are the most sensitive detectors in detecting the tiny changes in magnetic flux, which take an account to the wide spectrum of application potential of SQUID devices (Liu *et al* 2009).

Multi Angle Laser Light Scattering (MALLS)

Vaults have a capsule-like structure with a very thin shell (approximately 2 nanometers) surrounding a large internal cavity. The vault particle in a nanocapsule has an incredible potential for compound encapsulation, protection, and delivery (Kedersha *et al* 1991). Vault conformation in solution is probed using the multiangle laser light scattering (Leonard *et al* 2003, Stephen *et al* 2001) to determine conditions that can stimulate the interconversion of opened and closed conformers. These studies enable the control of entrapment and release of encapsulated materials. Vaults containing binding sites for the toxic metals have importance in environmental and medical detoxification (Sangwoo *et al* 2010).

FT-IR analysis

The presence of characteristic peaks is confirmed by using the FTIR analysis. The peaks indicate the characteristic functional groups of compound (Bouchemal *et al* 2004, Benvenutti *et al* 2002).

Applications of nanocapsules

The nanocapsules are found to be suitable for various applications (Table 2). Due to the micronized size, they have a wide range of applications and high reproducibility, which can be used significantly in life-science applications. They have the potential applications in various fields like agrochemicals, cosmetics products, genetic engineering techniques, wastewater treatments, cleaning products, and componential adhesive applications. They also find applicability in encapsulating the enzymes, organic or inorganic catalysts, oils, adhesives, surface polymers, inorganic micro-particles and nanoparticles, latex particles, or even biological cells.

Table 2. Applications of nanocapsules

Application	Drug	Mode of Preparation	References
Agrochemicals	Abamectin-nanocapsules	Emulsion polymerization	Shang *et al* 2006
	Cypermethrin nanocapsules	Microemulsion polymerization	Cheng *et al* 2008
	Pyrethrum Nanocapsules	Microemulsion polymerization	Wu *et al* 2008
Anti-inflammatory drugs	Diclofenac sodium	Sol-gel method	Adriana *et al* 2008, Kortesuo *et al* 2000
	Indomethacin loaded nanocapsules	Interfacial polymerization	Bernardi *et al* 2009
Antiseptics	Monodisperse polymer nanocapsule	Precipitation	Umapom *et al* 2007
Cosmetics	Hinokitiol-loaded poly (epsilon-caprolactone) nanocapsules	Emulsion-diffusion method	Hwang *et al* 2008
Diabetes	Insulin loaded Biodegradable poly (isobutyl-cyanoacrylate) nanocapsules	Interfacial polymerization	Huguette *et al* 2002, Graf *et al* 2009
Nanocapsules for cancer	Artemisinin	Nanoencapsulation method	Andrieu *et al* 1989
	Camptothecin (CPT) and doxorubicin	Sol-gel method	Shen *et al* 2010
	Cisplatin	Repeated freezing and thawing of a concentrated solution of Cisplatin in the presence of negatively charged phospholipids.	Burger *et al* 2002
	Indomethacin-loaded polyisobutylcyanoacrylate nanocapsules.	Interfacial polymerization	Andrieu *et al* 1989, Raffin *et al* 2002, Guterres *et al* 2000
	Lipid nanocapsules loaded with Rhenium-188 (LNC188Re-SSS)	Phase-inversion process	Vanpouille *et al* 2011
Nanocapsule for Topical use	Chlorhexidine	Interfacial Polymerization method	Lboutounne *et al* 2004

Nanocapsules for drug delivery

Nanocapsules, which measure 1 thousandth of a millimeter, can be coated with an antibody on the surface, which assists in directing them from the blood stream to an induced tumor. After reaching to the tumor, an instant blast occurs that makes the capsules to open up and discharge their therapeutic contents. On the surface of the polymer, there are tiny gold particles in the range of 6 nm i.e. 6 millionth of a millimeter which stick across and are specific to the laser light and lead the capsules to position their drug load capacity at the desired time. The rupturing of the capsule can be seen when near infrared light hits the gold spots and they melt instantaneously without harming the content.

Nanocapsules for oral delivery of peptides and proteins

Nanocapsules are used as carriers for oral administration of peptides and proteins, particularly biodegradable poly (isobutylcyanoacrylate) nanocapsules (Puglisi *et al* 1995, Hildebrand *et al* 2000). However, the development of suitable carriers remains as a challenging technique due to the characteristic bioavailability of these molecules. They are restricted due to the gastrointestinal barriers of the epithelium and by their degradation of digestive enzymes. By the technique of encapsulation which provides the bioactive molecules from enzymatic and hydrolytic degradation e.g., the loaded insulin nanoparticles, the impact has been observed in diabetic rats following the oral administration (Damge *et al* 1990). The nanocapsules are suitable for the entrapment of bioactive peptides.

Treatment of hormone dependent breast cancer

The study of Jack *et al* (2008) shows that specific siRNAs encapsulated in nanocapsules can be used to target estrogen receptor alpha (ERα). The intravenous injection of these nanocapsules into estradiolstimulated MCF-7 cell xenografts led to a significant decrease in tumor growth and a decrease in ERα expression in tumor cells. This indicates that a novel strategy, based on ERα−siRNA delivery, could be developed for the treatment of hormone dependent breast cancers.

MRI-guided nanorobotic systems for therapeutic and diagnostic applications

The nanorobotic systems are exercised for the diagnosis and curative or reconstructive treatments of the human body at the cellular and sub-cellular levels in a controllable manner guided by the Magnetic Resonance Imaging (MRI). The concept of an MRI guided nanorobotic system (Panagiotis *et al* 2011) is based on an MRI scanner, which induces the required outer driving forces to explode magnetic nanocapsules to a directed target. The latest technique control algorithms and computational tools of engineering have been developed to gain benefit for real time drive force followed by the administration of nanocapsules.

Nanocapsules for liver cell-type delivery of plasmids in vivo

The efficient delivery afforded by viral vectors, (Betsy *et al* 2006) and the use of non-viral vectors for gene therapy has been hindered by the lack of adequate *in vivo* delivery systems. Hepatocytes (heps) states about the

aisaloglycoprotein receptors (ASGPr) and liver sinusoidal endothelial cells (LSECs) express the hyaluronan receptors (HAr) in high abundance and provide the ideal targets for ligand mediated receptor uptake. Using a novel dispersion atomization method that forms sub 50 nm nanocapsules with the receptor ligand noncovalently bound to the capsule coating, a red fluorescent protein (DsRed2) reporter plasmid encapsulated using either asialoorosomucoid (ASOR) for hep or HA for liver sinusoidal endothelial cells (LSEC) uptake has been applied successfully. ASOR and HA targeted nanocapsules can deliver the plasmids *in vivo* to heps or LSECs, respectively.

Nuclear nanocapsules treatment for cancer by using radioactive materials

The radioactive compound Astatine, like radium and uranium, emit high velocity alpha particles by the procedure of radioactive decay, which is about 4,000 times faster than the beta decay of the emitted electrons, and is most commonly used to treat cancer. The unique combination of the low penetrating power as well as large particle size make the alpha particle unique for targeting tumor at the single cellular level (Deutsch *et al* 1986).

Nanocapsules for self-healing materials

Damages in the materials of coating of the polymer, components of adhesives, and microelectronics, as well as structural composites can span longer durations (Dong *et al* 2001). The new method of self-healing has been achieved using polymer microcapsules that contain the healing agent. It also possesses adequate strength, longer shelf life, and excellent binding to the host material. Nanocapsules with functionalized surface areas and their walls with the possibility of forming and taking nanometer sized objects, have become popular to forward future with miniaturized tool leading completely to novel therapeutic applications in the research of medicine and technology.

Liposomal nanocapsules in food Science and agriculture

Liposomes, the spherical bilayer vesicles form the dispersion of polar lipids in hydrophilic solvents. They have an ability to act as efficient drug delivery vehicles by protecting most reactive and sensitive compounds immediate to release. Liposomal entrapment has resulted in the stabilization of encapsulated therapeutic materials against the wide range of chemical and environmental changes, including their enzymatic and chemical modifications, as well as changes in buffering against the levels of extreme pH, conditions of temperature, and the ionic strength.

In vivo hair growth promotion effects of cosmetic preparations containing hinokitiol- loaded poly (epsilon-caprolactone) nanocapsules

Nanocapsules containing hinokitiol (HKL) and prepared by an emulsion diffusion method (Hwang *et al* 2008) show the growth promotion and offer good promising results with their structural and histological changes of the hair follicles, when compared with the solutions of standard.

Sun screen cosmetics comprising TiO_2 nanocapsules

A UV blocking cosmetic product containing TiO_2 nano capsule, which is produced by dispersing TiO_2 with surfactant, is provided to improve the stability and UV protection effect without any harm to the body. The oleophilic surface treatment is performed with surface treating agent containing isostearic acid or aluminum stearate.

Molecular design of protein based nanocapsules for stimulus responsive characteristics

Hsp16.5, a small heat shock protein (sHSP) (Sao *et al* 2009) from hyperthermophilic archaeon, forms a homogeneous complex. It is comprised of 24 subunits with a molecular weight of 400 kDA and exhibits very high thermal stability. Functionalization of the nanocapsule to regulate the structural response of external stimuli like protease signal and the temperature by using numerous mutations (Mutant 01-10) to form a cleavage site for a specific protease (an enzyme), Factor Xa, is being experimented to release on the external surface of the nanocapsule using a genetic engineering strategy. The resulting mutants were expressed to high levels in *Escherichia coli.* One of the mutants (Mutant 06) which has the most permissible cleavage located at the site of triangular pore on the capsule surface, formed a spherical assembly which is similar to that of observed in the wild type protein. The results of above-mentioned study revealed that Mut6 acts as a stimulus responsive nanocapsule. A characteristic protein-based nanocapsule has an applicable potential as a versatile intelligent system.

Nanocapsules against melanomas

Melanomas (cancer) are the highly aggressive tumors associated with dismal prognosis especially when they have metastasized. Despite of significant efforts to develop adjuvant therapies, the best response rate with the standard FDA approved treatment dacarbazine (Marie Curie *et al* 2011) is as low as 16%. Specific cancer cell targeting should be achieved by:

i) Passive enhanced permeability retention phenomenon due to the composition, size and stealth properties of the nanocapsules,
ii) Active targeting by coupling with various antibodies.

Various nanocapsule types have been utilized to evaluate their physico-chemical properties, half-life in blood, accumulation in the tumor models and therapeutic benefits. The polylactic-co-glycolic nanocapsules loaded with the magnetic nano-sized particles and Selol (a selenium based anti-cancer drug), provides a novel and strategic magnetic drug delivery system suitable for the treatment of cancer by the way of active drug and magnetohyperthermia (Falqueiro *et al* 2011).

Self-assembled DNA nanocapsules for drug delivery

DNA has become a basic material for nanotechnology researchers (Michael Berger *et al* 2009). Nanofabrication is a technique by which the cube octahedron and a tetrahedron are formed by the molecular self-assembly in simple DNA. These molecules encapsulate within DNA polyhedral, designing proteins, which can bind to these structures on their outer surfaces. The delivery of these drug molecules in various tissues or cells is then studied.

Future nanocapsule bandages to fight against infection

The conventional dressings require to be taken out if the skin becomes affected or it slows the healing (Radhika *et al* 2011). In contrast, nanocapsular dressings trigger automatically to discharge antibiotics when the wound becomes infected. They do not require to be removed, thereby enhancing the chances of healing wound without scarring. Nanocapsular bandages can also be used for additional types of wounds like ulcers and most consistently by the military people on the battlefield. These medicinal dressings release antibiotics from the nanocapsules activated by the presence of disease causing pathogenic or causative bacterial organism, targeting the treatment prior to the infection aggravates. The bacterial toxins burst the capsules comprising the antibiotics, which cover as the dressings. In this way, antibiotics are produced when needed; thus, it reduces the risk of the evolution of antibiotic resistant microbes such as Methicillin resistant *Staphylococcus aureus* (MRSA).

Conclusion

Nanocapsules are a contribution to the methodological development for formulation by various methods, mainly the interfacial polymerization and interfacial nano-deposition. They can also be released as the monodisperse particles with well-defined biochemical, electrical, optical, as well as magnetic properties. In drug delivery system, they are confined to suit the complexity of the application as they intend to produce contents in response to a specific bimolecular triggering action mechanism. Nanocapsules also have the efficient applications in various fields of the agrochemicals, wastewater treatments, genetic engineering, cosmetics, cleaning products, as well as in adhesive component. They are also used in encapsulation of enzymes, adhesives, catalysts, polymers, oils, inorganic micro and nanoparticles, latex particles, and even the biological cells. In conclusion, they can be used in the delivery of active pharmaceutical ingredients (APIs). They provide the novel effective drug delivery systems in the up-coming future.

Ethical issues

There are no applicable ethical issues in this paper.

Conflict of interests

Authors declare no conflict of interests.

Acknowledgments

The authors gratefully thank V. Shanmugan, the Chairman, and S. Nandha Kumar Pradeep, Secretary of Nandha College of Pharmacy and Research Institute, Erode, Tamilnadu, India for their support.

References

Adriana RP, Letıcia SF, Rodrigo PS, Alberto MD, Edilson VB, Tania MHC, *et al.* **2008**. Nanocapsule@xerogel microparticles containing sodium diclofenac: A new strategy to control the release of drugs. *Int J Pharm.*, 358(1-2), 292–95.

Adriana RP, Leticia C, Graziela M, Leonardo US, Nadya PD and Silvia SG. **2007**. Structural model of polymeric nanospheres containing indomethacin ethyl ester and *in vivo* antiedematogenic activity. *Int J Nanotechnol*, 4(5), 454–67.

Aiyer HN, Seshadri R, Raina G, Sen R and Rahul R. **1995**. Study of Carbon Nanocapsules (Onions) and Spherulitic Graphite by Stm and Other Techniques. *In: Fullerene Sci Tech*, 3 (6), 765-777.

Andrieu V, Fessi H, Dubrasquet M, Devissaguet JP, Puisieux F and Benita S. **1989**. Pharmacokinetic evaluation of indomethacin nanocapsules. *Drug Des Deliv* 4(4), 295- 302.

Arenas LT, Dias SLP, Moro CC, Costa TMH, Benvenutti EV, Lucho AMS, *et al*. **2006**. Structure and property studies of hybrid xerogels containing bridged positively charged 1 4-diazoniabi cycle [2. 2. 2] octane dichloride. *J Colloidal Interface Sci*, 297(1), 244–50.

Beduneau A, Saulnier P, Anton N, Hindre F, Passirani C, Rajerison H, *et al.* **2006**. Pegylated nanocapsules produced by an organic solvent free method: Evaluation of their stealth properties. *Pharm. Res*, 23(9), 2190-99.

Benita. S. 1998. Microparticulate drug delivery systems: release kinetic models. Microspheres, Microcapsules and Liposomes (the MML Series). R. Arshady (Ed.), Citrus Books, London, pp. 255- 278.

Benvenutti EV, Pavan FA, Gobbi SA and Costa TMH. **2002**. FTIR thermal analysis on anilinepropylsilica xerogel. *J Therm Anal Calorym*, 68(1), 199–206.

Berger M. **2006**. Rare-earth nanocapsules as a new type of nanomaterial for cryogenic magnetic refrigerators. Nanowerk Spotlight. Available form: http://www.nanowerk.com/spotlight/spotid=991.php [Retrieved April 04, 2012].

Bernardi A, Zilberstein AC, Jager E, Campos MM, Morrone FB, Calixto JB, *et al*. **2009**. Effects of indomethacin loaded nanocapsules in experimental models of inflammation in rats. *Br J Pharmacol*, 158(4), 1104-11.

Betsy TK, Gretchen MU, Mark TR and Clifford JS. **2006**. Targeted Nanocapsules for Liver Cell-Type Delivery of Plasmids *in vivo. Mol Ther*, 13, S415.

Bingyun S and Daniel TC. **2003**. Spatially and temporally resolved delivery of stimuli to single cells. *J Am Chem Soc*, 125(13), 3702–03.

Boal AK, Ilhan F, Derouchey JE, Thurn AT, Russell TP and Rotello VM. **2000**. Self-assembly of nanoparticles into structured spherical and network aggregates. *Nature*, 404(6779), 746–48.

Bouchemal K, Briançon S, Perrier E, Fessi H, Bonnet I and Zydowicz N. **2004**. Synthesis and characterization of polyurethane and poly (ether urethane) nanocapsules using a new technique of interfacial polycondensation combined to spontaneous emulsification. *Int J Pharm*, 269(1), 89–100.

Boudad H, Legrand P, Lebas G, Cheron M, Duchene D, Ponchel G, *et al*. **2001**. Combined hydroxypropyl-[beta] -cyclodextrin and poly (alkylcyanoacrylate) nanoparticles intended for oral administration of saquinavir. *Int J Pharm*, 218(1-2), 113-24.

Bruce MN. **1993**. Hybrid nanocomposite materials between inorganic glasses and organic polymers. *Adv Mater*, 5(6), 422–33.

Burger KN, Staffhorst RW, de Vijlder HC, Velinova MJ, Bomans PH, Frederik PM, *et al*. **2002.** Nanocapsules: lipid-coated aggregates of cisplatin with high cytotoxicity. *Nature Medicine*, 8(1), 81- 84.

Cha CH, Saif MW, Yamane BH and Weber SM. **2010.** Hepatocellular carcinoma: current management. *Curr Probl Surg*, 47(1), 10–67.

Cheng XM, Yu J, Zhou YF and Nie WY. **2008**. Applied Research of Polymerizable Emulsifier on the Preparation of Cypermethrin Nanocapsules. *J Adv Mater Res*, 236(12), 2024-27.

Couvreur P, Barratt G, Fattal E, Legrand P and Vauthier C. **2002.** Nanocapsule technology- A Review. *Crit Rev Ther Drug Carrier Syst*, 19(2), 99-134.

Daniel TC, Polina BS and Kimberly AD. **2010**. Investigating Lyophilization of Lipid Nanocapsules with Fluorescence Correlation Spectroscopy. *Langmuir*, 26(12), 10218–22.

Damge C, Michel C, Aprahamian M, Couvreur P and Devissaguet JP. **1990.** Nanocapsules as carriers for oral peptide delivery. *J Control Release*, 13(2-3), 233-239.

Deutsch E, Libson K, Vanderheyden JL, Ketring AR and Maxon HR. **1986**. The chemistry of rhenium and technetium as related to the use of isotopes of these elements in therapeutic and diagnostic nuclear medicine. *Int J Rad Appl Instrum B*, 13(4), 465–77.

Diaspro A, Krol S, Cavalleri O, Silvano D and Gliozzi A. **2002**. Microscopical characterization of nanocapsules templated on ionic crystals and biological cells toward biomedical applications. *IEEE Trans Nanobioscience, 1*(3), 110-15.

Dong XT, Zhang L, Zhang W, Wang LP and Hong GY. **2001.** Preparation and Characterization of Nanometer-sized CeO^2 /Polystyrene Hybrid Material. *Acta Phys Chim Sin*, 17(8), 739-42.

Dongwoo K, Eunju K, Jiyeong L, Soonsang H, Wokyung S, Namseok L, *et al*. **2010**. Direct Synthesis of Polymer Nanocapsules: Self-Assembly of Polymer Hollow Spheres through Irreversible Covalent Bond Formation. *J Am Chem Soc*, 132 (28), 9908–19.

Douglas AW and Zeno WW. **1999**. Blocked isocyanates III: Part A. Mechanisms and chemistry. *Progress in Organic Coatings*, 36(3), 148–72.

Dunne M, Corrigan OI and Ramtoola Z. **2000.** Influence of particle size and dissolution conditions on the degradation properties of polylactide-co-glycolide particles. *Biomaterials*, 21(16), 1659-68.

Falqueiro M, Primo FL, Morais PC, Mosiniewicz S, Suchocki P and Tedesco AC. **2011**. Selol-loaded magnetic nanocapsules: A new approach for hyperthermia cancer therapy. *J Appl Phys*, 109, 07B306.

Graf A, Rades T and Hook SM. **2009**. Oral insulin delivery using Nanoparticles based on micro emulsions with different structure types: Optimization and *in vivo* evaluation. *Eur J Pharm Sci*, 37(1), 53-61.

Guterres SS, Weiss V, de Lucca FL and Pohlmann AR. **2000**. Influence of benzyl benzoate as oil core on the physicochemical properties of spray-dried powders from polymeric nanocapsules containing indomethacin. *Drug Deliv*, 7(4), 195–99.

Haolong L, Yang Y, Yizhan W, Chunyu W, Wen L and Lixin W. **2011**. Self-assembly and ion-trapping properties of inorganic nanocapsule-surfactant hybrid spheres**.** *Soft Matter*, 7(6), 2668-73.

Heurtault B, Saulnier P, Pech B, Proust JE, Benoit JP. **2002**. A novel phase inversion based process for the preparation of lipid nanocarriers. *Pharm Res*, 19(6), 875–80.

Hildebrand GE and Tack JW. **2000**. Microencapsulation of peptides and proteins. *Int J Pharm*, 196(2), 173–76.

Hsieh BT, Hsieh JF, Tsai SC, Lin WY, Huang HT, Ting G, *et al*. **1999**. Rhenium-188-Labeled DTPA: a new radiopharmaceutical for intravascular radiation therapy. *Nucl Med Biol*, 26(8), 967–72.

Huguette PA, Malam A, Danielle J, Patrick C and Christine V. **2002.** Lipid Nanocapsules Loaded with Rhenium-188 Reduce Tumor Progression in a Rat Hepatocellular Carcinoma Model. *IEEE Trans Nanobiosci*, 1(3), 110-15.

Huguette PA, Malam A, Danielle J, Patrick C and Christine V. **2003**. Visualization of insulin-loaded nanocapsules: *in vitro* and *in vivo* studies after oral administration to rats. *Pharm Res*, 20(7), 1071-84.

Hwang SL and Kim JC. **2008.** *In vivo* hair growth promotion effects of cosmetic preparations containing hinokitiol-loaded poly (ε-caprolacton) nanocapsules. *J Microencapsul.* 25(5), 351-56.

Ingersoll JC, Markandeyulu G, Murty VS and Ramarao KVS. **2005**. Magnetic properties of Sm Tb Fe17-x Gax (0< x<8) *Appl Phys*, 97(10), 109-11.

Irii S and Shiozaki T. **1987**. Manufacture of microcapsules. JP patent 62193641, Japan.

Jack MR, Celine B, Laurence M, Herv H, Vronique M, Elisabeth C, *et al.* **2008**. Physicochemical characteristics and

preliminary *in vivo* biological evaluation of nanocapsules loaded with siRNA targeting estrogen receptor alpha. *Biomacromolecules*, 9(10), 2881–90.

Jackson LS and Lee K. **1991**. Microencapsulation and the food industry. *Lebensmittel- Wissenschaft und -Technologie*, 1(1), 289–97.

Jager A, Stefani V, Guterres SS and Pohlmann AR. **2007**. Physico-chemical characterization of nanocapsule polymeric wall using fluorescent benzazole probes. *Int J Pharm*, 338(1-2), 297–305.

Jang J, Bae J and Park E. **2006.** Selective fabrication of poly (3, 4-ethylenedioxythiophene) nanocapsules and mesocellular foams using surfactant-mediated interfacial polymerization. *Adv Mater*, 18(3), 354–58.

Jason CHC, Jian KW, Chao MH, David Y, Huanga DY, Huangd SH, *et al*. **2002**. Radiation induced liver disease after radiotherapy for hepatocellular carcinoma: clinical manifestation and dosimetric description. *Radiother Oncol*, 63(1), 41–45.

Kedersha NL. **1991**. Vault ribonucleoprotein particles open into flower-like structures with octagonal symmetry. *J Cell Biol*, 112(2), 225-35.

Kensuke N, Hideaki I and Yoshiki C. 2**003**. Temperature-dependent reversible self-assembly of gold nanoparticles into spherical aggregates by molecular recognition between pyrenyl and dinitrophenyl units. *Langmuir* 19(13), 5496-501.

Kepczynski M, Bednar J, Lewandowska J, Staszewska M and Nowakowska M. **2009.** Hybrid silicasilicone nanocapsules obtained in catanionic vesicles. Cryo-TEM studies. *J Nanosci Nanotechnol*, 9(5), 3138-43.

Kimberly AD, Knut D, Magnus WL, Thomas M, Werner S, Reine W, *et al.* **2004.** Synthesis of branched 'nanotrees' by controlled seeding of multiple branching events. *Nat. Mater*, 3(6), 380-384.

Kompella UB, Bandi N and Ayalasomayajula SP. **2003**. Subconjunctival Nano- and Microparticles Sustain Retinal Delivery of Budesonide, a Corticosteroid Capable of Inhibiting VEGF Expression. *Invest Ophthalmol Vis Sci*, 44(3), 1192-201.

Kortesuo P, Ahola M, Kangas M, Kangasniemi I, Yli-Urpo A and Kiesvaara J. **2000**. *In vitro* evaluation of sol–gel processed spray dried silica gel microspheres as carrier in controlled drug delivery. *Int J Pharm*, 200(2), 223–29.

Kumar MNVR, Bakowsky U and Lehr CM. **2004**. Preparation and characterization of cationic PLGA nanospheres as DNA carriers. *J Biomaterial*, 25(10), 1771-77.

Lambert G, Fattal E, Pinto-Alphandary H, Gulik A and Couvreur. **2000**. Polyisobutylcyanoacrylate nanocapsules containing an aqueous core as a novel colloidal carrier for the delivery of oligonucleotides. *Pharm Res*, 17(6), 707-14.

Lboutounne H, Faivre V, Flson F and Prot F. **2004**. Characterization of chlorhexidine-loaded nanocapsules through hairless and wistar rat skin. *Skin Pharmacol Physiol.* 17(4), 176-82.

Leonard HR, Hal M, Bruce D, Jeffrey Z and James H. **2003**. The Development of Vault Nano Capsules. *NSF Nanoscale Science and Engineering Grantees Conference*, 1-3.

Li YP, Pei YY, Zhou ZH, Zhang XY, Gu ZH, Ding J, Zhou JJ, Gao XJ, *et al*. **2001**. PEGylated polycyanoacrylate nanoparticles as tumor necrosis factor-[alpha] carriers. *J Control Release*, 71(3), 287-96.

Liu XG, Li B, Geng DY, Cui WB, Yang F, Xie ZG, *et al*. **2009**. (Fe, Ni)/C nanocapsules for electromagnetic-wave-absorber in the whole Ku-band. *Carbon*, 47 (2), 470-74.

Marie Curie. **2011.** Novel lipid nanocapsules of anti alpha 1 sodium pump subunit SiRNA to specifically target metastatic melanomas. *European commission euraxess*, 11, 37.

Matkan J and Treleaven RJ. **1987**. Particles containing releasable fill material and method of making same. US patent 4681806, USA.

Michael Berger. **2009.** Integrating nanotube-based NEMS into large scale MEMS. *Nanowerk LLC*, 5, 316-22. Available on: http://www.nanowerk.com/spotlight/spotid=11804.php

Mohanraj VJ and Chen Y. **2006**. Nanoparticles-A review. *Trop J Pharm Res*, 5(1), 561- 573.

Morgan PW. **1987**. Interfacial polymerisation. *Encyclopaedia of Polymer Science*. 2nd ed. Wiley, New York, pp. 231–237.

Panagiotis V, Matthieu F, Antoine F and Constantinos M. **2011.** MRI-Guided Nanorobotic Systems for Therapeutic and Diagnostic Applications. *Annu Rev Biomed Eng*, 13(1), 157-84.

Pohlmann R, Beck RCR, Lionzo MIZ, Coasta TMH, Benvenutti EV, Re MI, *et al*. **2008**. Surface morphology of spray-dried nanoparticle-coated microparticles designed as an oral drug delivery system. Braz J Chem Eng, 25(2), 389-98.

Puglisi G, Fresta M, Giammona G and Ventura CA. **1995**. Influence of the preparation conditions on poly (ethylcyanoacrylate) nanocapsule formation. *Int J Pharm*, 125(2), 283-87.

Qiang Z, Zancong S and Tsuneji N. **2001**. Prolonged hypoglycemic effect of insulin-loaded polybutylcyanoacrylate nanoparticles after pulmonary administration to normal rats. *Int J Pharm*, 218(1-2), 75-80.

Qingyi L, Feng G and Dongyuan Z. **2002.** The assembly of semiconductor sulfide nanocrystallites with organic reagents as templates. *Nanotechnology*, 13(6), 741-45.

Radhika PR, Sasikanth and Sivakumar T. **2011**. Nanocapsules: A new approach for drug delivery. *Int J Pharma Sci Res*, 2(6), 1426-29.

Raffin PA, Weiss V, Mertins O, Pesce SN and Stanisçuaski GS. **2002**. Spray-dried indomethacin-loaded polyester nanocapsules and nanospheres: development, stability evaluation and nanostructure models. *Eur J Pharm Sci*, 16 (4-5), 305-12.

Redhead HM, Davis SS and Illum L. **2001**. Drug delivery in poly (lactide-co-glycolide) nanoparticles surface modified with poloxamer 407 and poloxamine 908: *in vitro* characterisation and *in vivo* evaluation. *J Control Release*, 70(3), 353-63.

Repka M. **2002.** Hot Melt Extrusion. *Encyclopedia of pharmaceutical technology*, 2nd ed.; Swarbrick J, Boylan J (Ed.), Marcel Dekker Inc, New York, 2, PP. 1488-1504.

Salaun F and Vroman I. **2009**. Curcumin-Loaded Nanocapsules: Formulation and Influence of the Nanoencapsulation Processes Variables on the Physico-Chemical Characteristics of the Particles. *Int J Chem Reac Eng*, The Berekly Electronic press, 7(1), 1-26.

Samy EM, Shautian L, Daniel G and Udo P. **1996**. Synthesis of nanostructured materials using a laser vaporization condensation technique. *Nanotechnology* (*ACS Symposium Series*), 622, 79–99.

Sangwoo P, Hong YC**,** Jeong YA, Yungwan K, Abiraman S, Jeffrey O, *et al*. **2010**. Photo-Cross-Linkable Thermoresponsive Star Polymers Designed for Control of Cell-Surface Interactions. *Biomacromolecules*, 11(10), 2647–52.

Sao K, Murata M, Umezaki K, Fujisaki Y, Mori T, Niidome T, *et al*. **2009**. Molecular design of protein-based nanocapsules for stimulus-responsive characteristics. *Bioorg Med Che,* 17(1), 85-93.

Sarah A, Ying WY, Niveen MK, Fraser JS and Jeffrey I. **2009**. Dual-controlled nanoparticles exhibiting and logic. *J Am Chem Soc*, 131(32), 11344-46.

Shang Q, Feng S and Zheng H. **2006.** Preparation of abamectin-nanocapsules suspension concentrates. *Agrochemicals*, 12.

Shen Y, Jin E, Zhang B, Murphy CJ, Sui M, Zhao J, *et al.* **2010**. Prodrugs Forming High Drug Loading Multifunctional Nanocapsules for Intracellular Cancer Drug Delivery. *J Am Chem Soc*, 132(12), 4259–65.

Slowing II, Trewyn BG, Giri S and Lin VSY. **2007**. Mesoporous silica nanoparticles for drug delivery and biosensing applications. *Adv Funct Mater*, 17(8), 1225– 36.

Song Ma, Dianyu G, Weishan Z, Wei L, Xiuliang, M and Zhidong Z. **2006**. Synthesis of a new type of GdAl2 nanocapsule with a large cryogenic magnetocaloric effect and novel coral-like aggregates self-assembled by nanocapsules *Nanotechnology*, 17(21), 5406–11.

Stenekes RJ, Loebis AE, Fernandes CM, Crommelin DJ and Hennink WE. **2001**. Degradable dextran microspheres for the controlled release of liposomes. *Int J Pharm*, 214(1-2), 17–20.

Stephen AG, Raval FS, Huynh T, Torres M, Kickhoefer VA and Rome LH. **2001**. Assembly of vault-like particles in insect cells expressing only the major vault protein. *J Biol Chem*, 276(26), 23217-20.

Sung OC, Eun JL, Hyeok ML, Yue L, Lan YH and Dong PK. **2007.** Hierarchical pore structures fabricated by electron irradiation of silicone grease and their applications to superhydrophobic and superhydrophilic films. *Macromol Rapid Commun*, 28(3), 246-51.

Umapom P, Pramuan T and Katharina L. **2007**. Antiseptic Nanocapsule Formation via Controlling Polymer Deposition onto Water-in-Oil Miniemulsion Droplets. *Macromolecular Symposia*, 251(1), 54–62.

Vanpouille CB, Lacoeuille F, Roux J, Aube C, Garcion E, Lepareur N, *et al.* **2011.** Lipid nanocapsules loaded with rhenium-188 reduce tumor progression in a rat hepatocellular carcinoma model. *PLoS One*, 6(3), e16926.

Vonarbourg A, Passirani C, Desigaux L, Allard E, Saulnier P, Lambert O, *et al.* **2009**. The encapsulation of DNA molecules within biomimetic lipid nanocapsules. *Biomaterials*, 30(18), 3197-204.

Wan LSC, Heng PWS, Chia CGH. **1992**. Spray drying as a process for microencapsulation and the effect of different coating polymers. *Drug Dev Ind Pharm*, 18(9), 997–1011.

Watnasirichaikul S, Davies NM, Rades T and Tucker IG. **2000**. Preparation of biodegradable insulin nanocapsules from biocompatible microemulsions. *Pharm Res*, 17(6), 684-89.

Wu J, Zhou Y, Chen J, Nie W and Shi R. **2008.** Applied Research of Polymerizable Emulsifier on the Preparation of Cypermethrin Nanocapsules. *J Polymer Materials Science & Engineering*, 02.

Xinfei Y, Sheng Z, Xiaopeng L, Yingfeng T, Shuguang Y, Ryan M, *et al.* **2010**. A Giant Surfactant of Polystyrene–(Carboxylic Acid-Functionalized Polyhedral Oligomeric Silsesquioxane) Amphiphile with Highly Stretched Polystyrene Tails in Micellar Assemblies. *J Am Chem Soc*, 132 (47), 16741-44.

Yang H, Mendon SK and Rawlins JW. **2008**. Ion of blocked isocyanates through aqueous emulsion polymerization. *eXPRESS Polymer Letters*, 2(5), 349–56.

Yosida Y, Shida S, Ohsuna T and Shiraga N. **1994**. Synthesis, identification and growth mechanism of Fe, Ni and Co crystals encapsulated in multivalled carbon nanocages. *J Appl Phys*, 76, 8-11.

Youfang C, Xianfu L, Hyunjin P, and Richard G. **2009**. Study of artemisinin nanocapsules as anticancer drug delivery systems. *Nanomed Nanotech Biol Med*, 5(3), 316-22.

Zhang ZD, Zheng JG, Skorvanek I, Wen GH, Kovac J, Wang FW, *et al***. 2001**. Shell/core structure and magnetic properties of carbon-coated Fe-Co(C) nanocapsules. *J Phys Condens Matter*, 13(9), 1921.

Zhang ZD. **2004**. Nanocapsules, Encyclopedia of Nanoscience and Nanotechnology, HS. Nalwa (Ed.), American Scientic Publishers, 6, 77-160.

Zhu YQ, Hsu WK, Zhou WZ, Terrones M, Kroto HW and Walton DRM. **2001.** Selective Cocatalysed growth of novel MgO fishbone fractal nanostructures. *Chem Phys Lett*, 347(4-6), 337- 343.

Ziyi Z, Huayi C, Songbei T, Jun D, Jianyi L and Kuang LT. **2000**. Catalytic growth of carbon nanoballs with and without cobalt encapsulation. *Chem Phys Lett*, 330(1-2), 41-47.