



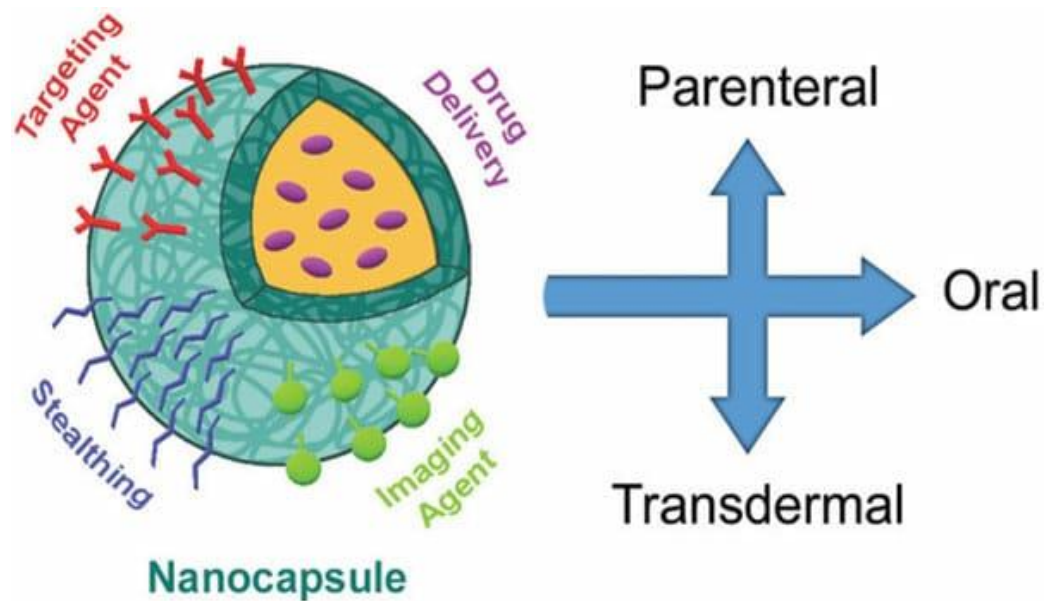
● REVIEW ON
NANOCAPSULES: THE
WAPEONS FOR NOVEL DRUG
DELIVERY SYSTEM.

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ABSTRACT.

Dispersed polymer Nano capsules can serve as Nano-sized drug carriers to achieve controlled release as well as

efficient drug targeting. The dispersion stability and the primary physiological response are mainly determined by the type of the surfactant and the nature of the outer coating.

Their release and degradation properties largely depend on the composition and the structure of the capsule walls.

Another important criterion is the capsule size, where an optimum is generally seen for radii ranging between 100 and 500 nm. Nanocapsules can be prepared by four principally different approaches: interfacial polymerization, interfacial precipitation, interfacial deposition, and self assembly procedures. All these procedures offer their individual advantages and disadvantages when it comes to the design of optimized

drug carrier systems. The most important capsule parameters such as capsule radius distribution, the capsule surface, the thickness and the permeability of the capsule membrane and its thermal or chemical decomposition, are discussed and examples are shown. In combination with efficient preparation procedures, nanocapsule dispersions allow for new and promising approaches in many kinds of pharmaceutical therapies.

A Nanocapsule consists of shell and a space in which desired substances may be placed. Drug-filled Nano capsules can be covered with antibodies or cell surface receptors that bind to cancer or various cells and release their biological compound on contact with that specific

tissue. Polymeric Nano capsules can now be made in specific sizes and shapes. These can then be functionalized by inserting molecules with a particular property onto the shell of Nano capsules. These molecules cause the release of the contents of the Nano capsule in response to a particular biomolecule which would be the triggering mechanism in a targeted drug delivery system. It is a sub microscopic colloidal drug carrier system. Nano capsules can be prepared by using natural or synthetic polymers. In Nano capsules drugs are placed into an inside core cavity, which provides protection from rapid degradation. It can be synthesized by various methods viz. nanoprecipitation, emulsion diffusion, double emulsification polymer

coating, and layer by layer . It is composed of an aqueous or an oily core surrounded by a thin polymer membrane. From the aqueous solutions, by sequential deposition of polymer layers onto a sacrificial template, capsules are generated. For the assembly of the multilayer shell, interactions such as electrostatics, covalent bonding, hydrogen bonding, etc. can be used as the driving force. Dissolution of the sacrificial template leads to the formation of the hollow capsules . Nano capsules are similar to a vesicular system that contains the drug inside its cavity, which consists of liquid core or polymer matrix surrounded by polymeric membrane.

The cavity encloses the active substances in the form of liquid or solid as a molecular dispersion. These hollow Nano capsules have the ability to encapsulate a variety of substances such as dyes, drugs, catalysts, and biopolymers such as proteins and nucleic acids.

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KEY WORDS:

Nanoparticles, Nano capsules, Drug carriers

INTRODUCTION:

The old and fascinating idea of a “magic bullet” in pharmaceutical therapy has triggered a wide range of research activities since it was brought up by Paul Ehrlich in the early 20th century. The approach which may come closest to the original intention may probably be found in the application of dispersed nano particles

loaded with an active ingredient . They ideally are small enough in size to pass through the patient's capillary system, consist of non-toxic and biodegradable material and combine suitable release and targeting properties. A general and widely accepted classification of nano particles has been given by J. Kreutzer.

According to this nomenclature, nano particles are solid colloidal particles with a diameter between 10 and 1000 nm.

Within the solid matrix of the particles, the active ingredient is either dissolved, entrapped or encapsulated. Among these colloidal particles, those formed by a shell-like wall with a liquid content may be accounted for as Nano capsules while their homogeneously solid counterparts are often referred to

as nanospheres. In many cases, nanocapsule walls consist of a biodegradable polymer and are typically formed on the spherical interface of particles or droplets or by self assembly of amphiphilic polymer molecules.

Especially therapeutic application of Nano capsules may be seen in connection with implant infections, especially if the infection is connected to the presence of a biofilm. The capsule surface may specifically interact with the polymer framework (extracellular polymeric substances – EPS) of the biofilm, e.g. by electrostatic interactions or polymer entanglements. If these interactions are selective enough, they may allow for a local accumulation of the capsules on the biofilm surface. Finally, the biological decomposition of the capsule wall will lead to a local release of the capsule contents. If the capsules are loaded with suitable active ingredients, this results in an efficient

drug delivery to the infected interface and could initiate new approaches to treat implant infections. Nano capsules can be distinguished from other Nano particles because they have well defined core and shell, whereas the latter do not. When it is made from polymers, Nano capsules can be referred as hollow polymer nanostructures. Technologies for microencapsulating materials have been around for several years, primarily for applications involving minimisation of hygroscopic and chemical interactions, elimination of oxidation, and controlled release of nutraceuticals.

Nano capsules, as characteristic class of nano particles, 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 nano capsules have attracted great interest because of their protective coating, which is usually

pyrophoric and easily oxidized. Nano particles 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 nano carriers and are referred as Nano medicines. 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. Nano capsules, which are submicron in size, when administered intravenously, reach to the target and release the encapsulated drug.

Polymeric nano particles are named nano capsules . when they contain a polymeric wall composed of non-ionic surfactants, macromolecules, phospholipids and an oil core . These are prepared mostly by two technologies: the interfacial polymerization and interfacial nano-deposition.

Nano capsules, 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.

The interest in research on magnetic nano capsules 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 intermetallic nano capsule that can be applied in cryogenic magnetic refrigerator devices .

Some drugs find difficulty in marketing due to their unpleasant side effects. However, when they are placed inside the cavity of nano capsule, 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, nano capsules possess greater capability to take on an extensive range of applications with extremely high efficient reproducibility. The production of nano capsules depends on their application and pharmaceutical, biochemical, electrical, optical or magnetic characteristics. The enhanced delivery of bioactive molecules through the targeted delivery by means of a nano capsule provides numerous challenges and opportunities for the research and future development of novel improved therapies.

MATERIAL AND METHODS-

Polymers

Gum Arabica, Hydroxypropylmethylcellulose (HPMC), Hydroxypropoxymethylcellulosephthalate (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 nano particles 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, Kumaret 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 (quaternary 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.

METHODS OF PREPARATION

Nano capsules composition

Nano capsules 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 nano capsules: 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 nano capsules (LNCs) as a nano vector-based formulation with biomimetic properties (Heurtault et al 2002) show 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 nano capsules, but mostly four different approaches are utilized, namely: methods of interfacial polymerization or interfacial precipitation or interfacial nanodeposition, and self-assembly methods. For designing the optimized drug carrier systems, each procedure offers its advantages and disadvantages. Nano capsules can also be prepared according to the nano precipitation 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 nano-capsules forming at the pores.

Methods of Preparation

Polymerization method

The monomers are polymerized in an aqueous solution to form nano particles followed by placing the drug either by dissolving in the medium of polymerization or by the adsorption of nano particles. Ultracentrifugation method, which has been utilized for purifying the nano particle 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 nano particles (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 $<5^{\circ}\text{C}$ before sonication using a Misonix sonicator 3000 (until a particle size $<250\text{ nm}$ 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

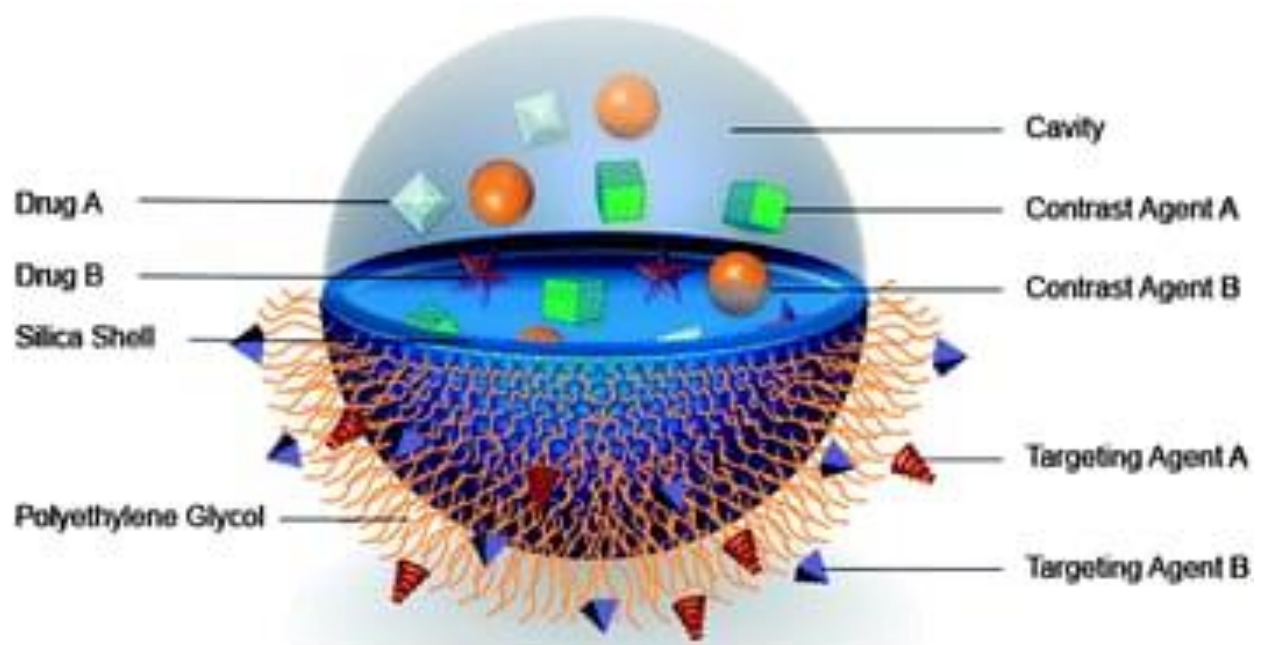
2003), organic reagent assisted method (Qingyi et al 2002), solution-liquid-solid method (Boal et al 2000) and catalytic vapor-liquid-solid growth (Zhu et al 2001).

Encapsulation of nanocapsules

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.

Structure of nanocapsules



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). Photon correlation spectroscopy or dynamic light scattering are used to determine the particle size.

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 bio-degradable copolymers of hydrophilic segments like poly-ethylene glycol (PEG), poly-ethylene oxide (PEO), poly-oxamer, poly-oxamine and poly-sorbate 80 (Tween 80). The zeta

potential of nanocapsule is efficiently used to characterize charge on the surface property of nanocapsule.

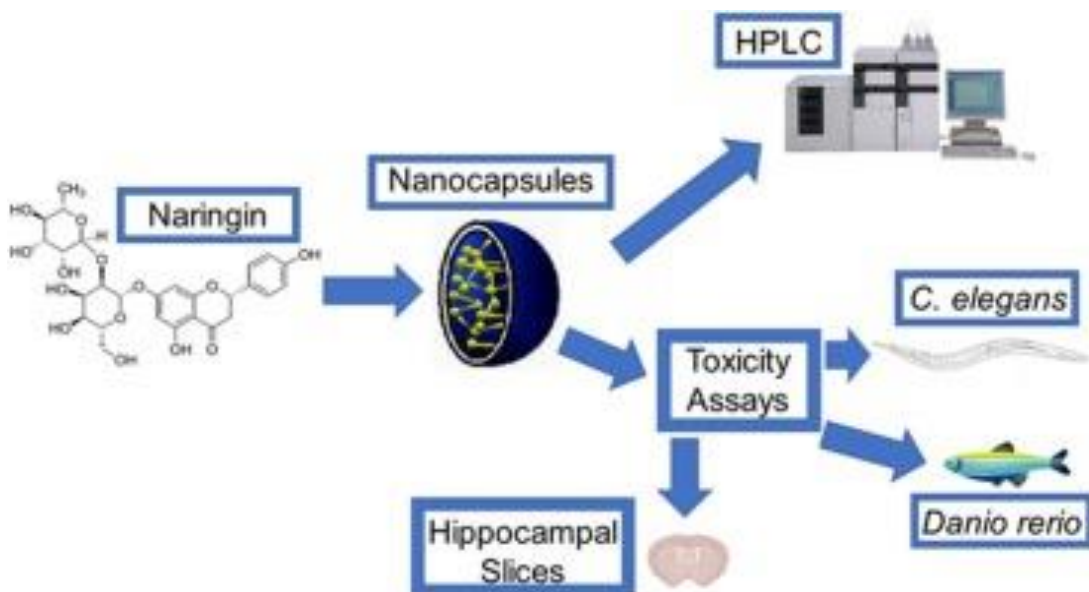
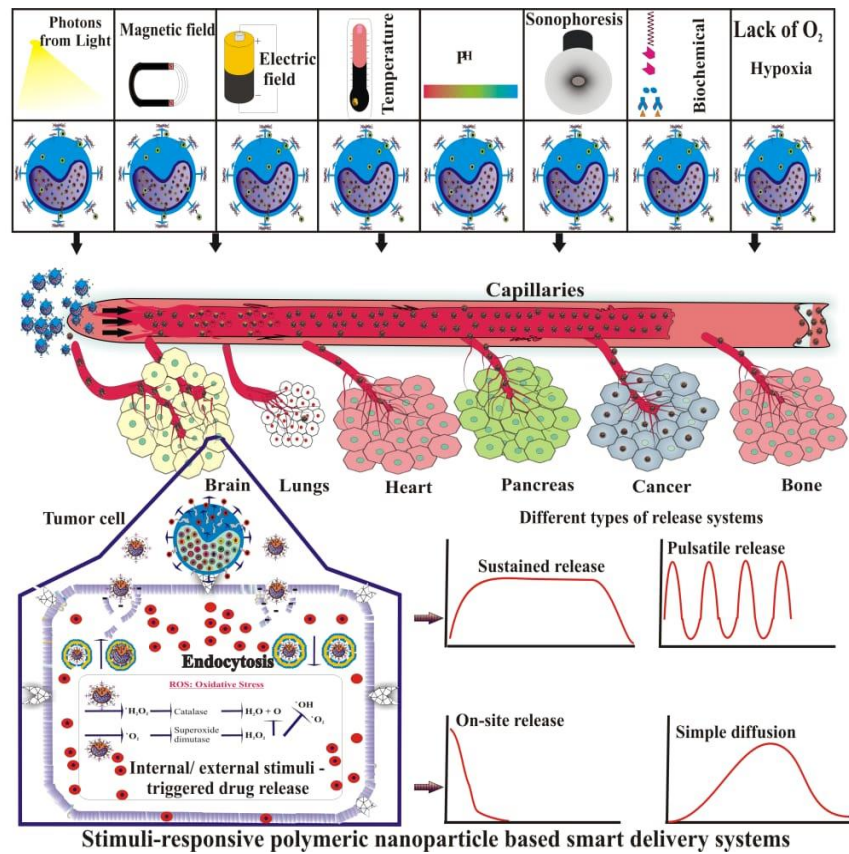
Evaluation studies

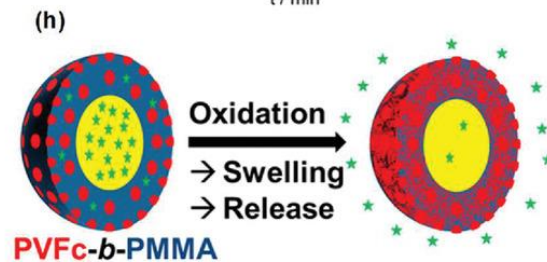
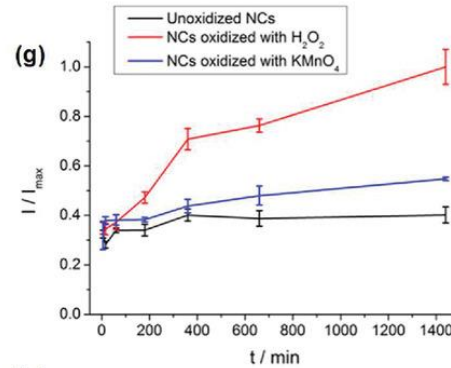
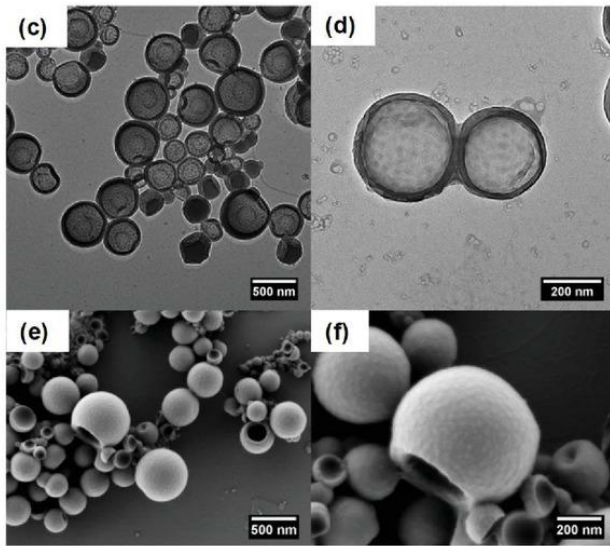
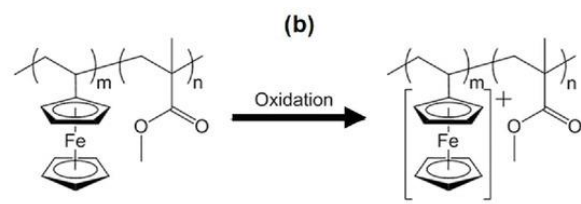
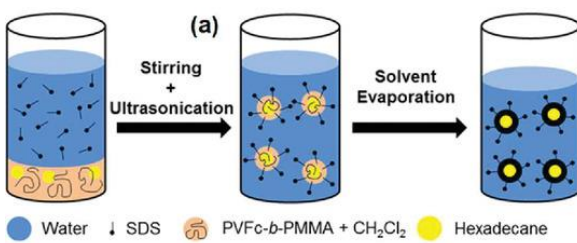
X-Ray Diffraction (XRD) studies

Phase analysis of the products is performed by powder XRD on a Rigaku D/max-2000 diffractometer with graphite monochromatized $\text{CuK}\alpha$ ($\lambda = 0.154056 \text{ nm}$) at a voltage of 50 kV and a current of 250 mA. The XRD pattern shows the phase composition of prepared products.

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.

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, Huguet 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 K α 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 series of 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 .

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.

FT-IR analysis

The presence of characteristic peaks is confirmed by using the FTIR analysis. The peaks indicate the characteristic functional groups of compound .

Applications of nanocapsules

to be suitable for various applications. 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 nano-particles, latex particles, or even biological cells.

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 ($ER\alpha$). The intravenous injection of these nanocapsules into estradiol stimulated MCF-7 cell xenografts led to a significant decrease in tumor growth and a decrease in $ER\alpha$ expression in tumor cells. This indicates that a novel strategy, based on $ER\alpha$ -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 asialoglycoprotein 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 TiO₂

nanocapsules A UV blocking cosmetic product containing TiO₂ nano capsule, which is produced by dispersing TiO₂ 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:

1. i) Passive enhanced permeability retention phenomenon due to the composition, size and stealth properties of the nanocapsules,
2. 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.

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.

RESULT

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.

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