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Review Article

A SYSTEMATIC REVIEW ON NANOCAPSULE: A NOVEL DRUG DELIVERY SYSTEM.

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Abstract

Nanocapsules, existing in miniscule size, which 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 great interest of attraction because of the protective coating, which are usually Pyrophoric and easily oxidized and delay the release of active ingredients.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.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.The enhanced delivery of bio-active 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.

KEYWORDS: Nanocapsule, X-ray diffraction, Radiotherapy, Spectroscopic techniques.

Introduction

In ancient times, humans have widely used plant based natural products as medicines against various diseases. Modern medicines are mainly derived from herbs on the basis of traditional knowledge and practices. Nearly, 25% of the major pharmaceutical compounds and their derivatives are obtained from natural resources (1.2). The discovery of novel drugs were based on the natural compounds with different molecular backgrounds. Natural products exhibit remarkable characteristic features such as extraordinary chemical diversity, chemical and biological properties with wide macromolecular specificity and with less toxicity. These lead to the discovery of novel drug delivery system.

Natural compounds are now being screened for treating several major diseases, including diabetes, cancer, cardiovascular, inflammatory, and microbial diseases, because natural drugs possess unique advantages, such as lower toxicity and side effects, low-price, and good therapeutic potential. Consequently, many natural compounds are not clearing the clinical trial phases because of these problems.(3)

Nanoparticle drug delivery systems are engineered technologies that use nanoparticles for the targeted delivery and controlled release of therapeutic agents.(4) Some major advantages of nanoparticles is their high surface-area-to-volume ratio, chemical and geometric tunability, and they have the ability

to interact with biomolecules to facilitate uptake across the cell membrane.
The surface area also has a large affinity for drugs and small molecules, like ligands or antibodies, for targeting and controlled release purposes. Nanoparticles refer to a family of materials both organic and inorganic. Each material has uniquely tunable properties and thus can be selectively designed for specific applications like:

1.Crossing the blood brain barrier (BBB) in brain diseases and disorder.
2. Enhancing targeted intracellular delivery to ensure the treatments reach the correct structures inside the cell.
3. Combining diagnosis and treatment.(5)

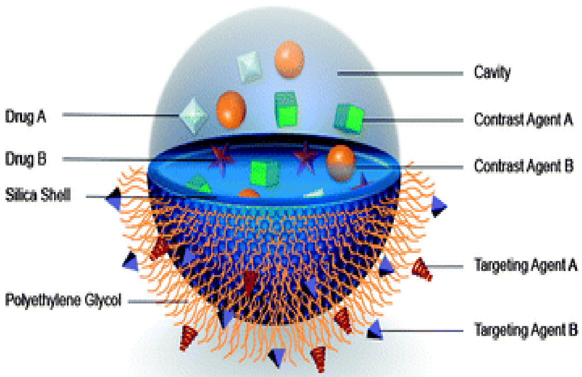

Figure1: Structure of Nanocapsule

Characterization Techniques:

Characterization of nanocapsules is difficult due to its small size and complex formation. Some of the techniques include quasi- elastic light scattering (QELS),Gel permeation Chromatography (GPC), Transmission Electron microscopy (TEM), Scanning Force Microscopy (SFM) and Scanning electron microscopy (SEM). But these techniques does not provided a clear picture of the Nanocapsules shell. The characteristics of interest of Nano capsules are morphology, size and size distribution, density and zeta potential.
The characterization of Nano particles deals with a branch called nanometrology.which deals with the characterization or measurement, of the physical and chemical properties of nanoparticles.They differ in other physical properties such as shape,size, surface properties, crystallinity, and dispersion state.

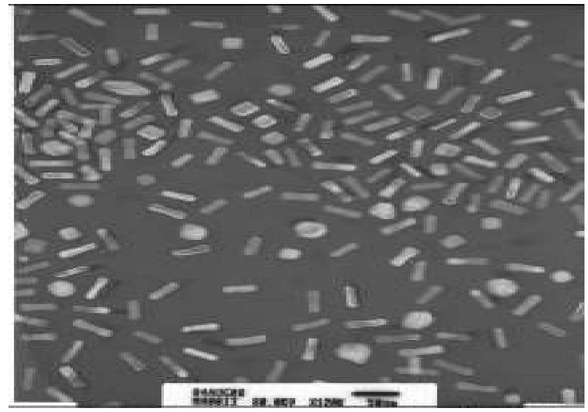

Figure 2: Nanoparticles which differ in Size, Shape, and Dispersion.

Methods of Characterization of Nanoparticles:

Microscopic Methods:
Microscopic methods generate images of individual nanoparticles to characterize their shape, size, and location. Electron microscopy and scanning probe microscopy are the preffered method to detect the Characterisation of Nanocapsules . Because nanoparticles have a size below the diffraction limit of visible light. Additionally, microscopy is based on single-particle measurements, meaning that large numbers of individual particles must be characterized to estimate their bulk properties. (6,7). A newer method,enhanced dark-field microscopy with hyperspectral imaging, shows promise for imaging nanoparticles in complex matrices such as biological tissue with higher contrast and throughput.(8)

Figure 3 : Electron Microscope scans the Individual Characterization of Nanoparticles.

Size and Dispersion:
External dimensions of a particle is the particle size, and Dispersity is a measure of the range of particle sizes in a sample. If the particle is elongated

or irregularly shaped, the size will differ between dimensions.

Size can be calculated from physical properties such as:

- Settling velocity
- Diffusion rate or coefficient, and
- Electrical mobility

Size can also be calculated from microscope images using measured parameters such as:

- Feret diameter
- Martin diameter and Projected area diameter.(9)

For airborne nanoparticles, techniques for measuring size include

- cascade impactors.
- electrical low-pressure impactors,
- mobility analyser and
- time of flight mass spectroscopy

For nanoparticles in suspension, techniques include

- dynamic light scattering,
- laser diffraction,
- Field flow fractionation
- particle tracking analysis
- size exclusion chromatography
- centrifugal sedimentation,and atomic force microscopy.(10)

Surface Chemistry and Charge:

The elemental or molecular chemistry of particle surfaces is called as Surface Chemistry. No proper definition exists for what constitutes a surface layer, which is usually defined by the measurement technique employed. For nanoparticles a higher proportion of atoms are on their surfaces relative to micron-scale particles, and surface atoms are in direct contact with solvents and influence their interactions with other molecules. Some nanoparticles such as quantum dots may have a core–shell structure where the outer surface atoms are different than those of the interior core.(11)

Surface charge generally refers to the charge from adsorption or desorption of protons on hydroxylated sites on a nanoparticle surface.Surface energy or wettability are also important for nanoparticle aggregation, dissolution, and bioaccumulation. They can be measured through heat of immersion microcalorimetry studies, or through contact angle measurements.

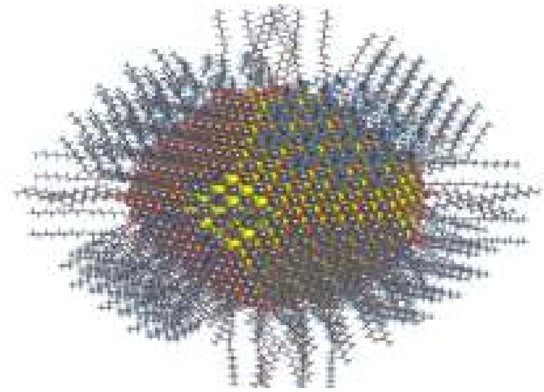

Figure 4: Surface of Nanoparticle

Determination of The Ph of Nanocapsule:

Nano capsules formulation pH was measured using a digital pH meter at room temperature. Nano capsules dispersion pH values fall within a range of 3.0-7.5.

Method of Preparation of Nanocapsule:

1. Nanoprecipitation Method:

The Nanoprecipitation method is also called solvent displacement or interfacial deposition. The polymers commonly used are biodegradable polyesters, especially poly-e-caprolactone (PCL), polylactide (PLA)and polylactide-co-glicolide PLGA.(12)

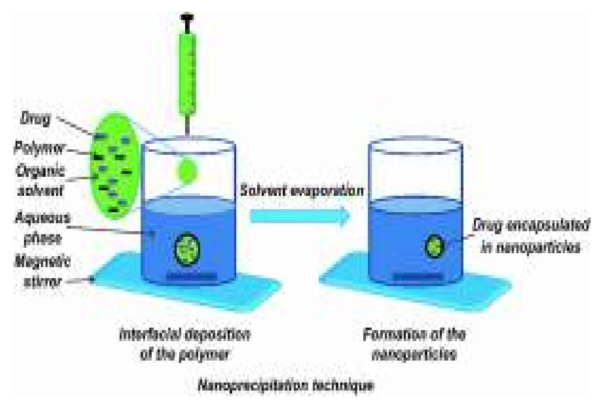

Figure 5: Preparation of Nanocapsules by Nanoprecipitation Method.

2. Polymerisation 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.The method for purifying the nanoparticle suspension, removes various stabilizers and surfactants employed for polymerization is Ultracentrifugation method. The nanoparticles are then resuspended in an isotonic surfactant medium. It has been suggested for making polybutyl cyanoacrylate or polyalkylcyanoacrylate nanopa rticles (13).

3. Emulsion–Diffusion Method:

In this method, the water miscible solvent along with a small amount of the water Immiscible organic solvent is used as an oil phase. Polymers commonly used are biodegradable polyesters, especially PCL, PLA and Eudragit. Poly (hydroxybutyrate-cohydroxyvalerate) (PHBHV) may also be used(14).

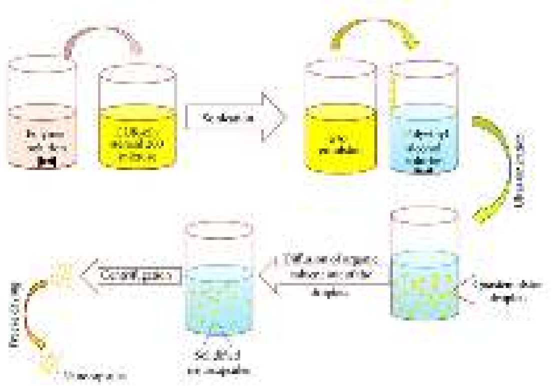

Figure 6: Polymerisation method of Nanocapsules.

4.Emulsion Polymerisation:

The M-6 Nanocapsule is an example of pre-emulsion preparation method (15). The pre Emulsion 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 pre-emulsion 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 , chemical vapor deposition (16).laser vaporization-condensation(17), charge transferring (18), organic reagent assisted method (19)solution-liquid-solid method and catalytic vapor-liquid-solid growth(20).

5. Polymer-Coating Method :

The layer-formed polymers used by them are poly (methyl methacrylate) (PMMA), poly(methacrylate) (PMA) and PCL. Nanocapsule formation is based on the mechanism of engulfment in three-phase systems (21).

6. Layer-by-Layer Method:

The layer-by-layer method makes used ofpolycations such as polylysine, chitosan, gelatin B, poly (allylamine) (PAA) poly (ethyleneimine) (PEI), aminidextran and protamine sulfate. The following polyanions are used(22):

- poly (styrene sulfonate) (PSS),
- sodium alginate,
- poly (acrylic acid),
- dextran sulfate,
- carboxymethyl cellulose,
- hyaluronic acid, gelatin A,
- chondroitin and Heparin.

Nano Based Drug Delivery Systems:

Recently, there has been enormous developments in the field of delivery systems to provide therapeutic agents or natural based active compounds to its target location for treatment of various aliments (23,24).There are a number of drug delivery systems successfully employed in the recent times, however there are still certain challenges that need to be addresses and an advanced technology need to be developed for successful delivery of drugs to its target sites.

Fundamentals Of Nanotechnology Based Techniques In Designing Of Drug:

Nanomedicine is the branch of medicine that utilizes the science of nanotechnology in the preclusion and cure of various diseases using the nanoscale materials, such as biocompatible nanoparticles (25) and Nanorobots (26)for various applications including, diagnosis (27)delivery (28) sensory (29) or actuation purposes in a living organism (30). Drugs with very low solubility possess various biopharmaceutical delivery issues including limited bio accessibility after intake through mouth, less diffusion capacity into the outer membrane, require more quantity for intravenous intake and unwanted aftereffects preceding traditional formulated vaccination process. However all these limitations could be overcome by the application of nanotechnology approaches in the drug delivery mechanism.

Drug Designing and Drug Delivery Processand Mechanism:
With the recent progression of nanomedicine and, due to the advancement of drug discovery/design and drug delivery systems, various therapeutic procedures have been proposed and traditional clinical diagnostic methods have been studied, to increase the drug specificity and diagnostic accuracy. For instance, new routes of drug administration are being explored, and they are being focusing on ensuring their targeted action in specific regions, thus reducing their toxicity and increasing their bioavailability in the organism (31).The advancements in computer sciences, and the progression of experimental procedures for the categorization and purification of proteins, peptides, and biological targets are essential for the growth and development of this sector(32,33).

In addition, several studies and reviews have been found in this area; they focus on the rational design of different molecules and show the importance of studying different mechanisms of drug release(34).Moreover, natural products can provide feasible and interesting solutions to address the drug design challenges, and can serve as an inspiration for drug discovery with desired physicochemical properties (35,36,37).Also, the drug delivery systems have been gaining importance in the last few years. Such systems can be easily developed and are capable of promoting the modified release of the active ingredients in the body.

Applications of Nanoparticles:

i) Nanocapsules as Drug Delivery Systems: Dispersed polymer Nanocapsule can serve as nano-sized drug carriers to achieve controlled release as well as efficient drug targeting.

ii) Medical sector : Cancer: Water-soluble polymer shells are being created to deliver a protein, apoptin, into cancer cells. The capsules are 100 nm in size.

iii) Future Nanocapsule Bandages to fight infection: This advanced dressing will speed up treatment because it is automatically triggered to release antibiotics only when the wound becomes infected,so that the dressing will not need to be removed, thereby increasing the chances of the wound healing without scarring. This Nanocapsules bandage might also be used for other types of wounds, such as ulcer and even by the military on the battlefield.

iv) Nutraceuticals: are substances that are placed infood to enhance nutrition. The increasedbioavailability of these substances is relative tothe size of the nanocarrier.

v) Drug administration : Nanocapsules have been proposed as drug delivery system for several drugs by different routes of administration such as oral, parenteral.

vi)New Cancer Weapon-Nuclear Nano cap sules: Chemists have found a way to package some of nature's most powerful radioactive particles inside DNA-sized tubes of pure carbon - a method they hope to use to target tiny tumors and even lone leukemia cells .

vii)Further Applications of Nanocap sules: Nanocapsules also have potential applications in agrochemicals, cosmetics, genetic engineering, wastewater treatments, cleaning products, and adhesive component applications. They can be used to encapsulate enzymes, catalysts, oils, adhesives, polymers,biomedicals, inorganic micro- and nanoparticles, latex particles, or even biological cells.

viii) Preparation of Biodegradable Insulin Nanocapsules: From Biocompatible Micro emulsions: Interfacial polymerization of spontaneously forming water-in-oil micro emulsions represents a convenient method for the preparation of poly (alkylcyanoacrylate) Nanocapsules suitable for the entrapment of bioactive peptides(39).
Drugs, growth factors or other biomolecules can be conjugated to nano particles to stop targeted delivery(40).This nanoparticle-assisted delivery allows for spatial and temporal controls of the loaded drugs to achieve the most desirable biological outcome.

Conclusion
The present review describes the advances in nanomedicines, including technological progresses that made the delivery of old and new drugs as well as novel diagnostic methodologies. A range of nano-dimensional materials, including nanorobots and nanosensors that are applicable to diagnose, precisely deliver to targets, sensesor activate materials in live system have been outlined. Initially, the use of nanotechnology was largely based on enhancing the solubility, absorption, bioavailability, and controlled-release of drugs. The efficacy of these natural products has greatly

improved through the use of nanocarriers formulated with gold, silver, cadmium sulphide, and titanium dioxide polymeric nanoparticles together with solid lipid nanoparticles, crystal nanoparticles, liposomes, micelles, superparamagnetic iron oxide nanoparticles and dendrimers.There has been a continued demand for novel naturalbiomaterials for their quality of being biodegradable, biocompatible, readily availability, renewable and low toxicity. Beyond identifying such polysaccharides and proteins natural biopolymers, research on making them more stable under industrial processing environment and biological matrix through techniques such as crosslinking is among the most advanced research area nowadays. Polymeric nanoparticles (nanocapsules and nanospheres) synthesized through solvent evaporation, emulsion polymerization and surfactant-free emulsion polymerization have also been widely introduced. One of the great interest in the development of nanomedicine in recent years relates to the integration of therapy and diagnosis.

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

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