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NANOCAPSULE - A NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT

Nano capsules are vesicular systems in which the drug is confined to a cavity consisting of an inner liquid core surrounded by a polymeric membrane. Nano capsules have various advantages and disadvantages. Two types of polymers are used for preparation of Nanocapsules they are: 1) Natural polymers 2) Synthetic polymers. Different methods are used for the preparation of Nanocapsules like 1) emulsification method 2) solvent evaporation method 3) polymer absorption method 4) Nano precipitation method 5) phase inversion method. 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 distinctive polymer membrane made up of natural or synthetic polymer. they have attracted a great interest as they contain a protective coating. different types of evaluation tests have been performed for nanocapsules.

KEYWORDS: Nanocapsules, polymeric membrane.

INTRODUCTION

Nanotechnology is the science of small.[1] Nanocapsules, as characteristic class of nanoparticles.[2] Nano derives from the Greek word "Nano" which means dwarf/small.[1] Their size ranges from 10nm to 1000 nm. In science and technology 'nano' stands for the order of magnitude 10-9 and thus describes very small dimension units between 'micro' (µ, 10-6) and 'pico' (p, 10-12). Hence, 1 nm is equal to 10-9 m. They are made up of one or more active materials (core) and a protective matrix (shell)[3] in which the therapeutic substance may be confined. Nanocapsules have been developed as drug delivery systems for several drugs by different routes of administrations such as oral and parental. Reduce the toxicity of drugs.] when polymeric nanoparticles contain a polymeric wall composed of non-ionic surfactants, macromolecules, phospholipids[4] and an oil core[5] they are names as "Nanocapsules".[6]

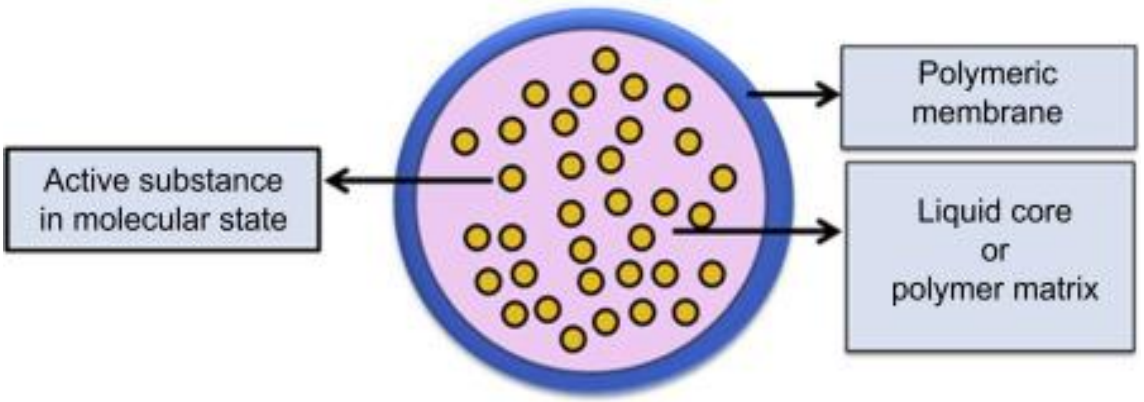

Fig. 1: Nano Capsule- An Overview.

USE OF NANOCAPSULES AS SMART DRUGS

Nanocapsules can be used as smart drugs that have specific chemical receptors and only bind to specific cells. It is this receptor that makes the drug 'smart,' allowing it to target cancer or disease.[7]

ADVANTAGES

- Higher dose loading with smaller dose volumes
- Longer site-specific dose retention
- More rapid absorption of active drug substances
- Increased bio-availability of the drug
- Higher safety and efficacy

- Improved patient compliance
- greater bio-availability
- Smaller drug doses.
- Reduction in fed/fasted variability.
- Less toxicity.[1]

DISADVANTAGES

- Discontinuation of therapy is not possible.
- Extensive use of poly vinyl alcohol as detergents issues with toxicity.
- Alveolar inflammation.
- Limited targeting abilities.
- Pulmonary inflammation And pulmonary carcinogenicity.[1]
- Cytotoxicity

POLYMERS USED IN PREPARATION

Preparation of Nano capsules can be used as a two types of polymers

1) Natural polymers 2) Synthetic polymers

NATURAL POLYMERS

The most commonly used natural polymers are

1) Chitosan
2) Gelatin
3) Sodium alginate
4) Albumin

SYNTHETIC POLYMERS

The most commonly used synthetic polymers are:

1) Polylactides(PLA).[1,8]
2) Polyanhydrides
3) Polyglycolides(PGA)
4) Poly orthoesters
5) Poly lactide co-glycolides(PLGA)
6) Poly glutamic acid
7) Poly cyanoacrylates
8) Poly malic acid
9) Poly carolactone
10) Poly methacrylic acid
11) Poly(N-Vinyl pyrrolidone)
12) Poly(ethylene glycol)
13) Poly (methyl metha-crylate)
14) Poly acrylamide
15) Poly (vinyl alcohol).[1]

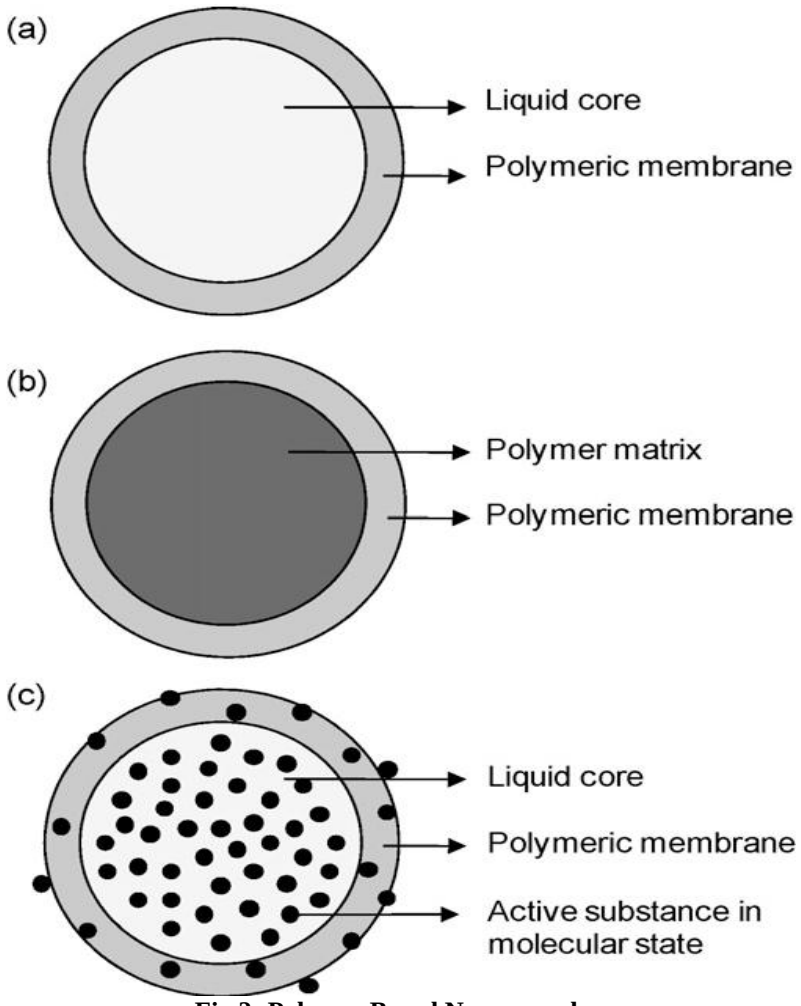

Fig 2: Polymer Based Nanocapsules.

METHODS FOR PREPARTION OF NANOCAPSULES

Nanocapsules are prepared by the following methods:

1. polymer absorption method
2. Nano precipitation method
3. Emulsification /solvent diffusion method
4. Solvent evaporation method
5. phase inversion method.[8]

1) POLYMER ABSORPTION METHOD/POLMERIZTION METHOD

Nanoparticles are formed by polymerising monomers in an aqueous solution followed by placing the drug either by the adsorption of nanoparticles or by dissolving in the medium of polymerization. Ultracentrifugation method, which is utilized for purifying the nano particle suspension, removes various stabilizers and surfactants employed for polymerization. The nanoparticles are then re-suspended in an isotonic surfactant free medium. It has been suggested for making polybutylcyanoacrylate or polyalkylcyanoacrylate nanoparticles. It is a very common method for preparation of nanomaterials. During polymerization, usually, the formation of micro-emulsion is a very important factor which has been the focus of extensive research worldwide due to its importance in a variety of technological applications. These applications include enhanced oil recovery, combustion, cosmetics, pharmaceuticals, agriculture, metal cutting, lubrication, food, enzymatic catalysis, organic and bio-organic reactions, chemical synthesis of nanoparticles and nanocapsules, etc.[9]

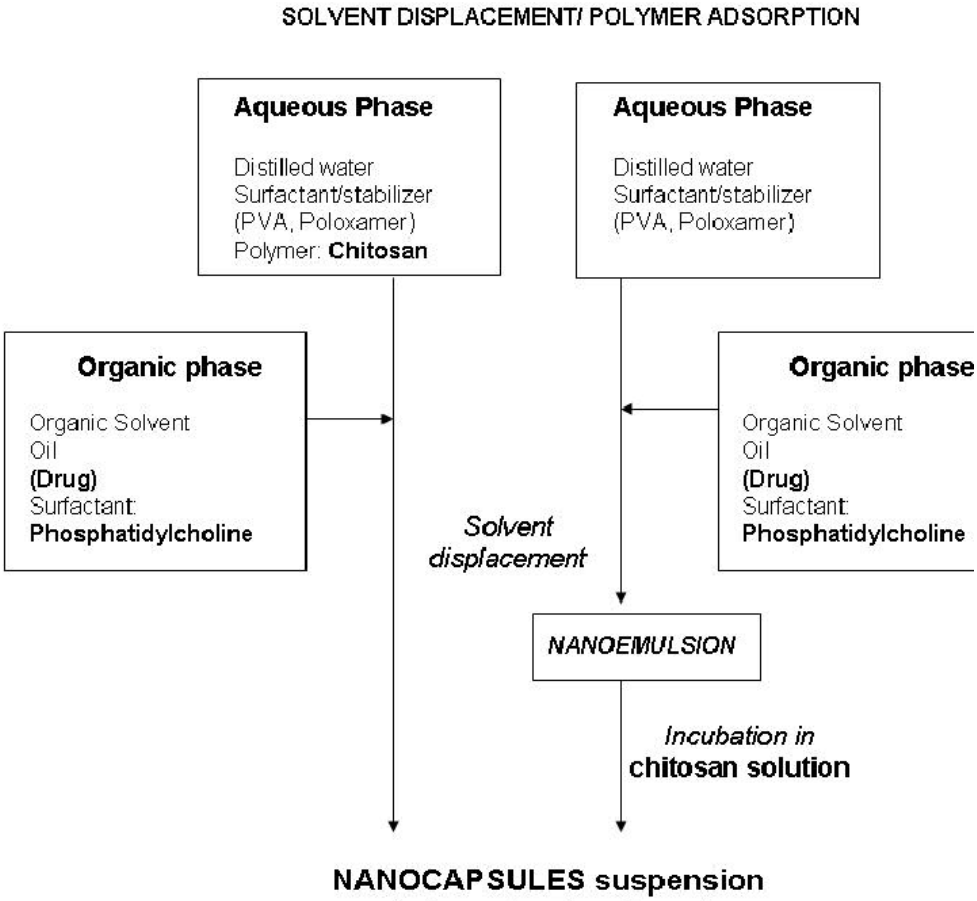

Fig 3: Polymer Absorption/Polymerization Method.

2) NANOPRECIPITATION METHOD

Nano precipitation is also called solvent displacement method. It involves the precipitation of a preformed polymer from an organic solution and the diffusion of the organic solvent in the aqueous medium in the presence or absence of a surfactant.[10] The solvent displacement technique allows the preparation of nanocapsules when a small volume of nontoxic oil is incorporated in the organic phase. considering the oil-based central cavities of the nanocapsules, high loading efficiencies are generally reported for lipophilic drugs when nanocapsules are prepared. the usefulness of this simple technique[11] is limited to water-miscible solvents, in which the diffusion rate is enough to produce spontaneous emulsification. then, even though some water-miscible solvents produce a certain instability when mixed in water, spontaneous emulsification is not observed if the coalescence rate of the formed droplets is

sufficiently high.[12] Although, acetone/dichloromethane (ICH, class 2) are used to dissolve and increase the entrapment of drugs, the dichloromethane increases the mean particle size[13] and is considered toxic. This method is basically applicable to lipophilic drugs because of the miscibility of the solvent with the aqueous phase, and it is not an efficient means to encapsulate water-soluble drugs. This method has been applied to various polymeric materials such as PLGA[14], PLA[15], PCL[16], and poly (methyl vinyl ether-comaleic anhydride) (PVM/MA),[17] This technique was well adapted for the incorporation of cyclosporin A, because entrapment efficiency is high as 98% were obtained.[18] Highly loaded nanoparticulate systems based on amphiphilic h-cyclodextrins to facilitate the parenteral administration of the poorly soluble antifungal drugs Bifonazole and Clotrimazole were prepared according to the solvent displacement method.[19]

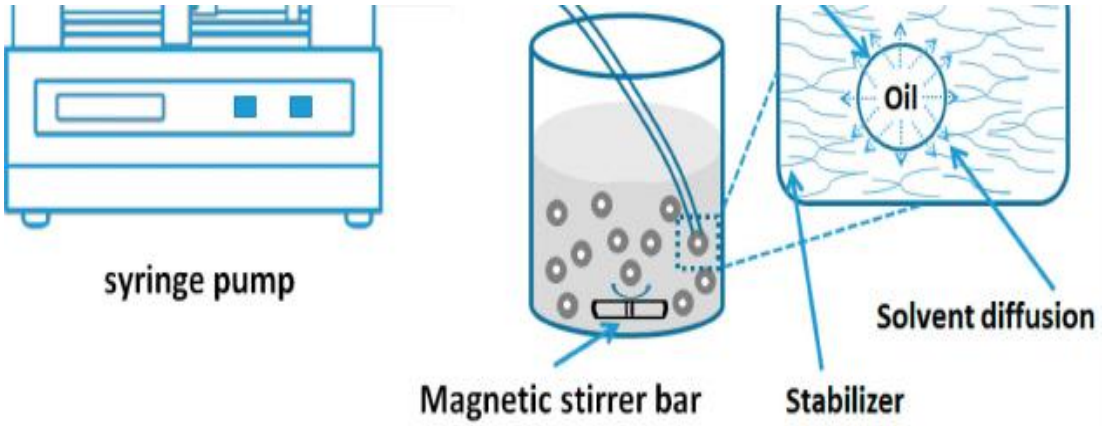

Fig 4: Nanoprecipitation Method.

3) EMULSIFICATION/SOLVENT DIFFUSION METHOD

This is a modified version of solvent evaporation method.[20] Preparation of nanocapsules by the emulsion-diffusion method allows both liphophilic and hydrophilic active substance nanoencapsulation. In this method of preparation required three phases those are organic phase, aqueous phase and dilution phase. The objective is the nano encapsulation of a liphophilic active substance, an organic solvent and oil partially miscible with water which should be water saturated. In this organic medium act as solvent for the different components of the organic phase. Inorganic phase can also include an active substance solvent (or) oil solvent. The aqueous phase comprises the aqueous dispersion of a stabilizing agent that is prepared using solvent-saturated water while the dilution phase is usually water. Polymers commonly used are biodegradable polyesters, especially PCL, PLA and Eudragit. Poly (hydroxyl butyrate-co-hydroxyvalerate) (PHBHV) may also be used. Inner phase contains the oil in addition to the active substance and solvent. In regarding to the external phase, the solvent used is water and poly(vinyl alcohol) (PVA) is preferred as the stabilizing agent. Other stabilizing agents such as poloxamer and ionic emulsifiers have been used. Suggested composition for preparation of nanocapsules is by emulsion-diffusion method. This technique presents several advantages, such as high encapsulation efficiency (generally >70%), no need for homogenization, high batch-to-batch reproducibility, ease of scale-up, simplicity, and narrow size distribution. Disadvantages are the high volumes of water to be eliminated from the suspension and the leakage of water-soluble drug into the saturated-aqueous external phase during emulsification, reducing encapsulation efficiency.[21,22]

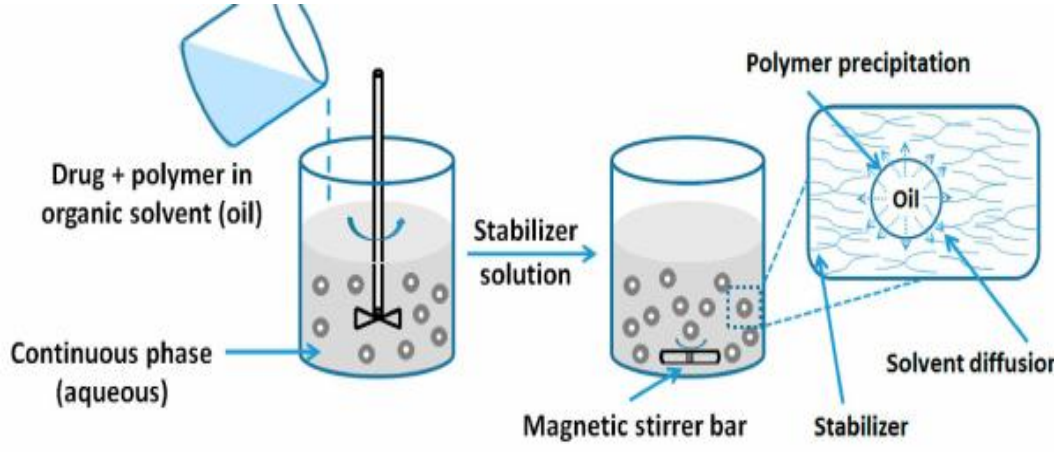

Fig 4: Emulsification Method.

4) SOLENT EVAPORATION METHOD

Solvent evaporation was the first method developed to prepare PNPs from a. In this method, polymer solutions are prepared in volatile solvents and emulsions are formulated. In the past, dichloromethane and chloroform preformed polymer[23] were widely used, but are now replaced with ethyl acetate which has a better toxicological profile. The emulsion is converted into a nanoparticle suspension on evaporation of the solvent for the polymer, which is allowed to diffuse through the continuous phase of the emulsion. In the conventional methods, two main strategies are being used for the formation of emulsions, the preparation of single-emulsions, e.g. oil-in-water (o/w) or double-emulsions, e.g., (water-in-oil)-in-water (w/o)/w. These methods utilize high-speed homogenization or ultrasonication, followed by evaporation of the solvent, either by continuous magnetic stirring at room temperature or under reduced pressure. Afterwards, the solidified nanoparticles can be collected by ultracentrifugation and washed with distilled water to remove additives such as surfactants. Finally, the product is lyophilized.[23,22] Lemoine et al[24] prepared PLGA nanoparticles of about 200nm by utilizing dichloromethane 1.0% (w/v) as the solvent and PVA or Span 40 as the stabilizing agent. Song et al.[25] prepared nanoparticles of PLGA with a typical particle size of 60–200nm by employing dichloromethane and acetone (8:2, v/v) as the solvent system and PVA as the stabilizing agent. Particle size was found to be influenced by the type and concentrations of stabilizer, homogenizer speed and polymer concentration. In order to produce small particle size, often a high-speed homogenization or ultrasonication may be employed.[8]

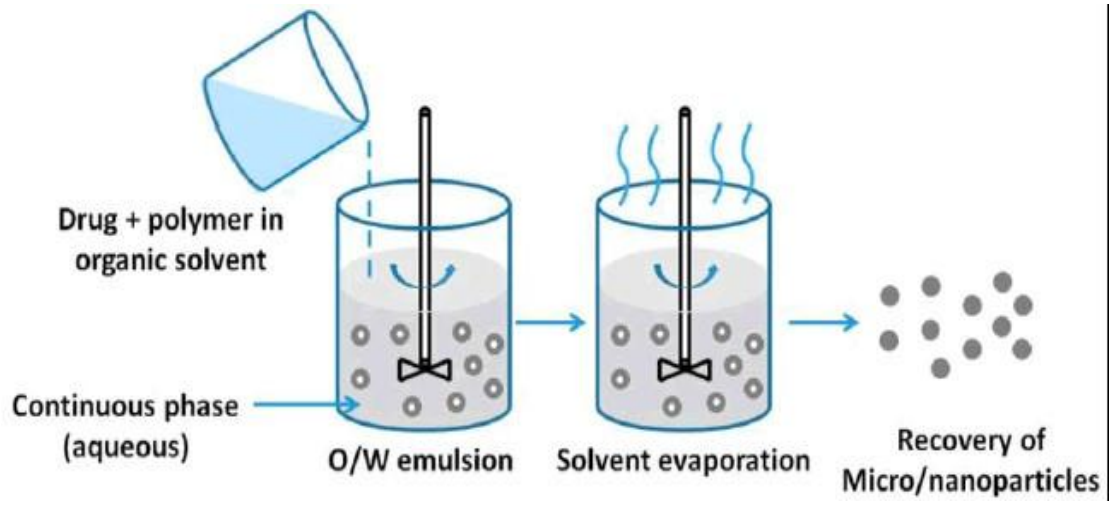

Fig 5: Solvent Evaporation Method.

5) PHASE INVERSION METHOD

This method for preparation of silica nanocapsules is by inter facial polymerization of nanoemulsions which are prepared by the phase inversion temperature(PIT) method. This is a low-pressure homogenisers. The nanoemulsions were prepared with decane as the oil phase, in which tetraethoysilane(TESO) was dissolved with an ethoxylated alcohol as the surfactant. The hydrolysis and polymerization of the TESO was performed under basic and acidic conditions using HCl and ammonia, respectively. The obtained nanocapsules have an average size between 100 and 300 nm, which

consists of an oil core(decane) and silica shell, which were characterized using dynamic light scattering, fourier transform infrared spectroscopy (FTIR), high-resolution scanning electron microscopy (HR-SEM) and by flourescence of an encapsulated aolvantochromic dye. The capsules could be positively or negatively charged by adsorption of ionic surfactants after they were formed.[26]

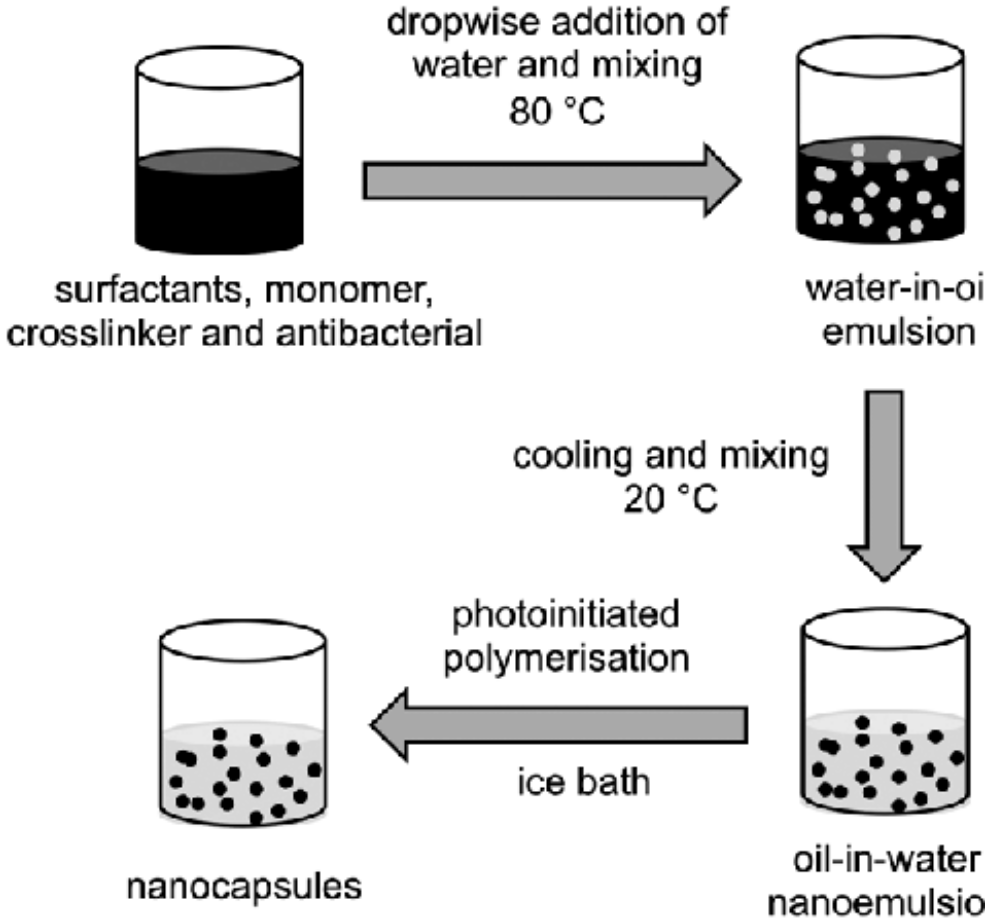

Fig 6: Phase Inversion Method.

EVALUATION OF NANOCAPSULES

1. **PARTICLE SIZE:** The smaller particles have greater surface area; therfore, most of the therapeutic agents associated at or near to the surface particle, lead to instant drug release, whereas, the larger particles having the larger core surfaes graduallt diffuse out.[27]
2. **DETRMINATION OF PH OF NANOCAPSULE:** Nanocapsules formulation pH was measured using a digital pH meter at room temperature. Nanocapsules dispersion pH value fall within a range of 3.0-7.5.
3. **DETERMINATION OF DRUG CONTENT:** Drug content was determined by dissolving 1ml of prepared nanocapsules in 20ml of acetonitrile. Appropriate quantity of sample was then subjected to the UV Spectrophotometer at 232nm. The absorbance for each sample was measured and compared with the standard.
4. **STRUCTURAL CHARACTERIZATION:** Structural characterization can be done by using field emission scanning electron microscopy (FE-SEM) and transmission electron microscopy (TEM) to determine the various attributes like shape, size and surface morphology. Micrographs of the nano capsules were obtained using a Phillips Cm 200 operated at 20-200 kv while the Fe-SEM was carried out using Hitachi S-4800 FE-SEM equipped with energy dispersion spectrometer (EDS).
5. **IN-VITRO DRUG RELEASE:** In vitro dissolution studies were carried out using USP type 11 dissolution apparatus. The study was carried out in 100 ml of buffer (PH 3.0). the nano capsules suspension was placed in dialysis membrane and dipped in dissolution medium which was kept inert thermostatically at 37±0.50C. The stirring rate was maintained at 100 rpm. At predetermined time intervals 5ml of sample were withdrawn and assessed for drug release spectrophoto metrically. After each withdrawal 5 ml of fresh dissolution medium was added to dissolution jar.[1]

CONCLUSION

The main goal of this review was to describe the different preparation techniques available for production of polymeric nanocapsules. It was observed that preparing PNCs is a state-of-art technology that requires

a suitable technique among the various possible methods. Nanocapsules preparation methods have been marked by three aspects: 1) need for less toxic reagents 2) simplification of the procedure to allow economic scale up and 3) optimization to improve yield and entrapment efficiency. limitations like one particular process or technique is not suitable to all drugs, post preparative steps, such as purification and preservation, incomplete or discontinuous film, inadequate stability of certain active components are remained to solve. Despite these technological challenges, nanocapsules have been showed great promise for the development of drug delivery system. They also have the efficient applications in various fields of the agrochemical, waste water treatments, genetic engineering, cosmetics, cleaning products, as well as in adhesive component. In up coming future they provide the noval effective drug delivery system.

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