NANOMATERIALS FOR ANTIFUNGAL DRUG DELIVERY

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1. Introduction:-

Drug delivery systems show how a pharmaceutical product is administered to the target site in order to provide therapeutic action.

Nowadays, Fungi are causing an increasing number of diseases all over the world. These infections are classified as superficial mycosis, cutaneous mycosis, subcutaneous mycosis, and systemic mycosis. The majority of these disseminated infections are caused by Candida, Cryptococcus, Aspergillus, and Pneumocystis species, which cause cryptococcosis, candidiasis, aspergillosis, and pneumocystis pneumonia, respectively.

Researchers believe that relying solely on currently available antifungal compounds will not be enough to treat these mycoses. The introduction of a completely new antifungal drug that acts on the target sites must go through a lengthy process of discovery, various clinical testing and trials on animals and humans, development, and regulatory approval before being released to the market. It is time-consuming, expensive, and likely to fail.

As a result, modifications to the existing drug delivery system have never been overlooked and are being pursued in a novel manner. Novel advances in antifungal drug delivery systems have been developed and managed to overcome the issues of solubility, stability, bioavailability, safety, and effectiveness present in conventional formulations and methods of administration. The four major groups of advances in antifungal drug delivery are vesicular systems, nanoparticulate-based systems, colloidal carriers, and miscellaneous drug delivery systems [1].

2. Need & Rationale:-

Fungal infections are a problem today on a global scale. There is no medical cover-up in the world regarding the significance of fungi as human pathogens. According to recent development, accurate diagnosis and treatment of these infections are crucial and required. Numerous factors influence the development of modern pharmaceutical products and the method of administration.

Development of a successful novel antifungal drug delivery system, it is essential to thoroughly investigate the relationships between the formulations, mode of administration, pharmacological properties, pharmacokinetics, pharmacodynamics, stability, efficacy, safety, and clinical indications [2].

The high prevalence of fungal infections has become a serious public health concern, exacerbated by an increase in host predisposition factors. Despite the fact that there are numerous drugs on the market to treat these diseases, their efficacy is questionable, and their side effects must not be overlooked. Keeping this in mind, it is critical to develop new and innovative carriers for these medicines not only to combat emerging fungal infections but also to prevent the spread of drug-resistant strains [3].

3. Advantages:-[4, 5]

- Target specific drug delivery
- Biocompatible and biodegradable nature
- Easy drug solubility
- Acts as drug reservoir
- Easy and convenient process
- Avoid Systemic first pass metabolism
- Patient compliance and Minimizing side effects of drug
- Help in reducing toxicity and increasing therapeutic efficacy
- Longer residence time at the site of action
- Controlled release of drug can be achieved

4. Disadvantages:-[4, 5]

- Time consuming and expensive process
- High pressure during production induced degradation of drug
- Unexpected crystallization of drugs
- Unpredictable particle growth and gelation tendency
- Lack of robust controlled release of drugs
- Loss of high amount of drugs
- Lack of stability during storage period
- Unexpected drug expulsion after lipid transition during storage
- Tedious to handle over conventional dosage form

5. An Overview of Novel Drug Delivery System:-

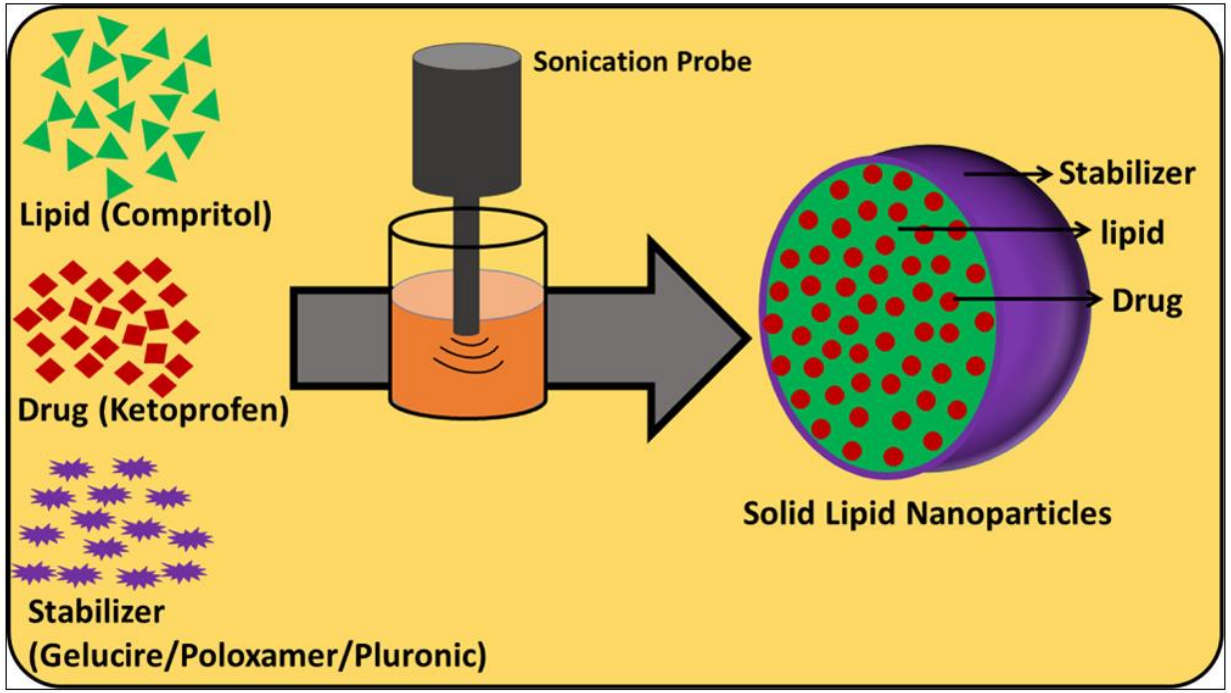
Novel drug delivery systems (NDDS) is one of the widely investigated topical formulation in pharmaceutical research. NDDS because of its unique ability to control release kinetics of encapsulate drugs, encapsulate a wide array of drugs and increase disease specific localization, reduces dosing frequency and enhance clinical efficacy. However, when implementing an appropriate topical formulation, one needs to understand the detail mechanism of antifungal therapeutics for maintaining adequate therapeutic performance.

Some examples of nanotechnology antifungal drug delivery are such as Solid lipid nanoparticles, Liposomes, Niosomes, Microoemulsion, Nanoemulsion, Metal nanoparticles, dendrimers, nanocrystals, nonogels etc.

6. Types of Novel Delivery Systems and their examples:-

6.1 Solid-Lipid Nanoparticles (SLN):-

- These are nano-lipid carriers where the active therapeutic is dispersed within a lipid core matrix.
- These are nanoparticle-imprinted matrices composed of lipids & surfactants.
- Solid lipid nanoparticles can be prepared using high homogenization or through the preparation of microemulsion.
- SLN's are w/o emulsion containing solids lipids as oil phase.
- The advantages of SLN's include low risk of toxicity (used lipids are physiologically same), hence biocompatible.
- The smaller size of lipid particles allows close contact with stratum corneum, facilitates dermal penetration of drug and controlled release of drug.
- Their formulation generates a film on the skin and prevent water evaporation.



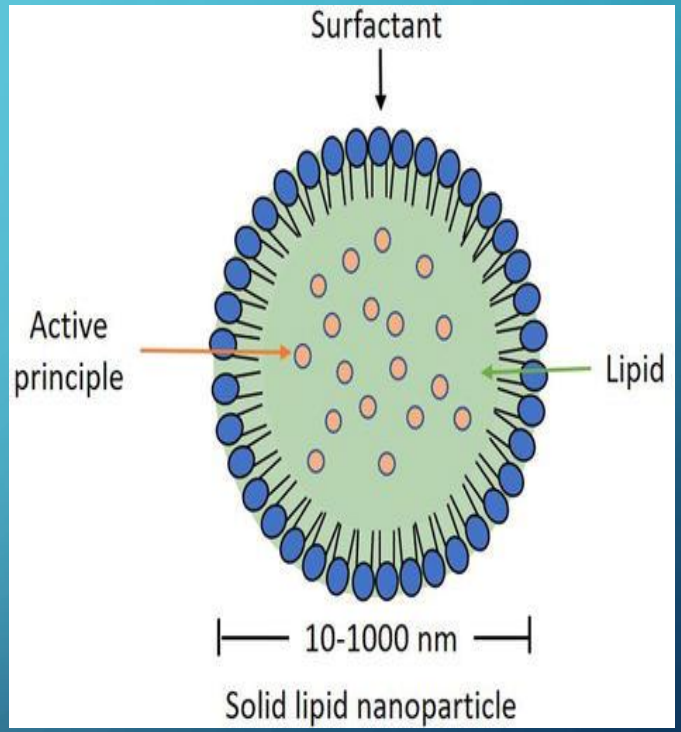


Figure 1: Method of Preparation and Structure of Solid Lipid Nanoparticles

6.2 Liposomes:-

- These are bilayer phospholipid spherical vesicles composed of amphiphilic lipids (phospholipids and cholesterol).
- They can accommodate a wide variety of drugs including both hydrophilic and lipophilic drugs.
- They may trap hydrophilic molecules in their aqueous core and lipophilic drugs in their lipid bilayer.
- Amphiphilic phospholipid and ultra flexible character of liposomes protect the drug from degradation and increase skin permeability.
- Due to their ability to alter the biodistribution profile of entrapped drug, these are considered suitable for topical drug delivery.
- They can be either adsorbed on the outermost skin surface or penetrate into deeper layers.

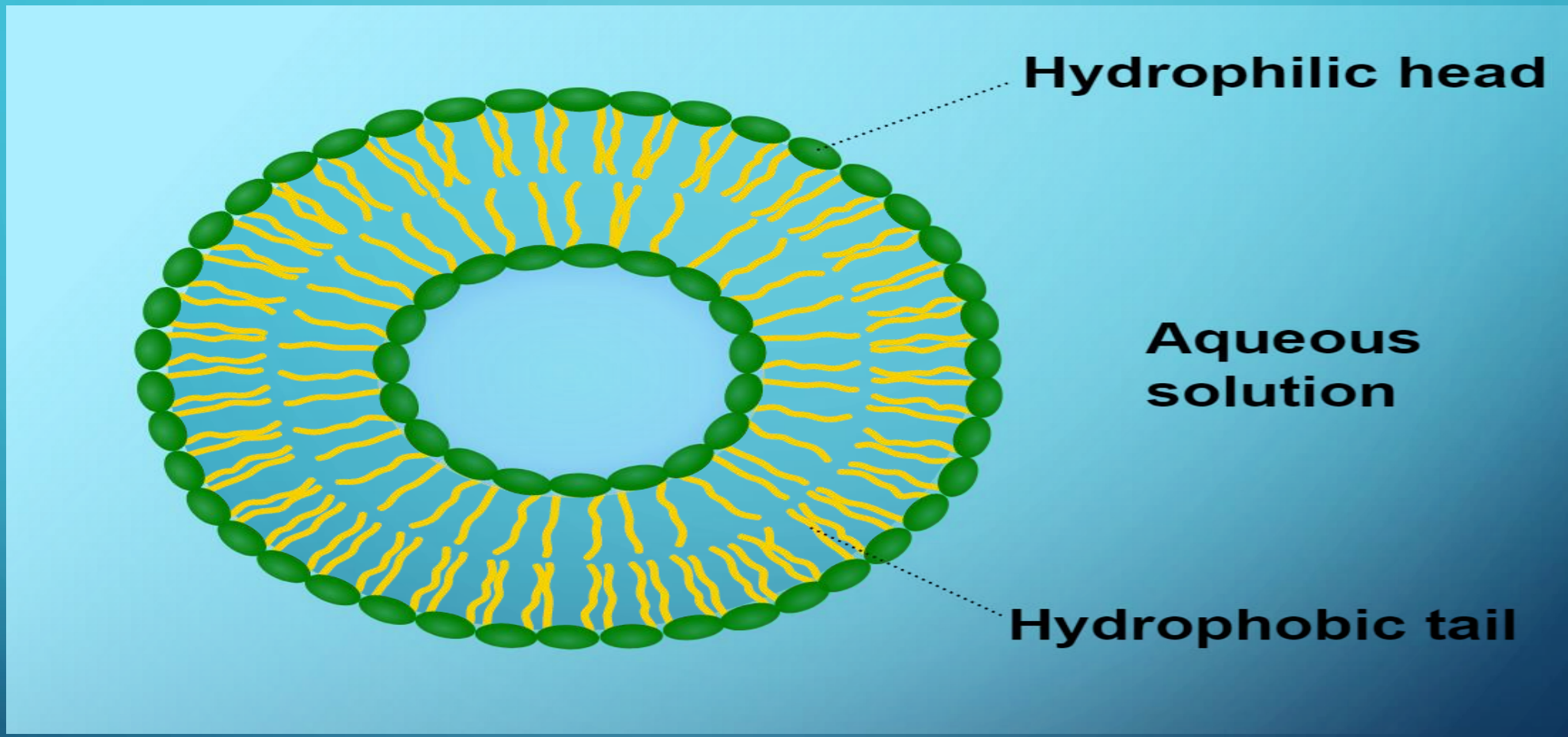
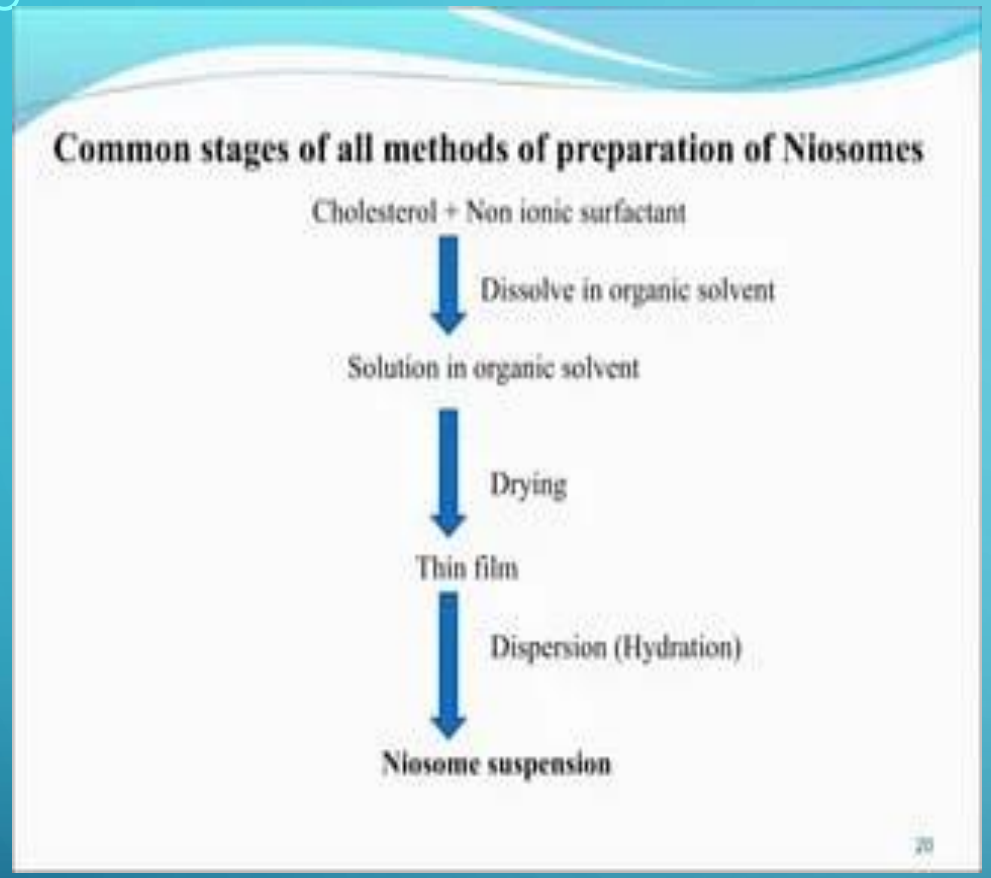


Figure 2: Structure of Liposomes

6.3 Niosomes:-

- These are a kind of spherical lipid vasical prepared by non-ionic surfactants.
- They interact with the stratum corneum, resulting in the reduction of transepidermal water loss.
- Its skin permeation depends on the types of surfactant, properties of drug used and morphological characteristics of niosomal preparations.
- These are a kind of bilayer lipid structure with non-ionic surfactants.
- They interact with the stratum corneum, resulting in reduction of transepidermal water loss.
- The degree of skin permeation depends on the interaction between noisome and skin, nature of drug, composition and morphology of noisome.



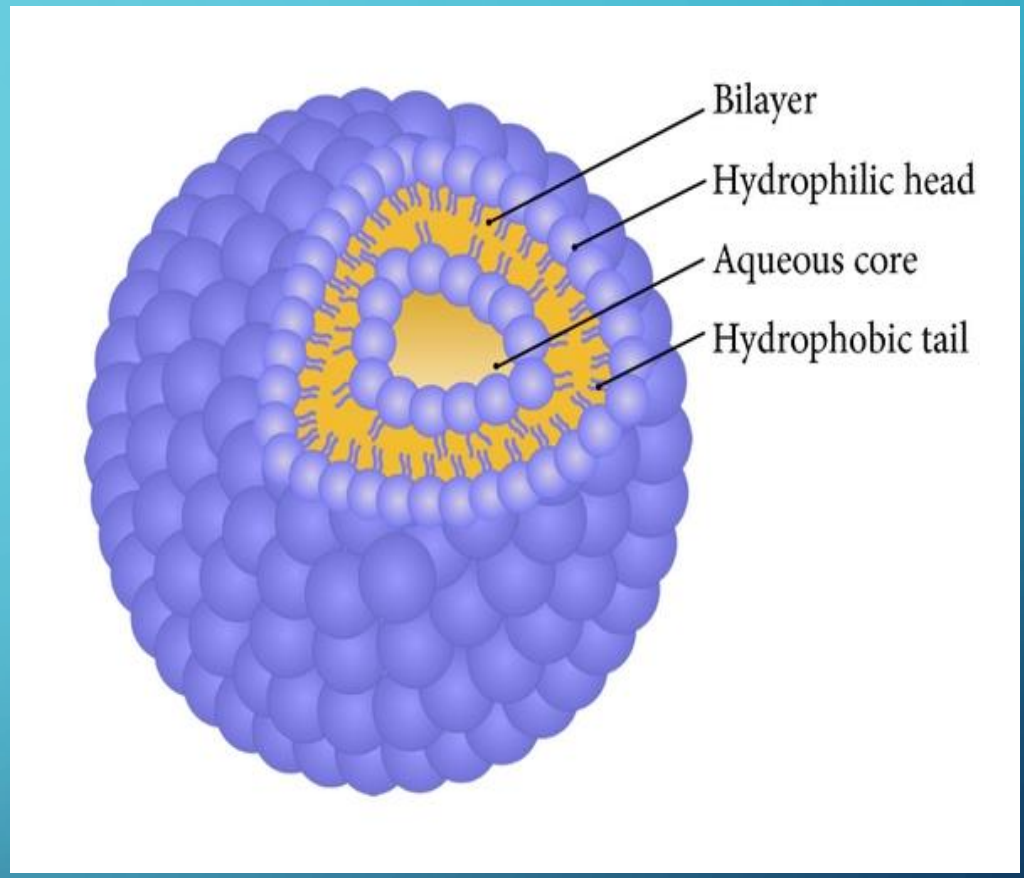
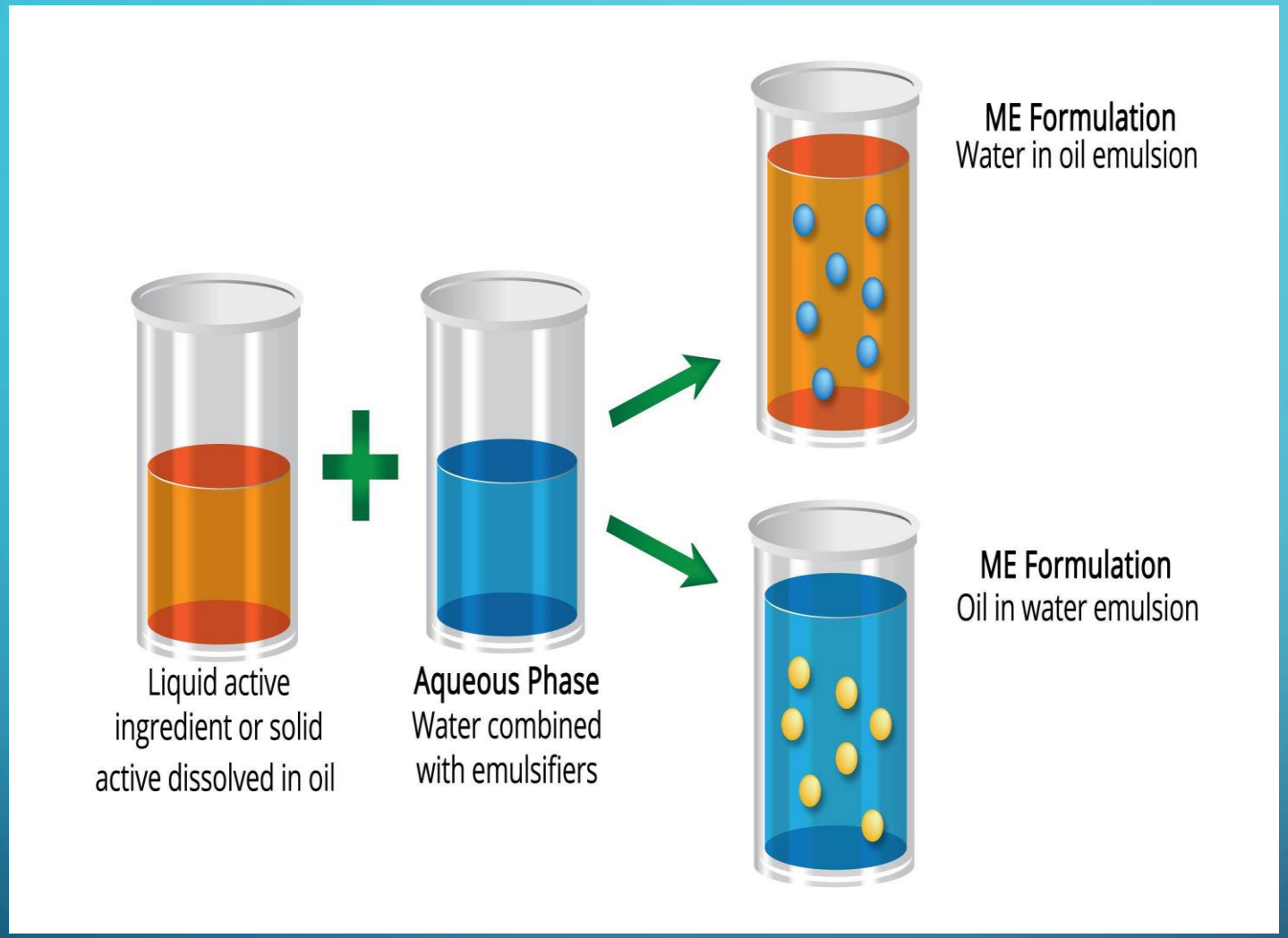


Figure 3: Stages of Preparation and Sructure of Niosomes

6.4 Microemulsion:-

- These are stable, translucent and isotropic dispersions of oil in water.
- These are stabilized by surfactants and co-surfactants for topical and transdermal administration of drugs with a droplet size of 0.1–1.0 μm.
- These have been reported very promising delivery system of anti-fungal agents due to their unique ability to enhance drug solubility.
- The antifungal spectrum of many azole drugs is compromised due to their low aqueous solubility.
- They offer the advantages like increasing drug solubility, high thermal stability, high permeability, easy manufacturing, optical clarity, and low cost.
- They show excellent biocompatibility because microemulsions are the appropriate delivery system for topical and transdermal systems.
- The presence of oils and surfactants in microemulsion formulation facilitate drug permeability across stratum corneum.



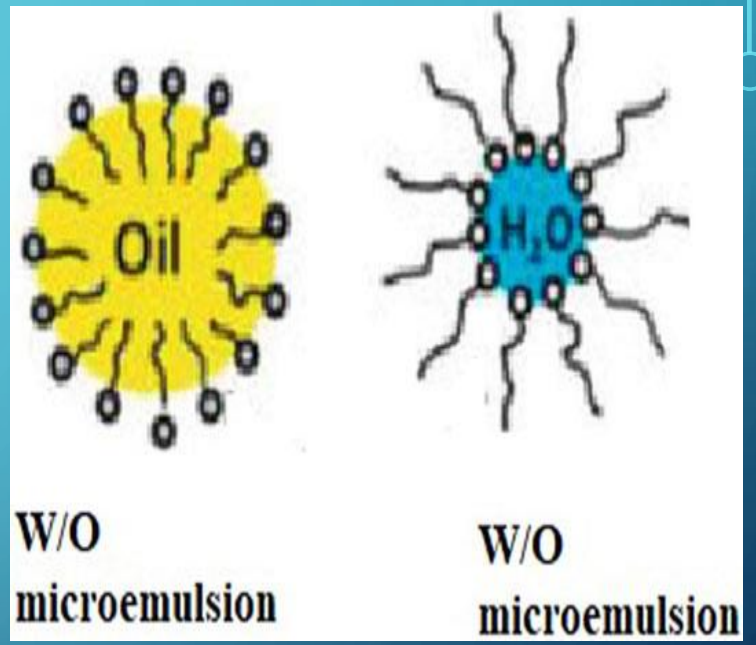
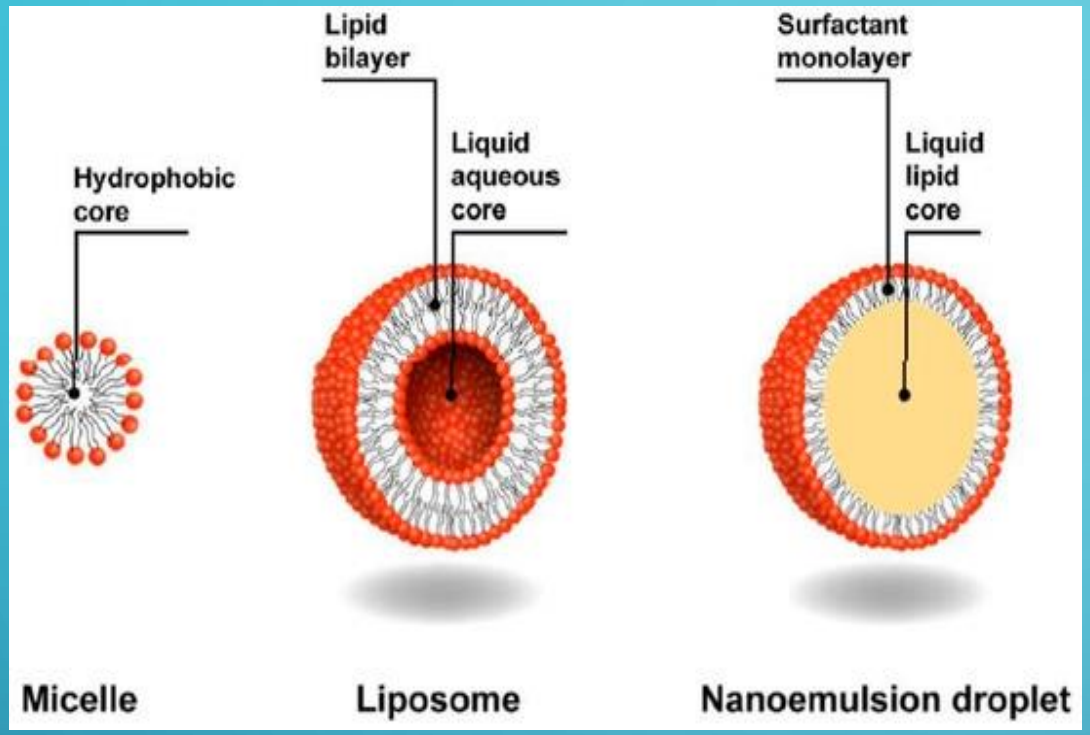


Figure 4: Method of Preparation and Structure of Microemulsion

6.5 Nanoemulsion:-

- It is a single phase, stable and isotropic dispersion consists of emulsified oil phase, water and amphiphilic molecules with droplet size ranging from 5-200 nm.
- These are thermodynamically and kinetically stable.
- Nanoemulsion because of high concentration of surfactants are considered suitable for skin permeation of both hydrophilic and lipophilic drugs.
- Nanoemulsion has immense potential to improve the solubility of lipophilic drugs.
- Nanoemulsions possess lot of commercial potentials owing to their reduced skin toxicity.
- They can usually be prepared using significantly less surfactant than microemulsion.



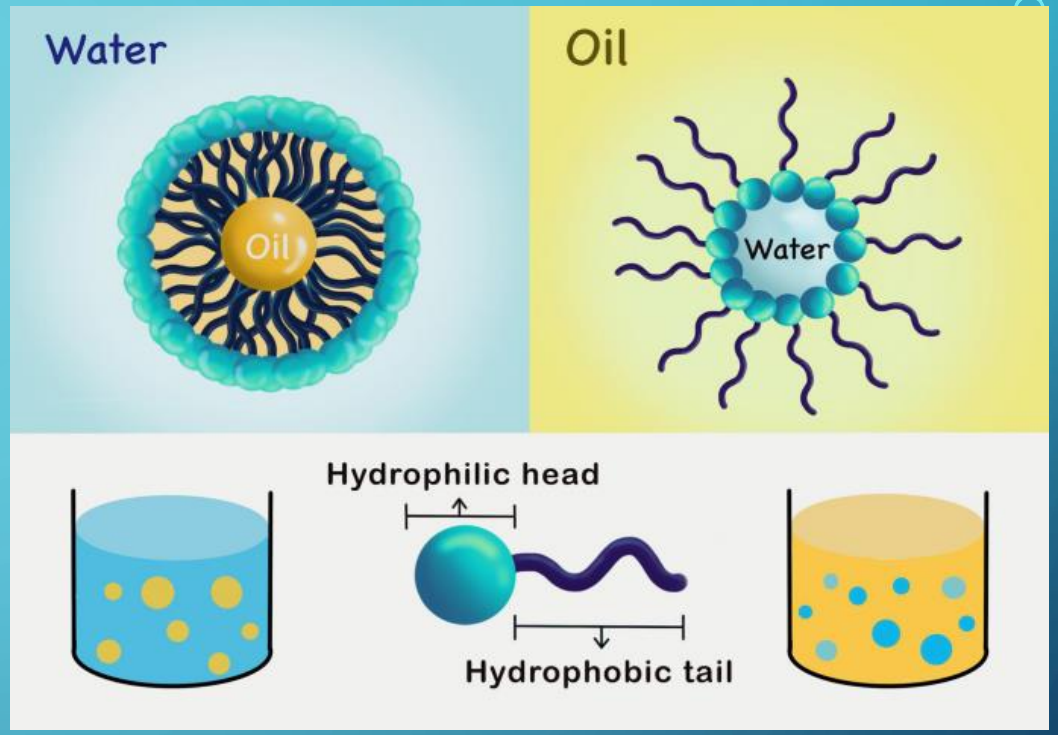


Figure 5: Method of Preparation and Structure of Nano-emulsion

6.6 Metal Nanoparticles:-

- Metal nanoparticles are small cluster of metal atoms with a size range of 10–100 nm and has distinct optical and functional properties.
- The optical properties of metal nanoparticles have clearly shown in case of gold nanoparticle.
- The nanoparticles due to their high aspect ratio make diffusion faster even below the critical temperature.
- The optical properties of gold, silver, lead, platinum nanoparticle arise from resonant oscillation of their free electrons in the presence of light, also known as Localized surface Plasmon resonance (LSPR).
- The advantages of these include strong plasma absorption, biological system imaging, determine chemical information on metallic nanoscale substrate, Surface-enhanced Raman scattering.
- Disadvantages of these include impurity, difficulty in synthesis, particle instability, biologically harmful.
- They should be prepared by a suitable method that is easily reproducible, available and economical with use minimum number of reagents that ay control the particle size.
- These are formed by physical, chemical and biological methods.
- Stabilization of metallic nanoparticles is done by electrostatic stabilization and steric stabilization.

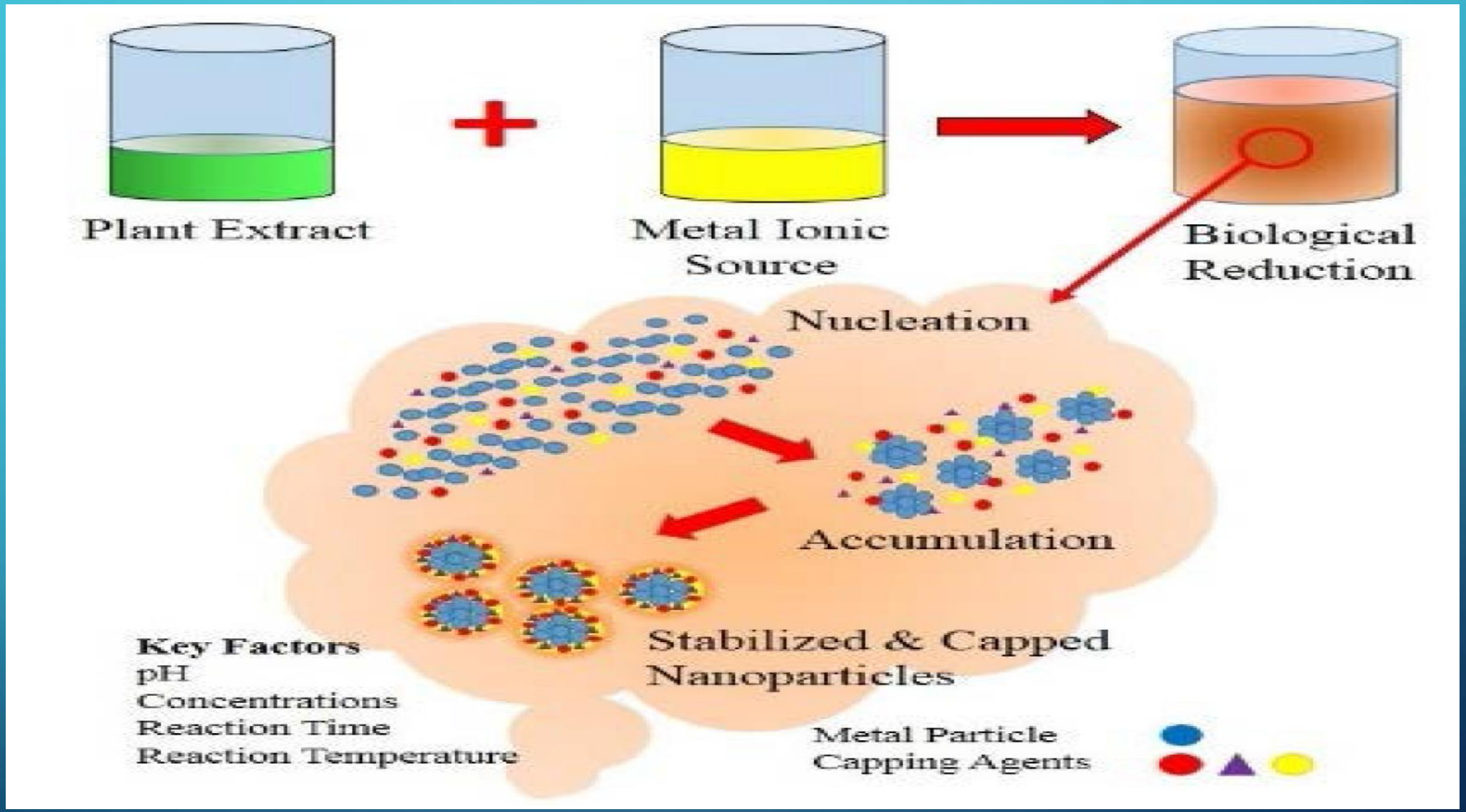
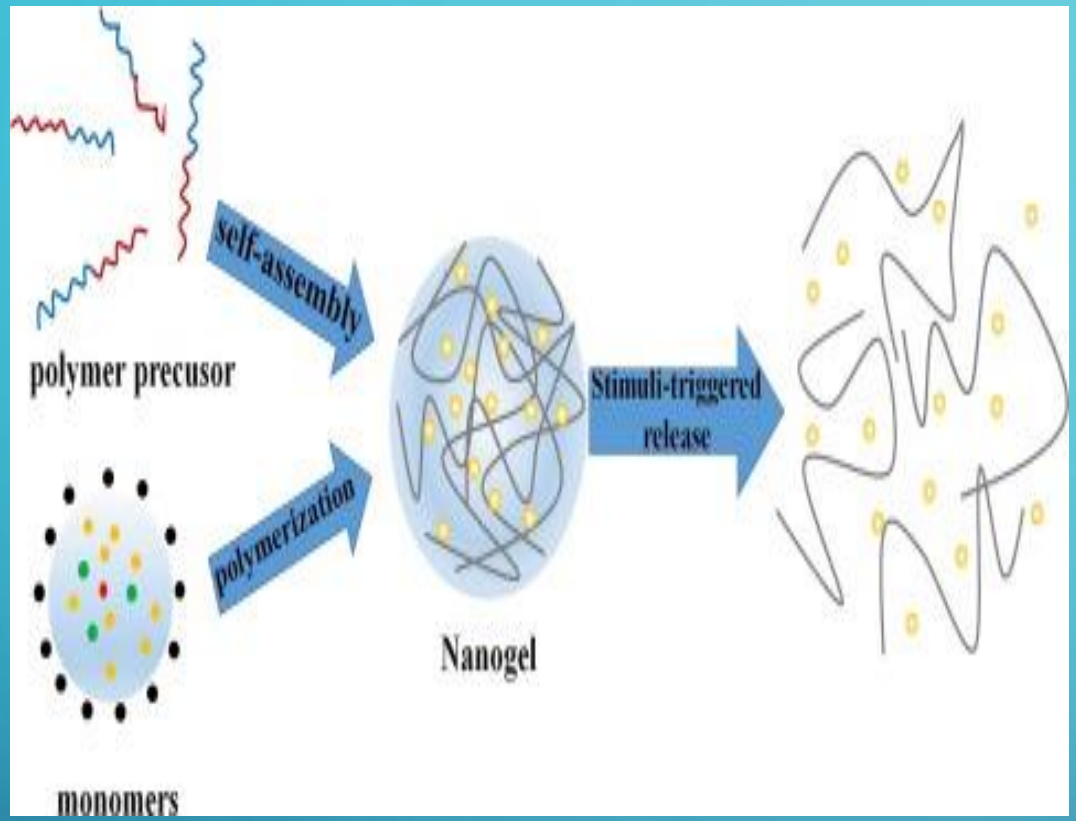


Figure 6: Method of Preparation and Structure of Metal Nanoparticles

6.7 Nanogels:-

- Nanogel is defined as nanoparticles made of cross-linked hydrophilic polymer ranging from 20-200 nm.
- They can be administered through different routes i.e. oral, topical, vaginal, ocular etc.
- Due to their smaller size and soft materials, they show better skin permeation and diffusion based swelling allowed desired drug release behavior.
- They have an excellent biocompatibility and high pay load of hydrophilic drugs.
- Nanogels possess a hydrophilic nature which limits good encapsulation property of hydrophobic drugs.
- Advantages of nanogel include high biocompatibility, high biodegradability, enhanced permeation capability, capability to cross the blood-brain barrier.
- Nanogel is found to be appropriate to administer a wide variety of drugs including hydrophilic and lipophilic drugs.
- The most common limitations of nanogel includes it is difficult to separate the surfactant and the solvent from the finished product even though the nanogel processing is not very pricey.



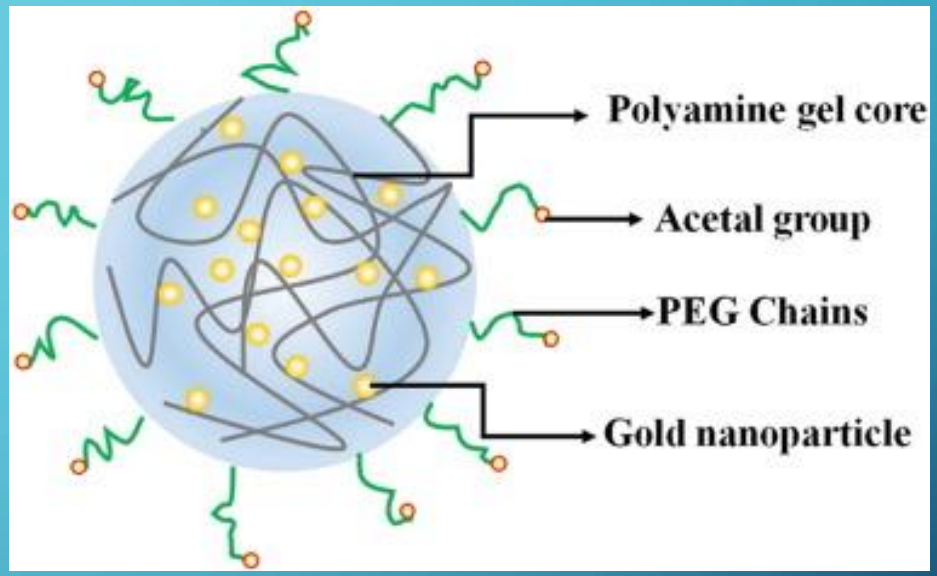


Figure 7: Method of Preparation and Structure of Nanogels

8. Novel Antifungal Preparations:-[2,4]

Sr. No.	Drug	Dosage Form	Brand Name
1.	Ketoconazole	Liposomes	--
2.	Nystatin	Niosomes	--
3.	Docetaxel	Solid Lipid Nanoparticles	Taxotere®
4.	Amphotericin B	Liposomes	Ambisome®
5.	Itraconazole	Microemulsion	--
6.	Clotrimazole	Ethosomes	--
7.	Econazole	Nanoemulsion	--

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Thank
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Any Questions?