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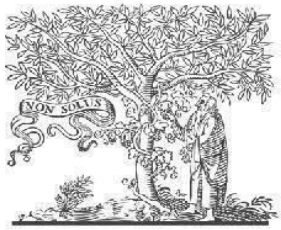

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NANOSPONGES: A REVIEW OF THEIR ANTIFUNGAL ACTIVITY

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ABSTRACT:

Recent advancements in nanotechnology have led to the development of targeted drug delivery systems. Effectively directing a molecule to a specific site requires a specialized delivery system. The discovery of nanosponges represents a significant breakthrough in addressing issues such as drug toxicity, poor bioavailability, and controlled drug release. Nanosponges can accommodate both hydrophilic and hydrophobic drugs due to their porous structure, which allows them to trap drug molecules and facilitate desired release patterns. Nanosponges are tiny, porous sponges that can circulate within the body, reaching specific sites and binding to surfaces to release drugs in a controlled and predictable manner. They are formulated by crosslinking cyclodextrins with carbonyl or decarboxylase crosslinkers. This technology has been extensively explored for the delivery of drugs through oral, topical, and parenteral routes. Additionally, nanosponges serve as effective carriers for enzymes, proteins, vaccines, and antibodies. This review highlights the methods of preparation, characterization, and the potential applications of nanosponges in drug delivery systems

KEYWORDS: Targeted drug delivery system, Nano sponges, Hydrophilic and Hydrophobic drug, β-Cyclohexatriene

INTRODUCTION

To achieve the desired results, targeting drug delivery systems has been a long-standing goal. Initially, the nanosponge drug delivery system was only used for topical applications. However, in the 21st century, nanosponges can now be administered orally as well as intravenously [1]. Nanosponges represent a modern class of materials made up of tiny particles with narrow cavities measuring just a few nanometers. These cavities can be filled with various substances. Due to their unique properties, nanosponges can carry both hydrophilic and lipophilic drug substances, enhancing the stability of poorly water-soluble drugs [2].

Nanosponges are three-dimensional scaffolds or networks of polyester that can naturally degrade. These polyesters are mixed with a cross-linker in a solution to form nanosponges. Since the polyester is biodegradable, it gradually breaks down in the body, releasing the loaded drug molecules in a controlled manner.

Advantages of Nanosponges:

1. **Increased Aqueous Solubility:** Nanosponges can enhance the solubility of poorly water-soluble drugs.
2. **Predictable Drug Release:** They can release drug molecules in a controlled and predictable fashion.
3. **Self-Sterilizing Properties:** Due to their tiny pore size (0.25 µm), bacteria cannot penetrate nanosponges, allowing them to act as self-sterilizers.
4. **Safety:** Nanosponge drug delivery systems are non-irritating, non-mutagenic, and non-toxic.
5. **Detoxification:** Nanosponges can help remove toxic and venomous substances from the body.
6. **Minimized Side Effects:** They reduce the side effects associated with drug therapy.
7. **Increased Formulation Stability:** Nanosponges enhance the stability and flexibility of drug formulations.
8. **Reduced Dosing Frequency:** They allow for less frequent dosing.
9. **Improved Patient Compliance:** The advantages of nanosponges lead to better patient compliance.

1.0.2 Disadvantages of Nanosponges:

- Nanosponges have the capacity to encapsulate small molecules, making them unsuitable for larger molecules.
- Dose dumping may occur at times.

1.2.0 Methods of Preparation:

1.2.1 Solvent Method:

In the solvent method, nanosponges are prepared by mixing polar aprotic solvents like Dimethyl sulfoxide (DMSO) and Dimethylformamide (DMF) with a polymer. A crosslinker is then added to this mixture in a 1:4 ratio. The reaction is carried out at temperatures ranging from 10°C to the reflux temperature of the solvent for 1 to 48 hours. Once the reaction is complete, the solution is cooled to room temperature, and the product is added to bi-distilled water. The product is then recovered by filtering under vacuum and refined using Soxhlet extraction with ethanol, followed by drying.

1.2.2 Emulsion Solvent Diffusion Method:

This method involves using different proportions of ethyl cellulose and polyvinyl alcohol to prepare nanosponges. Two phases are utilized: dispersed and continuous. The dispersed phase contains ethyl cellulose and the drug, dissolved in 20 ml of dichloromethane, with some polyvinyl alcohol (PVA) added to 150 ml of the continuous phase (aqueous). The mixture is stirred at 1000 rpm for about 2 hours. The resulting nanosponges are collected by filtration and dried in an oven at 400°C.

1.3.0 Mechanism of Drug Release from Nanosponges:

Nanosponges have an open structure without a continuous membrane. The active substance is encapsulated within the nanosponges and added to the vehicle. The encapsulated substance moves freely from the nanosponges into the vehicle until saturation and equilibrium are reached. Upon application to the skin, the vehicle becomes unsaturated, disrupting the equilibrium and allowing the active substance to flow from the nanosponges into the

epidermis until the vehicle is absorbed or dried. The nanosponges remain on the skin's surface (stratum corneum) and continue to release the active substance over an extended period.

1.4.0 Factors Influencing the Formulation of Nanosponges:

1.4.1 Nature of Polymer:

The polymer used in the preparation of nanosponges can significantly influence their formation and pre-formulation. The cavity size of a nanosponge should be large enough to encapsulate a drug molecule of a specific size for complexation

Method of Preparation:

The method of drug loading into nanosponges can influence the complexation between the drug and the nanosponges. The success of this process largely depends on the characteristics of both the drug and the polymer. Additionally, freeze-drying can also affect the drug-nanosponge complexation in certain cases.

Characteristics of Nanosponges:

- Nanosponges are porous particles primarily used to encapsulate poorly soluble drugs.
- They have high aqueous solubility and can carry both lipophilic and hydrophilic drugs.
- Nanosponge formulations are stable across a pH range of 1 to 11 and temperatures up to 300°C.
- They are non-irritating, non-mutagenic, non-allergenic, non-toxic, and protect the drug from physiological degradation.
- Nanosponges can encapsulate various types of drug molecules by forming inclusion and non-emulsion complexes.

Particle Size Determination:

The particle size of nanosponges is crucial for optimizing their properties. It affects both the drug release and solubility. Particle size can be determined using instruments like laser light diffractometers or zeta sizers. The cumulative percentage drug release from nanosponges of different particle sizes can be plotted against time to study this effect. Particle sizes larger than 30 μm may feel gritty, whereas sizes ranging from 10 to 25 μm are preferred for topical drug delivery.

Solubility Studies:

Higuchi and Connors described the phase solubility method to study inclusion complexation. This method is used to examine the effect of nanosponges on drug solubility, indicating the degree of complexation.

Microscopy Studies:

Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) can be employed to study the microscopic aspects of drug and nanosponge formulations. SEM is used to examine the morphology of nanosponges. Differences in the crystallization state of raw materials and final formulations, observed under an electron microscope, indicate the formation of inclusion complexes.

IR Spectroscopy:

IR spectroscopy estimates the interaction between drug molecules and nanosponges in the solid state. Changes in IR spectra can indicate complex formation. If less than 25 percent of

the drug molecule is encapsulated, the IR spectrum will show bands assigned to the included part of another molecule. IR spectroscopy is particularly useful for drugs containing carbonyl or sulfonyl groups and provides information about functional groups in the drug.

Zeta Potential:

Zeta potential, measured using a zeta sizer, quantifies the surface charge of nanosponges. It indicates the magnitude of the electrical surface charge at the double layer. A zeta potential value greater than 30 mV suggests good stability of the formulation.

Loading Efficiency:

The loading efficiency of a nanosponge particle can be determined by estimating the drug loaded into the nanosponge using UV spectrophotometry and high-performance liquid chromatography.

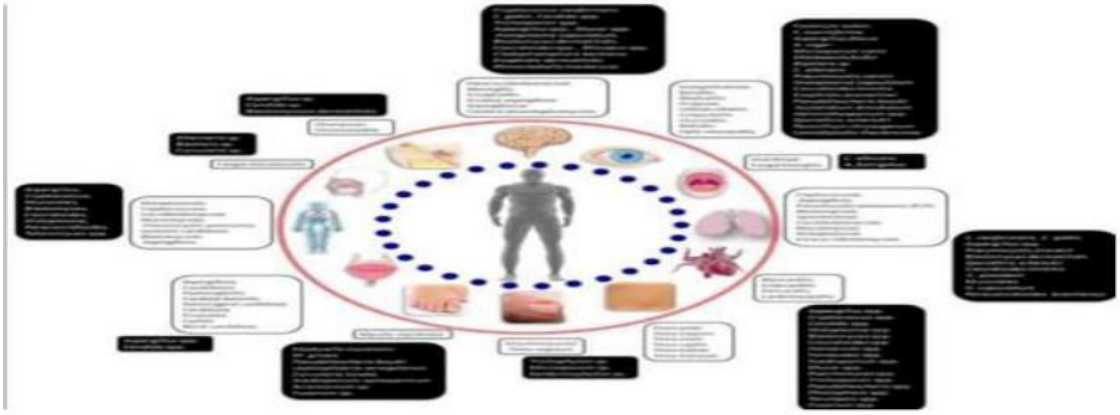

Fig No:-1 [Types of fungal infection]

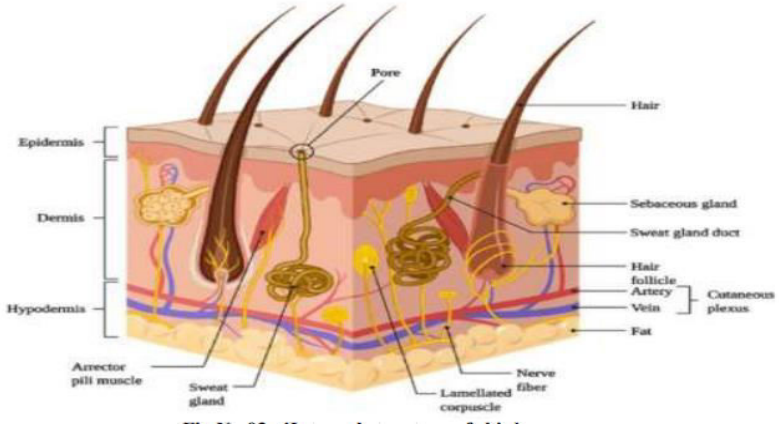

Fig.No.02 [Internal structure of skin]

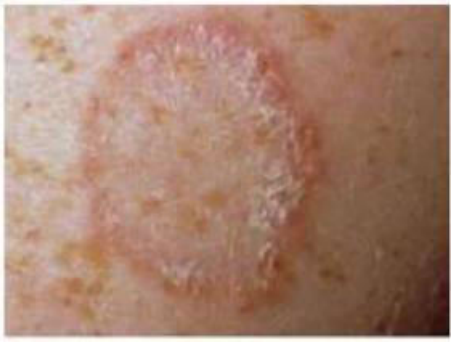

Fig no:-03 [Fungal infection on skin]

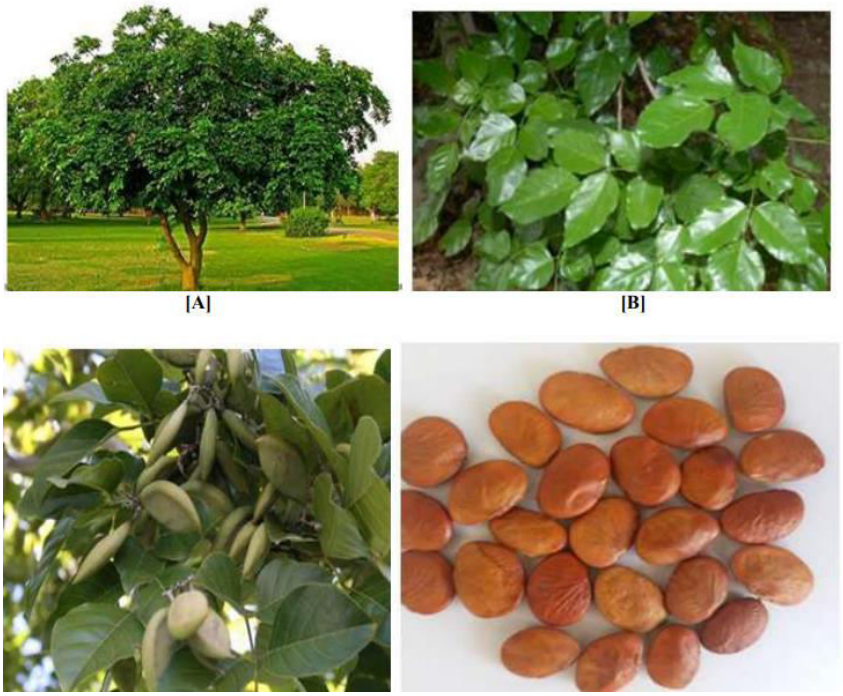

Fig No:-04 Pongamiapinnata: - [A] The whole plant [B] Leaves [C] Fruits [D] Seeds

NEEM:

Azadirachta indica, commonly known as neem, is native to India and has been naturalized in many tropical and subtropical regions around the world. It has significant medicinal value and is widely distributed globally. Neem contains numerous biologically active compounds, including alkaloids, flavonoids, triterpenoids, phenolic compounds, carotenoids, steroids, and ketones. The most biologically active compound is azadirachtin, which is a mixture of seven isomeric compounds labeled as azadirachtin A-G, with azadirachtin E being the most effective. Other biologically active compounds include salannin, volatile oils, meliantriol, and nimbin.

Neem leaves exhibit antifungal activity against pathogenic fungi such as Aspergillus flavus, Alternaria solani, and Cladosporium. A 5% aqueous leaf extract of neem has been shown to inhibit the growth of six tested fungal pathogens (Aspergillus fumigatus, Aspergillus niger, Aspergillus terreus, Candida albicans, and Microsporum gypseum).

Taxonomical Classification:

- **Kingdom**: Plantae
- **Order**: Rutales
- **Suborder**: Rutinae
- **Family**: Meliaceae
- **Subfamily**: Melioideae
- **Tribe**: Melieae
- **Genus**: Azadirachta
- **Species**: A. indica

Active Compounds of Azadirachta indica L. (Neem):

Azadirachta indica L. (neem) plays a therapeutic role in health management due to its rich source of various active ingredients. The most important active constituent is azadirachtin. Other significant compounds include nimbolinin, nimbin, nimbidin, nimbidol, sodium

nimbinate, gedunin, salannin, and quercetin. Neem leaves contain ingredients such as nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol, amino acids, 7-desacetyl-7-benzoylazadiradione, 7-desacetyl-7-benzoylgedunin, 17-hydroxyazadiradione, and nimbiol.

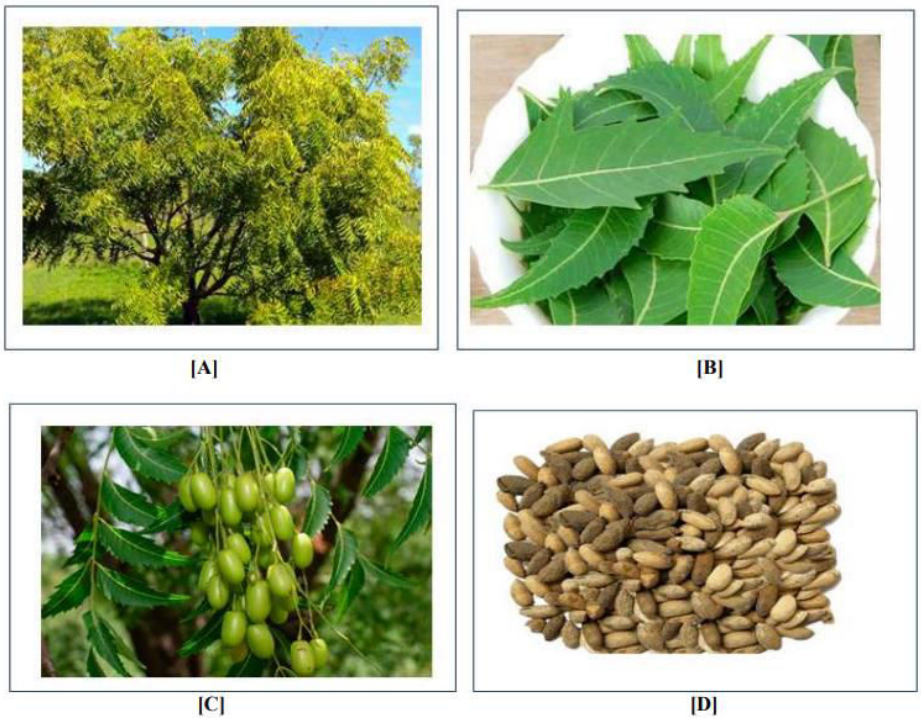

Fig No: -05 [Neem]

Preparation of Emulgel:

Emulgels are prepared by combining a gel with an emulsion. The emulsion and gel are made separately before being mixed together. To prepare the emulsion, the aqueous phase and oil phase are taken separately and then combined. The gel is prepared using a gelling agent. Once both the gel and emulsion are ready, they are mixed together with gentle stirring. The oil phase can include substances like castor oil, clove oil, and liquid paraffin, while the aqueous phase typically consists of water and alcohol.

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