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ANTIFUNGAL NANOCREAM AS A TOPICAL DRUG DELIVERY SYSTEM

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Abstract:

When it comes to delivering active ingredients to and through the skin for a variety of medicinal uses, nanoformulations have a certain position. These provide notable delivery advantages over coarse emulsions and are attractive, reasonably easy to manufacture, and reasonably inexpensive. A key technology opening the door for cutting-edge goods is nanotechnology. By using materials on a microscopic scale, nanotechnologies can give them new qualities not found in their bigger form. Furthermore, a vast range of consumer goods that are now available on the market and used in daily life can be altered by this technology. Nanocosmetics is one such fascinating area since nanomaterial can be used to create innovative products. On the other hand, the manufacturing of UV filters for sunscreens in because they behave differently than larger forms, nanoforms may be more dangerous than larger ones. Numerous studies conducted in the last few decades have shown how successful these delivery technologies are. Furthermore, the creation of novel excipients with prospective applications in nanoformulations keeps opening up new possibilities for formulations with high distribution capacities and low toxicity and irritation. In order to assess the durability of nano-cream preparation, droplet size, electrical conductivity, drug content, pH, and rheological characteristics have all been investigated at various temperatures. Thus, the extraordinary behaviour and features of nanomaterials have the potential to significantly alter both industry and human life. It is likely that in the future, new topical and transdermal delivery nanoemulsions solutions will be introduced.

***Index Terms*:** Nanocosmetics, Nanomaterials, Nanoemulsions.

I. INTRODUCTION

Fungal infections can result in more serious, invasive, and systemic disorders of the internal organs. They can also affect the skin and mucous membranes. The heart and lungs may also be impacted by fungal infections. Fungal infections that are spread through the air are more common in people with weakened or unbalanced immune systems. Alternative medicines based on nanoparticles have drawn a lot of scientific interest lately. Nano-carriers have the ability to improve the effectiveness of antifungals by binding to the fungal cell wall and so raising the medication concentration near fungus.[1] The four forms of these illnesses are subcutaneous, cutaneous, superficial, and systemic mycosis. Researchers claim that using the antifungal drugs that are now on the market alone would not be able to treat these mycoses. Before being put on the market, a novel antifungal medication that targets the sites of action must undergo an extensive phase of discovery, several human and animal clinical studies, development, and regulatory approval [2]. Advanced topical carriers solve biopharmaceutical problems including inadequate bioavailability and poor retention linked to traditional drug delivery systems because of their unique structural and functional features. Topical nano-carriers with antifungal drugs are the least toxic and exhibit superior therapeutic response. Nanoparticle-based alternative medicines have drawn a lot of scientific interest recently. Numerous research have addressed the impact of serum, size, and charge of the nanoparticles on the interactions between bacteria and nanomaterials [3]. Nanocream is one of the technological advances found in the cosmetic refining system on cosmetic items. Nanocream is a stable emulsion dosage form that is semisolid, with droplet diameters ranging from 20 to 500 nm. The benefit of using nanocream as a topical dose form is that it can improve the skin's ability to absorb active ingredients. Furthermore, the dosage forms for nanocream are more pleasant, easier to apply, and spreadable on the skin [4]. The only research groups working on nanoparticles in the

1990s were Muller, Gasco, and Western. Over 20 research groups are currently working on lipid nanoparticles at the India Institute of Chemical Technology in Mumbai, where lipid nanoparticle research is being actively pursued. One of the most intriguing instances of nanotechnology in antiquity was displayed by the Romans in the fourth century AD, when they employed nanoparticles and structures. "A cosmetic formulation that carries actives or other nanostructured ingredients, which has superior properties regarding its performance if compares with other conventional products" is how Fronza and collaborators defined nanocosmetics in 2007 [5]. Improved stability of cosmetic components and targeted delivery of ingredients to the desired position are the main advantages of using nanoparticles in Cosmeceuticals (Mu & Sprando, 2010). The formulation of cosmetics employing nanotechnology as a delivery system to enhance the efficacy of bioactive chemicals is known as nanocosmetics. Potential antibacterial, antifungal, and therapeutic effects of silver nanoparticles are demonstrated. Because of its antimicrobial qualities, it can be utilized as a preservative in cosmetic items. Topical cosmetic formulations can benefit from the use of silver nanoparticles. Nanoparticles can permeate skin at concentrations of 0.2–2% and do not exhibit any toxicity at this level (Campbell, Contreras-Rojas, Delgado-Charro, & Guy, 2012). Garlic and ginger extract were used to create zinc oxide and silver nanoparticles. Nanoparticles that were synthesized were described. A cream was created and various amounts of manufactured nanoparticles were added [6].

The typical skin's physiology

Three layers make up the skin: the epidermis (50–100 µm),

Dermis (1-2 mm)

Hypodermis (1-2 mm) [7].

Benefits

• Preventing first-pass metabolism.

• Practical and simple to use.

• The drawbacks of intravenous therapy and the various absorption conditions, such as pH fluctuations, enzyme presence, gastric emptying time, etc.

• Continuous drug input leads to efficacy with a reduced total daily dosage of the drug.

• Prevent intra- and inter-patent fluctuations in medication levels. (Surver and others, 2002).

Disadvantages

• The medication and/or excipients may cause skin irritation or contact dermatitis.

• Some medications' poor skin permeability

• The potential for allergic responses

• Applicable exclusively to medications whose actions depend on extremely low plasma concentrations

• It is difficult for drugs with bigger particle sizes to get through the skin. (Mishra and others, 1990)[8]

II. Techniques for making nano cream

Both high and low energy methods can be used to create nano cream, however high energy methods are preferred. External power is not required for low energy methods, whereas mechanical devices are employed in high energy methods to deliver high disruptive power. The majority of methods utilized to produce nano cream are low energy ones. Low energy techniques are gentle and non-destructive.

1. High energy emulsification method:

Because they are non-equilibrium systems, nanocream and nano emulsions cannot form quickly. High disruptive forces are delivered via mechanical devices. The majority of the time, high energy technologies are used to prepare nano creams. Ultrasonic generators, high pressure homogenizers, and high shear stirring all apply mechanical energy.[9] The high energy used causes the phases of water and oil to be disrupted, forming cream. Energy density of the input is -108-1010 W kg-1. The system receives a high energy supply in a brief period of time, which causes homogeneous tiny particle production [10].

2. High- Pressure Homogenization Method:

This is among the most often used methods for making nano cream. This technique can be used to prepare nanoparticles as small as 1 nm. Improved product stability, homogeneity, consistency, viscosity, and color are among the advantages of this process. In the personal care and

pharmaceutical industries, it is a routine industrial procedure. Increased pressure results in increased disruption efficiency. It uses non-thermal technology. By exerting pressure between 500 and 5000 psi, the nano emulsion is forced to flow through a tiny hole during this procedure. Tiny droplets created by combining several forces, such as cavitation, strong turbulence, and hydraulic shear [11].

The polydispersity index, or PDI, describes how uniformly droplet sizes are distributed in nanoemulsions.
Unmixed samples: PDI less than 0.08

Normal size distribution: PDI is in the 0.08–0.3 range.
PDI > 0.3 for a broad size range
Proteins, enzymes, and nucleic acids are examples of thermo labile substances that degrade when exposed to high energy and rising temperatures.

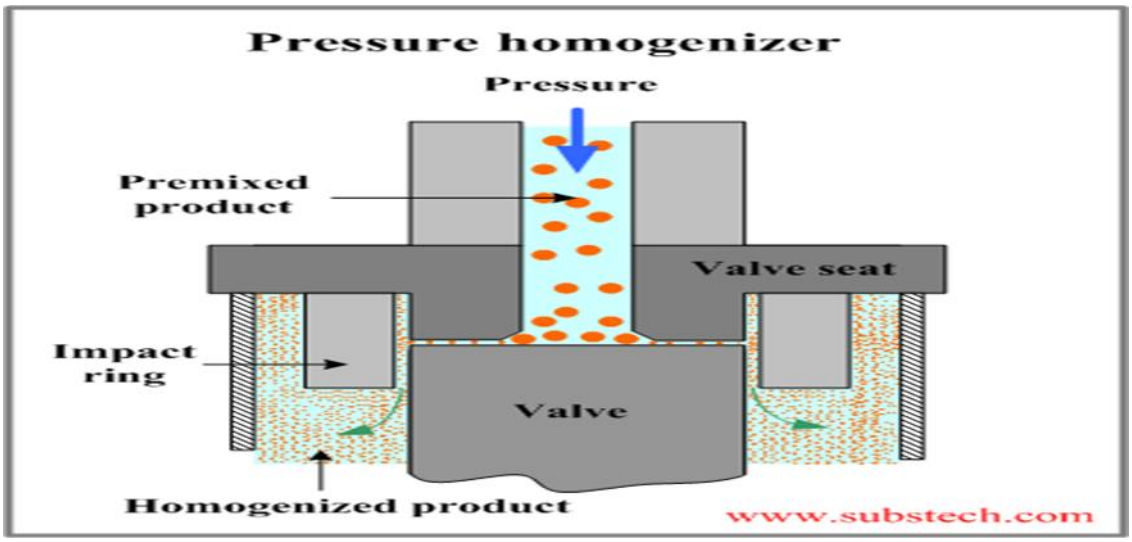

Fig: High pressure homogenization method

3. High-Shear Stirring:

Incorporate the usage of rotor-stator systems and high-energy mixers in the process of creating nanoemulsion. The size of the internal phase droplets is inversely correlated with the mixing intensity of these devices. It is challenging to prepare nanoemulsions with size ranges of 200–300 nm.[12]

4. Ultrasonic Emulsification

It is a special method for creating nanoemulsions. It's a very special and effective method. These are high-energy techniques. Ultrasound equipment produces shock waves. Ultrasonic emulsification is a process that involves two mechanisms. The oil stage scatters as beads in the nonstop stage in the first step because the acoustic field creates interfacial waves.
The second stage is when ultrasound induces acoustic cavitation, which results in the individual formation and disintegration of micro bubbles as a result of a single sound wave's weight shift. This method has the potential to result in lipid oxidation, polysaccharide depolymerisation, and protein denaturation.[13][14]

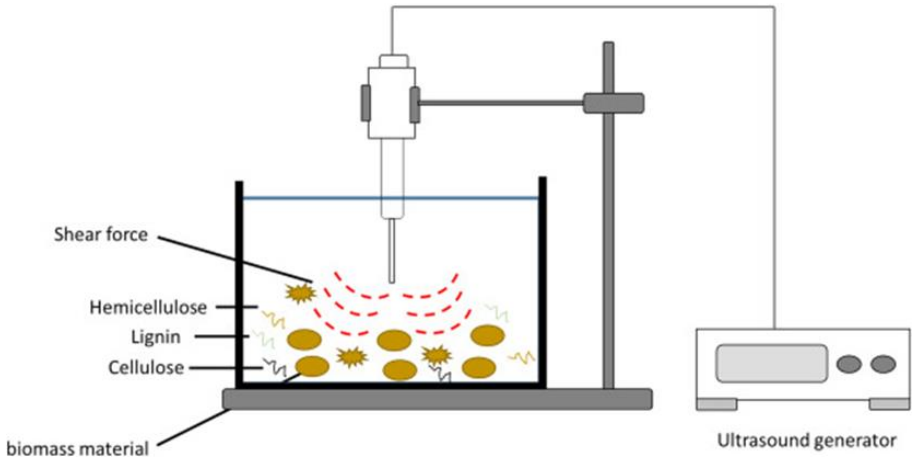

Fig: Ultrasonic Emulsification

5. Microfluidization

The most popular technique in the pharmaceutical business for creating tiny particles. A microfluidizer is utilized in this procedure. It has the capacity to create particles with more consistent sizes. This technique uses a high pressure force to generate particles that are 200–400 microns in size. Nano cream and nano emulsion can be produced by adjusting pressure and repeating the procedure.[15]

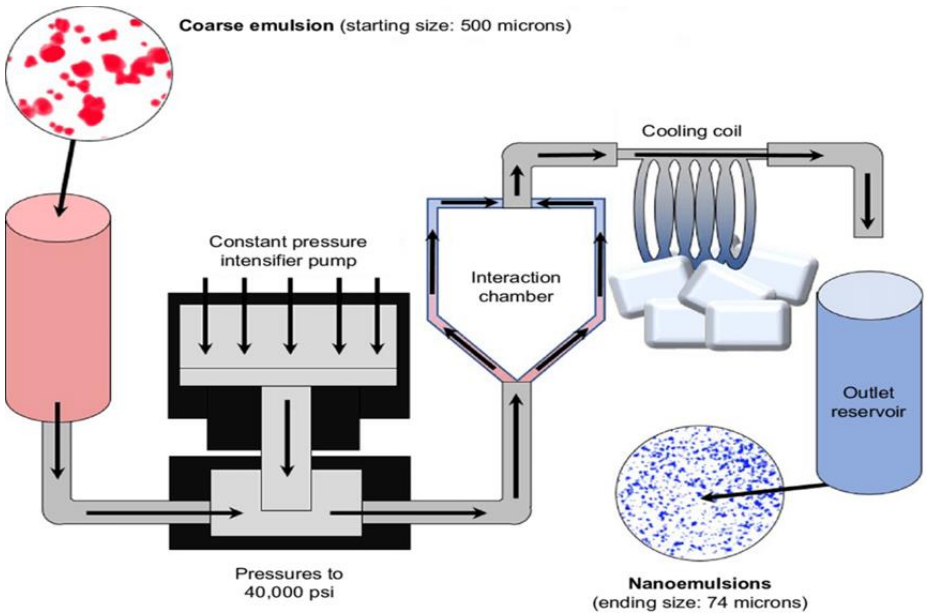

Fig: Microfluidization

6. Phase Inversion Temperature

This process turns o/w emulsion into w/o emulsion. It is an important process variable. A crucial role is played by non-ionic surfactants with temperature-dependent solubility, such as polyethoxylated surfactants. The process of emulsification involves altering the temperature-dependent affinities of surfactants for both water and oil. [16] The dehydration of polyoxy ethylene groups causes polyethoxylated surfactants to become lipophilic when heated. Rapid cooling of the emulsion at PIT 1281 temperature has been reported to produce stable and fine particle droplets. Within the PIT technique, both the droplet sizes and the interfacial tensions approach their minimal value. [17]

7. Phase Inversion Composition

This approach maintains a steady temperature.

It is among the best techniques for large-scale production.

It is simpler to include various extra substances into an emulsion.

III. General Parameters for The Evaluation of Nano cream

1. Weigh the cream's pH

Five grams of the prepared cream were combined with fifty millilitres of distilled water, and the pH was measured at 27 °C using a pH meter. [18][19]

2. Properties of Formulation examined based on outward look and traits.

3. The existence of foreign particles to check for foreign particles, place a small bit of cream on a glass slide made of grease and examine it under diffused light.

4. Synthetic involves paying attention to the color, odor, and texture.

5. Test for Nanocream Type

Methylene blue was poured into the preparation and the mixture was placed on a watch glass to conduct the nano cream type test. Water in oil type (W/O) or oil in water type (O/W) can be found in a nano cream formulation. The variations in the kind of nano cream point to instability in the emulsion.

6. Test of Spreadability

The preparation was weighed to a maximum of 0.5 grams and then placed on a square glass to assess its spreadability. Next, a second glass was placed on top of the glass. Subsequently, the glass is filled with 50, 100, 150, and 200 gram loads for a minute, and a caliper is used to measure the dispersion's diameter. Spreadability was calculated using the following equation:

$S = M \times L/T.$

where L is length and M is the weight (gm) taken.[20][21]

7. Particle size measurement

The test was conducted utilizing a Particle Size Analyzer (PSA) and the Dynamic Light Scattering (DLS) method. To determine the droplet size, the nanoemulsion was put into a cuvette and put into the particle size analyzer.

8. Uniformity

The final Nano cream recipe is applied on a glass piece and examined to determine whether or not the ingredients are well combined. It is expected that the stable nano cream will have a uniform configuration both prior to and following rapid storage [22].

9. Cream's partition coefficient

The drug's partition coefficient between n-hexane and phosphate buffer solution (pH 7.4) was calculated at (370 C + 0.20 C). 50 mg of cream, which was an excess, was placed in a separating funnel with a 1:1 ratio of buffer 7.4 to hexane. It spent a full day in a water bath. Every so often, the solution was shook. Following their separation and filtering through a 2u filter, the absorbance of each was measured using a UV spectrophotometer to ascertain the amount solubilized in each phase. The polarity of hexane is zero. It is therefore selected for the partition coefficient investigation.[23]

10. Diffusion Research in Vitro

The final formulations were subjected to in vitro diffusion testing. Franz Diffusion Cell This cream-filled cell is secured to a stand, submerged in 1000 cc of phosphate buffer, and continually agitated with a magnetic stirrer. After withdrawing 5 ml of the sample, 5 ml of phosphate buffer is added back in. The absorbance of the extracted samples is determined.[24][25]

11. Stickiness

A tiny smear of the cream formulation was applied to the skin's surface, and its greasiness was assessed.[26][27]

12. Irritancy

Make a mark on the dorsal surface of the left hand. After that, the time was recorded while the cream was applied to the afflicted area. Its level of irritancy is then assessed 24 hours later.[28][29].

13. Stability tests

1. Agitation test:

Is conducted with the use of a reciprocating shaker by placing the needed quantity of non-aqueous cream container on shaker at room temperature for 24 hours (60 cycles per minute) and noticed symptoms of separation.

2. Centrifugation test:

5 g of non-aqueous cream is placed in a centrifuge tube and centrifuged at 3500 rpm for 30 minutes, observing signs of separation.[30]

3. Accelerated stability testing.

It was carried out by keeping the formulation at 40°C 1°C for 7 days. And the other two formulations at 40°C +1°C for 20 days at room and observed on the first, fifth, tenth, fifteenth, and twentieth days [31]

IV. Nanocream formulation currently available in the market.

Table. Nanocream formulation currently available in the market.

Name	Brand	Treatment	Manufactured By	Country of Origin
Luliconazole Cream IP 1% w/w	Lulqbit	Athletes foot, jock itch, and ringworm	Aitine Life sciences	Made in India
Silsolve nano cream	EFzed	Antibacterial cream used to treat wounds and burns	Best Bio Tech, Vijayawada	Made in India
Dermrid Miconazole Nitrate Cream	Dermrid	Treat Skin Infections	Scythian Healthcare	Made in India
Nanowhite	Nano white	Lightens Dark Spot and Pigmentation	Tohtonku Sdn Bhd	Malaysia
Tarrago HighTech Nano Cream	Tarrago	Cleaning, nourishing and waterproofing balm	-	US

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