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A COMPREHENSIVE REVIEW ON NANOEMULGEL

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ABSTRACT:

A topical gel with a gel matrix that contains a dispersed nanoemulsion is known as a nanoemul- gel. The nanoemulsion is composed of oil phase droplets dispersed in an aqueous phase stabilized with stabilizers or surfactants, and is typically prepared using high shear mixing techniques. The use of nanoemulgels has increased recently as a result of their enhanced patient acceptance, high therapeutic and safety profile, non-greasy, convenient spreadability, and ease of application. The aim of this review is to highlight the importance of nanoemulgel as a delivery system for medications. The components of the system have been examined, and both high- and low-energy preparation methods have been discussed.

KEYWORDS: Nanoemulgel, Nanoemulsion, Gel, Surfactants, Viscosity.

INTRODUCTION:

Nanotechnology is one of the fast growing technical applications that has been used in a number of demands, particularly in the food, pharmaceutical, and cosmetics industries. Due to its superior properties, such as increased distribution of active ingredients, small droplet size with large interfacial area, and higher solubilization capacity, products using nanotechnology have a prospective market. The nanolipoidal delivery system is one kind of innovative pharmaceutical delivery technology that is mainly used for different stabilizing activities and to boost bioavailability. Solid lipid nanoparticles (SLNs), liposomes, microemulsions, and nanostructured lipid carriers are a few examples of nanolipoidal delivery systems.[1]

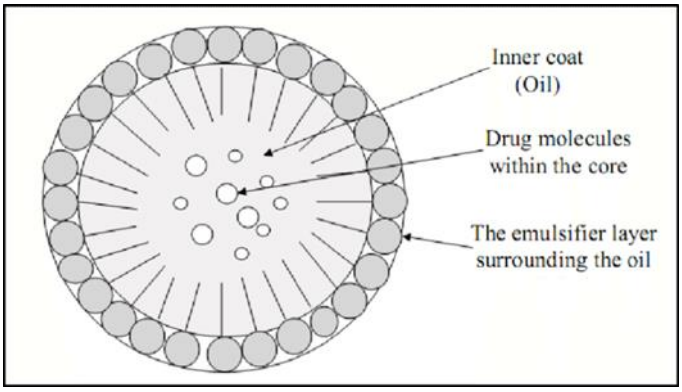

Fig.1: Structure of Nanoemulsion[2]

For the majority of medications, the nanoemulsion system is the best method of drug administration since it maximizes effectiveness while minimizing toxicity. Researchers have progressed from basic drug delivery to highly polished new dosage formulations. When the right surfactant and co-surfactant with the right HLB scale value are added to two immiscible liquids (oil and water), the combination becomes homogenous. This is known as a nanoemulsion. The range of this thermodynamically stable system is between 10 and 100 nm.[3]

The combination of two systems, the hydrogel system and the nanoemulsion system, is called nanoemulgel. A few drawbacks exist for both systems: hydrogels are unable to include lipophilic molecules, whereas nanoemulsions have low spreadability and retention. With a droplet size range of 5 to 500 nm, nanoemulgel contains a variety of polymeric components, surfactants, and fatty compounds of natural, synthetic, and semisynthetic provenance. The limitations of both technologies can be addressed via nanoemulgel. The lipophilic drug dissolves in the oil phase of the nanoemulsion, which is then combined with the hydrogel foundation to produce the nanoemulgel. This process allows the lipophilic drug to be incorporated into a hydrogel while also increasing the viscosity of the nanoemulsion. Nanoemulgel serves as a reservoir for transdermal medication administration.[4]

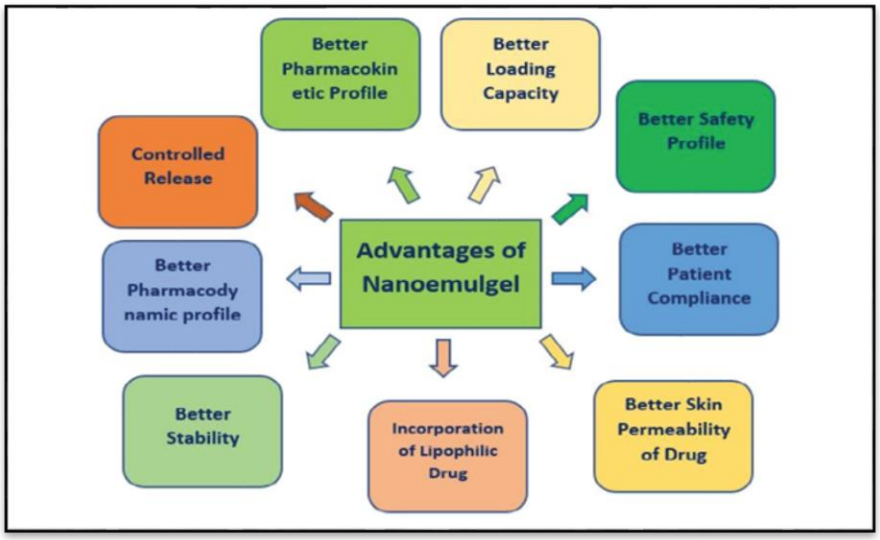

Fig. 2: Advantages of Nanoemulgel[5]

COMPONENTS OF NANOEMULGEL:

The main components of nanoemulgel are;

- **Oil**

Choosing the oil phase is the most crucial step in producing a stable nanoemulsion and enabling the most medication to solubilize it. Usually, the oil having the highest ability to solubilize a specific medication candidate is selected as the oily phase for making nanoemulsions. This helps to maximize the dosage of medicine that is incorporated into the nanoemulsion. Using an oil combination is another way to solubilize the most medication possible. The several oils used in the nanoemulsion formulation are listed in Table 1.

Table 1: Lists of oil used in nanoemulsion

Oils	**Botanical names**
Arachis oil	*Arachis hypogaea*
Brahmi oil	*Baopa monnieri*
Clove oil	*Syzygium aromaticum*

Table 1: Lists of oils used in nanoemulsion

Surfactants are necessary components for maintaining the stability of the nanoemulsion system. Anionic, cationic, and nonionic surfactants were used in this system. Selecting the appropriate surfactant (Table 2) is crucial for achieving a reliable delivery system due to their chemical differences. Surfactants with a high HLB value are necessary for stable nanoemulsion synthesis.

Table 2: Lists of surfactants used in nanoemulgel

Surfactants	**Chemical names**
Kolliphor RH 40	Macrogolglycerol hydroxystearate
Plurol Oleique CC 497	Polyglyceryl-3 dioleate
Labrafil M 1944 CS	Oleoyl polyoxylglycerides

Table 2: Lists of Surfactants used in nanoemulgel

- **Co-Surfactants**

In order to create a stable nanoemulsion and reduce the polarity of the surfactant, co-surfactant is essential. Co-surfactants that interact with the surfactant interface are included in Table 3, including alcohols with short to medium chains (C3–C8). Additionally, they help to enhance oil penetrability, which results in a stable formulation.

Table 3: Lists of Co-surfactants used in nanoemulgel

Co-Surfactants	**Molecular Formula**	**Molecular Weight**
Transcutol P	$C_6H_{14}O_3$	134.175 g/mol
Glycerol	$C_3H_8O_3$	92.09382 g/mol
Ethanol	C_2H_6O	46.068 g/mol

Table 3: Lists of Co-surfactants used in nanoemulgel

- **Gelling agents**

Certain interest in drug delivery applications can be attributed to the distinct physical characteristics of hydrogels. These are semisolid systems comprising a three-dimensional, inter connected network of inorganic and organic molecules, which are inhibited by liquid because of their great porosity. There is a dramatic transition that welcomes the new nanogel systems because of the quick advancements in nanotechnology. The important components of an efficient drug delivery system design are their high drug loading capacity, biocompatibility, and biodegradability.

Table 4: Examples of gelling agent

Name of the gelling agent	Molecular Formula	Molecular Weight (g/mol)
Poloxamer	$C_5H_{10}O_2$	102.133
Polyacrylamide	C_3H_5NO	71.077
Carbomer 934	$C_3H_4O_2$	3,000,000

Table 4: Examples of gelling agent

METHODS FOR PREPARING STABILISED NANOEMULSION:

Appropriate fabrication techniques should be used in order to provide stable and transparent nanoemulsion compositions. reducing the droplet size to the nanoscale requires the use of these techniques.

1) Using High Pressure Homogenization

With this technique, the oil phase is broken down into nano sized droplets that are easily dispersed in a hydrophilic gel matrix using a high-pressure homogenizer. High shear forces produced by the homogenization process aid in reducing droplet size and producing a stable nanoemulgel.[7]

2) Solvent Evaporation Technique

Using this technique, a drug solution is prepared and then emulsified in a separate liquid that isn't the drug's solvent. As the solvent evaporates, the medicine precipitates. High shear forces can be produced by a high-speed stirrer, which can be used to regulate particle aggregation and crystal formation.[8]

3) Microfluidization

Microfluidization is a patented mixing technique that uses a device called a microfluidizer. This technology creates a very small submicron particle by forcing the medicinal product through an interaction chamber under high pressure. The process is carried out several times to obtain the necessary particle size in order to produce a homogenous nanoemulsion.[9]

4) Spontaneous Emulsification Method

To prepare the nanoemulsion using this approach, three stages were needed. The first step of the procedure was making an organic solution using oil, lipophilic and hydrophilic surfactants in a solvent that was miscible with water. To create the o/w emulsion, this organic phase was then injected into the aqueous phase and magnetically agitated. In the third stage, evaporation was used to get rid of the organic solvent.[10]

5) Solvent Displacement Method

In order to prepare polymeric nanoparticles via the nano-precipitation process, a solvent displacement approach is designed and applied in order to prepare nanoemulsion. Organic solvents such as ethanol, acetone, and ethyl methyl ketone are used to dissolve the oily phase in the solvent displacement procedure. The rapid diffusion of organic solvent creates a spontaneous nanoemulsion when the organic phase is introduced to an aqueous phase containing surfactant. vacuum evaporation or other appropriate techniques may be utilized to eliminate the organic solvents that were used. nanoemulsion can occasionally occur even in the absence of surfactant usage.

Parenteral formulations may be made using this procedure, which could be completed at room temperature with just a little stirring. The high solvent ratio required to produce the proper droplet range is one of the method's main drawbacks.[11]

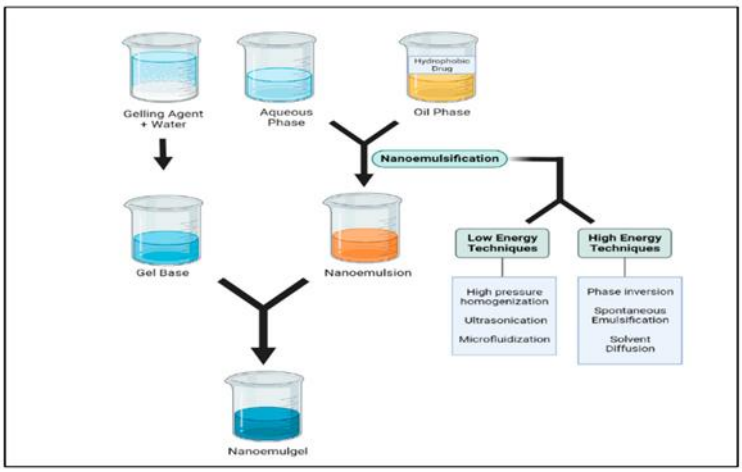

Fig.3: Steps to formulate the nanoemulgel

EVALUATION OF NANOEMULGEL:

- **Appearance**

The prepared formulation's color, homogeneity, and clarity are confirmed as well as its physical appearance.[13]

- **Determination of Rheological properties**

A Brookfield viscometer is used to measure the viscosity of 20 g of nanoemulsion-gel in a 25 ml beaker.[14]

- **Globule size and its determination in nanoemulgel**

Malvern zetasizer determines the size and distribution of globules. A homogenous dispersion is achieved by dissolving a 1 g sample in filtered water and agitating it. The zetasizer's photocell is injected with sample. The distribution and mean globule diameter are found.[15]

- **Drug content determination**

The right amount of nanoemulgel formulation mixed with a suitable solvent yields the drug content. Subsequently, the mixture is run through whatman filter paper, and the filtrate is subjected to UV spectrophotometric analysis using the same standard plot and the absorbance value reported by More et al. to determine the drug content.[14]

- **Spreadability**

Nanoemulgel spreadability is determined by measuring the diameter of the nanoemulgel circle that forms when the nanoemulgel is sandwiched between two glass plates of a specific weight. 350 mg of emulgel is weighed out and placed on one glass plate; another glass plate is dropped from 5 Cm away. The spread nanoemulgel circle's diameter is measured. It is calculated by using the following formula:

Spreadability (S) = M x L/T

Whereas M= Weight fastened to the top slide

L= Glass slide length

T= Distance traveled by upper slide in time[16]

- **In Vitro release study**

Drug release investigations employ the Franz diffusion cell, which has an effective diffusion area of 3.14 Cm^2 and a cell volume of 15.5 ml. The diffusion cell's donor and acceptor chambers are encased in an even layer of the nanoemulsion that is applied to the membrane. To dissolve the medication, fresh phosphate-buffered saline (pH 5.5) is added to the receptor compartment. magnetic stirrer is used to stir the receiving chamber. Gather samples (aliquots of 1.0 ml) at appropriate intervals. Following the appropriate dilution, UV-Vis was used to determine the drug content of the sample. Calculate the total amount of medication that has been released via the dialysis membrane.[17]

- **pH determination**

Using a pH meter, the pH of various topical preparations was found to be between 5 and 6.1 g of gel is dissolved in 10 ml of water for testing. To prevent errors, the pH of every formulation is measured three times.[18]

APPLICATIONS OF NANOEMULGEL:

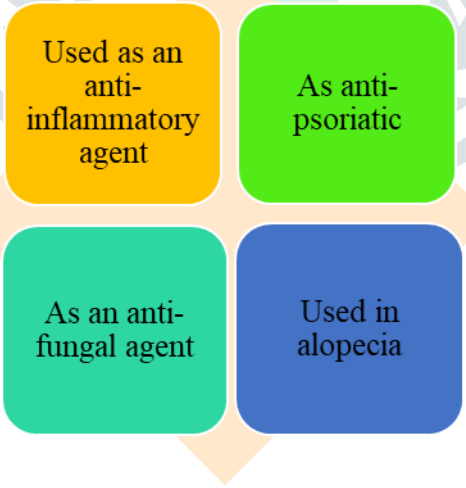

Fig.4: Applications of Nanoemulgel[19]

CONCLUSION:

A gelling agent is incorporated into the system based on nanoemulsion and provides the three-dimensional structure of nanoemulgel. One of the advantage of nanoemulgel is its range of nano size particles, which makes deep penetration easier. Through the use of nanoemulgel, a stable nanoemulsion formulation can be improved by reducing surface and interfacial tension, which increases the aqueous phase's viscosity.

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