JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

NANOEMULGEL: AN INVENTIVE APPROCH FOR TOPICAL BASED FORMULATIONS

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ABSTARCT:

The nanoemulgel drug delivery system is a formulation related intervention to improve drug absorption and therapeutic profile of lipophilic drugs. An increasing trend in nanoemulgel use in recent years has been noticed because of the better acceptability of the preparation to the patients due to their non-greasy, convenience spreadability, and easy applicability and good therapeutic and safety profile. Transdermal delivery of drug is promising but challenging system is available for local as well as systemic effect of drug. The prolonged residence of drug formulation in the skin is important for transdermal drug delivery. The main objective of this article is to give rise about nanogel used for topical application. Nanogels are able to carry encapsulated drug molecules to targeted tissues or cell structures without premature leakage of the drug into the blood stream or other tissues.

KEYWORDS: Nanoemulgel, Nanoemulsions, Topical Formulations, Methods Nanoemulgel

INTRODUCTION:

Emulgel is a combination of gel and emulsion where emulsion used can be both type W/O and O/W as a vehicle for purpose to deliver selected drug to the skin. Water Phase containing the gelling agent converts a classic emulsion in emulgel. Dermatological use of Emulgel has many favourable properties like easy spreadable, greaseless, being thixotropic, water-soluble, easy removal, longer shelf life, non-staining, and bio-friendly. The Nanoemulgel drug delivery system is a formulation related intervention to improve the systemic delivery and therapeutic profile of lipophilic drugs. Nanoemulgel is an amalgamated formulation of two different systems in which nanoemulsion containing drug is incorporated into a gel base. The fusion of the two systems makes this formulation advantageous in several ways. Lipophilic drugs can be easily incorporated and the skin permeability of the incorporated drugs can be enhanced in several folds due to the finely distributed droplets of nanoemulsion phase. As a result, the pharmacokinetic and pharmacodynamic profiles of the lipophilic drugs are improved significantly. An increasing trend in topical nanoemulgel use in recent years has been noticed because of the better acceptability of the preparation to the patients due to their non-invasive delivery, avoidance of gastrointestinal side effects, easier applicability and good therapeutic and safety profile. Despite of having

few limitations, nanoemulgel formulation can be considered as a potential and promising candidates for topical delivery of lipophilic drugs in the future

PROPERTIES :'

1. **Biocompatibility and degradability:** Nanogel is made up of either natural or synthetic polymers. They are highly biocompatible and biodegradable thereby avoiding its accumulation in the organs.
2. **Swelling property in aqueous media:** Due to the fact that Nanogels are very small, soft materials, they have the ability to swelling presence of an aqueous medium. It is considered to be the fundamental property influencing the mechanism of action followed by this drug delivery system. It depends on:
   a) Structure
   b) Environmental parameters
3. **Higher drug loading capacity:** Just like any other nanodelivery system, nanogels are expected to have greater loading capacity compared to conventional dosage forms. This is mainly due to the swelling property which allows the formulation to absorb large quantity of water. Thus, upon incorporation and loading the water will provide cargo space sufficient to contain salts and biomaterials
4. **Permeability and particle size:** What distinguishes nanodelivery systems is that a tiny manipulation in particle size, surface charge and hydrophobicity can remarkably improve permeability. In spite of the fact that nanoparticles are capable of permeation by diffusion through tissues or compromised areas of endothelium and in some cases through a particular transport system, they created a challenge crossing Blood Brain Barrier (BBB)
5. **Colloidal stability:** When handling nanoparticle, there is always a propensity of aggregation that compromises the colloidal stability. Formulators tend to alter the surface charge to avoid the formation of aggregates in bloodstream and further complications. It can be achieved through increasing zeta potential (minimum of ± 30 mV) that results in larger repulsive forces between particles that electrostatically stabilize them. Other techniques involve the incorporation of a surface modifier like PEG that produce steric effects and hydration forces to give a stable nanosuspension . If we compare polymeric micellar nanogel systems and surfactant micelles on basis of stability we will find that the former exhibits better stability lower critical micelle concentrations, decrease in dissociation rates, and longer retention of loaded drugs. They also have a high water content that assure good dispersion stability

ADVANTAGES:

1. Greater biocompatibility
2. Greater degradability.
3. Enhanced permeation capability.
4. Enhanced penetration.
5. Rapid responsiveness to environmental factor such as ph.

DISADVANTAGES:

1. Skin irritation on contact dermatitis.
2. Bubbles formed during emulgel formulation.
3. Possibility of allergenic reactions.
4. Drugs having large particle size (>400 daltons) are not easily absorb or cross through the skin barrier.

NANOEMULSIONS:

Nanoemulsion system is an ideal drug delivery for most of the drugs with objective of maximizing efficacy while minimizing toxicity. In the advancement of research, researchers have excogitate the simple drug delivery to eminently refined novel dosage forms. Nanoemulsions are mixtures of two immisible liquids (water and oil) to form homogeneous system by addings suitable surfactant and co-surfactants with appropriate HLB scale value. This thermodynamically stable system ranges from 10-100 nm.

Nanoemulsions preferred topical route as compare to oral administrative due to bitter taste With the help of suitable gelling agents or polymers, these nanoemulsions will show better results when applied topically.

NANOEMULGES:

Formation containing Nanoemulsion in gel base are called nanoemulgel, is the addition of Nanoemulsion system intergraded into gel matrix which influences a better skin permeation. This mixture of nanomulgel acts as drug reservoirs, influencing the release of drug from inner phase to outer phase and further. Nanoemulgel on intact with skin release the oil droplets from the gel and this oil droplets penetrate into the SC of the skin and deliver the drug to intended site. Nanoemulsion-gel have a good adhesion property and high solubilising of drug in oil phase leads to larger concentration gradient towards the skin that further increase skin penetration of drug. Also patient compliance is improved due to increased spared ability compare to creams and ointments and decreased stickiness.

MECHANISM:

There are multiple number of mechanisms such as:

1. PH responsive mechanism
2. Thermosensitive and volume transition mechanism.
3. Photoisomerisation

1.PH responsive mechanism:

As the name indicates, drug release responds to pH changes in the surrounding environment. In other words, the release of drug can take place in physiological environments that acquire ĚŝīĞrĞnł pH values. The most release will take place in the appropriate pH which means that the release is mainly achieved in a targeted area of the body that possesses that pH. This mechanism is based on the fact that polymers employed in the synthesis of a nanogel contain pH Ɛ groups that deionize in the polymeric network. The results in increase in pressure, swelling and porosity of the polymer which triggers the release of the bound molecules

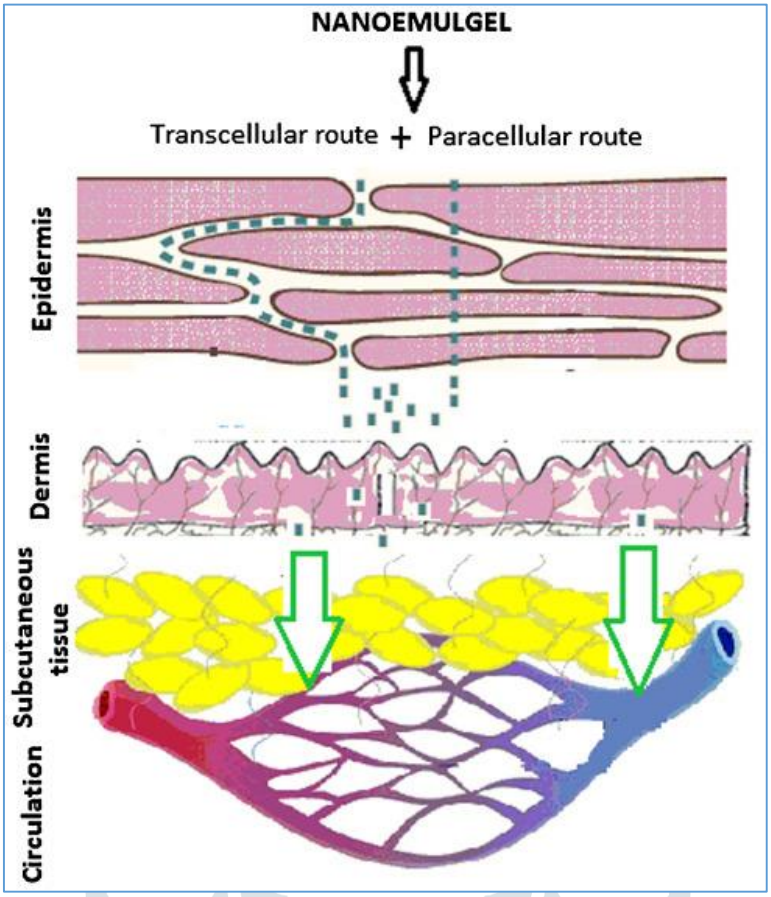

Fig 1. Mechanism of nanoemulgel

METHOD OF PREPARATION:

Methods of Formulation of Nanoemulsion-gel can be summarized in to following steps,

a. Screening of components
b. Preparation of Nanoemulsion
c. Preparation of Nanoemulgel

a. Screening of components: Drug Solubility was determined in different oils by excess addition of drug into different components followed by continuously stirred 72 hours to achieve equilibrium. After that samples centrifuged and supernatant was taken and solubility was determined by appropriate analytical methods. Then, excipients in each category with the highest solubility of drug are selected for further studies. Psedoternary phase diagram: Surfactant and cosurfactant (Nmix) were mixed in different ratios (2:1, 3:1 and 5:1). Each ratio chosen in increasing amount of surfactant respect to co surfactant for a study on the phase diagrams. Here aqueous phase (Distilled water) used as dilution media. Oil and Nmix was mixed at different ratios from 9:1 to 1:9 in different vials for each Nmix. Main objective for this is to cover for the study to decide boundaries of phases formed in the diagrams. It was developed using titration method with help of water as aqueous media. Slow titration of oil and Nmix is performed and visual observations are made for transparency of Nanoemulsion. The state of Nano emulsion is marked on one axis of aqueous phase, the second one of oil and the third one of N mix (surfactant and co-surfactant)

b. Preparation of Nanoemulsion: The drug is then solubilized in oil and oil is addend in to Nmix, this mixture is diluted with water to form of Nanoemulsion of given drug.

c. Preparation of Nanoemulgel: Gel base is prepared using 1g of the Carbopol in a required quantity of water. After complete swelling and dispersion of Carbopol solution during 24 hours period, prepared Nanoemulsion

is slowly added under continues stirring. Addition of Triethanolamine gives homogeneous gel dispersion. Finally required

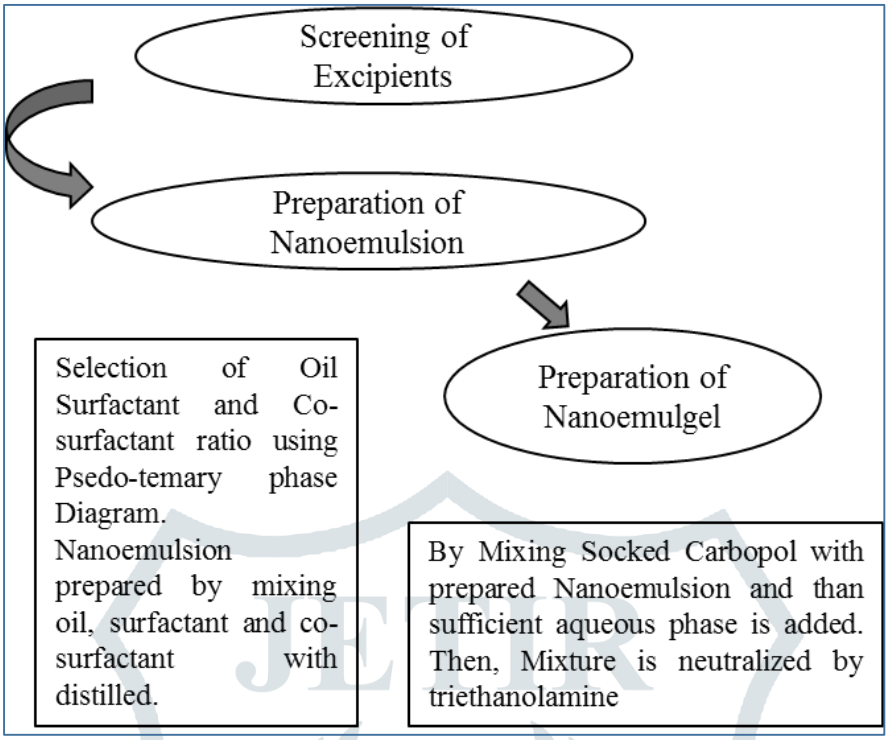

Fig 2: Flowchart of process of formulation of nanoemulgel.

OPTIMISATION AND EVALUATION:

- Apperance
- PH
- Size of globules
- Swelling index
- Bioadhesive strength
- Skin irritation test
- Invitro diffusion study
- viscosity
- % drug content.
- Stability study
- Assay.

CONCLUSION:

Topical Nanoemulgels have proven as better option for effective and convenient drug delivery system. Gel and non-greasy like properties are giving more patient compliance and lacks of oily as a base provides better drug release compared to other formulations. Incorporation of Nanoemulsion into gel matrix makes formulation dually control released system, Problems like creaming and phase separation which is associated with classical emulsion gets resolved with improved spraredability. Nanoemulsion loaded gel gives higher effectiveness in some topical disorders.

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