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# A Review on NANOEMULGEL

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**ABSTRACT**

An emulsion that has been gelled with the aid of a gelling agent is referred to as nanomulgel. They can be produced in w/o or o/w types. Introduction, preformulation, excipient selection criteria, formulation, and preparation technique are all included in the domain formulation and characterization of nanoemulgel. It also covers packing, labeling, documentation, stability studies, and evaluation.

**KEY WORDS: NANOEMULGEL**

## INTRODUCTION

A nanoemulsion is a transparent (translucent) oil-water dispersion with globule sizes ranging from 1 to 100 nm that is thermodynamically stable because it contains surfactant and cosurfactant molecules. The phrase "Nanoemulgel" refers to the mixture of emulsion and gel. Compared to conventional formulations like emulsions and gels, several medicines exhibit greater transdermal penetration when applied as nanoemulsions. Both in vitro and in vivo, the nanoemulsion exhibits improved transdermal and dermal transport capabilities. Due to its small globule size and high loading capacity, the medication enters the skin easily and has a short half-life of therapeutic activity.[1]

## ADVANTAGES OF NANOEMULGEL

- Using water/oil/water emulsions, hydrophobic drugs can be quickly implemented into the gel base.
- Improved stability and load capacity.
- Easy for production and a low-cost mechanism.
- Avoid gastrointestinal incompatibility.
- Target drug delivery on the body.
- Improved patient compliance.

## DISADVANTAGES OF NANOEMULGEL

- The drug and/or excipients can lead to skin irritation in people with contact dermatitis.
- Some medications have low permeability through the skin.
- Possibility of allergeic reactions.
- Larger-particle-size drugs are not easily incorporated into the skin[2]

## PREFORMULATION /STEPS IN FORMULATION DEVELOPMENT

An important phase in the creation of emulgel formulations is preformulation. To get crucial data and knowledge on the mechanical, chemical, and physical characteristics of the substances and their compatibility, a number of tests and research are conducted.

### *(A) IDENTIFICATION AND CHARACTERIZATION METHODS OF DRUG*

Understand the chemical and physical properties of the active ingredients (e.g., drugs or bioactives) you plan to incorporate into the emulgel.

**Characterization of Excipients**:

Determine the properties of the excipients used in the emulgel, such as the emulsifying agents, gelling agents, preservatives, and antioxidants. This includes particle size, solubility, and other relevant characteristics.

**Solubility Studies:**

Determine the solubility of the active ingredients in different oils, water, and various solvents. This helps in selecting the most suitable oil phase and solubilizers for the emulgel.

**Thermodynamic Studies:**

Analyze the phase behavior of the emulgel components, including the oil, water, and surfactants. This can help in choosing the right emulsifying agents and optimizing the emulsion.

**Viscosity Studies:**

Measure the viscosity of the gelling agents or polymers to understand their rheological properties and their effect on the formulation's texture.

**Stability Testing:**

Perform stability studies to assess the emulgel's physical and chemical stability under various storage conditions, such as temperature, humidity, and light exposure.

**pH Determination:**

Determine the pH of the emulgel and assess its effect on the stability and skin compatibility of the product.

**Microbiological Evaluation:**

Test the emulgel for microbial contamination and preservative efficacy to ensure its safety for use.

**Rheological Studies:**

Conduct rheological tests to understand the flow and deformation behavior of the emulgel. This information helps in optimizing the product's texture and ease of application.

**In vitro Release Studies:**

Evaluate the release rate of the active ingredients from the emulgel using in vitro release tests, which can help in predicting the product's performance.

**Safety Assessment:**

Assess the skin irritation potential of the emulgel through in vitro and in vivo studies, if required.[9]

### *B) EXCIPIENT DRUG COMPATIBILITY STUDIES*

Examine whether the active components, excipients, and formulation as a whole work well together. To find possible interactions or incompatibilities, this may entail methods such as Fourier-transform infrared (FTIR) spectroscopy and differential scanning calorimetry (DSC).

Initial Compatibility Screening: Mix the active drug with individual excipients, one at a time, in various ratios. Perform the following tests:

**a. Visual Inspection:** Examine the mixtures for any signs of incompatibility, such as phase separation, color changes, precipitation, or texture alterations.

**b. Differential Scanning Calorimetry (DSC):** Use DSC to detect changes in thermal behavior, like melting or decomposition points, which can indicate compatibility issues.

**c. Fourier-Transform Infrared (FTIR) Spectroscopy:** Use FTIR to identify any new chemical bonds, shifts in peak frequencies, or other changes in the spectra that suggest interactions.

### *C) CRITERIA FOR EXCIPIENT SELECTION*

Inert materials called excipients are employed as diluents or delivery systems for drugs. Within the pharmaceutical sector, it has multiple subcategories that consist of diluents or fillers, lubricants, glidants, disintegrants, binders or adhesives, flavors, colors, and sweeteners. All of these must meet certain criteria as follows,

a) Physiologically inert.

b) Acceptable to regulatory agencies.

c) Physiologically and chemically stable.

d) Free from bacteria.

e) Should not interfere with the bioavailability of the drug.

f) Commercially available in the form and purity commensurate with pharmaceutical standards.

g) Low cost, inexpensive.

h) Meet the standards of regulatory requirements.

***D) FORMULATION OPTIMIZATION TECHNIQUE***

**DOE (DESIGN OF EXPERIMENT)**

- Design of experiment is a powerful statistical technique for improving product / process designs and solving process /production problems
- DOE makes controlled changes to input variables in order to gain maximum amounts of information on cause and effect relationship with a maximum sample size
- When analyzing a process experiments are often used to evaluate which process inputs have a significant impact on the process output and what the target level the input should be to achieve a desired result (out put)
- Design of experiments (DOE) Is also referred to as designed experiments or experimental design
- Reduce time to design/develop new products and processes
- Improve performance of existing processes
- Improve reliability and performance of products
- Achieve product and process robustness
- Perform evaluation of materials, design alternatives, setting component and system tolerance

## FACTORS:

Factors are inputs to the process

Factors can be classified as either controllable or uncontrollable or uncontrollable variables.

In this case, the controllable factors are flour, flour, eggs, sugar, and oven.

Potential factors can be catogerized using the cause and effect diagram

## LEVELS:

Levels represent settings of each factor in the study

Examples include the oven temperature setting, number of spoons of sugars, number of cups of flour, and number of eggs

## RESPONSE

Response is output of the experiment

In the case of cake baking, the taste, consistency, and appearance of the cake are measurable outcomes potentially influenced by the factors and their respective levels[3]

## FORMULATION

An emulgel is made by following a set of stages that combine the characteristics of a gel with an emulsion, such as water in oil or oil in water, to produce a stable and functional product.[10] Emulgels are frequently utilized in cosmetics and pharmaceuticals.. Here is a general outline of the formulation procedure:

***Ingredients Needed:***

1. Oil Phase:

- Lipophilic substances (e.g., oils or active ingredients in oil form)

- Lipophilic emulsifiers (e.g., Span or Montanox series)

2. Aqueous Phase:

- Hydrophilic substances (e.g., water)

- Hydrophilic emulsifiers (e.g., Tween or Montanox series)

- Active ingredients in water-soluble form

3. Gelling Agent:

- Carbomer, HPMC, sodium carboxymethylcellulose, or other suitable gelling agents

4. Preservatives: (as required for microbial stability)

- Methylparaben, propylparaben, or any other approved preservative

5. Co-solvents: (optional, for enhancing solubility or texture)

- Propylene glycol, glycerin, etc.

6. Neutralizing Agent: (to adjust the pH)

- Triethanolamine or sodium hydroxide (for carbomer-based gels)

7. Colorants and Fragrance: (optional, for aesthetic appeal)[11]

***Procedure:***

- Prepare the Oil Phase:
- Weigh and heat the lipophilic ingredients and lipophilic emulsifiers in a heat-resistant container until they melt.
- Mix thoroughly to ensure uniform dispersion.
- Prepare the Aqueous Phase:
- Weigh and heat the hydrophilic ingredients, hydrophilic emulsifiers, and co-solvents (if used) in a separate container.
- Heat to the same temperature as the oil phase.
- Add the Gelling Agent
- Sprinkle the gelling agent (e.g., carbomer) into the aqueous phase while stirring continuously.
- Allow the gelling agent to hydrate and thicken the mixture. This may take some time, and additional mixing might be needed.
- Combine the Phases:
- Slowly pour the oil phase into the aqueous phase while stirring continuously.
- Ensure a uniform mixture by thorough mixing.
- Neutralize and Adjust the pH:
- If using carbomer, neutralize the mixture with a neutralizing agent (e.g., triethanolamine) while monitoring the pH. Adjust to the desired pH (typically in the range of 6.0 to 7.0).
- For other gelling agents, follow the specific instructions for neutralization or pH adjustment.
- Add Preservatives:
- Add the chosen preservatives to the emulgel formulation while ensuring they are adequately dispersed.
- Incorporate Colorants and Fragrance:
- If desired, add colorants and fragrance to the formulation to enhance aesthetics.

- Homogenize:
- Use a high-shear mixer or homogenizer to further ensure uniform distribution of all ingredients and to reduce particle size if necessary.
- Cool and Package:
- Allow the emulgel to cool to room temperature before transferring it to suitable packaging containers.
- Test for Stability:
- Conduct stability tests, including temperature cycling and microbial testing, to ensure the product's stability over time.

The specific ingredients and their quantities will vary depending on the intended application and the formulation requirements. Additionally, it's important to consider the compatibility of the ingredients and their solubility in the chosen phases to achieve a stable and effective emulgel formulation.[7]

## EVALUATION OF NANOEMULGEL

**Determination of homogeneity:**

The prepared gels were visually inspected for clarity and color. The prepared gels were also evaluated for the presence of any particles. Smears of gels were prepared on glass slide and observed under the microscope for the presence of any particle or grittiness.

**Determination of pH:**

The pH of the prepared nanoemulgel was measured using digital pH meter (Micropro Gradmate). The average of three readings was taken.[13]

**Determination of viscosity:**

The viscosity of gels is dependent on the type andconcentration of polymer used. The viscosity of different .Nanoemulgel was determined using a Brookfield digital rheometer (DV III+) with spindle #7 at 200 RPM with torque ranging from 10-100%. Average of three determinations was recorded.

**Determination of Zeta potential:**

The zeta potential of nanoemulsion was determined usingnano zeta sizer Horiba scientific SZ-100. Determination of Spreadability:Spreadability of the gels was determined by glass slides and wooden block which was provided by a pulley at one end. Aground glass slide was fixed on this block. An excess of gel(about 1 gm) of different formulation were placed on the ground slide. The gel was then pressed between the same shaped slides. Excess of the gels was scrapped off from the edges. The top plate was then subjected to pull 20 gms, lesser the time taken for separation of two slides better the spreadability.

**In-vitro drug release study:**

In-vitro drug release study was determined with a Franz diffusion cells, using dialysis membrane molecular weight cut off 12000-14000 Da, (Hi-Media, India). This was mounted between both chambers of the Franz diffusion cell. The receiver chamber was filled with Phosphate buffer pH 6.4 as diffusion medium and the whole assembly was placed on magnetic stirrer with 50 rpm. 1 gm. of nanoemulgel was placed on the donor chamber equally distributed on the membrane. Samples was withdrawn from the receiver solution at predetermined time intervals of 1st hr., 2nd hr., 3rd hr., 4th hr., 5th hr., 6th hr., 7th hr., 8th hr., 24th hr., and the cell was replenished to their marked volumes with fresh buffer solution. The samples were filtered and analyzed for the % of drug release.

## STABILITY STUDIES

The duration of a pharmaceutical product's physical, chemical, microbiological, and pharmacokinetic features and characteristics over the course of its shelf life after manufacture is referred to as the stability study of the product. The product's shelf life is determined by the substance's reduction to 90% of its initial concentration. The term "shelf life" refers to the product's stability and is commonly used interchangeably with "expiration date." Every medicinal preparation has a different expiration.

## STABILITY TESTING METHODS

Stability testing is a procedure performed for all the pharmaceutical products at various stages of the product development. In the early stages, the stability testing is performed by the accelerated stability studies which mainly are performed at high temperature/ humidity. Depending upon the aim, steps followed, the stability testing procedures have been categorized into four types and they are :-

## REAL TIME STABILITY TESTING

It is normally performed for a long duration of time to allow significant degradation of the product under the storage conditions recommended. The period of time for the test of the product depends on the stability of the product.

## ACCELERATED STABILITY TESTING

It is done at higher temperatures and that decomposition the product is determined. The information is used to predict the shelf life or used to compare the relative stability of alternative formulations The accelerated stability studies are easily predicted by the Arrhenius equation:

K=Ae-Ea./RT K= Specific rate constant

A= Frequency factor or Arrhenius factor

Ea= Energy of activation

R= Real gas constant 4.184 j/mol. K

T= Absolute temperature,

In this method the drugs are stored at different temperatures such as 40°C, 60°C, 70°C, 80°C, 100°C etc. These studies are to be done at room temperature and at refrigerator temperatures. During different intervals the samples are collected and examined for the stability. The sampling is done at 3 months in the first year and 6 months interval the next year and yearly thereafter.

## RETAINED SAMPLE STABILITY TESTING

In this type of testing, the stability is done by selecting one batch for a year. The samples stability studies help to predict the shelf life. The maximum shelf life of every product predicted could be 5 years which is conventional to the test samples at 3, 6. 9, 12, 18, 24, 36, 48 and 60 months.

## CYCLIC TEMPERATURE STRESS TESTING

In this method, cyclic temperature stress tests are designed knowledge of the product so as to mimic likely conditions in the market place storage. In this testing the sampling is considered to be conducted by a cycle of 24 hours which is known as the rhythm of the earth is 24 hours[8]

## PACKAGING AND LABELLING OF TABLETS PACKAGING: -

A device or material that holds a pharmaceutical product, whether or not it comes into direct touch with the substance, is called a pharmaceutical package container. A sturdy container is necessary for pharmaceutical packaging.

## TYPES OF PACKAGES

1.PRIMARY PACKAGING

Primary packaging is those packages which are in direct contact with the pharmaceutical formulation. The main aim of primary package is to protect the formulation from environmental, chemical, mechanical and/or other hazards

2.SECONDARY PACKAGING

The package external to Primary package is known as secondary package. This package provides additional protection during warehousing and also provide information about drug product for e.g., Leaflets.

3.TERTIARY PACKAGING

It is outer package of secondary packaging & prevents damage to the products. It is used for bulk handling & shipping. Examples: Barrel, crate, container, pallets, slip sheet.

## LABELLING LABEL:

Label means a display of written, printed or graphic matter upon immediate container or the wrapper of a drug package.

TYPES OF LABELS

I. Manufacturer label

II. Dispensing label

MANUFACTURER LABEL

A label which contains drug information for the use of medical practitioners, pharmacists, or nurses supplied by the manufacturer, packer, or distributor of the drug (FDA).

LEGAL REQUIRMENTS OF A MANUFACTURER LABEL

➢ The name of preparation

➢ Strength and dosage form.

➢ Quantity.

➢ Instructions for the use.

➢ Precautions & warnings.

➢ Registration number.

➢ Batch number.

➢ Manufacturing & Expiry date.

➢ Price

➢ The name and address of pharmaceutical industry

DISPENSING LABEL

Dispensing label is defined as the label used for dispensing, bearing the name and address of the supplier, the nature of the medicine and any other prescribed directions, the name of patient and the date of dispensing.[10]

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