# FORMULATION, EVALUATION AND OPTIMIZATION OFDICLOFENAC MULTIPLE EMULSION DRUG

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## ABSTRACT

*Multiple emulsions represent a promising approach for improving drug delivery systems, offering the potential for enhanced bioavailability and therapeutic efficacy. This study focuses on the formulation, evaluation, and optimization of diclofenac sodium multiple emulsions, a non-steroidal anti-inflammatory drug. The primary goal is to create a formulation that ensures controlled and sustained release of diclofenac, potentially improving therapeutic outcomes and patient compliance.*

*Preparation entails the creation of the primary emulsion by skillfully mixing the oil and water phases. Subsequently, this primary emulsion is transformed into a multiple emulsion to optimize drug encapsulation.*

*In the pursuit of this goal, various aspects of formulation and optimization were examined. Multiple emulsions were prepared with careful consideration of the selection of oil phase, surfactants, and co-surfactants to achieve stability and drug. Formulation optimization was based on the collected data, with adjustments made to improve drug delivery and therapeutic outcomes. This optimization process aimed to strike a balance between emulsion stability and drug release rate, changes made in the formulation to meet the desired performance criteria.*

*This work represents a crucial step in the development of innovative pharmaceutical formulations with the potential to enhance patient care.*

**Keyword :** - *Formulation1, Multiple emulsion2, Diclofenac3, Optimization4, Evaluation5, and Distribution6 etc….*

## INTRODUCTION

Multiple emulsions are novel carrier systems which are complex, poly-dispersed,multiphase systems consisting of at least two immiscible liquids i.e., both w/o and o/w emulsions exists simultaneously in a single system. Lipophilic and hydrophilic surfactants are used for stabilizing these two emulsions respectively.The droplets of dispersed phase contain even smaller dispersed droplets themselves, thus also called as “emulsions of emulsions”. The inner dispersed droplets in multiple emulsions are separated from outer liquid phase by a layer ofanother phase. The solute

has to transverse from inner miscible phase to outer miscible phase via middle immiscible organic phase, prior to release at absorptionsite, thus also known as liquid membrane system. Partition and diffusion coefficient of drug and strength of middle membrane phase, which is a multi- molecular layer of oil, water and emulsifier at both the interfaces of multiple emulsion, controls the drug release from these systems. This extends the classicaldefinition to include "liquid droplets and/or liquid crystals dispersed in liquid" These are heterogeneous preparation composed of two immiscible liquids, i.e. oiland water, one of which is dispersed as fine droplets uniformly throughout the other. The phase presented as small droplets are called dispersed, discontinuous or internal phase and the supporting liquid is known as continuous or external phase. Droplet diameter in multiple emulsions may range from 0.1 to 100 µm. Itconsists of large and poly dispersed droplets that are thermodynamically unstablewith a strong tendency for coalescence, flocculation and creaming. This may lead emulsions to reverse back to separate oil and water phase by fusion or coalescenceof droplets, thus it is required to add third component which kinetically stabilizesmultiple emulsions, known as emulsifying agent/emulsifier.

Multiple emulsions are prepared from oil and water by emulsification of an existing emulsion so as to provide two dispersed phases. These emulsions have promising applications in various fields such as chemistry, pharmaceutics, cosmetics etc., and have also been investigated as controlled-release drug delivery systems (CDDS), as „emulsion liquid membranes" for various applications These may be used as intermediate products in preparation of inorganic particles, lipid nanoparticles, polymeric microspheres, biodegradable microspheres, gel microbeads and vesicles such as polymers. Many potential pharmaceutical applications for multiple emulsions are aimed for slow and sustained release of active matter from an internal reservoir into continuous phase. They can also serve as an internal reservoir to entrap matter from outer diluted continuous phase into inner confined space. The active matter will dissolve in part in inner phase, in part at the internal and occasionally at external interface. Protection of sensitive and active molecules from oxidation in external phase can also be observed.

Types Based on nature of dispersed medium multiple emulsions are of two types, oil-in-water-in-oil (O/W/O) and water-in-oil-in-water (W/O/W). The most common multiple emulsions are W/O/W type; however for some specific applications O/W/O emulsions can also be used.

### 1.1 W/O/W emulsion system

In W/O/W system, an organic phase (hydrophobic) separates internal and external aqueous phases. In other words, W/O/W is a system in which oil droplets may be surrounded by an aqueous phase, which in turn encloses one or more water droplets. The immiscible oil phase, which separates two miscible aqueous phases is known as "liquid membrane" and acts as a diffusion barrier and semipermeable membrane for the drugs or moieties entrapped in internal aqueous phase.

### 1.2 O/W/O emulsion system

In O/W/O system, an aqueous phase (hydrophilic) separates internal and external oil phase. In other words, O/W/O is a system in which water droplets may be surrounded in oil phase, which in turn encloses one or more oil droplets.

## 2. METHOD AND MATERIAL

Materials: Diclofenac sodium and all formulation excipients (Paraffin oil, Span 80, Tween 20, Water) were obtained from Pharmaceutics Laboratory.

Methods: The parameters of authentication and pre-formulation is carried out by pure drug Diclofenac sodium for maintaining their quality, purity and standard.

### 2.1. Method of preparation a specific multiple emulsion of diclofenac Prepare the oil phase:

Weigh and measure the diclofenac sodium, Span 80, and oils according to the formulation. First take (50 ml) caster oil in a beaker ,then add span 80 (2 gm ) and last add Diclofenac sodium. Mix them together thoroughly to dissolve the diclofenac sodium.

Prepare the inner aqueous phase (water –in-oil): In a separate container, combine water and the Tween 80 from the water phase. Stir well until the surfactant is completely dissolved.

Form the water-in-oil (W/O) Emulsion: Slowly add the inner aqueous phase to the oil phase slowly while continuously stirring or using a high-shear mixer. Continue to mix until you achieve a stable water-in-oil emulsion. This can take some time, so patience and thorough mixing are essential.

Prepare the External aqueous phase: In another container, mix water and Tween 80 from the external aqueous phase. Add preservatives (methylparaben and propylparaben), as well as any other desired additives, and mix well.

Form the water-in-oil-in-water (W/O/W) Multiple Emulsion: Slowly add the water-in-oil emulsion to the external aqueous phase formed while continuing to mix. Ensure thorough mixing to form the stable water-in-oil-in-water multiple emulsion. Add Stabilizers, Thickeners, pH Adjusting Agents, Antioxidants, Chelating Agents, and Co-solvents:

Gradually add and mix the stabilizers (xanthan gum and carbomer), adjusting agents (sodium hydroxide or hydrochloric acid for pH adjustment), antioxidants (Vitamin E), chelating agents (EDTA), and co-solvents (if needed) as per the formulation.

Final Adjustments: the pH and adjust if necessary to meet the desired pH range. Continu e to mix until you achieve a homogeneous and stable multiple emulsion.

Package and Store: Transfer the multiple emulsion to appropriate packaging and ensure it's sealed properly to prevent contamination. Store the product under suitable conditions, considering stability requirements.

**Table -1:** Material Required for specific multiple emulsion of diclofenac in a 100 ml

| **Formulating a specific multiple emulsion of diclofenac in a 100 ml** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Oil Phase** | **Water phase** | **External aqueous phase** | **Stabilizer and thickeners** | **pH adjustment** | **Antioxidant** | **Chelating agent** | **Co solvent** |
| Diclofenac sodium | Water | Water | Xanthan Gum | Sodium hydroxide solution | Vitamin E | EDTA | Ethanol |
| Castor oil | Tween 80 | Tween | Carbomer | | | | glycerine |
| Span 80 | | Methylparaben | | | | | |
| | | Propylperaben | | | | | |

**2.2 Optimization of Formulation**

During the optimization process, there are some adjusting in the concentration of ingredients, surfactants, or stabilizers. i.e - Quantity of castor oil is change few time to get proper mixing of Drug in the oil phase. These adjustments make a positive impact on the final formulation and stability.

For instance, we observed that the quantity of castor oil needed some fine-tuning to ensure the proper mixing of the drug within the oil phase. These adjustments were made with a keen eye on achieving a homogenous formulation that would ensure uniform drug distribution and, consequently, therapeutic efficacy.

| **Optimization Of Diclofenac Multiple Emulsion** | | | | | | |
|---|---|---|---|---|---|---|
| | **Material** | **F1** | **F2** | **F3** | **F4** | **F5** |
| **Oil Phase** | Diclofenac sodium | 1 gm | 1.5gm | 2 gm | 2.5 gm | 2 gm |
| | Span 80 | 1 gm | 1.5 gm | 2.5 gm | 3 gm | 2 gm |
| | Castor oil | 10 ml | 20 ml | 30 ml | 40 ml | 50 ml |
| **Water Phase** | Water | 45 ml | 50 ml | 60 ml | 30 ml | 45 ml |
| | Tween80 | 4 gm | 6 gm | 6.5 gm | 5.5 gm | 5 gm |
| | | | | | | |
| **External Water Phase** | Water | 35 ml | 30 ml | 2o ml | 25 ml | 35 ml |
| | Tween80 | 3.5 gm | 3.5 gm | 4 gm | 5 gm | 3 gm |
| | Methylparaben | 0.2 gm | 0.2 gm | 0.2 gm | 0.2 gm | 0.2 gm |
| | Propylparaben | 0.1 gm | 0.1 gm | 0.1 gm | 0.1 gm | 0.1 gm |

## 3. RESULT

The multiple is pale yellow (dull yellow) in color , with characteristics smell. There is No any phase separation or instability issues. The physical characteristics of the diclofenac multiple emulsion are key indicators of its quality and suitability for pharmaceutical use. The emulsion exhibits a pale yellow (dull yellow) color, which not only reflects its appearance but also provides a visual cue for users, helping them to identify the product easily. The presence of a characteristic smell further adds to the sensory attributes of the emulsion, offering a familiar and consistent olfactory experience for patients. An especially positive aspect of the formulation is the absence of any phase separation or instability issues. This indicates that the emulsion has been carefully prepared and is likely to maintain its homogeneity throughout its shelf life. This stability is crucial in ensuring that the product remains efficacious and safe for use. In summary, the favorable physical characteristics, color, and odor, coupled with the absence of instability concerns, contribute to a pharmaceutical product that is not only effective but also user-friendly and visually appealing.

**Fig -1**: Formulating a specific multiple emulsion of diclofenac in a 100 ml

### 3.1 Optimization result

During the optimization process, there are some adjusting in the concentration of ingredients, surfactants, or stabilizers. i.e - Quantity of castor oil is change few time to get proper mixing of Drug in the oil phase. These adjustments make a positive impact on the final formulation and stability. For instance, we observed that the quantity of castor oil needed some fine-tuning to ensure the proper mixing of the drug within the oil phase. These adjustments were made with a keen eye on achieving a homogenous formulation that would ensure uniform drug distribution and, consequently, therapeutic efficacy. Importantly, these refinements in the formulation had a positive impact on the final product's stability. A stable formulation is crucial to ensure that the product remains consistent and effective over its shelf life. By addressing and rectifying issues during the optimization process, we have not only enhanced the overall quality and performance of the emulsion but also increased its potential for success in practical clinical applications. This demonstrates the importance of a methodical and adaptable approach in pharmaceutical formulation, where each adjustment brings us one step closer to an ideal product

## 4. CONCLUSIONS

Multiple Emulsions is one of the advanced drug delivery systems for improvement of various characteristics of drugs like bioavailability, taste, release rate etc. The advances include various novel formulations for betterment of the drug administration and improvement in the palatability of drug by incorporating them into various formulations. These are used in various pharmaceutical applications as it has a remarkable degree of biocompatibility, completely biodegradable, hydrophilic and hydrophobic drugs can be entrapped, protection from inactivation by the endogenous factors etc. These can be used in many applications like taste masking, sustained release, delivering the unstable drug etc.

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