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DESIGN AND EVALUATION OF NANOEMULSION FOR DELIVERY OF DICLOFENAC SODIUM

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Abstract

Diclofenac Sodium is an acetic acid NSAIDs with analgesic and antipyretic properties. Diclofenac sodium is also used to treat dysmenorrheal, ocularthritis and rheumentoid arthritis. The aim of the present study is to formulate and evaluate nanoemulsion for delivery of Diclofenac Sodium. The nanoemulsion was prepared by (oil in water) nanoemulsion technique. In this method, olive oil, Tween 80 and SLS (cosurfactant) was used. The nanoemulsion was evaluated for viscosity, particle size, conductivity test, drug content uniformity test, flocculation test, shelf life test, stability test and dissolution test. Diclofenac Sodium nanoemulsion was found to be white in color, having particle size 18.37, showed conductivity (67.7µs). The prepared emulsion was stable. The maximum percentage drug release was 1.71 % in 180 mins.

Key words: *Nanoemulsion , Diclofenac sodium, nonsteroidal anti-inflammatory drugs*

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Introduction

Nanotechnology comprises of the technological developments on the nanometer scale. The use of nanotechnology in pharmaceuticals is termed as "NANOPHARMACEUTICALS". The various nanopharmaceuticals currently being used or in the process of development are Nanoemulsions (submicron sized emulsions), Nanosuspensions (submicron sized suspensions), Nanospheres (drug nanoparticles in polymer matrix), Nanotubes (sequence of nanoscale arranged in a long thin cylindrical structure), Nanoshells (concentric sphere nanoparticles consisting of a dielectric core and a metal shell), Nanocapsules (encapsulated drug nanoparticles), lipid nanoparticles (lipid monolayer enclosing a solid lipid core) and dendrimers (nanoscale three-dimensional macromolecules of polymer).[1,2]

Nanoemulsions (NEs) are a group of dispersed particles used for pharmaceutical and biomedical aids and vehicles that show great promise for the future of cosmetics, diagnostics, drug therapies and biotechnologies. NEs can be defined as oil-in-water (o/w) emulsions with mean droplet diameters ranging from 50 to 1000 nm. Usually, the average droplet size is between 100 and 500 nm. The particles can exist as water-in-oil and oil-in-water forms, where the core of the particle is either water or oil, respectively. NEs are made from surfactants approved for human consumption and common food substances that are "Generally Recognized as Safe" (GRAS) by the FDA. These emulsions are

easily produced in large quantities by mixing a water-immiscible oil phase into an aqueous phase with a high-stress, mechanical extrusion process. [3]

The NEs are also referred to as mini emulsions, ultrafine emulsions and submicron emulsions. Phase behavior studies have shown that the size of the droplets is governed by the surfactant phase structure (bicontinuous, microemulsion or lamellar) at the inversion point induced by either temperature or composition. Due to their small droplet size, NEs the disperse phase (the so-called mini emulsion polymerization method) where NE droplets act as nano reactors. Another interesting application which is experiencing an active development is the use of NEs as formulations, viz. for controlled drug delivery and targeting.[4] NEs posses various advantages as these provide a much higher surface area and free energy than macro emulsions. [5]

Diclofenac Sodium is a widely used acetic acid non-steroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties. Nowadays research on increasing the bio-availability and patient compliance is the main field of attraction and nano-emulsions fulfill these required parameters. The present research work was aimed at formulation and evaluation of nanoemulsions for the delivery of Diclofenac Sodium.

2. Materials and Methods

2.1 Materials

Diclofenac sodium was used as an active ingredient, Tween 80 (CDH, New Delhi) as surfactant, olive oil (Qualikems Fine Chemicals ,New Delhi) and sodium lauryl sulfate (Qualigens GlaxoSmithKline Pharmaceuticals, Mumbai) as co-surfactant.

2.2 Method

2.2.1 Preparation of Nanoemulsion

The true NEs was prepared by dissolving Diclofenac sodium in appropriate quantity with co-surfactant (SLS). Then surfactant (Tween-80) and oil (olive oil) were added slowly. Then sufficient quantity of distilled water was added to get the final preparation 50 % w/w.

2.2.2 Evaluation of Nanoemulsion:

Ingredient	Quantity
Diclofenc	0.595g
Tween80	16.85g
Olive oil	2.5g
Sodium lauryl surfactant	5.6g
Water	50g

Table-1 Composition of nanoemulsion Diclofeanac Sodium

Viscosity Viscosity is a measure of the resistance of a fluid which is being deformed by either sheer stress or tensile stress. In everyday terms (and for fluids only), viscosity is "thickness" or "internal friction". Viscosity describes a fluid's internal resistance to flow and was determined by the Brookfield viscometer. [9]

Determination of particle size A Stage Micrometer is simply a microscope slide with a finely divided scale marked on the surface. Using the procedure explained below a 'conversion factor' can be derived. This will enable the user to convert the apparent size of a subject as seen through the eyepiece scale, into a real world. An accurately derived conversion factor will compensate for any of the errors discussed earlier. To measure an object's length, note the number of divisions spanned by the object, then multiply by the conversion factor for the magnification used. The conversion factor is different at each magnification. [9]

Conductometry In these methods, we measure the EMF of a galvanic cell which is operating near zero current. Because this EMF is a function of the ionic activities within the cell, it can be used to measure ionic concentrations in titration, water samples, biological samples and other industrial and environmental samples. The study of electro-analytical technique called conductometry is one of the oldest and in many ways simplest among other electro-analytical techniques. This technique is based on the measurement of electrolytic conductance. [9]

Drug Content Nanoemulsions were dissolved in 20 ml of water and different dilutions were prepared using distilled water. The solutions were filtered through a filter paper, diluted suitably and absorbance of Diclofenac Sodium

by UV-Visible spectrophotometer.[10]

Stability Testing

1. Test for Flocculation: Flocculation is defined as the association of particle within an emulsion to form large aggregates. However these aggregates can easily be re-dispersed upon shaking. It was observed visually.
2. Coalescence (Cracking): It is the process in which the emulsified particles join to form larger particles. The major factor which prevents coalescence is the mechanical strength of electrical barrier. After keeping the prepared NEs for 6 hours the phase separation was observed and so after repeated stirring.

In Vitro Dissolution: The release of the drug (Diclofenac Sodium) from NEs was determined following dialysis method using egg membrane as a semi-permeable membrane, where 500 ml of dissolution medium (pH 6.8) was used at 37± 0.5 °C and magnetic stirrer was maintained at 100 rpm for 3 hours. Sample (5 ml) was withdrawn at predetermined time intervals, filtered through filter paper (0.45 μ) and replaced by an equal volume of dissolution medium. Drug content in the dissolution sample was determined by UV Spectrometer.

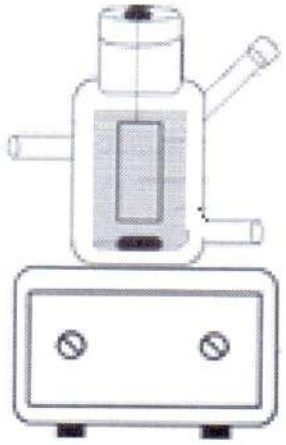

Fig 1. Image of the in vitro dissolution by Dialysis Method

3. Results and discussions

After the preparation of Diclofenac nanoemulsion the present investigation showed that its viscosity was 17550 cps at 10 rpm and the average size of the globule was 18.37 μm.

No of division	Cofactor	No of division ×Cofactor
10	3.5	35μm
5	3.5	17.5μm
4	3.5	14μm
6	3.5	21μm
8	3.5	28μm
3	3.5	10.5μm
5	3.5	17.5μm
6	3.5	21μm
3	3.5	10.5μm
4	3.5	14μm
5	3.5	17.5μm
4	3.5	14μm

Table-2 Particle size of nanoemulsion Diclofeanac sodium

The conductivity of the nanoemulsion was found to be 67.7μs. In the present study the drug content of Diclofenac sodium in nanoemulsion was found to be 0.483g. There was not any flocculation and cracking in the prepared nanoemulsion.

(III) In Vitro dissolution

Sr. No.	Time (in min)	Absorption	Drug release	Drug release % Drug Release
1.	0	0	0	0
2	30	8.92	0.0075	0.75
3	60	10.52	0.0085	0.885
4	90	12.02	0.0101	1.01
5	120	14.36	0.012	1.2O5
6	150	18.96	0.015	1.595
7	180	20.34	0.017	1.71

Table 3. Invitro Drug Release of Diclofenac sodium from prepared nanoemulsion

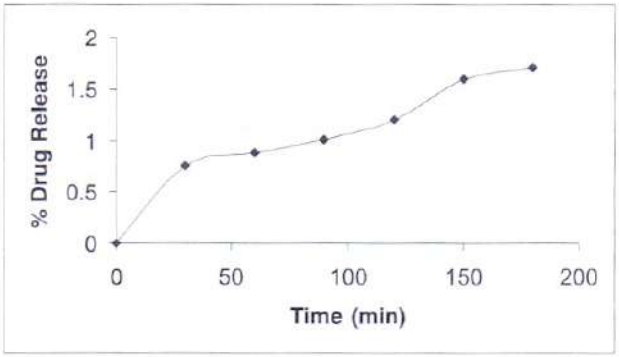

Fig 2. In vitro Drug Release profile of Diclofenac sodium from prepared nanoemulsion

Conclusion

The present study showed that the prepared emulsion was stable. The maximum percentage drug release was 1.71 % in 180 mins. As the prepared nanoemulsion has comparatively good conductivity and viscosity, it can be utilized for sustained and controlled drug delivery of Diclophenac Sodium. The present research provides a better sustained and controlled formulation of Diclofenac Sodium to the field of medicine.

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