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Preparation and Development of Diclofenac Loaded Aloevera Gel Nanoparticles for Transdermal Drug Delivery Systems

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Abstract:- The objective of this study was to preparation and development of Diclofenac loaded aloevera gel nanoparticles for transdermal drug delivery system. The application of CCD is a useful tool for optimizing DC-loaded alovera gel nanoparticles prepared by the emulsion solvent evaporation technique. The optimized nanoparticles obtained displayed an average particle size of 226.83 nm with a norrow polydispersity index (0.271), an EE of 49.9 % and a slow and prolonged drug release over a period of 24 hours. Ethylcellulose nanoparticles of Diclofenac sodium can be of significant practical use for a sustaining drug release and decreasing side effects.

Keywords:- *Extrudability, Spreadability, Evaluation, Viscosity, Homogeneity.*

I. INTRODUCTION

Nanoparticles are one of the promising drug delivery systems for controlling particle size, surface properties and release of therapeutic ingredients in order to reach the target at the therapeutic desirable proportion and rate regimen. Biocompatible, biodegradable and non-biodegradable polymers as Chitosan derivatives, PLA, PLGA, EC, are used for the preparation of polymeric nanoparticles by dissolution, entrapment, encapsulation or attachment of a drug to a nanoparticle matrix. NP matrix carriers can improve the encapsulation efficiency and stability of the drugs inside the NPs and provide effective drug levels over longer periods of time compared to traditional therapy. Different methods are used for the preparation of nanoparticles. One of the most used is the solvent evaporation method. Uniform concentration of drug at the site of absorption, maintaining of stable plasma concentration and reducing toxic effects can be achieved by developing controlled-release drug delivery systems.

Diclofenac sodium (DC) is a non-steroidal anti-inflammatory drug used for treatment of inflammatory diseases. DC has a short half-life of 1-2h and should be administered frequently at a high dose, which leads to severe undesirable effects and rises the possibility for missing a dose. The development of sustained dosage release forms was needed to ovoid theses inconveniences . It allows the finding of the optimal conditions for the best responses of experiments and understand the relationship between the dependent and independent variables in the formulation or process development. The response surface methodology (RSM) is the combination of statistical and mathematical techniques based on the recapitulation of experimental data from experimental design.

II. MATERIALS AND METHODS

A. Materials

Aloe vera was collected from Bhopal city (Madhya Pradesh, India). Diclofenac sodium, hydroxyl ethyl cellulose (HEC), Glycerol 85 % ,methyl parabean 0.1%, propyl parabean 0.01% from chemical store of NRI institute of Pharmaceutical Sciences ,Bhopal (M.P). The filter discs were purchased from chemical and drug market of Govindpura, Bhopal, (M.P). All the preparations were done by using deionized water.

B. Methods

➢ *Preparation of nanoparticles*

DC loaded EC nanoparticles were prepared by the W/O/W emulsion solvent evaporation method. First, 1mL of a DC aqueous solution (the internal aqueous phase) was emulsified by vigorous magnetic stirring into a 5mL of EC organic solution (ethyl acetate). Then this primary emulsion (W/O) was diluted in 10 mL of PVA aqueous solution (the external aqueous phase) while stirring using a homogenizer (KINEMATICA, Polytron PT 2500 E) in order to create the W/O/W emulsion. The NP suspension was obtained after solvent evaporation under magnetic stirring at room temperature. NP were separated by centrifugation (Sigma 3-30 KS, Germany) at 20.000 rpm for 20 min. The supernatant was kept for drug assay.

➢ *Characterization of nanoparticles*

- *Entrapment efficiency (EE)*

For measuring drug entrapment efficiency in the NPs, the supernatant part of the centrifuged NPs sample was carefully removed and examined to determine the amount of non-encapsulated drug after dilution with purified water and analysis by UV-visible spectroscopy (Shimadzu, UV 1800, Japan) at 276 nm. Entrapment efficiency (EE) was calculated as follows:

EE=Intial weight of feeding drug-Weight of not encapsulated drug in supernatantIntial weight of feeding drug×100**(1)**

- *Average particle size*

The particle size of nanoparticles was determined using dynamic light scattering technique at 25ºC using a Zetasizer (Horiba scientific, nano partica SZ-100). All measurements were performed in triplicate.

- *In vitro dissolution study*

In vitro dissolution studies were performed using USP Type II dissolution test apparatus (Paddle) (Distek 2500, Inc., USA) at 50 rpm and a temperature of 37 °C ± 0.5. In a dialysis bag, 18.7 mg of the optimized NPs containing 4.6 mg of DC was diluted by Phosphate buffered saline solution (PBS, pH=7.4), then was immersed into a Pyrex flask that contains 500 mL of PBS (pH=7.4). At predetermined intervals, 3mL of aliquots were withdrawn and replaced by the same volume of PBS (pH= 7.4). Then the aliquots were filtered using a 0.45 μm membrane filter, diluted suitably, and analyzed by a UV spectrophotometer at 276 nm. The dissolution study was carried out in triplicate and their average was used for determining the release kinetics.

➢ *Preparation Of Aloevera Gel Nanoparticle*

To prepare Aloe vera gel Methyl paraben sodium and were dissolved in water. Gelling agentwas added to it and stirred continuously till it got swollen completely. Triethanolamine was slowly added to the dispersion with continuous stirring which resulted in a stiff gel. Aloe extract was added to it and stirred for 15 min. Volume was made with water and stirred continuously till a uniform gel was formed.

1. Take a fresh aloe vera leaf wash with water and dry it extract aloe vera gel in a beaker mixing filter with filter paper collect aloe vera juice in a beaker and heat on a heating mental at 50-60 degree C for 1-3 min and cool it.
2. Take 50 ml purified water in beaker and add 0.01g methyl parabean .Heat on a water bath dissolve properly and Cool it and then add corbapol 934 (0.5g) Mixing with the help of magnetic stirrer.
3. Take 35ml aloe vera juice in a beaker add into paraben and carbapol 934solution and transfer into china dish. Add 2ml glycerine add in few drop of sandal wood oil. Add clouring agent and mix it and add 7-8 drop of triethanolamine.
4. After addition of all the ingredients the complete formultation is stirred with homogenizer or magnetic stirrer with 100 RPM speed for 8 hrs at room temperature 37ºc.
5. After that nanoparticles were were cooled and analysed in zetasizer for size and SEM study is also done for paticle size estimation.

➢ *Evaluation of Gel Nanoparticle*

- *pH:*

1.0 g gel was accurately weighed and dispersed in 100 ml purified water. The pH of the dispersion was measured using digital pH meter, which was calibrated before use with standard buffer solution at 4.0, 7.0 and 9.0. The measurements of pH were done in triplicate and average values were calculated.

- *Spreadability*

One of the criteria for a topical formulation to meet the ideal qualities is that it should possess good spreadability. It is the term expressed to denote the extent of area to which formulation readily spreads on application to skin or affected part. The therapeutic efficacyof a formulation also depends upon its spreading value. To determine the spreadability of formulation, 0.5 g of gel was placed within a circle of 1 cm diameter pre-marked on a glass plate of 20 × 20 cm, over which a second glass plate was placed. A weight of 500 g was allowed to rest on the upper glass plate for 5 min. The increase in the diameter due to gel spreading was noted.

- *Extrudability*

To determine extrudability a closed collapsible tube containing formulation was pressed firmly at the crimped end. When the cap was removed, formulation extruded until the pressure dissipated. Weight in grams required to extrude a 0.5 cm ribbon of the formulationin 10 sec was determined. The average extrusion pressure in g was reported.

- *Viscosity:*

The viscosity of the formulations was determined as such without dilution by R/S CPS PlusRheometer (Brookfield Engineerring Laboratorie, Inc., Middleboro, MA,USA) using spindle #C 50-1 having diameter of 50 mm using software RHEO3000.

- *Homogeneity:*

The developed formulations were tested for homogeneity by visual inspection after the gel had been filled in the container. They were tested for their appearance and presence of anyaggregates.

III. RESULT AND DISCUSSION

➢ *Formulation of Aloevera Gel Nanoparticles*

Table 1. Shows formulation of nanoparticles of alovera gel

Formulation (%w/w)	F1	F2	F3
Diclofenac sodium	1	1	1
HEC	2	2.5	3
Glycerol	10	10	10
Methyl paraben	0.1	0.1	0.1
Propyl paraben	0.01	0.01	0.01
Water up to	50	50	50

Table 2:- In Vitro Cumulative % Drug Release

Time (mint.)	F1	F2	F3
0	0	0	0
30	18.9	19.9	15
1	25.7	26.9	22.6
1.5	30.6	31.7	27
2	35	36.2	32
2.5	40.8	41.3	36.3
3	48.1	49.8	46
3.5	57.7	58.5	54.5
4	65.2	66.8	60.4
4.5	75.5	76.2	66.6
5	84.9	85.7	78.5
5.5	86.8	87.4	83.9
6	89.7	95.8	89.9

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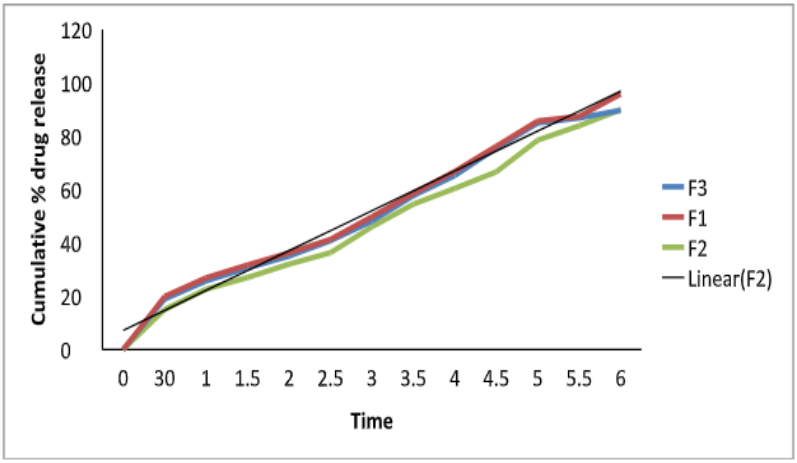

Fig 1 Evaluation of Gel Nanoparticle

Table 2: Physicochemical characteristics of diclofenac Aloe vera gel formulation

Formulation	Homogeneity	pH ± SD	viscosity (mPas) 6rpm	12rpm	Drug content (%) ±SD
F1	++++	7.33 ± 0.016	15000	10000	102.7 ± 7.40
F2	++	8.06 ± O.153	12000	9500	103.3 ± 4.10
F3	+++	7.63 ± 0.080	18000	16000	109.4 ± 1.80

IV. SUMMARY AND CONCLUSION

The application of CCD is a useful tool for optimizing DC-loaded alovera gel nanoparticles prepared by the emulsion solvent evaporation technique. The optimized nanoparticles obtained displayed an average particle size of 226.83 nm with a norrow polydispersity index (0.271), an EE of 49.9 % and a slow and prolonged drug release over a period of 24 hours. Ethylcellulose nanoparticles of Diclofenac sodium can be of significant practical use for a sustaining drug release and decreasing side effects.

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