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### FORMULATION AND DEVELOPMENT OF CATAFLAM SODIUM MICROSPHERES LOADED MICROEMULSION

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#### ABSTRACT

The present aim to formulate microspheres of diclofenac sodium loaded into micro emulsions, to attain sustained release of drugs in oral route of administration and minimize dosing frequency through site specific or pH Dependent drug delivery system. The method of proposed work performed in two steps. In first step, the production of microspheres by emulsification method using eudragit RS100 polymer as a coating material in presence of methanol as a solvent and then performed the evaluation studies like particle size and entrapment efficiency to select the Optimize microspheres. In the second step followed the phase titration method in which the optimized Microspheres loaded into aqueous phase in presence of emulsifying agent (tragacanth) to get micro emulsion then carried out in-vitro evaluation, viscosity and stability studies. The results found to be microspheres shows good entrapment efficiency and proper size distribution. On the basis of *In vitro* dissolution data found that, all formulations (F1-F6) were showed the drug release after defines the lag period made possible. The study revealed that entrapment efficiency and in-vitro release was best in F4 formulation was concluded. It will recommend as novel approach for future research.

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## INTRODUCTION

A range of parameters like solubility, stability at room temperature, compatibility with solvent, excipient, and photo stability play a critical role in the successful formulation of drugs [1]. Till date, more than 40% of the new chemical entities being generated through drug discovery programs are lipophilic or poorly water soluble compounds. Many formulation approaches are available to solve the problems of low solubility and low availability of drugs like micro ionization, use of fatty solutions, use of penetration enhancer or co solvents, surfactant dispersion method, salt formation, precipitation, etc., but these techniques having limited utility in solubility enhancement for poorly soluble drugs. [4]. To overcome these limitations, the present research focused to formulate polymeric coated micro spheres (by emulsification method) which are turned to micro emulsions by phase titration method to improve bioavailability of conventional drugs (BCS class-II, IV), minimizing side effects [6] and minimize dosing frequency. To achieve site specific drug delivery applications like, Oral drug delivery, Gene delivery, local drug delivery, Buccal drug delivery, Gastrointestinal drug delivery, Transdermal drug delivery, Colonic drug delivery, vaginal drug delivery [10, 11].

## METHODOLOGY:

### Preformulations Studies:

Pre-formulation studies may be described as a phase of the research and development process where the formulation scientist characterizes the physical, chemical and mechanical properties of new drug substances (in order to develop stable, safe and effective dosage forms) like, organoleptic properties, particle size determination (microscopic method), solubility analysis, melting point the melting point of drug was determined by capillary method, and matched with standards. Determination of  $\lambda_{\max}$ : the uv-spectrum of the pure drug sample was analyzed in phosphate buffer of pH 8.0 in the range of 200 to 400 nm and  $\lambda_{\max}$  was determined. Standard curve of diclofenac sodium drug: the calibration curve is based on the spectro photometry. Drug powder was characterization for bulk density, tapped density [4- 6].

### Formulation of microspheres by emulsification method [4- 6]:

Microspheres of diclofenac sodium prepared by transfer of required quantity of methanol into the beaker then add weighed quantity of drug and polymer to the content of beaker placed under the laboratory stirring by maintaining cold temperature (ice bath) to get the drug microspheres.

**Table no: 1 Formulation of microspheres loaded micro emulsion of diclofenac sodium.**

Formulation code	Drug polymer	API (D.S) (mg)	Eudragit RS100	Methanol	Tragacanth	Water (ml)
F1	1: 0.5	100	50	10ml	100	200
F2	1:1	100	100	10ml	100	200
F3	1:1.5	100	150	15ml	100	200
<b>F4</b>	<b>1:2</b>	<b>100</b>	<b>200</b>	<b>10ml</b>	<b>100</b>	<b>200</b>
F5	1:2.5	100	250	15ml	100	200
F6	1:3	100	300	15ml	100	200

### Evaluation of microspheres [7, 20]:

Particle size and shape: The most widely used procedures to visualize micro particles are conventional light microscopy (LM).

Drug entrapment efficiency: Drug entrapment efficiency can be calculated using following equation,

$$\% \text{ Entrapment} = \frac{(\text{Actual content/Theoretical content}) \times 100}{\text{Theoretical yield.}}$$

### Preparation of Micro Emulsion:

By phase titration method (2:2:1 ratio of water, oil, gum respectively) adding selected emulsifying agent (tragacanth) to twice of its weight of aqueous phase with continuous stirring to get gum mucilage then the oil phase (micro spheres) added slowly in portions with continuous trituration to emulsify the drug microspheres. The result products were evaluated (dissolution studies, viscosity) to find out the optimized one among all formulations.

## RESULTS AND DISCUSSION

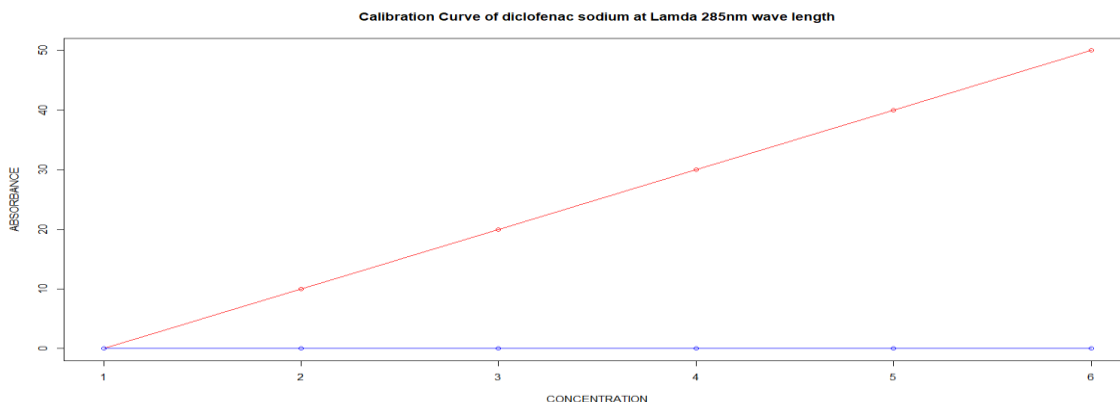
**Pre-formulation tests** were performed as per procedures given in standard references. The results were illustrated that the drug showed within the limits.

### Particle size determination:

Microscopic method can be used as the absolute method of particle size analysis. The average diameter of diclofenac sodium pure drug was found to be 24  $\mu\text{m}$ , compared with standards and that found to be within the range.

**Calibration curve of diclofenac sodium at  $\lambda_{\text{MAX}}$  285 nm wave length:**

The maximum absorption was observed at 276nm. It obeyed beer's law in the concentration range of 10-50 $\mu\text{g/ml}$ .

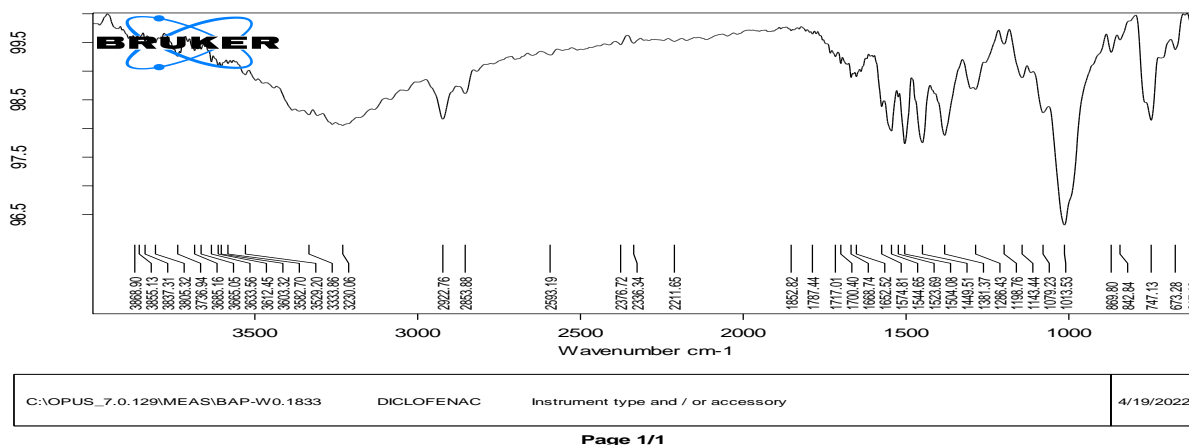


**Figure No: 1 Calibration Curve of Diclofenac Sodium.**

**Compatibility studies:**

The IR spectrum of pure drug and physical mixture of drug and polymer were studied. From the above results functional groups and type of vibrations are noted. In case of FTIR study there was no disappearance of already existing peaks. Hence, drug was found to be compatible with excipient.

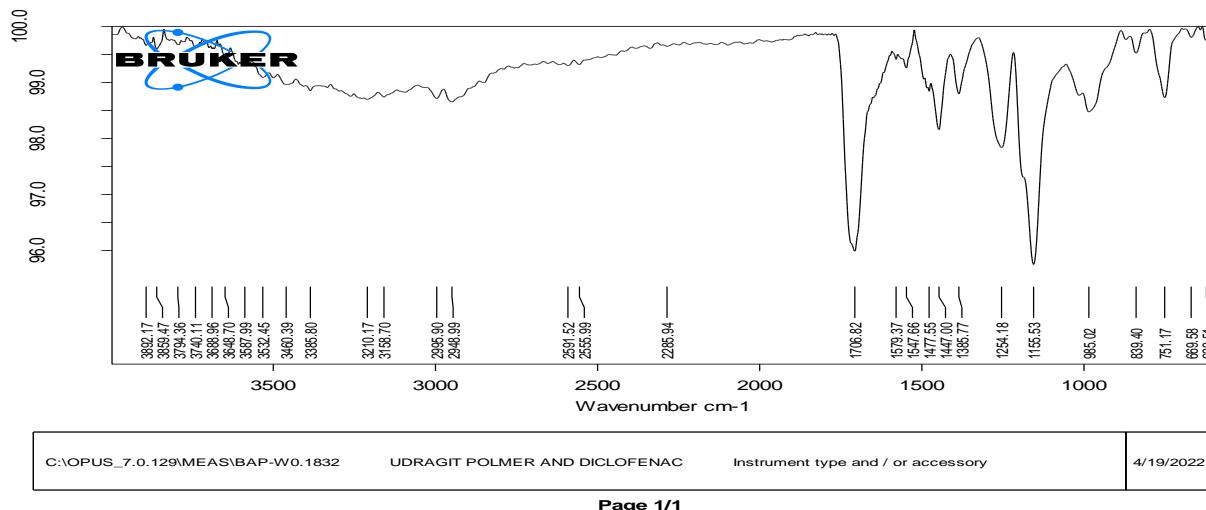
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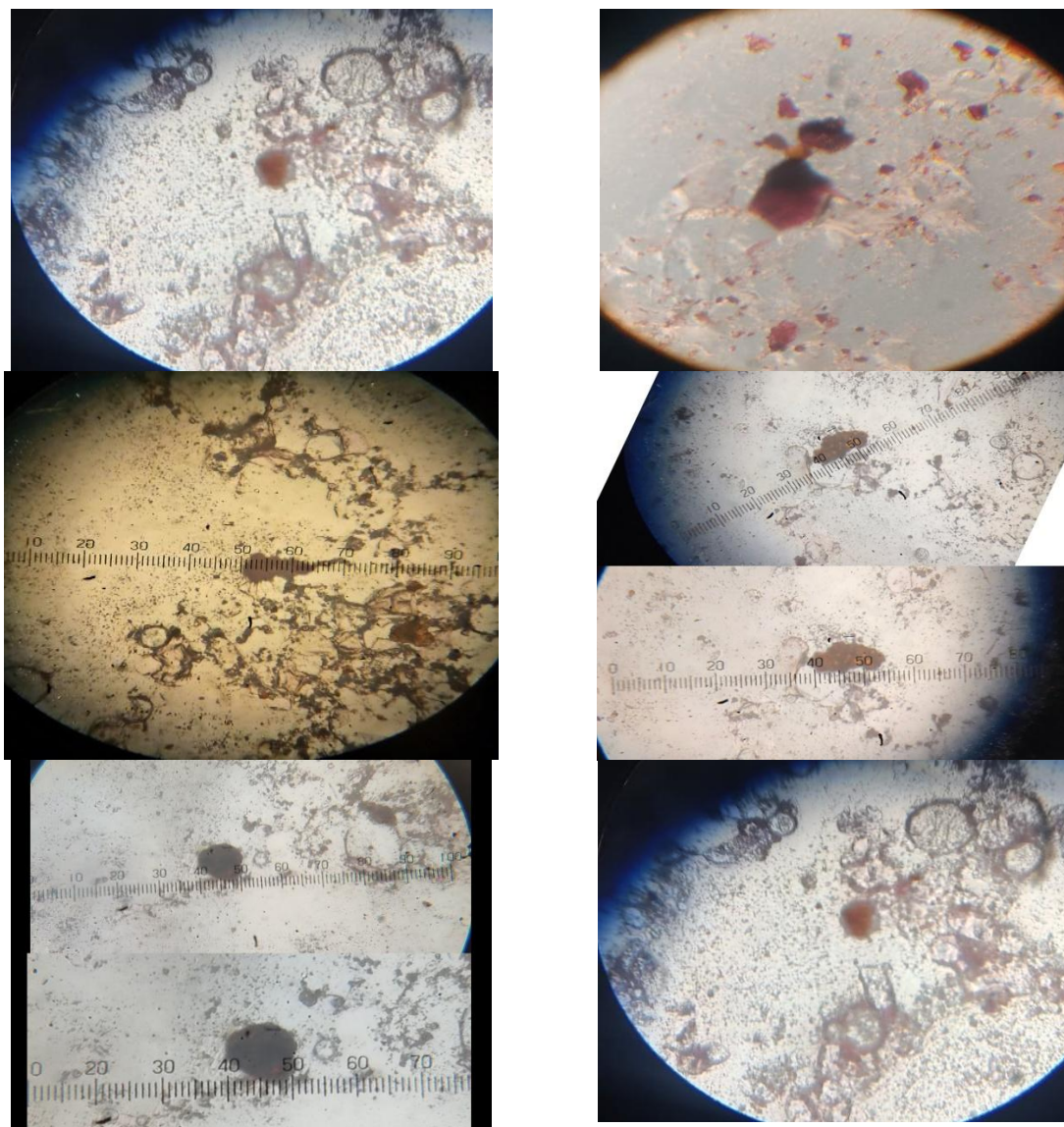
**Figure no:2 FTIR spectrum of pure diclofenac sodium.**

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**Figure no:3 FTIR spectra of diclofenac sodium with eudragit polymer.**

**Particle size determination of microspheres in emulsion:****Figure no: 4 Particle size of microspheres of F1-F6 respectively.**

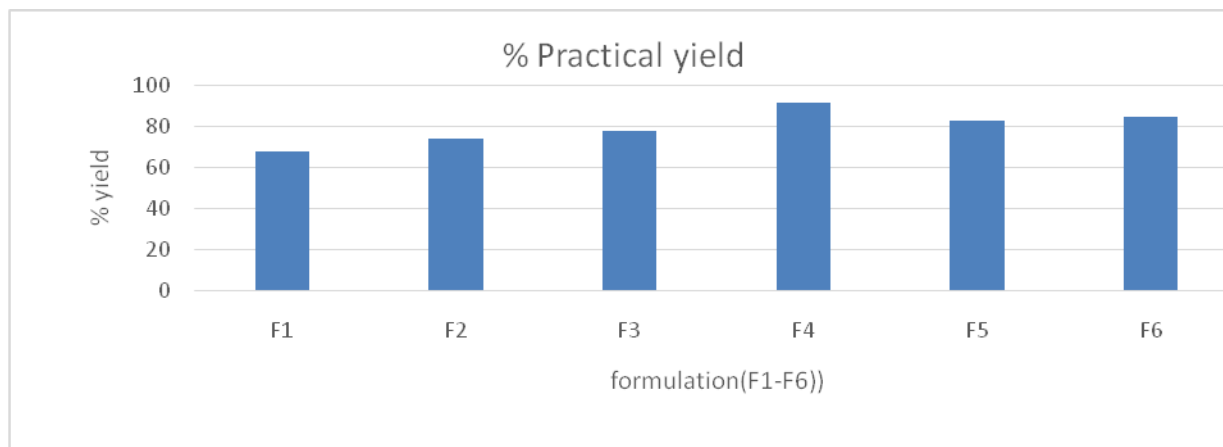
The mean particle size of the diclofenac sodium micro capsules was found to be proper distribution of polymeric layer surrounded the drug with normal frequency distribution were obtained

**Evaluation of microspheres:**

Entrapment efficiency: All the formulations were subjected for evaluation of entrapment efficiency. On the basis of entrapment efficiency evaluation data found that, all formulations (F1-F6) were showed good entrapment by polymer and F4 formulation shows maximum entrapment among them.

**Table no: 2 percentage entrapment of formulation(F1-F6):**

Formulation code	% Practical yield	Percentage entrapment (%)
F1	68	68
F2	74	74
F3	78	78
<b>F4</b>	<b>92</b>	<b>92</b>
F5	83	83
F6	85	85



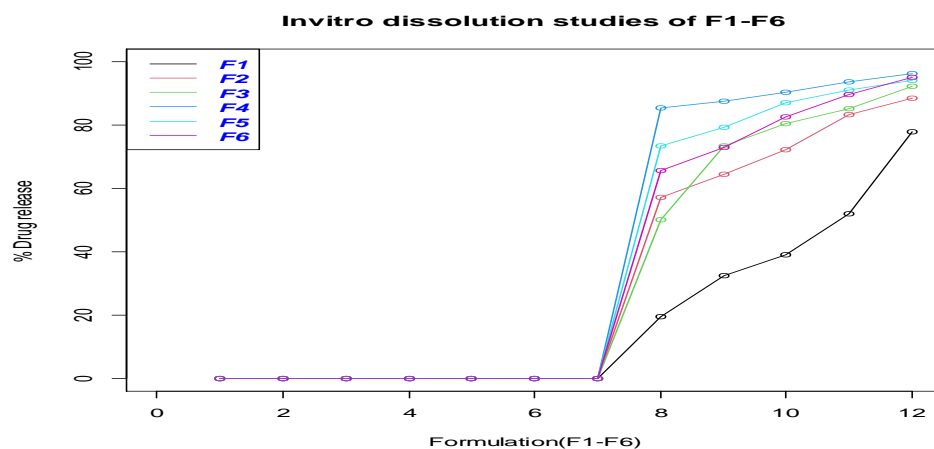
Graph no: 1 percentage entrapment of formulations.

**Invitro Dissolution studies:**

All the formulations were subjected for *Invitro* dissolution studies. On the basis of *Invitro* dissolution data found that, all formulations(F1-F6) were showed the drug release after define the lag period made possible due to pH dependent and site specific drug release polymer and F4 formulation shows better drug release as 96.2% at end of 12 hours.

Table no: 3 in vitro dissolution data of F1-F6.

TIME IN HOURS	F-1	F-2	F-3	F-4	F-5	F-6
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0
7	0	0	0	0	0	0
8	19.5	57.2	50.05	85.8	73.45	65.65
9	32.5	64.35	73.45	87.5	79.3	72.86
10	39	72.15	80.6	90.35	87.1	82.55
11	52	83.2	85.15	93.6	91	89.7
12	78	88.4	92.3	96.2	94.25	95.1



Graph no: 2 Invitro dissolution studies of F1-F6.



## CONCLUSION

The concept of formulating diclofenac sodium microsphere contain micro emulsion offers a suitable practical approach to achieve a prolonged therapeutic effect by releasing the medication over extended period of time. In present work, micro emulsions of diclofenac sodium microspheres was prepared successfully by emulsification method using eudragit as a polymer and then phase titration method. As the ratio of polymer was increased, the mean particle size of diclofenac sodium micro spheres was decreased. Diclofenac sodium microspheres with normal frequency distribution were obtained and the deviation was within the acceptable limit. The study also revealed that the drug entrapment and *in vitro* release of drug in micro emulsion are good. The optimized and best in F-4 formulation was concluded. This novel approach would be recommended for system for future aspects.

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## Conflicts of interest:

Nil.

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