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Dissolution Enhancement of Diclofenac Sodium by Self Emulsifying Technique

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ABSTRACT

The present investigation was aimed to dissolution enhancement of didofenac sodium by using Self emulsifying Technique using lemon oil as a oil, Tween 80,Tween 20,as a surfactant, span 20, span 80 as a co solvent etc. using in this technique. Pellets are prepared by Extrusion process. The solid self-emulsifying drug delivery systems were characterized by particle size analysis, Drug content, in vitro and in vivo pharmacokinetic studies. .Highest dissolution is found in f 9 formulation in Phosphate buffer Ph 6.8 as compared to other formulation.

Key words: *Diclofenac sodium, Self-emulsification technique, Drug release study, Pellets formulation.*

INTRODUCTION

Diclofenac sodium (2-[(2,6-diclorophenyl)-amino]-phenyl Acetate) has a antipyrytic, analgesic, and anti-inflammatory activity.it is a potent realitively non-selectively cyclooxygenase inhibitor [1]. Diclofenac is completely absorbed after oral administration. Peak concentration in Plasma is reached in 2-3 hours. The drug is extensively Bind to plasma protein (99%) and half life in plasma is 1-2 hours [2]. It inhibit the synthesis of prostaglandin synthesis. It has low aqueous solubility and, as a consequence, has low oral bioavailability. Therefore, the improvement of dissolution. from its oral solid dosage forms is essential for enhancing its bioavailability and therapeutic efficacy. Poor oral bioavailability of a drug is often due to low solubility, degradation in gastrointestinal tract (GIT), low permeability and high first pass metabolism [3].

Approximately 40% of new drug candidates have poor water solubility and the oral delivery of such drugs is frequently associated with low bioavailability, high intra- and inter-subject variability, and a lack of dose proportionality [4]. To overcome these problems, a variety of strategies have been developed including the use of surfactants, lipids, permeation enhancers, micronization, salt formation, cyclodextrins, nanoparticles and solid dispersions, and self emulsifying drug delivery system, etc. self-emulsifying drug delivery systems to improve the oral bioavailability of lipophilic drugs [5]. Self-emulsifying drug delivery systems SEDDSs has gained exposure for their ability to increase solubility and bioavailability of poorly soluble drugs. SEDDSs are isotropic mixtures of oils and surfactants, sometimes containing cosolvents, and can be used for the design of formulations in order to improve the oral absorption of highly lipophilic compounds [6].

Hence in the present study, an attempt has been made to formulate and evaluate self emulsifying drug delivery systems of Diclofenac sodium in the form of pellets.

MATERIAL AND EQUIPMENT

Diclofenac sodium was obtained as gift sample from Aldoc Pharmaceutical, kota Rajasthan, India. Oleic acid, Lemon oil, Microcrystalline cellulose Lactose, Polyvinylpyrrolidone (PVP K30) Tween 20, Span 20, Span 80, Tween-80 and Propylene glycol (PG) were purchase from Central drug house, New Delhi. All the chemicals and reagents used were of analytical grade.

Preparation of self emulsified pellets: [8]

The molten blend was prepared by mixing surfactants (teween 20 or tween 80) in co solvents (propylene glycol or span 20 or span 80) with oil (oleic acid or lemon oil) in different proportions (According to table) in a china dish at 70°C, followed by mixing the prepared blend with drug until a creamy dispersion was produced. Blending of excipients (MCC PH101, lactose and PVP K30) was carried out by physical mixing in different proportions. Creamy dispersion was then mixed thoroughly until a mass suitable for extrusion was obtained. Pellets were prepared by using syringe.

Table No. 1: Ingredients of Diclofenac sodium pellets

Ingredient % w/w	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug	4	4	4	4	4	4	4	4	4
Tween 20	---	---	7	7	---	---	7	7	7
Tween 80	7	7	---	---	7	7	---	---	---
PG	5	---	5	---	5	---	5	---	---
Span 20	---	---	---	---	---	---	---	---	5
Span 80	---	5	---	5	---	5	---	5	---
Lemonoil	---	---	---	---	2.5	2.5	2.5	2.5	---
Oleic acid	2.5	2.5	2.5	2.5	---	---	---	---	2.5
Lactose	15	15	15	15	15	15	15	15	17.5
Mcc	15	15	15	15	15	15	15	15	17.5
Pvp k 30	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5

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Fig. 1: Pelles formulation (F9)

1. Lamda max (λ) of Diclofenac sodium:

Weighing 100 mg drug in 100 ml. Phosphate buffer Ph 6.8 in volumetric flask. after 10ml solution withdrawal from above solution .and volume make up this solution 100ml by Phosphate buffer. Now 10 ml withdrawal and volume make up up to 100ml by Phosphate buffer. Now lamda max (λ) is Cheeked in UV apparatus at different nanometer.

2. Calibration curve of the Diclofenac sodium:

Calibration curve of the drug was estimated in phosphate buffer pH 6.8 and the suitably diluted solutions were analyzed by spectrophotometrically using double beam UV spectrophotometer at 276 nm. The estimation was performed in triplicate and the regression co-efficient was derived to ensure the linearity of the calibration curve.

3. Solubility: [7]

For the determination of solubility, excess quantity of Diclofenac sodium and pellets were taken in 10 ml (phosphate buffer pH 6.8) separately, kept on a shaking water bath (100 agitations/min) for 24h at room temperature. The solutions were then filtered through filters and the amount of the drug dissolved was analyzed spectrophotometrically at 276nm.

4. Drug content: [6]

Drug from pre-weighed SEDDS is extracted by dissolving in suitable solvent. Drug content in the solvent extract was analyzed by suitable analytical method against the standard solvent solution of drug.

5. Dissolution studies:

The *in vitro* dissolution studies were carried out using USP type II dissolution apparatus in phosphate buffer pH 6.8. The paddle rotation speed was 50 rpm. Temperature is maintained at 37°C.The samples were withdrawn at predetermined time intervals subsequently replaced with fresh media. The sample solutions were then filtered through 0.45µm membrane filters and the drug concentration was analyzed spectro photometrically at 276nm.

RESULT AND DISCUSSION

1. Lamda (λ_{Max}) of drug:

In uv spectrophotometer check Absorption at various wavelength 230-400 nm.highest absorption foundat276 nm Highest absorption represented its l λ_{max} of drug.

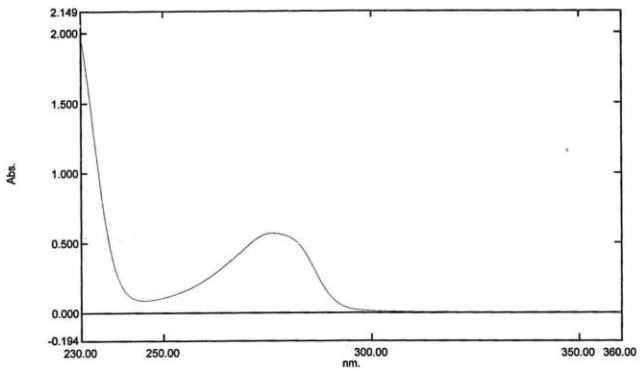

Fig. 2: Lamda (λ_{max}) of diclofenac sodium

2. Standard curve of Diclofenanc Sodium:

Tabel No. 2: Standard curve of Dioclofenac sodium

S.No	Concentation(ug/ml)	Absorbance
1	2	0.145
2	4	0.308
3	6	0.515
4	8	0.712
5	10	0.926

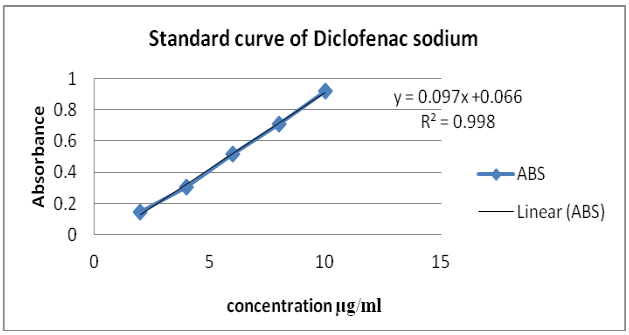

Fig. 3: Standard curve of Diclofenac sodium in phosphate buffer pH 6.8

3. Drug content:

The drug content was found to be uniform among the different batches of prepared pellets and ranged from 92.45 -95.23 %.

4. Solubility:

Solubility of drug was found to be increased for all the prepared batches of pellets and the formulation F9 showed the maximum solubility.

5. Dissolution studies:

Dissolution study of Pure drug and various formulation done in usp dissolution apparatus using phosphate buffer Ph 6.8, and maintain sink condition. Highest dissolution rate is found in formulation f 9.as compared to other formulation.

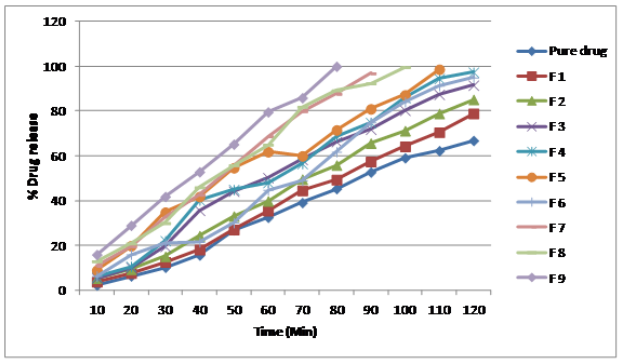

Fig. 4: In vitro Release of pure drug and all formulation in phosphate Buffer Ph 6.8

CONCLUSION

The used self emulsification technique in an aqueous system found to be economic and free from organic solvent. The mean and size distribution, Drug content and in-vitro drug release studies on Diclofenac sodium .the formulation F9 was found to be good enough and feasible technique for the formulation. Among the nine formulations, the formulation F9 exhibited significantly optimised release profile. The Diclofenac sodium formulated with the tween 80,tween 20,PG, Sspan 80,laose,lemon oil, etc may be good choice for the improvement of Dissolution.

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