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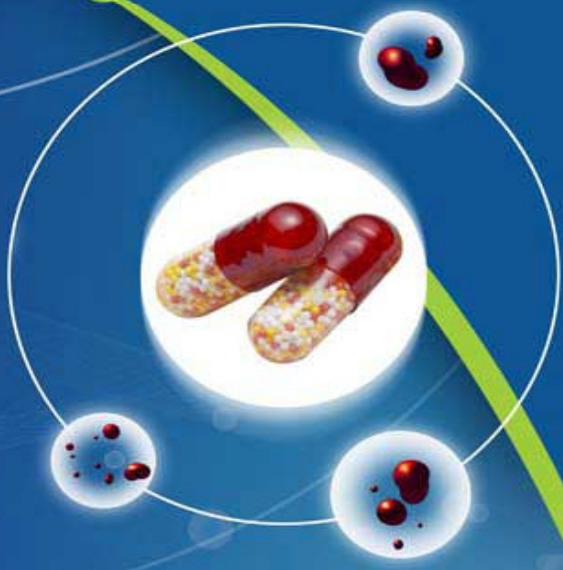

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Research Article

DEVELOPMENT, CHARACTERIZATION AND DISSOLUTION STUDY OF SOLID DISPERSION OF DICLOFENAC SODIUM BY KNEADING TECHNIQUE

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ABSTRACT

The present investigation was aimed to dissolution enhancement of diclofenac sodium by using Solid dispersion Technique using Mannitol, Sodium starch glycolate,Polymer.using in this technique. Solid dispersion are done by kneading method and solvent evaporation method..The solid dispersion characterized by particle size analysis,Drug content, in vitro and in vivo pharmacokinetic studies. .Highest dissolution is found in f 1 formulation in Phosphate buffer Ph 6.8 as compared to other formulation.

Key words: *Diclofenac sodium, Solid dispersion, Drug release study*,

INTRODUCTION

Diclofenac sodium (2-[(2,6-dichlorophenyl)-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].

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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 micronization, salt formation, cyclodextrins, nanoparticles, self emulsifying

drug delivery system and solid dispersions, etc. Solid dispersions have attracted considerable interest as an efficient means of improving the dissolution rate and
hence the bioavailability of a range of hydrophobic drugs. Much of the research that has been reported on solid dispersion technologies involves drugs that are poorly water-soluble and highly permeable to biological membranes as with these drugs dissolution is the rate limiting step to absorption[5]. Hence, the hypothesis has been that the rate of absorption in vivo will be concurrently accelerated with an increase in the rate of drug dissolution. In the Biopharmaceutical Classification System (BCS) drugs with low aqueous solubility and high membrane permeability are categorized as Class II drugs Therefore, solid dispersion technologies are particularly promising for improving the oral absorption and bioavailability of BCS Class II drugs.
Hence in the present study, an attempt has been made to formulate and evaluate solid dispersion of Diclofenac sodium.

MATERIAL AND METHOD

Diclofenac sodium was obtained as gift sample from Aldoc Pharmaceutical, kota Rajasthan, India. Mannitol, sodium starch Glycolate and Ethanol by Central drug house, New Delhi. All the chemicals and reagents used were of analytical grade.

METHOD

Kneading method- Polymer (mannitol or ssg) was added to the mortal and some quantities of 50% v/v ethanol were added while triturating to get slurry like consistency .The slowly drug was incorporated in to slurry and trituration was continued further for 1 hrs. The slurry was then air dried at 25ᵒc for 24 hrs. Pulverized and passed through sieve no.100 and stored in dessicator over fused calcium chloride.[7]

Evaluation of Diclofenac sodium solid dispersion

Percent practical yield

Solid dispersion were collected and weighed to determine practical yield from following equation- practical yield = [Practical weigh of solid dispersion] / [Theoretical mass of solid dispersion] *100

Drug content

Drug from pre-weighed Solid dispersion 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.
%drug content =Actual diclofenac sodium content in weight quantities of solid dispersion / theoritcal amount of diclofenac sodium solid dispersion *100

Solubility

For the determination of solubility, excess quantity of Diclofenac sodium and Solid Dispersion 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.

In Vitro dissolution study

Dissolution studies were performed assuring sink condition .the dissolution medium containing 900 ml phosphate buffer pH6.8 ,Temp.37ᵒC.The solid dispersion containing 500 mg of diclofenac was taken in muslin cloth and kept in basket of dissolution apparatus.sample is taken about 5 ml.in 10 min.interval .sample was analyzed in uv spectra at 276 nm

Table 1; Formulation ingredient preparation method of Diclofenac sodium solid dispersion

S.No	Batch code	Material	Method	Ratio
1	F 1	Drug +mannitol	Kneading Method	1:1
2	F 2	Drug+mannitol	Kneading Method	1:5
3	F 3	Drug+mannitol	Kneading Method	1:7
4	F 4	Drug + ssg	Kneading Method	1:1
5	F 5	Drug +ssg	Kneading Method	1:5
6	F 6	Drug+ ssg	Kneading Method	1:7

F 1

F 5

RESULT AND DISCUSSION

Percent Practical Yield

The Percent Practical Yield **was** found to be uniform among the different batches of prepared Solid Dispersion and ranged from 85-96 %.

Drug content

The formulation F1 showed the maximum solubility.

The drug content was found to be uniform among the different batches of prepared Solid Dispersion and ranged from 44-62 %.

Solubility

Solubility of drug was found to be increased for all the prepared batches of Solid Dispersion and

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 1.as compared to other formulation.

CONCLUSION

The used Solid Dispersion 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 F 1 was found to be good enough and feasible technique for the formulation. Among the Six formulations, the formulation F 1 exhibited significantly optimised release profile. The Diclofenac sodium formulated with ssg and mannitol, etc may be good choice for the improvement of Dissolution.

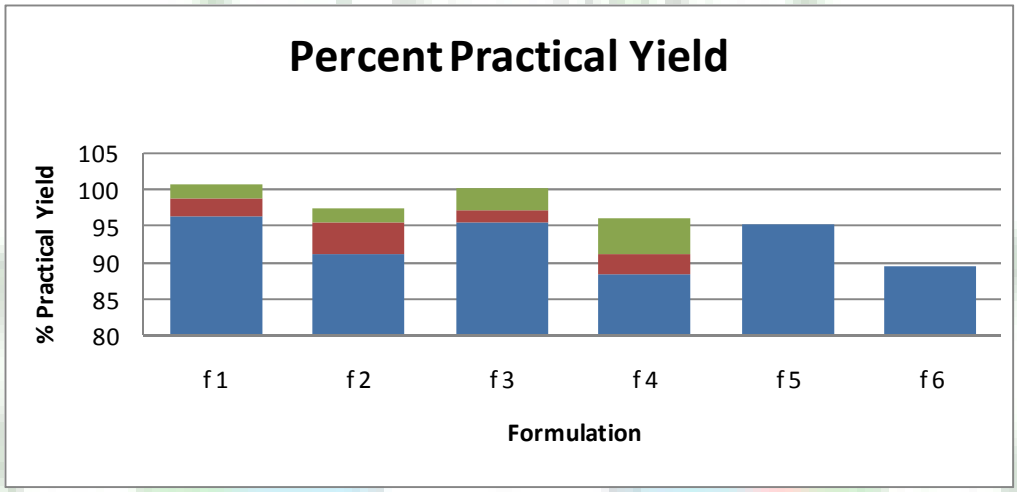

Fig: 1. Percent Practical Yield Graph

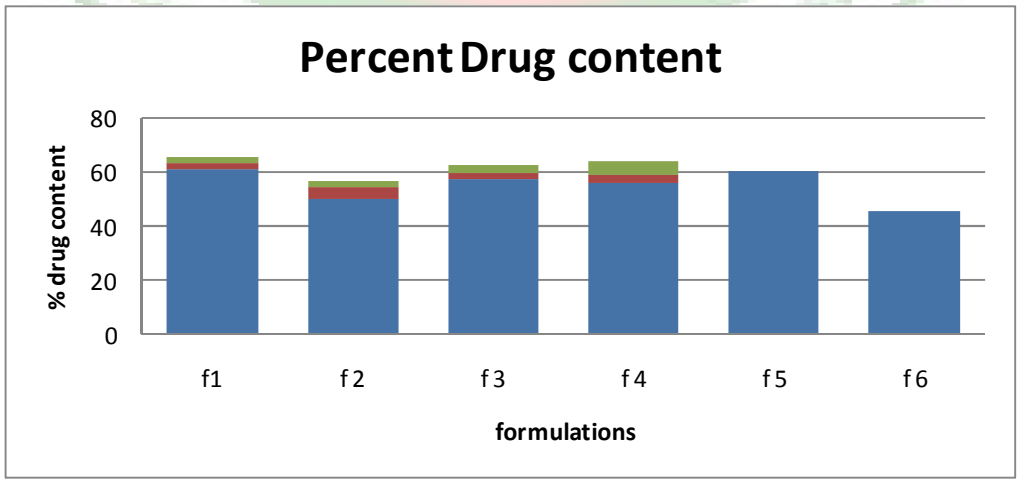

Fig.2 Drug content graph

In vitro Release of pure drug and all formulation in phosphate Buffer Ph 6.8 in different Dissolution model

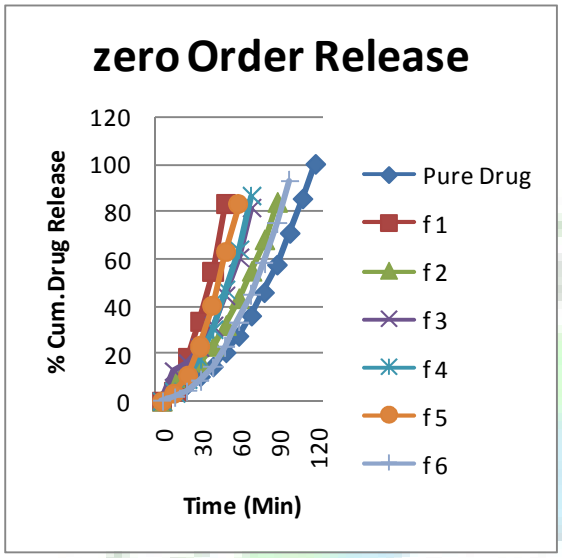

Fig.3 Zero Order Release

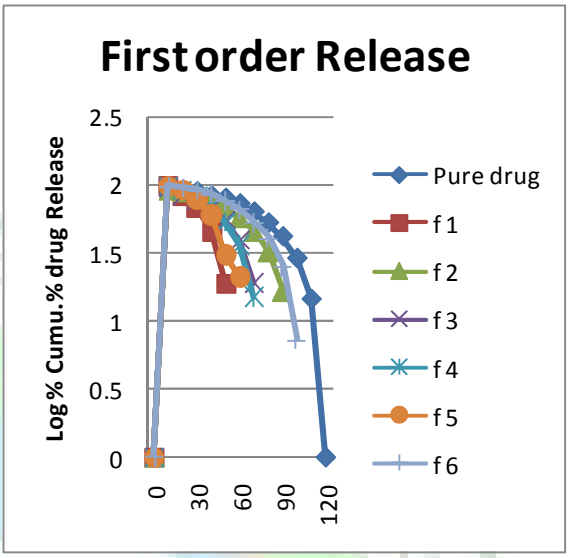

Fig.4 First Order Release

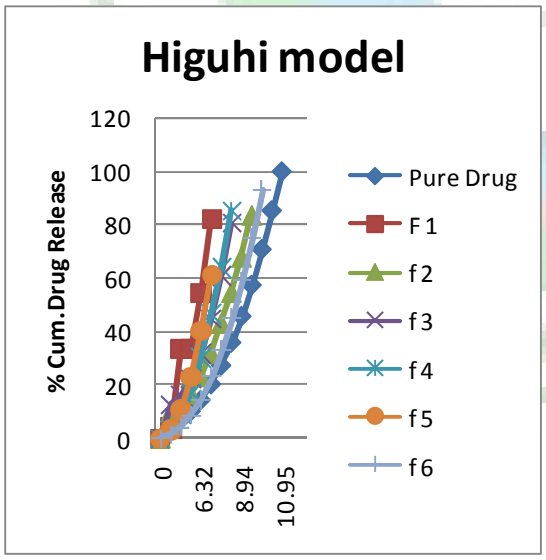

Fig.3 Higuchi Model

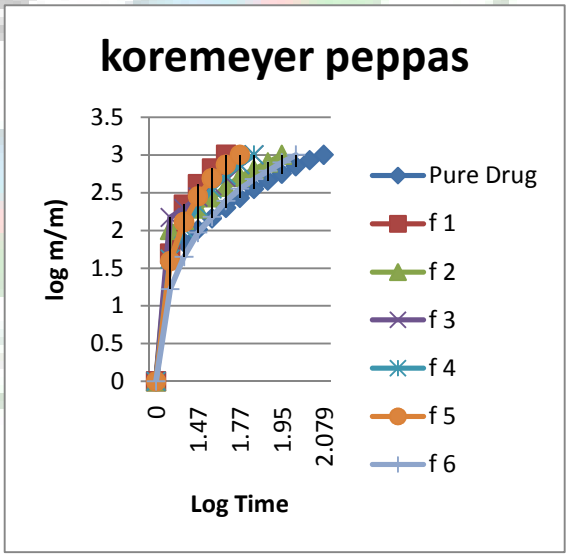

Fig.4 Koremeyer Peppas

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