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FORMULATION AND EVALUATION OF CEFIXIME DRY EMULSION

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ABSTRACT

Liquid emulsions have distinct advantages over the other oral dosage forms by improving the bio availability and by reducing the side effects, but the number of emulsion formulations currently in use are few compared with other oral dosage forms due to physical- chemical and compliance problems. To overcome these problems dry emulsions are prepared. Dry emulsions are prepared by drying liquid emulsions containing a solid carrier in the aqueous phase. Dry emulsions are lipid based powder formulations from which an emulsion can be reconstituted. Dry emulsions can be prepared by spray drying, lyophilization and rotary evaporation. Unfortunately the dry emulsions are cohesive powders. The cohesiveness can be reduced by addition of sucrose. In this study the oils used are Sesame oil, Olive oil and Peppermint oil. By conducting Pre formulation studies the best gum for the preparation of Dry emulsion was found to be HPMC and the Organic filler used was Mannitol. Observations were carried out and it was found that by formulating as dry emulsion the bioavailability and stability of drug were enhanced.

KEY WORDS: Cefixime, Dry Emulsion, Immediate Release.

1. INTRODUCTION

The dry Emulsion formulation aim to improve the bioavailabilityof drug substances and reduce their side effects.Dry Emulsions are attractive because they are physically and microbiologically stable formulations. They represent a potential oral drug delivery system for lipophilic and low soluble drug substances. Dry Emulsions are prepared by techniques like Lyophilization, Spray drying, and Rotary Evaporation. For preparing dry Emulsions the organic fillers used are Lactose, Mannitol, Malto-dextrins. Commonly used co-solvents are Polyethylene glycol, Propylene glycol, Glycerol etc. The thickening agents used are Natural and synthetic gums, Cellulose derivatives, colloidal silica.The sweetening agents used are Glucose, Aspartame, Sucrose etc. For preparing oil in water emulsions medium chain triglycerides are generally used as lipid phase so the preferred oils are sesame oil, olive oil and peppermint oil. Cefixime is a third generation Cephalosporin antibiotic, it has very low solubility in biological fluids. So to enhance the bioavailability and stability of drug it is formulated as a dry Emulsion.

2. MATERIALS AND METHODS

Materials: Cefixime was received as a gift sample from Oscar Remedies,Himachal Pradesh. HPMC E5 obtained from Ontop pharmaceuticals, Bangalore. Olive oil, Sesame oil and Peppermint oil were obtained from Empire Scientific Company. Propylene glycol, Tween 80 and Span 80 were received from kiran scientific Company.

Method of preparation of dry emulsion: The drug was thoroughly mixed with propylene glycol by using a magnetic stirrer.In another beaker aqueous phase was taken and to this gum, organic filler, surfactant and sweetening agent were added and stirred well until a homogenous solution was formed.Then the propylene glycol with drug was added to this solution and mixed thoroughly.The above mixture was kept on magnetic stirrer and the oil phase was added drop by drop.The stirring was continued until a milky white emulsion with desired droplet size was obtained.Now for drying this emulsion. The samples were taken in Petri plates and kept in incubator at four different temperatures.The temperatures were 40^0c, 50^0c, 60^0c, 70^0c, Out of these 60^0Cwas chosen for drying the emulsion. The emulsion was dried thoroughly and the dried powder of emulsion was collected and stored in a well closed container.

Preparation of solution for calibration curve: From the working standard solution (100µg/ml) 2-30µg/ml solutions were prepared, and calibration curve was plotted by taking 2, 4, 6, 8, 10&12µg/ml concentrations. Standard calibration curve of cefixime in 7.2 phosphate buffer at 287nm was plotted by taking absorbance on Y-axis and concentration on X-axis and it follows beer's law.

Pre-formulation Studies:

Drug excipient compatibility studies: Before formulation of drug substances into a dosage form, it is essential that it should be chemically and physically characterized. Pre-formulation studies give the information needed to define the nature of the drug substance and provide a framework for the drug combination with pharmaceutical excipients in the fabrication of a dosage form. In this Compatibility studies one of the requirements for the selection of suitable polymers or carriers for pharmaceutical formulation is its compatibility.

FTIR study: FTIR studies were performed by Potassium bromide pellet method.

Determination of melting point: Melting point of cefixime was determined by capillary method.

Solubility: The solubility of cefixime was determined by adding excess but measured amount of drug in 100ml volumetric flask containing 7.2 phosphate buffer and kept under agitated conditions at 37^0c± 0.5 in water bath shaker for 2hrs. The dispersions were filtered through whatmann filter paper and analyzed for the quantity of drug dissolved.

Cefixime pure drug analysis: The absorbance of the prepared solutions was checked using a UV spectrophotometer at 287 nm. Ph 7.2 Phosphate buffer was used as the blank.

Evaluation studies for the formulated dry emulsion: Dry emulsion is subjected to the following evaluation tests

Drug entrapment: Thedrug entrapment of the prepared dry emulsion should be in the range of 98.672 to 101.04%w/w.

In-vitro dissolution studies: Dissolution profiles of pure drug, dry emulsion and dry emulsion, dry suspension and tablet were compared on the basis of time required to release maximum drug. Cumulative percent drug release at 15, 30, 45, 60, 120, 180, 240, 300, 360, 420, 480 minutes were observed.

In-vitro Drug Entrapment Studies: The formulations of dry emulsions were subjected to evaluation of drug entrapment. The % drug entrapment of dry emulsion formulation with peppermint oil (Formulation 4) was 99.3%, and with olive oil (Formulation 3) was found to be 98.5%, with Sesame oil using single surfactant (Formulation 1) was 97.1% and with combination of surfactants (Formulation 2) was 97.9%.this shows that Cefixime dry emulsion formulation with peppermint oil shows high drug entrapment efficiency.

In-vitro drug release studies: On comparing the in vitro drug release studies of dry emulsion formulations prepared with the three oils, the dry emulsion formulation prepared with peppermint oil showed an immediate release of the drug enhancing its bioavailabiity. Then the invitro release of this peppermint dry emulsion formulation was compared with marketed products like cefixime dry suspension and tablet and with pure cefixime. When compared to other dosage forms like dry suspension and tablet the dry emulsion formulated with peppermint oil showed immediate release of drug. Thus the objective of the study was met.

The cumulative % drug release for formulations F1, F3, F5 and F7 at the end of 8hrs is 39.13, 97.44, 29.14 and 85.62 respectively. At the end of 5 hrs formulation F6 showed cumulative % drug release of 86.742. At the end of 4hrs formulation F2 showed cumulative % drug release of 90.15 and at the end of 2 hrs formulations F4 showed cumulative % drug release of 98.126. Stability studies were conducted for a period of 3 months.

Table.1.Formulation Table

Ingredients	F1	F2	F3	F4
Cefixime	2gm	2gm	2gm	2gm
Peppermint oil	-	-	-	8ml
Olive oil	-	-	16ml	-
Sesame oil	16 ml	16ml	-	-
Propylene Glycol	4ml	4ml	4ml	4ml
Tween 80	4ml	3ml	3ml	3ml
Span 80	-	2ml	2ml	2ml
Methocel K4M	4gm	4gm	3gm	1gm
HPMC	-	-	1gm	3gm
Mannitol	10gm	10gm	10gm	10gm
Sucrose	2gm	2gm	2gm	2gm
P Water	Q.S to 100ml	Q.S to 100ml	Q.S to 100ml	Q.S to 100ml

Table.2. In-Vitro Drug Entrapment Studies

Formulation code	Entrapment efficiency
F1	97.1%
F2	97.9%
F3	98.5%
F4	99.3%

Table.3.Comparision studies ofCumulative % Drug Release data for the Formulations

Time (min)	Cumulative % Drug Release Data						
	F1	F2	F3	F4	F5 (Pure drug)	F6 (Dry Suspension)	F7 (Tablet)
15	8.67	7.3	5.7	36.88	6.78	10.236	27.77
30	9.94	10.6	7.71	45.078	7.78	14.912	35.058
45	11.19	13.68	9.97	65.568	9.35	30.278	40.522
60	12.12	17.5	11.86	75.358	11.17	33.694	48.548
120	15.2	35.97	18.80	98.126	12.54	47.354	55.322
180	18.56	70.5	32.55	-	14.13	61.014	63.518
240	23.2	90.15	38.24	-	19.09	72.626	67.844
300	29.3	-	54.63	-	20.52	86.742	71.258
360	32.5	-	70.57	-	22.28	-	76.042
420	38.2	-	75.35	-	23.90	-	79.91
480	39.13	-	97.44	-	29.14	-	85.62

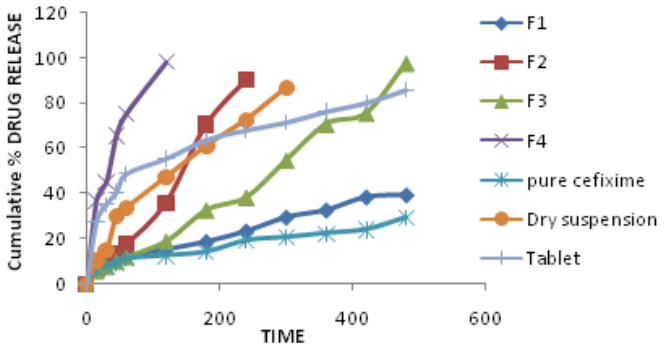

Figure.1.Plot of Cumulative % Drug Release vs. Time for Formulations

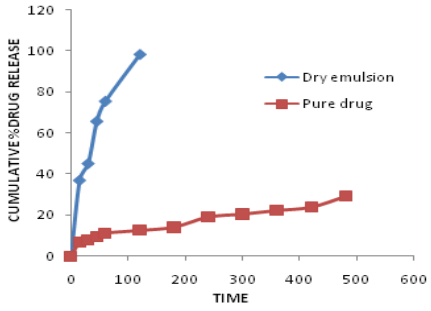

Figure.2.Plot representing comparison between pure Cefixime and Dry Emulsion

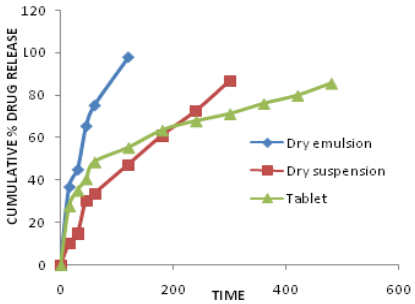

Figure.3.Plot representing comparision between Dry Emulsion, Dry Suspension and Tablet

4. CONCLUSION

By formulating Cefixime as Dry Emulsion its solubility and dissolution rate had been enhanced. The dry emulsion formulation was analysed for the stability studies for 3months at 45 ºC with 75±5% RH The emulsion was analyzed for drug entrapment and cumulative % drug release till a period of 3 months, no variations in results were observed. After three months the dry emulsion was reconstituted and the emulsion formed was stable with desired consistency and viscosity and without any signs of instability.On comparision of dissolution rate of Cefixime formulations it was found that,Pure Cefixime < Tablet < Dry suspension <Dry Emulsion. From the above study it can be concluded that the Dry

Emulsion formulation (F4) showed an immediate release of drug when compared with pure Cefixime and other marketed formulations.

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