Research Article

Design, Development and Evaluation of Dry emulsion of Cephalexin Monohydrate

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ABSTRACT

The aim of the present investigation is to improve the bioavailability and dissolution of cephalexin monohydrate by preparing dry emulsion. Dry emulsions are prepared by drying liquid o/w emulsions containing a solid carrier in the aqueous phase. The solid carrier provides the dry emulsions with bulk and mass. In this preparation of dry emulsion, propylene glycol in which drug is soluble, mannitol as organic filler and sucrose as sweetening and surfactant was used. Dry emulsion was evaluated for drug content, Globular size determination, Density, Moisture content and Surface characterization, In vitro drug release of dry emulsion was studied by USP type II paddle dissolution apparatus. This study revealed that solid dry emulsion technique was proved to be promising and useful for improvement of dissolution.

Keywords: cephalexin monohydrate, Dry emulsion, Mannitol.

INTRODUCTION

Liquid emulsions have distinct advantages over the other oral dosage forms by improving the bioavailability[1] 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 lack of physical-chemical and compliance problems.

To overcome these problems dry emulsions are prepared[2].Dry emulsions are attractive because they are physically and microbiologically stable solid formulations.

Dry emulsions are prepared by drying liquid o/w emulsions containing a solid carrier in the aqueous phase.

The solid carrier provides the dry emulsions with bulk and mass.

Dry emulsions are lipid based powder formulations from which an O/W emulsion[3,4] can be reconstituted *in-vivo* or *in-vitro*.

When exposed to an aqueous solution and thus they present a potential for drug delivery system.

For the preparation of dry emulsions we use drug, solid carrier, aqueous phase and lipophilic solvent.

The solid carriers used to prepare dry emulsions are gelatin, lactose, maltodextrin, mannitol, povidone, sucrose etc.

Insoluble carrier like colloidal silica can also be used. Dry emulsions can be prepared by spray drying[5-8], Lyophilization[9,10] and rotary evaporation.

The solid carrier may undergo partial or complete transformation into an amorphous state.

Since the amorphous carrier exhibits a strong tendency to crystallize at a particular elevated temperature and relative humidity[12], physical stability problems may arise.

Stability tests for amorphous solid carriers like lactose, maltodextrin, mannitol and sucrose will be carried out.

To avoid stability problems water soluble polymers[11] like hydroxyl propyl methyl cellulose, methyl cellulose and povidone are used as solid carriers.

MATERIALS AND METHODS

Cephalexin was received as a gift sample from Oxar remedies, Himachal Pradesh, HPMC E5 obtained from Top pharmaceuticals, Banglore.

Olive oil, Sesame oil and coconut oil were obtained from Empire scientific company. Propylene glycol, Tween 80, 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 strrier. In another beaker aqueous phase was taken and to this gum organic filler, surfactant[13] and sweetening agent were added and stirred well until a homogenous solution was formed.

Then the propylene glycol with Cephalexin monohydrate was added to this solution and mixed thoroughly.

The above mixture is 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. The samples were taken in petriplates and kept in incubator at four different temperatures to dry the emulsion.

The temperatures were 40˚C, 50˚C, 60˚C, 70˚C. Out of these 70˚C was choosen for drying the emulsion.

The emulsion was dried thoroughly and the dried powder of emulsion was collected and stored in a well closed container. The stability[14] of emulsion is checked by keeping it for 48 h.

Table 1: Compositions of Dry Emulsions

S. No	Ingredients	F1	F2	F3
1	Cephalexin Monohydrate	2g	2g	2g
2	Olive Oil	16ml	-	-
3	Coconut Oil	-	16 ml	-
4	Sesame Oil	-	-	16ml
3	Tween 80	3ml	3ml	3ml
4	Span 80	2ml	2ml	2ml
5	Methocel K4M	3g	3g	3g
6	HPMC	1g	1g	1g
7	Mannitol	10g	10g	10g
8	Propylene Glycol	4ml	4ml	4ml
9	Sucrose	2g	2g	2g
10	Water	Upto 100ml	Upto 100ml	Upto 100ml

Table 2: Drug Entrapment Efficiency and Drug Content Data of Dry emulsions

Formulation Code	Drug Entrapment Efficiency	Drug Content
F1	98.67 ± 0.52	95.24 ± 0.14
F2	95.38 ± 0.96	90.45 ± 0.75
F3	96.11 ± 0.75	88.36 ± 0.91

All values are expressed as mean ± standard deviation, (n=3)

Table 3: Globule Size Distribution of Dry Emulsion before and after Reconstitution

S. No.	Range in Micrometer	No. of Globules Before Reconstitution			No. of Globules After Reconstitution		
		F1	F2	F3	F1	F2	F3
1	1-14	413	388	363	400	347	355
2	15-28	40	69	72	45	52	54
3	29-42	14	25	86	26	20	31
4	43-56	0	16	24	5	11	8

Table 4: Cummulative Percent Drug Release of Different Formulations

S. No	Time (min)	% Drug Release				
		F1	F2	F3	Marketed Suspension	Pure Drug
1	0	0	0	0	0	0
2	15	32.03 ± 0.35	21.36 ± 0.75	15.39 ± 0.94	16.97 ± 0.39	12.34 ± 0.68
3	30	47.90 ± 0.21	38.25 ± 0.54	29.36 ± 0.46	36.26 ± 0.54	22.64 ± 0.39
4	45	56.93 ± 0.85	43.89 ± 0.91	35.78 ± 0.82	50.28 ± 0.16	31.62 ± 0.46
5	60	65.62 ± 0.95	51.32 ± 0.86	46.89 ± 0.18	59.98 ± 0.42	40.32 ± 0.82
6	75	74.18 ± 0.34	65.97 ± 0.44	59.33 ± 0.65	67.52 ± 0.19	50.22 ± 0.99
7	90	95.69 ± 0.11	71.35 ± 0.14	68.32 ± 0.33	74.68 ± 0.88	61.16 ± 0.17

All values are expressed as mean ± standard deviation, (n=3)

Characterization and Evaluation of Dry emulsion

Pre-formulation Studies

Pre-formulation investigations are done to characterize properties of raw materials including their physico-chemical, biopharmaceutical, and mechanical properties, as well as compatibility.

Determination of Melting Point

The melting point is determined by using a melting point apparatus by capillary method.

Solubility

The solubility of cephalexin was determined by adding excess but measured amount of drug in 100 ml volumetric flask containing excess water and kept under agitated conditions at 37°C ± 0.5 in water bath shaker for 2hrs. The dispersions were filtered through whatmann filter paper and analyzed for the quantity of drug dissolved.

Cephalexin Monohydrate Pure Drug analysis

The absorbance of the prepared solutions was checked using a UV spectrophotometer at 262 nm. Water was used as the blank.

Evaluation Studies for the Formulated Dry Emulsion[15]

Dry emulsion is subjected to the following evaluation tests.

Drug entrapment

The drug entrapment of the prepared dry emulsion should be in the range of 98.672 to 101.04% w/w.

In-vitro dissolution studies[16-18]

In-vitro drug release studies from dry emulsions were performed using USP Type 2 dissolution apparatus (paddle apparatus) at 25 rpm. Dry emulsions preparation equivalent to 125 mg of cephalexin monohydrate was taken. The dissolution medium consisted of 900 ml of distilled water maintained at 37 ±0.5°C. At predetermined time intervals 5ml of aliquot was withdrawn, and an equivalent volume of fresh dissolution medium was immediately added. The amount of drug released was estimated by measuring absorbance at 262 nm using a spectrophotometer. Cumulative percent drug release at five minutes interval of time were observed.

Dissolution profiles of pure drug, dry emulsion and dry suspension were compared on the basis of time required to release maximum drug.

Particle Size Analysis

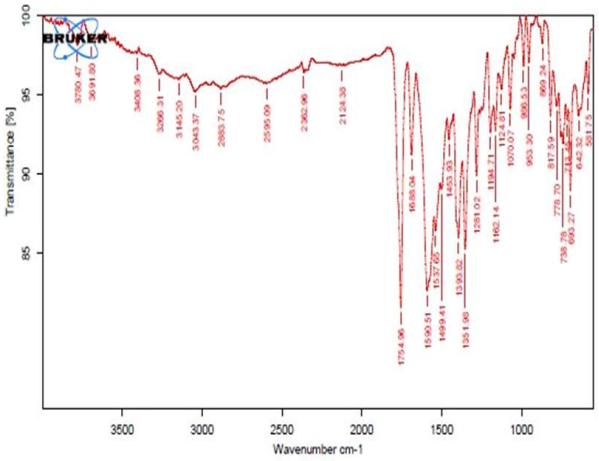
The particle sizes of loaded formulations were measured by an optical microscope fitted with an ocular and stage micrometer and particle size distribution was calculated.

The Olympus model (SZX-12) having resolution of 30 x was used for this purpose. The instrument was calibrated at 1unit of eyepiece micrometer was equal to 1/30 mm (33.33 µm). In all measurements at least 100 particles in five different fields were examined Each experiment was carried out in triplicate. Dry emulsions were diluted to 100 ml with distilled water. The droplet size distributions and poly dispersibility index of the resultant dry emulsions were determined using particle size analyzer.

RESULTS AND DISCUSSION

Pre-formulation Studies

FTIR Studies



Determination of Melting Point

Melting point of cephalexin monohydrate was determined by capillary method. The melting point was found to be 190 °C.

Evaluation Studies for the Formulated Dry Emulsion

Dry emulsion is subjected to the following evaluation tests.

Drug Entrapment Efficiency

The drug entrapment of the prepared dry emulsions was in the range of 96.11-98.672 and the values are shown in the Table 2.

Drug Content Estimation

The percent drug content of dry emulsion formulations was estimated by dissolving appropriate quantity of dry emulsion equivalent to 100 mg in water. The samples were mixed thoroughly to dissolve the drug in water. The samples were sonicated using ultrasonicator for 15 min and analyzed using UV spectrophotometer and absorbance was recorded. The drug content for the formulations F1, F2, F3 was found to be 95.24, 90.45, 88.36 % respectively.

Globule Size Determination

Microscopic examination of the emulsion before and after reconstitution was observed, the minimum size of oil globule in micrometer range is important since reduction in surface area leads improvement in solubility and dissolution rate of an emulsion. Globule size distribution was analyzed and calculated. Before reconstitution suggests that the size of the globule has

been reduced which contributes to high dissolution rate of dry emulsion and of after reconstitution suggests that the size of the globules remain nearly same, and also suggests stability of emulsion after reconstitution.

In-vitro Drug release studies[19,20]

On comparing the *in vitro* drug release studies of dry emulsion formulation prepared when compared to other dosage forms like dry suspension, the dry emulsion formulated with olive oil showed immediate release of drug.

The cumulative % drug release for formulation at the end of 90 min was shown in Table 4.

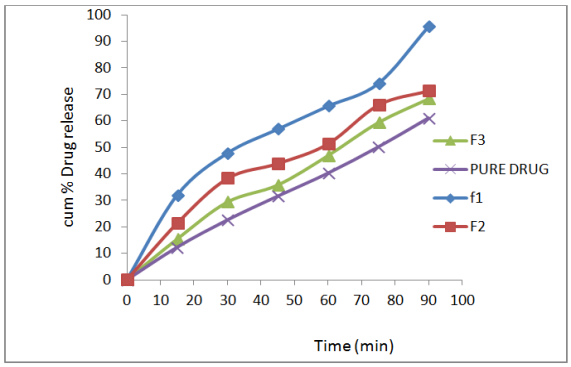


Figure 1: *In-vitro* Drug release of Dry Emulsions

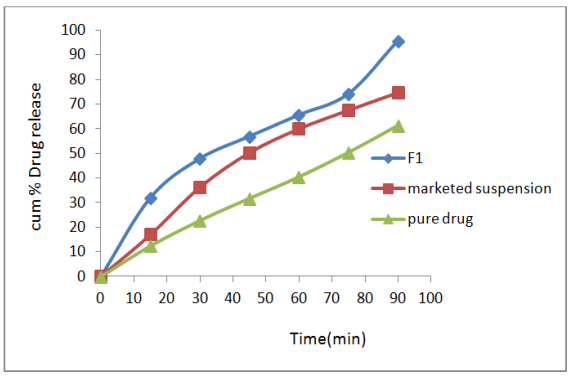


Figure 2: Comparison of *In-vitro* drug release of Dry Emulsion with Marketed formulation

CONCLUSION

By formulating Cephalexin monohydrate as Dry Emulsion its solubility and dissolution rate has been enhanced.

The dry emulsion formulation was analysed for the stability studies for 3 months at 45 °C 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 comparison of dissolution rate of Cephalexin monohydrate formulations it was found that, Pure Cephalexin < Dry suspension < Dry Emulsion.

From the above study it can be concluded that the Dry Emulsion formulation showed an immediate release of drug when compared with pure Cephalexin and other marketed formulations.

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