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Original Research Article

Formulation and evaluation of Loratidine solid dispersions by solvent evaporation technique

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ABSTRACT

Aim: The present investigation was aimed to prepare loratidine solid dispersions by solvent evaporation method using gelucire 44/14 and 50/13 as hydrophilic carriers.

Material and methods: Solid dispersion of loratidine with Gelucire 44/14 and Gelucire 50/13 were prepared using different weight ratios of three different hydrophilic carriers were prepared by the solvent evaporation method. Accurately weighed amount of drug and polymers in various ratios dissolved in ethanol in a round bottom flask and the solvent was evaporated at 45°C temperature.

Result: From the in vitro drug release studies the optimized formulation F3 containing gelucire 44/14 showed almost complete drug release within the 15 min. The percent drug release in 15 min (Q15) and initial dissolution rate (IDR) for optimized formulation (F3) was 94.22±1.08%, 9.26%/min. These were very much higher compared to the pure drug (23.87±1.13%, 2.38%/min). The improvement in the dissolution characteristics of a drug described in terms of dissolution efficiency (DE) and relative dissolution rate (RDR). The RDR was found to be 2.14. The DE was found to be 67.52 and it is increased by 4.0 fold with optimized FDT formulation compared to conventional tablets.

Conclusion: In conclusion, development of the solid dispersions can be a promising alternative method to attain the fast dissolution rate and absorption for water-insoluble drugs like loratadine and it was achieved with Gelucire 44/14 as a carrier.

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INTRODUCTION

Oral drug delivery is the simplest and easiest route of administrating drugs because of smaller bulk, accurate dosage and easy production (Ceballos et al., 2005). Solid dosage forms have many advantages over other types of oral dosage forms. Therefore, most of the new chemical entities (NCE) under development these days are intended to be used in a solid dosage form that originates an effective and reproducible in vivo plasma concentration after oral administration (Dannenfelser et al., 2004). However, the formulation of poorly water-soluble drugs has always been a challenging problem faced by pharmaceutical scientists and it is expected to increase because approximately 40% or more of the NCE being generated through drug discovery programs have the problem in water- solubility (Craig, 2002).

Solid dispersion technique is one of the promising strategies to formulate poorly soluble compounds that show dissolution-rate-limited absorption. The formulation of drugs having low aqueous solubility using solid dispersion technology has been an active research area since 1960. This technique was most successful in improving the dissolution and bioavailability of poorly soluble drugs because it is simple and economic. The term solid dispersion refers to a group of solid products consisting of at least two

different components, generally a hydrophilic matrix and a hydrophobic drug (Chiou and Riegelman, 1971). The matrix can be either crystalline or amorphous. The drug can be dispersed molecularly, in amorphous particles (clusters) or in crystalline particles. The carrier used has traditionally been a water-soluble or water-miscible polymers such as polyethylene glycol (PEG) or polyvinylpyrrolidone (PVP), low molecular weight materials such as urea, citric acid and mannitol (Desai, 2006) or more recently, carriers with surface activity such as Gelucire.

MATERIALS AND METHOD

Materials: Loratidine (LTD), Gelucires, Avicel PH 102, Crosspovidone, Magnesium Stearate,Talc.

Method: Solvent evaporation method.

The solid dispersion of loratadine with Gelucire 44/14 and Gelucire 50/13 was prepared using different weight ratios of three different hydrophilic carriers were prepared by the solvent evaporation method. Solid dispersions of loratidine of various polymers were prepared by as follows (Nair et al., 2002). Accurately weighed the amount of drug and polymers in various ratios dissolved in ethanol in a round bottom flask and the solvent was evaporated at 45°C temperature. Solid dispersions were subsequently stored in a vacuum oven at room temperature for 48 h to remove the residual solvent. The dried solid dispersions were ground in a mortar and pestle and passed through sieve # 60. The samples were stored in desiccators until use.

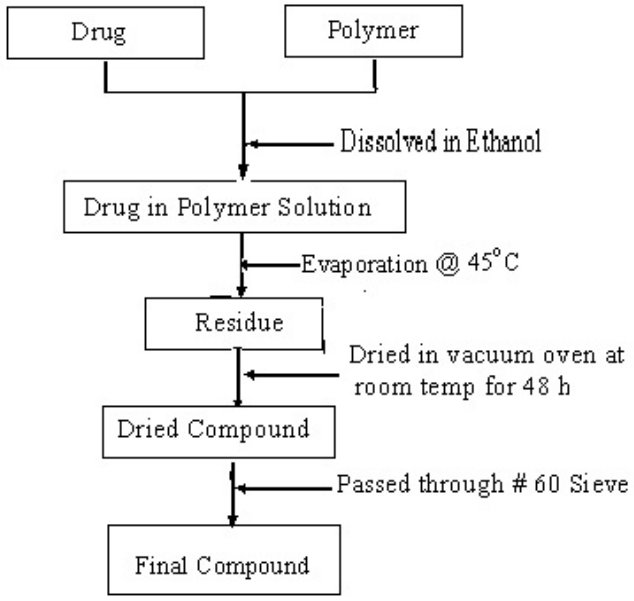

Table 1. Formulations of Loratidine solid dispersions with different ratios.

Formulation Code	Ingredients in (mg)			
	Loratidine	Gelucire 44/14	Gelucire 50/13	Drug, carrier Ratio
F1	10	10	-	1:1
F2	10	20	-	1:2
F3	10	30	-	1:3
F4	10	40	-	1:4
F5	10	50	-	1:5
F6	10	-	10	1:1
F7	10	-	20	1:2
F8	10	-	30	1:3
F9	10	-	40	1:4
F10	10	-	50	1:5

RESULTS

Table 2. Dissolution studies of LTD Solid Dispersions Gelucire 44/14.

Time (min)	F1	F2	F3	F4
0	0	0	0	0
5	35.21 ± 2.01	40.96 ± 2.76	61.11 ± 1.12	48.80 ± 0.99
10	44.36 ± 1.98	51.28 ± 1.89	81.22 ± 1.98	67.77 ± 1.22
15	61.85 ± 1.56	70.96 ± 1.90	95.48 ± 1.08	89.92 ± 1.76
20	78.61 ± 2.11	81.35 ± 0.98	99.31 ± 1.78	98.56 ± 1.67
30	88.21 ± 0.33	94.28 ± 0.09	-	-
45	93.08 ± 0.45	-	-	-
60	98.21 ± 0.99	-	-	-

Table 3. Dissolution studies of LTD Solid Dispersions using Gelucire 50/13.

Time (min)	F6	F7	F8	F9
0	0	0	0	0
5	17.53 ± 2.76	23.64 ± 2.21	30.54 ± 1.94	31.24 ± 2.31
10	28.63 ± 3.09	32.52 ± 2.66	40.85 ± 2.18	42.25± 3.45
15	39.12 ± 4.34	43.51± 3.01	52.31 ± 1.06	57.08 ± 2.91
20	52.66 ± 1.56	55.28 ± 1.87	79.64 ± 1.62	77.63 ± 1.34
30	61.82 ± 2.32	69.56 ± 1.18	98.97 ± 1.21	93.98 ± 1.08
45	65.23 ± 0.58	74.53 ± 2.76	-	-
60	72.65 ± 0.67	81.46 ± 0.87	-	-

The in vitro dissolution studies, the results were shown in Table 2 &7 From all these formulations, solid dispersions containing Gelucire 44/14 in 1:3 ratio (F3 formulation) showed highest dissolution rate within 15 min i.e. 94.22±1.08 %. From the dissolution studies, in case of different formulations, formulations with gelucire 44/14 were showed increased dissolution rate when compared to 50/13. From the in vitro dissolution studies, LTD in the form of solid dispersion showed the significant increase in dissolution rate. Many factors contributed to faster drug release rate such as the decrease in particle size, decrease in agglomeration of particles, increase wettability and decrease in crystallinity of the drug.

Table 4. Dissolution parameters of LTD conventional and F3 optimized tablets.

Formulation	(Q_{15})*	IDR (%/min)	DE	RDR
Optimized (F3)	94.22±1.08	9.26	67.52	2.14
Conventional tablet	39.62±1.29	2.38	15.27	

Mean ± SD n=3.

The percent drug release in 15 min (Q15) and initial dissolution rate (IDR) for optimized formulation (F3) was 94.22±1.08%, 9.26%/min. These were very much higher compared to the pure drug (23.87±1.13%, 2.38%/min). The improvement in the dissolution characteristics of a drug described in terms of dissolution efficiency (DE) and relative dissolution rate (RDR). The RDR was found to be 2.14. The DE was found to be 67.52 and it is increased by 4.0 fold with optimized FDT formulation compared to conventional tablets (Table 2). The overall increase in the dissolution performance of the optimized formulations described in terms of dissolution parameters (IDR, DE, RDR) compared to conventional tablets.

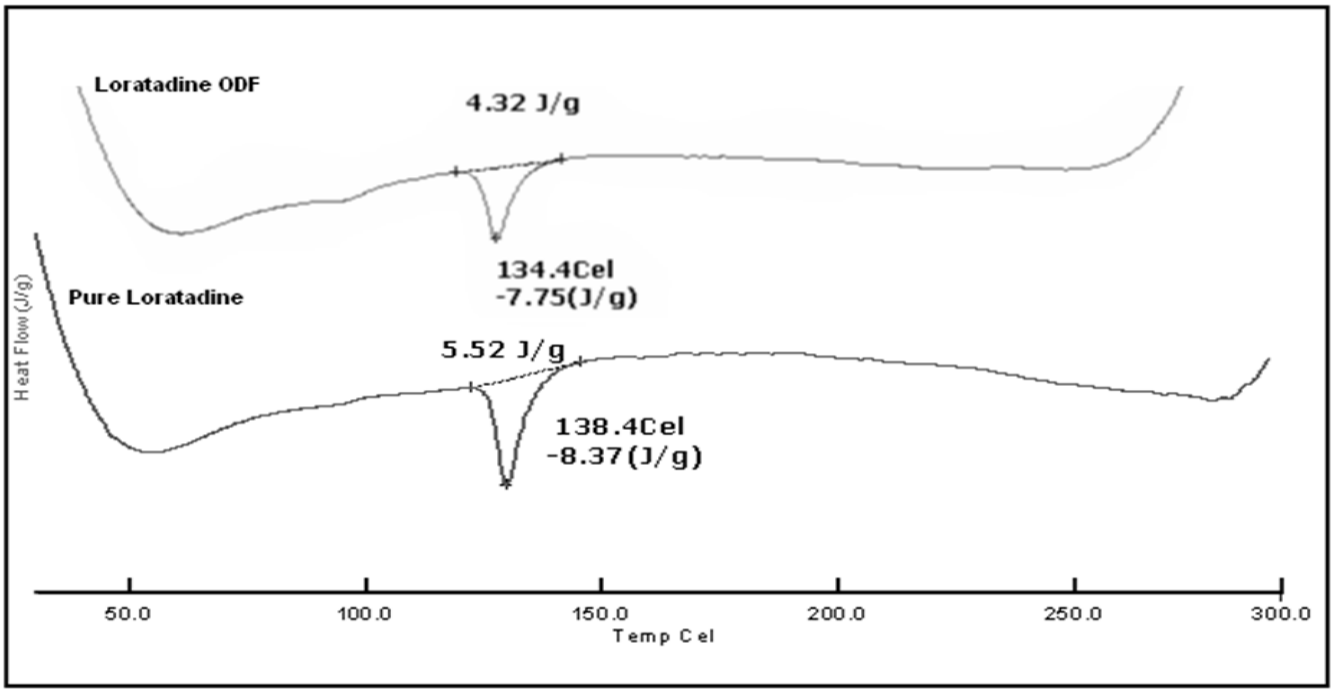

Figure 3. DSC thermograms of 1) LTD 2) F3 solid dispersion.

The thermograms of the LTD, solid dispersion of LTD with gelucire 44/14 were shown in Figure 4. The DSC thermograms of LTD exhibited a sharp endothermal peak around 134.4 o C corresponding to melting point. The thermogram of solid dispersions with gelucire 44/14 showed a short endothermal peak of drug at 138.4 o C indicating that slight shift in peak i.e., change in drug crystallinity due to solid dispersions.

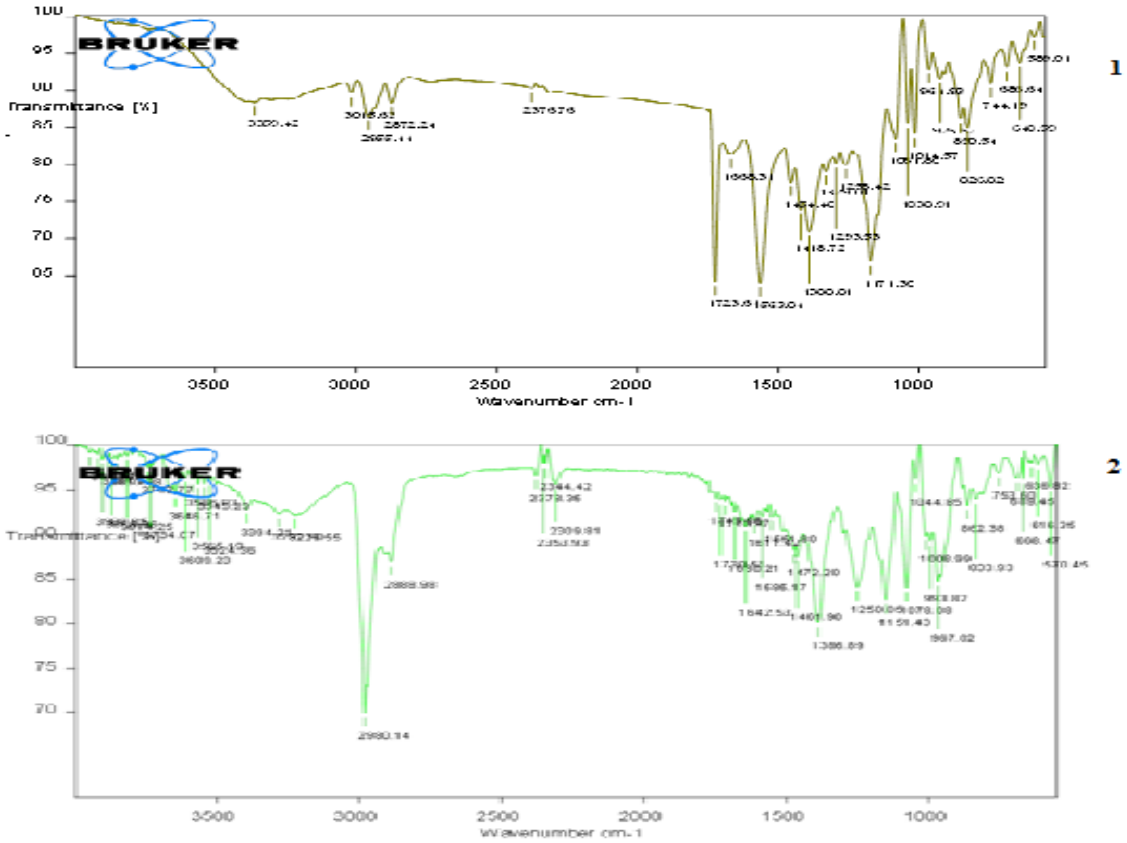

Figure 4. FTIR spectra of 1) LTD 2) F3 solid dispersion.

DISCUSSION

The design of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the proper time at the desired concentration level. For poorly water-soluble drugs dissolution rate is the rate-limiting step (Goldberg et al., 1965). The solid dispersion method is one of the widely used methods to increase the dissolution rate and is confirmed by the experiment results using Loratidine as a model drug. In the present investigation, an attempt was made to formulate fast dissolving tablets of loratadine by solid dispersion method using Gelucire 44/14 and 50/13 as hydrophilic carriers. All the formulations were subjected to solubility studies, powder analysis for drug-excipient interactions and for flow properties and also for drug release studies (Highuchi and Connors, 1965). All the prepared tablets were evaluated for different physical parameters of tablets and they were compared with Indian pharmacopoeial limits. From the in vitro drug release studies the optimized formulation F3 containing gelucire 44/14 showed almost complete drug release within the 15 minutes (Sekiguchi and Obi, 1961). The percent drug release in 15 min (Q 15) and initial dissolution rate (IDR) for optimized formulation (F3) was 94.22±1.08%, 9.26%/min. These were very much higher compared to the pure drug (23.87±1.13%, 2.38%/min). The improvement in the dissolution characteristics of a drug described in terms of dissolution efficiency (DE) and relative dissolution rate (RDR). The RDR was found to be 2.14. The DE was found to be 67.52 and it is increased by 4.0 fold with optimized FDT formulation compared to conventional tablets.

In the present study, various weight ratios of Loratidine and carriers were prepared and evaluated for Physiochemical properties. The dissolution rate of all formulations was shown greater than the conventional tablets due to intermolecular interactions between the polymer and drug. The percent drug release in 15 min (Q15) and initial dissolution rate (IDR) for optimized formulation (F3) was 94.22±1.08%, 9.26%/min. These were very much higher compared to the pure drug (23.87±1.13%, 2.38%/min). The improvement in the dissolution characteristics of a drug described in terms

of dissolution efficiency (DE) and relative dissolution rate (RDR). The RDR was found to be 2.14. The DE was found to be 67.52 and it is increased by 4.0 fold with optimized FDT formulation compared to conventional tablets.

CONCLUSION

In conclusion, development of the solid dispersions can be a promising alternative method to attain the fast dissolution rate and absorption for water-insoluble drugs like loratadine and it was achieved with Gelucire 44/14 as the carrier. Further, the pharmacokinetic evaluation is needed to prove the capability of Gelucire 44/14 solid dispersions to improve the bioavailability of loratadine.

CONFLICT OF INTEREST

None declared.

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