International Journal of Pharmacy and Pharmaceutical Sciences

Print ISSN: 2656-0097 | Online ISSN: 0975-1491 Vol 11, Issue 6, 2019

Original Article

FORMULATION AND EVALUATION OF LIQUISOLID COMPACTS OF LORNOXICAM

ASMA A. MOKASHI[a*], SNEHALATA L. GAIKWAD[b]

[a]M. C. E Society's Allana College of Pharmacy, Azam Campus, Camp, Pune (MS) India, [b]Quality Assurance Executive, Encube Ethicals Pvt. Ltd., Mumbai (MS) India
Email asmapathan9@gmail.com

Received: 06 Jul 2018 Revised and Accepted: 16 Apr 2019

ABSTRACT

Objective: Objective of the present investigation was to enhance the solubility and dissolution rate of poorly water-soluble drug lornoxicam using liquisolid technique with comparative determination of *in vitro* release profile of liquisolid compacts and conventional formulation of lornoxicam.

Methods: Formulation was prepared by a liquisolid technique using different drug concentration in a liquid vehicle and different carrier/coating ratio. Prepared liquisolid compact was evaluated for Fourier transform infrared (FTIR) spectra analysis, differential scanning calorimetry (DSC), X-ray diffraction (P-XRD), scanning electron microscopy (SEM) and *in vitro* dissolution study.

Results: The result showed that liquisolid compacts of lornoxicam displayed significantly higher drug release rate as compared to pure drug and conventional tablet prepared. The results of both DSC and X-ray crystallography indicated loss of crystallinity of the drug upon formulated into the liquisolid compact.

Conclusion: Dissolution rate of the drug from liquisolid compacts was affected by changing the drug concentration and excipient ratio. The liquisolid technique appeared to be a promising approach for improving the dissolution of poorly soluble drug lornoxicam.

Keywords: Lornoxicam, Liquisolid compact, *In vitro* dissolution study, Solubility

DOI: http://dx.doi.org/10.22159/ijpps.2019v11i6.28328

INTRODUCTION

The increased emergence of poorly water-soluble active compounds presents specific obstacles for the development of both immediate release and modified release dosage forms. The challenge for poorly water-soluble drugs is to enhance the rate of dissolution [1]. Various techniques have been used to formulate the oral drug delivery system that would enhance the dissolution profile and in turn, the absorption efficiency of the water-insoluble drug. Among them, the liquisolid compacts technique is one of the most promising and a new technique which promotes dissolution rate of water-insoluble drugs [2]. The term "Liquisolid systems" refers to immediate or sustained-release tablets or capsules that are prepared using the technique described under liquisolid systems, combined with the inclusion of appropriate adjuvants required for tableting or encapsulation, such as disintegrant for immediate release and binders for sustained release action [3]. In the liquisolid system, the liquid portion is a drug suspension, liquid drug, or drug solution made in suitable non-volatile liquid vehicles [4]. The present research involves enhancement of the solubility and dissolution rate of poorly water-soluble drug lornoxicam using the liquisolid technique with comparative determination of *in vitro* release profile of liquisolid compacts and conventional formulation of lornoxicam.

MATERIALS AND METHODS

Materials

Lornoxicam (Cirex Pharmaceuticals Ltd. Andhra Pradesh, India), PEG 400 (Research Lab, Mumbai, India), Polysorbate 80 (Research Lab, Mumbai, India), Propylene glycol (Finer chem. Ltd. Ahmedabad, India), Avicel PH200 and 102 (Microcrystalline cellulose) (Maple Biotech Pvt. Ltd Pune, India), Florite® R (Calcium Silicate) (Tomita Pharmaceutical Tokushima, Japan), Neusilin US2, (Fuji Chemical Industry Co., Ltd), Lactose (Research Lab, Mumbai, India), Crospovidone, PVPK-30 (BASF, Germany).

Solubility studies

The drug content was determined using double beam UV-spectrophotometer (UV 1800 Shimadzu) at 375 nm. The results were extrapolated to determine the solubility (mg/ml) of lornoxicam in its saturated solution with the solvent under investigation [3].

Determination of optimal flowable liquid retention potential (Φ value) for carrier and coating material

The optimal flowable liquid retention potential of the carrier (AvicelΦ) and coating (Florite R) material in a liquid vehicle was calculated based on the angle of slide measurement θ [5, 6]. The calculated Φ value was plotted against the corresponding angle of slide θ. The Φ value corresponding to an angle of slide 33° represented the flowable liquid retention potential **(**Φ value) of powder excipients [7].

Preparation of liquisolid compact

Lornoxicam was dispersed in Polyethylene glycol 400 to make 10–50% w/w solutions (denoted as LS-1 to LS-6). A carrier material containing Avicel PH 200 was added to the liquid medication containing the drug and PEG 400 under continuous mixing in a mortar. Further addition of coating material containing Florite R converted the damp mass into a free-flowing powder at a fixed carrier: coating ratio 20:1. Depending upon the type of vehicle in the formulation, different liquid load factors were employed in liquisolid preparations. Different carrier: coating ratio of Avicel PH 200 and Florite R were also used to prepare different liquisolid formulation. liquisolid formulation LS-N is prepared using Neusilin US2 as a carrier and Florite R as a coating material. The high liquid loading capacity of this Neusilin US2 may be explained by its extremely high specific surface area of 339±1 m^2/g as well as its good flow and tableting properties. Finally, 5% w/w of crospovidone as a super disintegrant and 3% w/w PVP K-30 as a binder were added in the above powder blend. Table 1 denotes the key formulation characteristics of lornoxicam liquisolid compacts with different drug concentration and different excipient ratio respectively [8].

Precompression studies of the prepared liquisolid powder system

Determination of flow properties

The flowability of the liquisolid formulation can be evaluated by using parameters such as the angle of repose, carr's index and hausner's ratio.

Table 1: Key formulation characteristics of lornoxicam liquisolid compacts

Liquisolid formulation	Drug conc. in liquid vehicle	R	L_f	Carrier (mg)	Coat (mg)	Unit dose weight (mg)
LS-1	10	20	0.139	576	28	755
LS-2	15	20	0.139	381.3	19	500.6
LS-3	20	20	0.139	288	14	377
LS-4	30	20	0.139	187	9	244.8
LS-5	40	20	0.139	144	7	188.6
LS-6	50	20	0.139	115.3	5.7	151
LS-N	30	20	0.869	65	3.3	103

FTIR spectra analysis

FTIR study was conducted to check compatibility between drug and excipients. Infrared spectrum of lornxicam, excipients, a drug with different excipients, physical mixture and the final liquisolid formulation was determined on FTIR Spectrophotometer (I. R Prestige-21 Shimadzu) using KBr dispersion method.

DSC analysis

Thermograms of the sample (lornoxicam and liquisolid system) were recorded on a DSC (SDT Q600 V20.9 Build 20). Thermal behavior of the samples was investigated under a scanning rate of 10 °C/min, covering a temperature range of 30-300 °C.

P-XRD analysis

X-ray diffractograms of lornoxicam, excipients, physical mixture and liquisolid formulation were performed by using Philips Analytical XRD (PW 3710) with a wavelength of 2.28970 °A. The scanning range was from 10-100 02θ.

SEM studies

The samples were fixed on aluminum stubs with double-sided tape, gold-coated sputter and examined in the scanning microscope (JSM 5600 LV Joel Japan) using an accelerating voltage of 15 kV, at a working distance of 8 mm.

Evaluation of liquisolid tablets

Prepared liquisolid tablets were evaluated for weight variation, hardness, friability, disintegration time and content uniformity [9].

***In vitro* dissolution studies**

In vitro dissolution studies were performed for LS-1 to LS–6, pure lornoxicam drug and conventional tablet, using USP dissolution apparatus II and specification in the BP. 5 ml sample was withdrawn at time intervals of 5, 10, 15, 20, 30, 45 and 60 min. Drug content in each withdrawn sample was determined using double beam UV spectrophotometer at 375 nm. Mean values of triplicate measurement were plotted versus time. Similar procedure was performed using 0.1N HCl and phosphate buffer pH 7.4 as a dissolution medium [10].

Stability study

Stability testing was performed as per FDA and ICH Guidelines of new drug products. The tablets were packed in the blister pack and were stored at 38.6 °C/75% relative humidity for 3 mo. After this period, stored tablets were evaluated (to study the effect of ageing on lornoxicamliquisolid tablets) via a dissolution test.

RESULT AND DISCUSSION

Solubility studies

Saturation solubility data for the lornoxicam is given in table 2.

Table 2: Saturation solubility data for the lornoxicam

Solvent	Solubility (mg/ml)
Propylene glycol	1.115
Tween 80	4.77
Glycerin	1.0385
Polyethylene glycol 400	8.954
Water	0.00728
phosphate buffer pH 6.8	0.0189
phosphate buffer pH 7.4	0.0137
0.1N HCl	0.0079

All readings are average±SD (n=3)

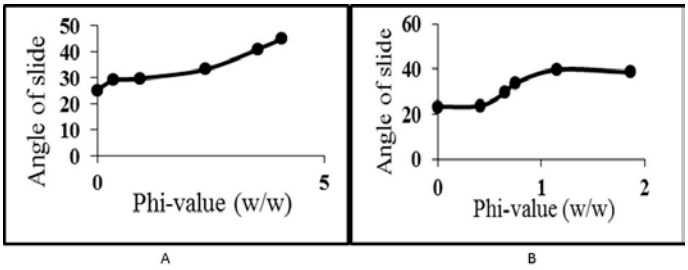

Fig. 1: Relationship between the angle of slide θ and Φ-value for (A) Florite R and (B) Neusilin US2

Determination of flowable liquid retention potential (Φ-value) for excipients

Fig. 1 shows the relationship between the angle of the slide and the corresponding Φ-value of Florite® R and Neusilin US2 determined in PEG 400 [3, 4].

Precompression studies of the prepared liquisolid powder system:

Determination of flow properties

LS-4showed good flow properties therefore considered as a liquisolid system with acceptable flowability [11]. Result of the flow properties of lornoxicam liquisolid systems is given in table 3.

FTIR spectra analysis

The spectrum of pure lornoxicam shows a characteristic peak at 1733.2 due to C=O stretch, 3067.91 due to N-H stretch, 738.77 due to C-Cl stretch. Appearance of these peaks in the physical mixture and liquisolid formulation indicate the absence of chemical interaction between the drug and excipients [11]. FTIR spectral data is shown in fig. 2.

Table 3: Flow properties of lornoxicam liquisolid system

Liquisolid system	Angle of repose (θ)	Carr's compressibility index (%)	Hausner's ratio
LS-1	33.46±0.95	14.72±0.50	1.23±0.07
LS-2	32.42±0.71	16.73±0.21	1.19±0.01
LS-3	36.43±0.70	17.59±0.60	1.17±0.03
LS-4	21.69±0.56	11.43±0.39	1.12±0.02
LS-5	35.20±0.77	15.54±0.30	1.18±0.02
LS-6	37.37±0.28	18.19±0.17	1.17±0.05
LS-N	21.69±0.56	16.73±0.21	1.18±0.17

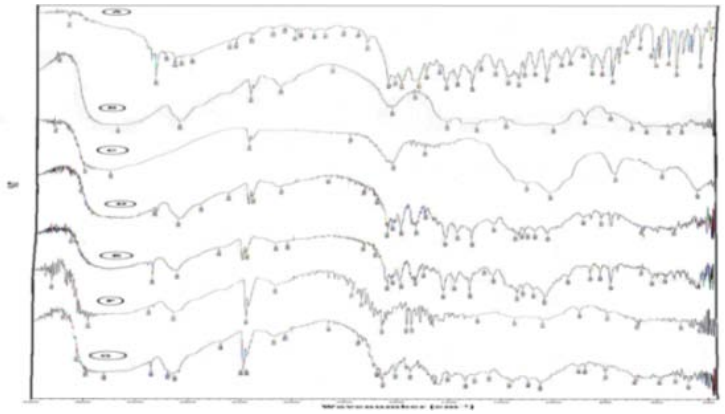

Fig. 2: Overlain FTIR spectrum of (A) lornoxicam (B) Avicel PH 200 (C) Florite R (D) lornoxicam: PEG400: Avicel PH 200 (E) lornoxicam: PEG400: Avicel PH 200: Florite R (F) physical mixture (G) liquisolid powder system

DSC analysis

DSC thermograms as shown in fig. 3 for pure lornoxicam show a sharp exothermic peak at 218.5 °C corresponding to its melting temperature (Tm); such sharp exothermic peak signifies that lornoxicam was in the pure crystalline state. This characteristic sharp melting peak of lornoxicam completely disappeared in DSC thermograms of LS-4 liquisolid formulation and a broadened peak with markedly reduced intensity was observed at approximately 115.5 °C [11].

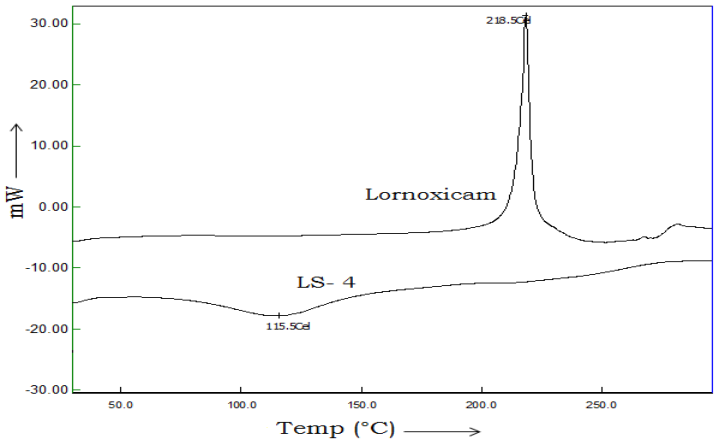

Fig. 3: DSC plot of lornoxicam and liquisolid formulation (LS-4)

P-XRD analysis

The P-XRD result as shown in fig. 4 is agreed well with the thermal analysis data. Pure lornoxicam was clearly in the crystalline state as it showed sharp distinct peaks notably at 2θ diffraction angles of 13.5 °, 24.3 °, 21.04 °, and 27.4 °. X-ray data supported the conclusion that the lornoxicam formed a solid solution within the carrier matrix [11].

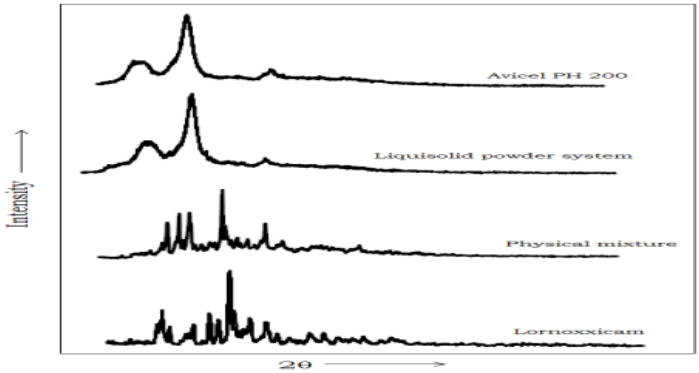

Fig. 4: Powder X-ray diffractograms of lornoxicam, physical mixture, liquisolid powder system, and Avicel PH 200

SEM studies

Fig. 5 displays SEM microphotographs of pure lornoxicam and liquisolid powder system. Pure lornoxicam appears to be crystals in nature as previously proven by DSC and XRD the particles consist of flat faces with sharp and well-defined edges. Further, the photomicrographs of the liquisolid powder system signify the complete disappearance of lornoxicam crystals, a fact that indicates that the drug was totally solubilized in the liquisolid system [11].

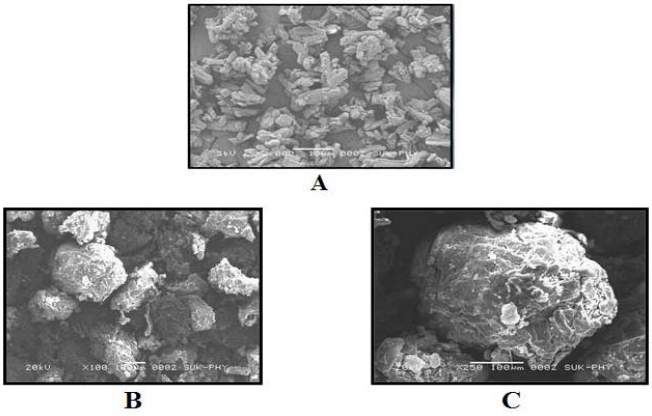

Fig. 5: SEM of (A) lornoxicam (2,000X), (B) liquisolid powder system (100X) and liquisolid powder system (250X)

Evaluation of lornoxicam liquisolid tablets

All prepared tablets complied with the pharmacopeial required specifications for the weight variation and friability. Results for hardness and weight variation, friability and disintegration time are represented in table 4. As the amount of Avicel goes on increasing, hardness also increases. With a decrease in R values, hardness was decreased [11]. This low hardness could be attributed to the less amount of added Avicel and poor compressibility of Florite R [7]. Microcrystalline cellulose has disintegration property, which could facilitate the disintegration of tablets and dissolution of drug [12]. The higher R values represent lead to a more uniform distribution of drug the drug by either adsorption onto or absorption into the carrier [7].

Table 4: Data for lornoxicam liquisolid tablets

Liquisolid system	Hardness (kg/cm²)	Wt. Variation (%)	Friability (%)	Disintegration time (sec)	% Drug content
LS-1	3.1±0.28	0.52±0.76	0.15±0.05	66.95±1.34	96.46±0.32
LS-2	3.3±0.24	0.57±0.32	0.19±0.05	75.12±0.55	96.07±0.33
LS-3	3.5±0.41	1.32±1.16	0.13±0.10	75.12±0.55	97.38±1.57
LS-4	4.3±0.52	0.41±0.70	0.15±0.05	29.30±0.43	99.03±0.27
LS-5	4.8±0.32	0.26±0.32	0.16±0.11	28.84±1.34	99.03±0.27
LS-6	4.6±0.28	1.84±0.41	0.15±0.05	66.95±0.97	98.05±1.39
LS-N	4.27±0.86	3.96±1.52	0.10±0.04	28.4±0.80	98.36±0.39

All readings are average±SD (n=3)

***In vitro* dissolution studies**

All the liqusiolid compacts showed higher drug release than the conventional tablet and the pure drug. It was observed from the Fig.6 that LS-4 shows the highest drug release 100±0.57% release at 60 min. Result is shown in fig. 6. Liquisolid compact LS–N shows higher drug release than a conventional tablet and pure drug but slower drug release as compared to LS–4 formulation this may be due to slower disintegration of LS–N as compared to LS-4.

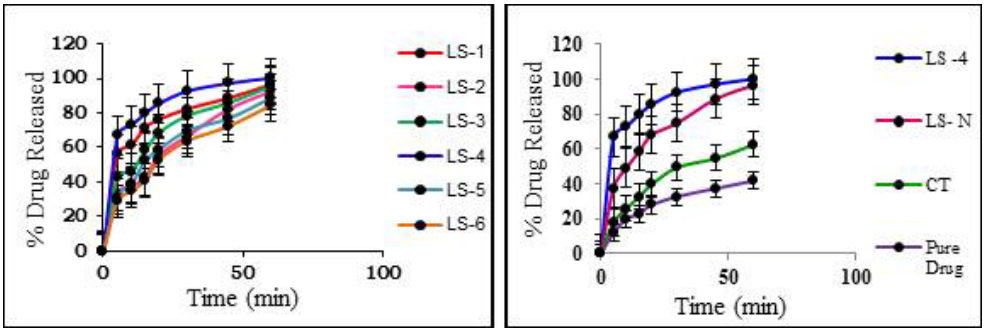

Fig. 6: Percentage drug released from liquisolid compacts

Stability study

3 tablets from LS-4 series were kept at 38.6 °C/75% relative humidity for 3 mo. Dissolution rate was measured for the aged tablets. Result is shown in fig. 7, with a calculated similarity factor (f2 value) of 67.18 and dissimilarity factor (f1 value) of 5.7.

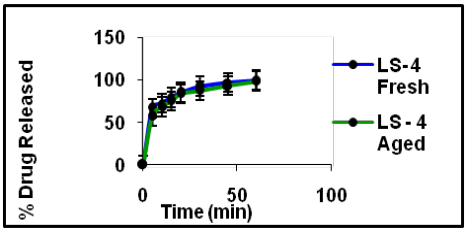

Fig. 7: Dissolution profile of fresh v/s aged LS-4 tablets

CONCLUSION

It can be concluded from the observations that formulation LS–4 optimally achieved the objectives of preparation of liquisolid compact of lornoxicam i.e. enhanced drug dissolution and solubility. The enhanced dissolution rate of lornoxicam from liquisolid tablets was due to an increase in wetting properties and surface area of drug particles available for dissolution. In this case, even though the drug is in a solid dosage form, it is held within the powder substrate in solution or in a solubilized, almost molecularly dispersed state, which contributes to the enhanced drug dissolution properties and the tablet properties were all within acceptable ranges. The results of both DSC and XRD suggested the loss of crystallinity of the drug upon liquisolid formulation indicating that the drug is held within the powder substrate in a solubilized state which contributed to the improvement in the dissolution rate and these results are supported by data from FTIR and SEM. Stability studies by means of dissolution testing showed that the liquisolid preparation produced were stable and not significantly affected by ageing.

ACKNOWLEDGMENT

The authors of the manuscript would like to acknowledge Meyer Organics Pvt. Ltd., for providing excipients and laboratory facilities to carry out this research work.

AUTHORS CONTRIBUTIONS

Experimental design, guidance, supervision, review work and writing of this manuscript for the research was done by Mrs. Asma Mokashi, Assistant Professor MCE Society's Allana College of Pharmacy, Azam Campus, Camp, Pune.

Experimental work and interpretation of result were done by Ms. Snehalata Gaikwad, Quality Assurance Executive, Encube Ethicals Pvt. Ltd., Mumbai. Both authors read and approve the final manuscript.

CONFLICTS OF INTERESTS

Authors have none to declare

REFERENCES

1. Charman SA, Charman WN. Oral modified release delivery systems. In: Rathbone MJ, Hadgraftb J, Roberts MS. Editors. Modified release drug delivery technology. New York: Marcel Dekker Inc; 2003.
2. Fahmy RH, Kassem MA. Enhancement of famotidine dissolution rate through liquisolid tablets formulation: *in vitro* and *in vivo* evaluation. Eur J Pharm Biopharm 2008;69:993-1003.
3. Spireas SS. Liquisolid systems and methods of preparing same. United State Patent no 5800834; 1998.
4. Panda S, Varaprasad R, Priyanka K, Swain R. Liquisolid technique: a novel approach for dosage form design. Int J Appl Pharm 2017;9:8-14.
5. Elkordy AA, Tan XN, Ebtessam EA. Spironolactone release from liquisolid formulation prepared with Capryol™ 90, Solutol® HS-15, Kollicoat® SR 30 D as non-volatile liquid vehicles. Eur J Pharm Biopharm 2013;83:203-23.
6. Spireas S, Sadu S. Enhancement of prednisolone dissolution properties using liquisolid compacts. Int J Pharm 1998;166:177-88.
7. Louis D, Soliman II, Tayel SA. Improvement of dissolution properties of carbamazepine through application of the liquisolid tablet technique. Eur J Pharm Biopharm 2008; 69:342-7.
8. Sanjaymitra PV, Ganesh GN. Dissolution and solubility enhancement strategies: current and novel prospectives. J Crit Rev 2018;5:1-10.
9. Banker GS, Anderson NR. Tablets. In: Lachman L, Lieberman HA. editors. The theory and practice of industrial pharmacy. 2nd ed. Noida: India Binding House; 2009. p. 293-45.
10. Noyes AA, Whitney WR. The rate of dissolution of solid substances in their own solutions. J Am Chem Soc 1897;19:930–4.
11. Khan A, Agrawal S. Formulation and evaluation of lumefantrine capsule prepared by using the liquisolid technique. Int J Curr Pharm Res 2018;10:43-50.
12. Hentzschel CM, Alnaief M, Smirnova I, Sakmann A. Enhancement of griseofulvin release from liquisolid compacts. Eur J Pharm Biopharm 2012;80:130-5.