Int J Pharm Bio Sci 2012 Oct; 3(4): (P) 591 - 603

Research Article **Pharmaceutics**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

FORMULATION DEVELOPMENT AND EVALUATION OF TAMOXIFEN CITRATE LIQUISOLID SYSTEM

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ABSTRACT

The *in vitro* dissolution property of poorly water soluble Tamoxifen citrate was improved by exploring the potential of Liquisolid system (LS). Different LS compacts were prepared using a mathematical model to calculate the required quantities of powder and liquid ingredients to produce acceptably flowable and compressible admixture. Avicel PH 102, Aerosil 200, Cross Carmellose Sodium and Propylene glycol were employed as carrier, coating material disintegrant and non volatile solvent respectively for preparing liquisolid compacts. The IR, DSC and XRD studies confirmed that there was no significant interaction between the drug and excipients used in LS compacts. The drug release rates of LS compacts were distinctly higher as compared to directly compressed tablets, which show significant benefit of LS in increasing wetting properties and surface area of drug available for dissolution. From this study it was concluded that the liquisolid technique is a promising alternative for improvement of dissolution property of water-insoluble drugs.

Keywords: Tamoxifen citrate, liquisolid tablets, dissolution rate, solubility.

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INTRODUCTION

Poorly water soluble drugs involve many difficulties in the development of pharmaceutical dosage forms for oral delivery systems due to their low bioavailability[1]. Bioavailability of poorly water-soluble hydrophobic drugs is limited by their solubility and dissolution rate. As a drug to be absorbed into the systemic circulation following oral administration, the drug must be dissolved in the gastric fluids. Development of solid dosage forms for water insoluble drugs has been a major challenge for pharmaceutical scientists for decades[2]. The active pharmaceutical ingredient in a solid dosage form must undergo dissolution before it is available for absorption from the gastrointestinal tract. For hydrophobic drugs, the dissolution process acts as the rate-controlling step and, which determines the rate and degree of absorption. Consequently, many hydrophobic drugs show erratic and incomplete absorption from the gastrointestinal tract of animals and humans. Thus, one of the major challenges to drug development today is poor solubility, nearly one-third of drugs in development are water insoluble and one-half fail in trials because of underprivileged pharmacokinetics [2, 3]. The use of water-soluble salts and polymorphic forms[4], solid dispersion[5], lyophilization[6], the formation of water-soluble molecular complexes[7], drug micronization, microencapsulation, co-precipitation, and the inclusion of drug solutions or liquid drugs into soft gelatin capsules are some of the major formulation tools which have been shown to enhance the dissolution characteristics of water-insoluble drugs, however, among them, the technique of ‘‘liquisolid compacts” is one of the most promising technique [8–9].

The technique of ‘liquisolid compacts’ is a new and promising recently developed additional technique towards the new approach of dissolution enhancement. The liquisolid systems are generally considered as acceptably flowing and compressible powdered forms of liquid medications (that implies liquid lipophilic (oily) drugs, or water-insoluble solid drugs dissolved in suitable water-miscible nonvolatile solvent systems). Such liquid medication may be converted into a dry-looking, nonadherent, free-flowing, and readily compressible powders by a simple admixture with selected powder excipients referred to as the carrier and coating materials[4]. However, even though in the liquisolid and powdered solution systems the drug might be in a solid dosage form, it is held within the powder substrate in solution, or in a solubilized, almost molecularly dispersed state. In such systems, the drug existed in a molecular state of subdivision and systems were free flowing, on-adherent, dry looking powders[10]. Therefore, due to their significantly increased wetting properties and surface of drug available for dissolution, liquisolid compacts of water-insoluble substances may be expected to display enhanced drug release properties, and consequently, improved bioavailability[11].

Tamoxifen citrate, (2-{4-[(1Z)-1,2-diphenylbut-1-en-1-yl]phenoxy}ethyl) dimethylamine, with potent antiestrogenic properties and estrogen receptor modulators that has been in routine use in the treatment of breast cancer and infertility in women’s for over 40 years. This agent belongs to class II drugs that its bioavailability is limited by its poor dissolution rate in GI. In fact, its solubility and dissolution rate are key factors in its bioavailability. The aim of present work is to increase the solubility and *in vitro* dissolution of practically insoluble drug Tamoxifen citrate, by formulating in to liquisolid tablet[12, 13]. In this study, Tamoxifen citrate a practically insoluble nonsteroidal anti-cancer drug was formulated into 10 mg liquisolid tablets consisting of Avicel PH 102, Aerosil PH 200, and PG as the liquid vehicle. The in-vitro release of such preparations were assessed and compared to this of commercial counterpart using a USP dissolution apparatus I (basket) in 900 ml 0.02N HCl for 60 minutes[11].

MATERIALS AND METHODS

Materials

The gift sample of Tamoxifen citrate was obtained from Apurva Biopharm, Mumbai. The following samples were purchased Avicel PH 102, Aerosil 200, propylene glycol (PG), Cross carmellose sodium (CCS) and methanol. All reagents used were of analytical grade (SD Fine chemicals, Mumbai).

Methods

Saturation solubility studies

To select the best nonvolatile solvent for preparation of liquid medication, saturated solubility studies were carried out in five different non volatile solvents, i.e. PEG 200, PEG 400, Glycerin, Polysorbate 80 and PG by preparing saturated solutions of the drug in these solvents and analyzing their drug content spectrophotometrically. The saturated solution of Tamoxifen citrate was prepared by adding drug in 5 ml of PEG 200, PEG 400, Glycerin, Polysorbate 80 and PG. These mixtures were sonicated for 24 hrs, after which the solutions were centrifugated, to get clear supernatant. The layers that were further diluted with methanol and analyzed spectrophotometrically at 275.6 nm for their drug content. Three determinations were carried out for each sample to calculate the solubility of Tamoxifen citrate.

PRECOMPRESSION STUDIES OF THE PREPARED LIQUISOLID POWDER SYSTEMS

Drug-Excipient compatibility study

Fourier Transform Infra Red (FTIR) spectroscopy

The IR spectra of powder mass of liquisolid tablets were recorded using Fourier Transform Infra-Red spectrophotometer (Shimadzu 84005, Japan) with diffuse reflectance principle. Sample preparation involved mixing the sample (2 mg) with Potassium bromide (KBr), triturating in glass mortar and finally placing in the sample holder. The spectrum was scanned over a frequency range 4000– 400 cm-1.

Differential Scanning Calorimetry (DSC)

DSC was performed using Differential Scanning Calorimeter, DSC-60 (Shimadzu, Japan), in order to assess the thermotropic properties and the thermal behaviors of the drug (Tamoxifen citrate) and liquisolid system prepared. Samples of 3–5 mg of the pure Tamoxifen citrate or the above-mentioned samples were sealed in aluminum pans at a constant heating rate of 10°C/min. in the scanning temperature range of 30 to 300°C. Empty aluminum pans were used as references and the whole thermal behaviors were studied under a nitrogen purge.

8.2.3. X-ray powder diffraction (XRD)

For characterization of crystalline state, the X-ray Diffraction (XRD) patterns for Tamoxifen citrate, physical mixture of Tamoxifen citrate: Avicel 102: Aerosil 200(1:1:1) and the liquisolid system prepared were determined using BRUKERs diffractometer (D8-Advanced). With a copper target, at a voltage of 40 kV and current of 20MA. The rate of the scanning was 0.30°C /min.

Mathematical model for formulation of liquisolid system

A powder can retain only limited amounts of liquid while maintaining acceptable flow and compression properties. To calculate the required amounts of powder excipients (carrier and coating materials) a mathematical approach for the formulation of liquisolid systems has been developed by Spireas.[5] This approach is based on the flowable **(Φ-value)** and compressible **(Ψ-number)** liquid retention potential introducing constants for each powder/liquid combination.

The **Φ-value** of a powder represents the maximum amount of a given non-volatile liquid that can be retained inside its bulk [w/w] while maintaining an acceptable flowability. The flowability may be determined from the powder flow or by measurement of the angle of repose. The **Ψ-number** of a powder is defined as the maximum amount of liquid the powder can retain inside its bulk [w/w] while maintaining

acceptable compactability resulting in compacts of sufficient hardness with no liquid leaking out during compression [5].

The compactability may be determined by the so-called **"pactisity"** which describes the maximum (plateau) crushing strength of a one-gram tablet compacted at sufficiently high compression forces. The terms "acceptable flow and compression properties" imply the desired and thus preselected flow and compaction properties which must be met by the final liquisolid formulation. Depending on the excipient ratio **(R)** of the powder substrate an acceptably flowing and compressible liquisolid system can be obtained only if a maximum liquid load on the carrier material is not exceeded. This liquid/carrier ratio is termed "liquid load factor L_f [w/w] and is defined as the weight ratio of the liquid formulation **(W)** and the carrier material **(Q)** in the system:

$$L_f = W/Q \quad \text{.....Eq. (1)}$$

R represents the ratio between the weights of the carrier (Q) and the coating (q) material present in the formulation:

$$R = Q/q \quad \text{.....Eq. (2)}$$

The liquid load factor that ensures acceptable flowability **(ΦL_f)** can be determined by:

$$\Phi L_f = \Phi + \varphi \cdot (1/R) \quad \text{..... Eq. (3)}$$

where Φ and φ are the Φ-values of the carrier and coating material, respectively. Similarly, the liquid load factor for production of liquisolid systems with acceptable compactability **(ΨLf)** can be determined by:

$$^{\Psi}L_f = \Psi + \psi \cdot (1/R) \quad \text{.....Eq. (4)}$$

Where Ψ and ψ are the Ψ-numbers of the carrier and coating material, respectively.

Therefore, the optimum liquid load factor (L o) required to obtain acceptably flowing and compressible liquisolid systems are equal to either ΦL_f or ΨL_f, whichever represents the lower value [5]. As soon as the optimum liquid load factor is determined, the appropriate quantities of carrier (Qo) and coating (qo) material required to convert a given amount of liquid formulation (W) into an acceptably flowing and compressible liquisolid system may be calculated as follows:

$$Q_o = W/L_o \quad \text{.....Eq. (5)}$$

And

$$q_o = Q_o/R \quad \text{.....Eq. (6)}$$

The validity and applicability of the above mentioned principles have been tested and verified by producing liquisolid compacts possessing acceptable flow and compaction properties [5].

Formulation of liquisolid system

Liquisolid compacts were prepared as follows. The desired quantities of the previously weighed of the solid drug and the liquid vehicle propylene glycol (PG) were mixed. The solution was then sonicated for 15 min until a homogeneous drug solution was obtained. Next, the calculated weight (W) of the resulting liquid medications (equivalent to 10 mg drug) were incorporated into the calculated quantities of the carrier material (Avicel PH102) (Q) and mixed thoroughly. The resulting wet mixture was then blended with the calculated amount of the coating material (Aerosil 200) (q) using a standard mixing process to form simple admixture. Several factors were varied like carrier: coat ratios (different R values) ranging from 8 to 19 was employed. Different liquid load factors (L_f) ranging from 0.345 to 0.518 were employed. Finally 5 % w/w of sodium starch glycolate as the disintegrant and 1% of magnesium stearate were mixed in final powder blend. The important formulation characteristics of liquisolid compacts are shown in Table 1.

Table 1
Composition of different Tamoxifen citrate liquisolid compacts according to mathematical model.

Liquisol system	Liquid load factor (L_f)	Powder Excipient ratio(R) Q:q	Avicel 102 (Q)	Aerosil 200 (q)	Mg. stearate	CCS	Tablet weight
			Quantity in mg				
LS-1	0.518	8	285.12	35.54	4.31	23.45	496.95
LS-2	0.492	9	300.60	33.40	4.52	24.09	510.51
LS-3	0.503	10	294.00	29.40	4.71	24.60	522.43
LS-4	0.472	11	326.00	29.60	4.89	25.17	533.56
LS-5	0.447	12	330.50	27.50	5.03	25.50	536.05
LS-6	0.426	13	347.10	26.70	5.21	26.08	552.99
LS-7	0.406	14	367.28	26.02	5.38	26.91	570.49
LS-8	0.392	15	377.29	25.15	5.50	27.51	583.35
LS-9	0.378	16	391.26	24.45	5.63	28.18	597.42
LS-10	0.365	17	405.20	23.83	5.76	28.84	611.53
LS-11	0.355	18	416.61	24.50	5.89	29.45	624.43
LS-12	0.345	19	428.69	22.50	5.99	29.95	635.03

***Mg. stearate- Magnesium stearate.**
***CSS-Cross Carmellose Sodium.**
***An appropriate amount of liquid medication containing 10 mg Tamoxifen citrate incorporated in Propylene glycol in each formulation.**
***Each compact containing 5% cross carmellose sodium and 1% magnesium stearate.**

Evaluation of precompressible blend flow properties of the liquisolid system

Determination of Angle of repose, Carr's index and Hausner's ratio were used to characterize flow properties of the liquisolid powder systems (Table 3). The Bulk density and Tap densities were determined for the calculation of Hausner's ratio and Carr's Index. The flowability of a powder is of critical importance in the production of pharmaceutical dosage forms in order to get a uniform feed as well as reproducible filling of tablet dies, otherwise, high dose variations will occur.

Evaluation of liquisolid tablet

Weight variation test [11]

The weight variation test was carried out as per USP 30. 20 tablets were weighed accurately and average weight was calculated. Results for all the batches of Tamoxifen citrate liquisolid compacts are shown in Table 4.

Hardness and friability [11]

The hardness of the liquisolid compacts prepared was evaluated using Monsanto hardness tester. It is expressed in kg/cm^2. The mean hardness of each formulation was determined. The friability of the prepared liquisolid tablets were measured in a Roche type apparatus and the percentage loss in weight was calculated and used as a measure of friability and the results for all the batches of Tamoxifen citrate liquisolid compacts are shown in Table 4.

Disintegration test [11]

The disintegration test was carried out using disintegration test apparatus as specified in the USP 30 and the results for all the batches of Tamoxifen citrate liquisolid compacts are shown in Table 4

Drug content uniformity[14]

Weigh and powder 20 tablets. Weigh accurately a quantity of the powder containing about 25 mg of Tamoxifen citrate, shake with 100 ml of Methanol for 15 minutes, add sufficient Methanol to produce 250.0 ml and filter. Dilute 10.0 ml of the filtrate to 100.0 ml with Methanol and measure the absorbance of the resulting solution at the maximum at about 275 nm.

In vitro drug release [11]

The USP basket apparatus I was used for all the *in vitro* dissolution studies. 900 ml 0.02 N Hydrochloric acid was used as dissolution media, at 100 rpm and 37 ± 0.5^{o}C. Appropriate aliquots were withdrawn at suitable time interval (5, 10, 20, 30, 40, 50, 60, min.) Sink conditions were maintained throughout the study. 5 ml of the samples were taken and filtered through a 0.45 mm Millipore filter. The dissolution media was then replaced by 5 ml of fresh dissolution fluid to maintain a constant volume. The samples were then analyzed at λ_{max} of 275.6 nm by UV/visible spectrophotometer.

RESULTS AND DISCUSSION

Saturated Solubility studies

The solubility of Tamoxifen citrate in PG, PEG 400, Tween 80, Tween 20 and Glycerin has been presented in the Table 2. The data reveals, Tamoxifen citrate has lowest solubility in glycerin. Solubility was found to be increased when semi polar solvents such as Polyethylene Glycol 400 were used. Solubility of Tamoxifen citrate was considerably increased in presence of Propylene glycol.

Table 2
Solubility of Tamoxifen citrate in various solvents

Sr. No.	Solvent	Solubility (%)w/v
1	PG	10.4 ±0.72
2	Glycerin	2.38 ±0.23
3	Tween 20	3.36 ±0.56
4	Tween 80	2.8 ±0.87
5	PEG 400	3.68 ±0.43
6	0.02 N HCl	0.23 ±0.56

Application of a mathematical model in designing the Tamoxifen citrate liquisolid system

To calculate the required ingredient quantities, the flowable liquid-retention potentials (Φ-values) and compressible liquid-retention potentials (Ψ-values) of powder excipients were used. From the calculations, in PG, the Φ-value was 0.17 for Avicel PH 102 and 3.33 for Aerosil 200. The Ψ-values was 0.28 for Avicel PH 102 and 1.92 for Aerosil 200. Therefore, the optimum liquid load factor (Lo) required to obtain acceptably flowing and compressible liquisolid systems are equal to either ΦL_f or ΨL_f, whichever represents the

lower value from equation 3 and 4, in accordance with equation 2 using a different R value (excipient ratio). The optimum quantities of carrier (Q_0) and coating material (q_0) were obtained from equations 5 and 6 respectively.

Drug-Excipient compatibility study

Fourier Transform Infra Red (FTIR) spectroscopy

The probable interaction between the drug and excipients was studied by FTIR. The FTIR spectral analysis reveals that there was absence of any characteristics peaks of pure drug Tamoxifen citrate as well as physical mixture of drug to polymer, which confirms the absence of chemical interaction between drug and polymers.

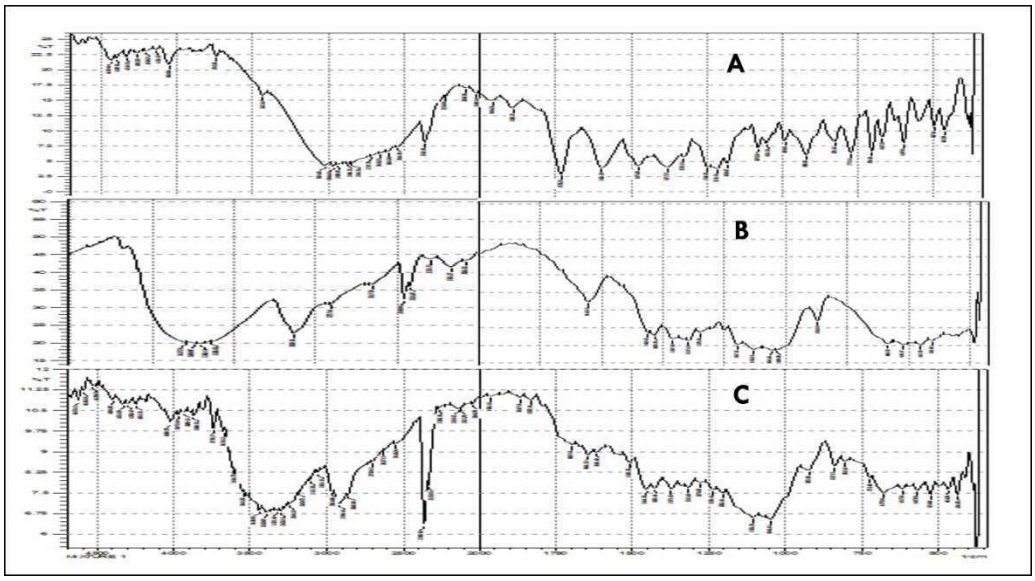

Figure 1

FTIR spectrum of A) Tamoxifen citrate B) Physical mixture C)Precompressible blend

Differential Scanning Calorimetry (DSC):

Tamoxifen citrate gave a sharp peak at 144.56°C corresponding to its melting and indicating its crystalline nature. The thermogram of physical mixture is shown in Figure 2 (B) and it exhibited a sharp exothermic peak corresponding to its melting point at 149.46°C. DSC study reveals that there is no interaction between the drug and excipients as well as any significant shift in the endothermic peak, indicating absence of physical change in drug in the liquisolid compacts. On the other hand, the thermogram of precompressible blend in Figure 2 (C), displayed complete disappearance of both characteristic peaks of Tamoxifen citrate; a fact that agrees with the formation of saturated drug solution in the liquisolid powdered system, i.e., the drug was molecularly dispersed within the liquisolid matrix.

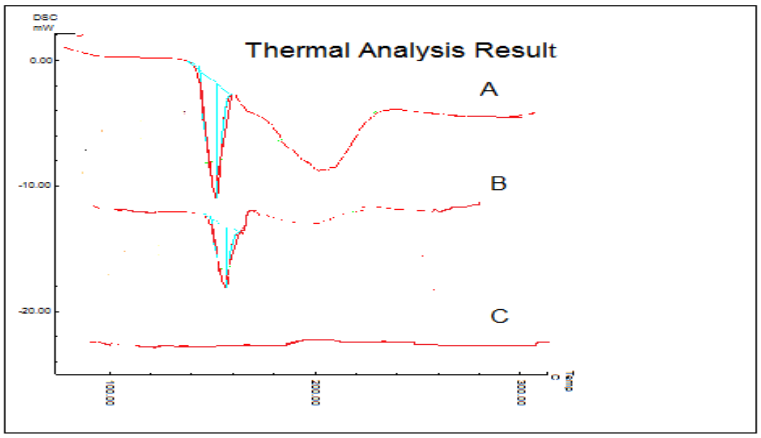

Figure 2
DSC thermograms of A) Tamoxifen citrate B) Physical mixture C) Precompressible blend.

X-ray powder diffraction (XRD)

X-ray diffraction pattern (A) revealed the crystalline state of Tamoxifen citrate. Tamoxifen citrate characteristic peaks were observed in the physical mixture (B), demonstrating that its crystalline structure remained unchanged during the physical mixing, and that the loss of crystallinity was due to liquisolid system formation. On the other hand, the liquisolid powder X-ray diffraction pattern (C) showed absence of Tamoxifen citrate constructive reflections (specific peaks) in the liquisolid X-ray diffractogram indicates that drug has almost entirely converted from crystalline to amorphous or solubilized form.

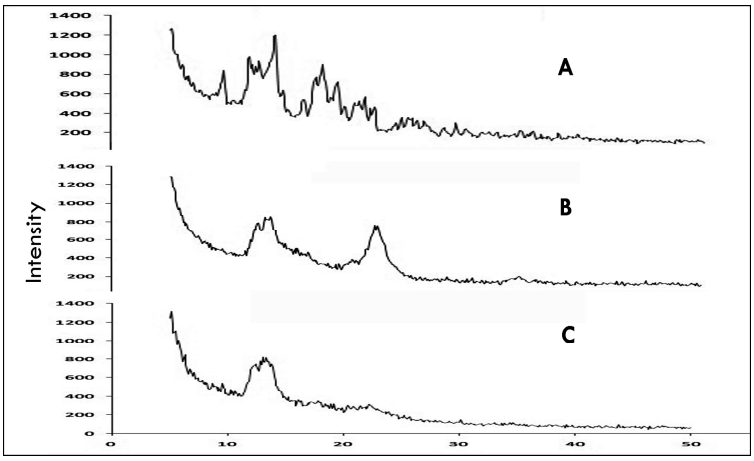

Figure 3
XRD pattern of A) Tamoxifen citrate B) Physical mixture C) Precompressible blend.

Precompression studies for liquisolid systems Flow properties

Flow properties are the important concern in the formulation and industrial production of tablet dosage form. Results of measurements such as Angle of repose, Carr's index and Hausner's ratio are represented in the Table 3. Angle of repose is characteristic to the flow rate of powder. In general, values of angle of repose >30 ° indicate satisfactory flow properties. Also values of Carr's index up to

15% result in good to excellent flow properties and Hausner's ratio values < 1.25 indicate good flow properties.

Table 3
Results of flowability parameters of liquisolid powder systems for different formulation

Liquisolid powder	Angle of repose	Density		Hausener s Ratio	Carr's index
		Bulk density	Tapped density		
LS-1	47.98 ±0.04	0.345±0.004	0.455±0.001	1.32 ±0.01	24.18 ±1.99
LS-2	44.79 ±1.27	0.278±0.002	0.400±0.001	1.44 ±0.02	30.50 ±0.56
LS-3	46.12 ±0.64	0.357±0.001	0.500±0.002	1.40 ±0.02	28.60 ±1.85
LS-4	37.56 ±0.24	0.307±0.004	0.412±0.003	1.02 ±0.01	18.21 ±0.57
LS-5	42.25 ±1.77	0.313±0.004	0.435±0.001	1.39 ±0.03	28.05 ±0.97
LS-6	37.99 ±0.35	0.395±0.002	0.411±0.005	1.28 ±0.01	15.97 ±1.00
LS-7	42.27 ±0.29	0.295±0.003	0.417±0.003	1.41 ±0.03	29.26 ±1.00
LS-8	33.69 ±0.20	0.357±0.001	0.455±0.002	1.27 ±0.02	21.52 ±0.74
LS-9	37.56 ±0.18	0.345±0.001	0.417±0.002	1.21 ±0.02	17.27 ±2.02
LS-10	34.07 ±0.09	0.417±0.003	0.476±0.001	1.14 0.00	12.97 ±0.98
LS-11	38.84 ±0.49	0.385±0.003	0.476±0.004	1.20 ±0.01	19.10 ±2.01
LS-12	34.77 ±0.43	0.313±0.004	0.400±0.004	1.28 ±0.02	21.75 ±0.58

Evaluation of liquisolid tablet

The results of weight, hardness, friability and drug content are represented in Table 4. Average weight of liquisolid tablet ranges from 501.35 ± 0.20 mg to 645.43 ± 0.50 mg. There should be certain amount of strength or hardness and resistance to friability for the tablet, so that tablet should not break during handling. However, it has also effect on tablet disintegration and drug dissolution. Average hardness of liquisolid tablet ranges from 4.6±0.32 to 6.3±0.05 kg/cm^2. Friability studies of liquisolid tablets are in the range of 0.245% to 0.417%. This indicates that acceptable resistance is shown by liquisolid tablets to withstand handling. It was observable that formulae LS-1 to LS-12 complied with the test of Tamoxifen citrate content uniformity according to the United States Pharmacopoeia by having the average Tamoxifen citrate content of 95.87% to 92.08% w/w.

Table 4
Results of weight, hardness, friability and drug content of liquisolid tablet formulation.

Formulation No.	Thickness (mm)	Hardness (kg/cm^2)	Average Weight Variation (mg)	Friability (%)	Drug Content (%)	Disintegration Time (Sec)
LS-1	2.1 ±0.1	4.6 ±0.32	501.35 ±0.20	0.417 ±0.002	92.08 ±0.86	160 ±1
LS-2	2.5 ±0.2	4.4 ±0.20	515.53 ±0.32	0.320 ±0.001	92.50 ±0.65	178 ±3
LS-3	3.3 ±0.23	4.8 ±0.28	525.98 ±0.22	0.324 ±0.003	93.33 ±0.60	165 ±4
LS-4	3.3 ±0.01	5.4 ±0.25	533.67 ±0.48	0.329 ±0.003	93.75 ±0.73	140 ±1
LS-5	3.4 ±0.01	5.3 ±0.05	539.15 ±0.20	0.416 ±0.001	94.16 ±0.65	160 ±3
LS-6	3.5 ±0.01	5.6 ±0.10	555.17 ±0.42	0.425 ±0.002	93.30 ±0.46	130 ±2
LS-7	3.6 ±0.03	5.8 ±0.20	574.89 ±0.20	0.418 ±0.004	94.50 ±0.73	149 ±1
LS-8	3.7±0.05	6.1 ±0.00	588.35 ±0.40	0.233 ±0.001	95.41 ±0.86	155 ±4
LS-9	4.1 ±0.02	6.0 ±0.10	601.12 ±0.20	0.256 ±0.002	95.83 ±0.65	130 ±3
LS-10	4.4 ±0.02	6.2 ±0.25	619.63 ±0.32	0.207±0.003	96.66 ±0.65	155 ±3
LS-11	4.4 ±0.01	6.3 ±0.04	632.13 ±0.42	0.232 ±0.00	94.16 ±0.86	145 ±1
LS-12	4.5 ±0.02	6.3 ±0.05	645.43 ±0.50	0.245 ±0.002	95.87±0.60	150 ±2

***In vitro* drug release**

The results of *in vitro* percentage amount of drug released at different time intervals have been plotted against time to obtain the release profiles. All the liquisolid compacts presented higher drug release than the pure drug. The enhanced dissolution rates of liquisolid compacts compared to pure drug can be attributed to the fact that, the drug is already in solution in PG, while at the same time, it is carried by the powder particles (Microcrystalline cellulose and Silica).Thus, its release is accerlated due to its markedly increased wettability and surface availability to the dissolution medium.From Figure 4, it is apparent that formulations LS 5 and LS 6 presented percent drug release 85.65 % and 87.83 % respectively. Whereas, formulations LS 1 and LS 2 revealed percent drug release 76.59 % and 78.40 % respectively. Lastly formulations LS 3 and LS 4 showed percent drug release 81.30 % and 83.84 % respectively. The powder excipient ratio was directly proportional to the in vitro release i.e., when the powder excipient ratio increased the release will increase.

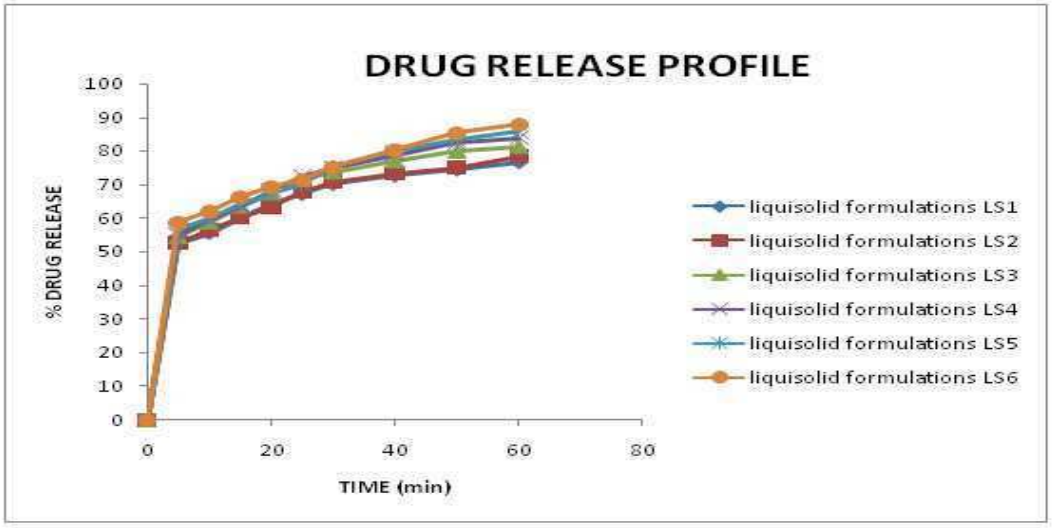

Figure 4
In-vitro drug release profile of tamoxifen citrate in 1 hr from formulations LS 1 to LS 6 in 0.02 N HCl

From figure 5, it was apparent that formula LS 10 and LS 11 presented the highest percent drug release 96.90 % and 95.81 % respectively. Wheres formulations LS 7 and LS 8 showed percent drug release 90.37 % and 92.54 % respectively. Lastly LS 9 and LS 12 showed percent drug release 94.36 % and 93.26 % respectively. As seen from Figure the drug release properties of liquisolid compacts were improved with an increase in powder excipient ratio R.

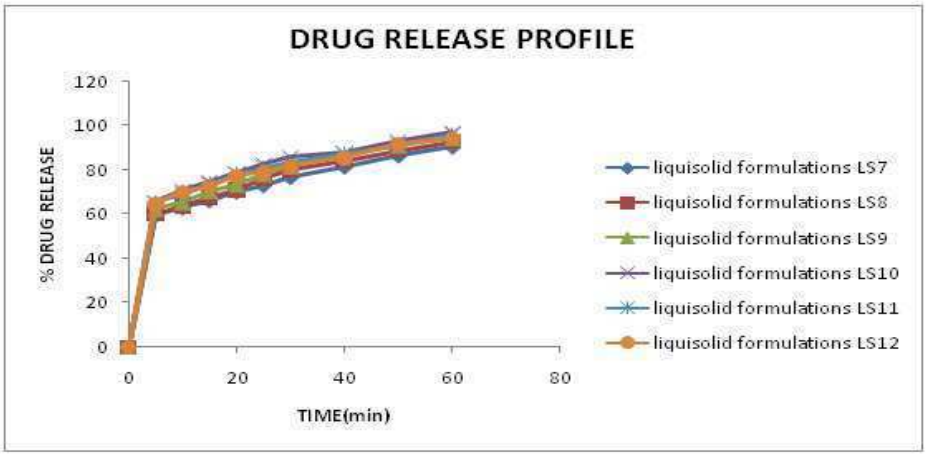

Figure 5
In-vitro drug release profile of Tamoxifen citrate in 1 hr from Formulations LS 7 to LS 12 in 0.02 N HCl

In Figure 6 the optimized formulation LS 10 was compaired with marketed tablet and pure drug. From the in-vitro drug release studies the optimized formulation LS 10 showed 96.90 % drug release, pure drug showed 24.75 % release the marketed tablet showed 70.42 % drug release in 60 minutes.

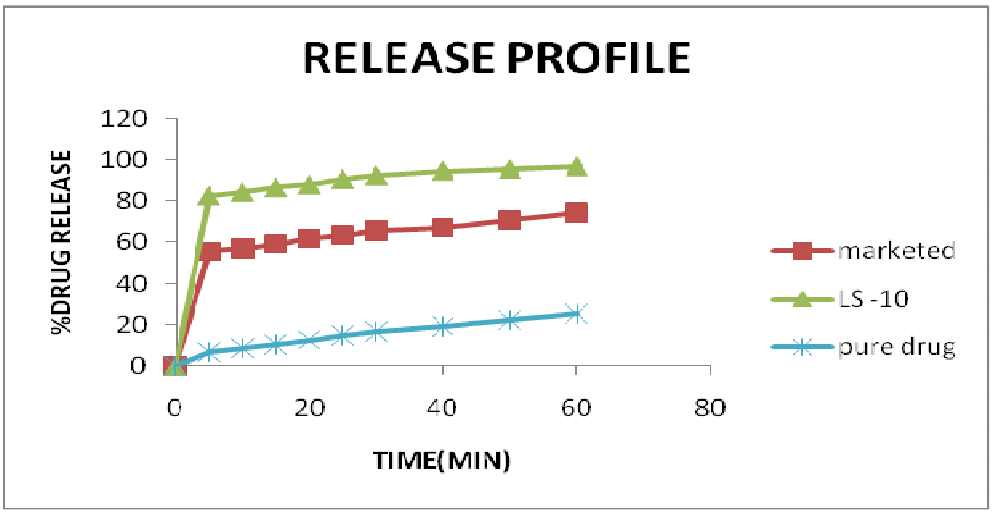

Figure 6
In-vitro drug release profile for tamoxifen citrate in 1 hr.from formulation LS 10, marketed tablet and pure drug in 0.02 N HCl

CONCLUSION

The Liquisolid technique is a promising alternative for improvement of dissolution property of water-insoluble drugs, such as Tamoxifen citrate as a model drug. The enhanced rate of Tamoxifen citrate dissolution from liquisolid tablets is probably 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. As compared to the pure drug and marketed tablet, liquisolid compacts of Tamoxifen citrate showed significantly enhanced *in vitro* drug release properties. In conclusion, development of the liquisolid compacts can be a promising alternative technique for BCS class II and IV drugs to achieve the improved dissolution rate.

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