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Liquisolid compact as an approach for Tenoxicam solubility enhancement using tween 80 as liquid vehicle

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ABSTRACT

Tenoxicam (Tnx) a nonsteroidal anti-inflammatory drug belonging to the oxim poorly water soluble drug and the rate of its oral absorption is often controlled by the dissolution rate in the gastrointestinal tract. Hence it is necessary to increase the solubility of the Tenoxicam. Different liquisolid (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. Liquisolid compacts were prepared using tween 80 as non-volatile solvent, Avicel PH102 as carrier, and colloidal silicon dioxide (Aerosil 200) as the coating material. Several liquisolid tablets formulations containing various drug concentrations in liquid medication (ranging from 10% to 35% w/w) were prepared. The ratio of Avicel pH 102 (carrier) to Aerosil 200 (coating powder material) were kept (20, 25). The formulations were then evaluated for their flow properties such as bulk density, tapped density, compressibility index, angle of repose and Hausner's ratio. FTIR, DSC, XRPD and SEM analysis were performed to know whether there is any interaction between drug and excipients interactions and also to study the changes in drug crystallinity and drug powder morphology. The liquisolid system showed acceptable flow properties. The IR, XRPD and DSC studies demonstrated that there is no interaction between the drug and excipients. The tabletting properties of the liquisolid compacts were within the acceptable limits. Liquisolid compacts demonstrated higher drug release rates than those of conventional and marketed tablet where select formula F9(R25, 30%) due to increasing wetting properties and surface area of the drug. This study shows that liquisolid technique is a promising alternative for improvement of solubility and the dissolution rate of water insoluble drug.

Keywords: Liquisolid compacts, Tenoxicam, tween 80, Aerosil 200, Avicel PH102

INTRODUCTION

Solubility is an important parameter for absorption of drugs especially for those which are water insoluble or poorly soluble drug. Low aqueous solubility is the major problem with formulation development of new discovery compound. Water is the solvent of choice for liquid pharmaceutical formulations. Most of the drugs are either weakly acidic or weakly basic having poor aqueous solubility [1]. Formulation of poorly water soluble compounds for oral delivery now presents one of the most frequent and greatest challenges to formulation scientists in pharmaceutical industry. The challenge for these poorly aqueous soluble drugs is to enhance the rate of dissolution. This in turn subsequently improves absorption and bioavailability [2].

Tenoxicam, 4-hydroxy - 2 - methyl -N-2- pyridinyl - 2H - thieno - [2,3e]1,2-thiazine-3-carboxamide-1,1-dioxide (Figure 1a) is a non-steroidal anti-inflammatory drug (NSAID), acting as a inhibitor of cyclooxygenase-2 and inhibitor of prostaglandin synthesis. It is very effective as analgesic and anti-inflammatory drug for the systemic

treatment of rheumatoid arthritis, osteoarthritis and other joint diseases [3,4]. It belongs to class II drugs, these types of drugs according to biopharmaceutical classification system characterize by low aqueous solubility and high permeability and often solubility is the rate-limiting step for absorption.

Different methods were used to improve the solubility of these drugs like solubilization, pH adjustment, cosolvents, microemulsion, self emulsification, polymeric modification, drug complexation, particle size reduction, use of a surfactant as a solubilizing agent. The pro-drug approach and solid dispersion. however, among them, the technique of ‘‘liquisolid compacts” is one of the most promising techniques. Liquisolid systems (LS) are acceptably flowing and compressible powdered forms of liquid medications. The term ‘liquid medication’ (that implies liquid lipophilic (oily) drugs, or water-insoluble solid drugs dissolved in suitable water-miscible, high boiling point non-volatile solvent systems). Such liquid medication may be converted into a dry-looking, non-adherent, free flowing and readily compressible powders by a simple admixture with selected powder excipients referred to as the carrier (Q) and coating (q) materials.

To attain the flowability and compressibility of liquisolid compacts, the ‘‘mathematical model for liquisolid systems” was employed as follows to calculate the appropriate quantities of carrier and coating materials required to produce liquisolid systems of acceptable flowability and compressibility properties of admixture based on new fundamental powder properties called the flowable liquid retention potential (Φ -value) . However, even though in the liquisolid 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. Therefore, due to their significantly increased wetting properties and surface area of drug available for dissolution media, liquisolid compacts of water-insoluble drugs may be expected to display enhanced drug solubility and release properties, and consequently, improved bioavailability . the present work is aimed towards enhancing the solubility, dissolution of Tenoxicam by using liquisolid compact technology[5,6].

EXPERIMENTAL SECTION

Materials

The following materials were used: tenoxicam (Sigma, Germany), avicel pH 102(JRS, Germany),Aerosil 200(Mingtai chemical, Taiwan), tween 80 (chemfine chemicals- Mumbai, India), sodium starch gluconate (ASG, India). All reagents used were of analytical grade.

Method

Saturation Solubility study

Saturated solutions were prepared by adding excess amount of the drug (tenoxicam) to the appropriate solvent (tween 80) sonicated for 30min then shaking on water shaker bath for 48 h at 25 ±0.5°C under constant vibrations. The solutions were filtered through a 0.45 µm. After this period the Filtered samples of non volatile liquid (1ml) were diluted with appropriate quantity of ethanol and analyzed by UV-visible spectrophotometer (Carry win UV, Varian, Australia) at 352 nm. The saturation solubility of the drug was also done in distill water, simulated gastric fluid pH 1.2 (SGF) and simulated intestinal fluid pH 6.8 (SIF). The average values of the three trials were taken [7].

Application of the mathematical model for designing the liquisolid compacts

In this study, tween 80, Avicel PH 102 (Micro crystalline Cellulose- MCC), and Aerosil 200 were used as a liquid vehicle, carrier, coating respectively. The concentration of the tenoxicam in tween 80 was varied as (10%, 15%, 20%, 25%, 30% and 35% w/w) and the carrier: coating ratio was 20:1 and 25:1. The ‘‘new formulation mathematical model of liquisolid systems” was employed as fallows to calculate the appropriate quantities of excipients required for producing liquisolid systems of acceptable flowability and compressibility properties.

The mathematical model was based on new fundamental powders properties (constants for each powder excipient with the liquid vehicle) called the flowable liquid retention potential (Φ-value) and compressible liquid retention potential ψ-number) of the constituent powders (carrier and coating materials). According to the new theories, the carrier and coating powder materials can retain only certain amounts of nonvolatile liquid while maintaining acceptable flow and compression properties. Depending on the excipients ratio (R) or the carrier: coating ratio of the powder system used, where

$$R = Q/q \quad ... (1)$$

As R represents the ratio between the weights of carrier (Q) and coating (q) materials present in the formulation. An acceptably flowing and compressible liquisolid system can be prepared only if a maximum liquid retain by carrier material is not exceeded; such a characteristic amount of liquid is termed the liquid load factor (Lf) and defined as the ratio of the weight of liquid medication (W) (weight of drug + weight of liquid) over the weight of the carrier powder (Q) in the system, which should be possessed by an acceptably flowing and compressible liquisolid system. i.e.:

$Lf = W/Q$ ... (2)

Spireas et al. used the Flowable liquid retention potentials (Φ - values) of powder excipients used to calculate the required excipient quantities, hence, the powder excipients ratios R and liquid load factors Lf of the formulations are related as follows:

$Lf = \Phi + \Phi (1/R)$ ... (3)

Where, Φ and Φ are flowable liquid retention potential of carrier and coating material respectively. So in order to calculate the required weights of the carrier and coating materials used, first, from Eq. (3), Φ and Φ are constants, therefore, according to the ratio of the carrier/ coat materials (R), Lf was calculated from the linear relationship of Lf versus 1/R. next, according to the used liquid vehicle concentration, different weights of the liquid drug solution (W) will be used. So, by knowing both Lf and W, the appropriate quantities of carrier (Q) and coating (q) powder materials required to convert a given amount of liquid medication (W) into an acceptably flowing and compressible liquisolid system could be calculated from equation (1) and (2) [5,6].

Preparation of directly compressible tablet (DCT) and liquisolid compact

Directly compressible tablets (DCT) of tenoxicam were prepared by direct compression using single tablet punch machine, each containing 20 mg tenoxicam, 208.25 mg Avicel pH 102, 8 mg Aerosil 200, where blend in mortar for 10 min then add 5 % w/w sodium starch gluconate as superdisintegrant mix for 10 min, 0.5 % w/w magnesium stearate add in the final step. Various LS compacts denoted (F1 to F12) containing 20 mg of tenoxicam were prepared by dispersing in non-volatile vehicles (Tween 80).Then a bindery mixture of carrier of carrier (Avicel pH 102) and coating material (Aerosil 200) was prepared in mortar and pestle at a ratio of 20:1 and 25:1 (trial and error methods were used, i. e. changing the carrier: coating material ratio (R) from 5, 10, 15, 20 and 25 until get good result (flow properties) is obtained. R 25 was used in all formulations since it gave the optimal flow property. This binary mixture was added to the admixture of drug and vehicle. Finally 5% sodium starch gluconate as superdisintegrant was added in above powder blend and mixed in all formulas. The final powder blend was subjected to compression [5, 6].

Evaluation of liquisolid system formulations

Precompression evaluation of the prepare liquisolid powders system

Flow properties of liquisolid system pwder

The flow properties of the liquisolid systems were 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 weight variations will occur. The flow properties of the liquisolid powders were estimated by determining the angle of repose, Carr's index and Hausner's ratio. The angle of repose was measured by the fixed funnel method. The bulk density and tap density were determined for the calculation of Hausner's ratio and Carr's index [8].

Fourier transforms spectroscopy (FTIR)

FTIR spectra were performed of optimized formulation by the KBr pellet method using the fourier transform infrared spectrophotometer (Shimadzu, Japan). A baseline correction was made using dried potassium bromide; Sample was scanned from 4000 to 400 cm-1. The FTIR spectra of Tenoxicam, excipients and liquisolid powder were performed to detect any sign of interaction which would be reflected by a change in the position or disappearance of any characteristic stretching vibration of the compound[9].

X-ray diffractometery (XRD)

The crystallinities of pure tenoxicam, excipients and liquisolid formula were evaluated by XRD measurement. It has been seen that polymorphic changes of the drug are important factors, which may affect the drug dissolution rate and bioavailability. The results were recorded over a range of 0-50° (2θ) using the Cu-target X-ray tube and Xe-filled

detector. The operating conditions were: voltage 40 kV, current 30 mA, scanning speed 1/min [9], using XRD shimadzu (6000, Japan) [10].

Differential scanning calorimetry (DSC)
DSC was performed using Shimadzu Japan differential scanning calorimeter Mettler, in order to assess the thermotropic properties and thermal behaviour of the pure tenoxicam, carrier, DCT and the liquisolid compacts. About 5 mg of the sample were sealed in the aluminium pans and heated at the rate of 10 °C/min, covering a temperature range of 30°C to 300°C under inert atmosphere flushed with nitrogen [11].

Scanning electron microscopy (SEM)
SEM is utilized to assess the morphological characteristics of the raw materials and the drug–carrier systems. In this study the photomicrographs were performed for the pure tenoxicam and liquisolid system. The samples were fixed on aluminum stubs with double-sided tape, gold-coated sputter and examined in the microscope using an accelerating voltage of 15 kV at a working distance of 8 mm using Tescan vegall (Czech) scanning electron microscopy [12].

Post compression evaluation of Tenoxicam liquisolid tablets
Hardness and Friability tests
The hardness of formulated liquisolid tablets was determined by using Erweka (Germany) TBH 100 hardness tester, and the mean hardness of 3 tablets from each of the prepared formulas was measured individually. The hardness was measured in terms of kg.

The friability of the prepared liquisolid tablets was measured using Erweka (Germany), TAR 120 type apparatus, and the drum was rotated for 4 min at 25 rpm (13). The losses of the mass of 20 tablets before and after rotation were determined, and by applying equation (4), the percentage of friability was calculated as follow:
%Friability = ((initial weight- final weight) / initial weight) x100 %… (4) [13]

Disintegration time
The disintegration test was performed at 37±0.5 °C in 0.1N HC1 (pH 1.2) for three tablets from each formula using the USP tablet disintegration apparatus (Disintegration tester ZT 322, Erweka, Germany) with a basket rack assembly containing six open-ended tubes and 10-mesh screen on the bottom .The tablet was placed in each tube of the basket and the time for complete disintegration of the six tablets was recorded. Generally, ideal tablet hardness should be produced without applying excessive compression force where rapid tablet disintegration and drug dissolution are maintained at the same time [14].

Content uniformity tests
Five tablets were weighed individually and powdered. The powder equivalent to 20mg of tenoxicam was weighed and dissolved in 10 ml of methanol and volume was adjusted to 100 ml with pH 6.8 buffer. The solution was sonicated for 30min then filtered and from this solution 1 ml was taken and make up with PH 6.8 buffer in 100 ml standard volumetric flask. The amount of drug present in each tablet was determined spectrophotometrically at 368nm using UV–visible spectrophotometer. The percentage content was determined using standard calibration curve [15].

In vitro dissolution studies of liquisolid tablets
The dissolution study was carried out using USP apparatus 2 paddle for the tablets. The dissolution test was used to compare between liquisolid tablets, DCT, and marketed tenoxicam tablet. The dissolution media were either 900 mL of SGF 0.1 N HCl pH 1.2 and SIF phosphate buffer pH 6.8, at 37 ± 0.5°C, tenoxicam tablets were kept in the paddle dissolution apparatus, at 50 ± 2 rpm. Sample of 5 mL were withdrawn at specific time intervals (5, 10, 15, 20, 30, 45, 60 min) and filtered through a 0.45 μm filter then analyzed spectrophotometrically at 363nm and 368 nm for HCl pH 1.2 and phosphate buffer 6.8, respectively (using Copley dissolution 8000 tester, Copley scientific, UK). The dissolution media was replaced with 5ml fresh dissolution media to maintain sinks conditions and constant volume. Each preparation was tested in triplicate and the mean values were calculated [16].

Similarity factor: The similarity factor (f2) is used to compare the dissolution profile of best formulation with that of marketed formulation. In this approach, recommended by the FDA Guidance for Industry, a value between 50

and 100 indicates similarity between two dissolution profiles. If the f2 value is close to 100, the profiles are nearly identical Similarity factors (f2) equation:

$f_2 = 50 \text{ x log } \{[1+ (1/n) \sum_{t=1}^{n} (Rt - Tt)^2]^{-0.5} \text{ x } 100\}$ ….(5)

Where, (n) number of time points at which percent dissolved was determined. (Rt) the percent dissolved of reference (marketed) formulation at a given time point. (Tt) the percent dissolved of the test formulation to be compared at the same time point [17].

RESULTS AND DISCUSSION

Solubility Studies

The solubility of Tenoxicam (Tnx) in various solvents is given in Table (1). The table shows that the solubility of (Tnx) was increased by the presence of non-volatile solvents (tween 80 and glycerine). The high solubility of the drug in tween 80 indicating the micellar solubilization in concentration higher than its critical micelle concentration. This suggested the nonpolar nature of (Tnx) and its presence in the hydrophobic interior of the micelle [16]. inThe table also shows that an increase in pH resulted in an increase in the solubility of (Tnx); this is because (Tnx) is acidic i.e (Tnx) become partially ionized by increase pH.

Table 1: Solubility of tenoxicam in various solvents

Solvents	Solubility (%w/w)
Distilled water	0.042
SGF(pH 1.2)	0.0888
SIF(phosphate buffer pH 6.8)	1.145
Tween 80	1.236
Glycerin	0.7866

Application of new mathematical model for design of liquisolid systems

Mathematical model equation for Avicel PH 102 and Aerosil 200 in tween 80 can be given according to values of (Φ) and (Φ) as given by Spireas et al [21] as follow:

Lf = 0.16 + 3.3 (1 / R) … (3)

Based on this equation, Lf is calculated by using different R values and based on value of W (liquid medication), amount of carrier can be calculated according to equation (2), and then amount of coating can be calculated by applying equation (1) depending on R value. The amount of superdisintegrant is equal to 5% of the tablet weight. Table (2) represents the exact qualitative and quantitative composition for each formula [5, 6].

Table 2: Composition of tenoxicam liquisolid formulas prepared using tween 80 as nonvolatile liquid according to mathematical model (All liquisolid formulas contain 20mg tenoxicam)

Liquisolid compact system code	Drug conce. In liquid medication (% w/w)	R ratio	Liquid loading factor (Lf)	Liquid vehicle (mg)	Carrier (Q)Avicel PH 102(mg)	Coating (q)Aerosil 200(mg)	Disintegrant sodium starch gluconate (mg) 5 % w/w	Total weight tablet (mg)
F1	20%	20	0.327	80	306.28	15.31	22.189	443.78
F2	25%	20	0.327	60	245.02	12.25	17.75	355.05
F3	30%	20	0.327	46.67	204.19	10.21	14.79	295.86
F4	35%	20	0.327	37.143	175.02	8.75	12.68	253.59
F5	15%	20	0.327	113.33	408.37	20.42	29.59	591.71
F6	10%	20	0.327	180	612.56	30.63	44.38	887.57
F7	20%	25	0.293	80	341.06	13.64	23.93	478.63
F8	25%	25	0.293	60	272.85	10.91	19.15	382.91
F9	30%	25	0.293	46.67	227.38	9.095	15.96	319.11
F10	35%	25	0.293	37.143	194.89	7.796	13.68	273.51
F11	15%	25	0.293	113.33	454.75	18.19	31.91	638.18
F12	10%	25	0.293	180	682.13	27.29	47.86	957.28

Precompression evaluation of the prepare liquisolid powders system

Angle of repose: the angle of repose (Ɵ) is a characteristic of the internal friction or cohesion of the particles, the value of the (Ɵ) will be high if the powder is cohesive and low if the powder is non-cohesive according to USP value. The result show in table (3), conclude that, the increase in concentration of drug in the liquid medication like (F9, F10) because reduction in the angle of repose and increase in flow ability of formula.

Carr's index, Hausner's ratio: were used also for evaluation powder flowability and most formulas have acceptable flowable evaluation where increase amount of carrier (avicel pH good flow properties) and coating materials lead to increase flow of admixture, where formulas(F9, F7) have the low value indicating good flowing [18].

Fourier transform spectroscopy: The FTIR spectrum of pure tenoxicam figure(1) showed the characteristic peak of the drug at 3434 cm-1 of O-H stretching vibration and other peaks at 1637 cm-1 due to amide carbonyl stretching,1384.6 cm-1 due to CH3 deformation, C=C stretching of aromatic group at 1608.34 cm-1 and 1423.21cm-1 due to C-H deformation.

Figure (2) showed the FTIR spectrum of DCT with the presence of the characteristic peaks of tenoxicam indicating that there was no interaction between drug- excipients used in the study and no hydrogen bond formation in DCT. Absence of the characteristic peak (3434 cm-1) of tenoxicam was observed in liquisolid formula figure (3), which might be due to formation of hydrogen bonding between the O-H of enol group of tenoxicam and the hydroxyl group of the liquid vehicle in liquisolid formula; this resulted in drug dissolution enhancement . It is observed that the peaks of major function groups of (Tnx), which are present in spectrum of pure drug, were present in Tnx liquisolid formula but the broadness of the characteristic peak of Tnx with shifting to lower frequency might be due to formation of hydrogen bonding between O-H of enol group of tenoxicam and the hydroxyl group of the tween 80 in liquisolid formula, this resulted in drug dissolution enhancement [9].

The X-ray diffraction: patterns in figure (5) revealed that pure Tenoxicam was clearly in crystalline state as it showed sharp distinct peaks notably at 2Ɵ diffraction angles of 12, 14.9, 16.5, 23.8, and 29.7. Tenoxicam characteristic peaks were observed in the conventional formulation figure (6), demonstrating that its crystalline structure remained unchanged during the physical blend, and that the loss of crystallinity was due to liquisolid system formation. On the other hand, the liquisolid powder X-ray diffraction pattern figure (8) showed only one sharp diffraction peak at 2 Ɵ angle of 22.5 belonging to carreier Avicel pH 102 figure (7), indicating that only Avicel pH 102 maintained its crystalline state. Such absence of Tenoxicam constructive reflections (specific peaks) in the liquisolid X-ray diffractogram indicates that drug has almost entirely converted from crystalline to amorphous or solubilized state, such lack of crystallinity in the liquisolid system indicates that Tenoxicam solubilization in the liquid vehicle. This amorphization or solubilization of Tenoxicam in the liquisolid system may contribute to the consequent improvement in the dissolution rate, apparent solubility and therefore the bioavailability of Tenoxicam [19]. Such results were also in good agreement with Mura et al. and Ghebremeskel et al [20].

Differential scanning calorimetry: DSC of pure tenoxicam showed a characteristic, sharp endothermic peak at 212°C which is associated with the melting point of the drug and indicated the crystalline nature of tenoxicam figure (9). The thermogram of DCT figure (10) exhibited endothermic peak at 213°C, which is the peak of the drug, indicated that there is no interaction between the drug and excipients used in the formulation. Figure (12) showed complete disappearance of characteristic peak of tenoxicam and this is due to the formation of drug solution in the liquisolid-powdered system, i.e., the drug is molecularly dispersed within the liquisolid matrix. This disappearance of drug characteristic peak upon formulation into a liquisolid system was in agreement with McCauley and Brittain who declared that the complete suppression of all drug thermal features undoubtedly indicates the formation of an amorphous solid solution. In addition, Mura et al. found out that the total disappearance of the drug melting peak indicates that drug amorphization had taken place [19,20].

Scanning electron microscopy: figure (13) illustrated the photomicrograph of the pure drug (Tenoxicam), it showed that the drug had crystalline nature as was proved previously by the DSC and XRD. figure (14) displayed the photomicrograph of the final liquisolid system and it showed the complete disappearance of telmisartan crystals. This fact indicates that even though the drug is in solid dosage form, it is held within the liquisolid powder substrate in solution or in solubilized, almost molecularly dispersed state which contributes to enhance drug dissolution property [21].

Table 3: Precompression Parameters of Tenoxicam liquisolid Formulations (F1-F12)

Formulation code	Angle of Repose (θ)	Hausner's ratio	%Carr's index
F1	40	1.177	15.05
F2	37.41	1.2	16.7
F3	35.15	1.25	20.2
F4	35.06	1.226	18.5
F5	42.5	1.28	21.05
F6	42.29	1.3	22.3
F7	39.3	1.17	14.8
F8	36.12	1.2	17.4
F9	33.9	1.15	13.4
F10	34.13	1.18	15.5
F11	40.4	1.27	20.92
F12	41.2	1.26	20.7
DCT	29.2	1.18	15.4

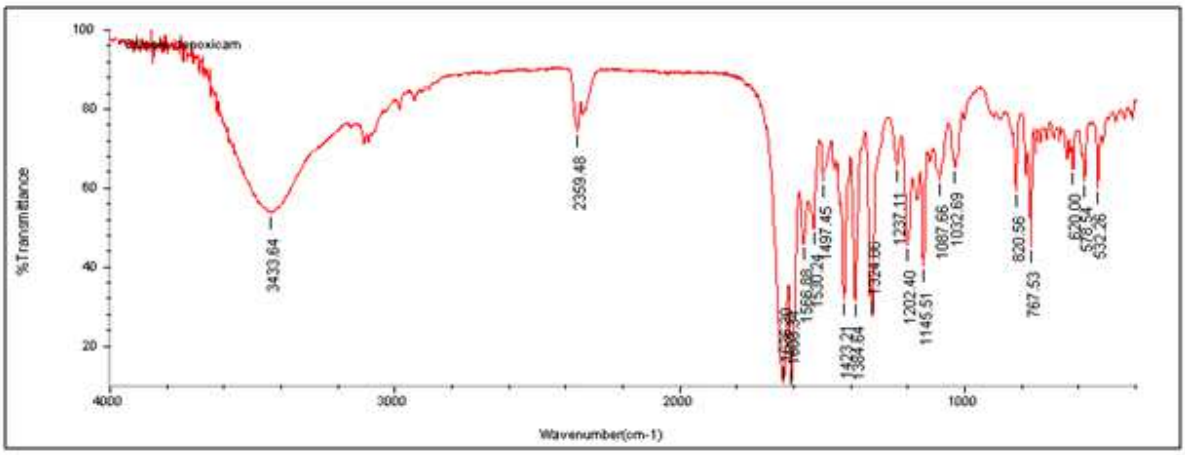

Figure 1: FTIR spectrum of pure tenoxicam

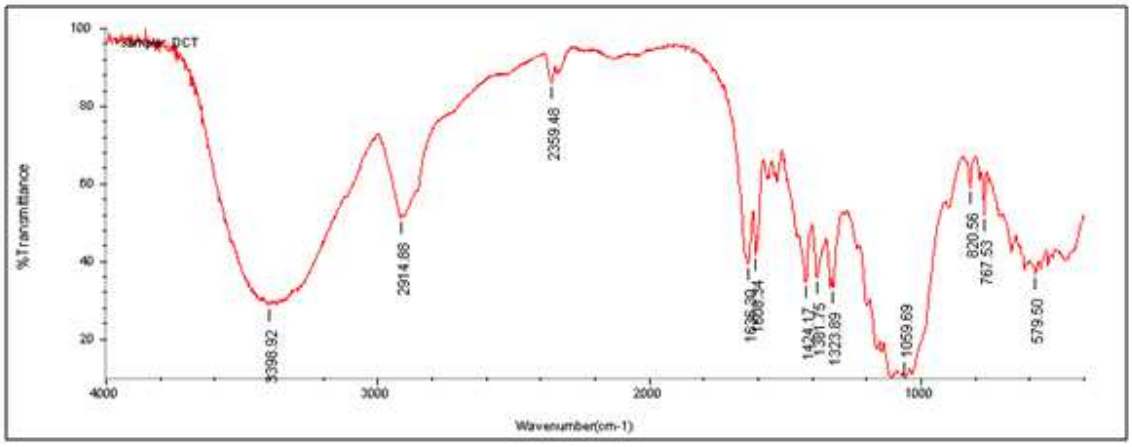

Figure 2: FTIR spectrum of pure DCT

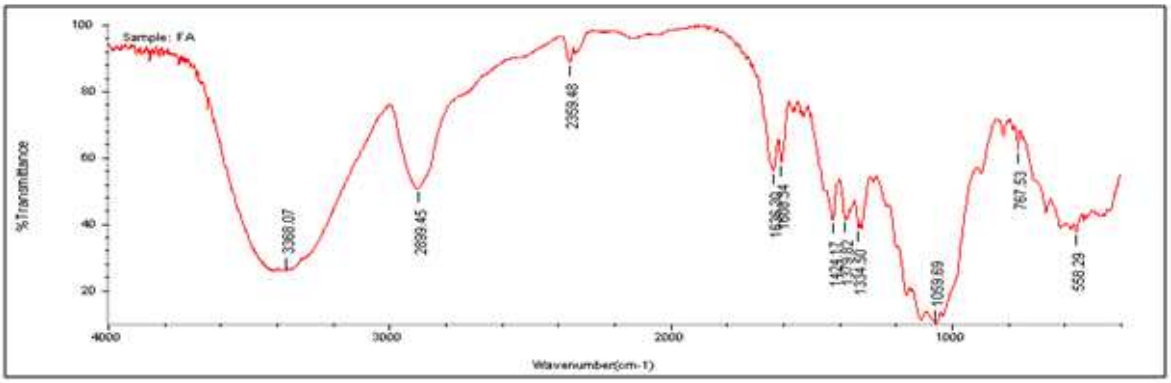

Figure 3: FTIR spectrum of liquisolid compact

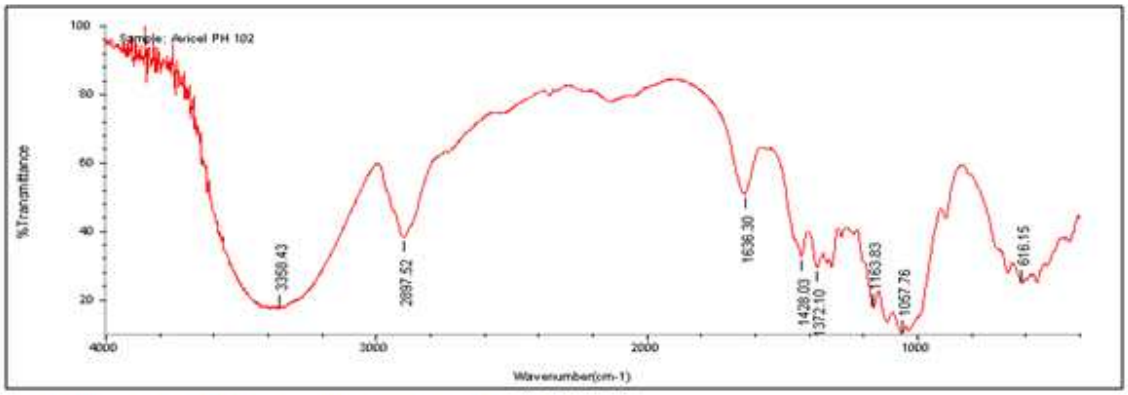

Figure 4: FTIR spectrum of Avicel pH 102

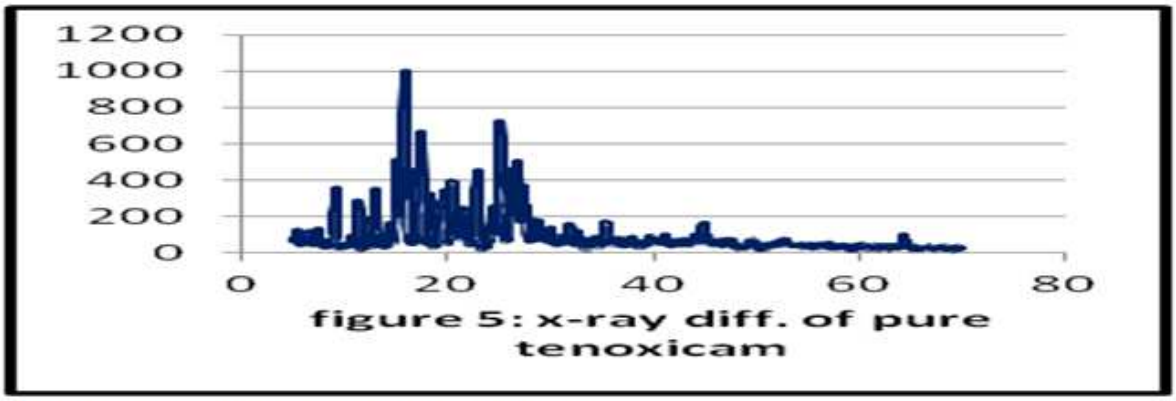

Figure 5: X-ray diffraction of pure tenoxicam

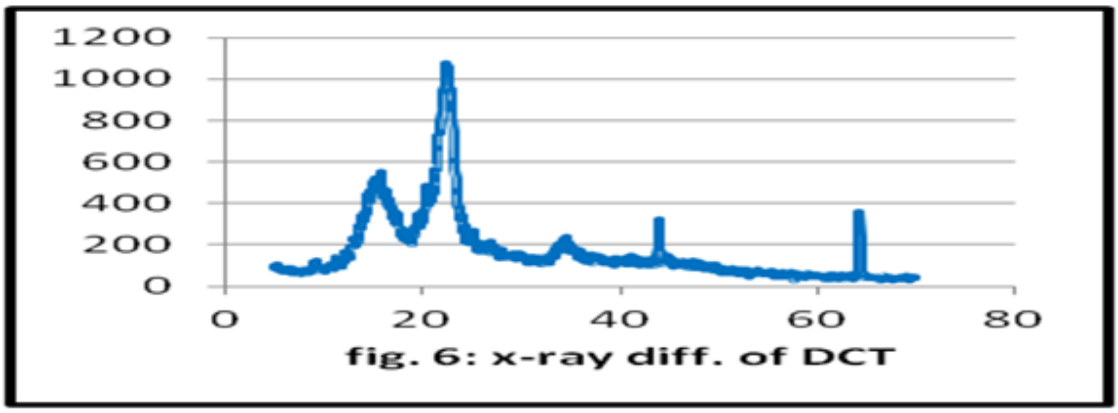

Figure 6: X ray diffraction of DCT

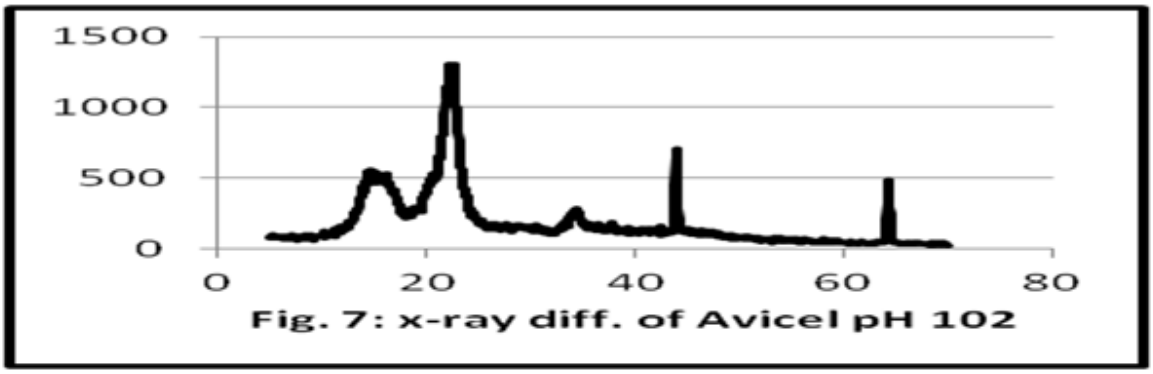

Figure 7: X ray diffraction of Avicel pH102

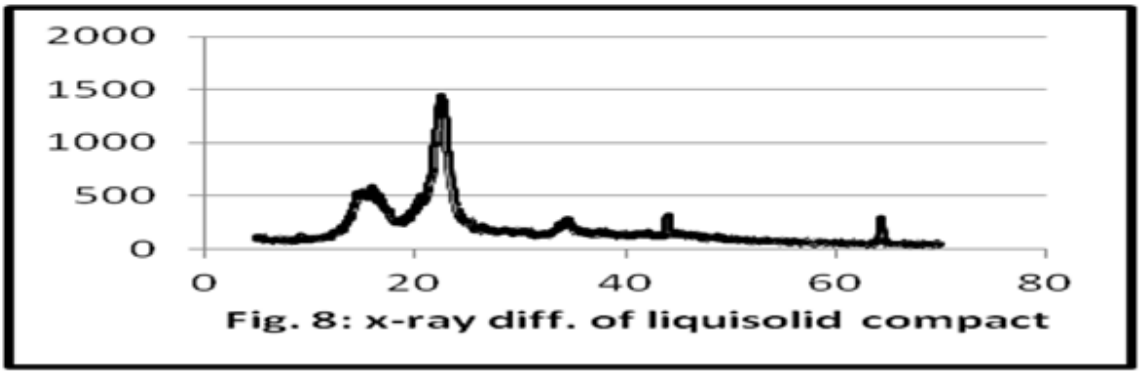

Figure 8: X ray diffraction of liquisolid compact

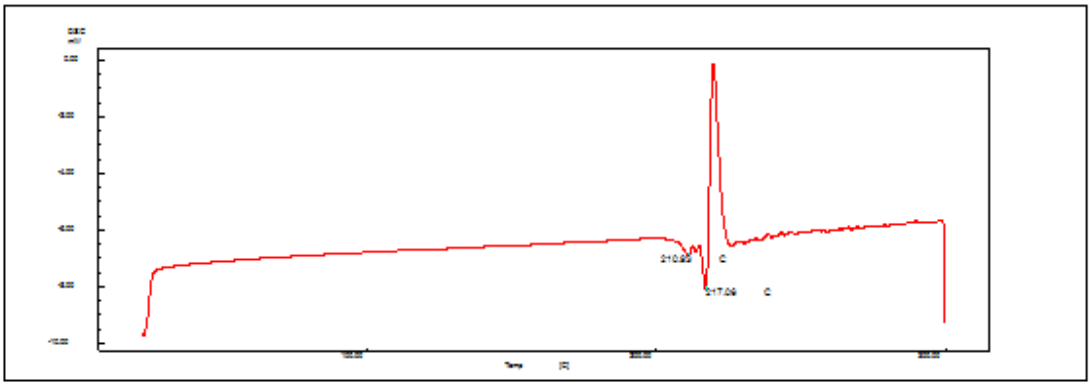

Fig. 9: DSC of pure Tenoxicam

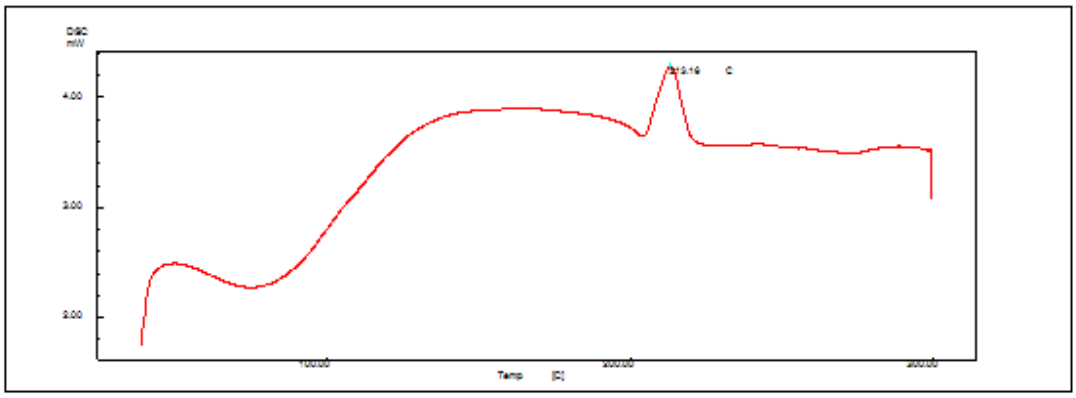

Fig. 10: DSC of DCT

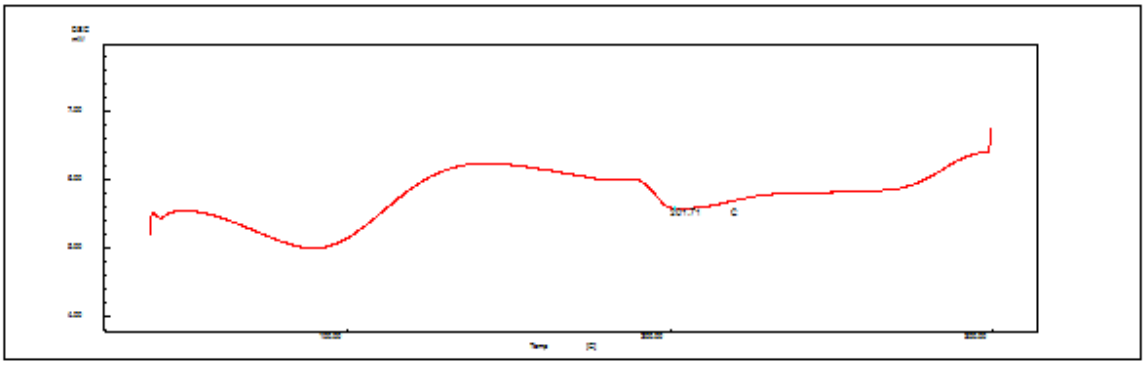

Fig. 11: DSC of Avicel pH

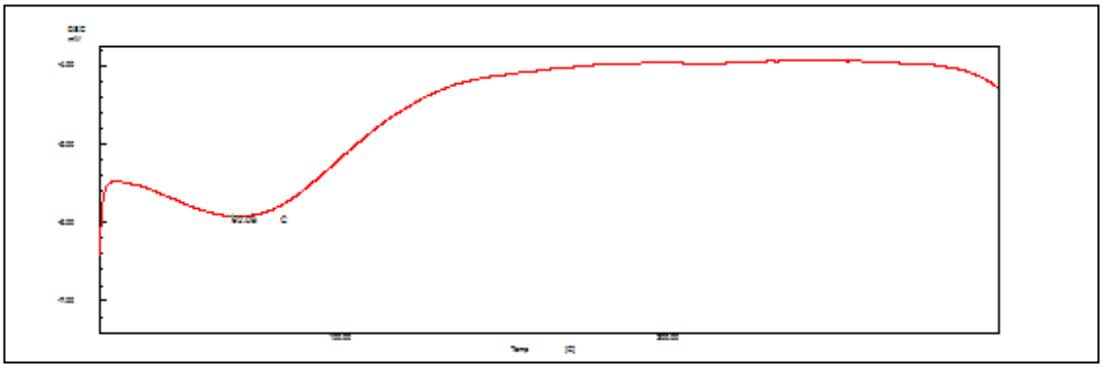

Fig. 12: DSC of liquisolid compact

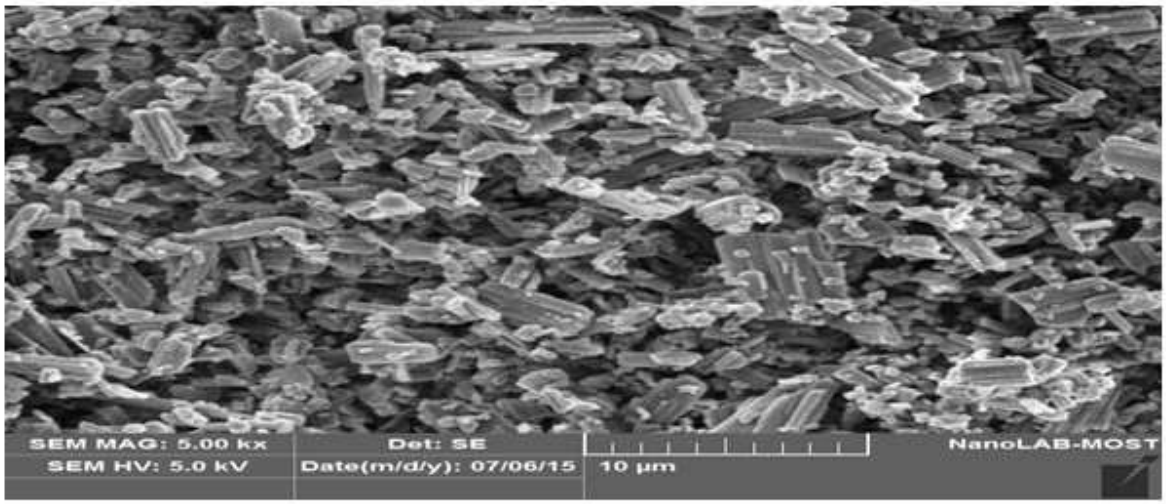

Fig. 13: SEM of pure tenoxicam

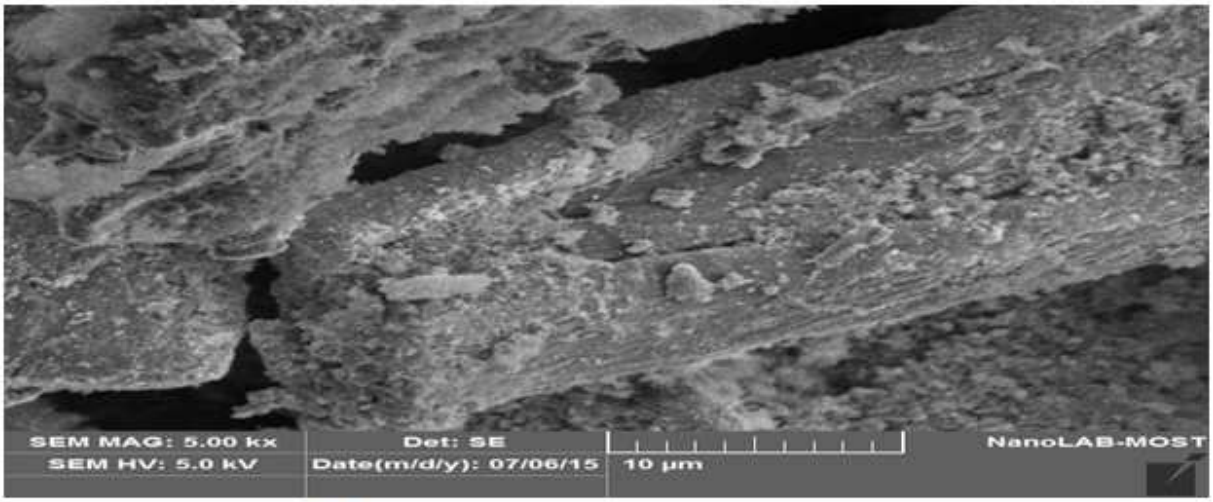

Fig. 14: SEM of liquisolid compact

Post compression evaluation of Tenoxicam liquisolid tablets

Hardness and friability: All the prepared batches had hardness in acceptable range, from 4 to 5.5 kg/cm2. Generally, the ideal tablet hardness should be produced without applying excessive compression force where rapid tablet disintegration and drug dissolution are maintained at the same time . It was seen that as the amount of Avicel pH 102 goes on increasing, hardness also increases. With a increase in R-values, hardness was found to increase .
All the liquisolid tablets showed acceptable friability, the percentage did not exceed 1% of the tablet weight, also, no tablet was cracked, split or broken or deformed. Hardness and friability were represented in table (4) [22].

Content uniformity: The percentage of content uniformity of all tenoxicam liquisolid compacts (table 4) was between 92.25% and 101.1%; this complied with pharmacopoeial requirements, in which each individual content was between 90% and 110% of the average content [15].

Disintegration time: All the prepared liquisolid tablets had a disintegration time less than 2.5 min. The batches prepared with increasing drug concentration exhibited an increasing disintegration time as shown in table (4).

Table 4: Hardness, Friability and disintegration percentage of Tenoxicam liquisolid formulation

Formulation	Hardness (kg/cm2)	% Friability	%Drug Content	Disintegration time (sec)
F1	4.5	0.55	95.79	115
F2	5.5	0.48	93.33	121
F3	5.09	0.51	98.5	128
F4	5.12	0.44	97.32	135
F5	4	0.65	94.88	108
F6	4	0.75	92.25	105
F7	4.24	0.5	95.46	112
F8	5.5	0.45	98.98	118
F9	4.5	0.42	101.1	122
F10	4.75	0.39	100	126
F11	4.75	0.55	96.5	90
F12	4.25	0.62	97.75	85
DCT	4.5	0.51	98.45	350

In-vitro drug release: Dissolution rates of liquisolid formulas were compared with conventional tablet (DCT) and marketed tablet as represented in figure (15, 16, 17 and 18). The concentration of drug in liquid medication is an important aspect as it affects drug release. From the obtained results it can be concluded from obtained data that there was a direct relationship between the powder excipient ratio (R) and the release of drug from liquisolid tablets, When R value increases, the release rate will also increase. i.e.: liquisolid tablets of (R 25) had higher drug release than liquisolid tablets of (R 20).

The percent of Tenoxicam released from liquisolid compacts containing varying amounts of carrier and coating material (from F1 to F12) was found to vary from 85.28% to 65.17% in 0.1N HC1 (pH 1.2) and from 88.79% to 73% in phosphate buffer (pH 6.8) in the first 20 min from results we can see the drug release profile in phosphate buffer high compare with pH 1.2 this may be to the solubility of drug in phosphate buffer . So, it can be concluded from given data that F9 was the best liquisolid formula having optimized fast release profile among all other preparations. From figures 12 and 13, it can be seen that the release rate of liquisolid compacts was markedly higher than that of DCT and marketed tablet, the percentage drug release in HCl pH 1.2 at first 20^{th} min were 85.28%, 36.17% and 60% for F9 (best formula), DCT and marketed tablet respectively figure (19, 20). And the percentage drug release in phosphate buffer (pH6.8) at first 20th min were 88.79%, 39.45% and 63% for F9, DCT and marketed tablet respectively. The similarity factor (f2) is used to compare the dissolution profile of best formulation with that of marketed formulation the result was 23.39 mean dissimilarity This increase in dissolution rate of liquisolid tablets is because these formulations contain a solution of the drug in non-volatile vehicle used for preparation of the liquisolid compacts; the drug surface area available for dissolution is significantly increased. Therefore, in the case of liquisolid compacts, the surface area of drug available for dissolution is much greater than that of the DCT and the marketed tablet.

Table 5: Similarity Factor Between Marketed and F9 Tenoxicam Liquisolid Compacts

Time	% drug release		Rt - Tt	(Rt – Tt)2	Similarity Factor f2
	Rt	Tt			
5	18.34	66.85	-48.51	2353.22	23.39
10	41.88	82.22	-40.34	1627.316	
15	50.11	87.55	-37.44	1401.754	
20	63	88.79	-25.79	665.1241	
30	55.37	89.49	-34.12	1164.174	
45	65.24	90	-24.76	613.0576	
60	79.23	96.28	-17.05	290.7025	
Total				8115.348	**Dissimilarity**

f2 > 50 show similarity

f2 = 50 x log {[1+ (1/n) $\sum_{t=1}^{n}(Rt - Tt)^2$] $^{-0.5}$ x 100}

= 50 x log {[1+ (1/7) 8115.348]$^{-0.5}$ x 100 }

= 50 x log {0.029357 x 100 }

= 23.39

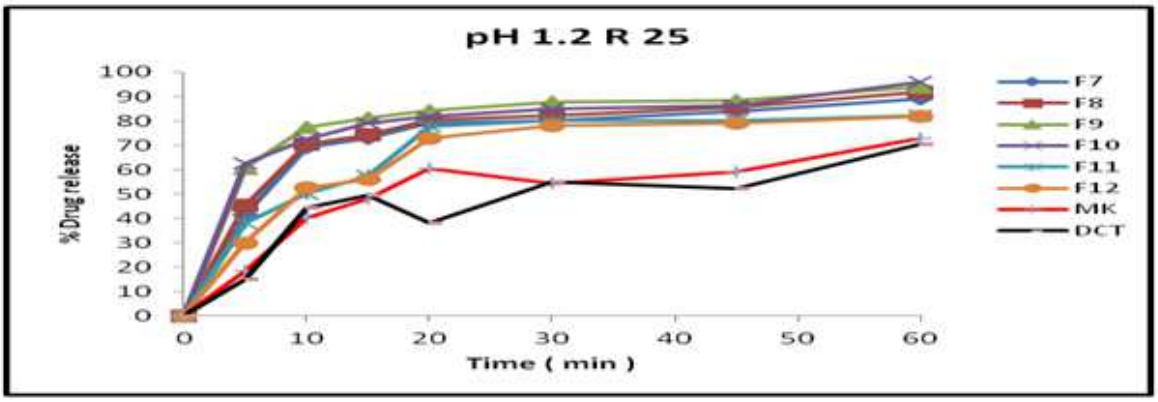

Figure 15: Dissolution profile of liquisolids, marketed and directly compressed tablet at pH 1.2, R25.

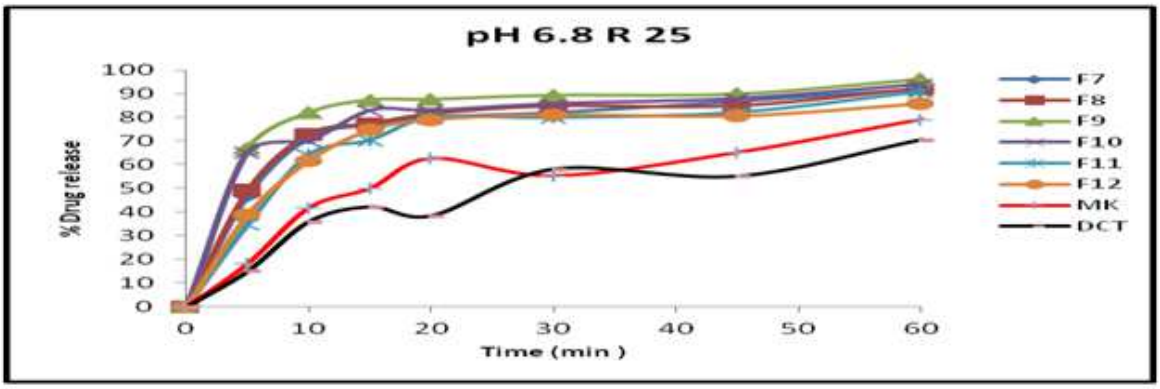

Figure 16: Dissolution profile of liquisolids, marketed and directly compressed tablet at pH 6.8, R25.

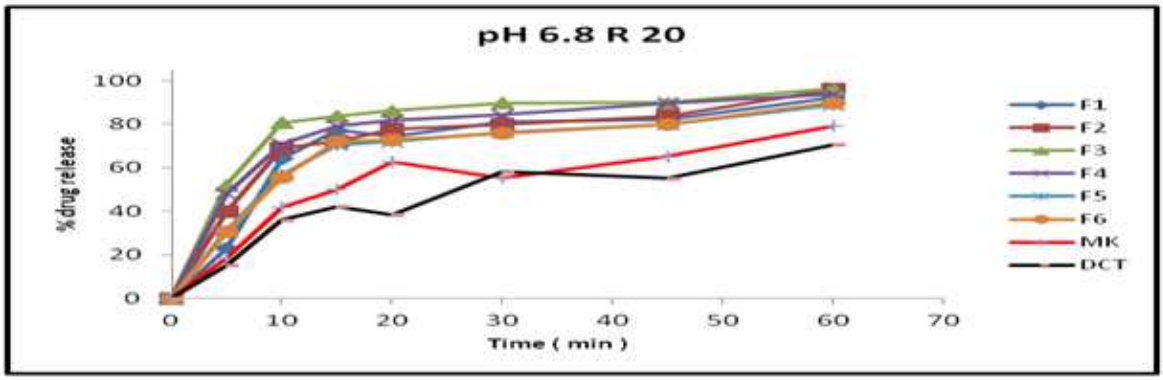

Figure 17: Dissolution profile of liquisolids, marketed and directly compressed tablet at pH 6.8, R20.

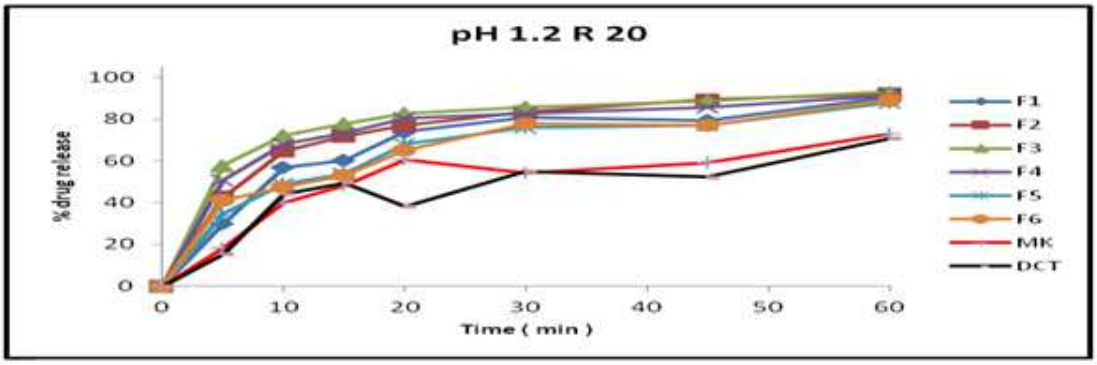

Figure 18: Dissolution profile of liquisolids, marketed and directly compressed tablet at pH 1.2, R20

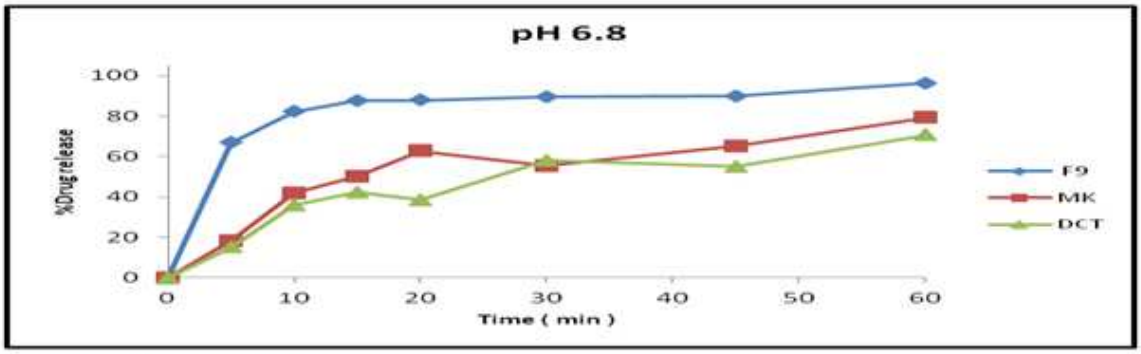

Figure 19: Dissolution profile of liquisolid F9 and marketed at pH 6.8.

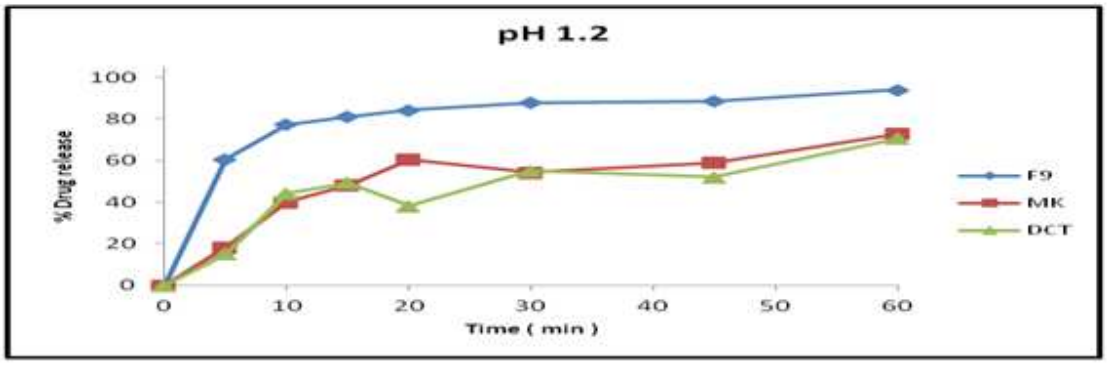

Figure 20: Dissolution profile of liquisolid F9 and marketed at pH 1.2.

CONCLUSION

The liquisolid compacts technique can be a promising alternative for the formulation of poorly water drugs, such as tenoxicam into rapid release tablets. The enhanced rate of drug dissolution from liquisolid tablets is probably due to an increase in wetting properties and surface area of drug particles available for dissolution, thus, liquisolid compacts technique leads to enhance dissolution rate and subsequently improve bioavailability of poorly water-soluble drugs as been shown that the solubility of the drug in the nonvolatile vehicle of the liquisolid compacts is directly proportional to their tenoxicam dissolution rates.

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