ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

# Dissolution Enhancement of Prednisolone using Liquisolid Compacts

**Prabhat Kumar Sahoo[1]*, Sujit Dash[1], Amaresh Chandra Sahoo[1], Biswanath Mishra[1]**
[1] *Institute of Pharmacy & Technology Salipur, Odisha*
Pravat.200581@gmail.com

**Abstract:**

Several liquisolid system of Prednisolone (LS-1 to LS-12) were prepared in 50 tablets batches & compressed into tablets of 5mg strength each. All liquisolid formulations contains microcrystalline cellulose as the carrier powder & silica as the coating material at a fixed powder excipients ratio (R) of 20 propylene glycol was used as liquid vehicle to prepare the liquid medication of the different drug concentration on ranging from 10-40%w/v, includes in the LS-1to LS-9 on the other hand formulation LS-10 to LS-12 contains liquid medication with a fixed 10%w/v drug concentration in different liquid vehicles, namely glycerin, PEG (LS-9) & Polysorbate 80(Tween80). Depending on the liquid vehicle & drug concentration in the liquid medication used, different liquid factor $L_f$ ranging from 0.132-0.165(w/w) were employed in our liquidsolid preparation. Finally a standard 10% (w/w) of the disintegrant sodium starch glycolate was added to all systems. The hardness of the tablets was found to be in the range of 4.0-6.0kg/cm$^2$. The percentage friability for all formulations was below 1% indicating that the friability is within the prescribed limits. The tablets were found to contain 95.8-99.2% of the labeled amount indicating uniformity of drug content.

The cumulative mean percentage drug release of Prednisolone released from liquisolid compacts containing same amount of carrier & coating material (From LS-1-LS-12) was found to vary from 19.23-44.63 in first 50min. This indicates the fast release of is observed from above formulations. The optimized formulations LS-1 showed the 45.98% drug release in the first hour where as the CT tablets(control) showed 20.28% in hour.

**Key words:** Liquisolid compact, Prednisolone, In-vitro dissolution, Polyethylene Glycol(PEG), Sodium starch glycolate

## INTRODUCTION

Formulation Development Techniques for BCS Class II Drugs pose challenging problems in their pharmaceutical product development process[1,2]. As the dissolution rate forms the rate limiting step in their bioavailability, enhancement of dissolution rate and achieving the target dissolution is a critical step in their formulation development[3,4]. Several conventional methods such as micronization, chemical modification, use of surfactants and solubilizers, solid dispersion and a few new emerging technologies such as cyclodextrin complexation, mucoadhesive microspheres, nanoparticles, nanosuspensions, micro emulsion and self-emulsifying systems are available to enhance the bioavailability of BCS Class II drugs[5,7]**.** When the drug dissolved in the liquid vehicle is incorporated into a carrier material which has a porous surface and closely matted fibres in its interior as cellulose, both absorption and adsorption take place; *i.e.* the liquid initially absorbed in the interior of the particles is captured by its internal structure, and after the saturation of this process, adsorption of the liquid onto the internal and external surfaces of the porous carrier particles occur. Then, the coating material having high adsorptive properties and large specific surface area gives the liquisolid system the desirable flow characteristics.

Components of Liquisolid Compact Formulations

Liquisolid compact mainly includes

1. Non volatile solvent
2. Disintegants
3. Carrier material
4. Coating material

## MATERIAL AND METHODS

Prednisolone was obtained from Zydus Cadila, Ahemadabad, India. Propylene glycol & PEG 400 was obtained from Glenmark, India Microcrystalline cellulose was obtained from IPT Salipur. Lactose was obtained from IPT Salipur. Sodium starch glycolate was obtained from IPT Salipur. Silicagel-G was obtained from IPT Salipur.

### Solubility Analysis

The solubility of prednisolone in water and the four liquid vehicles used to prepare the liquisolid systems, namely, propylene glycol, polyethylene glycol 400, glycerin & polysorbate 80, were studied by preparing saturated solutions of the drug in these solvents and analyzing their drug content spectrophotometrically . Specifically, prednisolone was mixed in 10ml test tubes with such amounts of each of the above solvents in order to produce systems containing an excess of drug. The mixture were sonicated for 24hr and then cooled down to 25$^0$c under constant vibration. After centrifugation, accurately weighed quantities of the filtered supernatant solutions were further diluted with methanol and analyzed spectrophotometrically at 246 nm for their drug content. The results were extrapolated to determine the %w/w of prednisolone in its saturated solution with the solvent under investigation.

### Melting Point

Melting point of Prednisolone was determined by two methods

1. Capillary method
2. Differential scanning calorimetry: (DSC)

### Formulation of Directly Compress Tablets

A conventional formulation of micronized Prednisolone, USP, (denoted as DC-1) was directly compressed into

tablets, each containing 5mg drug. In addition, each DC-1 tablet contained the following powder excipients
1.70mg coarse granular microcrystalline cellulose (Avicel PH 200)
2.35mg Lactose monohydrate
3.5mg nm-sized silica (cab-O-Sil)
4.10mg sodium starch glycolate
A 100 tablet batch was mixed in mortar & pestle for 10min. & compressed using compression machine. Sufficient compression loads were applied in order to produce tablets of 5-6 kp hardness, as determined using a pfizer hardness tester.

**Liquisolid compacts**:-
Several liquisolid system of Prednisolone (LS-1to LS-12) were prepared in 50 tablets batches & compressed into tablets of 5mg strength each.
All liquisolid formulations contains microcrystalline cellulose as the carrier powder & silica as the coating material at a fixed powder excipients ratio (R) of 20 propylene glycol was used as liquid vehicle to prepare the liquid medication of the different drug concentration on ranging from 10-40%w/v, includes in the LS-1to LS-9 on the other hand formulation LS-10 to LS-12 contains liquid medication with a fixed 10%w/v drug concentration in different liquid vehicles , namely glycerin, PEG (LS-9) & Polysorbate 80(Tween80)
Depending on the liquid vehicle & drug concentration in the liquid medication used, different liquid factor $L_f$ ranging from 0.132-0.165(w/w) were employed in our liquisolid preparation.
Finally a standard 10% (w/w) of the disintegrant sodium starch glycolate was added to all systems. Important formulations characterized of the prepared prednisolone liquisolid.

**Mixing & Compression**
The mixing procedure was conducted in 3 stages. During the first stage, the system was blended at an approximate mixing rate of one rotation/second for approximately one minute in order to evenly distribute the liquid medication into the powder. In the second mixing stage, calculated quantities of coating material was added to the system & blended for two minute. The liquid/powder admixture was evenly spread as a uniform layer on the surfaces on the mortar & left standing for approximately for five minutes to allow the drug solution to be absorbed in interior of the powder particles. In the third stage the powder was scrapped off the mortar surfaces by means of aluminium spatula then producing the final liquisolid formulation to be compressed. Similar formulation are prepared by using Microcrystalline cellulose, Lactose monohydrate, sodium starch glycolate as carrier materials.

**Characterization of Prepared tablets**
The prepared tablets were studied for their physical properties like weight variation, hardness, friability & drug content uniformity.

Tablet hardness
The strength of tablet is expressed as tensile strength in $kg/cm^{2.}$ The tablet crushing load which is the force required to break a tablet into halves by compression. It was measured using a tablet hardness tester (pfizer tablet hardness tester)
Weight variation test
It is done by weighing 20 tablets individually calculating the average weight & comparing the individual weight to the average.
Friability
This test is performed to assess the effect of friction & shocks which may upon during handling, packaging & shipping operation to detect capping & lamination problem. Roche friabilator was used to measure the friability of the tablets.
Drug content uniformity
For estimation of drug content tablets were crushed & the aliquot of powder equivalent to 5mg of drug was dissolved in suitable quantity of distilled water & 0.1N HCL. Solution was filtered, diluted & drug content determine by UV visible spectrophotometer (SHIMADZU UV1700) at 246nm. Drug concentration was calculated from Calibration curve.
*In vitro* dissolution
The USP paddle (electrolab) was used for all the invitro dissolution studies. In this method 0.1N HCL & distilled water was used as dissolution medium. The rate of stirring was 50 rpm. The amount of prednisolone was 5mg in all formulation. The dosage forms were placed in the 900ml of 0.1N HCL maintained at 37±2° c at appropriate intervals 10ml of the sample were taken & filtered through a 0.45um milipore filter. The dissolution media was then replaced by 10ml fresh 0.1N HCL to maintain a constant volume. After proper dilution the samples were then analysed at 246nm by UV visible spectrophotometer then the mean of three determinations was used to calculate the drug release from each of the formulations. Cumulative % drug release was plotted as a function of time & drug release in 5 minutes (Q%) was calculated.
Drug Release Kinetics
Data obtained from *In-vitro* release studies were fitted to various kinetics models to find out the mechanism of drug release from liquisolid tablets**.** Kinetics models used for *In-vitro* drug release from tablets:
• Zero order release kinetic model.
• First order release kinetic model.
• Higuchi Model.
*Zero order Kinetics*
According to this model, under standard condition of temperature and agitation, the dissolution medium, the dissolution rate model can be described by the equation.
$dq/dt = K_0$
or, Expressing in an integrated form
$q = K_0t$
Where, q = amount of drug released per unit surface area.
$K_0$ = zero order release rate constant
t = time
A plot of q vs. t gives a straight line.

*First order Release Kinetics (Noyes Whitney's Equation):*
According to Noyes Whitney, under standard condition of agitation and temperature, the dissolution rate process for solids can be described by the equation.
$dq/dt = K_1(Cs–Ct)$
Under Sink condition, i.e. when Ct < 0.15 Cs, the equation becomes,
$dq/dt = K_1Cs$

**Table-1 Solubility of Prednisolone in Various solvents**

| Liquid vehicle | Solubility(mg/ml) |
|---|---|
| Polyethylene glycol 400 | 4.7348 |
| Propylene glycol | 10.4772 |
| Polysorbate 80(tween 80) | 3.6420 |
| Glycerin | 5.8227 |
| Distilled water | 0.0142 |

or in an integrated form
$\ln q_0/q = K_1Ct$
Where, q=amount of drug released per unit surface area.
$K_1$=First order release rate constant
$q_0$= initial amount.
Cs= Saturation solubility
Ct = Concentration at time t.
A plot of log % amount drug release vs time gives a straight line with a negative slope.
*Higuchi Model Kinetics*
For coated or matrix type dosage form, the dissolution medium enters the dosage form in order for the drug to be released and diffused into the bulk solution. In such cases, often the dissolution follows the equation proposed by Higuchi.

$$Q = \left[ D_E(2A - EC_s)\frac{C_s}{t} \right]^{0.5}$$

or, $Q = K_{HG}\, t^{0.5}$
Where, Q= Amount of drug released per unit surface area of the dosage form
D = Difusion Co-efficient of the drug.
E = Porosity of the matrix.
T = Tortuosity of the matrix.
$C_s$ = Saturation solubility of the drug in the surrounding liquid.
$K_{HG}$ = Higuchi release rate constant.
t = time
Fitness of the data into various kinetics models were assessed by determining the correlation co-efficient, the rate constants, for respective models were also calculated from slope.
*Korsmeyer-Peppas Model*
Korsmeyer *et al*. (1983) derived a simple relationship which described drug release from a polymeric system. To evaluate the mechanism of drug release from matrix tablet, data for the first 60% of drug release were plotted in Korsmeyer et al's equation as log cumulative percentage of drug released vs. log time and the exponent n was calculated through the slope of the straight line.
$Mt/M8 = K\, t^n$
where Mt/M*8* is the fractional solute release, t is the release time, K is a kinetic constant characteristic of the drug/polymer system, and n is an exponent that characterizes the mechanism of release of tracers. For cylindrical matrix tablets, if the exponent n = 0.45, then the drug release mechanism is Fickian diffusion, and if 0.45 < n < 0.89, then it is non-Fickian or anomalous diffusion. An exponent value of 0.89 is indicative of Case-II Transport or typical zero-order release.

**Stability Study:**
Acclerated stability studies were carried out for the optimized formulation as per ICH guidelines. Optimized tablet formulation (LS-1) were packed and stored at 40ºC/75% RH upto **one months** in stability chamber. In the specified time interval the In-vitrodrug release rate was determined.

## RESULT AND DISCUSSION

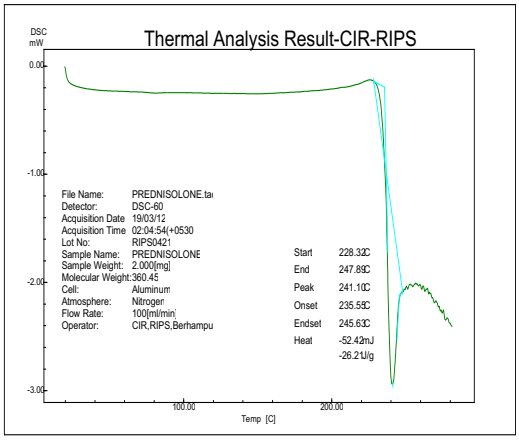


**Fig-1 DSC of Pure Prednisolone**

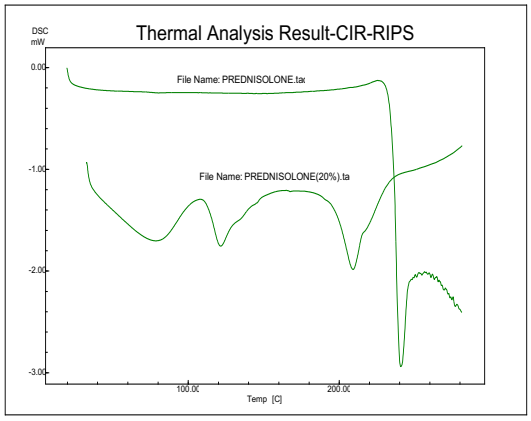


**Fig-2 Comparison between DSC of pure Prednisolone & optimized formulation**

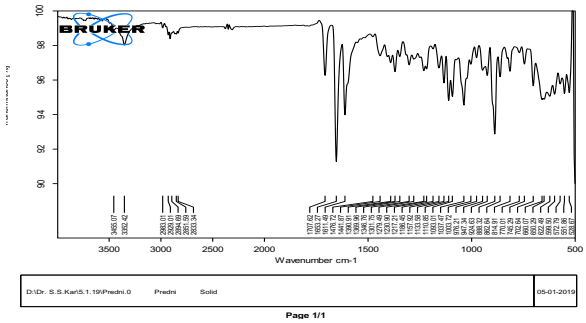


**Fig-3 FTIR of pure Prednisolone**

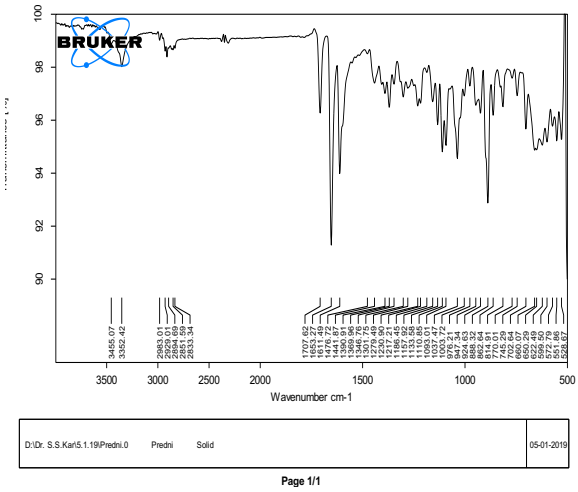


**Fig-4 FTIR of Optimized liquisolid compact (LS-1) of Prednisolone**

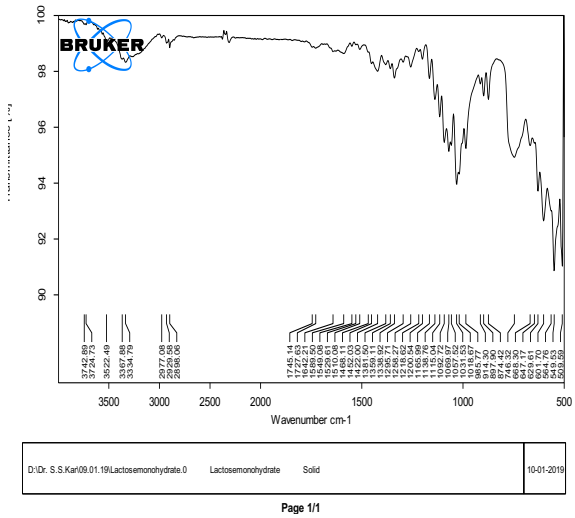


**Fig-5 : FTIR of Prednisolone with lactose monohydrate as a carrier**

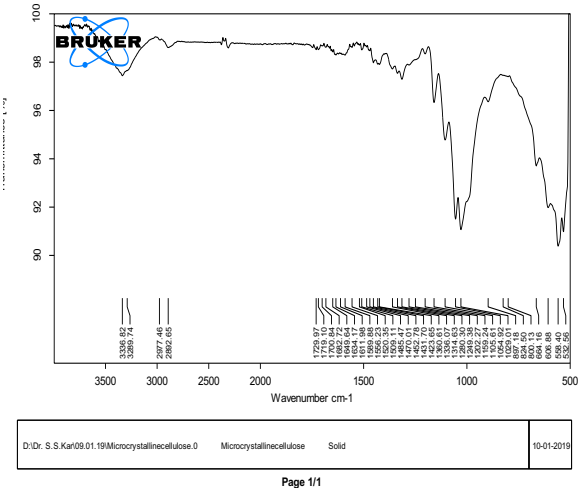


**Fig-6: FTIR of Prednisolone withmicro crystalline celluloseas a carrier**

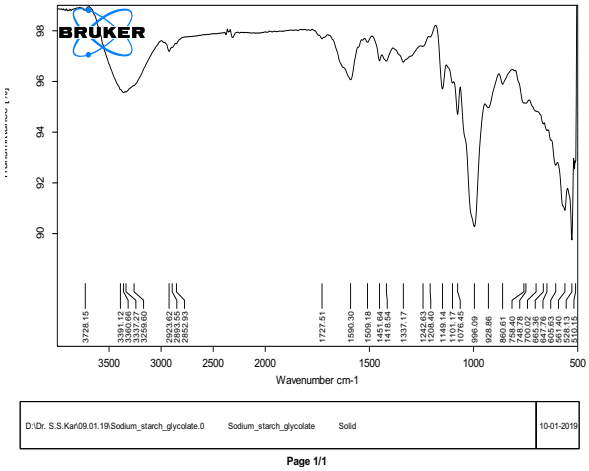


**Fig-7: FTIR of Prednisolone with sodium starch glycolates a carrier**

**Analytical methods used for estimation of Prednisolone**

An accurately weight of 0.05gm Prednisolone was taken in a clean 100ml volumetric flask, then volume was makeup up to 100ml with Acetonitrile:Methanol in ratio of 30:70 & shaken vigorously to yield a clear solution of 500µg/ml by using Acetonitrile:Methanol .Then different concentration like 4µg/ml,8µg/ml,12µg/ml,16µg/ml,20µg/ml was prepared

**Determination of $\lambda_{max}$**

A particular concentration from the stock solution was scanned from 200-300nm wavelength range in UV visible spectrophotometer (double beam UV visible spectrophotometer shimadzu uv-1700). From the scanning report it was evident that the wavelength of maximum absorbance λmax of prednisolone was found at 246nm as show in Fig.

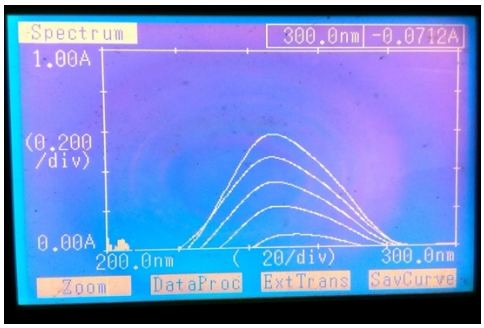


Fig 7 Spectrum of Prednisolone

**Table- 2 Calibration table of Prednisolone.**

| Sl.no | Concentration | Absorbance |
|---|---|---|
| 01 | 00 | 00 |
| 02 | 8µg/ml | 0.1875nm |
| 03 | 12µg/ml | 0.3117nm |
| 04 | 16µg/ml | 0.4529nm |
| 05 | 20µg/ml | 0.5582nm |

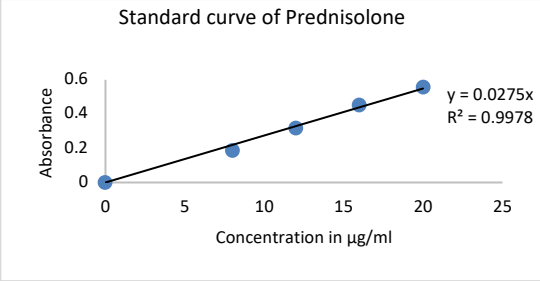


**Fig.8 Standard curve of Prednisolone in Propylene glycol**

**Table 3: Formulation design of prednisolone directly compressed tablet**

| Ingredients | Directly compressed (DC-1)mg |
|---|---|
| Prednisolone | 5mg |
| Microcrystalline cellulose | 80mg |
| Lactose monohydrate | 40mg |
| Silica gel G | 10mg |
| Sodium starch glycolate | 10mg |
| Unit Weight | 145mg |

**Table 4: Formulation characteristics of prepared prednisolone liquisolid compacts**

| Liquisolid system | Liquid vehicle | Drug concentration %w/w | $R_f$value | Liquid load factor | Unit dose weight(mg) |
|---|---|---|---|---|---|
| LS-1 | PG | 10 | 12 | 0.165 | 142.5 |
| LS-2 | PG | 12.5 | 12 | 0.155 | 135.5 |
| LS-3 | PG | 15 | 12 | 0.136 | 140.5 |
| LS-4 | PG | 17.5 | 12 | 0.132 | 138.5 |
| LS-5 | PG | 20 | 12 | 0.145 | 152.6 |
| LS-6 | PG | 22.5 | 12 | 0.149 | 139.3 |
| LS-7 | PG | 25 | 12 | 0.138 | 148.7 |
| LS-8 | PG | 30 | 12 | 0.152 | 131.9 |
| LS-9 | PG | 40 | 12 | 0.156 | 121.6 |
| LS-10 | GLY | 10 | 12 | 0.163 | 165.9 |
| LS-11 | PEG | 10 | 12 | 0.156 | 143.8 |
| LS-12 | T80 | 10 | 12 | 0.146 | 149.6 |

**Table-5 Physical Properties of Prednisolone Liquisolid compacts**

| Formulation | Weight Variation(mg) | Hardness ($Kg/Cm^2$) | Friability(%) | Drug Content Uniformity (%) |
|---|---|---|---|---|
| LS-1 | 132.5±0.15 | 5.5±0.15 | 0.15 | 95.8±1.74 |
| LS-2 | 145.23±1.05 | 5.3±0.28 | 0.22 | 97.2±0.28 |
| LS-3 | 133.2±0.83 | 5.6±0.67 | 0.18 | 93.4±0.49 |
| LS-4 | 138.22±1.44 | 5.4±0.72 | 0.24 | 99.1±0.71 |
| LS-5 | 144.23±.79 | 5.0±.96 | 0.21 | 99.2±0.35 |
| LS-6 | 135.45±0.33 | 5.9±.74 | 0.14 | 98.2±0.70 |
| LS-7 | 135.87±0.34 | 4.35±0.23 | 0.23 | 98.34±0.45 |
| LS-8 | 134.45±0.98 | 5.1±0.56 | 0.34 | 97.34±0.67 |
| LS-9 | 138.23±0.24 | 5.4±0.34 | 0.23 | 98.34±0.87 |
| LS-10 | 137.12±0.78 | 4.9±0.87 | 0.45 | 97.67±0.34 |
| LS-11 | 136.32±0.62 | 4.34±0.56 | 0.23 | 98.23±0.65 |
| LS-12 | 138.31±0.11 | 5.1±0.34 | 0.43 | 96.34±0.67 |
| DC-1 | 135.25±0.21 | 5.3±0.31 | 0.36 | 95.34±0.65 |

**Table-6 Drug Release profile for Conventional liquisolid compacts of Prednisolone (DC-1)**

| TIME IN MIN | % CUMULATIVE DRUG RELEASE |
|---|---|
| 0 | 0 |
| 5 | 15.31±0.23 |
| 15 | 16.37±0.31 |
| 30 | 17.37±0.52 |
| 45 | 19.27±0.45 |
| 60 | 20.28±0.32 |
| 75 | 22.21±0.12 |
| 90 | 23.23±0.31 |
| 105 | 24.26±0.46 |
| 120 | 25.29±0.73 |
| 135 | 27.24±0.89 |
| 150 | 28.29±0.14 |
| 165 | 29.34±0.36 |
| 180 | 31.31±0.36 |

**Table-7 Drug Release profile for liquisolid compacts (LS-1)**

| TIME IN MIN | % CUMULATIVE DRUG RELEASE |
|---|---|
| 0 | 0 |
| 5 | 30.85±0.79 |
| 15 | 34.56±0.45 |
| 30 | 36.52±0.63 |
| 45 | 42.63±0.52 |
| 60 | 45.98±0.36 |
| 75 | 47.36±0.47 |
| 90 | 52.96±0.95 |
| 105 | 55.36±0.85 |
| 120 | 59.21±0.96 |
| 135 | 63.36±0.68 |
| 150 | 67.25±0.57 |
| 165 | 71.25±0.63 |
| 180 | 73.12±0.96 |

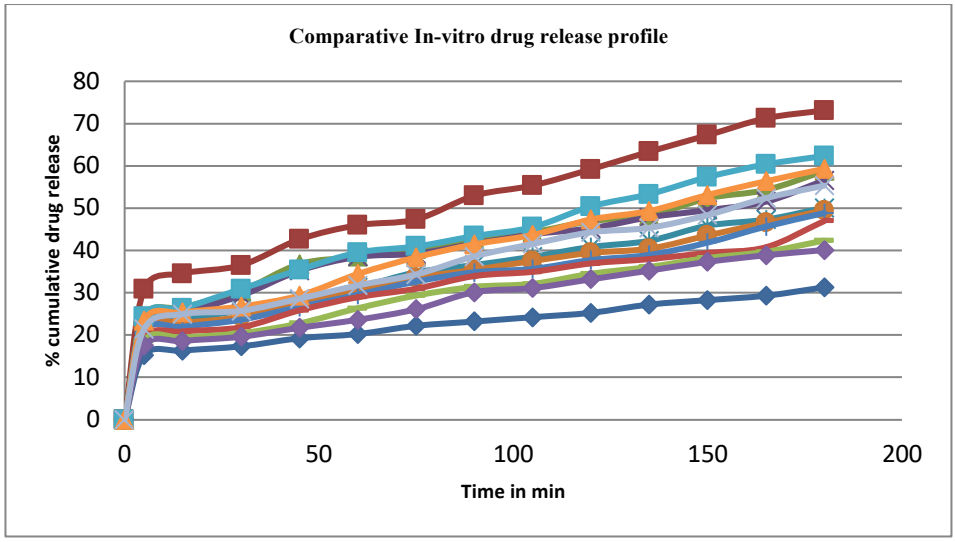


**Fig 9 Comparative In vitro drug Release profile of different Prednisolone liquisolid Tablet**

**Table 8 Release kinetics of different liquisolid formulation LS-1-LS-12**

| Formulation | Zero order($R^2$) | First order($R^2$) | Higuchi($R^2$) | Korsemeyer-peppas ($R^2$) |
|---|---|---|---|---|
| LS-1 | 0.995 | 0.975 | 0.976 | 0.995 |
| LS-2 | 0.937 | 0.870 | 0.989 | 0.964 |
| LS-3 | 0.926 | 0.875 | 0.988 | 0.970 |
| LS-4 | 0.897 | 0.860 | 0.965 | 0.932 |
| LS-5 | 0.995 | 0.978 | 0.969 | 0.989 |
| LS-6 | 0.880 | 0.819 | 0.965 | 0.934 |
| LS-7 | 0.853 | 0.804 | 0.949 | 0.923 |
| LS-8 | 0.759 | 0.695 | 0.892 | 0.845 |
| LS-9 | 0.997 | 0.985 | 0.964 | 0.987 |
| LS-10 | 0.945 | 0.892 | 0.983 | 0.970 |
| LS-11 | 0.939 | 0.880 | 0.981 | 0.964 |
| LS-12 | 0.929 | 0.867 | 0.982 | 0.961 |

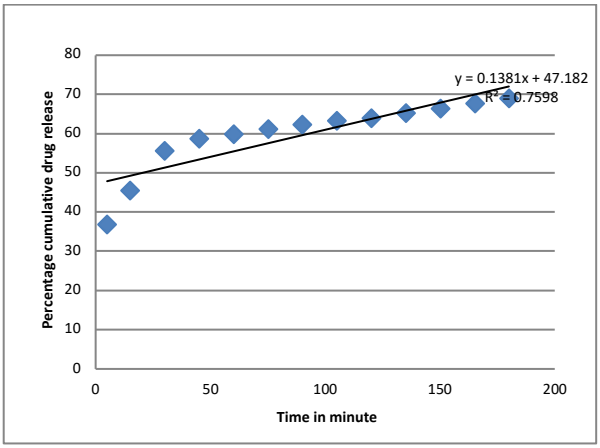


**Fig 10 Zero order kinetics of optimized formulation**

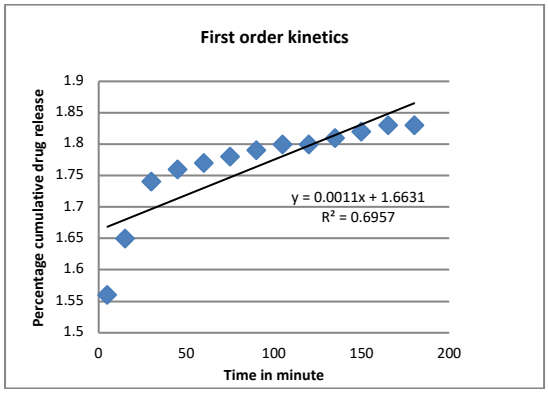


**Fig 11 first order kinetics of optimized formulation**

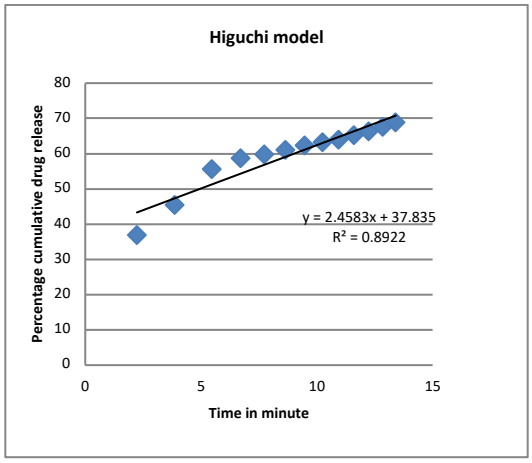


**Fig 12 Higuchi kinetics of optimized formulation**

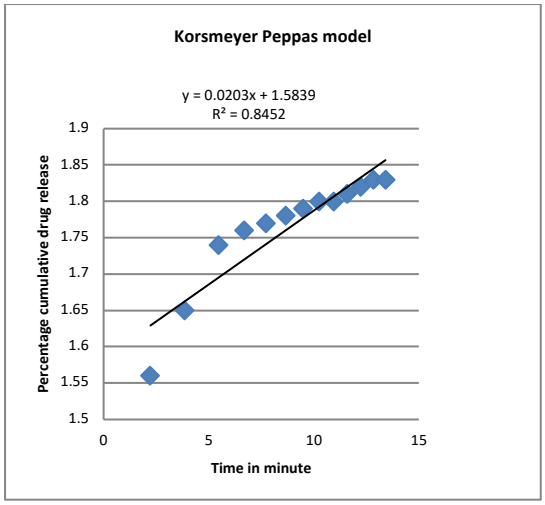


**Fig 13 Korsmeyer Peppas model of optimized formulation**

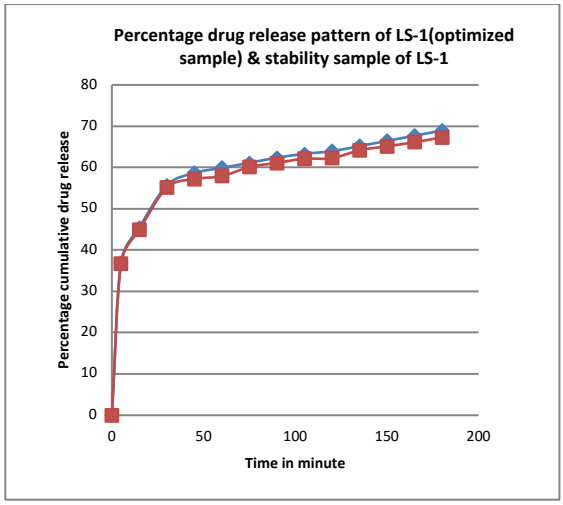


**Fig14 Comparative percentage drug release study between LS-1 & stability sample of LS-1**

**Table 9- Stability Study of optimized formulation (LS-1)**

| Parameters | Initials | 5th day ($40^0$c/75%RH) | 10th day ($40^0$c/75%RH) | 15th day ($40^0$c/75%RH) | 20th day ($40^0$c/75%RH) | 25th day ($40^0$c/75%RH) | 30th day ($40^0$c/75%RH) |
|---|---|---|---|---|---|---|---|
| Description | Yellowish white | Same | Same | Same | Same | Same | Same |
| Av.weight(mg) | 143.2 | 143.1 | 143.1 | 143.1 | 143.1 | 143.1 | 143.1 |
| Hardness(kg/cm$^2$) | 5.1 | 5.1 | 5.2 | 5.1 | 5.1 | 5.1 | 5.2 |
| Dissolution(min) | | | | | | | |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 30.85 | 30.86 | 30.87 | 30.87 | 30.87 | 30.87 | 30.87 |
| 15 | 34.56 | 34.57 | 34.58 | 34.58 | 34.58 | 34.58 | 34.58 |
| 30 | 36.52 | 36.53 | 36.54 | 36.54 | 36.54 | 36.54 | 36.54 |
| 45 | 42.63 | 42.64 | 42.65 | 42.65 | 42.65 | 42.65 | 42.65 |
| 60 | 45.98 | 45.99 | 45.99 | 45.99 | 45.99 | 45.99 | 45.99 |
| 75 | 47.36 | 47.37 | 47.37 | 47.37 | 47.37 | 47.37 | 47.37 |
| 90 | 52.96 | 52.97 | 52.97 | 52.97 | 52.97 | 52.97 | 52.97 |
| 105 | 55.36 | 55.37 | 55.37 | 55.37 | 55.37 | 55.37 | 55.37 |
| 120 | 59.21 | 59.22 | 59.22 | 59.22 | 59.22 | 59.22 | 59.22 |
| 135 | 63.36 | 63.37 | 63.37 | 63.37 | 63.37 | 63.37 | 63.37 |
| 150 | 67.25 | 67.26 | 67.27 | 67.27 | 67.27 | 67.27 | 67.27 |
| 165 | 71.25 | 71.26 | 71.27 | 71.27 | 71.27 | 71.27 | 71.27 |
| 180 | 73.12 | 73.13 | 73.14 | 73.14 | 73.14 | 73.14 | 73.14 |

## CONCLUSION

An attempt was made to develop the liquisolid compacts of Prednisolone to achieve fast dissolving effect and to enhance the bioavailabilty. From the in-vitro drug release studies the optimized formulation LS-1 showed fast drug release when compared to the conventional tablet. The dissolution efficiency was found to increase by two times with compared to conventional tablet. In conclusion, the liquisolid compacts technique can be a promising alternating for the formulation of water insoluble drugs, such as Prednisolone into rapid release tablets. The higher dissolution rates displayed by liquisolid compacts may also imply enhanced oral bioavailability due to the increased wetting properties & surface of drug available for dissolution.

## REFERENCES.


1. Javadzadeh Y. Siahi-Shadbad M.R., Barzegar-Jalali M., Nokhodchi A. “Enhancement of dissolution rate of piroxicam using liquisolid compacts.”Il Farmaco . 2005;60(4):361-365.z
2. Javadzadeh, Mohd.lezasiahi,asnaashari solmaz. “An investigation of physicochemical properties of piroxicam liquid-solid compacts”. Pharmaceutical development and technology. 2007 ;( 12):337-343.
3. Spireas, S . Sadu, S : Grover, R. “In vitro release evaluation of hydrocortisone liquisolid tablets”.J-pharm-sci.1998;87(7):867-872.
4. Yousef Javadzadeh, Baharak Jafari-Navimipour, Ali Nokhodchi “.Liquisolid technique for dissolution rate enhancement of a high dose water-insoluble drug” (carbamazepine)Inter J Pharm. 2007;341( 1-2):26-34.
5. Ngiik Tiong and Amal A. Elkordy. “liquisolid technique in improving the dissolution profiles of naproxen in a solid dosage form.” Euro J Pharm And BioPharm. 2009;73(3):373-384.
6. Rania H. Fahmy, Mohammed A. Kassem “Enhancement of famotidine rate through liquisolid tablets formulation in vitro and in vivo evaluation.”Euro J Pharm and Biopharm. 2008; 69(3):993-1003.
7. VB Yadav, AV Yadav, “Improvement of solubility And dissolution Of Indomethacin by liquisolid compact granulation technique”. J.Pharm Sci& Research;2009(1):44-51.