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DEVELOPMENT OF FAST RELEASE FORMULATION FOR DISSOLUTION RATE ENHANCEMENT

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ABSTRACT

The present work are to enhance the drug loading capacity in liquisolid system, increase the flow property due to decrement in required volume of nonvolatile solvent and enhance the solubility of drug in nonvolatile solvent by using mixed solvency concept. Naproxen was selected as model poorly water soluble drug for exploring the mixed solvency concept to enhance the solubility and hence to enhance the release rate of drug. The proposed formulation is aimed to enhance solubility of naproxen by employing mixed solvency concept and to develop the fast release capsule of naproxen by using liquisolid technique.

KEYWORDS: Liquisolid system, Naproxen, mixed solvency concept.

INTRODUCTION

There are following approaches can be employed to enhance the aqueous solubility of poorly soluble drugs.[2]

- ✓ Alteration of pH
- ✓ Use of co solvents
- ✓ Effect of dielectric constant
- ✓ Use of surface active agents
- ✓ Complexation
- ✓ Hydrotropic solubilization
- ✓ Chemical modification of the drug

The above mentioned approaches have been used widely in various fields of pharmacy. However, applications of 'Hydrotropic' and 'Mixed Hydrotropic Solubilization' have not been explored to appreciable extent in various fields of pharmacy.

Mixed Solvency

Mixed solvency approach has been applied for enhancement of aqueous solubility of poorly water soluble drug .All substances whether liquids, gases or solids possess solubilizing power and hence concentrated aqueous solution containing various dissolved substances can also improve the solubility[1] of poorly water soluble drugs.In supercritical fluid technology liquefied carbon dioxide acts as solvent for many insoluble substances. These points indicate that all substances possess some solvent character.[3,4]

Application

In Pharmaceutical Analysis

In Pharmaceutical Formulation Development

Methods employed for developing Fast-release Dosage form[5]

Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to obtain rapid and complete systemic drug absorption. Such fast-release system results in relatively rapid drug absorption and fast onset of action. There have been a number of formulation approaches explored and widely practiced in the pharmaceutical industry to improve delivery of poorly water soluble compounds especially in development of fast release dosage forms. These delivery approaches are based on various techniques, such as

- ✓ Particle size reduction
- ✓ Formation of the prodrugs/ salts
- ✓ Use of co-solvent
- ✓ Complexation with the excipients such as cyclodextrin
- ✓ Solid dispersion
- ✓ Liquisolid dispersion

Liquisolid Technique[6]

Liquisolid technique is the most promising method for promoting dissolution rate of poorly water-soluble drugs. liquisolid compacts were evolved from Powdered Solutions' which depended on preparing a true solution of the drug in a high boiling point, water miscible

solvent, which was carried out on the extensive surface of an inert carrier such as silica. "Liquisolid system refers to formulations formed by conversion of liquid drugs, drug suspensions or drug solution in non-volatile solvents into dry, nonadherent, free-flowing and compressible powder mixtures by blending the suspension or solution with selected carriers and coating materials". Liquisolid system is a novel concept of drug delivery via oral route. This technique is applied to water insoluble drugs and lipophilic drugs to sustain their release.[7]

General method of preparation of Liquisolid[6]

A drug substance is initially dispersed in the nonvolatile solvent systems (Polysorbate 80, PEG-200) termed as liquid vehicles with different drug: vehicle ratios. Then a mixture of carrier or different polymers and excipients is added to the above liquid medication under continuous mixing. Then to the above binary mixture the disintegrant like sodium starch glycolate and other remaining additives are added and mixed for a period of 10 to 20 min. The final mixture is compressed in the formulation of tablets (or encapsulated in hard gelatin capsules) using the tableting machine. The final liquisolid granules are characterized for solubility, dissolution,flowability, compressibility and other physicochemical properties.

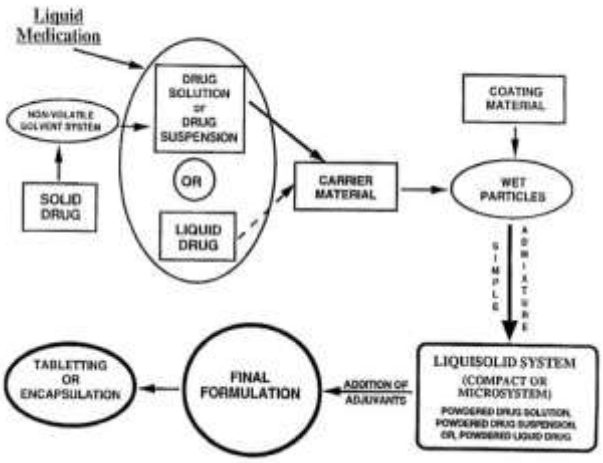


Fig. 1.3: Flow diagram of liquisolid system[8].

2. Advantages [6,9]

Liquisolid systems are low cost formulations than soft gelatine capsules.

Production is similar to that of conventional tablets.

Drug release can be modified using suitable formulation ingredients Drug can be molecularly dispersed in the formulation.

Capability of industrial production is also possible.

Enhanced bioavailability can be obtained as compared to conventional tablets.

3.Applications [6]

Solubility and Dissolution Improvement Flowability and Compressibility

Designing of Controlled Release Tablets Bioavailability Enhancement

4.Evaluations [6]

Flow Behavior

Angle of Repose

Differential Scanning Calorimetry (DSC)

Powder X-Ray Diffraction

Scanning Electron Microscopy (SEM)

Dissolution Testing of Liquisolid Formulations

Material and Methods

Drug- Naproxen

Propylene glycol	solvent
Microcrystalline amorphous cellulose-(Avicel PH 102	carrier
Silicon dioxide-(Aerosil 200)	coating material
PVP, PEG,SB (diff. grade)	solubilizer
Tween 80	Dissolution media

Preformulation studies of Naproxen

Calibration curve of Naproxen in Methenol

Accurately weighed quantity of naproxen (50 mg) was dissolved in about 35 ml of methanol in 50 ml volumetric flask and the volume was made upto 50 ml by methanol. The concentration of this resulting solution (stock solution) was 1000 µg/ml. Aliquots of the above solution were taken and diluted with methanol to get naproxen concentration in the range of 40-160 µg/ml. The resulting dilutions were analyzed at 332 nm on Shimadzu -1700 UV spectrophotometer against methanol blank. The absorbance data are shown in the table and graphically represented in fig.

Table 1: Calibration curve data of naproxen in methanol at 332 nm.

S. no.	Concentration (□g/ml)	Absorbance (mean ± S.D.) (N=3)
1.	0	0 ± 0
2.	40	0.419 ± 0.005
3.	80	0.825 ± 0.017
4.	120	1.21 ± 0.009
5.	160	1.61 ± 0.014

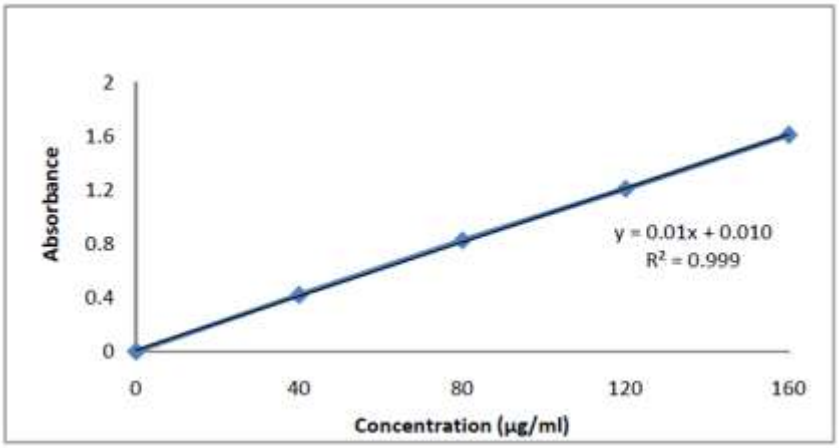


Fig. 1: Calibration curve of naproxen in methanol at 332 nm.

Determination of Solubility

About 5 ml of D.M. water was taken in a vial and excess amount of drug was added. The vial was sealed with rubber closure and aluminium seal. It was shaken for 12 hr in Orbital Flask Shaker (Khera Instruments Pvt. Ltd., India) and allowed to equilibrate for 24 hrs in undisturbed condition. Then the solution containing the excess undissolved drug was centrifuged at 2200 r.p.m. for 5 minutes in ultra-centrifuge and was filtered through Whatman grade 5 filter. Aliquot was suitably diluted with demineralised water and analyzed using UV spectrophotometer at 330.0 nm. Same procedure was repeated for remaining solvent except one thing in case of viscous solvent like PEG 200, 300, 400 and PG (these were not filtered after centrifuge and clear supernatant were taken with the help of micropipette from centrifuge tube) to determine the solubility of naproxen. Results are shown in table.

Table 2: Solubility of naproxen in various solvents.

S.no.	Solvent	Solubility of naproxen (mg/ml)
1	D. M water	0.0855
2	SGF	0.0241
3	Ethanol	41.097
4	Methanol	53.277
5	PEG 200	81.463
6	PEG 300	118.848
7	PEG 400	111.979
8	Propylene glycol	33.585

Drug excipient interaction study

This study was performed to determine any physical change in the drug when kept in contact with solubilizers/excipients under different storage conditions for one month. Drug and solubilizers/excipients were mixed in 1:1 ratio and divided into three parts. These parts were sealed in vials and kept under different conditions. Two vials of each sample were kept at room temperature, in the oven at 40ºC and in refrigerator for one month period. After every seven days for one month, the vials were withdrawn and any change in physical appearance and color of the contents were observed. The observations are recorded in table

Table 3: Physical interaction studies of drug with solubilizers/excipients.

S. N.			Refrigerator Roomc)								
			wk	wk	wk	wk	wk	wk	wk	wk	wk
1.	Naproxen + SB	White powder	NC	NC	NC	NC	NC	NC	NC	NC	NC
2.	Naproxen + PEG 4000	White powder	NC	NC	NC	NC	NC	NC	NC	NC	NC
3.	Naproxen + PEG 200	Transparent liquid	NC	NC	NC	NC	NC	NC	NC	NC	NC
4.	Naproxen + PVP	White powder	NC	NC	NC	NC	NC	NC	NC	NC	NC
5.	Naproxen + Urea	White powder	NC	NC	NC	NC	NC	NC	NC	NC	NC
6.	Naproxen + Niacinamide	White powder	NC	NC	NC	NC	NC	NC	NC	NC	NC
7.	Naproxen + Avicel PH 102	White powder	NC	NC	NC	NC	NC	NC	NC	NC	NC
8.	Naproxen + Aerosil 200	White powder	NC	NC	NC	NC	NC	NC	NC	NC	NC
9.	Naproxen + PG	Transparent liquid	NC	NC	NC	NC	NC	NC	NC	NC	NC

NC – No change, wk - Week

SB – Sodium Benzoate, PG – Propylene glycol

Development of Fast-release Formulation

1. Selection of solvent

Development of fast release formulation by liquisolid system, a non-volatile solvent is required. Non-volatile solvent should be inert, high boiling point, preferably water-miscible

and not highly viscous organic solvent systems like propylene glycol, liquid polyethylene glycols, polysorbates, glycerin etc.

Drug should be in dispersion or solution form in non-volatile solvent. If it is in solution form then chances of fast dissolution will be more.

PEG 200 was selected as non-volatile solvent but since it was not found good solvent for sodium benzoate &niacinamide, therefore 20% water was incorporated to enhance the solubility of sodium benzoate &niacinamide in PEG 200.

Propylene glycol was found a good solvent for PEG 4000 & PVP (M.wt. 40,000).
PVP 40,000 was used in complete experiment.

Solubility can be increased by mixed-solvency concept and either increases the drug loading capacity in system or decreases excipients ratio to achieve free flow of formulation and make them as a strong solvent for naproxen

Selection of carrier material

Carrier material should be porous which has sufficient absorption properties such as microcrystalline and amorphous cellulose, which has to contribute in liquid absorption. Literatures revealed that microcrystalline cellulose has greater absorption capacity and hence it is first line material for liquisolid technique.

Avicel PH 102 was selected as the carrier material after thorough literature survey.

Selection of Coating material

Coating material should be very fine and possessing highly adsorptive property such as various types of amorphous silicon dioxide (silica). Coating material contributes in covering the wet carrier particles and adsorbs excess liquid and gives the dry looking powder. Due to coating material, flow property of liquisolid mass also increases.

Aerosil 200 was selected as the coating material after thorough literature survey.

Effect of various parameters on Dissolution rate of Liquisolid Dispersion

Various parameters effect the dissolution property of liquisolid system. Effect of following parameters or factors on dissolution property of liquisolid system were studied.

Type of Non-Volatile Solvent System

Two non-volatile solvents, blend A [PEG 200: Water (8:2)] and propylene glycol were selected to observe the effect on dissolution rate of liquisolid system.

Type of Solubilizers And Drug Loading

Effect of solubilizers on dissolution rate of liquisolid system was also studied. Different solubilizers were taken in formulation and the effect on dissolution rate was observed.

Carrier to Coating Material Ratio

Effect of carrier to coating material ratio on dissolution rate of liquisolid system was also studied. For this study 22:1, 18:1, 14:1 and 10:1 ratio of carrier to coating material were taken in formulation.

Revolution Per Minute (Rpm)

50 and 100 rpm were selected to observe the effect of rpm on dissolution rate in liquisolid system. USP apparatus –I (basket type) was selected for this purpose.

Dissolution Media

Simulated gastric fluid and simulated gastric fluid containing 0.75% v/v tween 80 were selected to observe the effect of dissolution media on dissolution rate in liquisolid system. Simulated gastric fluid containing 0.75% v/v tween 80 provided the sink condition.

Preparation of Liquisolid Dispersion

Preparation of Drug Solution

To prepare the drug solution, required quantity of non-volatile solvent blend A [PEG 200 : Water (8:2)] or propylene glycol was taken in the vial. Solubilizers were added into this and vortexing was done for 15-30 min. To dissolve solubilizers in propylene glycol, 30 min heating was required at 50ºC after vortexing. After complete dissolution of solubilizers, calculated amount of naproxen was added and vortexing was done for 15 min to dissolve it. Thus drug solution of naproxen was prepared.

Table 4: Selected non-volatile solvent with different solubilizers for optimization of Batches.

S.no.	Non-volatile solvent	Solubilizers	Solubility (% w/v)	Considered solubility (% w/v)
1	Blend A	15% SB	16.03	15
2	Blend A	5%PVP+5%PEG4000+5%N+5%SB	8.47	8
3	Propylene glycol	40% PEG 4000	11.30	10
4	Propylene glycol	20% PVP+20% PEG 4000	13.93	12

Preparation of Liquisolid mass

To prepare liquisolid mass, required amount of drug solution was taken in mortar and 1/3rd portion of avicel PH102 was added into it and 10 min mixing was done using pestle. Rest two parts of avicel were also added by geometric dilution method into it and mixed well for 10-10 min. Above powder mixture was taken out from mortar and required quantity of aerosol 200 as adsorptive material was taken in mortar. Small-2 portion of above powder mixture was added and mixed well. The above powder blend was mixed with aerosil 200 by geometric dilution method using pestle & mortar. After proper mixing about 30 min., the liquisolid dispersion; so obtained, was passed through sieve no. 80.

Dissolution rate study

Dissolution tests are one of the most widely used tests in quality control of dosageforms. Dissolution tests become especially important when dissolution is the ratelimiting step as in the case of B.C.S. class II or B.C.S. class IV drugs.

In order to select the optimum batch of liquisolid dispersion for final formulation, dissolution rate studies were performed. The ratio of carrier to coating material inliquisolid dispersion with highest dissolution rate i.e. fastest dissolution was selectedfor preparing immediate release of the final formulation.

Procedure

Required number of capsules containing liquisolid dispersion and pure drug equivalent to 50 mg of naproxen were tested in dissolution rate studies using U.S.P. XXIV (type I) dissolution test apparatus (Model TDT6P, Electro lab Mumbai, India) with basket rotation at 50 and 100 r.p.m. Dissolution studies were conducted in two media, 900 ml of simulated gastric fluid (pH 1.2) and simulated gastric fluid containing 0.75% tween 80 (pH 1.2). Temperature was maintained at 37+ 0.5°C. At definite time intervals 5 ml of the sample was withdrawn and

filtered through Whatman grade 5 filter and analyzed for drug content spectrophotometrically at 332 nm. Withdrawn samples were also replaced with fresh dissolution media. Calculations for the amount of drug were done using respective regression equations.

In order to obtain the sink condition for dissolution rate, solubility of naproxen was determined in SGF containing different concentration of tween 80. The results are shown in **table.**

Table 5: Determination of tween 80 concentration in SGF for sink condition.

S.no.	Concentration of tween 80 (% v/v)	Solubility of Naproxen(%w/v)	Minimum volume required for 3 times the sink conditions (ml)
1	0	0.0024	2083.33
2	0.5	0.0106	1402.23
3	0.75	0.0173	866.91
4	1.0	0.0228	657.68
5	1.5	0.0316	474.46
6	2.0	0.0500	299.67
7	2.0	0.0592	253.25
8	3.0	0.0693	216.38
9	3.5	0.0778	192.67
10	4.0	0.0900	166.56
11	4.5	0.1053	142.35
12	5.0	0.1196	125.42

Table shows solubility of naproxen at different concentrations of tween 80 in simulated gastric fluid needed for sink condition. 0.75% v/v tween 80 was sleeted as a solubilizer to provide the sink condition.

Optimization studies

Preparation of Different batches for optimization studies

Batches of liquisolid dispersion were prepared by the similar procedure which was described in table shows the composition of different batches of liquisolid dispersion.

Blend A [PEG200 : Water (8:2)] as a non -volatile solvent and 15% sodium benzoate (w/v) as a solubilizer was used for batches LSD1 to LSD4 for preparing liquisolid dispersion.

Blend A [PEG200 : Water (8:2)] as a non -volatile solvent and 5%PVP+5%PEG4000+ 5%N +5%SB (w/v) as a solubilizers were used for batches LSD5 to LSD8 for preparing liquisolid dispersion.

Table 7.1: Composition of liquisolid dispersion in different batches.

S. no.	Batch code	Carrier : Coating	Quantity taken		Aerosil (mg)	Total weight (mg)
			*Drug solution (w/v) (mg)	PH102 (mg)		
1	LSD1	22:1	191.5	818.4	37.2	1047.1
2	LSD2	18:1	191.5	669.6	37.2	898.3
3	LSD3	14:1	191.5	520.8	37.2	749.5
4	LSD4	10:1	191.5	372.0	37.2	600.7
5	LSD5	22:1	372.0	818.4	37.2	1227.6
6	LSD6	18:1	372.0	669.6	37.2	1078.8
7	LSD7	14:1	372.0	520.8	37.2	930.0
8	LSD8	10:1	372.0	372.0	37.2	781.2
9	LSD9	22:1	208.0	818.4	37.2	1063.6
10	LSD10	18:1	208.0	669.6	37.2	914.8
11	LSD11	14:1	208.0	520.8	37.20	766.0
12	LSD12	10:1	208.0	372.0	37.2	617.2
13	LSD13	22:1	245.0	818.4	37.2	1100.6
14	LSD14	18:1	245.0	669.6	37.2	951.8
15	LSD15	14:1	245.0	520.8	37.2	803.0
16	LSD16	10:1	245.0	372.0	37.2	654.20

***Weight of drug solution containing 25 mg of naproxen

Propylene glycol as a non-volatile solvent and 20% PVP + 20% PEG 4000 (w/v) as a solubilizers were used for batches LSD9 to LSD12 for preparing liquisolid dispersion.

Propylene glycol as a non-volatile solvent and 40% PEG 4000 (w/v) as a solubilizer was used for batches LSD13 to LSD16 for preparing liquisolid dispersion.

Determination of drug content in Liquisolid Dispersion

Powdered liquisolid dispersion equivalent to 25 mg of naproxen was accurately weighed and transferred into a 50 ml volumetric flask. Approximately 25 ml of methanol was added and flask was shaken about 10 min and kept for sonication about 15 min to dissolve the drug. Further 20 ml of methanol was added and sonicated about 15 min again. Finally volume was made upto the mark with methanol. After filtration through Whatman grade 5 filters. One ml of the filtrate was diluted upto 10 ml with methanol and absorbance of the solution was measured spectrophotometrically at 332 nm against methanol as blank. Results of the analysis are shown in table.

To confirm drug content uniformity drug content was determined in triplicate for each batch. Upper, middle and lower, three points were selected for triplicate study for each batch.

Table 7.2: Drug content of naproxen in liquisolid dispersion.

S. no.	Batch code	Drug present in liquisolid dispersion equivalent to 25 mg of naproxen (Mean ± S.D)
1	LSD1	23.33 ± 0.38
2	LSD2	23.60 ± 0.20
3	LSD3	22.86 ± 0.35
4	LSD4	23.13 ± 0.25
5	LSD5	23.90± 0.36
6	LSD6	23.26 ± 0.15
7	LSD7	22.53 ± 0.21
8	LSD8	22.30 ± 0.20
9	LSD9	23.03 ± 0.25
10	LSD10	23.63 ± 0.21
11	LSD11	23.40 ± 0.20
12	LSD12	22.66 ± 0.25
13	LSD13	23.23 ± 0.25
14	LSD14	23.53 ± 0.25
15	LSD15	22.26 ± 0.15
16	LSD16	23.13 ± 0.25

Dissolution rate study of all batches of Liquisolid Dispersion

Dissolution studies were conducted in two media, 900 ml of simulated gastric fluid (pH 1.2) and simulated gastric fluid containing 0.75% tween 80 (pH 1.2) and dissolution procedure of the batches of liquisolid dispersion were carried out by the similar procedure which was described in section 7.6 and cumulative drug release for different batches are shown in table 7.7 to 7.14 and graphically represented from fig. 7.3 to 7.18

Table 7.3: Dissolution rate studies of liquisolid dispersion in simulated gastric fluid (SGF) pH 1.2.

S.no.	Time (min.)	% Cumulative drug release at 50 r.p.m					% Cumulative drug release at 100 r.p.m				
		PD	LSD 1	LSD 2	LSD 3	LSD 4	PD	LSD 1	LSD 2	LSD 3	LSD 4
1	0	0	0	0	0	0	0	0	0	0	0
2	2	1.58	4.89	4.39	3.24	2.90	2.41	3.24	2.74	1.91	4.89
3	5	3.08	7.89	6.89	5.57	6.22	3.74	10.02	7.87	7.04	7.23
4	10	5.74	14.04	12.71	11.54	10.05	5.91	20.65	18.65	16.00	12.22
5	15	7.42	18.08	15.09	13.75	12.92	6.77	26.87	22.55	20.22	16.25
6	30	8.62	20.99	17.82	16.80	15.14	11.26	34.29	29.12	22.31	19.97
7	45	9.16	24.08	22.04	19.37	18.19	18.43	42.57	36.71	27.06	22.73
8	60	10.20	25.69	23.65	21.62	20.44	19.69	45.94	42.03	30.18	26.81

PD- Pure drug

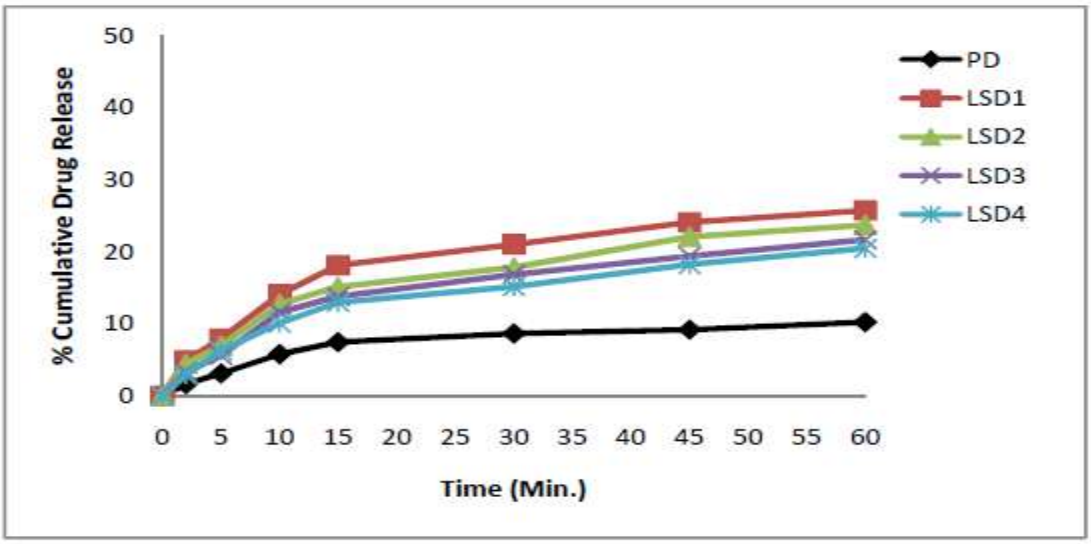


Fig. 7.1: Dissolution rate of naproxen from liquisolid dispersion in SGF at 50 r.p.m.

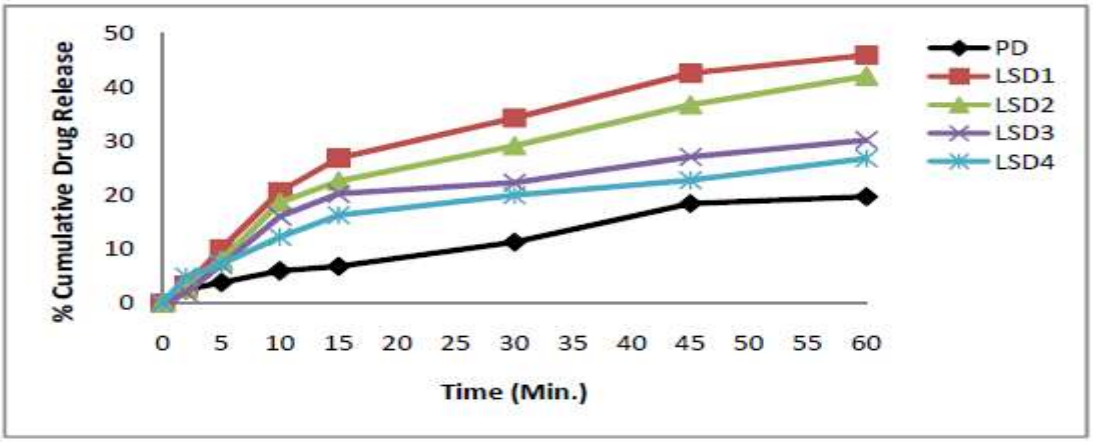


Fig. 7.2: Dissolution rate of naproxen from liquisolid dispersion in SGF at 100 r.p.m.

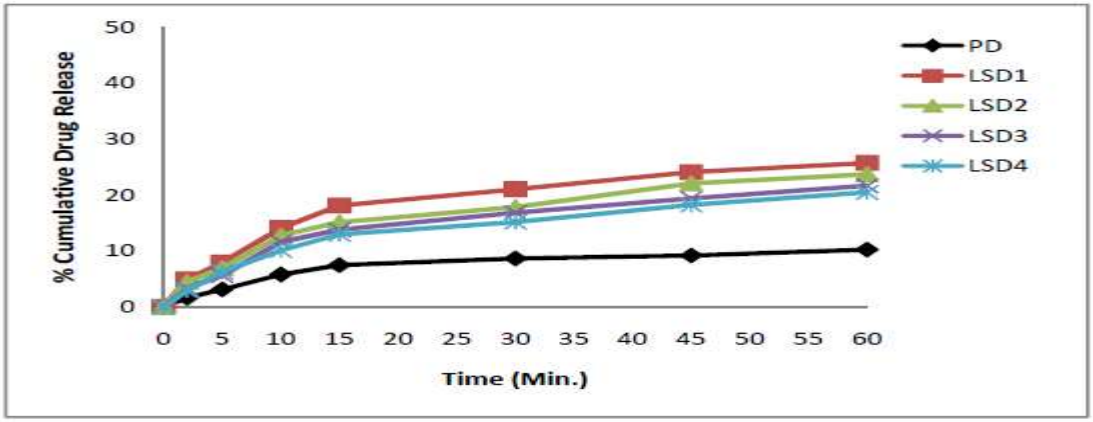
Discussion:-In case of LSD1 to LSD 4, dissolution rate was greater as compared to pure drug. Formulation LSD1 showed better dissolution rate at both rpm as compared to rest three batches.

Dissolution rate was decreased as carrier to coating ratio was decreased and increasedas rpm was increased.

Table 7.4: Dissolution rate studies of liquisolid dispersion in simulated gastric fluid (SGF) pH 1.2.

S.no.	Time(min.)	% Cumulative drug release at 50 r.p.m					% Cumulative drug release at 100 r.p.m				
		PD	LSD 5	LSD 6	LSD 7	LSD 8	PD	LSD 5	LSD 6	LSD 7	LSD 8
1	0	0	0	0	0	0	0	0	0	0	0
2	2	1.58	5.05	4.72	3.57	2.74	2.41	4.23	5.22	3.73	2.57
3	5	3.08	8.55	7.06	6.23	5.40	3.74	11.85	12.35	10.69	7.04
4	10	5.74	10.91	8.42	9.07	7.41	5.91	19.84	18.53	16.86	13.69
5	15	7.42	13.77	11.44	10.61	10.26	6.77	24.74	24.41	20.75	17.89
6	30	8.62	17.88	15.14	13.97	13.12	11.26	32.80	29.83	23.17	20.80
7	45	9.16	20.39	17.53	16.69	14.35	18.43	38.27	33.46	24.29	22.73
8	60	10.20	23.47	20.93	18.59	15.91	19.69	40.13	35.62	25.58	24.18

PD- Pure drug



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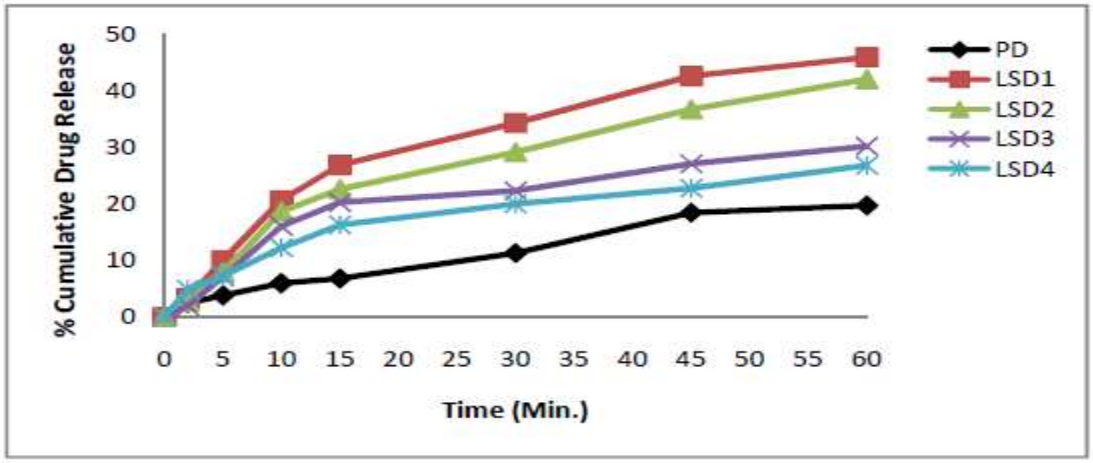

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		PD	LSD 5	LSD 6	LSD 7	LSD 8	PD	LSD 5	LSD 6	LSD 7	LSD 8
1	0	0	0	0	0	0	0	0	0	0	0
2	2	1.58	5.05	4.72	3.57	2.74	2.41	4.23	5.22	3.73	2.57
3	5	3.08	8.55	7.06	6.23	5.40	3.74	11.85	12.35	10.69	7.04
4	10	5.74	10.91	8.42	9.07	7.41	5.91	19.84	18.53	16.86	13.69
5	15	7.42	13.77	11.44	10.61	10.26	6.77	24.74	24.41	20.75	17.89
6	30	8.62	17.88	15.14	13.97	13.12	11.26	32.80	29.83	23.17	20.80
7	45	9.16	20.39	17.53	16.69	14.35	18.43	38.27	33.46	24.29	22.73
8	60	10.20	23.47	20.93	18.59	15.91	19.69	40.13	35.62	25.58	24.18

PD- Pure drug

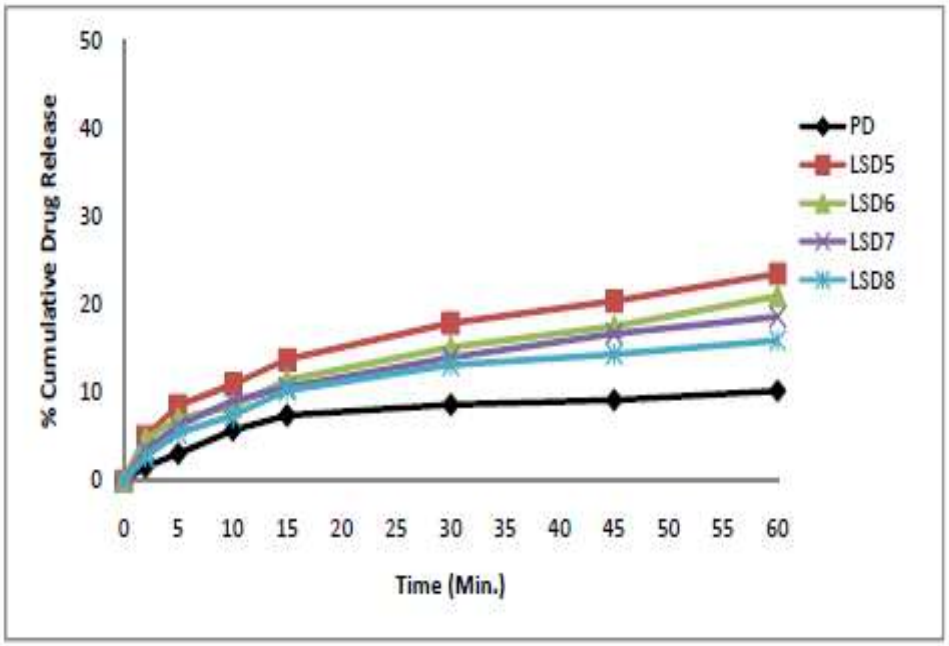

Fig. 7.3: Dissolution rate of naproxen from liquisolid dispersion in SGF at 50 r.p.m.

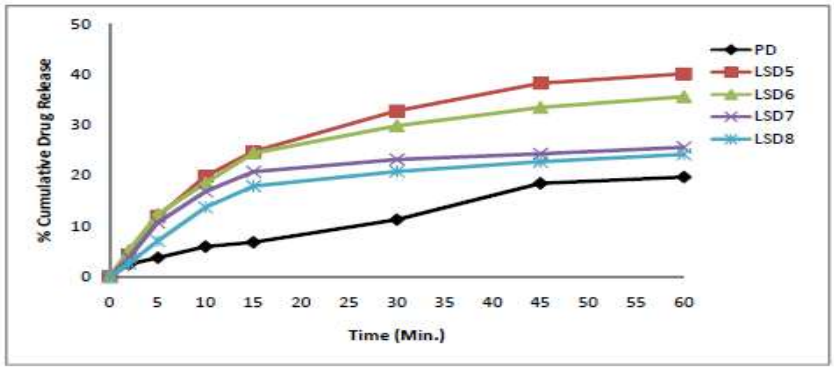

Fig. 7.4: Dissolution rate of naproxen from liquisolid dispersion in SGF at 100 r.p.m.

Discussion: In case of LSD5 to LSD 8, dissolution rate was greater as compared to pure drug. Formulation LSD5 showed better dissolution rate at both rpm as compared to rest three batches.

Dissolution rate was decreased as carrier to coating ratio was decreased and increased as rpm was increased.

Table 7.5: Dissolution rate studies of liquisolid dispersion in simulated gastric fluid (SGF) pH 1.2.

S. No.	Time (min.)	% Cumulative drug release at 50 r.p.m					% Cumulative drug release at 100 r.p.m				
		PD	LSD 9	LSD10	LSD11	LSD12	PD	LSD 9	LSD10	LSD11	LSD12
1	0	0	0	0	0	0	0	0	0	0	0
2	2	1.58	5.22	4.06	6.70	3.07	2.41	3.90	3.40	5.55	2.24
3	5	3.08	10.72	8.71	11.69	6.56	3.74	12.67	7.55	13.51	9.52
4	10	5.74	15.38	14.21	17.87	12.70	5.91	24.30	21.96	24.31	19.15
5	15	7.42	17.94	15.77	19.95	15.25	6.77	29.72	26.54	32.87	22.89
6	30	8.62	21.34	19.49	22.70	18.47	11.26	35.66	33.29	48.57	29.13
7	45	9.16	24.43	22.40	26.46	20.88	18.43	48.57	42.72	50.65	35.57
8	60	10.20	26.88	24.84	30.07	22.98	19.69	49.83	47.25	52.25	39.56

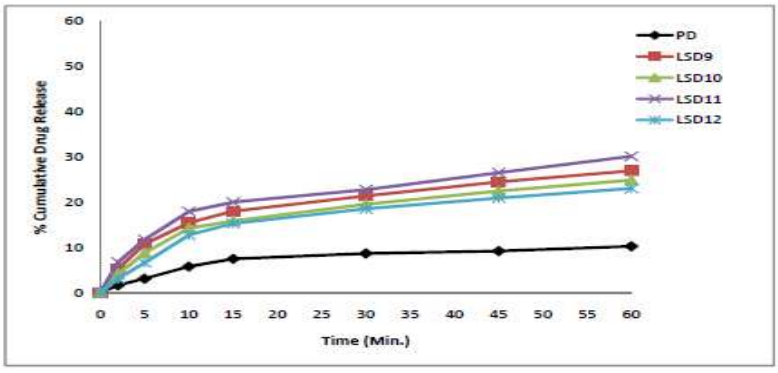

Fig. 7.5: Dissolution rate of naproxen from liquisolid dispersion in SGF at 50 r.p.m.

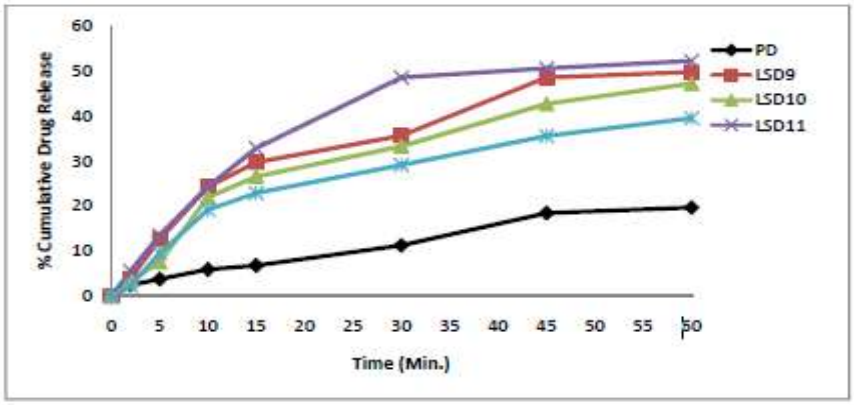

Fig. 7.6: Dissolution rate of naproxen from liquisolid dispersion in SGF at 100 r.p.m.

Discussion: In case of LSD9 to LSD 12,dissolution rate was greater as compared to pure drug. Formulation LSD11 showed greater dissolution rate at both rpm as compared to rest three batches. Dissolution rate was increased in liquisolid dispersion as rpm increased.

RESULT AND DISCUSSION

The fast release formulation of naproxen was prepared by liquisolid technique using propylene glycol and blend A [PEG 200: Water 8:2] as a non-volatile solvents and microcrystalline cellulose (avicel PH102) as carrier material or Aerosil 200 as a coating material. Factors, that effect the dissolution rate, studied were type of solubilizers, non-volatile solvents, ratio of carrier to coating material, dissolution media and rpm of basket The liquisolid dispersion of naproxen with propylene glycol containing 20% PEG 4000 & 20% PVP 40,000 as solubilizers significantly increased the drug dissolution rate.The solubility of a large number of poorly soluble drugs has been enhanced by mixed solvency concept.

The fast release capsule of naproxen was developed using propylene glycol with 20% PEG 4000 & 20% PVP 40,000 and 14:1 ratio of avicel to aerosil containing liquisolid dispersion. The developed capsule of liquisolid dispersion exhibited about upto 83.64% drug release in 45 min. The optimized batch LSD11 showed the better dissolution behavior compared to pure drug and optimized batch evaluated for the weight variation, drug content, disintegration and drug release.

The optimized batch was evaluated using scanning electron microscopy, X-ray diffraction, and DSC. The results suggest complete solubilized of naproxen in the liquisolid dispersion.

Based on the above findings, it may be concluded that fast release capsules of naproxen can be prepared for its dissolution rate enhancement. The formulation developed in the present studies can be further evaluated by bioavailability and scale-up studies.

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