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COMPARATIVE STUDIES OF VARIOUS ADSORBENT CARRIERS FOR ENHANCING DISSOLUTION PROFILE OF KETOPROFEN

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ABSTRACT

In recent times, a large number of studies concerning the improvement of the dissolution rate of poorly water-soluble drugs is focused on the application of various porous materials as the drug carriers. These materials have attracted the attention of researchers owing to their outstanding properties such as large surface area, high pore volumes, microporosity and possibility of surface functionalization. In the present study, the biopharmaceutical performance of porous adsorbents as a carrier for the poorly water soluble drug Ketoprofen was investigated. Ketoprofen loaded different adsorbents with high specific surface area were used like Neusilin, Sylysia, Fujicalin and Aerosil, and it was done by solvent evaporation method. It was noticed that porous structure is responsible for an amorphous state of the drug and thus the improvement of its dissolution rate. From this research work it can be concluded that although the porous carrier particles help to enhance dissolution rate, including stability studies.

KEYWORDS: Ketoprofen; Solvent evaporation method, Adsorbent carrier like Neusilin, Sylysia, Fujicalin and Aerosil, dissolution rate, stability study.

INTRODUCTION

The novel approaches have been attempted to increase the gastrointestinal absorption and bioavailability of BCS class II drugs and decrease variability in the plasma concentration-time profiles with the purpose of increasing dissolution rate and bioavailability respectively. Solubility depends upon drug category, types of polymer, temperature and pH etc.

Many active pharmaceutical ingredients show inadequate physicochemical (aqueous solubility, stability) and/or biopharmaceutical (dissolution rate, permeability) properties which significantly limit their oral bioavailability and hence oral delivery. Some of the various approaches employed to enhance the bioavailability of poorly soluble drugs include salt formation, micronization, co-solvency, hydrotropy, cyclodextrin complexation, micellar solubilization, pH modification, solid dispersions, nanosuspension, spherical crystallization, etc. In recent times, porous materials have been reported to be a step ahead for increasing oral bioavailability. The presence of porous structure like microporous, mesoporous and macroporous structure was found to be essential in providing the sustained drug delivery systems, floating drug delivery systems and improvement of poorly water soluble drugs etc.

This carrier are mainly used to increases the surface area of material and to shows greater solubility of poorly soluble drug by forming it in to amorphous form by using Solvent Controlled Precipitation Method. There has been a great interest in the pharmaceutical field in the use of silicates for the development of oral dosage forms, especially to enhance dissolution rate and bioavailability of poorly water soluble drugs by adsorbing them onto silicates in amorphous forms or as solutions. Having high surface area and commonly being porous, silicates are capable of adsorbing liquids, often as much as 2 to 3 times their own weights. They were first utilized for adsorbing organic solutions of poorly water-soluble drugs and in more recent years, they were investigated for adsorbing self-emulsifying drug delivery systems to convert them into dry powders.

EXPERIMENTAL

Materials

Ketoprofen were obtained as a gift sample from B.E.C. Chemicals, Pvt. Ltd. Roha, Dist –Raigad. Sylysia@350FCP,Sylysia770 from Sylysia Chemical Ltd, Aichi,Japan and other excipients from Fine Chemical, Mumbai.

Preparation of adsorption solvent evaporation method by using Ketoprofen and adsorbent carrier

To prepare amorphous powder by adsorbent using solvent evaporation method. Different ratio 50, 100,400

mg of each adsorbent carrier was suspended in 10 ml of Ketoprofen solutions in ethanol. The suspensions obtained were evaporated at 40^0c. The obtained dried mass was crushed & passes through glass tube further studied for evaluation tests.

Table No 1: Batches of Pure Ketoprofen with different adsorbent carrier ratios.

Batch Code	Ketoprofen	Sylysia350	Ratio
S1	100 mg	50 mg	1 : 0.5
S2	100 mg	100 mg	1 : 1
S3	100 mg	400 mg	1 : 4

Batch Code	Ketoprofen	Sylysia770	Ratio
P1	100 mg	50 mg	1 : 0.5
P2	100 mg	100 mg	1 : 1
P3	100 mg	400 mg	1 : 4

Batch Code	Ketoprofen	Neusilin	Ratio
N1	**100 mg**	**50 mg**	**1 : 0.5**
N2	100 mg	100 mg	1 : 1
N3	100 mg	400 mg	1 : 4

Batch Code	Ketoprofen	Aerosil 200	Ratio
A1	100 mg	50 mg	1 : 0.5
A2	100 mg	100 mg	1 : 1
A3	100 mg	400 mg	1 : 4

Batch Code	Ketoprofen	Fujicalin	Ratio
F1	100 mg	50 mg	1 : 0.5
F2	100 mg	100 mg	1 : 1
F3	100 mg	400 mg	1 : 4

Drug content determination

The drug content was determined by dissolving prepared formulation equivalent to10 mg Ketoprofen in 10 ml ethanol. It was sonicated for 10 min.The solutions was filter through whatmann filter paper, suitably diluted and analyzing spectrophotometrically at 256nm.Each sample was prepared and analyzed in triplicate.

DRUG AND EXCIPIENTS COMPATIBILITY STUDY

Differential Scanning calorimetry

Thermo grams of pure ketpprofen were taken for DSC study. An empty aluminum pan was used as a reference. DSC measurements were performed at a heating rate of 5^0C/min from 50 to 400^0C using aluminium sealed pan. The sample size was 5 mg of pure drug and 5 mg of amorphous powder for measurements. During the measurement, the sample cell was purged with nitrogen gas at 40 ml/min. The results were mentioned in section 7.4.4 and figure 7.15, 7.16 and 7.17.

X-Ray Diffraction (XRD)

To determine the physical state of Ketoprofen and amorphous powder X-ray was applied. A transmission diffractometer (rigaku miniflex, Mumbai, India) was used to investigate crystallinity in prepared solid dispersion, inclusion complex, physical mixture and Ketoprofen. Diffraction patterns were obtained at a voltage of 45 kV and at a current of 40 mA. Samples were scanned in a 2 θ range from 5^0 to 70^0 with a scanning speed of 2^0/min and an intensity of 1000 cps.

Scanning Electron Microscopy (SEM)

The surface morphology of the amorphous powder of prepared Ketoprofen was analyzed by a scanning electron microscope model JEOL, JSM-5400 (Japan) coupled with energy dispersive X-ray analysis (EDAX).

Preparation of dissolution media

0.1N HCl: 8.33ml of Conc. HCL was dissolved in 1000 ml of distilled water.

The dissolution tests of prepared formulation of Ketoprofen (amorphous powder), mixture were performed using the United States Pharmacopoeia (USP) dissolution apparatus II at 50 rpm. Formulations were placed in the dissolution vessel containing 900 ml of 0.1 N HCL in purified water maintained at 37 ± 0.5^0c.At appropriate intervals, samples from the dissolution medium were withdrawn and concentration were determined spectrophotometrically at 256 nm.

Stability study of Ketoprofen & optimized batches of amorphous powder

The optimized batch of amorphous powder was stored at 40^0C±2°C/75 ±5% RH for 1 month in a stability chamber and the effects of storage condition on the preparation were studied by Drug content & In vitro dissolution studies.

RESULT AND DISCUSSION

In the present work a successful attempt was made to achieve a rapid dissolution of Ketoprofen by preparing the formulation by with different ratios. Effect of polymer and their molar ratios on in vitro dissolution of drug was also carefully deliberated. Optimized batch was characterized for FTIR, DSC, XRD & SEM studies. The formulated formulations of optimized batches were evaluated for invitro dissolution & for stability study (short term)

Fourier Transform Infra-Red Spectroscopy

The FTIR spectrum of Ketoprofen was recorded using FTIR (cary-630 Agilent technology). The spectrum was recorded over the range of wave no. 4000 to 400 cm^{-1}. The spectrum observed is shown in fig.0.5. The values of major peaks in FTIR spectrum of Ketoprofen are mentioned in table 2 from the observed peak it is clear that Ketoprofen is in the pure form.

Table No 2: FTIR Interpretation of Ketoprofen.

Sr. no.	Functional Group	Peak (wave number) cm^{-1}
1	OH str.	3050.166
2	CH str.	2644.006
3	CH df.	1284.104
4	C=O str.	1695.602
5	Ar-H	787.989

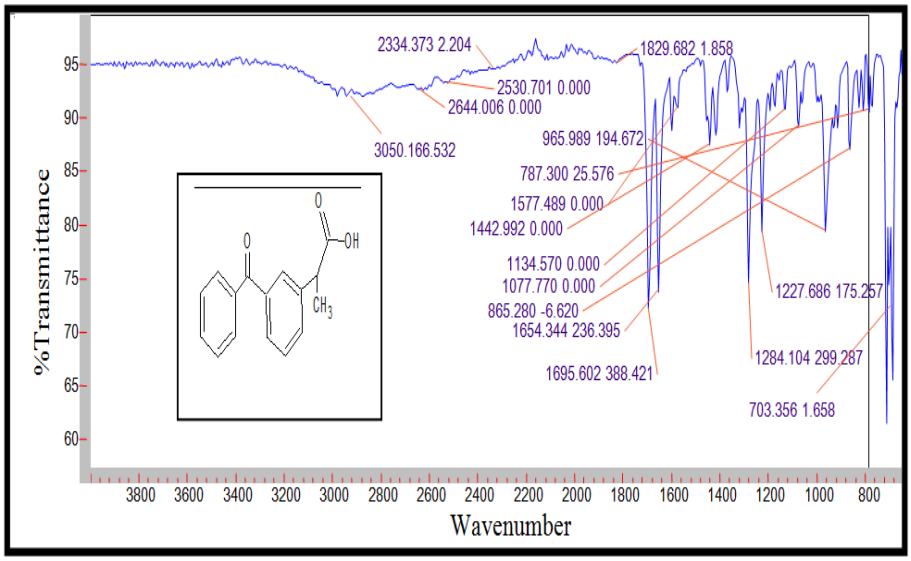

Fig 0.5: FTIR spectra of Ketoprofen.

Experimental Study

Preparation of adsorption solvent evaporation method by using Ketoprofen and adsorbent carrier.

The formulated batches has been found in form of free flowing powder without any agglomeration of particles within the batches, This powder batches are then stored at in well sealed container for its further characterization like drug content, dissolution study etc.

Drug Content determination using UV spectroscopy

The drug when loaded on adsorbent carriers usually dispersed on the large surface area of the carrier at a molecular/supramolecular or particulate level. Further increase in carrier surface area may not lead to further subdivision of the drug due to increased cohesive forces/surface tension among the drug particles thus leading to the limiting value of effective surface area. This may reason drug content may increase with carriers.

We observed % Drug Content is 98.25%, 94.02%, 96.81%, 94.88%, and 97.09% respectively. And Optimized batches are S2, P2 N2, A2, & F2 respectively.

Table No: 3% Drug Content.

Sr. No.	Batch No.	Ratio	Drug content
1	S1	1:0.5	76.06±0.011
2	**S2**	**1:1**	**98.25±0.001**
3	S3	1:4	85.93±0.045
4	P1	1:0.5	82.11±0.012
5	**P2**	**1:1**	**94.02±0.012**
6	P3	1:4	87.79±0.036
7	N1	1:0.5	76.41±0.001
8	**N2**	**1:1**	**96.81±0.009**
9	N3	1:4	81.14±0.044
10	A1	1:0.5	79.98±0.005
11	**A2**	**1:1**	**94.88±0.036**
12	A3	1:4	80.47±0.025
13	F1	1:0.5	82.14±0.048
14	**F2**	**1:1**	**97.09±0.042**
15	F3	1:4	87.65± 0.05
Mean ± S.D., n=3			

Solubility studies of prepared Ketoprofen and adsorbent carrier using solvent evaporation method

Saturation solubility is important parameter that will affect the bioavailability of drug because of its poor solubility in aqueous media it posses limitation in absorption of drug. Here saturation solubility of all prepared amorphous powder batches with different ratios was performed in water. The prepared amorphous powder batches with different ratios shows increased solubility as compare to pure Ketoprofen. The Saturation solubility of Ketoprofen was increased in 9 times due to

adsorbent carrier. This effect may be due to wetting of drug particles and localization solubilisation caused by hydrophilic carrier as well as decrease in particle size by precipitation. Saturation solubility data indicates that the solubility of Ketoprofen was enhanced by prepared solvent evaporation technique using Sylysia 350, Sylysia 770, Neusilin, Aerosil, & Fujicalin.

Drug solubility may be increased with increase in adsorbent carrier concentration but at molecular level, this may be the reason because of which 1:1 ratio batches has higher solubility than 1:0.5, 1:4 batches.

These results clearly revealed that the highest drug solubility was observed in S1-S3 Batches are S2, in P1-P3 Batches are P2 & in N1-N3 Batches are N2 & in A1-A3 Batches are A2 & in F1-F3 Batches are F2.

Table No 4 Saturation solubility of Ketoprofen with adsorbent carrier in water.

Sr. No.	Adsorbent carrier used	Batch Code	Drug: Polymer ratio	Solubility in Distilled water (µg/ml
1	Sylysia 350	S1	1:1	58.01±0.032
2		S2	1:1.5	77.86±0.021
3		S3	1:2	47.53±0.013
4	Sylysia 770	P1	1:1	47.60±0.001
5		P2	1:1.5	69.53±0.002
6		P3	1:2	52.89±0.051
7	Neusilin	N1	1:1	50.20±0.021
8		N2	1:2	68.57±0.042
9		N3	1:3	62.25±0.031
10	Aerosil	A1	1:1	48.04±0.014
11		A2	1:2	62.74±0.052
12		A3	1:3	51.09±0.074
13	Fujicalin	F1	1:1	68.01±0.074
14		F2	1:2	88.99±0.096
15		F3	1:3	62.05±0.001
Mean ± S.D., n=3				

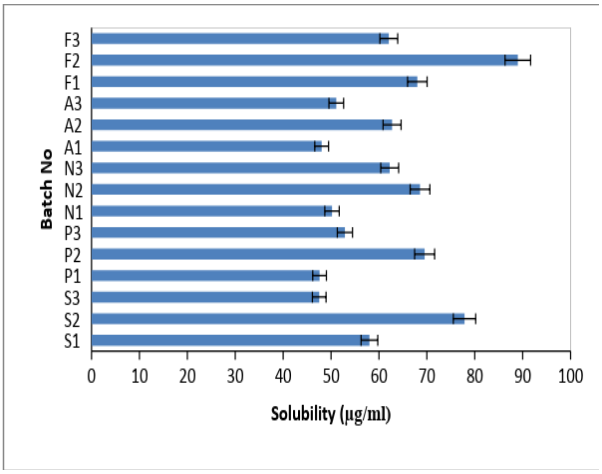

Fig 1: Saturation solubility of prepared amorphous powder batches.

Drug Excipients compatibility study

It is well known that interactions between the active substance and excipients can influence the pharmacological properties and behavior of drugs in biological systems. In this study, mixtures of polymers and Ketoprofen as the active substance were ground together and analyzed by FTIR, DSC, XRD and SEM. Besides the active substance itself, Ketoprofen amorphous powder contains the following polymers: Sylysia350, Sylysia770, Neusilin, Aerosil and Fujicalin as adsorbents in the formulation.

Fourier Transform Infrared

FTIR of Ketoprofen: Sylysia350 Batches S1, S2, S3 ratio

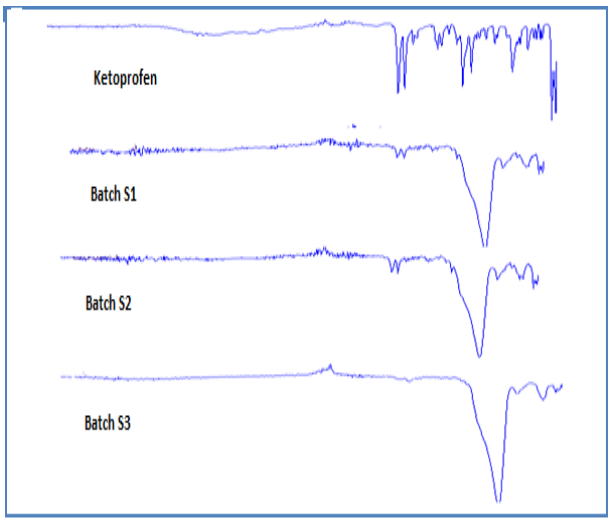

Fig 2: FTIR of Ketoprofen: Sylysia350 Batches S1, S2, S3 ratio.

Table No.5: FTIR Interpretation of Ketoprofen: Sylysia350 Batches S1, S2, S3 Ratio.

Sr. no.	Functional Group	Ratio Batch S1 (observed frequency)cm^{-}	Ratio Batch S2 (observed frequency)cm^{-}	Ratio Batch S3 (observed frequency)cm^{-}
1	OH str.	-	-	-
2	CH str.	-	-	-
3	CH df.	1091.853	1091.506	1085.549
4	C=O str.	1697.985	1696.298	-
5	Ar-H	764.607	787.409	800.152

Band broadening and merging can be observed in the CH deformation region between 1050 and 1125cm−1 and also C=O stretching between 1670 and 1720cm−1. No differences were found between spectra of the Ketoprofen and Sylysia350 Batches. It can be postulated that only weak van der Waals or hydrogen forces are involved in binding Ketoprofen onto Sylysia surfaces, thus enabling easy desorption of the drug during dissolution. In the Sylysia pores, the drug is adsorbed to a certain extent as a thin layer or small particles of the drug. The high specific surface area of these particles contributes to improved dissolution compared to pure drug.

FTIR of Ketoprofen: Sylysia770 of Batches P1, P2, P3 ratio

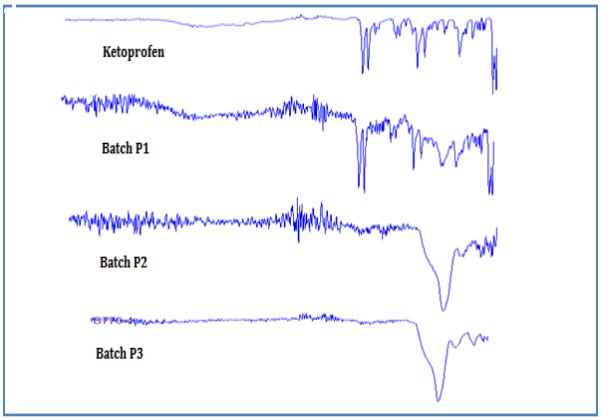

Fig 3: FTIR of Ketoprofen: Sylysia770 of Batches P1, P2, P3 ratio.

Table No 6: FTIR Interpretation Ketoprofen: Sylysia770 of Batches P1, P2, and P3 Ratio.

Sr. no.	Functional Group	Ratio Batch P1 (observed frequency)cm^{-}	Ratio Batch P1 (observed frequency)cm^{-}	Ratio Batch P1 (observed frequency)cm^{-}
1	OH str.	3194.282	-	_
2	CH str.	2440.282	2676.556	_
3	C=O str.	1697.122	1863.015	_
4	CH df	1060.441	1083.600	1087.387
5	Ar-H	864.835	799.409	793..397

Band broadening and merging can be observed in the CH deformation region between 1050 and 1125cm−1, CH stretching region between 2400 to 2500cm-1 and also C=O stretching between 1670 and 1720cm−1. No differences were found between spectra of the ketoprofen and Sylysia770 Batches. It can be postulated that only weak van der Waals or hydrogen forces are involved in binding Ketoprofen onto Sylysia surfaces, thus enabling easy desorption of the drug during dissolution. In the Sylysia pores, the drug is adsorbed to a certain extent as a thin layer or small particles of the drug. The high specific surface area of these particles contributes to improved dissolution compared to pure drug.

FTIR of Ketoprofen: Neusilin of Batches N1, N2, N3 ratio

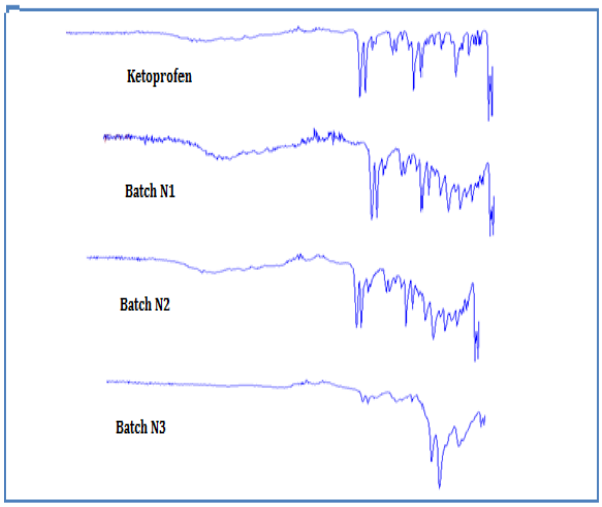

Fig 4: FTIR of Ketoprofen:Neusilin of Batches N1,N2,N3 ratio.

Table No.7: FTIR Interpretation of Ketoprofen: Neusilin of Batches N1, N2& N3 Ratio.

Sr. no.	Functional Group	Ratio Batch N1 (observed frequency)cm^{-}	Ratio Batch N2 (observed frequency)cm^{-}	Ratio Batch N3 (observed frequency)cm^{--}
1	CH str.	2536.526	2465.2	2396.1
2	C=O str.	1655.082	1655.018	1657.262
3	CH df	966.531	1000.381	1000.754
4	Ar-H	773.845	778.870	-

Bands characteristic of ketoprofen and Neusilin Batches N1, N2& N3 were found at ranging 2530 to 2356 cm−1 (CH valence vibration), 1690 to 1630 cm−1 (CO R vibration), 1090 to 960cm−1 (range of CH deformation). In FTIR spectra of Ketoprofen: Neusilin Batches N1, N2& N3 may suggest that hydrogen bond between carbonyl group of Ketoprofen and Neusilin group of adsorbent take part in formation of amorphous state of Ketoprofen.

FTIR of Ketoprofen: Aerosil of Batches A1, A2, A3 ratio

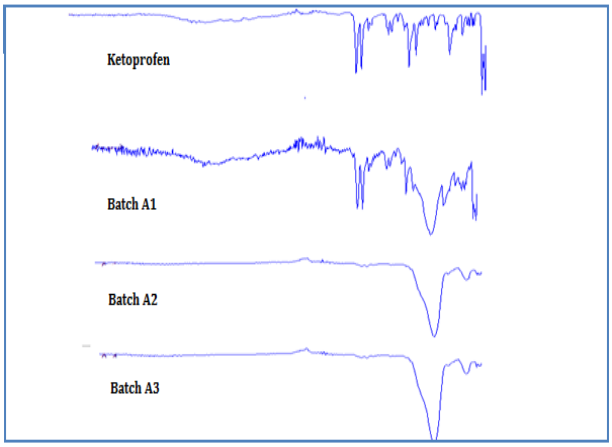

Fig 5: FTIR of Ketoprofen: Aerosil of Batches A1, A2, A3 ratio.

Table No.8: FTIR Interpretation of Ketoprofen: Aerosil of Batches A1, A2, A3 Ratio.

Sr. no.	Functional Group	Ratio Batch A1 (observed frequency)cm	Ratio Batch A2 (observed frequency)cm	Ratio Batch A3 (observed frequency)cm
2	CH str.	2536.529	2318.413	2337.066
3	C=O str.	1694.895	1653.25	1695.23
4	CH df	1073.812	1078.579	1080.552
5	Ar-H	809.685	809.088	809.611

FTIR spectra of Ketoprofen showed major peaks at ranging 1700 to 1630 cm−1(C=O stretching), 2937 to 2500 cm−1 (CH stretching of CH2), 1090 to 950 cm−1, (CH Deformation). Aerosil Batches A1, A2, A3 showed characteristic bands at 1100, 808 cm−1. It suggests that the possibility of change in hydrogen bonding between Ketoprofen and Aerosil of Batches A1, A2, A3.

FTIR of Ketoprofen: Fujicalin of Batches F1, F2, F3 ratio

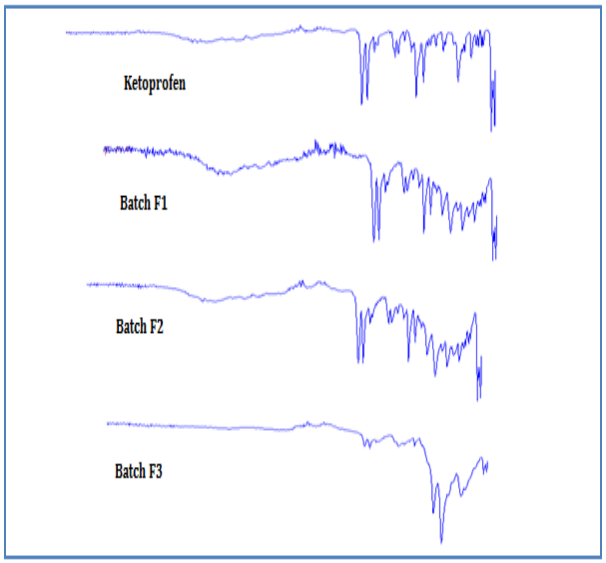

Fig 6 FTIR of Ketoprofen: Fujicalin of Batches F1,F2,F3 ratio.

Table No.9 FTIR Interpretation of Ketoprofen: Fujicalin of Batches of F1,F2,F3.

Sr. no.	Functional Group	Ratio Batch F1 (observed requency)cm	Ratio Batch F2 (observed frequency)cm	Ratio Batch F3 (observed frequency)cm
1	OH str.	3047.640	-	_
2	CH str.	2641.454	2626.506	_
3	C=O str	1694.749	1695.121	1577.722
4	CH df	1059.476	1059.310	1203.145
5	Ar-H	863.557	863.471	791.541

Bands characteristic of ketoprofen and Fujicalin Batches F1, F2, F3 were found at ranging 2530 to 2356 cm−1 (CH valence vibration), 1690 to 1630 cm−1 (CO R vibration), 1090 to 960cm−1 (range of CH deformation). In FTIR spectra of Ketoprofen: Fujicalin Batches F1, F2, and F3 may suggest that there is no chemical interaction between drug and fujicalin.

Differential Scanning Calorimetry (DSC)

Differential scanning calorimetry (DSC) is a fast and reliable method to screen drug-excipient compatibility and provides maximum information about the possible interactions. In DSC, an interaction is concluded by elimination of endothermic peak(s), appearance of new peak(s), and change in peak shape and its onset, peak temperature/melting point and relative peak area or enthalpy.

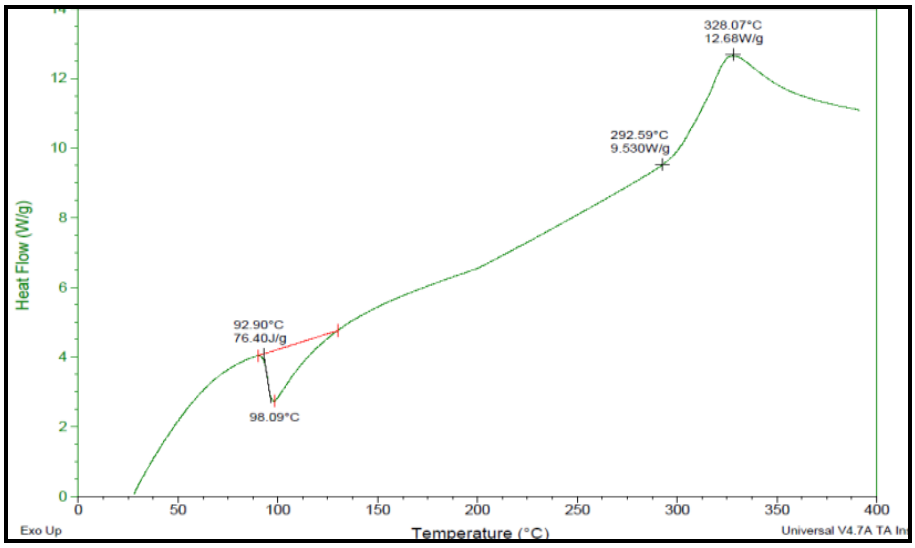

Fig.7 DSC of Ketoprofen at Temp.98.09

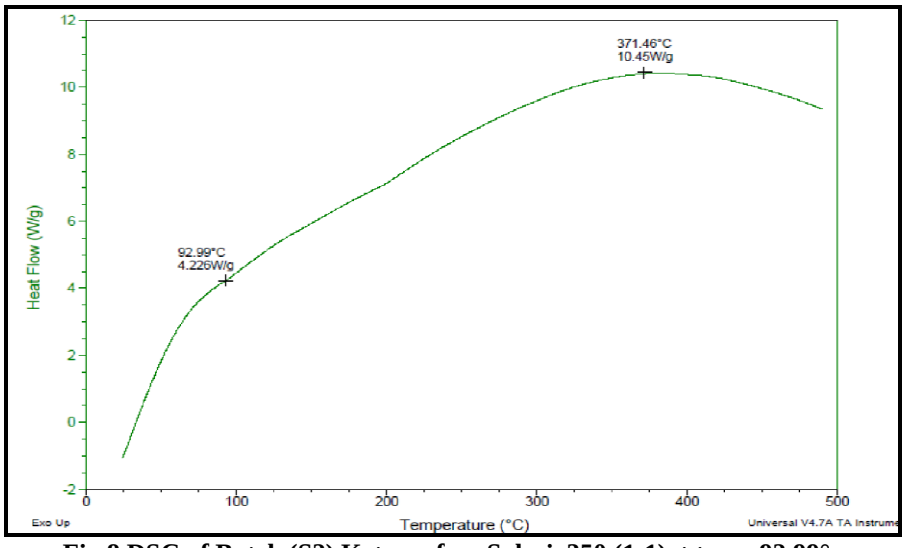

Fig 8 DSC of Batch (S2) Ketoprofen: Sylysia350 (1:1)at temp 92.99°c

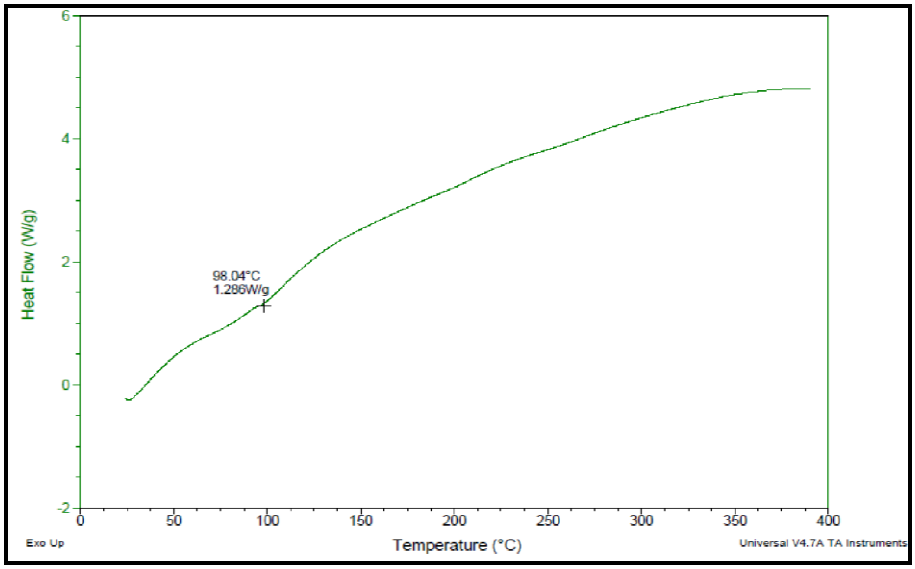

Fig.9 DSC of Batch (P2) Ketoprofen: Sylysia770 (1:1) at temp 98.04°c

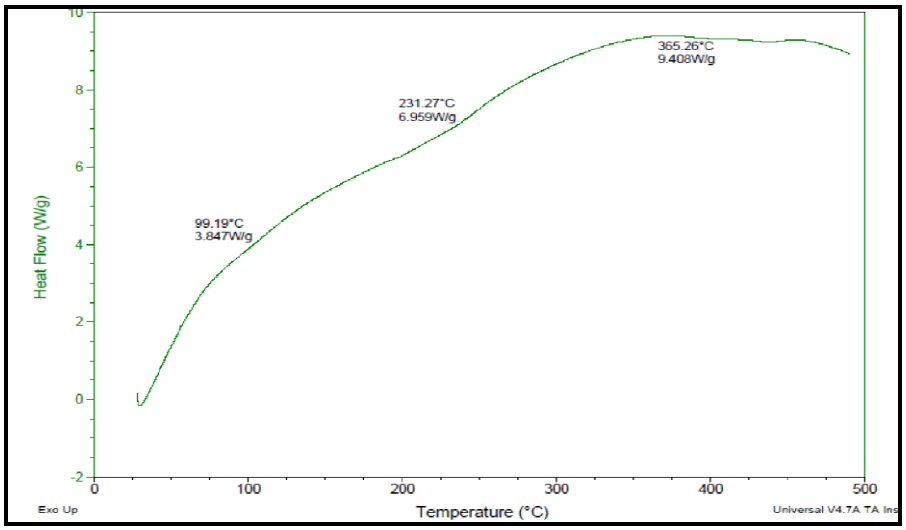

Fig.10 DSC of Batch (N2) Ketoprofen: Neuosilin(1:1) at temp 99.19°

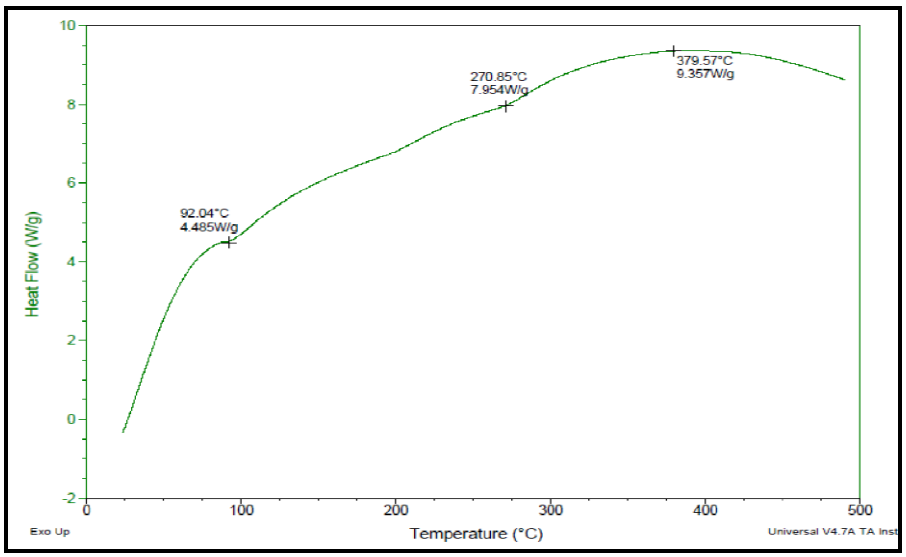

Fig.11 DSC of Batch (A2) Ketoprofen: Aerosil (1:1) at temp 92.04°c

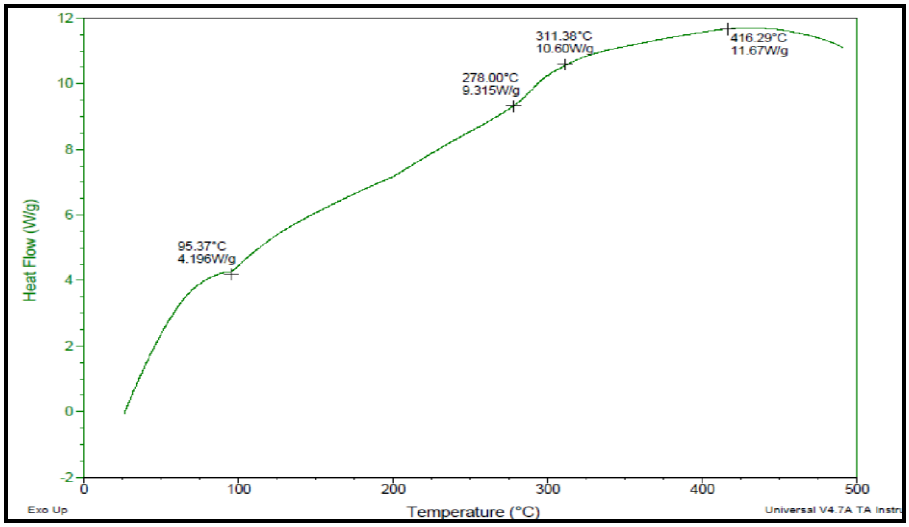

Fig.12: DSC of Batch (F2) Ketoprofen:Fujicalin(1:1) at temp 95.37°c.

A figure 8 - 12 shows the DSC thermo gram over the temperature range 40-150°C. The melting point and melting enthalpy of crystalline Ketoprofen were 98.09°C &76.40J/g respectively. It is clearly indicate that distinct melting point of Ketoprofen 98.09°C changes to for Batches Ketoprofen:sylysia350 (Batch S2) 92.99^0, Ketoprofen: sylysia (BatchP2) 770 98.04^{0}c, Ketoprofen: Neusilin (BatchN2) 99.19^{0}c, Ketoprofen: Aerosil (BatchA2)92.04^{0}c, Ketoprofen: Fujicalin(BatchF2) 95.37^{0}c were found. This implies that Formulations which were prepared shows the endotherm peak very near about defined temperature range to the pure ketoprofen drug. The shifting of endotherm peak and change in peak shape because of concentration of adsorbent carrier. Hence it indicates the physical incompatibility between Ketoprofen and adsorbent carrier.

Powder X-Ray Diffraction (PXRD)

Fig.13 shows X-Ray diffraction pattern of pure Ketoprofen, less diffused peaks in the X-Ray diffraction spectrum indicates that Ketoprofen present as a crystalline material. From X-ray diffraction of formulations of formulated batches Fig 14, 15, 16, 17,& 18 is showed that there is formation of amorphous nature form of the drug because there is decrease in intensity of than its API. Batches as The S2, P2, N2, A2, F2.shows intensity respectively300, 260, 325, 320, 425.It was clearly found that the amorphous nature of formulations.

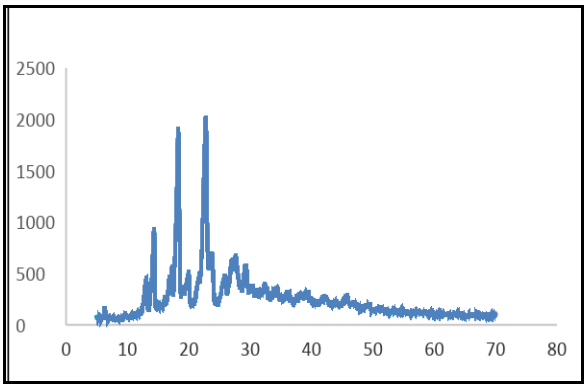

Fig 13 XRD of Ketoprofen

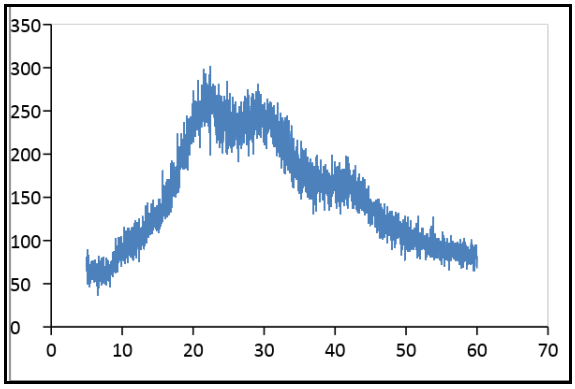

Fig. 14 XRD Pattern of Batch S2

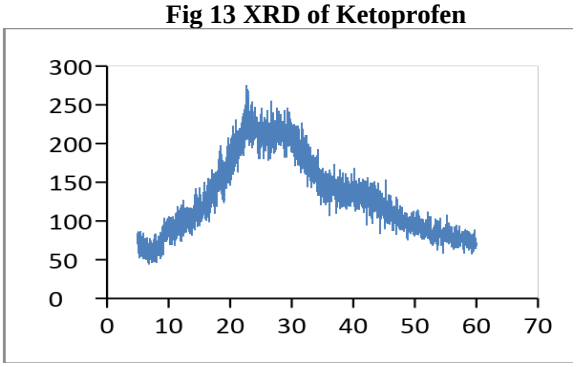

Fig.15 XRD Pattern of Batch P2

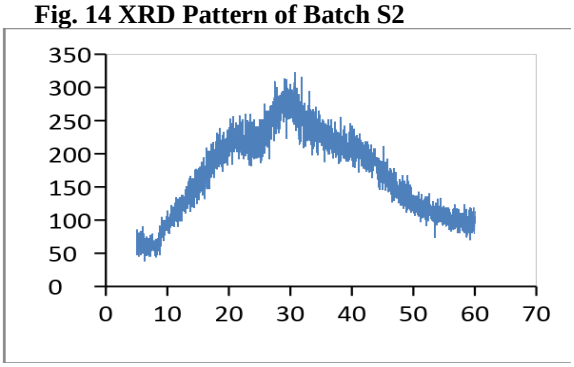

Fig.16 XRD Pattern of Batch N2

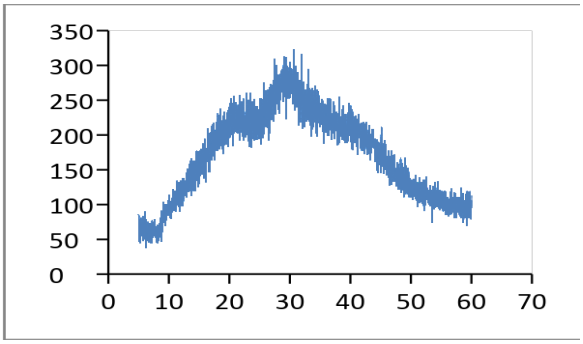

Fig 17 XRD Pattern of Batch A2

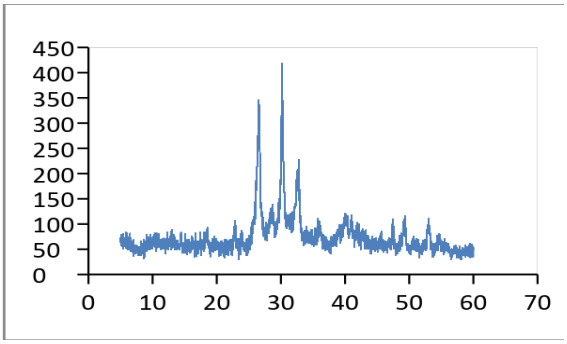

Fig.18 XRD Pattern of Batch F2

Scanning Electron Microscopy (SEM)

From Differential Scanning Calorimetry (DSC), Powder X-Ray Diffraction (PXRD) study two batch optimize S2, F2 and done its Scanning Electron Microscopy (SEM) SEM micrographs of pure ketoprofen, and Batch S2 and Batch F2 showed in Fig. 19, 20 & 21.

The surface morphology of pure Ketoprofen in intensity with 500µ-50µm, Batch S2 2000µm-10µm and Batch F2 2000µm-10µm were studied by SEM. As showed in Figuer. 19, 20 & 21. Ketoprfen appears crystalline, almost rectangular in shape while Batch S2 and D2 exhibited a significant change in shape and Particles appeared irregular in shape with smooth surface, probability due to complete miscibility of the drug and fujicalin and sylysia.

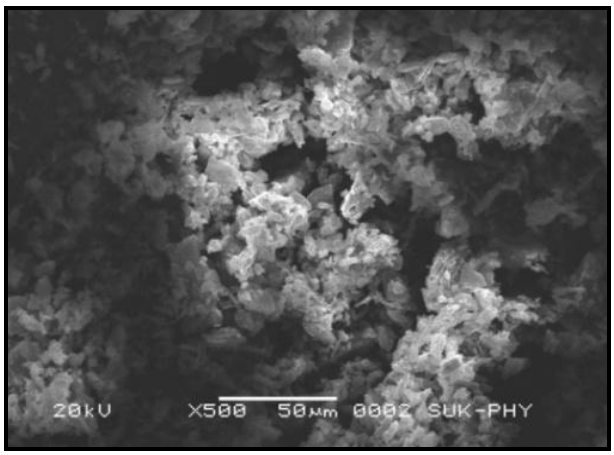

Fig. 19 SEM of Ketoprofen.

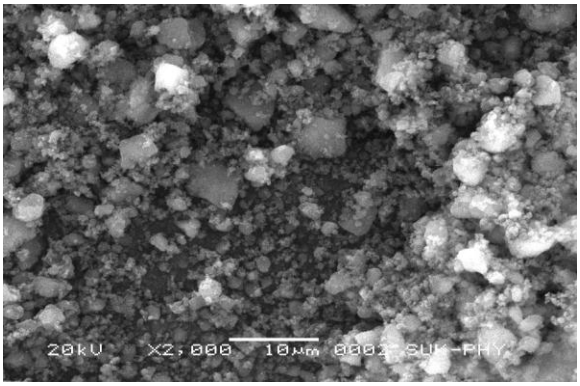

Fig. 20 SEM of S2 Batch

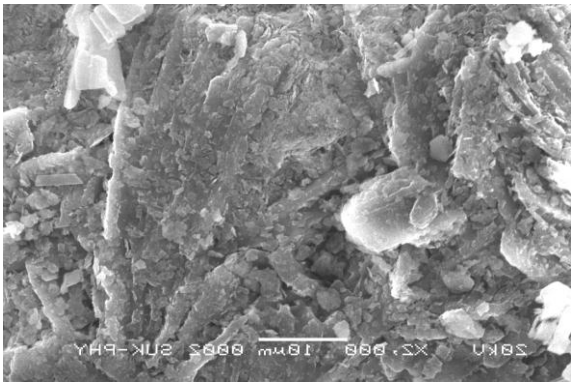

Fig.21 SEM of F2 Batch

***In vitro* Dissolution study**

The *in vitro* dissolution study in an important parameter to determine % cumulative drug release in the dilution media. The *in vitro* dissolution study of prepared amorphous powder and Ketoprofen were performed in the USP dissolution test apparatus. 0.1N HCL was selected as the dilution media jar.

Table No.10: % Cumulative drug release.

Time (min)	% Cumulative drug release		
	Ketoprofen	Batch S2	Batch F2
5	1.53±0.015	45.87±0.034	30.17±0.156
10	3.25±0.104	59.11±0.305	49.95±0.025
15	8.68±0.062	67.18±0.015	63.36±0.050
20	10.26±0.010	74.22±0.035	71.85±0.036
25	11.23±0.015	76.68±0.078	78.36±0.060
30	16.54±0.032	78.42±0.025	80.25±0.025
35	20.24±0.436	80.39±0.030	81.33±0.017
40	23.85±0.505	84.93±0.020	84.14±0.030
45	26.15±0.032	89.66±0.036	87.74±0.025
50	27.91±0.015	93.09±0.015	89.72±0.640
55	30.23±0.015	95.87±0.034	90.36±0.060
60	32.54±0.032	96.11±0.305	92.25±0.025
Mean ± S.D., n=3			

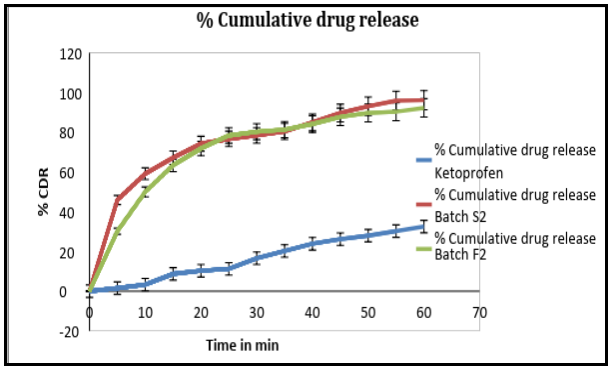

Fig. 22: % Cumulative drug release.

Figure 22 represent a comparison of the dissolution profiles of pure Ketoprofen and the batches of Ketoprofen with using sylysia350 and fujicalin containing 92 & 96% of the drug in 0.1NHCl. However, drug release from solvent evaporation and solvent deposition technique was significantly improved its solubility as compared to the dissolution of pure Ketoprofen and its batches. Comparing the solvent evaporation and solvent deposition technique prepared by evaporation shows increasing release rates with increasing drug content. This can be explained by decreases in surface area available for dissolution due to pore filling, and decreases in wettability due to increases in drug content in the dispersion. Also, the proportion of larger drug particles that precipitate in Sylysia pores and need more time to dissolve probably increases along with increasing drug content in the dispersion.

Stability study of Ketoprofen & optimized batches of amorphous powder

The optimized batch of amorphous powder was stored at 40^0C±2°C/75 ±5% RH for 1 month in a stability chamber and the effects of storage condition on the preparation were studied by Drug content & In vitro dissolution studies.

Experimental Study

Percentage Drug content after stability

Table No.11 % Drug content of Stability batches reading at 40^0C for 0 months &1 month.

Period	% Drug content.	
	Batch S2	Batch F2
0 Month	96.06%	92.02%
1 Month	94.98%	91.83%
Mean ± S.D., n=3		

The drug content which is shown in table no.11 it shown that there is decrease the % drug content of Batches S2& F2 hence these formulation should be stable for temperature 40^0C ±2.

***In-Vitro* dissolution Studies after Stability**

Table.No.12 % Cumulative drug release

Time (min)	% Cumulative drug release		
	Ketoprofen	Batch S2	Batch F2
5	0.43±0.015	42.87±0.034	30.17±0.156
10	1.22±0.104	48.51±0.305	38.95±0.025
15	4.68±0.062	59.18±0.015	48.36±0.050
20	9.26±0.010	62.22±0.035	54.85±0.036
25	9.48±0.015	66.68±0.078	54.85±0.060
30	10.74±0.032	70.42±0.025	61.35±0.025
35	14.09±0.436	73.39±0.030	66.23±0.017
40	18.58±0.505	78.93±0.020	71.34±0.030
45	22.18±0.032	81.66±0.036	76.14±0.025
50	25.41±0.015	85.099±0.015	85.72±0.640
55	29.87±0.015	90.87±0.034	88.36±0.060
60	31.44±0.032	93.87±0.305	90.05±0.025
Mean ± S.D., n=3			

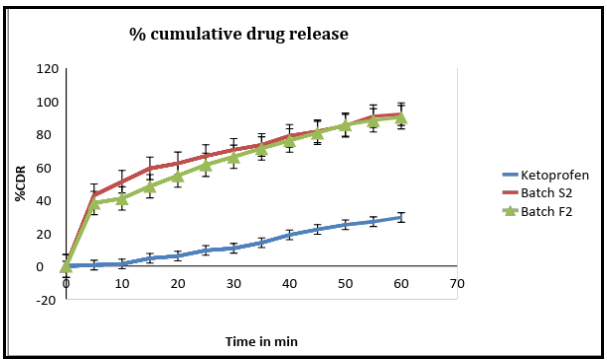

Fig.23 % Cumulative drug release.

In-Vitro dissolution Studies Table No.12 Shows that, The % CDR of Batches S2 & F2 of formulation with Ketoprofen amorphous powder after stability shows that formulation are stable at room temperature & 40^0C±2°C/75 ±5% RH for 1 month.

CONCLUSION

Amorphous solid mixture of Ketoprofen was successfully prepared by adsorption with solvent evaporation technique using adsorbents carrier. The adsorbents carrier increases the water solubility and dissolution profile of Ketoprofen. The solid state studies

confirmed that amorphization of adsorbents with an adsorbents carrier by decreasing crystallinity and there is no any chemical interaction. It shows significant improvement of the in vitro dissolution rate. The research work have shown increase in solubility of Ketoprofen with increase in dissolution rate may be attributed to increase surface area due to use of absorbent carrier.

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