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Dissolution Enhancement of Poorly Soluble Aceclofenac by Solid Dispersion Technique and Its Comparison with Marketed Formulations

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Abstract: The development of a meaningful dissolution procedure for drug product with limited water solubility has been a challenge to both the pharmaceutical industry and the agencies that regulate them. These challenges include developing and validating the test methods, ensuring that method is appropriately discriminatory and addressing the potential for an *in vivo- in vitro* correlation (*IVIVC*). Aceclofenac (BCS Class II drug) comes under Non Steroidal Anti-Inflammatory Drugs and widely used as an analgesic. Aceclofenac is poorly soluble in water and aqueous buffers in the gastrointestinal pH range (1.2 – 7.5), which leads to the failure of dissolution of aceclofenac. Here an attempt has been made to enhance the dissolution of aceclofenac by solid dispersion technique. Solid dispersion of Aceclofenac was tried with PEG- 6000, Beta Cyclodextrin, Gelatin Hydrolysate, SLS and Croscarmellose. It was found that the aceclofenac – croscarmellose complex has given the best solubility results. The Infra Red spectra revealed that there is no incompatibility between the drug and excipients. The DSC thermogram shows the complete complexation between drug and aceclofenac. The dispersible tablets of the selected Aceclofenac-Croscarmellose solid dispersions were prepared and compared with *in – vitro* dissolution profiles of Aceclofenac without Croscarmellose and marketed tablets. The drug release from the Aceclofenac-Croscarmellose solid dispersions tablets was found to be 94.95% within 10 min. It was comparatively faster than the drug release of Aceclofenac tablets with Croscarmellose and marketed tablets which was found 35.14% and 32.78% within 10 min respectively. The T_{50} values of Aceclofenac-Croscarmellose solid dispersions tablets, Aceclofenac with Croscarmellose tablets and marketed tablets were found to be 3min, 16 min and 21 min respectively. The results showed that the rapid dissolution was the characteristic behavior of solid dispersion of Aceclofenac-Croscarmellose solid dispersions tablets.

Keywords: Aceclofenac, Croscarmellose, Infra Red spectra, DSC, Solid Dispersion.

INTRODUCTION

Drug dissolution testing is an analytical technique used to assess release profiles of drugs from pharmaceutical products, generally solid oral products such as tablets and capsules. If a drug from its dosage form has to produce its effect, it must be released from the product and should generally be dissolved in the fluids of the gastrointestinal tract. Drug dissolution testing plays an important role, as a routine quality control test, for characterizing the quality of the product, for accepting product sameness under SUPAC (Scale up and Post Approval Changes) related changes, to waive bioequivalence requirements for lower strengths of a dosage form and to support waivers for other bioequivalence requirements. (1) Dissolution from the dosage form involves mainly two steps (2) – liberation of the drug from the formulation matrix (disintegration), followed by the dissolution of the drug (solubilization of the drug particles) in the liquid medium. The overall rate of dissolution depends on the slower of these two steps. In the first step of dissolution, the cohesive properties of the formulated drug play a key role. For solid dosage forms, these properties include disintegration and erosion. If the first step of dissolution is rate limiting, then the rate of dissolution is considered *disintegration controlled*. In the second step of dissolution (i.e., solubilization of drug particles), the physicochemical properties of the drug such as its chemical form (e.g., salt, free acid, free base) and physical form (e.g., amorphous or polymorph and primary particle size) play an important role. If this latter step is rate limiting, then the rate of dissolution is *dissolution controlled*. This is the case for most poorly soluble compounds in immediate release (IR) formulations whose solubility is less than 1 to 2 mg/Liter in the pH range of 2 to 8. Recent advanced technologies like combinatorial chemistry and high throughput screening are effectively discovering new drugs with good pharmacological activities. (3) About 35 to 40 % of the drugs discovered by these technologies are having poor aqueous solubility. (4) Aceclofenac (BCS Class II drug) comes under Non Steroidal Anti- Inflammatory Drugs and widely used as an analgesic. Aceclofenac is poorly soluble in water and aqueous buffers in the gastrointestinal pH range (1.2 – 7.5), which leads to the failure of dissolution of aceclofenac. In 1965, Tachibana and Nakamura described a new approach utilizing water- soluble polymers for the preparation of aqueous dispersions of β- carotene. (5) Mayersohn and Gibaldi applied the same approach to improve the solubility and dissolution characteristics of griseofulvin. (6) The dispersion method allows the preparation of physically modified forms of the drug that are much more rapidly soluble in water than the pure compound. The most commonly used hydrophilic carriers for solid dispersions include polyvinyl pyrrolidone, polyethylene glycols and plasdone-S630. Many times surfactants may also used in the formation of solid dispersion. Surfactants like Tween-80, Myrj-52 and Pluronic-F68 and sodium lauryl sulphate are used.

Here an attempt has been made to enhance the dissolution properties of Aceclofenac by making Solid dispersion of Aceclofenac with PEG- 6000, Beta Cyclodextrin, Gelatin Hydrolysate, SLS and Croscarmellose.

EXPERIMENTAL

Materials

Aceclofenac was obtained from Astro Pharmaceutical Ltd, Mumbai. The assay of the drug, as given the certificate of analysis was of 99 to 101 %. Polyethylene Glycol was obtained from SD fine chemicals Ltd, Mumbai. B-Cyclodextrin was obtained from Himedia Laboratories Pvt. Ltd, Mumbai. Gelatin Hydrolysate was obtained from Sterling Biotech Ltd, Ooty. Sodium Lauryl Sulphate was obtained from SD fine chemicals ltd, Mumbai. Croscarmellose was obtained from Sigma chemical Ltd, Bangalore. All other reagents and solvents used were analytical grade.

Dissolution test apparatus USP 30, Lab India DS 8000, Mumbai was used for the dissolution. Friability test apparatus manufactured by India Equipment corporation, Mumbai and Disintegration test apparatus manufactured by Veego Instruments Co, Mumbai were used for the evaluations. Shimadzu UV - Visible Spectrophotometer - 1800, Perkin Elmer – 1600 IR Spectrophotometer were used for Calibration Curve and Incompatibility Studies. Weighing, drying, sieving, filtering and other operations were carried out using laboratory equipments.

Methods

Preformulation Studies

Development of Calibration Curve

A stock solution of Aceclofenac (1mg/ml) was prepared by dissolving 100 mg of drug in 100 ml of Acetone. From this 5, 10, 15, 20, and 25 µg/ml dilutions were prepared. The wavelength of maximum absorbance (λmax) was determined by scanning one of the dilutions from 400 to 200 nm in the spectrophotometer and the spectrum was recorded. The absorbance of all the dilutions were measured at the λmax 275nm and a standard curve between the concentration and their respective absorbance was plotted. The intercept (B) and the slope (K) of the straight line were calculated.

Determination of aqueous solubility of a drug

Dissolved 100mg equivalent quantity of the drug in 100 ml water to make a saturated solution. The

solution was filtered using Whitman filter paper. If necessary, the filtrate was diluted suitably and its absorbance was measured using a UV spectrophotometer at 275 nm. The quantity of drug dissolved in water was determined using the following formula;

$$\text{Amount dissolved (mg/ml)} = \frac{[\text{Absorbance} \times \text{slope} + \text{intercept}] \times \text{bath volume}}{1000}$$

Infra Red Spectrophotometry

Infra-red spectral matching approach was employed to detect any possible chemical interaction between drug and carriers. Potassium bromide was used to make pellet with all compounds. About 100mg of the compound was compressed to form a transparent pellet in hydraulic press at 15 tons pressure. The pellet was scanned from 4000-400 cm^{-1} in FT-IR spectrometer. IR spectrum of individual materials was also recorded. I.R. studies were taken for the sample of Aceclofenac, β-Cyclodextrin, Polyethylene Glycol 6000 (PEG-6000), Gelatin Hydrolysate, Sodium Lauryl Sulphate, Croscarmellose, Aceclofenac+ β-Cyclodextrin, Aceclofenac+ Polyethylene Glycol 6000 (PEG-6000), Aceclofenac+ Gelatin Hydrolysate, Aceclofenac+ Sodium Lauryl Sulphate, and Aceclofenac+ Croscarmellose.

Preparation and evaluation of Solid Dispersion

Thirty batches of solid dispersions were prepared using Aceclofenac as a drug and various carriers like β-cyclodextrin, PEG – 6000, gelatin hydrolysate, sodium Lauryl Sulphate and Croscarmellose corresponding to the ratios of 1:1 and 1:2. The solid dispersions were prepared by three methods such as physical mixture, kneading method and solvent evaporation method. Six batches of Aceclofenac-β-Cyclodextrin solid dispersions were prepared using 1:1 and 1:2 ratios. The prepared solid dispersions were evaluated for angle of repose, bulk density, compressibility, moisture uptake, solubility and drug content.

Differential scanning calorimetry (DSC) Studies of Aceclofenac, Croscarmellose and Aceclofenac-Croscarmellose solid dispersion

The DSC thermograms of Aceclofenac, Croscarmellose and Aceclofenac – Croscarmellose solid dispersions were studied for the evalution of physical modifications.

Preparation of dispersible tablets containing Aceclofenac- Croscarmellose solid dispersions and Aceclofenac only

The dispersible tablets of the selected Aceclofenac-Croscarmellose solid dispersions were prepared. The simple Aceclofenac tablets with Croscarmellose were prepared.

Evaluation of Prepared and marketed Tablets

The prepared tablets of Aceclofenac-Croscarmellose solid dispersions, only Aceclofenac with Croscarmellose tablets and marketed tablets were evaluated for average weight, friability, hardness, drug content and disintegration.

***In-vitro* dissolution studies**

Dissolution studies were carried out using the Aceclofenac-Croscarmellose solid dispersions, Aceclofenac with Croscarmellose and marketed tablets. The dissolution study was performed using USP Apparatus 2 (Lab India DS 8000, India) at 37 ± 0.5^0C with paddle speed 75 ± 5 rpm in 900ml water as dissolution medium. A 10ml sample was withdrawn at different time interval and filtered (Cut – off 0.2µm, Ministart SRP 25, Sartorius, Germany) and analyzed spectrophotometrically at 275nm. Withdrawn samples were replaced with 10ml of fresh medium.

Table 1 Characteristic peaks of the Aceclofenac and carriers in I.R.

Aceclofenac	β-CDs	Aceclofenac + β-CDs	PEG – 6000	Aceclofenac + PEG – 6000	Gelatin Hydrolysate	Aceclofenac + Gelatin Hydrolysate	SLS	Aceclofenac + SLS	Croscarmellose	Aceclofenac + Croscarmellose
3853.8	3903.2	3852.5	3923.4	3903.8	3903.2	3904.0	3858.0	3820.9	3813.5	3799.7
3649.3	3853.0	3837.3	3904.7	3809.9	3890.6	3891.5	3676.6	3746.6	3769.1	3659.0
3630.3	3837.9	3820.2	3854.2	3853.5	3870.7	3871.3	3492.5	3735.5	3732.4	3582.0
3587.9	3820.7	3800.5	3839.1	3839.9	3853.5	3854.2	2957.9	3724.7	3667.6	3441.5
3317.9	38..7	3749.3	3821.8	3820.5	3839.9	3840.2	2919.1	3649.6	3654.0	3119.6
3279.6	3768.1	3733.8	3807.3	3805.4	3820.8	3821.2	2849.8	3318.5	3585.6	2933.7
3071.0	3749.5	3710.2	3802.4	3769.1	3805.2	3802.2	2358.9	2957.0	3379.6	2647.8
3027.2	3563.6	3688.5	3758.8	3750.2	3778.4	3780.2	2344.8	2918.7	3107.3	2271.1
2970.4	3509.0	3674.3	3750.9	3735.1	3768.3	3769.3	1684.9	2849.4	2919.6	1920.8
2936.2	3385.2	3646.9	3421.5	3724.9	3478.9	3750.9	1654.6	2344.8	2329.8	1846.7
2863.2	2926.4	3585.4	2886.9	3710.9	3323.3	3735.5	1560.3	1942.5	1715.5	1770.9
2345.1	2376.4	3318.7	2739.6	3689.8	3077.0	3723.9	1468.6	1920.9	1601.8	1729.2
2304.9	2344.4	2933.9	2694.5	3675.7	2958.8	3566.8	1619.9	1911.3	1522.1	1567.7
2103.8	2080.4	2367.0	2606.8	3648.9	2877.3	3307.7	1363.4	1870.5	1505.2	1442.0
1941.5	1869.8	2343.6	2506.8	3628.7	2365.4	3076.9	1223.0	1846.6	1424.8	1247.3
1920.6	1792.4	1921.3	2378.0	3618.4	2343.4	2935.0	1160.6	1792.8	1377.7	1099.1
1911.3	1772.5	1845.8	2345.0	3566.8	1653.9	2877.6	1132.7	1772.2	1323.7	898.1
1846.5	1733.5	1829.5	2238.4	3527.1	1450.0	2368.6	1112.9	1716.7	1267.4	839.0
1830.1	1717.7	1771.7	2165.5	3422.6	1398.4	2344.6	1084.4	1655.0	1238.4	769.8
1771.3	1700.1	1716.8	2098.2	2887.1	1333.6	1869.2	1045.3	1648.6	1160.6	653.7
1716.7	1683.2	1653.3	1968.5	2740.7	1241.9	1844.7	1019.6	1638.7	1056.4	472.3
1618.3	1653.3	1646.6	1870.0	2694.4	1201.2	1654.8	996.3	1629.7	991.3	438.0
1604.2	1646.8	1589.6	1830.0	2626.5	1162.8	1534.2	918.6	1618.3	898.9	434.3
1589.1	1559.4	1577.7	1811.9	2379.1	1081.1	1448.8	890.8	1604.7	722.7	410.5
1577.4	1541.3	1567.6	1793.4	2344.6	1030.8	1399.4	830.5	1589.1	679.9	-
1567.1	1506.9	1560.5	1773.5	2239.1	975.5	1332.7	763.1	1577.6	554.1	-
1534.5	1418.0	1508.3	1751.0	2167.2	921.0	1238.7	721.5	1567.3	460.0	-
1508.4	1368.5	1453.0	1734.7	1968.6	683.7	1161.1	669.3	1560.8	-	-
1480.7	1336.8	1438.7	1718.6	1869.9	660.1	1081.5	633.5	1543.2	-	-
1452.3	1302.2	1418.5	1706.8	1811.3	605.7	1030.8	590.7	1533.9	-	-
1438.7	1243.8	1367.3	1684.7	1772.1	525.7	976.3	482.0	1508.6	-	-
1417.9	1157.8	1344.8	1669.8	1734.7	504.9	922.0	428.4	1468.9	-	-
1344.3	1080.4	1301.6	1654.4	1700.7	493.2	660.8	-	1453.7	-	-
1301.5	1027.4	1292.5	1647.4	1684.7	-	427.2	-	1438.8	-	-
1291.0	946.4	1281.5	1637.1	1669.5	-	418.3	-	1417.8	-	-
1281.1	937.4	1256.8	1617.9	1661.9	-	407.5	-	1380.4	-	-
1247.5	887.8	1248.1	1609.8	1654.2	-	-	-	1344.2	-	-
1198.1	856.9	1199.0	1577.2	1647.1	-	-	-	1230.3	-	-
1149.7	755.7	1155.3	1570.2	1636.9	-	-	-	1180.4	-	-
1101.0	707.3	1079.2	1560.0	1617.5	-	-	-	1149.7	-	-
1055.4	609.0	1026.8	1542.3	1589.0	-	-	-	1084.6	-	-
964.30	577.9	944.8	1533.4	1577.5	-	-	-	1056.3	-	-
809.25	528.1	899.1	1522.0	1569.4	-	-	-	-	-	-
749.09	-	851.2	1507.8	1560.0	-	-	-	-	-	-
427.86	-	780.6	1467.8	1541.1	-	-	-	-	-	-
-	-	749.8	1412.9	1507.4	-	-	-	-	-	-
-	-	715.8	579.2	1467.3	-	-	-	-	-	-
-	-	-	528.8	1455.5	-	-	-	-	-	-
-	-	-	508.8	1413.1	-	-	-	-	-	-
-	-	-	-	1360.2	-	-	-	-	-	-
-	-	-	-	1642.9	-	-	-	-	-	-
-	-	-	-	1280.7	-	-	-	-	-	-
-	-	-	-	1242.4	-	-	-	-	-	-
-	-	-	-	1149.3	-	-	-	-	-	-
-	-	-	-	1113.1	-	-	-	-	-	-
-	-	-	-	778.4	-	-	-	-	-	-
-	-	-	-	748.4	-	-	-	-	-	-
-	-	-	-	721.1	-	-	-	-	-	-
-	-	-	-	578.8	-	-	-	-	-	-
-	-	-	-	529.1	-	-	-	-	-	-
-	-	-	-	508.8	-	-	-	-	-	-

Table 2 Physical Evaluation of Aceclofenac

S.No.	Evaluation	Mean ± SD value
1.	Angle of Repose	24.19 (± 0.24)
2.	Bulk density (g/cc)	0.92 ± (0.20)
3.	Compressibility (%)	27.08 (± 2.9)
4.	Moisture uptake (%)	7.34 (± 0.91)
5.	Solubility (mg/ml)	0.78 (±0.21)

Value in parentheses represent SD n=3

Table 3 Physical Evaluation of β-Cyclodextrin

S.No.	Evaluation	Mean ± SD value
1.	Angle of Repose	32.59 (± 1.13)
2.	Bulk density (g/cc)	0.88 (± 0.55)
3.	Compressibility (%)	25.36 (± 1.11)
4.	Moisture uptake (%)	11.18 (± 0.46)

Value in parentheses represent SD n=3

Table 4 Physical Evaluation of Polyethylene Glycol 6000

S.No.	Evaluation	Mean ± SD value
1.	Angle of Repose	32.56 (± 1.34)
2.	Bulk density (g/cc)	0.85 (± 0.10)
3.	Compressibility (%)	26.44 (± 2.91)
4.	Moisture uptake (%)	10.54 (± 1.01)

Value in parentheses represent SD n=3

Table 5 Physical Evaluation of Gelatin Hydrolysate

S.No.	Evaluation	Mean ± SD value
1.	Angle of Repose	45.61 (± 0.96)
2.	Bulk density (g/cc)	0.64 (± 0.68)
3.	Compressibility (%)	27.72 (± 0.02)
4.	Moisture uptake (%)	9.46 (± 0.98)

Value in parentheses represent SD n=3

Table 6 Physical Evaluation of Sodium Lauryl Sulphate

S.No.	Evaluation	Mean ± SD value
1.	Angle of Repose	24.02 (± 1.07)
2.	Bulk density (g/cc)	0.88 (± 0.46)
3.	Compressibility (%)	24.34 (± 1.03)
4.	Moisture uptake (%)	9.65 (± 1.06)

Value in parentheses represent SD n=3

Table 7 Physical Evaluation of Croscarmellose

S.No.	Evaluation	Mean ± SD value
1.	Angle of Repose	22.79 (± 0.97)
2.	Bulk density (g/cc)	0.66 (± 0.17)
3.	Compressibility (%)	28.80 (± 1.75)
4.	Moisture uptake (%)	10.54 (± 1.25)

Value in parentheses represent SD n=3

Table 8 Physical Evaluation of Solid Dispersions containing Aceclofenac and β-Cyclodextrin

Evaluation	Physical Method (1:1)	Kneading Method (1:1)	Solvent evaporation Method (1:1)	Physical Method (1:2)	Kneading Method (1:2)	Solvent evaporation Method (1:2)
Angle of Repose (degrees)	24.72 (±3.93)	26.49 (±3.23)	26.29 (±3.20)	24.88 (±3.76)	24.34 (±4.85)	24.21 (±3.31)
Bulk density (g/cc)	0.91 (±3.51)	0.93 (±1.52)	0.94 (±1.15)	0.92 (±2.64)	0.89 (±5.85)	0.89 (±6.81)
Compressibility (%)	15.89 (±1.63)	17.07 (±0.93)	16.16 (±0.98)	15.17 (±1.18)	15.63 (±2.32)	16.23 (±1.47)
Moisture uptake (%)	10.04 (±1.06)	10.73 (±0.43)	9.83 (±0.64)	10.00 (±1.65)	9.87 (±1.19)	11.08 (±1.05)
Solubility (mg/ml)	1.60 (±0.08)	3.40 (±0.39)	1.94 (±0.36)	1.17 (±0.29)	1.53 (±0.85)	1.79 (±0.60)
Drug content (%)	99.98	99.90	98.35	99.25	99.46	98.26

Value in parentheses represent SD n=3

Table 9 Physical Evaluation of Solid Dispersions containing Aceclofenac and PEG- 6000

Evaluation	Physical Method (1:1)	Kneading Method (1:1)	Solvent evaporation Method (1:1)	Physical Method (1:2)	Kneading Method (1:2)	Solvent evaporation Method (1:2)
Angle of Repose (degrees)	28.51 (±0.84)	29.51 (±0.70)	30.21 (±1.29)	25.09 (±1.86)	29.94 (±0.55)	30.80 (±1.37)
Bulk density (g/cc)	0.72 (±0.45)	0.66 (±0.88)	0.64 (±0.35)	0.71 (±1.52)	0.65 (±0.37)	0.70 (±0.60)
Compressibility (%)	36.22 (±0.60)	39.21 (±0.66)	37.75 (±0.60)	38.86 (±0.54)	37.11 (±0.99)	37.09 (±1.67)
Moisture uptake (%)	10.51 (±1.11)	11.11 (±0.47)	11.79 (±1.85)	11.45 (±1.85)	10.62 (±0.87)	10.17 (±0.95)
Solubility (mg/ml)	1.63 (±4.57)	2.60 (±0.16)	2.52 (±0.17)	1.29 (±0.24)	3.72 (±0.20)	3.49 (±0.17)
Drug content (%)	99.28	99.34	99.34	98.25	99.66	99.86

Value in parentheses represent SD n=3

Table 10 Physical Evaluation of Solid Dispersions containing Aceclofenac and Gelatin Hydrolysate

Evaluation	Physical Method (1:1)	Kneading Method (1:1)	Solvent evaporation Method (1:1)	Physical Method (1:2)	Kneading Method (1:2)	Solvent evaporation Method (1:2)
Angle of Repose (degrees)	25.29 (±3.0)	24.94 (±4.24)	25.07 (±5.79)	25.05 (±3.15)	26.62 (±2.73)	26.17 (±4.51)
Bulk density (g/cc)	0.92 (±0.26)	0.93 (±0.60)	0.82 (±0.81)	0.84 (±0.64)	0.88 (±0.13)	0.87 (±0.11)
Compressibility (%)	27.38 (±2.69)	26.47 (±2.64)	25.38 (±3.03)	25.58 (±0.81)	26.27 (±2.99)	25.31 (±3.06)
Moisture uptake (%)	10.25 (±1.09)	9.96 (±0.45)	9.69 (±0.69)	10.61 (±1.29)	10.44 (±1.06)	10.05 (±0.51)
Solubility (mg/ml)	1.96 (±0.54)	1.30 (±0.26)	1.73 (±0.27)	0.74 (±1.79)	1.09 (±0.41)	1.03 (±0.12)
Drug content (%)	93.98	95.90	99.15	98.13	98.86	99.38

Value in parentheses represent SD n=3

Table 11 Physical Evaluation of Solid Dispersions containing Aceclofenac and Sodium Lauryl Sulphate

Evaluation	Physical Method (1:1)	Kneading Method (1:1)	Solvent evaporation Method (1:1)	Physical Method (1:2)	Kneading Method (1:2)	Solvent evaporation Method (1:2)
Angle of Repose (degrees)	22.39 (±2.38)	21.46 (±1.70)	22.90 (±1.82)	22.70 (±1.54)	20.87 (±0.14)	21.28 (±2.32)
Bulk density (g/cc)	1.92 (±4.58)	0.88 (±5.03)	0.90 (±1.52)	0.92 (±3.21)	0.89 (±2.64)	0.86 (±2.51)
Compressibility (%)	14.29 (±1.46)	14.75 (±2.77)	16.16 (±1.78)	15.57 (±2.36)	17.95 (±3.72)	16.92 (±4.85)
Moisture uptake (%)	8.61 (±0.74)	9.06 (±0.85)	8.72 (±1.27)	8.24 (±0.96)	7.76 (±0.79)	8.76 (±0.53)
Solubility (mg/ml)	1.49 (±0.55)	0.99 (±0.53)	2.87 (±6.42)	1.53 (±0.14)	1.34 (±0.27)	2.69 (±0.20)
Drug content (%)	98.58	99.93	98.67	98.64	98.46	99.91

Value in parentheses represent SD n=3

Table 12 Physical Evaluation of Solid Dispersions containing Aceclofenac and Croscarmellose

Evaluation	Physical Method (1:1)	Kneading Method (1:1)	Solvent evaporation Method (1:1)	Physical Method (1:2)	Kneading Method (1:2)	Solvent evaporation Method (1:2)
Angle of Repose (degrees)	22.05 (±2.24)	21.45 (±1.03)	23.49 (±2.58)	22.01 (±1.90)	23.07 (±3.66)	21.87 (±1.16)
Bulk density (g/cc)	0.91 (±0.52)	0.93 (±0.30)	0.90 (±0.20)	0.90 (±0.57)	0.92 (±0.15)	0.89 (±0.31)
Compressibility (%)	14.58 (±1.01)	15.30 (±1.42)	14.23 (±0.35)	16.19 (±0.26)	15.13 (±1.16)	14.45 (±1.16)
Moisture uptake (%)	9.63 (±1.46)	10.12 (±0.60)	9.21 (±1.05)	10.65 (±0.75)	10.44 (±1.05)	9.80 (±0.73)
Solubility (mg/ml)	5.30 (±0.16)	3.52 (±0.13)	5.31 (±0.10)	9.63 (±0.13)	5.70 (±0.20)	15.152 (±0.24)
Drug content (%)	100.98	101.91	99.96	99.94	99.98	99.99

Value in parentheses represent SD n=3

Table 13 Formula for the tablets containing Solid Dispersion

S. No.	Ingredient	Quantity per 1 tablet (gm)
1.	Complex(Aceclofenac+ Croscarmellose)	0.300
2.	Mannitol	0.073
3.	Lactose	0.073
4.	Sodium carboxy methyl cellulose (5%)	0.025
5.	Croscarmellose (2%)	0.010
6.	Magnesium stearate (1%)	0.005
7.	Talc (3%)	0.015
8.	Saccharin	q.s.
9.	Lemon yellow	q.s.

Table 14 Formula for the tablets containing Aceclofenac only

S. No.	Ingredient	Quantity per 1 tablet (gm)
1.	Aceclofenac	0.100
2.	Mannitol	0.073
3.	Lactose	0.073
4.	Sodium carboxy methyl cellulose (5%)	0.025
5.	Croscarmellose (2%)	0.010
6.	Magnesium stearate (1%)	0.005
7.	Talc (3%)	0.015
8.	Saccharin	q.s.
9.	Lemon yellow	q.s.

Table 15 Evaluation of Prepared and Marketed Tablet

S.No.	Evaluation	Tablet of Aceclofenac & Croscarmellose complex	Tablet of Aceclofenac with Croscarmellose	Marketed tablet
1.	Average weight (mg)	511.57 (±1.10)	506.45 (±1.17)	300.57 (±0.58)
2.	Friability (%)	0.341 (±0.11)	0.43 (±9.05)	0.39 (±0.18)
3.	Hardness (kg)	4.0 (±0.50)	4.33 (±0.57)	5.0 (±0.50)
4.	Disintegration (min)	8.66 (±1.52)	39.66 (±1.53)	43.33 (±1.62)
5.	Drug content (%)	100.60 (±0.57)	100.23 (±0.30)	100.44 (±0.61)

Value in parentheses represent SD n=3

Table 16 In-vitro dissolution studies of Prepared and Marketed Tablets

S.No.	Time (min)	Cumulative % drug release of Tablet containing Aceclofenac & Croscarmellose complex	Cumulative % drug release of Tablet containing Aceclofenac without Croscarmellose	Cumulative % drug release of Marketed tablet	Mean ± Standard deviation values (n=3)
1.	0	0	0	0	0
2.	5	81.55	27.32	23.81	44.22±2.37
3.	10	94.95	35.14	32.78	54.29±5.28
4.	15	98.06	48.32	44.66	63.68±2.83
5.	30	99.34	70.58	66.21	78.71±1.99
6.	45	99.94	79.58	73.94	84.86±3.67
7.	60	100.93	91.21	82.97	97.69±1.61

RESULTS AND DISCUSSIONS

The calibration curve was obtained in the range of 5 to 25 µg/ml with a good regression (r^2) of 0.9956. The infra red spectra of the drug, excipients and prepared solid dispersions reveal that there is no interaction between the drug and excipients, as shown in the Table1.

Aceclofenac and the carriers were characterized for angle of repose, bulk density, compressibility, moisture uptake and solubility as shown in the Tables 2 to 7. The results were satisfactory. The solid dispersions were prepared by three methods. The prepared solid dispersions were also evaluated for Angle of Repose (degrees), Bulk density (g/cc), Compressibility (%), Moisture uptake (%), Solubility (mg/ml) and Drug content (%) as shown in Tables 8 – 12. The results showed that the prepared solid dispersions were well within the limits for further studies. Among all the solid dispersions batches, the solubility of Aceclofenac-Croscarmellose solid dispersions were found highest in solvent evaporation method in 1:2 ratio which was more than 15 times as compare to the free drug solubility. So the batch of Aceclofenac-Croscarmellose solid dispersions was selected as an ideal batch. The selected ideal batch of Aceclofenac-Croscarmellose solid dispersions was confirmed by Differential scanning calorimetry (DSC) studies. Figure 1 shows the DSC data. The thermogram of Aceclofenac showed by first line was a sharp endothermic peak given at 154.57 ^{O}C corresponding to its melting Point. The DSC thermogram of Cross Caremellose was characterized by a small endothermic peak at about 163.81 ^{O}C. The endothermic peak at 145.06 ^{O}C was found for the Aceclofenac + Cross Caremellose complex which was shown in last line in graph. The complete disappearance of the Aceclofenac endothermic peak in these systems indicates the formation of a true chemical complex.

The dispersible tablets of the selected Aceclofenac-Croscarmellose solid dispersions were prepared using the formula given in Table 13. The simple Aceclofenac tablets with Croscarmellose were prepared using the formula given in Table 14. The prepared tablets of Aceclofenac-Croscarmellose solid dispersions, only Aceclofenac with Croscarmellose tablets and marketed tablets were evaluated for Average weight, Friability, Hardness, and Drug content as shown in Table 15. Dissolution studies were carried out using the Aceclofenac-Croscarmellose solid dispersions, Aceclofenac with Croscarmellose and marketed tablets. The drug release from the Aceclofenac-Croscarmellose solid dispersions tablets was found to be 94.95% within 10 min. It was comparatively faster than the drug release of Aceclofenac tablets with Croscarmellose and marketed tablets which was found 35.14% and 32.78% within 10 min respectively. The T_{50} values of Aceclofenac-Croscarmellose solid

dispersions tablets, Aceclofenac with Croscarmellose tablets and marketed tablets were found to be 3min, 16 min and 21 min respectively. Rapid dissolution was the characteristic behavior of solid dispersion of Aceclofenac-Croscarmellose solid dispersions tablets. It was easily being understood that the tablets of Aceclofenac-Croscarmellose solid dispersions were found to be good. The results are shown in Table 16 and the cumulative graph is shown Figure 2.

Figure 1 Differential scanning calorimetry (DSC) Studies of Aceclofenac, Croscarmellose and Aceclofenac-Croscarmellose solid dispersion

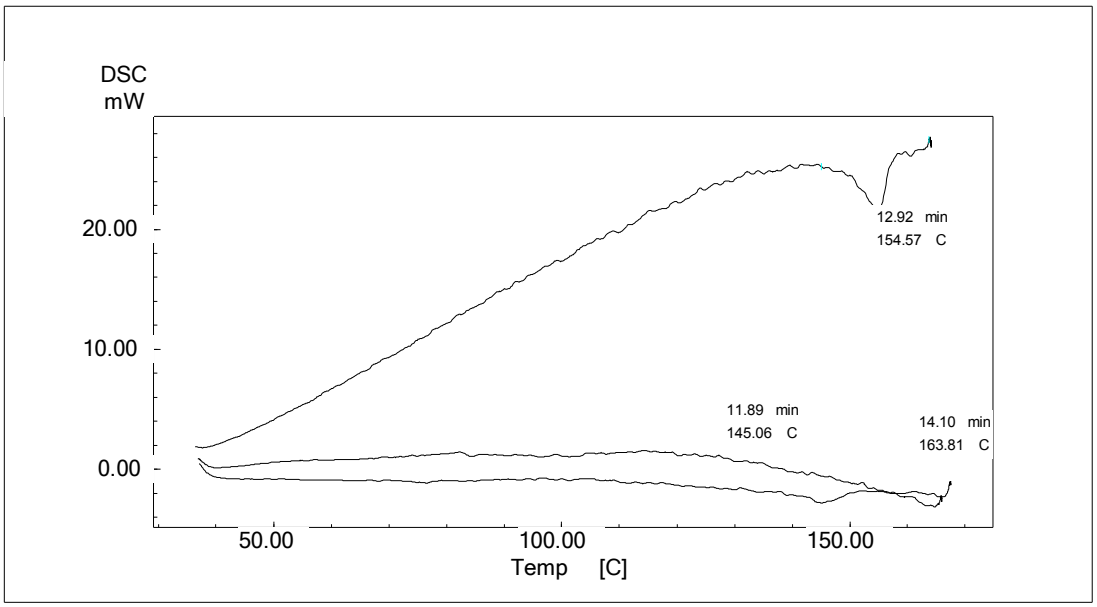
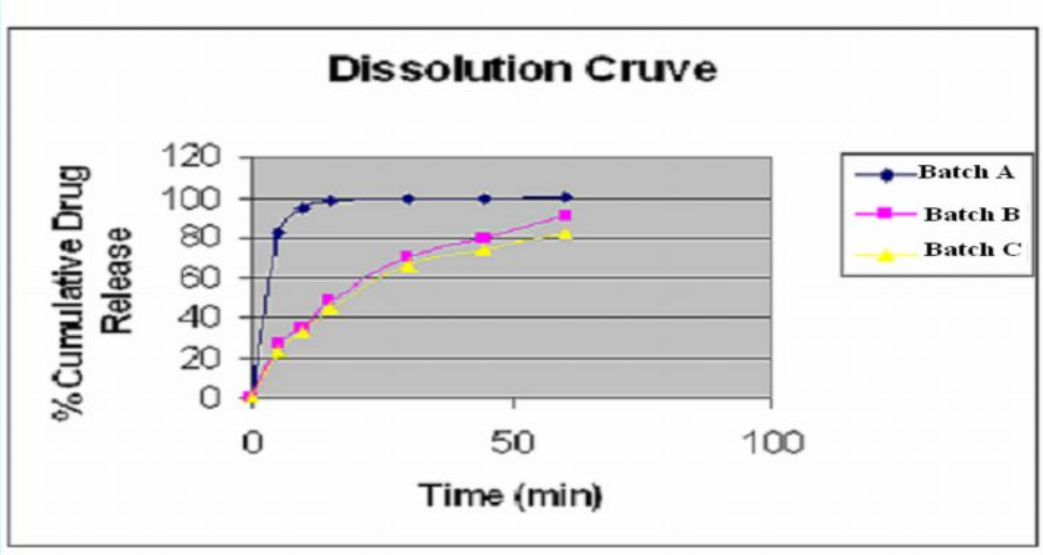


Figure 2 Cumulative Graph of tablets containing Aceclofenac and Croscarmellose, Aceclofenac drug only and marketed tablet



Batch A - Tablet containing Aceclofenac and Croscarmellose solid dispersion
Batch B - Tablet containing Aceclofenac drug only
Batch C - Marketed tablet

CONCLUSION

The Aceclofenac and Croscarmellose solid dispersions tablets was shown the maximum % drug release which was much more than 90% as compared to simple Aceclofenac tablets and marketed tablets.

From the in vitro drug release it was found that the solid dispersion complex of drug was giving good dissolution property than the simple and marketed tablets. Hence, it can be concluded that the dispersible tablets of Aceclofenac and Croscarmellose solid dispersions may be better than simple Aceclofenac tablets for getting better therapy. There was a 15.152 % increase in dissolution of the solid dispersions when compared to marketed drug. This in turn can reduce the dose of Aceclofenac, which is expected to reduce dose related adverse effects and cost of therapy. It is worthwhile for further investigations on long time stability and bioavailability evaluations in human subjects can be confirmed the optimal formula.

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