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Original Research Paper

SOLUBILITY ENHANCEMENT OF POORLY WATER SOLUBLE DRUG ATORVASTATIN CALCIUM BY SOLID DISPERSION TECHNIQUE USING NATURAL CARRIER

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ABSTRACT

Atorvastatin calcium (ATC) is an oral anticholesteremic agent. ATC belongs to BCS class II drug having high permeability but low aqueous solubility. In order to get beneficial therapeutic effects, its water solubility needs to be increased. In the present study, attempt was made to improve solubility and dissolution rate of ATC by formulating it into solid dispersion using maltose monohydrate as a highly water soluble carrier. Three methods were used for preparing solid dispersion, namely, physical mixture, kneading and solvent evaporation method in 1:1, 1:3 and 1:5 drug-carrier ratios. The FTIR study of ATC, its combination with the carrier, and of the sold dispersion indicated no interaction between drug, carrier and other excipients used. The prepared solid dispersion showed improved solubility and dissolution rate as compared to pure drug. The improvement in solubility may be attributed to the improved wettability of ATC due to uniform dispersion into the carrier. The optimized batch was K2, which was prepared by kneading method in 1:3 ratios. The optimized batch released 99.59 % drug within 60 min and had solubility almost five folds higher than pure ATC. From the solubility values it was clear that kneading method was more suitable than the other two methods used for preparing solid dispersion. The XRD studies revealed that the crystalline nature of ATC was reduced when formulated into solid dispersion. The optimized batch of solid dispersion was chosen for formulating immediate release tablet into three batches by direct compression method by varying the concentration of superdisintegrant, crosscarmellose sodium. Tablet prepared with 20% cross carmellose sodium showed 99.41% drug release in 60 min, this drug release was higher compared to the other two batches of tablet prepared.

Keywords: Atorvastatin calcium (ATC), Solid dispersion, Solubility, Dissolution.

INTRODUCTION

Most of the newly discovered chemical entities, in spite of high therapeutic activity, have low aqueous solubility and poor bioavailability, leading to poor absorption in the gastrointestinal tracts.[1] Drug absorption from the gastrointestinal (GI) tract can be limited by a variety of factors. Poor aqueous solubility and/or poor membrane permeability of the drug molecule is the most important factor governing the drug absorption from the GIT.[2] For an oral dosage form to elicit therapeutic effect, it is required to first dissolve in gastrointestinal fluids before permeating the membranes of the GI tract to reach systemic circulation. Therefore, a drug with poor aqueous solubility will typically exhibit dissolution rate limited absorption as it will not face any problems in permeating the membranes whereas the drug with poor membrane permeability will typically exhibit permeation rate limited absorption even though it shows good aqueous solubility.[3] Hence two areas of pharmaceutical research that focus on improving the oral bioavailability of active

agents include enhancing solubility and dissolution rate of poorly water-soluble drugs and enhancing permeability of poorly permeable drugs.[4] Alteration of the solid state at the particle or molecular level involves a physical change in the drug and is an attractive option for improving drug solubility.[5] Solid dispersions contribute by enhancing wettability and modulating the properties of the solvent. It is one of the widely and effective used techniques for dissolution enhancement.[6] The two basic procedures used to prepare solid dispersions are the melting or fusion and solvent evaporation method.[7] Atorvastatin is one such drug belonging to class II according to Biopharmaceutical classification system which shows poor water solubility but has good membrane permeability. Thus formulation of atorvastatin should be such that it should have enough aqueous solubility. Solid dispersion method serves this purpose as it increases the solubility as well as dissolution rate as compared to the pure atorvastatin. The study involves formation of solid dispersion of atorvastatin using natural polymer, maltose monohydrate which is highly water soluble. Thus using solid dispersion method, the solubility barrier of atorvastatin in water can be overcome.

MATERIALS AND METHODS

Materials

ATC was obtained as a gift sample from Microlabs Pvt. Ltd., Bangalore (India). All other chemicals and reagents were of analytical grade purchased from Himedia Laboratories Pvt. Ltd., Mumbai. FTIR spectra were taken using Shimadzu FTIR-8700 spectrophotometer; DSC thermograms were obtained by differential scanning calorimeter (DSC 60; Shimadzu) where as XRD patterns were recorded using Philips diffractometer (PW3710; Almelo, Netherland).

Methods

Preformulation parameters

Determination of Absorption Maxima (λ max) of ATC

Approximately 10 mg of ATC was dissolved in 0.1 N HCl and volume was made up to 100 ml to get 100 µg/ml stock solution. It was further diluted to get concentrations from 10-50 µg/ml. The solutions were analysed by UV-spectrophotometer to find the maximum absorption at a particular wavelength. The λ max was found to be 241 nm. Similarly, absorption maxima were carried out in distilled water and it was also found to be 241 nm.

Standard Calibration Curve of ATC

Standard Calibration Curve of ATC was carried out both in distilled water and in 0.1 N HCl

Procedure

A standard solution of 100 µg /ml was prepared by dissolving 10 mg of ATC in 100 ml 0.1 N HCl. From the above stock solution, aliquots of 1-5 ml were withdrawn and were diluted with 0.1 N HCl up to 10 ml. It was further diluted to get concentrations from 10-50 µg/ml. The resultant dilutions were analysed by UV at 241 nm and absorbance values were noted for each dilution. Finally, a graph of absorbance vs concentration was plotted.

Melting Point Determination

Melting point was determined by using glass capillary method. The Thieles tube filled with paraffin oil was used, in to which a capillary containing the drug was placed along with the thermometer. The paraffin oil was then heated continuously till the powder melts and corresponding temperature was noted and recorded as melting point of drug.

FTIR Studies of Drug and Carrier

Drug-carrier compatibility study was done to study the interaction between drug and carrier used in the preparation of solid dispersion. FTIR spectrum of pure drug ATC, carrier-maltose monohydrate and of drug-carrier combination was recorded. The drug and carriers separately and in combination were mixed with KBr for determination of spectrum. The range selected was from 4000 cm^{-1} - 400 cm^{-1}.

Determination of Micromeritic Properties of Atorvastatin Calcium

Micromeritic properties of ATC such as bulk density, tapped density, Hausner's ratio,

compressibility index and angle of repose were determined.

Solubility Determination of Pure ATC

Solubility studies were carried out in distilled water. Solubility studies were performed according to the method described by Higuchi and Connors.[8] For solubility determination, excess of ATC was added in vials containing distilled water. The vials were subjected to shaking for 24 hrs on a magnetic stirrer. The

Physical Mixture[9]

In this method, the drug ATC and the carrier maltose monohydrate were simply mixed using spatula and gently triturated to get uniformly mixed drug-carrier mixture. The mixture was prepared in 1:1, 1:3 and 1:5 ratio of drug-carrier respectively. The resultant mixture was stored until further use.

Kneading Method [10]

In this method, the physical mixture of ATC and carrier maltose monohydrate was kneaded using methanol to form a thick paste. The thick paste obtained was then dried in hot air oven 60^0C and then pulverised to obtain fine particles, which were further passed through sieve no.60.

Solvent Evaporation Method[11]

Atorvastatin and maltose were added in methanol in a mortar and the solution was vigorously stirred until entire methanol was evaporated to obtain a clear solvent free film. The film was then pulverised and passed through sieve no.60.

Evaluation of Solid Dispersion

Solubility Studies of Atorvastatin Solid Dispersion

The solubility studies of ATC solid dispersion were carried out in distilled water. Solubility studies were performed according to the method described by Higuchi and Connors**.** Solid dispersion equivalent to 10 mg of ATC was shaken with 10 ml distilled water in vials on magnetic stirrer for 24 hours at room temperature. Then, the solutions were filtered through Whatman filter paper no 1. Filtered solution was diluted properly with distilled water. The diluted resultant suspension was then filtered through Whatmann filter paper no.1 and suitably diluted with distilled water. Finally, the samples were analysed by UV-spectrophotometer at 241 nm.

Preparation of Solid Dispersion

Formulation of solid dispersion was done after studying the drug-carrier compatibility using FTIR. Three methods, namely physical mixture, kneading and solvent evaporation were used for preparation in 1:3 drug: carrier ratio.
solution was analyzed for the ATC using UV-spectrophotometer at 241 nm.

Determination of Drug content

Solid dispersion equivalent to 10 mg of ATC was weighed accurately and dissolved in 10 ml of methanol. The solution was filtered, diluted suitably and drug content was analyzed at 241 nm by UV spectrophotometer.[12]

% Drug content = $(Mact/M_t) \times 100$

Mact = Actual amount of drug in solid dispersion.
Mt = Theoretical amount of drug in solid dispersion.

FTIR Studies of Solid Dispersion

FTIR spectrum of the prepared solid dispersion was taken for checking the interaction of the drug with carrier and other excipients used. The solid dispersion was mixed with KBr for determination of spectrum. The range selected was from 4000 cm^{-1} – 400 cm^{-1}. Instrument used was Shimadzu FTIR-8700 spectrophotometer

Differential Scanning Calorimetry (DSC)

DSC was used to detect the occurrence of thermal events in drug and the formulation mixture. The samples were weighed in 40 ml aluminium pans, approximately 2 to 4 mg, and were sealed. An empty aluminium pan was used as a reference. DSC thermograms were obtained by differential scanning calorimeter (DSC 60; Shimadzu) at a heating rate of 10^0C/min from 0 to 300^0C in nitrogen atmosphere.

X-Ray Powder Diffraction (XRD)

X-ray powder diffraction was used as a rapid analytical technique for detecting the amount of crystallinity in a powder sample. X-ray diffraction (XRD) studies of pure drug ATC and solid

dispersion were carried out to detect the changes in the crystallinity when ATC was converted to solid dispersion. XRD patterns were recorded using Philips diffractometer (PW3710; Almelo, Netherland) and Cu-ka radiation (l = 1.6418 Å), monochromatised by a secondary flat graphite crystal. The scanning angle ranged from 1° to 40° and the counting time was 1 s/step. The current used was 30 mA and the voltage was 40 kV.

Dissolution Studies of Solid Dispersion

The dissolution rate of pure Atorvastatin solid dispersion was studied in 900 ml of 0.1 N HCl using USP type II (Paddle type) dissolution test apparatus with a Paddle stirrer at 50 rpm. A temperature 37±0.5^{o}C was maintained throughout the study. Drug or solid dispersion equivalent to 25 mg of Atorvastatin was used in each test. Samples of dissolution media (5ml) were withdrawn through a filter (0.45µ) at different intervals of time, suitably diluted and assayed at 241 nm. The samples of dissolution fluid withdrawn at each time were replaced with 5 ml of fresh fluid.

Preparation of Immediate Release Tablet from Solid Dispersion by Direct Compression Method

The best batch of solid dispersion (Prepared by kneading method-formulation code K2) was chosen and formulated into immediate release tablet equivalent to 40 mg dose of ATC. Formulations were prepared by using superdisintegrant cross carmellose sodium and other excipients such as magnesium stearate, talc and microcrystalline cellulose. Immediate release tablets were prepared by direct compression method. Required quantities of solid dispersion (equivalent to 40 mg of ATC), filler and other excipients were blended together for some time (10 min) after passing through 60 mesh screen and mixed with magnesium stearate and talc. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 300 mg using concave punch of size 7 mm.

Evaluation of Tablet

The prepared tablets were evaluated for hardness, thickness, friability, weight variation, *In-vitro* disintegration time and for drug release.

Dissolution Studies

The *in-vitro* drug release studies for all formulations were studied using USP type - II (Paddle) dissolution test apparatus. 900 ml of 0.1N HCl solution was used as dissolution medium. The speed of the paddle was set at 50 rpm and the temperature of the medium was maintained at 37 ± 0.5°C and 5 ml sample was withdrawn at predetermined intervals up to 50 min and replacements were done with fresh dissolution medium. The samples were suitably diluted and analysed for drug content by UV spectroscopy at 241 nm.

RESULTS

UV- Spectra (λ max) of ATC in 0.1 N HCl

UV- spectra (λ max) of ATC was carried out in 0.1 N HCl. The λ max was found to be 241 nm. The UV- spectra is shown in Fig.1.

Standard Calibration Curve of ATC

Standard calibration curve of ATC was carried out both in distilled water and in 0.1 N HCl. The readings from calibration curves in 0.1 N HCl and distilled water are shown in Table 2 and 3 respectively. Calibration curves in 0.1 N HCl and in distilled water are shown in Fig. 2 and 3.

Fourier Transforms Infra Red Spectroscopy

The prominent peaks observed in the graph of pure ATC were also observed in the graph involving ATC-maltose and in the solid dispersion as well. The FTIR Spectra of pure ATC, ATC-maltose combination and of solid dispersion is shown in Fig. 4, 5 and 6 respectively.

Determination of Micromeritic Properties of Atorvastatin Calcium

Micromeritic properties of ATC such as bulk density, tapped density, Hausner's ratio, compressibility index and angle of repose are mentioned in Table 4.

Melting Point Determination

Melting point was determined by using glass capillary method. The melting point of ATC was found to be 179^{0}C.

Solubility Studies of Atorvastatin Solid Dispersion

Solubility value of pure ATC and solid dispersion is mentioned in Table 5. Solubility of ATC was found to be 10.31µg/ml in distilled water. Solid dispersion prepared by three methods had higher solubilities compared to pure ATC.

Determination of Drug content

The percent drug content of solid dispersion prepared by three methods is mentioned in table 5. Batch K2 has the highest drug content (98.35%).

X-Ray Powder Diffraction (XRD)

The XRD images of pure ATC and solid dispersion are shown in Fig. 7 and 8 respectively**.** XRD pattrern of solid dispersion shows reduced peak intensities as compared to pure ATC.

Differential Scanning Calorimetry (Dsc)

The DSC thermogram of ATC and solid dispersion is shown in Fig. 9 and 10 respectively.

Percent Drug Release from Solid Dispersion

The percent drug release from all the batches of solid dispersion was studied in 0.1 N HCl. The percent drug release is shown in table 6. A graph of time vs percent drug release from solid dispersion is depicted in Fig. 12.

Formulation of Tablet from Solid Dispersion

Formula for different batches of tablet is shown in Table 7.

Evaluation of Tablet

Tablet prepared from solid dispersion by direct compression method were evaluated for thickness, hardness, friability, weight variation, disintegration for all the batches. Table 8 evaluates the above mentioned parameters of tablet.

Percent Release of Drug from Tablet

Percent release of drug from three batches of tablet is shown in Table 9 and fig 13.

Stability Study of Immediate Release Tablet

The Optimized batch of immediate release tablet (F3) was subjected for one month stability study according to ICH guidelines by exposing the tablets in their final packaging mode to the temperature 40 $\pm 2^0$C and relative humidity 75 ± 5% in programmable environmental test chamber. At the end of one month, the tablets were analyzed for *in vitro* dissolution. Table 10 shows percent drug release from tablet after stability study.

DISCUSSION

UV- Spectra ((λ max) of ATC in 0.1 N HCl

Accurately weighed 10 mg of ATC was dissolved in 0.1 N HCl and volume was made up to 100 ml to get 100 µg/ml stock solution. From the above stock, serial dilutions were made by withdrawing 1, 2, 3, 4 and 5 ml solution and diluting up to 10 ml with the same stock solution to get 10, 20, 30, 40 and 50 µg/ml solutions. The solutions were analysed by UV-Spectrophotometer to find the maximum absorption at a particular wavelength. The λ max was found to be 241 nm.

Standard Calibration Curve of ATC

Standard calibration curve of ATC was carried out both in distilled water and in 0.1 N HCl. Standard curve of ATC was prepared in 0.1 N HCl, ATC followed Beer Lambert's law in the concentration range of 2-14 µg/ml. The equation of line(s) was found to be: Y= 0 .012 x + 0.033 (R^2=0.997). Correlation coefficient values indicated the linear correlation between concentration and absorbance. The calculations of drug content and *in vitro* drug release are based on respective standard curve.

Micromeritic Properties of ATC

Properties such as bulk density, tap density, carr's index, Hausner's ratio and angle of repose were studied. The bulk density of drug was found to be 0.087 gm/ml; tap density value obtained was 1.073 gm/ml while the Hausner's ratio was 1.19. The angle of repose and carr's index values found out were 38.31 and 20.9 respectively. Both values indicated that the flow of the powder was fair and passable

Fourier Transforms Infra Red Spectroscopy

The FTIR spectra of pure ATC showed characteristic peaks at 2955.15 cm^{-1} (C-H - stretching), 3055 cm^{-1} (C-HO - stretching alcoholic group), 3363 cm^{-1} (N-H stretching amidic group), 1656.97 cm^{-1} (C=C - bending),

696 cm^{-1} (C-F - stretching), 1110 cm^{-1} (O-H - bending). The prominent peaks observed in the graph of pure ATC were also observed in the graph involving ATC-maltose and in the solid dispersion as well. This indicates that the drug and the carrier are compatible with each other.

XRD Studies

The XRD pattern of pure drug ATC produced several diffraction peaks at 2θ=17.078 19.43, 21.58 indicating the crystalline nature of ATC. The XRD of solid dispersion exhibited crystallinity with reduced intensity as compared to pure ATC. XRD of solid dispersion showed reduced peak height areas compared to pure drug. Some major peaks displayed in the XRD image of pure ATC got disappeared in the XRD pattern of the formulated solid dispersion, indicating the existence of amorphous ATC in the solid dispersion of ATC-maltose monohydrate. Absence of sharp characteristic peaks in the formulation suggests the conversion of crystalline ATC to amorphous.

Differential Scanning Calorimetry (DSC) studies

The DSC thermogram of ATC showed an endothermic peak at 172^{0}C, corresponding to its melting point. This peak indicates the crystallinity of ATC. Only one sharp peak was observed which confirmed that ATC is free from impurities. The DSC thermogram of the solid dispersion involving ATC showed endothermic peak at lower temperature i.e 169 ^{0}C compared to the peak of pure ATC at 172 ^{0}C.This may be attributed to uniform dispersion of ATC into the carrier, maltose.

Percent Drug Release from Solid Dispersion

Solid dispersion prepared by kneading method in 1:3 ratio showed maximum drug release (99.59%) corresponding to 75 minutes. Hence this ratio was selected for the preparation of immediate release ATC tablet. Solid dispersion formulated using physical mixture had 86% drug release in 75 minutes, while the release by kneading and solvent method were 99.59 and 91.32 % drug in the same time. It was clear from the observed values that kneading method 1:3 ratio had better drug release than the other included methods, hence this method and ratio was selected for formulating immediate release ATC tablet. The reasons for improved drug release may be

- The strong hydrophilic character of maltose monohydrate which improves the water penetration and wettability of the ATC.
- Reduction in crystallinity of ATC when formulated in solid dispersion, absence of crystal indicates lower energy required for dissolution.

Formulation of Tablet from Solid Dispersion by Direct Compression Technique

The tablet was prepared from optimized batch of solid dispersion (K-2) by direct compression method using different excipients such as microcrystalline cellulose, cross carmellose sodium, talc and magnesium stearate. The sold dispersion was selected in such a ratio that it would contain the drug-carrier in 1:3 optimized ratio in all three batches. Solid dispersion equivalent to 40 mg ATC was taken and tablets were formulated into three batches namely F-1, F-2 and F-3 by varying the concentrations of superdisintegrant, cross carmellose sodium. A plain tablet of ATC was also prepared for comparing the release. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 300 mg using concave punch of size 7 mm.

Evaluation of Tablet

Tablet prepared from solid dispersion by direct compression method can be evaluated for thickness, hardness, friability, weight variation, disintegration for all the batches. All the tablets passed the tests and were within the range specified in Pharmacopoeia.

Stability Study of Immediate Release Tablet

Stability studies were carried out at 40 ± 2^{0}C and relative humidity 75 ± 5 % for 30 days. No significant change in the drug release profile of the tablet (F3) was observed during the stability study period. Hence the preparations were sufficiently stable as per the regulatory requirement.

CONCLUSION

The objective behind preparing solid dispersion of ATC with maltose was to improve its solubility and dissolution rate as it is a poorly water soluble drug. The solubility and dissolution studies showed improved solubility of ATC through solid dispersion with maltose. The solubility value of the optimized batch, K2 was found to be 5 folds higher than the pure drug, whereas dissolution rate of ATC improved to more than 20 % as compared to the pure drug. Further, all the solid dispersions showed higher aqueous solubilities and better drug release as compared to pure ATC. The IR spectra indicated no interaction between the drug and carrier. A maximum increase in dissolution rate was obtained with ATC: maltose solid dispersion in 1:3 ratio prepared by kneading method. The solubility and dissolution rates obtained by kneading method were found to be better as compared to physical mixture and solvent evaporation method. Tablets were prepared from optimized batch of solid dispersion (K-2) by direct compression method and studied for percent release of drug. Batch F3 showed 99.41 % drug release. Batch F3 had the highest amount of superdisintegrant.

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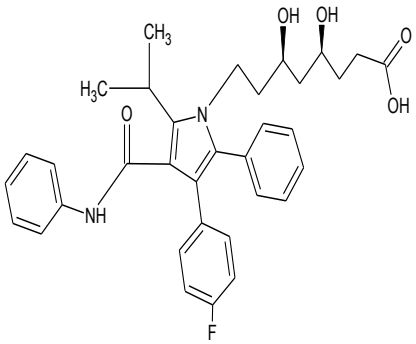

Structure of ATC

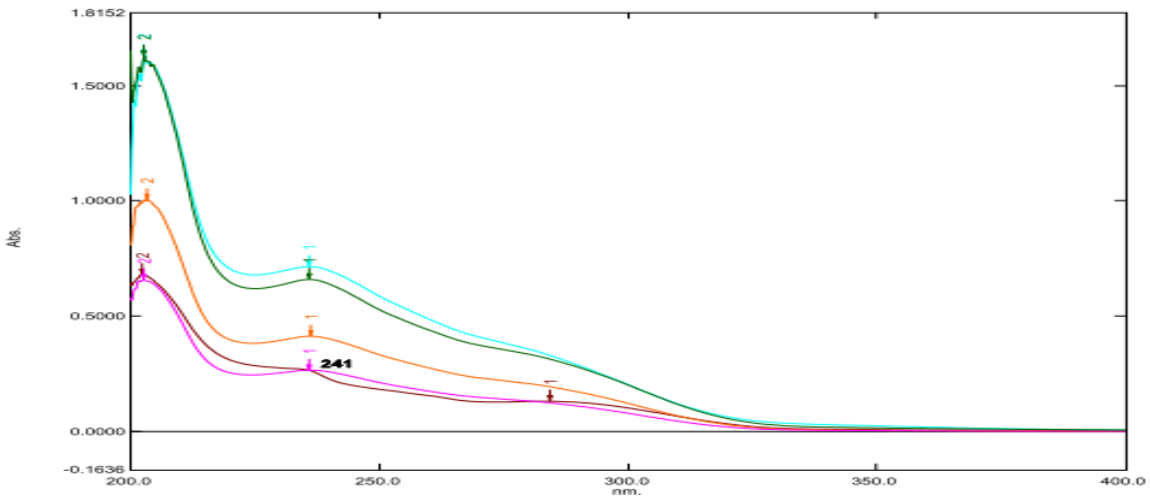

Figure 1: λ max of ATC in 0.1 N HCl

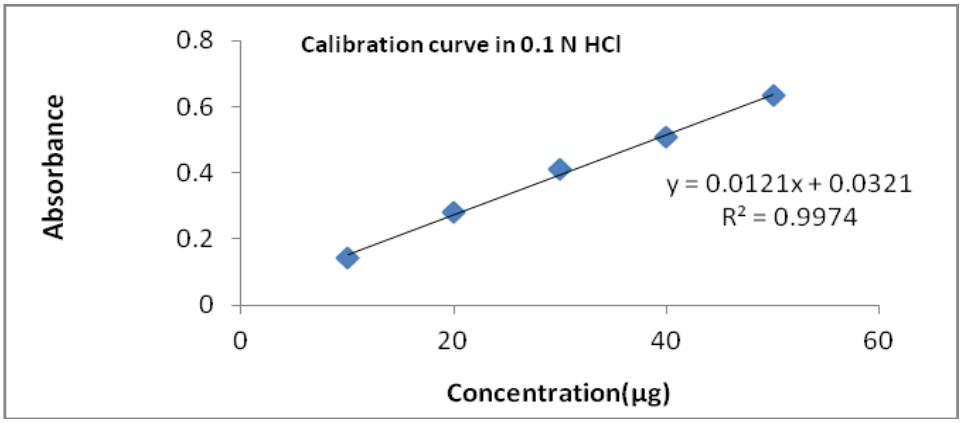

Figure 2: Calibration curve of ATC in 0.1 N HCl

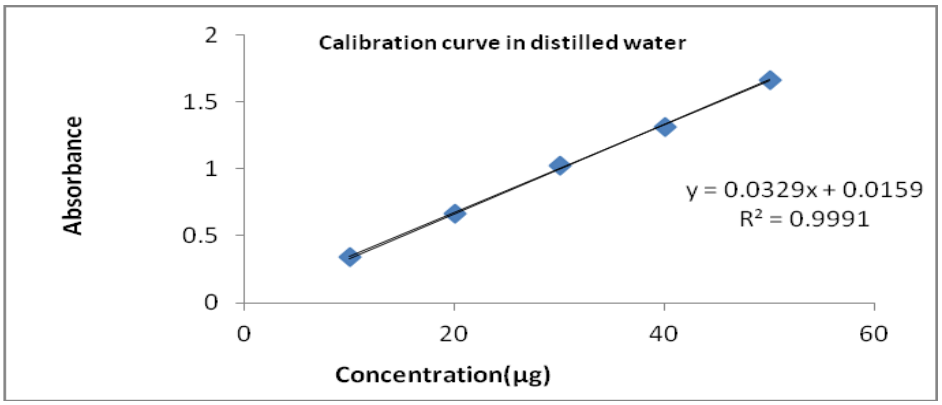

Figure 3: Calibration curve of ATC in distilled water

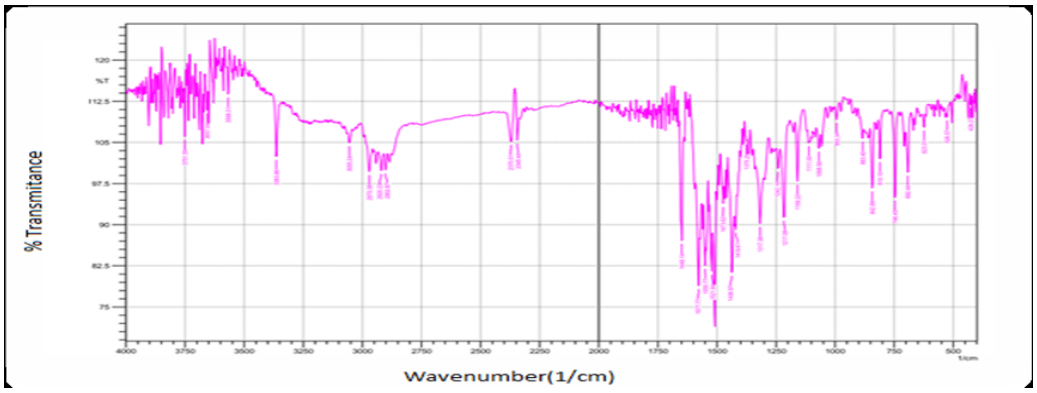

Figure 4: FTIR Spectra of ATC

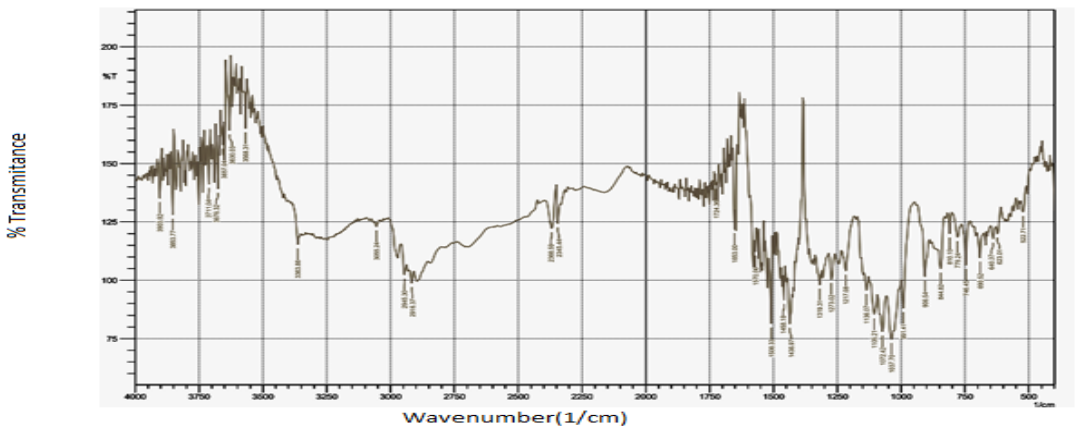

Figure 5: FTIR spectra of ATC-maltose monohydrate

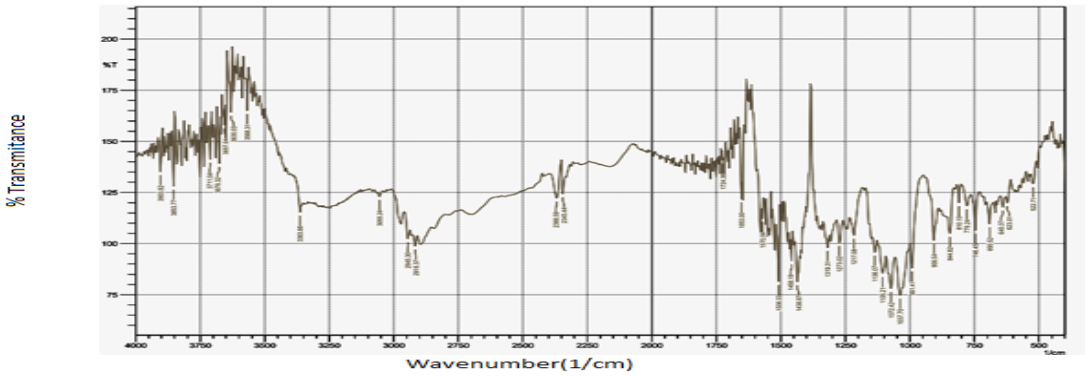

Figure 6: FTIR spectra of solid dispersion

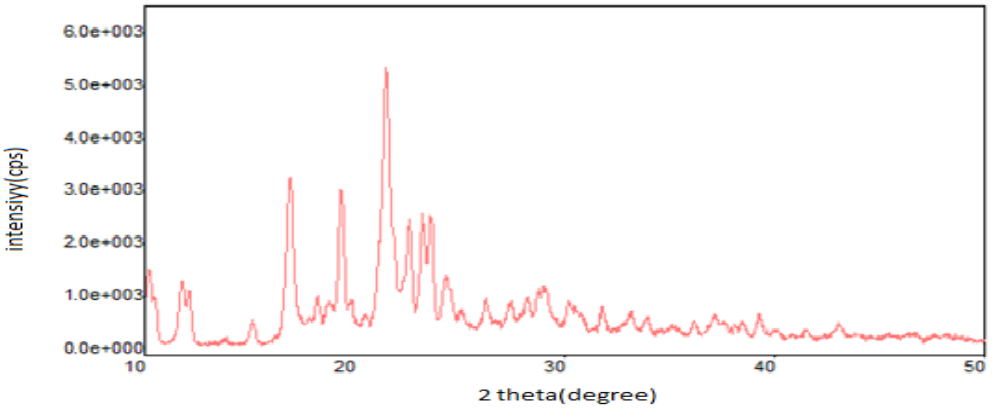

Figure 7: XRD image of ATC

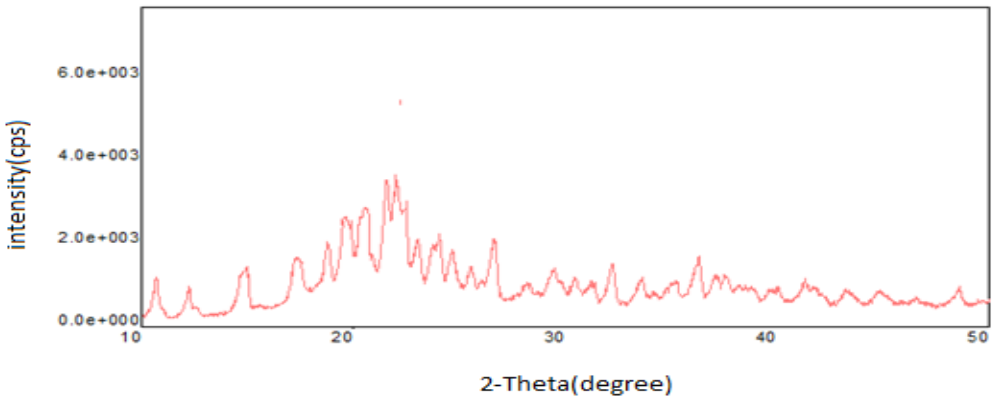

Figure 8: XRD image of solid dispersion

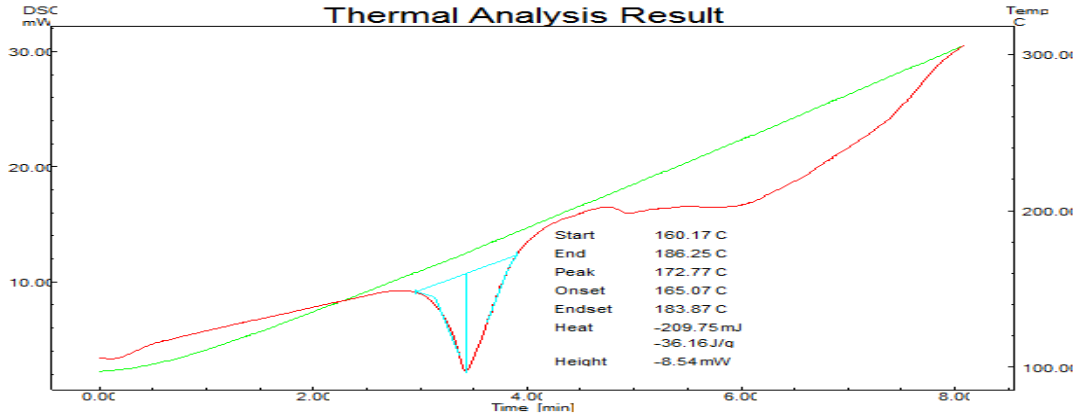

Figure 9: DSC thermogram of pure ATC

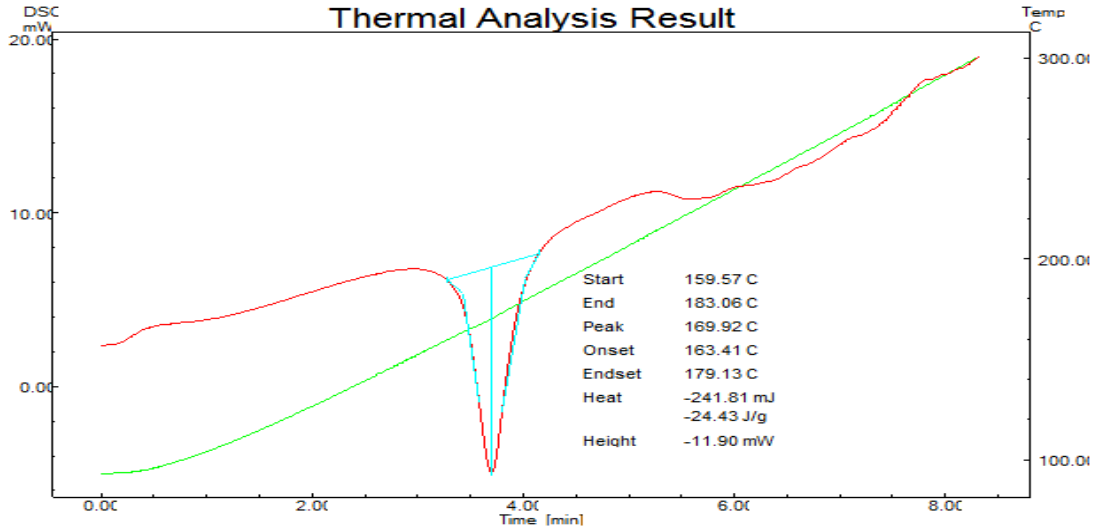

Figure 10: DSC thermogram of solid dispersion

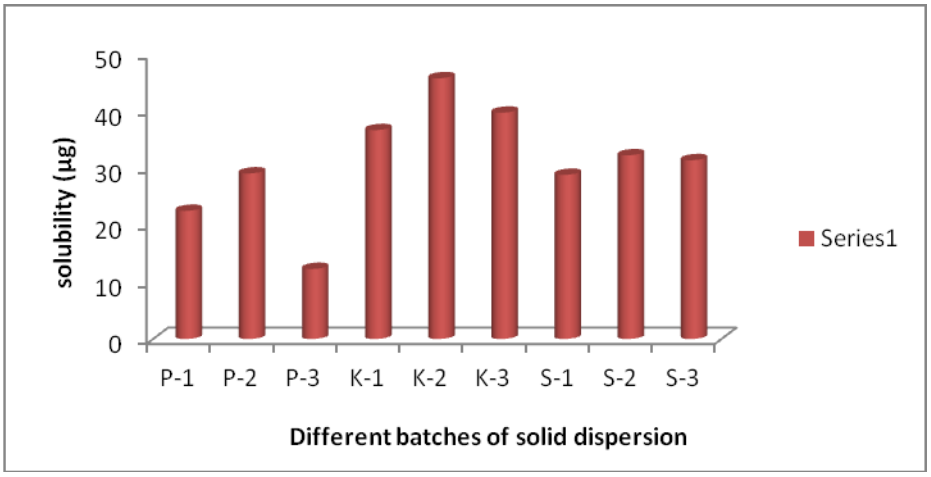

Figure 11: Solubility values of solid dispersion of different batches

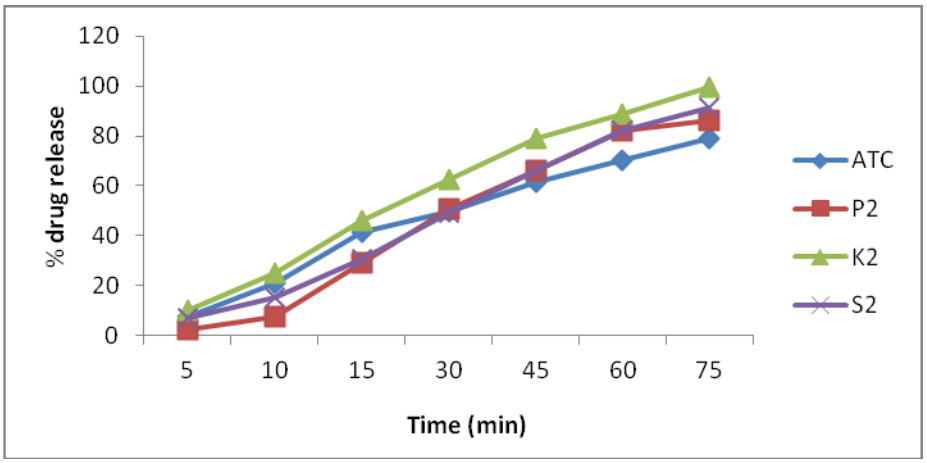

Figure 12: Percent drug release from solid dispersion

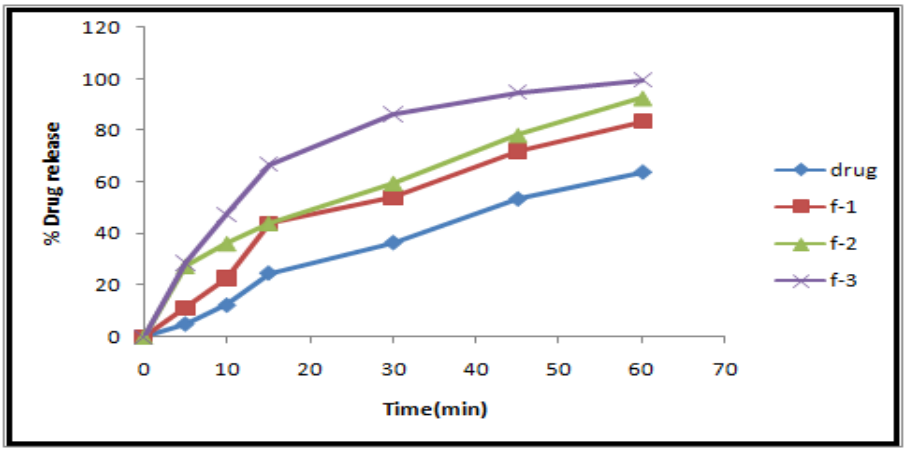

Figure 13: Percent drug release from tablet

Table 1: Drug-carrier formulation in various ratios

Method	Drug-Carrier ratio	Formulation code
Physical Mixture	1:1	P1
	1:3	P2
	1:5	P3
Kneading Method	1:1	K1
	1:3	K2
	1:5	K3
Solvent Evaporation	1:1	S1
	1:3	S2
	1:5	S3

Table 2: Readings from calibration curve in 0.1 N HCl

Concentration (µg/ml)	Absorbance (at 241 nm)
10	0.144
20	0.281
30	0.410
40	0.510
50	0.735

Table 3: Readings from calibration curve in distilled water

Concentration (µg/ml)	Absorbance (at 241 nm)
10	0.3452
20	0.7714
30	1.027
40	1.7159
50	1.7715

Table 4: Micromeritic properties of Atorvastatin calcium

Test	Observation
Bulk density (gm/ml)	0.087 ± 0.03
Tapped density (gm/ml)	1.073 ± 0.07
Carr's index	20.09 ± 4.22
Hausner's ratio	1.19 ± 0.04
Angle of repose (θ)	37.31 ± 2.194

Table 5: Solubility values and percent drug content of solid dispersion

Formulation code	Drug : carrier ratio	Solubility (µg/ml)	Solubility Increase (Folds)	% Drug content
-	**Drug-ATC**	10.31	-	
P-1	1:1	22.46	2.17	92.44
P-2	1:3	29.03	2.185	91.19
P-3	1:5	12.28	1.91	93.03
K-1	1:1	36.62	3.55	93.60
K-2	1:3	45.71	4.43	98.35
K-3	1:5	39.62	3.84	96.04
S-1	1:1	28.78	2.79	93.32
S-2	1:3	32.21	3.12	94.25
S-3	1:5	31.34	3.03	93.32

Table 6: Percent drug release from solid dispersion (in 0.1 N HCl)

Time (min)	% Drug release			
	Pure Drug-ATC	Physical Mixture	Kneading	Solvent Evaporation
5	7.5	2.30	10.38	6.92
10	21.05	7.63	24.99	15.27
15	41.53	29.17	46.03	30.67
30	49.49	50.96	62.46	49.01
45	61.28	66.06	79.07	66.16
60	70.2	82.10	88.93	82.13
75	79.20	85.98	99.59	91.32

Table 7: Formula for different batches of tablet

Ingredients (in mg)	Batch-F1	Batch-F2	Batch-F3
Solid dispersion (40 mg ATC)	160	160	160
Magnesium stereate	4	4	4
Cross carmellose sodium	10	15	20
Microcrystalline cellulose	122	117	112
Talc	4	4	4
Total	300 mg	300 mg	300 mg

Table 8: Evaluation of tablet

Formulation code	Hardness Kg/cm2	Thickness (mm)	Friability (%)	Weight variation (mg)	Disintegration time (sec)
F1	21.7	8.2±0.01	0.16	6.5	80
F2	22.1	8.5±0.03	0.17	8	73
F3	22.5	8.9±0.02	0.20	7.2	53

Values are mean ± SD n=3

Table 9: Percent release of drug from tablet

Time(min)	% Drug release			
	Pure ATC	Batch F-1	Batch F-2	Batch F-3
5	5	11.25	27.50	28.75
10	12.30	22.75	36.18	47.44
15	24.67	43.82	44.08	66.76
30	36.43	53.90	59.59	86.20
45	53.3	71.99	78.21	94.64
60	66.63	83.24	92.96	99.41

Table 10: Percent drug release from Tablet after stability study

Sr. No.	Time (min)	% Drug release before stability study	% Drug release after stability study
1	5	28.75	27.283
2	10	47.44	45.254
3	15	66.76	65.335
4	30	86.20	84.917
5	45	94.64	92.744
6	60	99.41	98.82

REFERENCES

1. Lipinski, C and Lombardo, F (1997), "Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings", ***Adv Drug Deliv Rev***, Vol. 23, 3–25.
2. Lachman, L (1991), "***The Theory and Practice of Industrial Pharmacy***", Edition 3, Varghese Publishing House, Bombay, 462-464.
3. Leuner, C and Dressman, J (2000), "Improving drug solubility for oral delivery using solid dispersions", ***Eur J Pharm Biopharm***, Vol.50, 47-60.
4. Patidar, K (2010), "Solid Dispersion Technology: A Boon for Poorly Water Soluble Drugs", ***Ind J NDDS***, Vol. 2, 349-357.
5. Pudipeddi, M and Serajuddin, A (2005), "Trends in solubility of polymorphs", ***J Pharm Sci***, Vol. 94, 929–939.
6. Chiou, WL and Riegelman, S (1971), "Pharmaceutical applications of solid dispersions", ***J Pharm Sci***, Vol.60, 1281–1302.
7. Sekiguchi, K and Obi, N (1961), "Studies on absorption of eutectic mixtures.A comparison of the behavior of eutectic mixtures of sulphathiazole and that of ordinary sulphathiazole in man", ***Chem Pharm Bull***, Vol. 9, 866-872.
8. Higuchi, T and Connors, K (1965), "Phase-solubility techniques", ***Adv Anal Chem Instrum***, Vol. 4, 117-212.
9. Ford, JL (1986), "The current status of solid dispersions", ***Pharma Acta Helv***, Vol. 61, 69-88
10. Sharma, SN and Ali, A (1991), "Preparation and evaluation of solid dispersions of Ibuprofen", ***Ind J Pharm Sci***, Vol. 53, 233-236.
11. Patil, SR; Patil, M and Kumar, R (2009), "Solid dispersion of Carbamazepine in PVPK30by conventional solvent evaporation and supercritical methods", ***Int J Pharm***, Vol. 272, 1-10.
12. Arunkumar, N and Deecaraman, M (2009), "Preparation and solid state characterization of Atorvastatin Nano-suspensions for enhanced solubility and dissolution", ***Int J Pharm Tech Res***, Vol. 1, 1725-1730.

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