Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 15s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Enhancement of Solubility, Dissolution Rate, and Bioavailability of Azilsartan Medoxomil Using the Solid Dispersion Technique

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Cite this paper as: Sanjeev Kumar, Tanveer Naved, Sanjar Alam, Reeta Chauhan, (2025) Enhancement of Solubility, Dissolution Rate, and Bioavailability of Azilsartan Medoxomil Using the Solid Dispersion Technique. *Journal of Neonatal Surgery*, 14 (15s), 119-133.

ABSTRACT

For increasing bioavailability and solubility of Azilsartan Medoxomil (AZM), a modified dosage form was developed in this study. Solid dispersion of Azilsartan Medoxomil was prepared through physical mixture and kneading method with β-cyclodextrin. Characterization is done by two main methods, Differential scanning calorimetry (DSC), and Fourier transform infrared spectroscopy (FTIR). The results confirmed that the use of solid dispersion in the modified dosage forms greatly enhanced the antihypertensive medications solubility and dissolution, which were previously weakly soluble in water. Furthermore, the pharmacokinetic study was performed on Wistar rats after oral administration of pure suspension and Azilsartan solid dispersion. The pharmacokinetic parameters i.e., Cmax and AUC for solid dispersions were reported to be significantly increased ($p < 0.05$) than that of pure API suspension. The formulation of SD-3 solid dispersion was shown best in improving solubility and dissolution. Overall, the study showed how altered dose forms may enhance the bioavailability and effectiveness of medications that are poorly soluble in water, which may result in better treatment outcomes for hypertension patients.

Keywords: *Azilsartan Medoxomil, Solid dispersion, Solubility enhancement, Pharmacokinetic, Bioavailability*

1. INTRODUCTION

Hypertension, is a chronic illness spreading in large people worldwide.[1] Because of its link to kidney and cardiovascular problems, management is essential.[2] Treatment typically involves the use of widely prescribed antihypertensive medications, viz. angiotensin-converting enzyme inhibitors, calcium channel blockers, and diuretics, to manage and control high blood pressure effectively. However, some of these medications have poor water solubility, which hampers their effectiveness. To address this, modified forms have been developed to improve solubility and absorption.[3] Such dosage forms are as solid dispersions, liposomes, and nanoparticles. These formulations offer benefits like improved patient compliance and reduced side effects. [4]

Azilsartan Medoxomil is an antihypertensive drug.[5] It belongs to the class of angiotensin II receptor blockers (ARBs).[6] Azilsatrtan Medoxomil, a prodrug, undergoes metabolism in the body to produce azilsartan. However, its low solubility poses challenges in drug delivery.[7] This indicates that medoxomil has low water solubility, which can make it challenging to deliver as a medication.[5,8] Azilsartan Medoxomil is frequently manufactured as calcium and potassium salt for increasing its solubility.[9] Salt forms of medoxomil are more soluble in water compared to the original medoxomil molecule. [10,11]

Improved dissolution rate and bioavailability of weekly decipherable pharmaceuticals have drawn attention to solid dispersions, especially those that use beta-cyclodextrin as a carrier.[12] Because of its solubility, biocompatibility, and regulatory permission for usage in pharmaceuticals, beta-cyclodextrin is preferred.[13] Creating azilsartan medoxomil as solid dispersion coupled with beta-cyclodextrin has the potential to improve treatment results.[14] Consequently, the objective of this work is to formulate and pronounce such a solid dispersion, as well as assess its physicochemical characteristics and drug release profile.

2. MATERIALS AND METHODS

A gift sample of Azilsartan medoxomil was obtained from Synokem Pharmaceuticals Ltd, located in Haridwar. A wide range of analytical grade chemicals and polymers were utilized in the study.

Melting Point Analysis

Azilsartan Medoxomil, melting point was evaluated using the capillary tube method, as per the U.S.P standard.

λmax Determination

A solution of Azilsartan Medoxomil prepared with Azilsartan Medoxomil (10mg) dissolved in methanol (5 ml). The solution was then further diluted with 0.1N HCl at a pH of 1.2, reaching a final volume of 100 ml. A dilute solution (10 µg/ml) was generated from the stock solution and thereafter subjected to 200 to 400 nm for UV-visible spectroscopy. The maximum absorption is taken as λmax.

Calibration curve plot

The plot of Azilsartan Medoxomil involved the serial dilutions with varying concentrations. The stock solution was made from a 0.1N HCl diluted to contain 10 mg/100 ml of Azilsartan Medoxomil. The drug's absorbance was subsequently measured at its maximum value. A graph showing the measured absorbances in relation to the appropriate concentrations was created.

Solid dispersion Solubility Calculation

The saturation solubility of solid dispersion, physical mixture and Azilsartan Medoxomil was assessed in various solutions, including water, 0.1N HCl with a pH of 1.2, and phosphate buffer solutions with pH values of 7.4 and 6.8.[16] An elevated quantity of each was introduced into 10 ml of each medium and placed in an incubator shaker at a temperature of 25±1 °C. After a period of 48 hours, the solution was subjected to centrifugation at 5000 rpm for a duration of 15 minutes. The supernatants underwent filtration with a particle size of 0.22 µm and were subsequently diluted using the appropriate solution. The absorbance was quantified utilizing an ultraviolet spectrophotometer, and subsequently, calculation of solubility was done.

Formulation Design:

Solid dispersion is one of the processes to enhance the solubility and rate of dissolution of medications with limited solubility is the solid dispersion. Solid dispersion was formulated by two methods.

By Physical Mixing Method:

The physical mixing method is a frequently applied method for the preparation of solid dispersions.[15] The API, and beta-cyclodextrin were mixed in a glass mortar for thirty minutes at various drug: carrier ratios, including 1:1, 1:2, 1:4, 1:6, and 1:8 subsequently, the mixes are filtered through sieve no-120 to ensure consistent size and then placed in a desiccator for storage (Table 1).

Table 1: Physical Mixtures Composition

Formulation code	Drug:βCD	Compositions (Drug:βCD)	
PM-1	1:1	120	120
PM-2	1:2	120	240
PM-3	1:4	120	480
PM-4	1:6	120	720

PM-5	1:8	120	960

By Kneading Method

Azilsartan Medoxomil and β-CD were measured and combined in molar ratios of 1:1, 1:2, 1:4, 1:6, and 1:8 in a mortar, along with a small amount of water-ethanol (1:1). The mixture was kneaded into a paste-like consistency for 30 minutes. The resulting dense mass was then placed in a desiccator for 48 hours to dry. After drying, the substance was crushed, sieved through a 120-mesh sieve, and stored in a desiccator.[17] (Table 2).

Table 2: Solid Dispersions Composition

Formulation code	Drug:βCD	Compositions (Drug:βCD)	
SD-1	1:1	120	120
SD-2	1:2	120	240
SD-3	1:4	120	480
SD-4	1:6	120	720
SD-5	1:8	120	960

Solid Dispersion Analysis

Medication Content

Precisely weighed solid dispersions and physical mixtures containing 10 mg of API were dissolved in 10 mL of ethanol. The solution underwent filtration, appropriate dilution, and subsequent analysis of drug content at a wavelength of 248 nm using a UV spectrophotometer. The drug content was determined by employing the subsequent equation in the following manner:

The absorbance of the test divided by the absorbance of the standard at the same dilution yields the drug content, which is then multiplied by 100.

Fourier transform infrared spectroscopy

This method is a very effective analytical method employed for characterizing the chemical composition and structural properties of various materials. The utilization of this technique has been extensively employed in the examination of solid dispersions, which refer to amalgamations of constituents in a solid form. The assessment of drug-polymer interaction is a prevalent application of FTIR in solid dispersion characterisation. Changes in peak positions in the Fourier Transform Infrared spectra can be used to determine changes in the functional groups of the drug and polymer.

Differential scanning calorimetry

This is a frequently employed method for characterizing solid dispersions. The thermal energy transfer between a sample and a reference material is measured as a function of temperature using the DSC technique, providing insights into their thermal properties. DSC can be employed to analyze solid dispersions to assess the thermal properties of the medication as well as the polymer matrix. A large endothermic peak in the DSC thermogram of a solid dispersion frequently signifies the drug and/or polymer melting. One can learn more about the degree of drug crystallinity and the level of drug-polymer interactions by measuring the peak temperature and melting enthalpy.

Drug release

A USP II dissolution equipment is utilized in the in vitro release investigation. The dissolution device was loaded with the prepared solid dispersion, physical mixture, and active pharmaceutical ingredient (API), and then immersed in the dissolution medium at a temperature of 37 °C ± 0.5 °C. Subsequently, the basket is adjusted to rotate at a pre-established velocity in order to guarantee optimal homogenization of the pharmaceutical product and dissolve media. Samples are collected from the dissolution medium at intervals of 5, 10, 15, 30, 45, 60, 75 and 90 minutes through a sampling port, and new dissolving

media is added to the removed volume. After that, these samples' medication concentration is determined using ultraviolet spectrophotometer at 248 nm. The charting of the total amount of drug released with time is necessary to determine the drug release profile.

Biological study [18-19]

The protocol IAEC/KSOP/E/20/12 was approved by KIET School of Pharmacy-Ghaziabad. Albino Wistar rats were used for the *in-vivo* investigation. Albino rats (weighing 200–250 g) were sourced from the institutional animal house and were stored under a 12-hour light/dark cycle with appropriate climatic conditions (25 ± 2 °C). The rats were provided with standard food and had unrestricted access to water. The drug plasma concentration was measured using HPLC

High performance liquid chromatography method [20]

HPLC method was validated for the routine analysis of Azilsartan Medoxomil. The method was reproduced as reported by AHER et al (2018) with little modification. The instrumentation details are given in the Table 3.

Table 3: Chromatographic condition

S.No	Process parameter	Optimized value
1	Instrument	SHIMADZU (LC-10AT vp)
2	Column	C_{18}
3	Mobile phase	Acetonitrile : water
4	Ratio of mobile phase	80:20 (v/v)
5	pH of mobile phase	7
6	Flow rate	1 mL min^{-1}
7	Run time	10 minute
8	Retention time	2.56 minute
9	Detector	UV-Spectrophotometer
10	Detection wave length	250 nm

i. Preparation of ammonium acetate buffer

Ammonium acetate is extensively used buffering chemical compound with the formula CH_3COONH_4 (Mol. Wt = 77.0825 g/mol), a white solid, which is derived from the reaction of ammonia and acetic acid. To prepare 0.05 mM ammonium acetate buffer, 3.85 g was solubilized in 1000 mL of HPLC water in volumetric decanter. The pH of the buffer (pH 7) was maintained with the help of acetic acid. The properly mixed buffer was filtered through 0.45 µm membrane before use.

ii. **Preparation of mobile phase**

The mobile phase was prepared by mixing methanol and previously prepared ammonium acetate buffer (80:20 v/v). Just before the HPLC analysis, the mobile phase was vacuum-filtered through a 0.45 µm membrane filter after being degassed by sonication.

iii. **Preparation of Drug Stock for calibration curve**

Calibration curve for Azilsartan Medoxomil was prepared using the strength of 0.25 to 10 µg/mL for routine *in vitro*, *ex vivo* and stability analysis. Ten milligram (mg) of Azilsartan Medoxomil was accurately weighed and taken in a 100 mL volumetric flask. To this 100 mL of HPLC water was added to obtain a stock of 100 µg/mL. Before making serial dilution, a secondary stock solution (10 µg/mL) was prepared. The serial dilutions from this stock solution were made by diluting the required stock solution with HPLC water (**Table 4**).

Table 4: Dilution scheme for calibration curve of Azilsartan Medoxomil in methanol

Stock volume (µL) (10 µg/mL)	**Added HPLC water (µL) q.s to 10 mL**	**Concentration (µg/mL)**

10,000	-	10
9000	1000	9
8000	2000	8
7000	3000	7
6000	4000	6
5000	5000	5
4000	6000	4
3000	7000	3
2000	8000	2
1000	9000	1
500	9500	0.5
250	9750	0.25
125	9875	0.125

Pharmacokinetic Study

Two groups of six rats each were created out of the rats. Group I was used for administering pure API, while Group II was used for solid dispersions. Before receiving the medication, the rats were fasted for 12 hours. To collect blood samples, a Smiths Medical™ Portex™ polyethylene catheter (Fisher Scientific Ltd., Loughborough LE11 5RG, UK) was inserted into the left jugular vein of each rat. Each rat was given an oral dose of either the solid dispersions (20 mg/kg) or the pure API suspension. Blood samples were collected from each rat at 0.25, 0.5, 1, 2, 3, 6, and 12 hours and placed in EDTA-filled Eppendorf tubes. To separate the plasma, the blood samples were centrifuged for 15 minutes at 4000 rpm. The plasma was then extracted using a micropipette and mixed with ethyl acetate and 0.2% formic acid to analyze the drug concentration. The resulting mixture was dried under vacuum. Following drying, a 0.45 µm cellulose membrane filter was used to filter the extract before it was reconstituted with the mobile phase. For analysis, a 20 µL sample was inoculated into the HPLC column. The run was carried out for ten minutes at room temperature and one milliliter each minute. By plotting the plasma drug concentration versus time and using a non-compartmental model, several pharmacokinetic parameters were calculated, including C_{max}, T_{max}, AUC_{0-t}, $AUC_{0-\infty}$, the elimination rate constant, and the half-life.

3. RESULT

Melting point

The solid Azilsartan medoxomil had a melting point ranging from 212 to 214°C.

Calibration curve of Azilsartan Medoxomil

Azilsartan Medoxomil content was measured using UV-visible spectroscopy at a wavelength of 248 nm. Figure 1 displays the maximum values of Azilsartan Medoxomil. The validation process of the analytical method was conducted to assess its specificity, linearity, accuracy, and precision. The outcomes of this validation are presented in Figure 2.

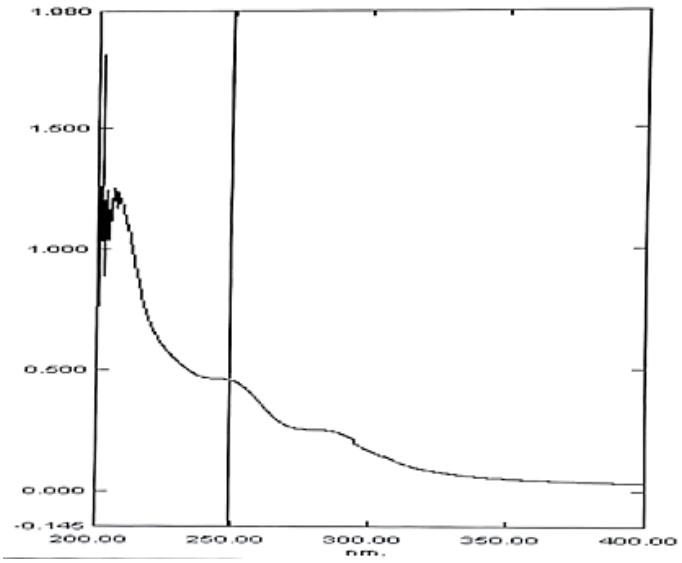

Figure 1: AZM λ_{max}

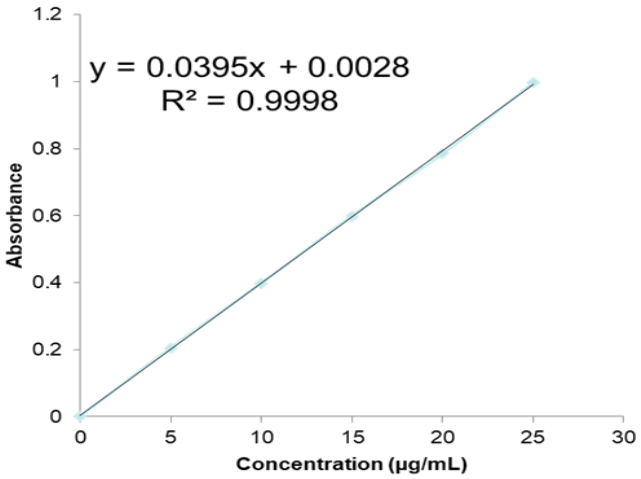

Figure 2: AZM Calibration curve in 0.1N HCl

Solubility Determination

Improving the solubility of AZM is the main goal of creating a solid dispersion of the medication. Using beta-cyclodextrin as the carrier material increased the solubility of AZM by up to 9 times. The findings (table 5 and figure 3) demonstrated that the both the prepared formulation improved the solubility of Azilsartan Medoxomil. However, the solid dispersions demonstrated a greater ability to increase solubility compared to the physical mixtures.

Table 5 : Solubility Profile of AZM, Physical Mixtures and Solid Dispersion

Solubility (µg/ml) ± SD; n=3

Formulation	pH 1.2 (HCl-0.1N)	pH 6.8 (Buffer-Phosphate)	pH 7.4 (Buffer-Phosphate)	Water
AZM Plain	17.23±0.4	20.32±0.7	23.26±0.5	15.52±0.8
Physical Mixture	85±0.6	120±0.4	140±0.7	90±0.6
Solid Dispersion	131±0.3	170±0.5	194±0.8	128±0.2

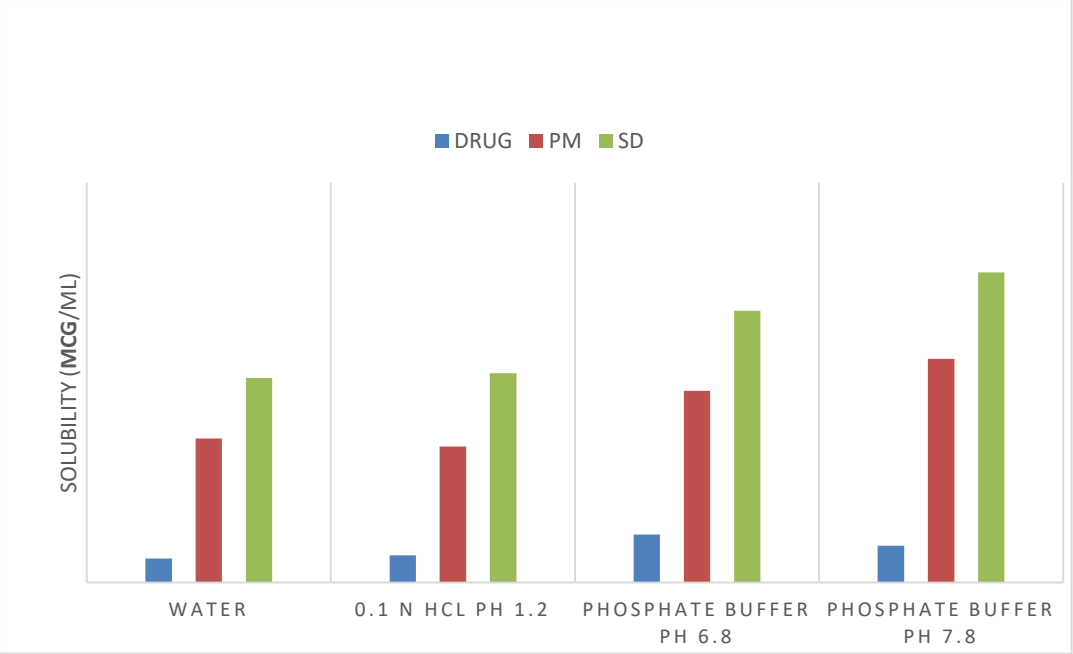

Figure 3: Solubility Profile of Drug, Physical Mixtures and Solid Dispersion

Fourier transform infrared spectroscopy (FTIR)

Figure 4 demonstrated FT-IR spectra of solid dispersions of pure Azilsartan Medoxomil. The pure Azilsartan Medoxomil spectrum showed 3398, 3352, and 3286 cm^{-1} peaks, corresponding to the stretching vibration and bending vibration, respectively. These peaks are associated with the amino group. Additionally, the spectrum displayed absorption peaks at 1561 is due to stretching vibration caused by asymmetry of carboxyl and of sulfonyl is 1322 cm^{-1}. The spectral analysis of beta cyclodextrin give band at 2954 cm^{-1} and 1670 cm^{-1} due to stretching (C-H) and from pairing (C=O) respectively. The absence of novel peaks in the solid dispersions, as well as the lack of variations in the locations of the absorption bands, suggests that there are no substantial interactions occurring between Azilsartan Medoxomil during the manufacturing and storage of the solid dispersions. Figure 5 and 6 displays FTIR spectra of Beta-Cyclodextrin and Azilsartan Medoxomil + Beta-Cyclodextrin respectively.

Figure 4: FTIR study of Azilsartan Medoxomil

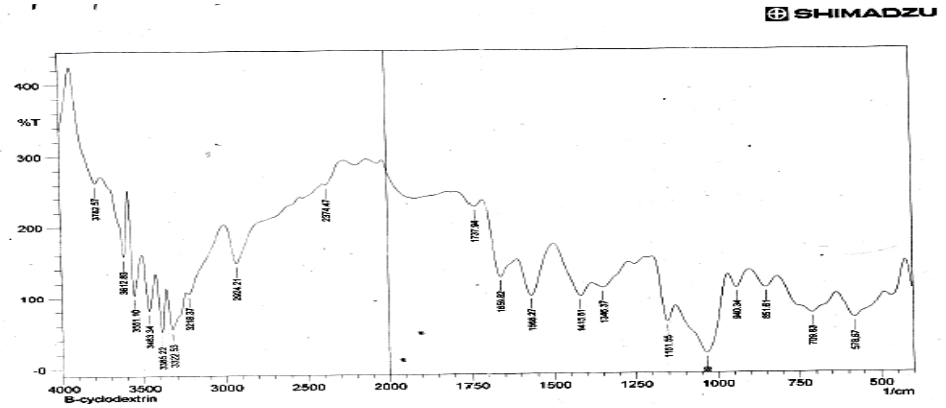

Figure 5: FTIR study of Beta-Cyclodextrin

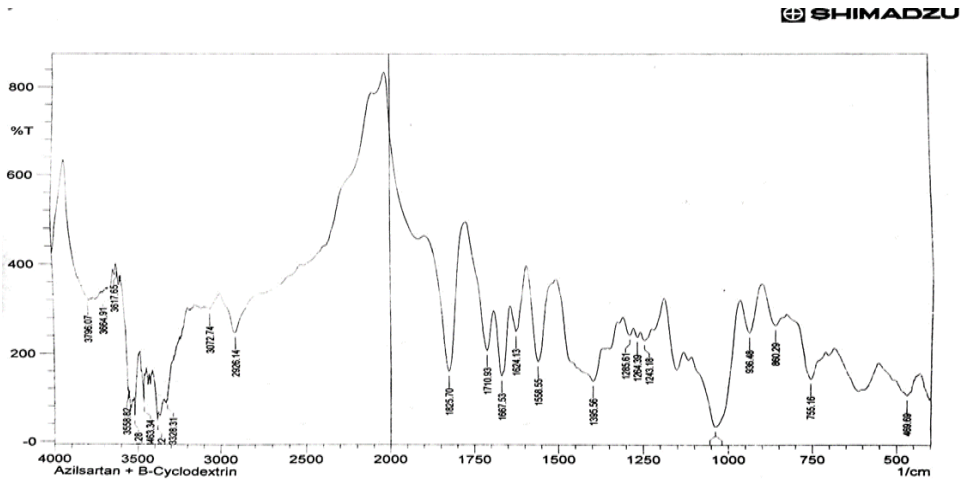

Figure 6: FTIR study of Azilsartan Medoxomil + Beta-Cyclodextrin

Differential scanning calorimetry

DSC research showed that the solid dispersion and pure drug did not differ in any statistically meaningful way in terms of their thermal properties. This suggests that there were no interactions between the excipient and the medication throughout the formulation process. Azilsartan Medoxomil crystals' melting point as ascertained by DSC analysis, is shown in Figure 7 to be between 200 and 250°C. The DSC graph of beta-cyclodextrin with Azilsartan Medoxomil is shown in Figure 8 and shows a single endothermic peak between 140 and 148°C. The breakdown temperature of Azilsartan Medoxomil is corresponding with this peak. As the amount of beta-cyclodextrin in the ground mixtures (GMs) enhanced, the melting peaks of Azilsartan Medoxomil in the GMs broadened and shifted towards a lower temperature. Melting peaks were visible on the DSC curves for all ground AZM crystals at 212-214°C.

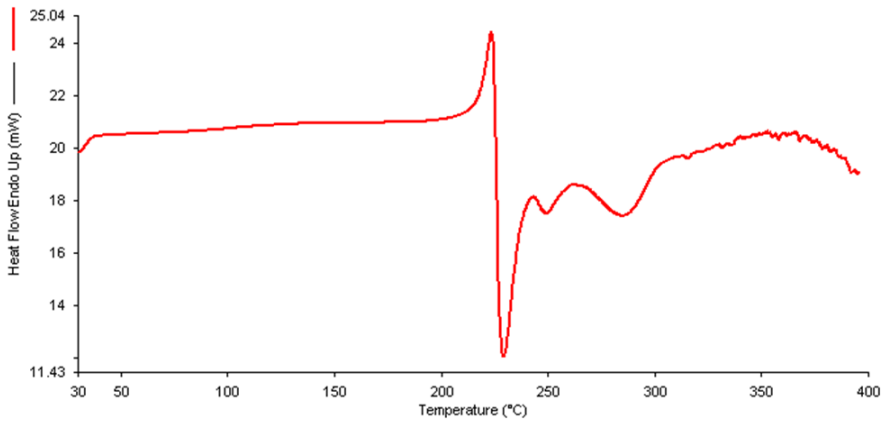

Figure 7: DSC Azilsartan Medoxomil

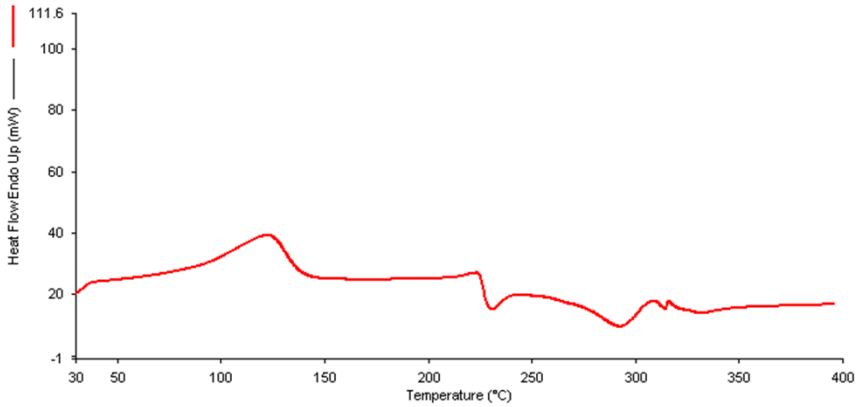

Figure 8: DSC Azilsartan Medoxomil and Betacyclodextrin

Medication Content

All formulations had medication content ranging from 97.05% to 99.01% suitable according to the approved monograph.

***In Vitro* release studies**

Release rate was analyzed by plotting dissolution curve up to a specific time point of AZM with Beta-cyclodextrin. The findings of these experiments indicate that the utilization of solid dispersion formulations can yield a substantial enhancement in the solubility rate of AZM in comparison monotherapy. Furthermore, the dissolution rate in the solid dispersion prepared by the kneading method is better than that of the physical mixture. According to a study, the dissolution rate of AZM was shown to be enhanced by as much as 82% in 90 minutes when it was prepared using selected polymer as the carrier material. The dissolution assays conducted shown a notable improvement in the dissolution rate of AZM when it was manufactured as a solid dispersion. This finding suggests that the formulation of Azilsartan Medoxomil as a highly soluble system was successful (Figure 9 and 10).

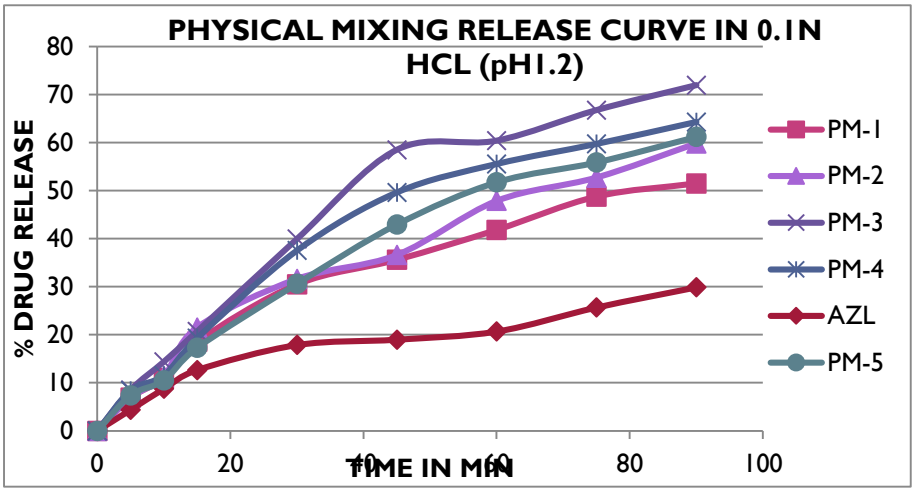

Figure 9: Dissolution Profile- Physical Mixtures in pH 1.2 (0.1N HCL)

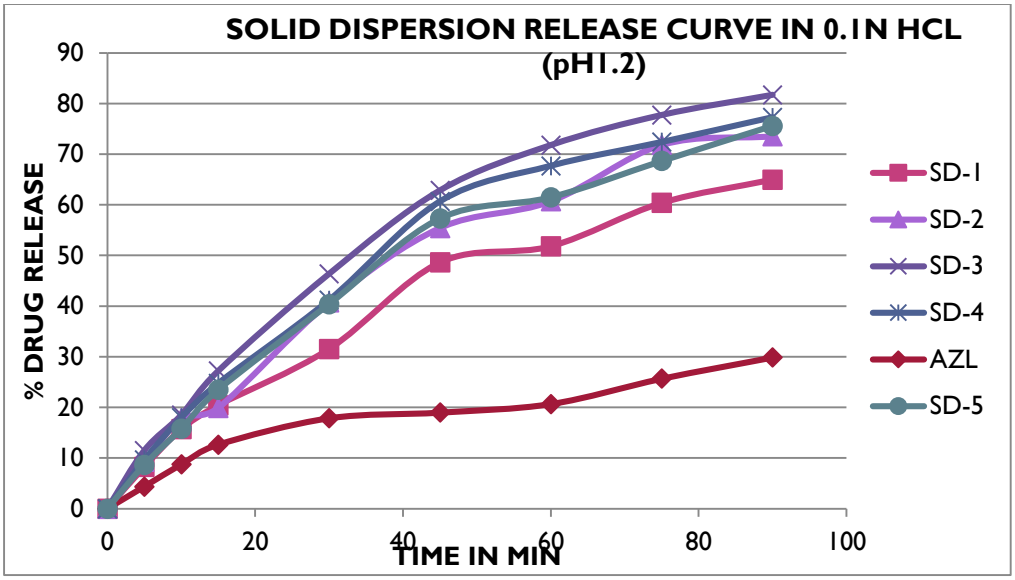

Figure 10: Dissolution Profile – Solid Dispersion in pH 1.2 (0.1N HCL)

Comparative Dissolution studies

The comparative dissolution studies between the selected solid dispersion (SD-3), the physical mixture (PM-3) formulation, and the pure AZM revealed that the cumulative percentage of drug release was 82% for the solid dispersion and 71% for the physical mixture, both significantly higher than the 30% release from the pure AZM (Figure 11).

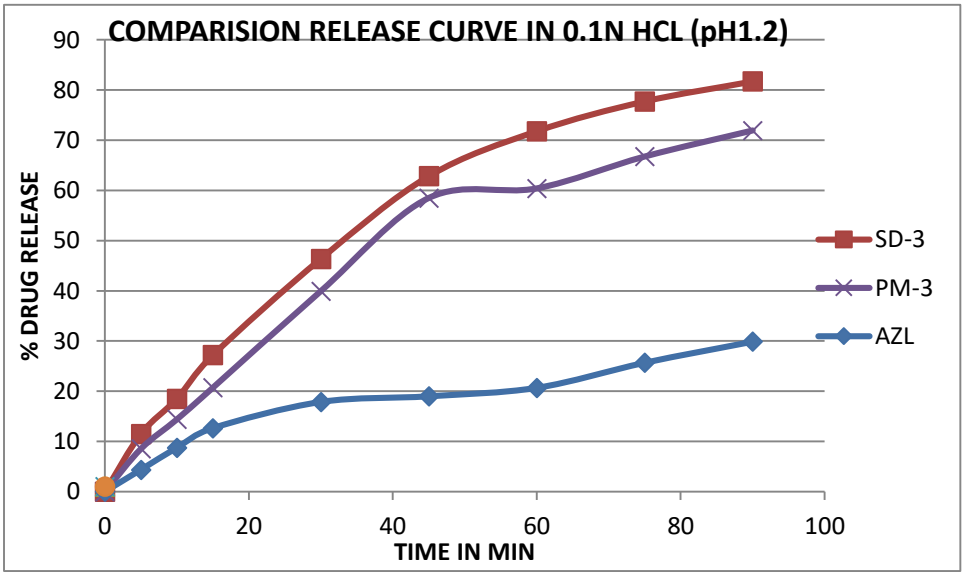

Figure 11: Dissolution Profile Comparison of SD-3, PM-3 and Pure Azilsartan Medoxomil.

High Performance Liquid Chromatography Method

The method was set with retention time of 2.56 min (Figure 12). Calibration curve was prepared using 0.125 to 10 µg/mL stock solution to determine linearity of the proposed method. The retention time of Azilsartan was found at 2.56 ± 0.1 min. The chromatogram showed good peak symmetry with no any tailing as already shown in the concentration of AZM and its respective area are documented in the Calibration curve was constructed by plotting peak areas versus concentrations, and the regression equation was calculated using average of triplicate observation. The mean calibration curve was given by the regressed equation y = 41054x + 1302, with a correlation coefficient, r^2 = 0.999, here Y represents peak area and x the concentration in µg /mL (Table 6 and Figure 13).

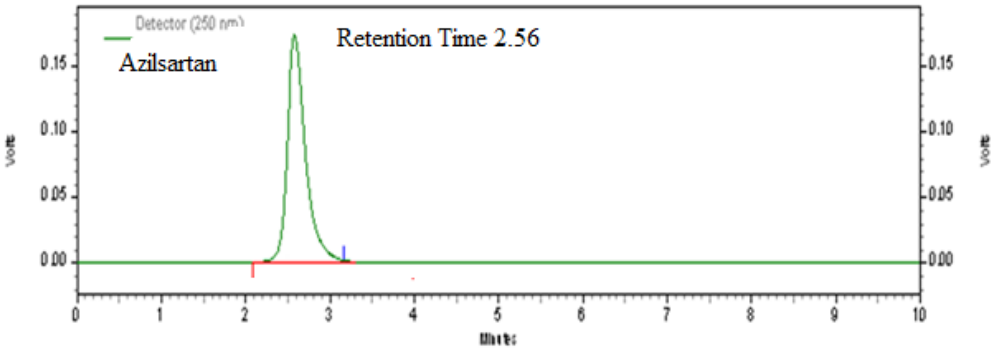

Figure 12: Representative HPLC chromatogram obtained for calibration curve

Table 6: Concentration and peak area ± S.D. obtained for calibration curve

Concentration (µg /mL)	Peak area	S.D. (n = 3)
10	414515	± 28632.32
9	366891.33	± 22871.96
8	325628.67	± 13501.74
7	293014.33	± 24012.83
6	251852.33	± 18902.84
5	209202.67	± 16632.07
4	159338	± 18890.32
3	121721.67	± 10343.95
2	85538.33	± 3792.983
1	43468.67	± 2207.361
0.5	22355.67	± 643.1332
0.25	11252.33	± 735.6122
0.125	6076.67	± 422.139

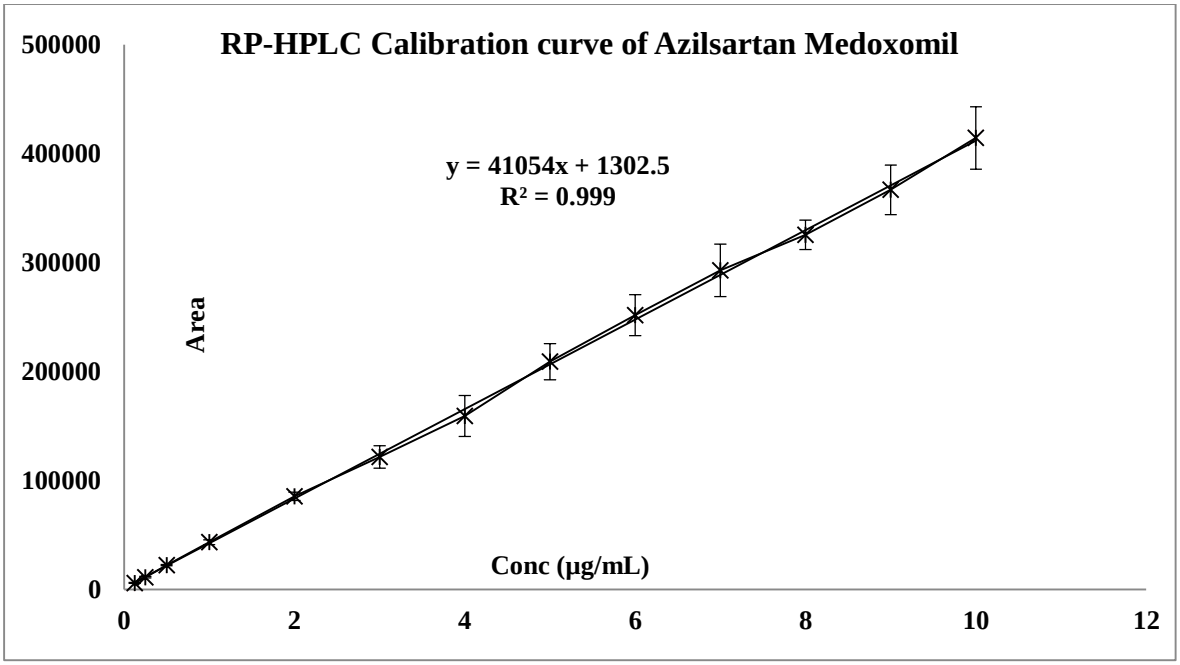

Figure 13: Calibration curve of Azilsartan Medoxomil by RP-HPLC method.

In Vivo studies

Wistar rats were administered oral doses of AZM solid dispersion and pure AZM suspension before participating in the pharmacokinetic study. It was found that the pharmacokinetic parameters, specifically C_{max} and AUC, were significantly ($p < 0.05$) elevated for the solid dispersions compared to the pure AZM suspension. For the solid dispersion, the T_{max} was 0.5 h, the half-life was 4.73 ± 0.85 h, and the elimination rate constant was 0.028 ± 0.031 h^{-1}. In contrast, the pure AZM suspension had a T_{max} of 2 h, a half-life of 11.22 ± 1.16 h, and an elimination rate constant of 0.0811 ± 0.001 h^{-1}. The C_{max} for the solid dispersions was approximately 23 times higher than that of the pure AZM suspension. Additionally, the oral bioavailability and AUC of the solid dispersions were 9.96 times greater than those of the AZM suspensions. The significant increase in bioavailability is likely due to the enhanced solubility of the solid dispersion (Table 7 and 8 and Figure 14)

Table 7: Pharmacokinetic Parameters Azilsartan Medoxomil Solid dispersion

P/K parameters	**Plasma**
Elim Rate Const	0.128±0.031
T_{max} (hr)	0.5±0.0
C_{max} (µg/ml)	295.02±47.89
$AUC_{o\sim t}$	1166.22±192.43
AUCo→inf	1207.64±233.37
AUMCo→t	4432.99±792.62
AUMCo→inf	5800.29±185.33
MRT (hr)	4.73±0.85

Table 8: Pharmacokinetic Parameters pure AZM Suspension

P/K parameters	Plasma
Elim Rate Const	0.081±0.01
Tmax (hr)	2.66±2.8
Cmax (µg/ml)	12.85±1.36
AUCo~t	117.86±33.24
AUCo→inf	136.97±38.28
AUMCo→t	866.11±38.64
AUMCo→inf	1561.25±555.43
MRT (hr)	11.22±1.16

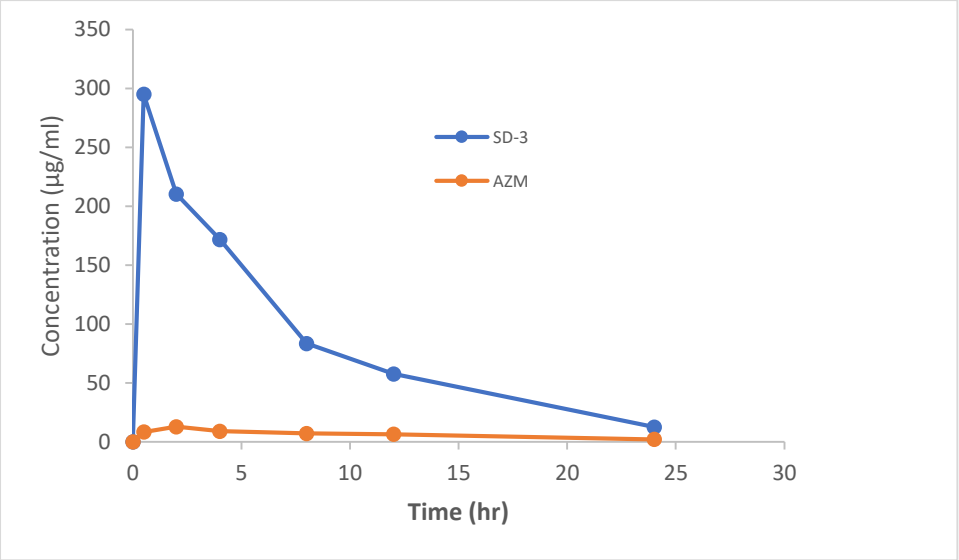

Figure 14: Plasma Concentration-Time Profile of Azilsartan Medoxomil after Oral Suspension and Solid Dispersion Administration

Stability Studies

Stability investigations were conducted on the prepared solid dispersion for 6 months at 40 °C ± 2 °C and 75 ± 5% relative humidity in accordance with ICH recommendations. Numerous factors, including medication content and *in vitro* release, were evaluated during the investigation. No color change was observed during the stability trial. Table 9 displayed the SD-3 *in vitro* drug release profile after 90 minutes. The results from the stability study indicate that the solid dispersion remained stable at 40 °C/75% relative humidity.

Table 9: Physicochemical Assessment of Solid Dispersion (SD-3) after Accelerated Stability Studies

S.N.	Time (Month)	% Medication Content	% Release Drug
1	0	98.87±0.27	82.14±0.23

2	2	97.79±0.51	81.87±0.19
3	4	98.11±0.38	80.91±0.42
4	6	97.97±0.30	80.12±0.13

4. CONCLUSION

This study demonstrated that the addition of Beta-cyclodextrin in varying proportions to solid dispersions of Azilsartan Medoxomil effectively increased the solubility and rate of dissolution of Azilsartan Medoxomil in water. The results of this study indicate that using Azilsartan Medoxomil as a solid dispersion has potential to improve the solubility and rate of dissolution of existing dosage forms. Increasing the time of grinding and partially changing it into an amorphous phase resulted in an increased solubility rate of Azilsartan Medoxomil. The solid dispersions produced using the kneading method exhibited greater enhancement in solubility. The pharmacokinetic study revealed that the C_{max} and AUC of the solid dispersion were significantly higher, being 23 times and 9.96 times greater, respectively, compared to the pure AZM suspension. Among prepared formulations, SD-3 having 1:4 (drug: carrier) ratio showed an eightfold increase in water solubility.

CONFLICTING INTEREST

Authors declare no conflicts of interest.

FUNDING

This study is done without funding.

Abbreviations

AZM: Azilsartan Medoxomil; **SD:** Solid Dispersion; **PM:** Physical Mixture; **DSC:** Differential scanning calorimetry; **FTIR**; Fourier Transform Infrared Spectroscopy; HPLC; High Performance Liquid Chromatography.

REFERENCES

[1] Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. *Nat. Rev. Nephrol. 2020;16(4):223-3. doi: 10.1038/S41581-019-0244-2. PMID: 32024986.*

[2] Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. *Circulation 2016:134:441-450. doi: 10.1161/CIRCULATIONAHA.115.018912. PMID 27502908.*

[3] Kario K, Hoshide S, Mogi M. Lifetime home BP-centered approach is the core from onset to aggravation of hypertension. *Hypertens. Res.2023:*46:553–555. doi: 10.1038/s41440-023-01174-5.

[4] Ražem D, Katušin-Ražem B. The effects of irradiation on controlled drug delivery/controlled drug release systems. *Radiat. Phys. Chem.2007:* 77:288–344. doi:.org/10.1016/j.radphyschem.2007.06.006.

[5] Pradhan A, Tiwari A, Sethi R. Azilsartan: Current Evidence and Perspectives in Management of Hypertension. *Int. J. Hypertens 2019:*2019:1824621. doi: 10.1155/2019/1824621.

[6] "Azilsartan: Side Effects, Dosage & Uses - Drugs.com." https://www.drugs.com/azilsartan-Medoxomil l.html (accessed Mar. 25, 2023).

[7] Kurtz TW, Kajiya T. Differential pharmacology and benefit/risk of azilsartan compared to other sartans. *Vasc. Health Risk Manag 2012:*8(1):133–143. doi: 10.2147/VHRM.S22595.

[8] Chand SP, Debnath S, Rahimi M, Ashraf MS, Bhatt P, Rahin SA. Contextualization of Trait Nexus and Gene Action for Quantitative and Qualitative Characteristics in Indian Mustard. *J. Food Qual 2022:2022(2). doi: 10.1155/2022/4387318.*

[9] Mei JQ, Zhou DN, Jin ZY, Xu XM, Chen HQ. Effects of citric acid esterification on digestibility, structural and physicochemical properties of cassava starch. *Food Chem 2015:*187:378–384. doi: 10.1016/j.foodchem.2015.04.076.

[10] De Caterina AR, Harper AR, Cuculi F. Critical evaluation of the efficacy and tolerability of azilsartan. *Vasc. Health Risk Manag 2012:*8:299–305. doi: 10.2147/VHRM.S22589. PMID: 22661897.

[11] Al-Snafi AE, Singh S, Bhatt P, Kumar V. A review on prescription and non-prescription appetite suppressants and evidence-based method to treat overweight and obesity. *GSC Biol. Pharm 2022:*19(03):148–155. doi: 10.30574/gscbps.2022.19.3.0231.

[12] [Gao Q, Xu L, Cai J. New drug targets for hypertension: A literature review. *Biochim. Biophys 2021(03):*1867:166037. doi: 10.1016/j.bbadis.2020.166037.

[13] Bhatt P, Kumar V, Goel R, Sharma SK, Kaushik S, Sharma S, Shrivastava A, Tesema M. Structural Modifications and Strategies for Native Starch for Applications in Advanced Drug Delivery. *Biomed Res. Int 2022:*2022:1–14. doi: 10.1155/2022/2188940. PMID: 35993055.

[14] Bhatt P, Singh S, Sharma SK, Rabiu S. Development and Characterization of Fast Dissolving Buccal Strip of Frovatriptan Succinate Monoydrate for Buccal Delivery. *Int. J. Pharm. Investig 2021:*11(1):69–75. doi: 10.5530/ijpi.2021.1.13.

[15] Beneš M, Pekárek T, Beránek J, Havlíček J, Krejčík L, Šimek M, Tkadlecová M, Doležal P. Methods for the preparation of amorphous solid dispersions – A comparative study. *J. Drug Deliv. Sci. Technol 2017:*38:125–134. 10.1016/j.jddst.2017.02.005.

[16] Veseli A, Žakelj S, Kristl A. A review of methods for solubility determination in biopharmaceutical drug characterization. *Drug Dev. Ind. Pharm 2019:*45(11):1717–1724. doi: 10.1080/03639045.2019.1665062. PMID: 31512934.

[17] Kanojiya PS, Charde YM, Wadetwar RN. Solid Dispersion of Artemether in Fast Disintegrating Tablet to Enhance Dissolution Rate and Oral Bioavailability. Indian J of Pharmaceutical Education and Research.2022;56(1):153-65. doi: 10.5530/ijper.56.1.18.

[18] Atef E, Belmonte AA. Formulation and in vitro and in vivo characterization of a phenytoin self-emulsifying drug delivery system (SEDDS). Eur J Pharm Sci. 2008;35(4):257–263. doi: 10.1016/j.ejps.2008.07.004. PMID: 18706499.

[19] Mohan A, Madhavi M, Swetha G, Jyosthna P. Preparation, in vitro and in vivo characterization of solid dispersions of lamotrigine using solvent evaporation technique. IOSR J Pharm. 2015;5(1):54–59.

[20] Aher SS, Saudagar RB, Kothari H. Development and validation of rp-hplc method for simultaneous estimation of azilsartan medoxomil and chlorthalidone in bulk and tablet dosage form. Int J Curr Pharm Res 2018:10(6):21-24. doi: 10.22159/ijcpr.2018v10i6.30967.