Section A-Research paper
ISSN 2063-5346

Development and Validation of rapid, Accurate chromatographic analytical method for Mini tablets containing Azilsartan Medoxomil

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Abstract:
To determine the concentration of azilsartan medoxomil (AM), a chromatographic technique, namely high-performance liquid chromatography with a polar mobile phase approach that is both straightforward and speedy, was designed and validated. The photodiode array detector was the instrument that was utilized for the detection. Chromatographic separation of the analyte AM was achieved in 5.047 minutes. The vital parameters of the Validation of the analytical method were carried out extensively. The detection and quantitation limits were 33.92 µg/ml and 102.78 µg/ml, respectively. Interday and intraday methods evaluated the precision parameter. The calibration curve was found to be linear. The 230 nm wavelength is used to perform detection. The newly developed RP-HPLC method passed Validation with flying colors and can now be used for assay and dissolution testing (AM1-AM11).

Keywords:
Method development, Validation, Azilsartan Medoxomil, HPLC, Mini tablet

INTRODUCTION

The chemical name for azilsartan medoxomil (AM) is 5-methyl-2-oxo-1,3-dioxol-4-yl)methyl2-ethoxy-1-([2'-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl)-1Hbenzimidazole-7-carboxylate. The molecular weight of AM, which has the chemical formula C25H20N4O5, is 456.46 g/Mol. AM is a white powder readily soluble in methanol but practically insoluble in water. Angiotensin receptor blocker AM reduces BP (Blood pressure) by inhibiting the action of the vasopressin hormone angiotensin II.

Mini tablets are single-unit solid dosage forms with a diameter of less than 3 mm. The sole change in manufacturing processes from conventional tablets is using several punches. They are useful for difficult swallowing patients and taking various pharmacological treatments. They offer a more efficient treatment by minimizing the drug's release profile variability. The process for formulation development and production is simple. There is little variation observed in inter as well as intra-individuals. The risk of local irritation is reduced. While

considering the number of advantages of mini tablets as a dosage form over single unit dosage forms, the present work aimed to develop the AM-loaded mini tablets.

The newly developed and validated analytical method ensures a specific, accurate, and exact approach for a given analyte. An accurate and validated analytical method is vital in developing a new formulation. A review of the literature indicates a few analytical techniques (Swamy and Seshagirirao et al., 2015; MadhuBabu and Bikshal et al., 2012; Neelima and Prasad et al., 2014; Naazneen et al., 2014; Vekariya and Joshi et al., 2013; Sunitha et al., 2015; Sandeep and Kumar et al., 2016; Karpe et al., 2016; Sravani et al., 2014) were researched and structured to determine the content of AM in combinations of the API in formulations. The authors have attempted to formulate the mini tablets of AM. The paper also represented the draft of an analytical method developed and validated, a simple, accurate RP-HPLC method for determining API and mini tablets.

MATERIAL AND METHOD

MATERIAL

AM was procured from Piramal Pharma Ltd. All the other HPLC-grade and AR-grade chemicals were bought from S. D. Fines.

METHOD

HPLC method development and Validation

The reported analytical methods could be more extensive. The method is time-consuming and tedious. As our developed formulation contain different excipients and polymer, we structured a new, simple analytical method and validated the HPLC method as described by ICH. The application of this method was further extended to pharmacokinetic study.

RP-HPLC was used to determine the amount of the drug in the sample. I was using the Agilent Tech. (1100) equipment, the determination was completed. The analytical method was developed using the reverse column as a stationary phase with a dimension of 100 * 4.6 mm with an inner diameter of 2.5 mm. The mobile phase was selected with 40% HPLC grade acetonitrile and 60% HPLC water. The pH of the solvent system was maintained at pH 5.4 by adding 0.1 % orthophosphoric acid. The eluent was flown through the column system at 0.75 ml/min, and the analyte was detected using a PDA detector at 230nm wavelength. The drug's quantitative value was calculated by calculating peaks with the help of the CHEMSTATION 10.1 program.

HPLC method Development (Creaven et al., 1982; Hema and Swati et al.,2017; Bhagat et al., 2019; ICH: Q2B, 1996; Patel et al., 2016; Sudev and Sree et al., 2019; Chauhan and Chauhan et al.,2015; Alquadeib et al., 2019;Sharma and Chauhan et al., 2018**)**

The RP-HPLC chromatographic parameters were optimized using various mobile phase compositions. Using the mobile phases acetonitrile and distilled water maintained at pH 5.4 using orthophosphoric acid (OPA) in the ratio of 40:60 v/v, the resolution and peak symmetry obtained were excellent, as was the symmetry of the peaks. The peak area was quantified at the determined wavelength based on the peak area. The proposed method's suitability for the proposed system was assessed. A prepared standard stock solution of AM was used to perform the system suitability to ensure it was as effective as possible. Various factors, such as resolution, HETP, and peak tailing, were investigated to determine the system's suitability.

- **Method validation parameters**

1. Linearity

It was determined that the calibration curve was linear across the concentration range of 150 to 750 microg/ml of Azilsartan medoxomil. The aliquots of each solution were injected into the chromatographic column under optimal chromatography conditions. The peak area versus AM concentration relationship was plotted to determine the regression equation and correlation coefficient.

2. Accuracy

The usual addition technique was used to assess the correctness of the procedure under consideration. On top of the previously examined sample solutions of the medicine were known quantities of standard solutions at various concentrations, such as 80, 100, and 120 percent. After extracting the powder, it was subjected to chromatographic analysis using an optimized mobile phase. The percentage of individuals who recovered and the percentage of RSD at each dose level of the medication were calculated and compared. In each level the responses were examined in three different levels.

3. Precision

When an analytical technique is used repetitively to do several samples of the same sample, its precision is measured by how well individual test results agree with one another.

Method precision (repeatability)

To test the device's repeatability, a solution of a medication with a concentration of 450 micro g/ml was injected many times. It is unacceptable for the RSD percentage to be higher than 2 percent.

Intermediate precision

Their effectiveness was evaluated using the intermediate precision's intraday and interday accuracy. The three distinct concentrations were used to examine intraday precision. By measuring the equivalent concentration three times on the same day and three times on different days, the accuracy within and between days was examined. The results were presented as a percent relative standard deviation.

4. Robustness

As per ICH guidelines, robustness is a parameter that measures the capacity of a developed analytical procedure to remain unchanged by minor but intentional changes in the parameters listed in the procedure documentation and to indicate its suitability during routine use.

The robustness of the method was examined by examining the effects of minute modifications on the composition of the mobile phase solution. In the current study, several chromatographic parameters, including mobile phase, flow rate, and detection wavelength (less than one nanometer), were purposefully changed to examine the performance of the approach. The percent RSD could be determined.

5. Detection Limit and Quantification Limit

The lowest concentration at which the method can correctly identify the analyte contained within the matrix is referred to as the limit of detection (sometimes written as detection limit or DL). The lowest concentration that can be reliably recognized from background noise is another name for it. The limit of quantitation (LOQ) (also known as the quantification limit,

QL) is the lowest concentration of the analyte that can be reliably measured by the method. Suitable precision and trueness must exist and be shown for something reliable.

For quantitative analysis, this must be coupled with an acceptable uncertainty range; for example, the generated analytical estimate must not depart from the true value by more than E/2.

The LOD and LOQ were calculated using the signal-to-noise ratio for AM. The S/N ratio was determined at a concentration until the LOD S/N ratio was 3 and the LOQ S/N ratio was 10.

Development of Mini tablets

Mini-tablets are a unit solid dosage form. It is a novel dosage form with a wide range of applications, defined as tablets with less than 3 mm diameter. Mini-tablets are a viable and modern method for administering oral medications to target populations like children, the elderly, and other patients with swallowing disorders. As multiple unit systems offer single-pattern or mixed-pattern modified release, mini-tablets might be effectively built. Mini tablets with various active ingredients combined and/or with various release profiles may lessen polypharmacy therapy and/or dose frequency issues.

The excipients include Avicel PH 102 and Mannitol (Pearlitol SD 100) used as tablet filler, Hypromellose (Methocel K 4 M) and Eudragit RS PO used as sustained release polymer, Hydroxypropyl Cellulose Klucel EF acts as a binder. Colloidal Silicon Dioxide (Aerosil 200 Pharma) is a glidant, and magnesium Stearate is a lubricant. Wet compression was used to create the AM micro pills. Each component listed in Table 1 below was precisely weighed using an electronic scale (AXE 200, Shimadzu, Japan), and each ingredient was then thoroughly blended using a "V" cone blender. Granulating the dry mix was done before lubrication. The lubricated blend was compressed using a multi-punch compression machine (Trover, Pharmamec, India) equipped with a tablet punch with a 3 mm diameter. According to dose and weight, mini-tablets were placed inside size 0 capsules.

Evaluation of developed mini tablets

All the compressed mini tablets were subjected to various parameters post-compression evaluation. These include assay, uniformity of weight and content, friability and hardness testing, tablet diameter and thickness (Madathilethu et al., 2018; Wood et al., 1906; Osei-Yeboah et al., 2015).

Weight variation

Twenty mini tablets were selected randomly from each prepared batch to perform the uniformity of weight. These were weighed on an electronic weighing balance, and the percentage weight variation was calculated and recorded (Moskalyk et al., 1961).

Friability

From each of the batches that were made, ten pre-weighed micro tablets were chosen at random and put into the friabilator's drum (Roche Friabilator). The experiment was carried out in triplicate, as described in Lachman et al., and the mean results were reported.

Hardness

A Monsanto hardness tester determined the average breaking strength of ten mini tablets. The mean response of hardness was recorded (Ridgway et al., 1970).

Diameter and thickness

The average diameter and thickness of the prepared mini tables were measured by experimenting thrice using a Vernier Caliper.

Disintegration test

Disintegration tests followed USP 38-NF33 specifications for tablets intended for sustained release. Six tablets were randomly selected from each experiment and placed in a USP disintegration test device (Erweka, ZT 320 series, Heusenstamm, Germany). The apparatus's basket rack assembly was submerged in 800 mL of distilled water at 37 0.5 °C. The original 10-mesh wire cloth was replaced at the base of the basket assembly with a 30-mesh woven stainless steel wire cloth with a plain square weave. When the tablet had completely broken down and nothing was left on the mesh, the disintegration time (DT) was measured in seconds. The mean and SD were computed for each batch. (Donauer et al., 2007).

Assay of Mini tablets

The above-validated HPLC method was employed to carry out the assay of formulated tablets. The drug's equivalent weight (0.100 gm) is weighed and transferred in a volumetric flask containing 5 ml of methanol. Dissolved the drug in methanol and made up the volume to 100 ml with Phosphate buffer pH 6.8. From the above-prepared stock solution, pipette 1 ml of solution and make volume up to 10 ml using phosphate buffer pH 6.8. The drug content in the sample was estimated by analyzing filtrate using Shimadzu UV-1800 at the wavelength 249 nm (Gawai et al., 2018). Calculate the percentage of drug loading.

RESULT AND DISCUSSION

Development and Validation of Method

The ICH guidelines aim to validate the created analytical method and ensure that it is appropriate for the purpose for which it was developed. Validation offers some direction on how to consider the various aspects of Validation for each analytical technique. The study also guarantees the formulations' or API's' quality. The effectiveness of AM was assessed in the current investigation. According to ICH criteria, the developed approach was extremely thoroughly validated. Numerous variables were examined. Ultimately, the validated approach was used for pharmacokinetic, dissolution, and assay studies. The created and approved procedure is used for assay and dissolution tests.

- **Optimization of RP- HPLC method**

The essential parameters that determine the optimization of any chromatographic method for analysis are good resolution, peak shape, theoretical plates, retention time, and asymmetry. Several circumstances of chromatographic procedures, such as varied compositions of mobile phase, flow rate, and various stationary phases, were optimized and evaluated for the assessment of AM to achieve all of these characteristics. With the mobile phase, the produced peak was excellent, crisp, symmetrical, and well-defined. Acetonitrile: water in a ratio of 40:60 v/v adjusted to 5.4 pH with OPA, with a flow rate of 0.75 ml/minute at 230 nm. The retention time of AM was observed at 5.59 min (Figure 1).

- **Method validation parameters**

1. Linearity

The method's linearity was established by diluting the standard stock solution to obtain concentration ranges of 150 to 750 µg/ml. The findings indicate that a strong connection between peak area and analyte concentration existed. The calibration curve was constructed and assessed using linear regression by graphing the AUC vs. the analyte concentration (Figure 2).

2. Accuracy

The medication recovered well at three distinct concentration levels, demonstrating that the procedure was accurate. In the pre-analyzed samples, a known quantity of standard medication (80, 100, and 120 percent) was added, and the samples were exposed to the suggested HPLC procedure. The percent recovery rate was determined to be within acceptable norms. (See also Table 3)

3. Precision

- **Method precision (repeatability)**

Table 3 presents the results of the repeatability test, often known as method precision. The method's precision was determined by repeatedly adding a concentration of azilsartan medoxomil equal to 450 microg/ml. Because the % RSD came out to be 1.06, it was determined that the newly devised approach was accurate.

- **Intermediate precision**

Tables 4,5, and 6 contain the findings for both intraday and interday. The study of three distinct standard solution concentrations (300, 450, and 600 g/ml) revealed good repeatability. For intraday precision, the % RSD was determined to be 1.91, 1.09, and 1.20; for interday precision, it was 1.83, 1.21, and 1.62.4.

Robustness

Robustness was achieved by making modest adjustments to the chromatographic settings, such as the flow rate of the mobile phase and the wavelength. It was noted that the chromatograms exhibited no discernible signs of alteration. The devised approach was determined to be reliable because the % RSD values were less than 2.0%. (Table 6,7, 8)

5. Limit of Detection (LOD) and Limit of Quantification (LOQ)

These findings demonstrated that the method used to determine azilsartan medoxomil had high sensitivity. It was determined that the LOD and LOQ should be set at 33.92 mcg/ml and 102.78 mcg/ml, respectively.

Evaluation of Developed Mini tablets

The tablets for sustained release were prepared and evaluated further for different parameters, including weight variation, friability, hardness, diameters, thickness, disintegration test (min), assay, and dissolution test (Table 9).

The prepared mini tablets of AM (AM1 to AM11) for sustained release were found to have sufficient mechanical strength, which was confirmed by their hardness (> 3kg/cm2), and the loss on friability was < 1%.

The prepared mini tablets of AM were observed to have uniformity in the weights, thickness, and uniformity in contents. The same mini tablets of AM were evaluated for assay content as specified in Indian Pharmacopoeia.

CONCLUSION

AM is used for the treatment of hypertension. The present work aimed to develop sustained released mini tablets as mini tablets provides less risk of dose dumping inter and intra-subject variability. The mini tablets have excellent size uniformity, regular shape, and a smooth surface. The dosage form also offers a high degree of dispersion in the GI tract, thus minimizing the risks of high local drug concentrations.

The prepared tablets were assessed for routine evaluation parameters. All the mini tablets were observed to have uniformity in the weight of the drug, good mechanical strength (hardness and friability), and uniformity in the drug content. Among the above formulations, CC1 showed better physicochemical constraints, including drug release, so they were subjected to evaluation of assay.

A simple, rapid, precise, and reliable method was developed to estimate the Azilisartan Medoxomil mini tablet formulation. Acetonitrile has been selected for chromatographic separation because of its low chemical reactivity, high miscibility with water, low viscosity, and low ultraviolet cut-off. The study also concluded that using acetonitrile during RP-HPLC development possesses higher elution strength, resulting in shorter analyte retention.

The outcomes are within the ICH guidelines' prescribed range. Using an analytical column with the mobile phase produces good separation and precise results. The method can be utilized for routine analysis in quality control laboratories because the retention time for API was good.

Overall, AM was the subject of an extensive study. AM was successfully developed as a sustained-release micro tablet by the authors.

ACKNOWLEDGMENTS

Nil

REFERENCES

1. Alquadeib BT: Development and Validation of a new HPLC analytical method for determining diclofenac in tablets. Saudi Pharmaceutical Journal 2019; 27(1):66-70.
2. Bhagat R and Saudagar RB: A Review on Analytical Method Development and Validation. Journal of Drug Delivery and Therapeutics 2019; 9(3-s):1064–1067.
3. Chauhan A, Mittu B, and Chauhan P: Analytical method development and Validation: a concise review. J Anal Bioanal Tech 2015; 6:1.
4. Creaven PJ. Cancer Chemother. Pharmacol. 1982;7:133.
5. Donauer N, Löbenberg R. A mini-review of scientific and pharmacopeial requirements for the disintegration test. International journal of pharmaceutics. 2007 Dec 10; 345(1-2):2-8.
6. Gawai M. N., Surwade K. S., Phadatare D. G. UV Spectrophotometric Method for estimating Azilsartan Medoxomil in Bulk Form. Asian J. Research Chem. 2018; 11(5): 791-793 doi: 10.5958/0974-4150.2018.00139.6

7. Hema and Swati Reddy G: A review on new analytical method development and Validation by RP-HPLC. Int Res J Pharm Biosci 2017; 4:41-50.
8. ICH: Q2B, Analytical Validation- Methodology, 1996.
9. Josilene Chaves Ruela Corrêa, Cristina Duarte Vianna-Soares, Hérida Regina Nunes Salgado, "Development and Validation of Dissolution Test for Fluconazole Capsules by HPLC and Derivative UV Spectrophotometry", Chromatography Research International, vol. 2012, Article ID 610427, 8 pages, 2012. https://doi.org/10.1155/2012/610427
10. Karpe S, S Sandeep, R Priya, K Sanjay. Development and Validation of a Bioanalytical RP-HPLC method for Azilsartan Medoxomil with liquid-liquid extraction. Int J Pharm PharmSci, 2016;8(2):164-168.
11. Lachman L, Schwartz JB. Herbert lie berman. Joseph L Kanig., The Theory and Practice and Industrial Pharmacy, Third edition. Page. (293–345).
12. Madathilethu J, Roberts M, Peak M, Blair J, Prescott R, Ford JL. Content uniformity of quartered hydrocortisone tablets in comparison with mini-tablets for pediatric dosing. BMJ pediatrics open. 2018; 2(1).
13. MadhuBabu K, BikshalBabu K. Reverse Phase-HPLC Method Development and Validation for the Simultaneous Estimation of Azilsartan Medoxomil and Chlortalidone in Pharmaceutical Dosage Forms. Journal of Atoms and Molecules 2012;2(1).
14. Moskalyk RE, Chatten LG, Cox CE, Pernarowski M. Uniformity of drug dosage in compressed tablets. Journal of pharmaceutical sciences. 1961 Aug; 50(8):651-7.
15. Naazneen A S. Stability-Indicating RP-HPLC Method for the Simultaneous Estimation of Azilsartan Medoxomil and Chlorthalidone in Solid Dosage Forms. Int J Pharm PharmSci, 2014;6(6):236-243.
16. Neelima K, Rajendra Prasad Y. Development and Validation of RP-HPLC Method for the Simultaneous Estimation of Chlorthalidone and Cilnidipine in Bulk and Combined Tablet Dosage Form. Pharmacophore 2014;5(4):442-450.
17. Osei-Yeboah F, Sun CC. Validation and applications of an expedited tablet friability method. International journal of pharmaceutics. 2015 Apr 30; 484(1- 2):146-55.
18. Patel A, Dwivedi N, Kaurav N, Bashani S, Patel S and Sharma HS: Chemical analysis of pharmaceuticals: a review. J Med Pharm Innov 2016; 3:4-7.
19. Ridgway K, Aulton ME, Rosser PH. The surface hardness of tablets. Journal of pharmacy and pharmacology. 1970 Dec; 22(S1):70S-8S.
20. Sandeep K, Kumar R, Mymoonaakhtar, Chandaranjan, Gitachawla. Development and Validation of RP-HPLC method for Simultaneous Estimation of Azilsartan Medoximil and Chlorthalidone in bulk form and formulation using quality by design. Int j pharm pharm sci, 2016;8(2):266–272.
21. Sharma S, Goyal S, and Chauhan K: A Review on Analytical Method Development and Validation. International Journal of Applied Pharmaceutics 2018; 10(6):8–15.
22. Sravani, SR Kumar, N Duganath,N Devanna. Method Development and Validation for the Simultaneous Estimation of Azilsartan and Chlorthalidone by RP-HPLC in Pharmaceutical Dosage Form. Int J Pharma Sci. 2014;4(5):725-729.

23. Sudev S and Sree Janardhanan. V: Review on HPLC Method Development Validation and Optimization. Int. J. Pharm. Sci. Rev. Res 2019; 56(2):28–43.
24. Sunitha, CM Subash, TS Sushma, A Venu, BV Narasimha Rao, B AppaRao – Method Development and Validation of Stability Indicating Rp-Hplc Method for Simultaneous Estimation of Azilsartan and Chlorthalidone in Pure And Pharmaceutical Dosage Form. World Journal of Pharmaceutical Research, 2015;4(4):966-974.
25. Swamy K, Rajendrakumar and Seshagirirao. A Novel Stability Indicating Validated RP-HPLC Method for Simultaneous Determination of Azilsartan and Amlodipine Besylate hydrochloride in bulk and tablet dosage form. ejbps, 2015;2(1):316-332.
26. Vekariya P, Joshi H. Development and Validation of RP-HPLC Method for Azilsartan Medoxomil Potassium Quantitation in Human Plasma by Solid Phase Extraction Procedure. ISRN Spectroscopy volume 2013;2013.
27. Wood JR. Tablet Manufacture; Its History, Pharmacy, and Practice. Lippincott; 1906.

TABLES

Table 1: Formula of sustained-release coated AM Mini Tablets

Ingredients	Weight of Ingredients in mg										
	AM1	**AM2**	**AM3**	**AM4**	**AM5**	**AM6**	**AM7**	**AM8**	**AM9**	**AM10**	**AM11**
Drug	21.34	21.34	21.34	21.34	21.34	21.34	21.34	21.34	21.34	21.34	21.34
Avicel PH 102	8.25	8.25	8.25	8.25	8.25	8.25	8.25	8.25	8.25	8.25	8.25
Mannitol (Pearlitol sd100)	7.00	7.00	7.00	7.00	7.00	7.00	7.00	7.00	7.00	7.00	7.00
Hypromellose (Methocel K 4 M)	4	8	8	12	12	12	12	12	4	8	4
Eudragit RS PO	12	8	8	4	4	12	4	12	4	8	12
Hydroxypropyl Cellulose Klucel EF	2	4	4	6	2	6	6	6	2	4	2
Colloidal Silicon Dioxide (Aerosil 200 Pharma)	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Magnesium Stearate	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25

Table 2: Recovery data of Azilsartan medoxomil

Level (%)	Drug Conc (mcg)	Amt added (mcg)	Average Amt recovered (mcg)	% Recovery	RSD*
80%	450	360	366.48	101.80	1.84
100%	450	450	454.74	101.05	1.72
120%	450	540	546.34	101.58	1.99

***N= 3**

Table 3: Precision study (repeatability) of Azilsartan Medoxomil

Conc µg/ml	Area	AVG	SD	%RSD*
450	12635	12560	133.36	1.06
450	15485			
450	12369			

***N= 3**

Table 4: Precision study (Intraday) of Azilsartan Medoxomil

Sr No.	Conc	Area			Mean	Amt Found	% Amt Fnd	SD	%RSD*
		I	II	III					
1	300	5369	5471	5264	5420.00	310.42	103.47	103.50	1.91
2	450	8705	8649	8521	8677.00	451.83	100.41	94.32	1.09
3	600	12142	12316	12025	12229.00	606.05	101.01	146.43	1.20

***N= 3**

Table 5: Precision study (Interday) of Azilsartan Medoxomil

Sr No.	Conc	Area			Mean	Amt Found	% Amt Fnd	SD	%RSD*
		I	II	III					
1	40	5461	5596	5659	5528.50	315.13	105.04	101.16	1.83
1	60	8969	8754	8858	8861.50	459.84	102.19	107.52	1.21
3	80	12432	12054	12142	12243.00	606.66	101.11	197.79	1.62

***N= 3**

Table 6: Robustness study with change in flow rate

Flow Rate = 0.65 ml/min			Flow Rate = 0.85 ml/min		
Sr No.	µgm/ml	Area	Sr No.	µgm/ml	Area
1	450	8795	1	450	8796
2	450	8769	2	450	8674
3	450	8744	3	450	8671
	Mean	8769.33		Mean	8713.67

	SD	18.38		SD	86.27
	%RSD*	0.21		%RSD*	0.99

***N= 3**

Table 7: Robustness study with change in wavelength

Wavelength= 232			**Wavelength= 234**		
Sr No.	**µgm/ml**	**Area**	**Sr No.**	**µgm/ml**	**Area**
1	450	8802	1	450	8905
2	450	8904	2	450	8804
3	450	8771	3	450	8798
	Mean	8825.7		Mean	8835.67
	SD	72.12		SD	71.42
	%RSD*	0.82		%RSD*	0.81

***N= 3**

Table 8: Robustness study with change in the mobile phase

Mobile Phase					
Acetonitrile: water (59:41)			**Acetonitrile: water (61:39)**		
Sr No.	**µgm/ml**	**Area**	**Sr No.**	**µgm/ml**	**Area**
1	450	8852	1	450	8747
2	450	8754	2	450	8752
3	450	8791	3	450	8854
	Mean	8799.0		Mean	8784.33
	SD	69.30		SD	3.54
	%RSD	0.79		%RSD	0.04

***N= 3**

Table 9: Evaluation of Mini Tablets with coating material for sustained release

Parameters	**AM1**	**AM2**	**AM3**	**AM4**	**AM5**	**AM6**	**AM7**	**AM8**	**AM9**	**AM10**	**AM11**
Average weight of powder (mg)	55.34	57.34	57.34	59.34	55.34	67.34	59.34	67.34	47.34	57.34	55.34
Weight variation (%)	0.1	0.14	0.14	0.12	0.15	0.14	0.12	0.1	0.15	0.15	0.11
Friability (%)	0.3	0.28	0.29	0.28	0.3	0.28	0.26	0.27	0.22	0.24	0.23
Hardness (Kg/cm^2)	4.1	5	4.6	4.8	5	5	4.9	5	4.7	4.8	5
Diameters (mm)	3	2.98	2.89	2.9	3	2.99	3	3	2.87	2.96	3

Thickness (mm)	2.57	2.84	2.56	2.98	2.88	2.76	2.82	2.94	2.78	2.64	2.82
Assay by HPLC	96.11±0.83	95.13±0.82	98.02±1.52	96.59±1.66	96.09±0.79	101.62±0.73	97.16±1.56	97.42±1.20	101.22±1.81	100.04±0.51	100.09±1.07

Figures

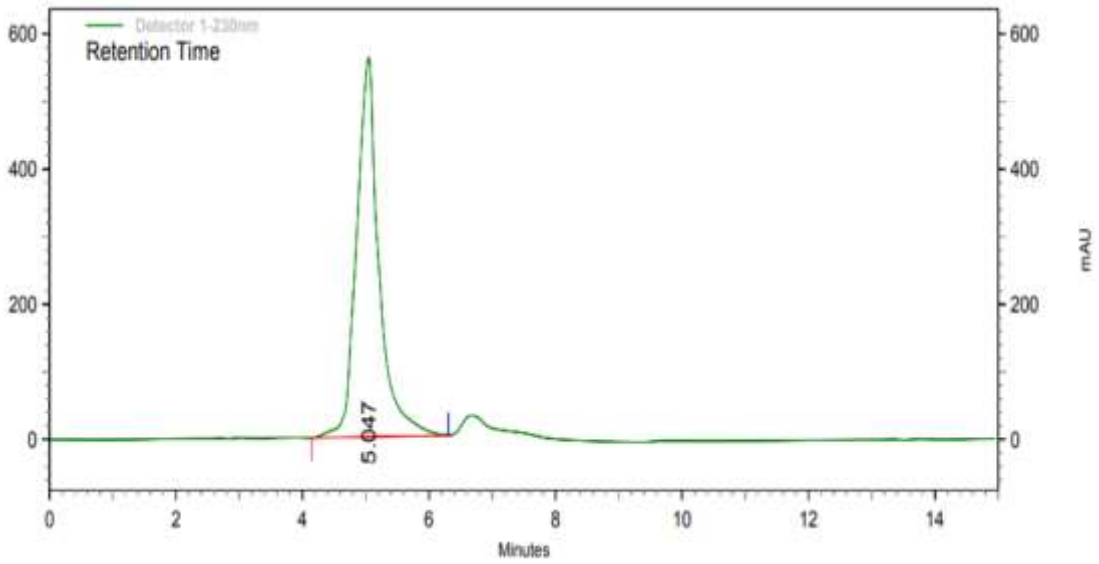

Figure 1: Chromatogram of Azilsartan

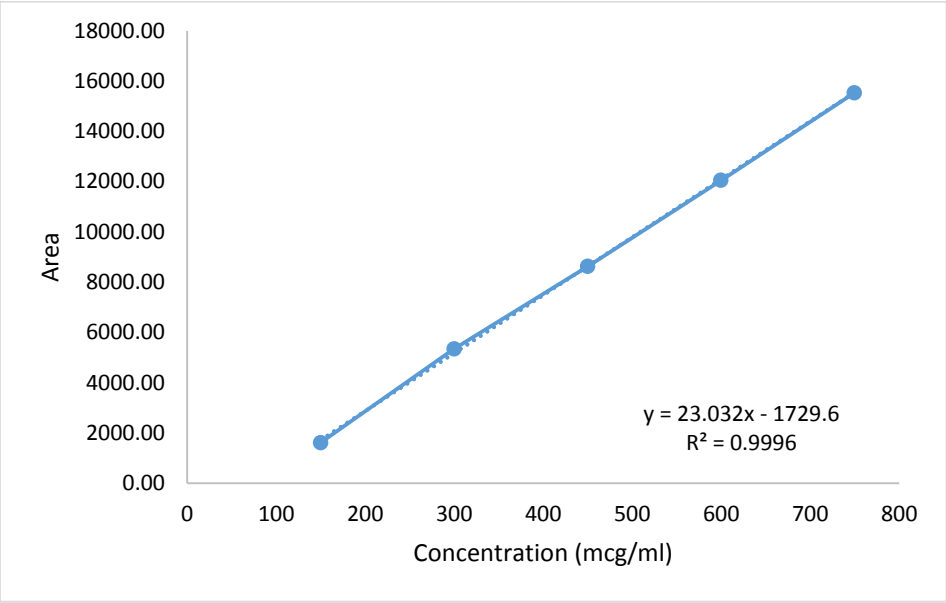

Figure 2: Linearity curve of Azilsartan Medoxomil

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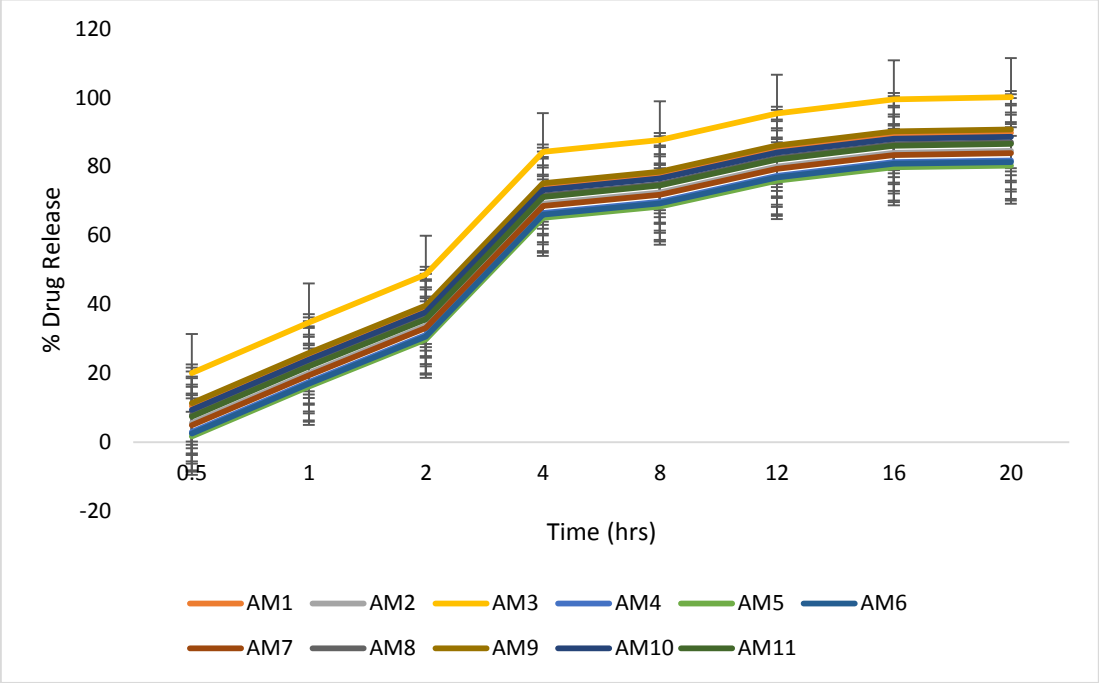

Figure 3: Graphical representation of percentage cumulative drug released from selected formulations using HPLC