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METHOD DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR SIMULTANEOUS ESTIMATION FOR AZELNIPIDINE & TELMISARTAN IN BULK & PHARMACEUTICAL DOSAGE FORM

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Abstract:

RP-HPLC method was developed for the estimation of Azelnidipine and Telmisartan in tablet dosage form. The proposed methods were applied for the determination of drug in tablet dosage form. Determination of Azelnidipine and Telmisartan is equation method. In this method concentration of each drug was obtained by using the absorptivity values calculated for drug wavelength 270 nm and solving the equation. A rapid and reliable RP-HPLC method was developed and validated estimation of Azelnidipine and Telmisartan in tablet dosage form. The RP-HPLC method was performed C18-(100mm x 4.6 mm,)2.5 ?m particle size in gradient mode, and the sample was analyzed using methanol 75 ml and 25 ml (pH 4.3 0.1% OPA with TEA) as a mobile phase at a flow rate of 0.8 ml/min and detection at 249 nm. By the retention time for Azelnidipine and Telmisartan found 3.20 and 6.23 min respectively. The method was applied to marketed tablet formulations. The tablet assay was performed for combination was validated for accuracy, precision, linearity, specificity, and sensitivity in accordance with ICH guidelines. Validation related the method is specific, rapid, accurate, precise, reliable, and reproducible. Calibration plots by both HPLC were linear over the 4-20 and 10-50 g/ml for Azelnidipine and Telmisartan respectively, and recoveries from tablet dosage form were between 100.34 and 101.68 %. The method can be used for routine of the quality control in pharmaceuticals. The RP-HPLC method was found to be simple, economical and rapid as compared to MS method was found to be more accurate, precise and robust. Both these methods can be used for routine analysis of Azelnidipine and Telmisartan in tablet dosage form.

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INTRODUCTION:

Azelnidipine is an antimetabolites which structurally related to normal compounds that exist within the cell. And interfere with purine /pyrimidine nucleotide precursors available by inhibit their synthesis, their maximum cytotoxic effect are in s-phase. The vitamin Telmisartan plays a central role in a variety of metabolic reactions involving the transfer of one carbon units and is essential for cell replication. Azelnidipine is structurally related to Telmisartan and acts as an antagonist of that vitamin by inhibiting dihydrofolate reductase. Telmisartan is obtained from dietary sources or from that produced by intestinal flora. It undergoes reduction to the tetrahydrofolate form via a reaction catalyzedby intracellular nicotinamide-adenine dinucleotidephosphate-dependent. Azelnidipine enters the cell by active-transport processes that normally mediate the entry of N5 -Methyl-FH4. Literature gave brief information of method development on bulk of Azelnidipineand Telmisartan followed validate that method as per ICH guideline on spectrophotometry and HPLC method. Specific method are reported for the analysis and determination of AZN&TLM in bulk and dosage form. The reported method is complex and time consuming hence there was a need for developing a validated method for estimation of AZN&TLM in pharmaceutical dosage form.[1]

Method development by RP-HPLC:

Using a trial-and-error approach, the process was developed by experimenting with various mobile phase ratios, column types, and flow rate variations.

Preparation of stock solution:

4 mg of Azelnidipinee and 40 mg of Telmisartan pure APIs were precisely weighed and transferred to a 50 mL volumetric flask. The flask's volume was adjusted using a diluent to obtain concentrations of 0.08 mg/mL and 0.8 mg/mL for Azelnidipinee and Telmisartan, respectively.

Preparation of standard solution:

In a 50mL volumetric flask, 40mg of Telmisartan API and 4mg of Azelnidipinee granules were precisely weighed and transferred, with the remaining capacity being filled with diluent. After transferring 1 mL of the final solution into a 10 mL volumetric flask, the remaining volume was once more filled with diluent to create a solution that contained 8 µg/mL and 80 µg/mL. The concentrations of Telmisartan and Azelnidipinee are regarded as 100%, respectively.

Preparation of sample solution:

A properly weighed tablet powder (Telmas-40) containing 40 mg of Telmisartan and 4 mg of Azelnidipine was transferred into a 50 mL volumetric flask, with the remaining volume being filled with diluent. To achieve solutions of 8 µg/mL and 80 µg/mL for Azelnidipinee and Telmisartan, respectively, which are regarded as 100% level concentrations, 1 mL of the resultant solution was put into a 10 mL volumetric flask, with the remaining capacity once more filled with diluent. A 0.4µm nylon filter was used to remove any particles before the injection sample solution was added.

Optimized method, in which the chromatographic conditions maintained as follow:

Mobile Phase	:	0.1 % OPA in water: Acetonitrile (40:60 v/v)
Column	:	Agilent C18(150 x 4.6mm, 5)
Flow Rate	:	1 mL/min.
Temperature	:	Ambient
Volume	:	10 µL
Detection wavelength	:	260nm

Method validation

System Suitability Test:

By injecting a 100% level of working standard concentration into six replicates, the current method's system suitability test was conducted. The chromatograms that were obtained were then subjected to evaluations of parameters such as the USP tailing factor (T), resolution (R), USP plate count (N), and percentage relative standard deviation (% RSD).

Linearity:

By injecting a series of working standard quantities, ranging from 2 µg/mL to 12 µg/mL of Azelnidipinee and 2 µg/mL to 12 µg/mL of Telmisartan, into the HPLC system under ideal chromatographic conditions, the linearity of the current approach has been achieved. Ultimately, the concentration versus peak area linearity graph was created, and the regression coefficient (R2) value was ascertained.

Transfer 0.25mL, 0.5mL, 0.75mL, 1mL, 1.25mL and 1.5mL of stock solution 0.08mg/mL of Azelnidipine and 0.8 mg/mL of Telmisartan in to individual 10ml volumetric flask, further made the volume with diluent to get the concentrations about 2, 4, 6, 8, 10,12 µg/mL of Azelnidipine and 20, 40, 60, 80, 100, 120 µg/mL of Telmisartan respectively.

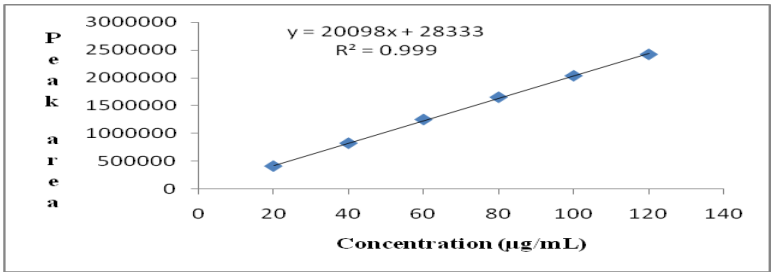

Figure-. Linearity graph of Azelnidipine

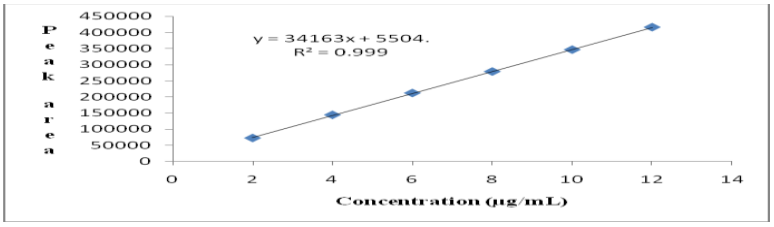

Figure-. Linearity graph of Telmisartan

Table-. Linearity data of Azelnidipine and Telmisartan

		Azelnidipine		Telmisartan	
S.no	**% Level**	**Concentration (µg/mL)**	**Peak area**	**Concentration (µg/mL)**	**Peak area**
I	25	2	72172	20	416015
II	50	4	143902	40	827348
III	75	6	211654	60	1253065
IV	100	8	278255	80	1652865
V	125	10	346128	100	2039015
VI	150	12	415778	120	2422755
Correlation coefficient (R^2)			**0.999**		**0.999**

Accuracy:
Recovery trials that involved the injection of a specified quantity of sample solution in triplicate at three distinct standard concentration levels—roughly 50%, 100%, and 150%—were used to verify the method's accuracy. At three distinct medication solution levels, the % mean recovery was computed.

Precision:
It can typically be done on various days (inter-day) and on the same day (intraday). By injecting 100% of the working standard concentration six times a day and three times a day for three consecutive days, the method's intraday and interday precision was tested. % RSD was computed for the obtained peak areas**.**

Specificity:
The following injection techniques were used for the 10 µL volume of prepared blank solution, 100% level pure working standard solution, standard solution with placebo, and forced degradation solution. To determine whether there had been any interference with the peaks of Azelnidipine and Telmisartan in the acquired chromatograms, the RT of two desired analytes in separate injections of standard, sample solution, forced degradation solution, and standard solution spiked with placebo were monitored.

Results of Specificity of Azelnidipine and Telmisartan

Name	RT (Min.)	
	Azelnidipine	Telmisartan
Standard	2.187	2.957
Sample	2.201	2.971
Blank	-	-

Robustness:
Modest adjustments to the optimised technique parameters, such as the mobile phase composition (± 1 ml), flow rate (± 0.1 mL/min.), and detection wavelength (± 2 nm), were made to test the resilience of the procedure. The percentage RSD value was calculated using important system suitability criteria.

Linearity:
Plotting a linear curve between each analyte's concentration and peak area response enabled the method to achieve an R2 value of 0.999 for concentrations ranging from 2 to 12 µg/mL and 20 to 120 µg/mL of Azelnidipine and Telmisartan, respectively

Table-. Linearity data ofbAzelnidipine and Telmisartan

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CONCLUSION:

Azelnidipine and Telmisartan in pure blended powder and their fixed-dose combination tablet form were analysed in parallel using a cost-effective, perceptive, accurate, trouble-free, and highly responsive reverse phase technique. Analyte studies under varied stressors attest to the method's stability and representative nature. Azelnidipine and Telmisartan were skilfully isolated from workable degradants produced with exquisite resolution using the proposed approach. The predicted approach is widely known in the pharmaceutical industry because it has a shorter retention period and is more sensitive for telmisartan and azelnidipine.

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