ISSN: 2395-0536

INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND NOVEL SCIENCES

IJPRNS

DEVELOPMENT AND ESTIMATION OF NIACIN AND SIMVASTATIN BULK AND IT'S FORMULATION USING RP-HPLC

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ABSTRACT

The estimation of Niacin and Simvastatin was done by RP-HPLC. The assay of Niacin and Simvastatin was performed with tablets and the % assay was found to be 99.32 and 99.39 which shows that the method is useful for routine analysis. The linearity of Niacin and Simvastatin was found to be linear with a correlation coefficient of 0.999 and 0.999, which shows that the method is capable of producing good sensitivity. The method shows precision 0.44 and 0.85 for Niacin and Simvastatin which shows that the method is repeatable. The recovery was found to be 99.95% and 100.15% for Niacin and Simvastatin. The LOD and LOQ for Niacin were found to be 2.96 and 9.96 and LOD and LOQ for Simvastatin was found to be 2.98 and 9.98.

Key Words: RP-HPLC, Niacin, Simvastatin, validation, ICH guidelines

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INTRODUCTION

Analytical chemistry is the science that seeks ever improved means of measuring the chemical composition of natural and artificial materials. Chemical composition is the entire picture (composition) of the material at the chemical scale and includes geometric features such as molecular morphologies and distributions of species within a sample as well as single dimensional features such as percent composition and species identity (1).

High performance liquid chromatography is a very quantitative and qualitative analysis of pharmaceuticals. The principle advantage of HPLC compared to classical column chromatography is improved resolution of the separated substance, faster separation times and the increased accuracy, precision and sensitivity (2).

Niacin ((pyridine-3-carboxylic acid) fig-1) a water-soluble vitamin of the B complex occurring in various animal and plant tissues. It is required by the body for the formation of coenzymes NAD and NADP. It has pellagra-curative, vasodilating, and antilipemic properties.

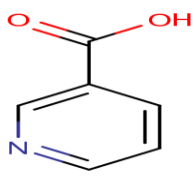

Figure-1 structure of niacin

Simvastatin (((1S,3R,7S,8S,8aR)-8-{2-[(2R,4R)-4-hydroxy-6-oxooxan-2-yl]ethyl}-3,7-dimethyl-1,2,3,7,8,8a-hexahydronaphthalen-1-yl 2,2-dimethylbutanoate) fig-2) is a lipid-lowering agent that is derived synthetically from the fermentation of Aspergillus terreus. It is a potent competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase (hydroxymethylglutaryl COA reductases), which is the rate-limiting enzyme in cholesterol biosynthesis. It may also interfere with steroid hormone production. Due to the induction of hepatic LDL receptors, it increases breakdown of LDL cholesterol.

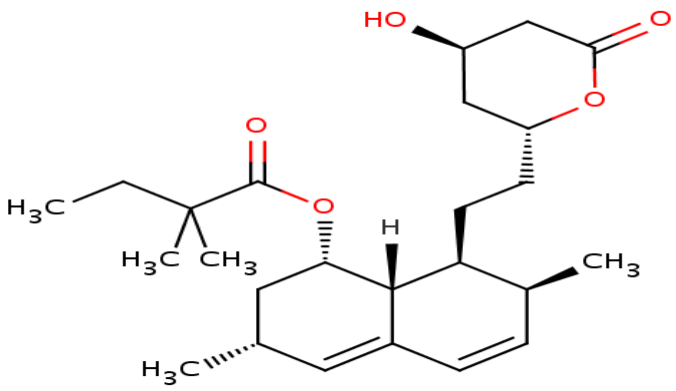

Figure-2 structure of Simvastatin

The literature review (3-9) reveals that few HPLC methods for the estimation of Niacin and Simvastatin alone and in combination with other drugs. Very few methods are reported for estimation of both drugs from formulation .We intends to develop RP-HPLC method by simultaneous determination with simple, rapid, greater sensitivity and faster elution.

The main objective of the present work is to establish a stability-indicating HPLC method for simultaneous determination of simvastatin and niacin in combined dosage form. The validated method would be applicable in both formulation development and routine quality control analysis.

MATERIALS AND METHODS

Wave length selection

UV spectrum of 10 µg / ml Niacin and Simvastatin in diluents (mobile phase composition) was recorded by scanning in the range of 200nm to 400nm. From the UV spectrum wavelength selected as 254. At this wavelength both the drugs show good absorbance.

Optimization of Column

Inertsil ODS C $_{18}$ (4.6 x 150mm, 5.0µm) was found to be ideal as it gave good peak shape and resolution at 1.0 ml/min flow.

Assay

Standard Solution Preparation

Accurately weigh and transfer 125mg of Niacin & 5mg of Simvastatin working standard into a 10ml clean dry volumetric flask add Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution). Further pipette 1ml of Niacin & Simvastatin of the above stock solution into a 10ml volumetric flask and dilute up to the mark with Diluents. Further pipette 3ml of Niacin & Simvastatin of the above stock solution into a 10ml volumetric flask and dilute up to the mark with Diluents.

Sample Solution Preparation

Accurately weigh and transfer equivalent to 125mg of Niacin & 5mg Simvastatin equivalent weight of the sample into a 10ml clean dry volumetric flask add about 7ml of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution). Further pipette 1ml of Niacin & Simvastatin of the above stock solution into a 10ml volumetric flask and dilute up to the mark with Diluents. Further pipette 3ml of Niacin & Simvastatin of the above stock solution into a 10ml volumetric flask and dilute up to the mark with Diluents (10, 11).

Inject 20 µL of the standard, sample into the chromatographic system and measure the areas for the Niacin & Simvastatin peaks and calculate the %Assay by using the formulae. Validation was done according to ICH guidelines (12, 13).

RESULTS AND DICUSSION

Optimized chromatographic conditions

Mobile phase- Phosphate buffer pH 3.0: ACN (50:50%v/v); Column- Inertsil ODSC18 5µm (4.6*150mm); Flow rate- 1.0 ml/min; Wavelength- 254 nm; Column temp- Ambient; Sample Temp- Ambient and Injection Volume-20 µl.

Assay

Standard and sample solution injected as described under experimental work. The corresponding chromatograms and results are shown below (Fig-3, 4 and table-1).

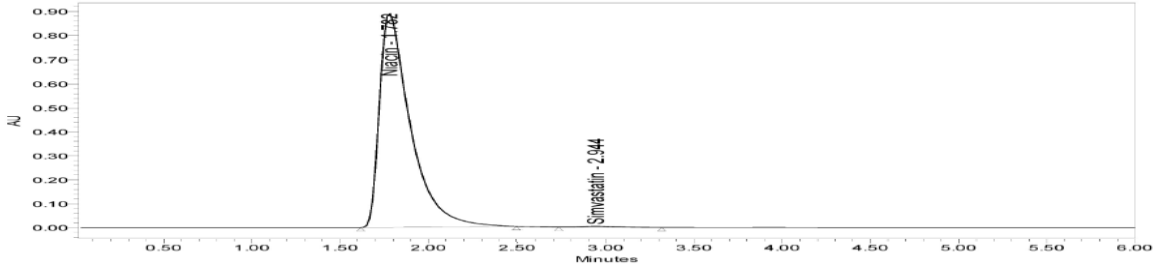

Figure-3 Chromatogram for Standard

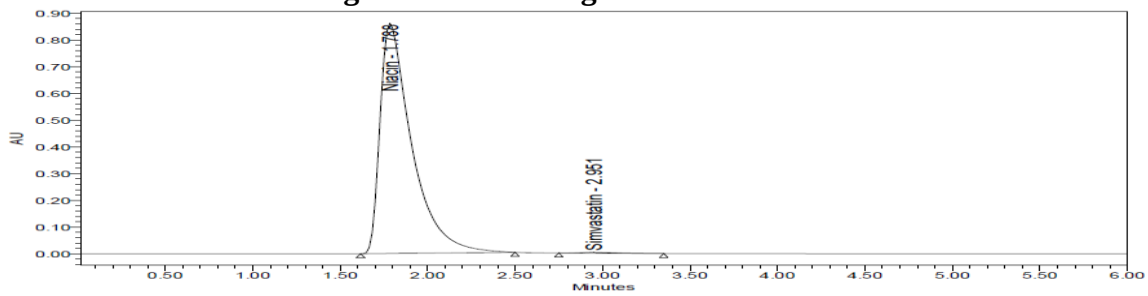

Figure-4 Chromatogram for Sample

Table-1 Results of Assay for Niacin and Simvastatin

	Label Claim (mg)	% Assay
Niacin	125	99.32
Simvastatin	5	99.39

Linearity

The linearity range was found to lie from 125µg/ml to 625µg/ml of Niacin, 5µg/ml to 25µg/ml of Simvastatin and chromatograms and calibration graphs are given below (fig-5-11).

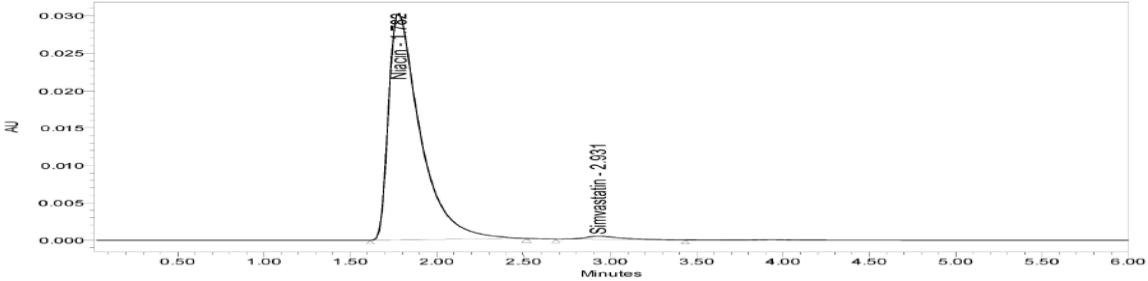

Figure 5- Chromatogram for linearity-1

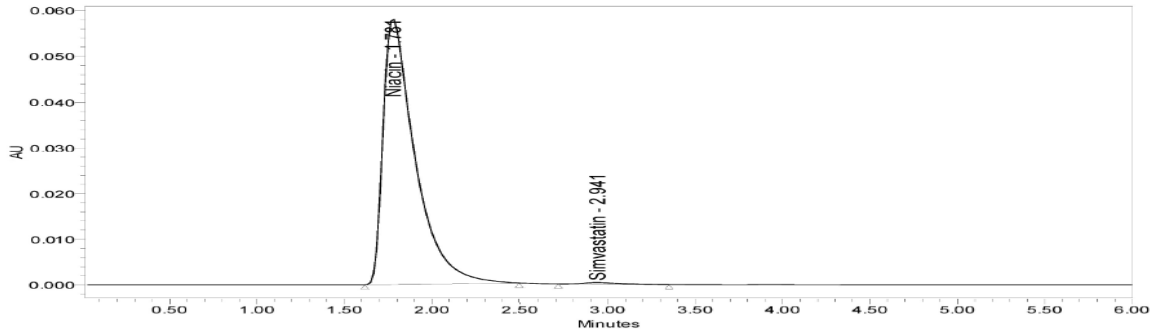

Figure 6- Chromatogram for linearity-2

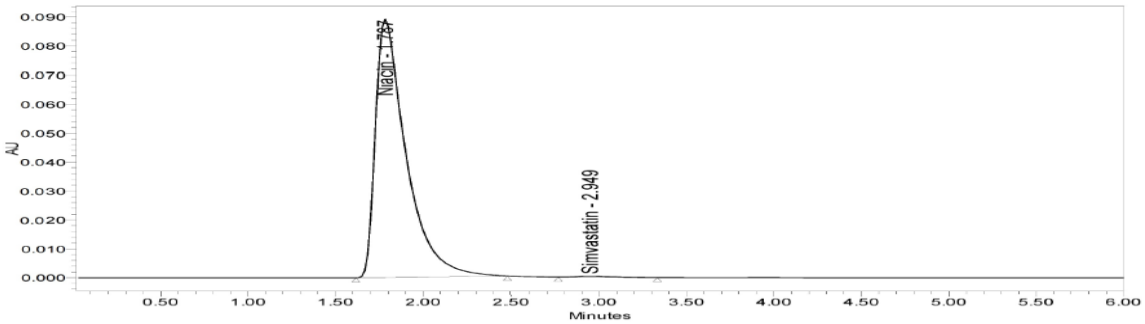

Figure 7- Chromatogram for linearity-3

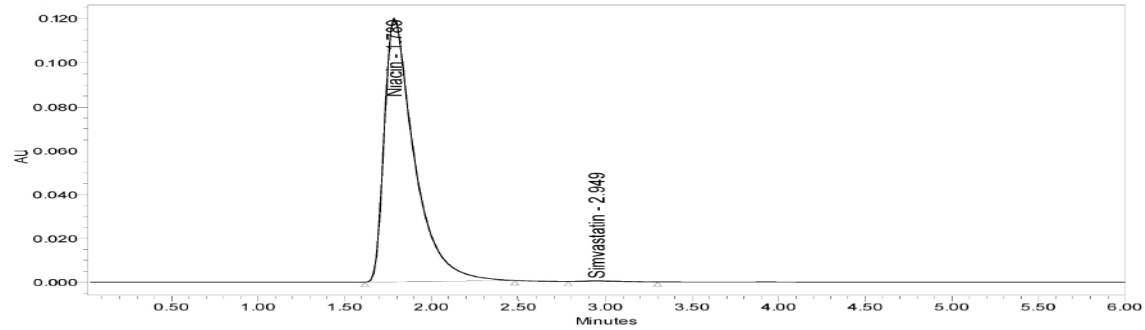

Figure 8- Chromatogram for linearity-4

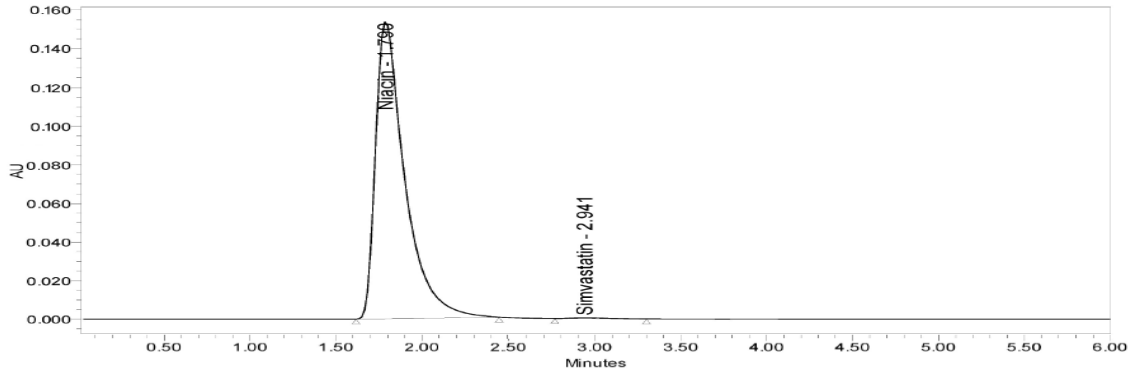

Figure 9- Chromatogram for linearity-5

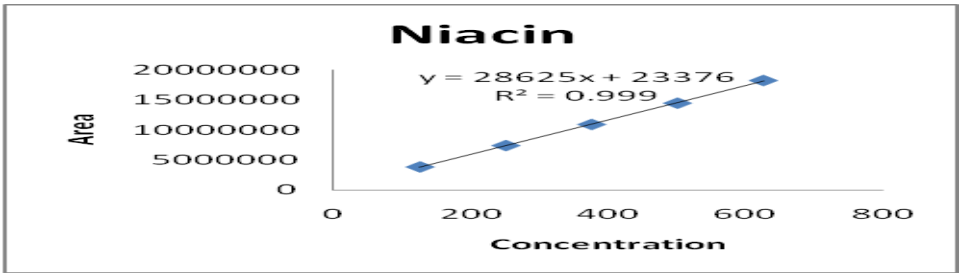

Figure 10- Calibration graph for Niacin

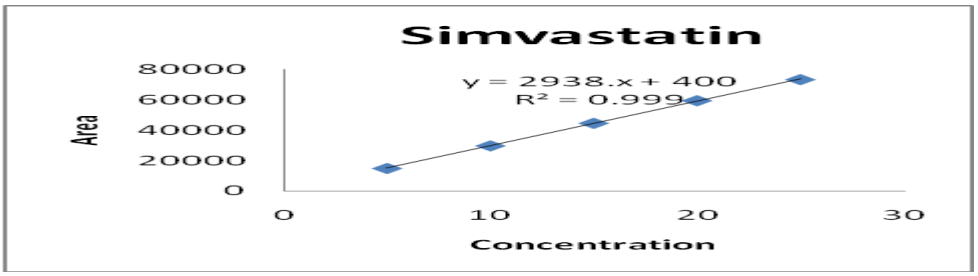

Figure 11- Calibration graph for Simvastatin

The correlation coefficient obtained was 0.999 which is in the acceptance limit.

Precision

Precision of the method was carried out for both sample solutions as described under experimental work. The %RSD for the standard solution is below 1, which is within the limits hence method is precise.

Accuracy

Sample solutions at different concentrations (50%, 100%, and 150%) were prepared and the % recovery was calculated (Table-2 and 3).

Table 2- Accuracy (recovery) data for Niacin

%Concentration (at specification Level)	Area*	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	5493305	62.5	63.26	100.87	99.95
100%	10816058	125	124.56	99.65	
150%	16171000	187.5	186.23	99.32	

*Average of three determinations

Table 3- Accuracy (recovery) data for Simvastatin

%Concentration (at specification Level)	Area*	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	22677	2.5	2.53	101.14	100.15
100%	44774	5	4.99	99.85	
150%	66890	7.5	7.46	99.45	

*Average of three determinations

The results obtained for recovery at 50%, 100%, 150% are within the limits. Hence method is accurate.

LOD and LOQ

The LOD and LOQ for Niacin was found to be 2.96 and 9.96 and LOD and LOQ for Simvastatin was found to be 2.98 and 9.98 respectively.

Robustness

The Retention time, USP plate count, USP tailing factor obtained for change of flow rate, variation in mobile phase was found to be within the acceptance criteria. Hence the method is robust.

CONCLUSION

The estimation of Niacin and Simvastatin was done by RP-HPLC. The assay of Niacin and Simvastatin was performed with tablets and the % assay was found to be 99.32 and 99.39 which shows that the method is useful for routine analysis. The linearity of Niacin and Simvastatin was found to be linear with a correlation coefficient of 0.999 and 0.999, which shows that the method is capable of producing good sensitivity. The acceptance criteria of precision is RSD should be not more than 2.0% and the method show precision 0.50 and 0.54 for Niacin and Simvastatin which shows that the method is precise. The acceptance criteria of intermediate precision is RSD should be not more than 2.0% and the method show precision 0.44 and 0.85 for Niacin and Simvastatin which shows that the method is repeatable when performed in different days also. The accuracy limit is the percentage recovery should be in the range of 97.0% - 103.0%. The total recovery was found to be 99.95% and 100.15% for Niacin and Simvastatin. The validation of developed method shows that the accuracy is well within the limit, which shows that the method is capable of showing good accuracy and reproducibility. The acceptance criteria for LOD and LOQ is 3 and 10. The LOD and LOQ for Niacin was found to be 2.96 and 9.96 and LOD and LOQ for Simvastatin was found to be 2.98 and 9.98. The robustness limit for mobile phase variation and flow rate variation are well within the limit, which shows that the method is having good system suitability and precision under given set of conditions.

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