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Simultaneous estimation of meclizine and nicotinic acid by using RP-HPLC

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ABSTRACT

A simple, accurate, rapid, precise and novel Reverse phase High Pressure liquid chromatographic method (RP-HPLC) has been developed and validated for simultaneous determination of Meclizine & Nicotinic acid in pharmaceutical dosage form. λ max of Meclizine was 220 nm and Nicotinic acid was 273 nm. The selected and optimized mobile phase was acetonitrile: potassium dihydrogen phosphate buffer (0.02M, pH 3.0) (55:45v/v) and conditions were flow rate (1.0 ml/minute), wavelength (234 nm), Run time was 20 min. The retention time were found to be 3.01 min and 6.07 min for Meclizine & nicotinic acid respectively. Linearity and range was found to be 0-140 µg/ml for Nicotinic acid and 0-150 µg/ml for Meclizine. The proposed chromatographic conditions were found appropriate for the quantitative determination of the drugs. The method was validated for accuracy, precision, specificity, linearity, robustness, sensitivity, LOD and LOQ. The proposed method was successfully used for quantitative analysis of tablets. No interference from any component of pharmaceutical dosage form was observed. Validation studies revealed that method is specific, rapid, reliable, and reproducible.

Keywords: RP-HPLC, Meclizine, Nicotinic acid and Acetonitrile.

INTRODUCTION

QUANTITATIVE ANALYSIS BY UV VISIBLE SPECTROPHOTOMETRY[1,2,3,4]

METHODS OF ESTIMATION OF SINGLE COMPONENT FORMULATIONS

Quantitative spectrophotometric assay of medicinal substance as a single entity can be carried out by preparing a solution in a transparent solvent and measuring its absorbance at a suitable wavelength, most preferably the wavelength maxima (λ_{max}). The concentration of the absorbing substance can be calculated from the measured absorbance using one of the four principle procedures.

- Use of a standard absorptivity value
- Use of a calibration graph
- Single or double point standardization
- Chemical derivatization method

METHODS OF ESTIMATION OF MULTI-COMPONENT FORMULATIONS

Simultaneous estimation of drug combination is generally done by separation using chromatographic

methods like HPLC, GC and HPTLC etc. These methods are accurate and precise with good reproducibility, but the cost of analysis is quite high owing to expensive instrumentation, reagent and expertise. Hence it is worthwhile to develop simpler and cost effective method for simultaneous estimation of drugs for routine analysis of formulation. Spectrophotometric analysis fulfills such requirement where the simultaneous estimation of the drug combination can be done with similar effectiveness as that of chromatographic methods.

ANALYTICAL METHOD DEVELOPMENT BY RP-HPLC METHOD DEVELOPMENT AND DESIGN OF SEPARATION METHOD[5]

Methods for analyzing drugs in multicomponent dosage forms can be developed, provided one has knowledge about the nature of the sample, namely, its molecular weight, polarity, ionic character and the solubility parameter. An exact recipe for HPLC, however, cannot be provided because method development involves considerable trial and error procedures. The most difficult problem usually is where to start, what type of column is worth trying with what kind of mobile phase. In general one begins with reversed phase chromatography, when the compounds are hydrophilic in nature with many polar groups and are water soluble.

The organic phase concentration required for the mobile phase can be estimated by gradient elution method. For aqueous sample mixtures, the best way to start is with gradient reversed phase chromatography. Gradient can be started with 5-10% organic phase in the mobile phase and the organic phase concentration (methanol or acetonitrile) can be increased up to 100% within 30-45min. Separation can then be optimized by changing the initial mobile phase composition and the slope of the gradient according to the chromatogram obtained from the preliminary run. The initial mobile phase composition can be estimated on the basis of where the compounds of interest were eluted, namely, at what mobile phase composition.

Changing the polarity of mobile phase can alter elution of drug molecules. The elution strength of a mobile phase depends upon its polarity, the stronger the polarity, higher is the elution. Ionic samples (acidic or basic) can be separated, if they are present in dissociated form. Dissociation of ionic samples may be suppressed by the proper selection of pH.

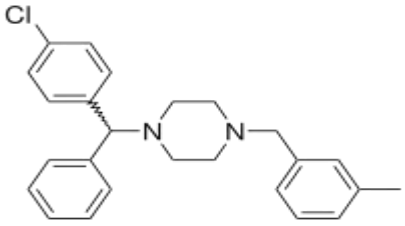
The pH of the mobile phase has to be selected in such a way that the compounds are not ionized. If the retention times are too short, the decrease of the organic phase concentration in the mobile phase can be in steps of 5%. If the retention times are too long, an increase of the organic phase concentration is needed.

DRUG PROFILE[6-11]

MECLIZINE

A histamine H1 antagonist used in the treatment of motion sickness, vertigo, and nausea during pregnancy and radiation sickness.

Molecular structure



Structure of Meclizine

Category: Anti-Allergic Agents, Histamine H1Antagonists, Antiemetics
Molecular weight: 390.948
Molecular formula: C25H27ClN2
Chemical name: 1-[(4-chlorophenyl) (phenyl) methyl]-4-[(3 methyl phenyl) methyl] piperazine
Metabolism: Hepatic
Half-life:6 hours

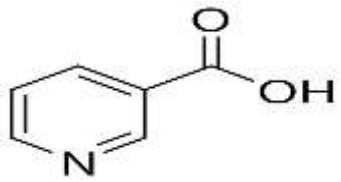
Pka: 8.16
Solubility: water soluble, methanol and acetonitrile soluble

NICOTINIC ACID

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

Physical properties: white, crystalline powder
Solubility: very soluble in water

Molecular structure



Structure of Nicotinic acid
Chemical name: pyridine-3-carboxylic acid
Molecular formula: $C_6H_5NO_2$
Molecular weight: 123.1094
Category: Antihyperlipidemic agent.
Pka: 4.75

MATERIALS AND METHODS

CHEMICALS

S.No.	Name	Specifications		Manufacturer/Supplier
		Purity	Grade	
1.	Doubled distilled water	----	----	In house laboratory.
2.	Methanol	99.9%	A.R.	Loba Chem; Mumbai.
3.	Sodium Hydroxide	96%	L.R.	SD fine-Chem ltd; Mumbai
4.	Acetonitrile	99.9%	HPLC	Loba Chem; Mumbai.

INSTRUMENTS

S. no.	Name of Instrument	Instrument Model	Name of manufacturer
1	UV-Visible double beam spectrophotometer	UV 1800	Shimadzu, corp. Japan.
2	HPLC	1575	Hitachi
3	Ultra sonicator	--------	Entrech electronics limited
4	Melting point appraturs	--------	

UV ANALYSIS FOR METHOD DEVELOPMENT AND ITS VALIDATION FOR SIMULTANEOUS ESTIMATION OF MECLIZINE & NICOTINIC ACID

Simultaneous estimation of meclizine & nicotinic acid as API Preparation of standard stock solution of meclizine

Accurately weighed Meclizine (10 mg) was transferred to 100 ml volumetric flask, dissolved in methanol: buffer (50:50) and made-up the volume to 100 ml with

same solvent system. The final solution contained 100 µg per ml of Meclizine solution.

PREPARATION OF STANDARD STOCK SOLUTION OF NICOTINIC ACID

Accurately weighed Nicotinic acid (10 mg) was transferred to 100 ml volumetric flask, dissolved in methanol: buffer (50:50) and made-up the volume to 100 ml with same solvent system. The final solution contained 100 µg per ml of Nicotinic acid solution.

METHOD DEVELOPMENT AND ITS VALIDATION FOR SIMULTANEOUS ESTIMATION OF MECLIZINE & NICOTINIC ACID BY RP-HPLC IN COMBINATION TABLET DOSAGE FORM

SELECTION OF WAVELENGTH

The λ_{max} of the two ingredients i.e. Meclizine & Nicotinic Acid, were found to be 220 nm and 273 nm respectively in methanol as solvent system. As both the drugs having almost near absorption max at 220 nm, it has been chosen as common absorption maximum for hplc analysis.

PREPARATION OF STANDARD SOLUTION OF MECLIZINE

10 mg of Meclizine was weighed accurately and transferred into 100 ml volumetric flask. About 20 ml of HPLC grade methanol was added and sonicated to dissolve. The volume was made up to the mark with same solvent. The final solution contained about 200 µg/ml of Meclizine.

PREPARATION OF STANDARD SOLUTION OF NICOTINIC ACID

10 mg of Nicotinic acid was weighed accurately and transferred into 100 ml volumetric flask. About 20 ml of HPLC grade methanol was added and sonicated to dissolve. The volume was made up to the mark with same solvent. The final solution contained about 400 µg/ml of Nicotinic acid.

RESULTS AND DISCUSSION

The selected and optimized mobile phase was acetonitrile: potassium dihydrogen phosphate buffer (0.02M, pH 3.0) (55:45v/v) and conditions optimized were: flow rate (1.0 ml/minute), wavelength (234 nm), Run time was 20 min. Here the peaks were separated and showed better resolution, theoretical plate count and symmetry.

METHOD VALIDATION

ACCURACY: RECOVERY STUDY

The mean recoveries were found to be 98.97, 99.54, 99.57 % for Meclizine and 99.67, 99.19, 99.49% for Nicotinic acid. The limit for mean % recovery is 98-102% and as both the values are within the limit, hence it can be said that the proposed method was accurate.

PRECISION

The repeatability study which was conducted on the solution having the concentration of about 100 µg/ml for Meclizine and 100 µg/ml for Nicotinic acid (n =5) showed a RSD of 0.7684% for Meclizine and 0.08488% for Nicotinic acid. It was concluded that the analytical technique showed good repeatability.

Intraday and interday studies show that the mean RSD (%) was found to be within acceptance limit (≤2%), so it was concluded that there was no significant difference for the assay, which was tested within day and between days. Hence, method at selected wavelength was found to be precise.

LINEARITY AND RANGE

Linearity and range was found to be 0-140 µg/ml for Nicotinic acid and 0-150 µg/ml for Meclizine. The correlation coefficients were found to be 0.995 & 0.994, the slopes were found to be 8031 & 41291 and intercept were found to be 10243 & 13551 for Nicotinic acid and Meclizine respectively.

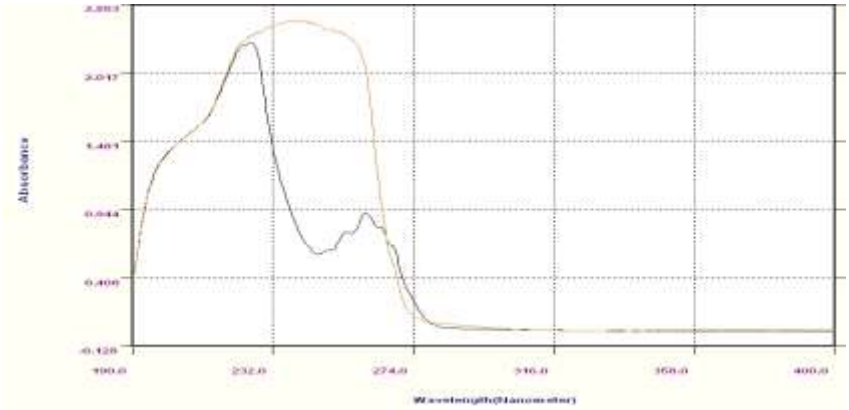
LOD & LOQ

The Minimum concentration level at which the analyte can be reliable detected (LOD) & quantified (LOQ) were found to be 0.05 & 0.15 µg/ml respectively for Meclizine

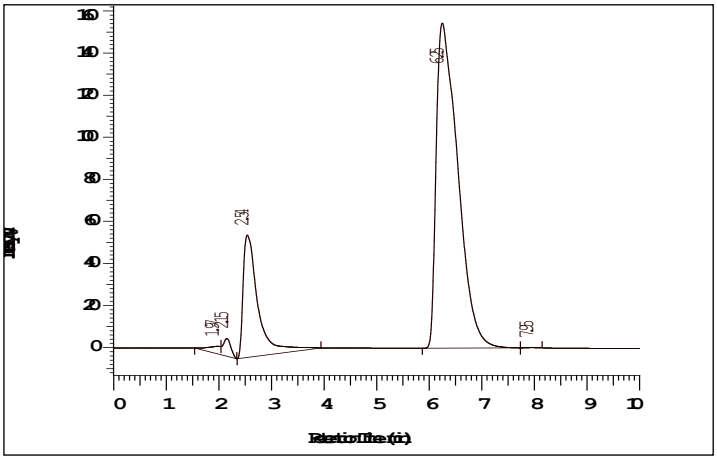
The LOD was found to be 0.452 µg/ml and LOQ was found to be 1.356 µg/ml for Nicotinic acid which represents that sensitivity of the method is high.

ASSAY OF MECLIZINE /NICOTINIC ACID TABLETS

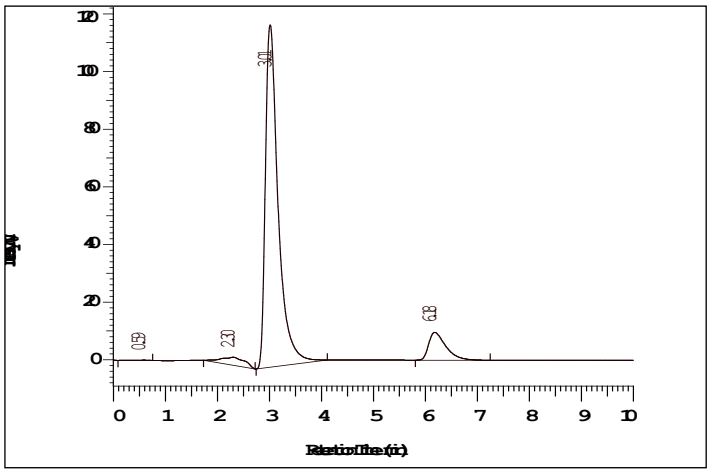
The assay of DILIGAN tablets containing Meclizine was found to be 100.065 %. & Nicotinic acid 99.62%.



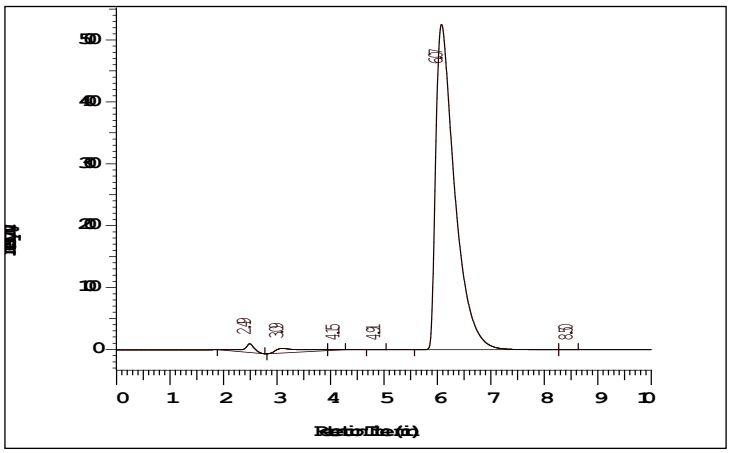
Overlain spectra of λ max. of Meclizine (220 nm) and Nicotinic acid (273 nm).



The chromatogram obtained after condition 5, Typical chromatogram of MECLIZINE (RT=2.54 min) and NICOTINIC ACID (RT= 6.25 min).



Chromatogram of Meclizine



Chromatogram of Nicotinic acid

TABLE.01.CHROMATOGRAPHIC CONDITIONS OF MECLIZINE & NICOTINIC ACID

Mobile phase	Acetonitrile:potassiumdihydrogen phosphate Buffer (55:45 v/v)
Stationary phase	Develosil ODS HG-5 RP C_{18}, 5µm, 15cmx7.6mm i.d.
Wave length	234nm
Run time	20 min
P.H of mobile phase	3.0
Flow rate	1.0 ml/min
Injection volume	20 µl
Temperature	Ambient
Mode of operation	Isocratic elution

SYSTEM SUITABILITY PARAMETERS OF ASSAY

Table.2. System suitability parameters for HPLC

Parameter	**Limit**
Capacity factor	K' > 2
Injection precision	RSD < 1% for ≥ 5
Resolution	Rs> 1.5
Tailing factor	T ≤ 2
Theoretical plate	N > 2000

Table:3.Validation results of Meclizine

Parameter	**Result**
Linearity	0-150 µg/correlation coefficient = 0.994
System precision	%RSD = 0.07
Accuracy	Mean recovery = 99.67
	ROBUSTNESS
	Change in flow rate

Flow rate (mL/min)	**%RSD**
1.1	0.07
0.9	0.02
Change in wave length	
Wavelength	**% RSD**
222	0.04
218	0.01
Change in Temperature	
Temperature	**% RSD**
27 C	0.09
23 C	0.13

Table:4.Validation results of Nicotinic Acid

Parameter	**Result**
Linearity	0-140 µg/mL Correlation coefficient = 0.995
System precision	%RSD=0.08
Accuracy	Mean recovery = 98.97
Change in flow rate	
Flow rate (mL/min)	**%RSD**
1.1	0.03
0.9	0.08
Change in wave length	
Wavelength	**% RSD**
222	0.82
218	0.46
Change in Temperature	
Temperature	**% RSD**
27 C	0.19
23 C	0.73

CONCLUSION

In the present work RP-HPLC method for simultaneous estimation of Meclizine & Nicotinic acid in tablet has been developed. The proposed methods are precise, accurate and do not suffer from any interference due to common excipients.

REFERENCES

[1] Skoog D.A., Holler F.J., Nieman D.A.," Principle of Instrumental Analysis", 6th ed Reprint, Thomson Brooks/Cole publication, 2004 ; 300-351.(UV)
[2] Sharma Y.R., "Elementary Organic Spectroscopy, Principle & Chemical Applications", S. Chand & Company Ltd., New Delhi, 2005; 8.
[3] Kalsi P.S., "Spectroscopy of Organic Compounds", 5th ed, New Age International Publishers New Delhi, 2002; 7.
[4] Braun R.D.,"Introduction to Instrument Analysis", Pharma Book Syndicate, Hyderabad, 2005; 261.
[5] Snyder L.R., Kirkland J.J. and Glajch L.J., "Practical HPLC Method Development", 2nd Edn., John Wiley and Sons, Inc., 1997; p.p. 2-18.
[6] http://www.mims.com/index.aspx?menuid=pgctrl&subid=brand&gen name=diclofenac sodium
[7] http://en.wikipedia.org/wiki/diclofenac sodium

[8] British Pharmacopoeia, Vol-I, The Department Of Health, The Stationery Office on behalf of the Medicines and Healthcare products Regulatory Agency (MHRA), London.
[9] http://en.wikipedia.org/wiki/rabeprazole
[10] http://chemicalland21.com/lifescience/uh/rabeprazole.htm.
[11] Indian Pharmacopeia, 2007, Vol I, Govt. of India, Ministry of Health and Family Welfare, Ghaziabad.

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