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Research Article

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Quantitative estimation of mefloquine HCl by RP-HPLC in pharmaceutical dosage form

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ABSTRACT

An approach for quantitative estimation of Mefloquin Hcl in formulation in presence of its degradation products. The method has shown adequate separation for Mefloquin Hcl from their associated main related compound and their degradation products. Separation was achieved on a Waters Symmetry, C18, 250 mm ×4.6 mm, 5 µ ,column at 25°C temperature by using a mobile phase consisting Buffer– Methanol (25:75 v/v) [Buffer: sodium hydrogen sulphate monohydrate in 1000 ml of water] at a flow rate of 0.7 ml/min, and UV detection at 280 nm. In the present study, comprehensive stress testing of Mefloquin Hcl was carried out according to ICH guideline Q1A (R2). The specificity of the method was determined by assessing interference from the placebo and by stress testing of the drug (forced degradation). Drug was subjected to Acid hydrolysis, Alkali hydrolysis, Oxidation, Dry heat and Photolysis to apply stress conditions. There were no other coeluting, interfering peaks from excipients, impurities, or degradation products due to variable stress conditions, and the method is specific for determination of Mefloquin Hcl in the presence of degradation products. The method was validated in terms of linearity, precision, accuracy, specificity, robustness and solution stability. The linearity of the proposed method was investigated in the range of 50-150 µg/ml (r^2 = 0.9995) for Mefloquin Hcl. Degradation products produced as a result of stress studies did not interfere in the estimation of Mefloquin Hcl and the assay can thus be considered stability-indicating.

Keyword: HPLC, Mefloquin Hcl, Estimation, Tablets.

INTRODUCTION

Mefloquine hydrochloride (Lariam, Mephaquin or Mefliam) is an orally administered medication used in the prevention and treatment of malaria. Mefloquine was developed in the 1970s at the United States Department of Defense's Walter Reed Army Institute of Research as a synthetic analogue of quinine. The brand name drug, Lariam, is manufactured by the Swiss company Hoffmann–La Roche. In August 2009, Roche stopped marketing Lariam in the United States. Generic mefloquine from other manufacturers is still widely available. Rare but serious neuropsychiatric problems have been associated with its use[1, 2, 3, 4].

EXPERIMENTAL SECTION

Materials

1)Mefloquine hydrochloride: - Working standard grade or Mefloquine hydrochloride Active Pharmaceutical Ingredient (API) was supplied by Mission Vivacare Research Centre (Indore, India), and its claimed purity was 98.20%.

2)Mefloquine hydrochloride Tablet (label claim 250 mg), Canfal 250mg Mfg.Lupin and placebo was manufactured and supplied Mission Vivacare Research Centre (Indore, India).

3)Mefloquine Related Compound A ((RS)-[2,8-bis(trifluoromethyl)quinoline-4-yl] [(2RS)-Piperidine-2-yl]methanol.Hydrochloride, Mefloquine Related Compound B ((RS)-[2,8-bis(trifluoromethyl)quinoline-4-yl]

[pyridine-2-yl] methanol), Mefloquine Related Compound C ((RS)-[2,8-bis(trifluoromethyl)quinoline-4-yl] [pyridine-2-yl] methanone) provided by Mission vivacare Ltd, R&D Department, Pithampur, Madhya pradesh
Note: Related compound A, Related compound B, Related compound C are known impurities of drug substance.

Reagents and Chemicals
1) Sodium hydrogen sulphate monohydrate - AR grade, Merck, India.
2) Methanol: - HPLC grade, Qualigens, India.
3) Milli-Q water: - It was purified by Millipore Corporation's system.
4) Hydrochloric acid: - Reagent Grade, Merck, India.
5) Sodium hydroxide: - Reagent Grade, Merck, India.
6) Hydrogen Peroxide (50%):- Reagent Grade, Merck, India.

Instruments, Apparatus and equipment
1) High Performance Liquid chromatography system (HPLC): Waters Liquid Chromatography with PDA detector
2) Analytical Balance: - AD 265S, Mettler Toledo, Schwerzenland.
3) pH Meter: - Labindia, India.
4) Sonicator: - 5510, Branson Ultrasonics Corporation, Danbury, CT, USA.
5) Hot air oven: - Labline, India.
6) Photo stability chamber: - UV/visible equipments, Germany

Chromatographic system
1) The reverse phase HPLC was selected for separation because it is convenient and rugged than other forms of the liquid chromatography and is more likely to result in a satisfactory final separation.
2) Degradation studies were carried out on a system consisted of Waters Liquid Chromatography with PDA detector Chromatographic software:– Empower PRO

METHODS
Standard preparation:
Standard stock solution was prepared by dissolving 50 mg of Mefloquine HCl reference standard to a 50 mL volumetric flask and dissolve and dilute up to the mark with diluent. Pipette out 5 ml of above solution in a 50 ml volumetric flask and make up the volume with diluents.

Sample preparation
Weigh accurately 20 tablet and triturate it take the powder equivalent to 50 mg of Mefloquine HCl and transfer it into 50 ml volumetric flask add about 10 mL of diluent, sonicate at for about 10 min with intermittent shaking, keep to achieve room temperature make up the volume with diluent. Pipette out 5 mL of the above solution and transfer to 50 mL volumetric flask and make up the volume with diluent.

Buffer Preparation
Dissolve 1.5 gm. of sodium hydrogen sulphate monohydrate in 1000 mL of milli Q water. Filter the solution through 0.45µ nylon filter paper.

Mobile phase
Mix 25 ml buffer solution and 75 ml of Methanol, sonicate and filter through 0.45µ membrane filter and degas.

Solvent Mixture
Buffer : organic (1:1) was used as diluent

Blank Solution: Use solvent mixture as blank.

Optimized RRLC Parameters:

Instrument	: Waters Liquid Chromatography with PDA detector
Column	: Waters Symmetry, C18, 250 mm × 4.6 mm, 5 µ
Flow Rate	: 0.7 mL/min
Injection volume	: 10 µL
Column temperature	: 25^{o}C
Sample cooler Temperature	: Ambient
Detection	: 280 nm
Run time	: 25 minutes

System Suitability Test

Inject Blank preparation in single injection, standard preparation in five replicate, record the chromatogram and calculate the system suitability parameters as given below:

Theoretical plate for Mefloquine HCl peak in five replicate standard injections : NLT 2500
% RSD for five replicate standard injections : NMT 2.0
Tailling Factor for Mefloquine HCl peak in five replicate standard injections : NMT 2.0
If system suitability passes then inject sample preparation in duplicate.

RESULTS AND DISCUSSION

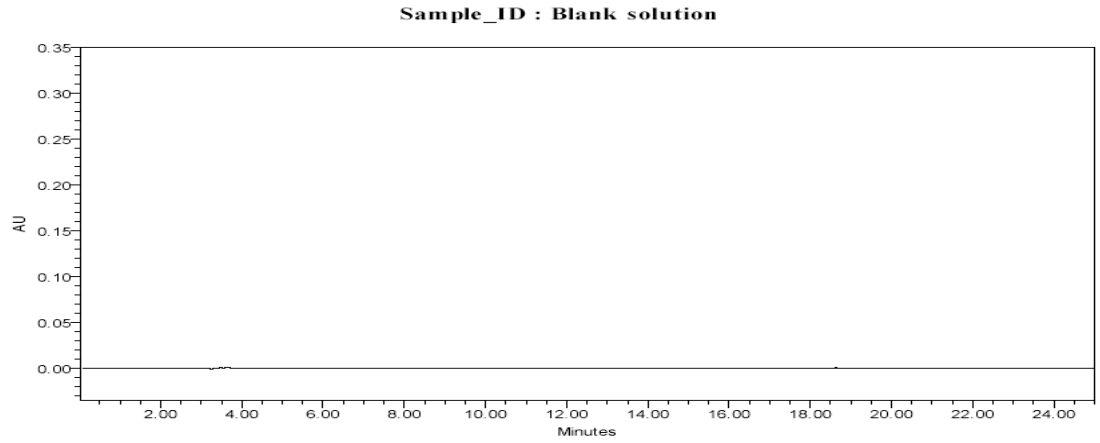

Figure 1: HPLC Chromatogram of Blank solution

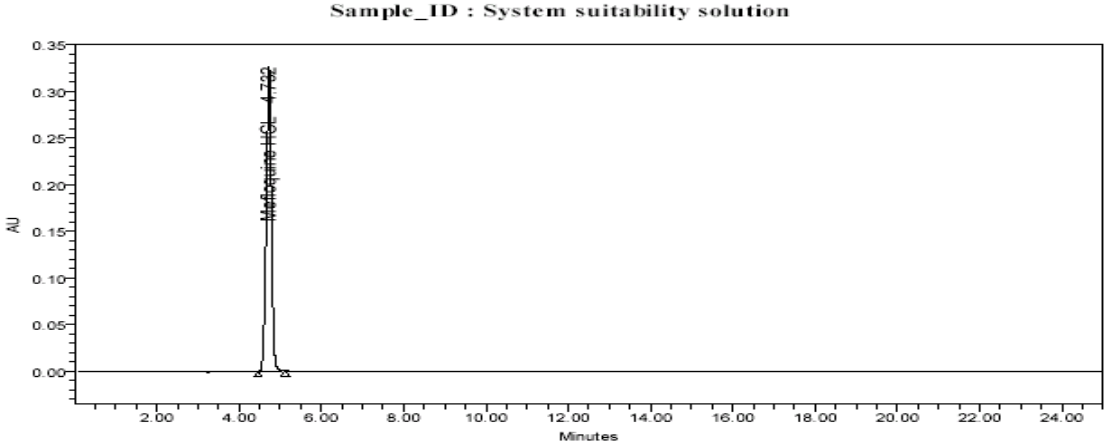

Figure 2: HPLC Chromatogram of system suitability (Standard) preparation with about RT-4.7 min

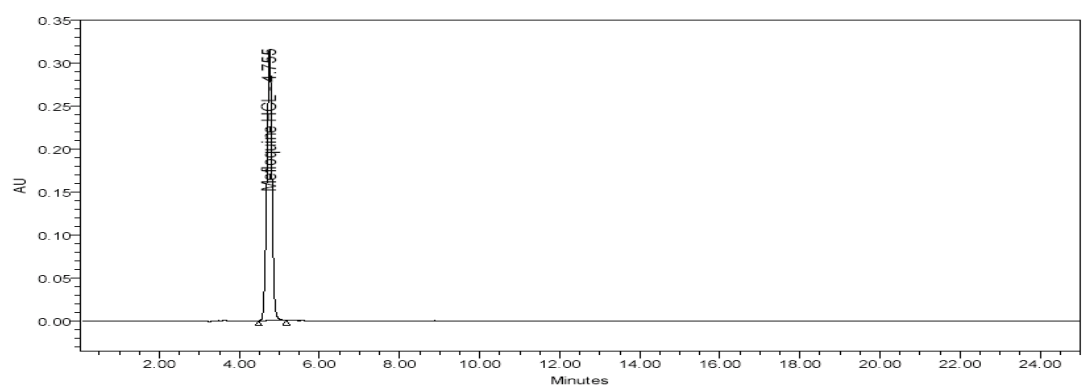

Figure 3: HPLC Chromatogram of Tablet preparation with about RT-4.7 min

Table 1 : Mean values of system suitability parameters

Sr. No.	Parameters	Mefloquine HCl
1.	Peak area	3652958
2.	No. of theoretical plates	8313
3.	Retention time (min)	4.732
4.	Asymmetry/USP Tailing	1.05
5.	% RSD	0.11

Table 2 : Response (Peak Area) and Assay of Sample Preparation

Sample Preparation No.	Sample		
	Area	Assay (%)	Assay (%)
1.	3639432	98.01	98.04
2.	3641342	98.06	

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