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REVIEW ON THE ANALYTICAL METHODS FOR THE ESTIMATION OF GARENOXACIN IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

This review explores Garenoxacin, a novel des-fluoro-6-quinolone antibiotic, highlighting its analytical methodologies. Garenoxacin exhibits broad spectrum activity against gram +ve & gram -ve organisms, including drug resistant strains. Its mechanism involves dual inhibition of DNA gyrase and topoisomerase IV, making it a potent candidate for the treating skin and soft tissue infections (SSSIs), respiratory tract infections, and other microbial conditions.. Analytical techniques such as HPLC (Concentration Range: 2–12 µg/mL, Wavelength: 280 nm, Stationary Phase: C18 (Princeton SPHERE ULTIMA, 250×4.6 mm, 5 µm), Mobile Phase: Acetonitrile: Water (60:40 v/v), ~0.1% orthophosphoric acid, Flow Rate: 1.0 mL/min, Detector: UV Diode Array (PDA)) , RPHPLC, (chromatographic conditions used in stationary phase zorbax eclipse XDB C18 250×4.6mm, 5m, mobile phase 0.1% orthophosphoric acid and acetonitrile in the ration of 50:50 (%v\v) and flow rate was maintained at 1.0ml\min, detection wavelength 240nm concentration range of 0.04 to 4µg\ml),and UV-spectrophotometry (Concentration Range: 3–18 µg/mL, Wavelength: 295 nm, Stationary Phase: Not applicable (UV method), Mobile Phase: Distilled water (aqueous solution) are discussed in the context of Garenoxacin quantification and validation, with emphasis on ICH and QbD guidelines. Clinical cases and studies underscore its effectiveness, safety and occasional adverse reactions, including hypersensitivity and fixed drug eruptions. The review also includes method development for pharmacokinetic studies and dosage form analysis, establishing garenoxacin's significance in therapeutic and analytical fields.

INTRODUCTION

Garenoxacin is considered as both API (bulk drug) and tablet formulation (solid oral dosage form).This study was carried out to assess the purity, quality and efficacy of using the new generation Garenoxacin these are the methods which effect the garenoxacin as: HPLC (High Performance Liquid Chromatography Effect of Garenoxacin: It has polar functional groups (carboxylic acid, piperazinyl, quinolone core), so it interacts well with reversed-phase C18 columns. Retention time depends on pH (since garenoxacin has ionizable groups). Detection: UV detection at ~ 270–295 nm due to quinolone chromophore. Mobile Phase: Usually a mixture of buffer (phosphate, acetate) and organic solvent (acetonitrile/methanol). UHPLC (Ultra High

Performance Liquid Chromatography) Effect of Garenoxacin: Same principles as HPLC, but smaller particle size columns (≤2 μm) are used. Garenoxacin gives sharper peaks, shorter run time, higher sensitivity compared to HPLC. Advantage: More efficient separation and reduced solvent consumption. Mass Spectroscopy (MS / LC–MS/MS) Effect of Garenoxacin: Because it contains nitrogen and fluorine atoms, garenoxacin ionizes well in Electrospray Ionization (ESI), usually in positive ion mode [M+H]+. Molecular ion peak: m/z ~ 402 (M+H)+ depending on the method. Useful for pharmacokinetic studies, metabolite identification, and trace level quantification. UV–Visible Spectrophotometer Effect of Garenoxacin: The quinolone nucleus has strong UV absorbance. Λmax usually around 272–290 nm. Can be used for simple estimation in bulk and formulations (though less specific than HPLC/LC-MS). Limitation: Cannot distinguish garenoxacin from degradation products or excipients as effectively as HPLC or LC-MS. HPLC/UHPLC → Used for assay, stability studies, dissolution. MS (LC–MS/MS) → highly sensitive, used for pharmacokinetics, plasma concentration analysis. UV spectrophotometer → Quick, simple method but less selective.

PHYSICAL AND CHEMICAL PROPERTY:

Table. No 1: Physical and chemical properties of Garenoxacin

Chemical name	1-Cyclopropyl-8-(difluoromethoxy)-7-[(1R)-1-methyl-2,3dihydro-1H-isoindol-5-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid mono methane sulfonate
CAS Number	194804-75-6
Molecular formula	C23H20F2N2O4CH4O3S
Molecular weight	522.52g|mol
Half life	20 hours
Solubility	Insoluble in water, sparingly soluble in methanol, very soluble in acetonitrile DMSO
Category	Antibiotic
BCS	Class II

CHEMICAL STRUCTURE OF GARENOXACIN:

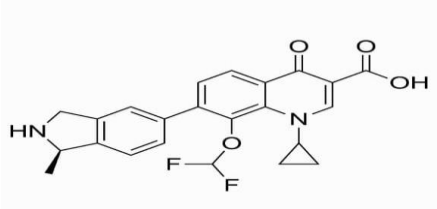

Fig.1: Chemical structure of garenoxacin

ANALYTICAL METHOD DEVELOPMENT:

The process of developing an accurate assay to ascertain the composition of formulations is known as analytical method development. Developing an analytical approach entails determining whether it is appropriate for use in laboratory. Analytical must adhere to GMP and GLP procedures and full fill ICH guide lines approval requirements.[18]

HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC):

In Garenoxacin the HPLC method was introduced by A. P. Edlabadkar and A. P. Rajput in 2017 and 2018. HPLC method for optimization of development and validation of garenoxacin Mesylate in bulk and tablets.

Originally called high pressure liquid chromatography, HPLC is a technique used in analytical chemistry to separate, identify, and quantify specific components in mixtures among other things; the mixtures may originate from liquid solutions that have been dissolved for biological, environmental, medicinal, chemical or dietary sources.[19]

Optimised condition in HPLC

Flow rate - 1.0 ml \ min

Detection wavelength – 280nm

Stationary phase\ column – Princeton SPHERE ULTIMA C18, 280nm, 5μm particle size

Column- C18 column

Mobile phase- formic acid in water (0.1%v/v): methanol [(60:40) %v/v]

ULTRA-HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (UHPLC):

Particles smaller than the 2.5-5um ones commonly employed in HPLC can be held in columns used in UHPLC. The fundamental premises of UHPLC, which operates under the same assumptions as HPLC that is efficiency and consequently, resolution accretion increase as column packing particle size decreases.

Smaller particle separations in columns result in increased efficiency per unit of time; however, efficiency cannot be reduced by higher mobile phase flow rates or linear velocities. Following characteristics, it is possible to achieve unprecedented levels of peak resolution and delicate particle speed. Linear velocity depends on the size of the particles packed into the analytical column. It is well known according to Van Deemter equations that the effectiveness of the chromatographic process is directly correlated with the reduction in particle size. His model-characterized band broadening demonstrates that the relationship between the height equivalent of a theoretical plate (HETP) and linear velocity depends on analytical column. [20]

REVERSE PHASE HIGH PERFORMANCE LIQUID CHROMATOGRAOHY (RPHPLC):

In Garenoxacin the RPHPLC was introduced by Ajitha Azhakesannn, Sujatha K, Abbulu K in April 2019. Bioanalytical method development and validation of garenoxacin Mesylate in human plasma by RP-HPLC.

A polar mobile phase and non-polar stationary phase are used in reversed phase liquid chromatography (RPLC) a kind of liquid chromatography, to separate organic molecules. The majority of separations and analyses carried out with HPLC in recent years have been carried out in the reversed phase mode. The components of the sample are kept in the system in reversed phase mode to a greater extent if they are hydrophobic. [21,22]

Stationary phase – zorbox eclipse XDB C18 (250×4.6mm, 5m)

Mobile phase – 0.1% orthophosphoric acid and acetonitrile

Ratio – 50:50 (%v\v)

Flow rate – 1.0 ml\min

Detection wavelength – 240nm

Retention time – 4.0 min

Concentration range - 0.04-4 µg\ml

MASS PECTROSCOPY:

D. A. Gajjar and colleagues (Bristol-Myers Squibb) used LC-MS/MS (mass spectrometry) for garenoxacin quantification in humans in 2003.

Mass percentage of Carbon (C), Hydrogen (H), Fluorine (F), Nitrogen (N), and Oxygen (O) in garenoxacin is 64.784%, 4.728%, 8.911%, and 15.008%. [23]

UV SPECTROPHOTOMETER:

Developed by: A. P. Edlabadkar & A. P. Rajput

Methods introduced: Four UV-spectrophotometric approaches (zero-order and first-order derivative, both with absorbance and AUC) for garenoxacin Mesylate assay

Publication source: Der Pharmacia Letters (mid-2010s; estimated ~2018)

Beer-lamberts range (ug/ml): 03-18 ug/ml

Spectral slit width: 1nm

Solvent: water

Lamda max: wave length maxima of garenoxacin with respected to adopted method like zero order, zero order-AUC, first order derivative, first order derivative AUC can be found as 274nm, 256.50-286nm, and 277.50-300nm. [24]

REPORTED METHOD FOR GARENOXACIN:

In 2016,A. P. Edlabadkar, and A. P. Rajput Der Pharmacia Letter on "Development of Four Simple UV-Spectrophotometry Methods for Estimation of Garenoxacin Mesylate in Bulk Material and Pharmaceutical Formulation." It details the development and validation of four UV-spectrophotometric methods for quantifying Garenoxacin Mesylate (GRN), a quinolone antibiotic used to treat respiratory and urinary tract infections, in bulk and tablet forms, using distilled water solutions were created using distilled water as a solvent.

The study was published in 2021 by Ajitha Azhakesannn A and her colleagues. ln order to develop and validate a novel stability-indicating method based on QbD for the assay and dissolution of garenoxacin in tablets. It describes how a Quality by Design (QbD) methodology was used to create and validate a novel stability-indicating method for the assay and dissolving of garenoxacin in 200 mg garenoxacin tablets. The des-fluoro (6) quinolone antibiotic garenoxacin Mesylate, which is sold under the brand name Geninax in Japan, has a broad-spectrum effect on antimicrobial resistance. With peak purity verified under stressful circumstances, the RP-HPLC test technique was linear, robust, accurate (99.8–100.5% recovery), and exact (RSD ≤ 0.48%). Variations in API particle size had no effect on the dissolving method's consistent drug release (Q ≥ 80% at30min).

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Spectrometric methods

Sakariya SV, mardia RB, Chauhan SP, Sahagia BN development of different spectrometric methods for the estimation of garenoxacin Mesylate in bulk and pharmaceutical formulations this was published by 2015, a different spectrometric method has been developed and validate for the determination of GRA in tablet dosage form, these are the solvents are used in the preparation of garenoxacin: garenoxacin Mesylate 0.1N HCL, 0.1N NaOH, distilled water. These are the concentration of HCL and NaOH are 10-50µg\ml. the maximum wavelength was observed at 347nm.

Linearity: 10-50µg\ml
LOD: 0.32µg\ml
LOQ: 1.09µg\ml

These are concentrations of HCL and distilled water are 10-50 µg\ml, the maximum wavelength was observed at 348nm.

Linearity: 10-50µg\ml
LOD: 0.46µg\ml
LOQ: 1.55µg\ml

CONCLUSION:

Garenoxacin analytical methods such as RP-HPLC, UHPLC, and UV-spectrophotometry have been successfully developed and validated for its quantification, adhering to ICH and QbD guidelines. Garenoxacin, a broad-spectrum fluoroquinolone antibiotic, can be effectively analyzed by several modern analytical techniques. UV spectrophotometry provides a simple and rapid method for its estimation, while HPLC and UHPLC offer accurate, precise, and reliable determination in pharmaceutical formulations and stability studies. Mass spectrometry, particularly LC–MS/MS, ensures highly sensitive detection and is indispensable in pharmacokinetic and bioanalytical applications. Thus, garenoxacin shows strong compatibility with spectroscopic and chromatographic methods, making it well suited for both qualitative and quantitative analysis. There was no colorimetric methods reported for estimation of garenoxacin was observed and this study is useful for further development of simple analytical methods for the estimation of garenoxacin in bulk and its formulations.

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