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Review Article

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF POSACONAZOLE IN PHARMACEUTICAL FORMULATIONS – A REVIEW

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ABSTRACT

Posaconazole marketed under the trade name Noxafil among others, is a medication used to treat serious fungal infection. Posaconazole, a broad-spectrum triazole antifungal agent, is approved for the preventionof invasive aspergillosis and candidiasis in addition to the treatment of oropharyngeal candidiasis. There is evidence of efficacy in the treatment and prevention of rarer, more difficult-to- treat fungal infections. Posaconazole oral suspension solution has shown limitations with respect to fasting state absorption, elevated gastrointestinal ph and increased motility. The newly approved delayed-release oral tablet and intravenous solution formulation provide an attractive treatment option by reducing interpatient variability and providing flexibility in critically ill patients. On the basis of clinical experience and further clinical studies, posaconazole was found to be a valuable pharmaceutical agent for the treatment of life-threatening fungal infection. This review will examine the development history of posaconazole and highlight the most recent advances.

Keywords: Posaconozole, Analytical Parameter, Antifungal, Validation.

INTRODUCTION

Posaconazole is a synthetic systemic triazole antifungal agent. It is used to treat invasive infection in severely immunocompromised patients those with acquired immunodeficiency syndrome and haemopietic stem-cell transplant recipients [1,2]posaconazole is 4-{4-[4-(4-(3R,5R)-5-(2,4-digluorophenyl)tetrahydro-5-(1H-1,2,4-triazol-1-ylmethyl)-tetraydrofuran-yl]methoxy}phenyl] piperazin-1-Yl]phenyl}-2-{1s,2s}-1-ethyl-2-hydroxy-propyl}-2,4-Dihydro-3H-1,2,4-triazol-3-one [3-4], is a triazole antifungal drug, approved by the Food Drug administration in 2006 and characterized for the broader spectra of action between triazole, besides the less potential of interaction. It is the 1st azoles agent to prove activity upon the zygomycetes, a difficult-to-treat family that involve Mucor and Rhizopus species. According to review of literature, It was known that analytical methods like HPLC and UPLC methods are available for the determination of posaconazole as alone or in composite with other Antifungal drugs in plasma and serum [5-10].So an attempt was made to develop a simple, precise, sensitive, rapid and accurate method for the Posaconazole detection using an economical mobile phase which is ecofriendly and validated the method by using RP-HPLC. Posaconazole is a new triazole with broad-spectrum antifungal activity against Candida, Aspergillus and Fusarium species, as well as against zygomycetes [11]. It has proven effective as a curative treatment of invasive fungal infections, mostly invasive aspergillosis and refractory mucosal candidiasis, and for antifungal prophylaxis in patients with graft-versus-host disease, as well as in patients with prolonged neutropenia in acute leukaemia [12-15]. Posaconazole is a highly lipophylic weak base structurally related to itraconazole. It belongs to

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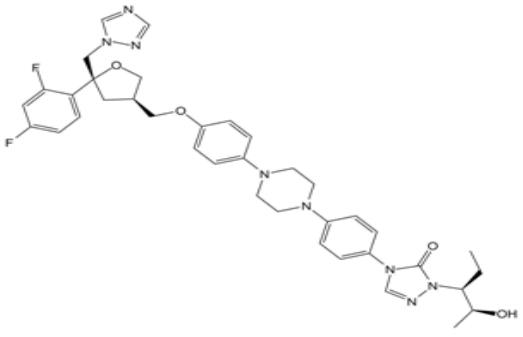
class II compounds, indicating that it is well absorbed but dissolves slowly in water (high permeability/low solubility)[16]. Similar to other triazoles, marked interpatient variability (between-patient variability in blood concentration after receiving the same dose), for both healthy volunteers and patient populations has been described. Several factors can impact posaconazole disposition: first, the only available formulation is an oral suspension that shows a great variability of absorption. Prandial state and meal composition (specifically fat), gastric pH or mucosal integrity impact significantly on posaconazole absorption [17]. Moreover, dose frequency has been proven to influence posaconazole disposition [18]. With regard to the pharmacodynamic endpoints associated with optimal treatment, certain evidence has suggested a relationship between exposure and efficacy for this compound [19]. Hence, the concept of posaconazole therapeutic drug monitoring should be explored at length in future clinical studies.To perform therapeutic drug monitoring, several quantification methods of posaconazole in serum by HPLC and by liquid chromatography–tandem mass spectrometry methods have been described in the literature [20-24]. As far as we know, only one microbiological method (bioassay) has been described for posaconazole monitoring [25].

IUPACNAME: 4-{4-[4-(4-(3R,5R)-5-(2,4-digluoropheny)-5-(1H-1,2,4-triazol-1-yl methyl)-tetraydrofuran-yl]methoxy}phenyl]piperazin-1-Yl]phenyl}-2-{1s,2s}-1-ethyl-2-hydroxy-propyl}-2,4-Dihydro-3H-1,2,4-triazol-3-one (FING. 1) {3-4},
Trade Name: Noxafil
Route of Administration: Oral dosage form
Bioavailability: 8% to 47%
Metabolism: uridine diphosphate(UDP)-glucuronyltransferase(UGT) enzyme pathway
Biological Half Life:15 to 35 hours
Molecular Formula:C37H42F2N8O4
Molecular Mass:700.8 g/mol
Pharmaceutical Dosage Form: Tablet, oral suspension.



AIM:

The work aims at review on comparison of developing newer analytical method for POSACONAZOLE In various dosage forms by RP-HPLC, and UPLC, UV Spectroscopy that are simple, accurate, precise, sensitive and reliable.

OBJECTIVE OF WORK:

Obtaining a conclusion with improved accuracy and precision techniques of analytical methods through comparison.

MATERIALS AND METHODS:

High Performance Liquid Chromatography:

HPLC stands for high performance liquid chromatography or high-pressure liquid chromatography. HPLC can separate, identify and quantify the compounds present in any sample which can be dissolved in liquid [26]. HPLC is primarily based on the use of a column that contains packing material (stationary phase), a pump that drives the mobile phase(s) across the column, and a detector that displays the molecule retention durations [27]. The are many types of HPLC, we will focus on only Normal phaseHPLC, Reversed-HPLC, size exclusion-HPLC. In normal phase-HPLC, a polar stationary phase and a non-polar mobile phase are used. The polar stationary phase interacted with and held the polar analyte [28].

- The HPLC method was performed by Grumurthy.Telugu using C18 Intertsil ODS-2V column and ACN: Water (90:10 v/v). It is detected at 262nm by PDA detector [29].
- The HPLC method was performed by E.Cendejas-buono using sunfire c18 column and acetonitrile:water(60:40).It is detected at 262 nm by UV spectrum[30]
- The HPLC method was performed by Dominic Storzinger using C8 column and phosphate buffer:acetonitrile:methonal(43:49:8 v/v/v).It is detected at 260 nm by UV detector[31]
- The HPLC method was performed by Cassia V.Garcia C 18 column using 0.09M ammonium phosphate buffer: acetonitrile: methyl chloride: triethyl amine (1060:940:10:1). It is detected at 262nm by UV detector [32]
- The HPLC method was performed by Peter H.Jang using ODS HYPERSIL column and ammonium acetate :water :acetonitrile(409:590:1 v/v/v).It is detected at 245nm(EX) and 380nm(Em) model 5440 FL detector.[33]
- The HPLC method was performed by S.Kathirvel using C8 Column and 0.09M ammonium phosphate buffer: acetonitrile: methyl chloride: triethyl amine (1060:940:10:1). It is detected at262 nm by UV detector .[34]

UV-VISIBLE SPECTROSCOPY:

In UV-visible spectroscopy, the amount of light absorbed at each wavelength of UV and visible region of electromagnetic spectrum is measured. This absorption spectroscopy uses electromagnetic radiations between 200 nm to 800 nm and is divided into the ultraviolet (UV, 200-400 nm) and visible (VIS, 400-800 nm) regions [35]. The principle of UV-Visible spectroscopy is based on the absorption of ultraviolet light or visible light by sample or chemical substance which results in the production of different spectra. Most commonly used solvents in UV spectroscopy are water, methanol, ethanol, ether, chloroform, carbon tetrachloride, cyclohexane and dichloroethane [36].

- The UV spectroscopy method for this drug was performed by Andressa da S.Bitencourt for this method methanol used as a solvent .It is detected at 260 nm by UV spectroscopy[37].

HIGH PERFORMANCE THIN LAYER CHROMATOGRAPHY:

High Performance Thin Layer Chromatography (HPTLC) is a sophisticated and automated form of the thin-layer chromatography (TLC) with better and advanced separation efficiency and detection limits. It is also known as High Pressure Thin Layer Chromatography/Planar chromatography or Flat-bed chromatography. It is a powerful analytical method equally suitable for qualitative and quantitative analytical tasks [38,39].

- The HPTLC method for this drug was performed by Vandana Jain , CAMAG twin through Glass chamber used for this analysis and Toluene: chloroform : ethanol (5:4:1 v/v/v) used as a mobile phase. It is detected at 265 nm by UV spectroscopy. [40]

ULTRA PERFORMANCE LIQUID CHROMATOGRAPHY:

UPLC is a modern technique which gives a new direction for liquid chromatography. UPLC refers to ultraperformance liquid chromatography, which enhance mainly in three areas: speed, resolution and sensitivity.Ultra performance liquid chromatography (UPLC) applicable for particle less than 2µm in diameter to acquire better resolution, speed, and sensitivity compared with high-performance liquid chromatography (HPLC). The unique feature of UPLC analysis is interconnected skeletons and interconnected flow paths (through-pores) which are found in monolithic columns make UPLC technique different from HPLC. In UPLC chromatogram it is found that better resolution and separation are found as compared to HPLC along with perform more sensitive analysis, reduce consumption of solvent and has high speed of analysis [41,42].

- The UPLC method for this drug was performed by vadlamanudurga prasad1* ,UPLC-BEG shield C18 column is used and water: acetonitrile (40:60) used as a mobile phase. It is detected at 210nm by UV detector.[43]

Table 1: High Performance Liquid Chromatography

S.NO	AUTHOUR	COLUMN	MOBILE PHASE	ELUTION METHOD	TEMP. (˚C)	RT	DETECTION VALUE
1.	Grumurthy. Telugu	C18 intertsil ODS-2V column (250*4.6,5µm)	ACN:WATER (90:10 v/v)	Isocratic elution method	30	3.98 min	PDA Dtector 262nm
2.	E.Cendejas-Bueno	Sunfire C18 (5µm, 4.6× 150mm	Acetonitrile:water (60:40)	Isocratic elution method	25	6.50±0.1 Min	UV Spectrum 262 nm
3.	Domincstorzinger	C8 column(150×4.6mm, 5µm)	Phosphate buffer: Acetonitrile: Methanol (43:49:8 v/v/v)	Gradient elution method	45	5.1 min	UV Spectrum 260 nm
4.	Cassia V.Garcia	C18 column	0.09M ammonium Phosphate buffer: Acetonitrile: Methyl chloride: Triethyl amine(1060:940:10:1)	Isocratic elution method	40	8.5 min	UV Dtector 262nm

5.	Peter H.Jang	ODS HYPERSIL,(5µM,250× 4.6 mm)	Ammonium acetate: Water: acetonitrile (409:590:1v/v/v)	Isocratic elution method	45	~6.4 min	Model 5440 FL detector 245nm(Ex) and 380nm(Em)
6.	S. Kathir vel	C 18 column	0.09M Ammonium phosphate buffer : acetonitrile : methyl chloride : triethlamine (1060 : 940 : 10:1)	Gradient elution method	25	26.31 min	UV Detector 262nm.
7.	Ana cristina souse gramozavil arinno Santana	C8 column (250mm×4.6mm;5µm Particle size)	Methanol : acetate buffer (ph3.5) (71:29)	Isocratic elution method	25	3.6 and 7.6 min	UV Detector 260nm.

Table 2: Uv-Visible Spectroscopy

S.NO.	AUTHOR	DRUG	SOLVENT	ABSORBAMCE	QUARTS CELL
1.	AndressadaS.Bitencourt	posaconazole	Methanol	260nm	1 cm

TABLE 3: HIGH PERFORMANCE THIN LAYER CHROMATOGRAPHY.

S.NO.	AUTHOR	COLUMN	MOBILE PHASE	ABSORBANCE	RF
1.	Vandana Jain	CAMAG twin through Glass chamber	Toluene: chloroform: ethanol (5:4:1 v/v/v)	265nm	0.331

Table 4: Ultra Performance Liquid Chromatography

S.NO.	AUTHOR	COLUMN	MOBILE PHASE	ELUTION METHOD	TEMP.	RT	DETECTION VALUE
1.	Vadlamanu DurgaPrasad 1*	UPLC-BEG shield C18 column (100mm length,2.1mm diameter,1.7µm particle size)	Water: acetonitrile (40:60)	Gradient elution method	18C	6.3 min	UV detector 210nm.

SUMMARY AND CONCLUSION:

A current review described the optimized validated method of RP-HPLC was developed using Mobile phase composed of acetonitrile and water (60:40) which all validation Parameters were found to be highly satisfactory, including linearity, selectivity, precision, accuracy, Robustness and limit of detection and quantification appropriate. This method uses lower amounts of organic solvent, does not Use buffer solution in mobile phase and produces lower level of waste. Hence it can be inferred that the Developed method is useful in routine laboratory analysis. Posaconazole, sold under the brand name Noxafil among others, is a triazole antifungal medication.

Determination of Posaconazole UV absorbance had been optimized by use of Methanol as solvent for effective absorbance and the method can be easily applied in routineQuality control laboratories.In this review article, we discussed about the analytical methods for estimation of posaconazolein different pharmaceutical dosage form. The proposed technique accomplished for posaconazole are HPLC,UV,HPTLC,UPLC. The Above data are helpful for further research studies in analysis of posaconazole.

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