Review Article

A Review on Analytical Methods for the Determination of Palonosetron in Pharmaceutical Formulation

N. Pooja Singh*, V. Mohan Goud, JVC Sharma, P. Sirisha, CH. Praveena Devi
Department of Pharmaceutical analysis, Joginpally B.R Pharmacy College, Yenkapally (V), Moinabad, R.R Dist., Telangana, India.
***Corresponding author's E-mail:** mohanvanga@yahoo.com

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ABSTRACT

Palonosetron is a second-generation 5-HT3 receptor antagonist with an extended half-life of approximately 40 hours and high binding affinity for the 5-HT3 receptor that is markedly different from other 5-HT3 receptor antagonists. Phase III trials demonstrate that a single dose of palonosetron compared with traditional 5-HT3 receptor antagonists is more effective in preventing chemotherapy-induced nausea and vomiting during the first 24 hours following chemotherapy, and also exhibits prolonged efficacy to provide significantly better protection from nausea and vomiting in the delayed and overall phases. This review article accentuates various analytical methods viz. HPLC, HPTLC, spectrophotometric, electrochemical, capillary electrophoresis and LC–MS for the estimation of palonosetron in pharmaceutical formulations and in biological matrices.

Keywords: Palonosetron, antiemetic drug, analytical methods.

INTRODUCTION

Palonosetron, chemically known as (3aS)-2-[(3S)-1-Azabicyclo [2.2.2] oct-3-yl]-2, 3, 3a, 4, 5, 6-hexahydro-1Hbenz [de]isoquinolin-1-one, is a specific and selective serotonin 5-HT3 antagonist with antinauseant and antiemetic activity. It is prescribed for the prevention of nausea and vomiting associated with cancer chemotherapy and postoperative nausea and vomiting. 3-5 Chemotherapeutic agents cause the release of serotonin, which then stimulates medullary vomiting center and 5-HT3 receptors and thus initiating the vomiting reflex, causing nausea and vomiting. The antiemetic activity of palonosetron is brought about by the inhibition of 5-HT_3 receptors present both in the medullary chemoreceptor zone and gastrointestinal tract[1-5].

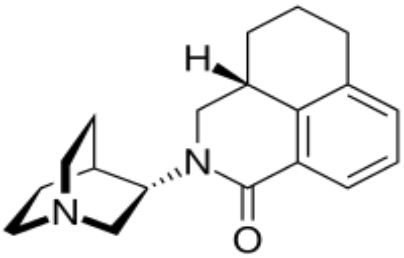

Figure 1: Structure of palonosetron

Mechanism of Action

Palonosetron is a 5-HT_3 antagonist, commonly known as a *setron*. These drugs act by blocking serotonin from binding to the 5-HT_3 receptor.

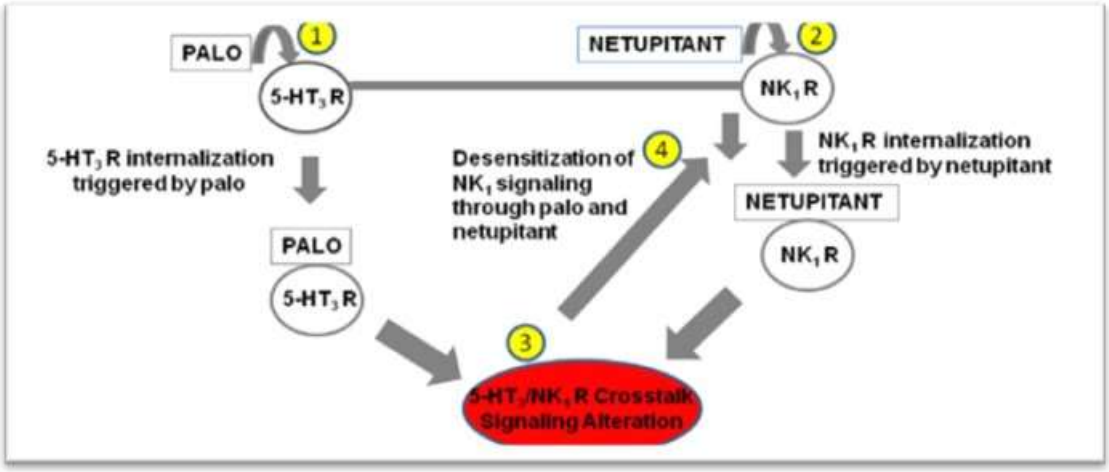

Figure 2: Mechanism of action of Palonosetron

Uses:

- This medication is used to prevent nausea and vomiting caused by cancer drug treatment (chemotherapy).
- It is also used to prevent nausea and vomiting after surgery.
- Palonosetron works by blocking one of the body's natural substances (serotonin) that causes vomiting.

Analytical Method

A. Compendial Method:

Monograph of palonosetron is not official in any pharmacopoeia.

B. Reported Method:

Chromatography Method:

Most of the reported methods for determination of palonosetron in pharmaceutical formulations are HPLC method. The HPTLC and GC methods are also used widely to determine the assay of palonosetron. The summary of reported methods is tabulated below.

Table 1: Summary of chromatography method of palonosetron

Title	Method	Mobile Phase	Stationary Phase	Wave Length	Retention Time/ Concentrations
Development of the chromatographic method for the estimation of palonosetron in palonosetron hydrochloride injection[6]	HPLC	Water: Acetonitrile: Trifluoro acetic acid (700:300:0.64)	RP Kromasil C8, (100*4.6mm), 5µ Make Akzonobel Column	210nm	3.6min
Novel RP-HPLC method development for the estimation of palonosetron hydrochloride in bulk and softule dosage forms[7]	RP-HPLC	Buffer (0.025M sodium di hydrogen orthophosphate pH adjusted 6.9 with TEA) : acetonitrile (65:35 %v/v)	ODSUG-5 column (250×4.6mm)	240nm	0.03µg/ml to 2µg/ml
Chemometrics assisted and RP-HPLC methods for quantification of netupitant and palonosetron hydrochloride by QbD approach: development and validation[8]	RP-HPLC	mixture of 10 mM sodium acetate buffer, adjusted to pH 3.5 using Glacial acetic acid: acetonitrile: methanol in ratio of (10:50:40 v/v/v)	Synchronies C-18 (250mm	240nm	3.55 min
Enantio separation of palonosetron hydrochloride and its related enantiomeric impurities by computer simulation and validation[9]	HPLC	n-hexane: ethanol: methanol: heptafluoro butyric acid: diethyl amine (70:15:15:0.05:0.1, v/v	Chiralcel-OD 250mm × 4.6mm	240nm	-
Direct enantiomeric separation of palonosetron hydrochloride by chiral HPLC[10]	HPLC	n-hexane, absolute alcohol and diethylamine (60:40:0.05)	CHIRALPAK AD-H(250 mm×4.6 mm, 5 µm) column	256nm	0.5 to 50 µg·mL
Liquid chromatography-electrospray quadrupole linear ion trap mass spectrometry method for the quantitation of palonosetron in human plasma and urine: application to a pharmacokinetic study[11]	LC-EQ/MS	methanol-1mM ammonium formate in water (containing 0.1% formic acid, v/v, pH=2.8	Zorbax Eclipse TC-C(18) column		0.01-5.00 ng/mL for plasma and 0.10-30.00 ng/mL for urine
Development and validation of a rapid LC-MS/MS method for simultaneous determination of netupitant and palonosetron in human plasma and its application to a pharmacokinetic study[12]	LC-MS/MS	acetonitrile and 10mM ammonium acetate buffer (pH 9.0) (89:11, v/v)	Phenomenex C18 column (50mm×2.0mm, 3µm)		0.02-10ng/Ml conc in plasma
A novel validated RP-HPLC-DAD method for the simultaneous estimation of netupitant and palonosetron in bulk and pharmaceutical dosage form with forced degradation studies[13]	RP-HPLC-DAD	0.01M Ammonium acetate buffer (pH adjusted to 3.5 with orthophosphoric acid) and Acetonitrile (65:35, v/v	Kromasil C18 column (250mm×4.6m, 5mm particle size), Waters Alliance e2695		99.73% to 100.03%

Table 2: Summary of UV Spectroscopic method of palonosetron

Drug	Method	Wavelength	Conc. Range	Recovery
Estimation of palonosetron hydrochloride (a 5-HT_3 antagonist) in pharmaceutical dosage form by U.V spectrophotometric method[14]	UV method	265 nm	7.5-25 µg/mL	99.3%

DISCUSSION

The most widely used method for determination of palonosetron was HPLC method. Some various chromatographic conditions are presented in table 1&2.

CONCLUSION

The Sensitivity, Specificity, and Better Separation Efficacy Enable HPLC to be used Frequently for Qualitative and Quantitative Determination of palonosetron. The presented Information is Useful for the Future Study for Researcher Involved in Formulation Development and quality control of palonosetron.

The optical isomers of palonosetron hydrochloride were resolved directly on AD-H chiral column. The developed method was simple and accurate for the chiral purity control of palonosetron hydrochloride.

A simple and sensitive stability indicating RP-HPLC method was explored for the determination of palonosetron in pure form and in commercially available tablet dosage forms. The method was validated as per ICH guidelines.

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