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REVIEW ARTICLE

Analytical Methods for Determination of Ondansetron hydrochloride and Pantoprazole

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1 | INTRODUCTION

Ondansetron hydrochloride (OND) is a 5-HT3 antagonist (5-HT3-receptor antagonist) with antiemetic activity.

It is used in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy. It is also used for the prevention and treatment of postoperative nausea and vomiting [1, 2]. Peak plasma concentrations of OND occur about 1.5 hours after an oral dose of 8 mg, and about 6 hours after a rectal dose [1]. OND is extensively distributed in the body; about 70 to 75% of the drug in plasma is protein bound. It is metabolized in the liver through multiple enzymatic pathways; OND is a substrate for cytochrome P450 isoenzymes, primarily CYP3A4, but also CYP1A2 and CYP2D6. Less than 5% of a dose is excreted unchanged in the urine [1].

Pantoprazole (PAN) is a proton pump inhibitor. It inhibits secretion of gastric acid by irreversibly blocking the enzyme system of hydrogen/ potassium adenosine triphosphatase (H+/K+ ATPase), the 'proton pump' of the gastric parietal cell. It is used in conditions where inhibition of gastric acid secretion may be beneficial, including aspiration syndromes, dyspepsia,gastro-esophageal

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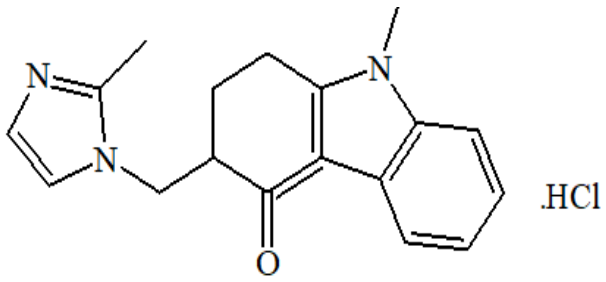
reflux disease, peptic ulcer disease, and the Zollinger-Ellison syndrome [1, 2]. After an oral dose Peak plasma-PAN concentrations are achieved about 2 to 2.5 hours. The oral bioavailability is about 77% with the enteric-coated tablet formulation, and does not vary after single or multiple doses. PAN is 98% bound to plasma proteins. It is extensively metabolized in the liver, primarily by the cytochrome P450, to desmethyl pantoprazole. Metabolites are excreted mainly (about 80%) in the urine, with the remainder being excreted in bile. The terminal elimination half-life is about 1 hour [1].

In this literature review, we will introduce most of up-to-date reported methods that have been developed for determination of OND and PAN in their pure form, combined form with other drugs, combined form with degradation products, and in biological samples.

1. Ondansetron hydrochloride



Chemical structure of OND

1.1. Chemical characters:

1.1.1. IUPAC name: 9-Methyl-3-(2-methyl-imidazol-1-ylmethyl)-1, 2, 3, 9-tetrahydro-carbazol-4-one hydrochloride

1.1.2. Molecular formula: C18H19N3O, HCL, 2H2O

1.1.3. Molecular weight: 356.9

1.2. Physical charecters:

1.2.1. Physical form: A white to off-white powder.

1.2.2. Melting point: 231C°.

1.2.3. Solubility: Sparingly soluble in water and in alcohol; very slightly soluble in acetone, in chloroform, and in ethyl acetate; slightly soluble in dichloromethane and in isopropyl alcohol; soluble in methyl alcohol [1].

1.2.4. Storage: Store in airtight containers at a temperature of 25C°, excursions permitted between 15 C° and 30 C°. Protect from light[1].

1.3. Review of analytical methods: Various techniques were used for the analysis of OND in pure forms, in their pharmaceutical formulations and in biological fluids. The available reported methods in the literature can be summarized as follows:

1.3.1. Spectroscopic methods:

1.3.1.1. Spectrophotometric methods:

Drugs	Method or reagent	λ_{max}	Ref
OND and MTC	First drivative spectroscopy	266 nm OND and 253 nm MTC	[3]
OND and PAN	Ratio drivative spectrophotometry	271.80 nm OND and 300.20 nm PAN	[4]
OND	Second drivative spectroscopy	248-254nm	[5]

1.3.1.2. Spectrofluorometric methods:

Drug	Fluorogenic reagent (method)	λex (nm)	λem(nm)	Ref
OND	Triton X 100 micellar system	317 nm	354 nm	[6]
OND	pararosaniline hydrochloride in dioxane	439 nm	493 nm	[7]

1.3.2. Chromatographic methods:

1.3.2.1. HPLC

Matrix	Column	Mobile phase	system	Ref.
Tablet	a Phenomenex C_{18} column	ACN: 50 mM KH_2PO_4 buffer: triethylamine (25 : 74 : 1; v/v; pH 4.0)	HPLC- DAD at 310 nm	[8]
Tablet	a Phenomenex C_{18} column	50 mM KH_2PO_4 (pH 6): ACN (60:40 v/v)	HPLC- UV at 222 nm	[9]
Tablet	a Waters Xterra C_{18}	A gradient elution with 10 mM ammonium formate (pH 3.0):methanol	HPLC – MS/MS	[10]
Tablet	Chiralpak AS-3R	methanol/water/diethylamine (85/15/0.1% v/v/v)	HPLC- UV at 222 nm	[11]
Plasma	a Agilent Zorbax Eclipse® C_{18}	ACN: water (50:50, v/v)	HPLC – MS/MS	[12]
Tablet	Thermo Hypersil BDS C_8	potassium dihydrogen orthophosphate buffer: ACN (pH 3.0) 60:40 v/v	HPLC- UV at 258 nm	[13]
Tablet	A kromasil C_8	phosphate buffer and methanol (50:50)	HPLC- UV at 250 nm	[14]

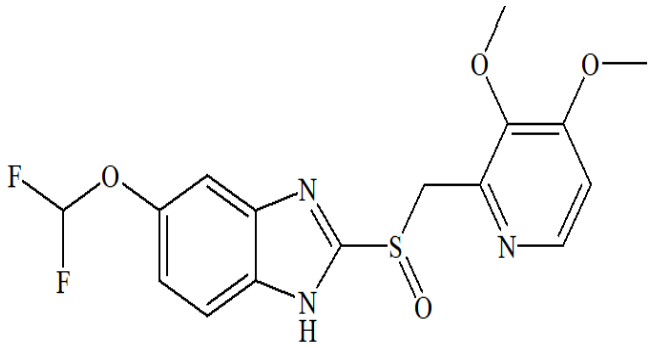
1.3.2.2. HPTLC

Matrix	Column	Mobile phase	system	Ref.
Tablet	silica-gel 60 F_{254} plate	Chloroform: ethyl acetate: methanol: ammonia (9:5:4:0.1 v/v).	UV 254 nm	[15]
Tablet	silica-gel 60 F_{254} plate	Methanol. Ethyl acetate – methanol – ammonia, (11:3.5:0.2, v/v)	UV 310 nm	[16]
Tablet	silica-gel 60 F_{254} plate	dichloromethane: methanol (9:1 v/v)	UV 309 nm, 294 nm	[17]
Tablet	silica-gel 60 F_{254} plate	Chloroform: methanol: ethyl acetate (7:2:1, v/v).	UV 302 nm	[18]

1.3.3. Other methods

Potentiometric [19].

2. Pantoprazole (PAN)



Chemical structure of PAN

2.1. Chemical characters:

10.1.1. IUPAC name: 5-Difluoromethoxybenzimidazol-2-yl 3, 4-dimethoxy-2-pyridylmethylsulphoxide

2.1.2. Molecular formula: C16H15F2N3O4S.

2.1.3. Molecular weight: 383.4.

2.2. Physical characters:

2.2.1. Physical form: A white to off white crystalline powder and is racemic.

2.2.2. Melting point: 124 C°.

2.2.3. Solubility: PAN is freely soluble in water, soluble in DMSO and methanol, very slightly Soluble in phosphate buffer pH 7.4, and practically insoluble in n-hexane [1].

2.2.4. Storage: Store in airtight containers at a temperature of 25C°, Protect from light [1].

2.3. Review of analytical methods:

Various techniques were used for the analysis of PAN in pure forms, in their pharmaceutical formulations and in biological fluids. The available reported methods in the literature can be summarized as follows:

2.3.1. Spectroscopic methods:

2.3.1.1.Spectrophotometric methods:

Drugs	Method or reagent	λ_{max}	Ref
PAN	bromothymol blue in aqueous acidic medium	428 nm	[20]
OND and PAN	Ratio drivative spectrophotometry	271.80 nm OND and 300.20 nm PAN	[4]
PAN	$FeCl_3$ and 1,10 phenanthroline 2, 2´-bipyridyl	510 nm 520 nm	[21]
PAN	spectral changes upon changing the pH	296 nm 0.1 HCl and 319 nm 0.1N NaOH	[22]
PAN and MS	first simultaneous equation Q value analysis method	274 nm (MS), 288.2 nm (PAN) 274 nm (MS), 302 nm (PAN)	[23]
PAN and ITP	First drivative spectrophotometry	238.5 (PAN) and 288 nm (ITP)	[24]

2.3.1.2.Spectrofluorometric methods:

Drug	Fluorogenic reagent (method)	λex (nm)	λem(nm)	Ref
PAN	SDS	306 nm	345 nm	[25]

2.3.2. Chromatographic methods:

2.3.2.1.HPLC

Matrix	Column	Mobile phase	system	Ref
Tablet	C_{18} column	ACN: water (90:10, v/v)	HPLC – MS/MS	[26]
Tablet	Inertsil C_{18}	ACN: phosphate buffer (60:40, v/v, pH 7.0)	HPLC- UV at 230 nm	[27]
Tablet	a Phenomenex C_{18}	phosphate buffer: ACN (55:45 v/v, pH 5.0)	HPLC- UV at 289 nm	[28]
Tablet	Tracer excel ODS C_{18}	phosphate buffer (10 mM)/ACN (53/47, v/v, pH 7.3)	HPLC- UV at 290 nm	[29]
plasma	an ovomucoid column	methanol: CAN: 10 mM ammonium formate (pH 7) (10.4:2.6:87, v/v/v)	HPLC – MS/MS	[30]
Tablet	a Hypersil ODS column	A gradient elution with 0.01 M phosphate buffer of pH 7 and ACN	HPLC- UV at 290 nm	[31]
Tablet	a Zorbax Eclipse XDB C18	Agradient elution with Acetate buffer (pH 4.5): ACN.	HPLC- UV at 290 nm	[32]
Tablet	A phenomenox C_{18}	30 mM ammonium sulphate buffer : ACN (50:50, v/v)	HPLC- UV at 275 nm	[23]
Plasma	an Lichrospher C_{18} column	methanol: water (60:40, v/v)	HPLC – MS/MS	[33]
Tablet	a Nucleodur C_8 column	0.1 M ammonium acetate solution : methanol (42:58, v/v)	HPLC- UV at 280 nm	[34]

2.3.2.2.HPTLC

Matrix	Column	Mobile phase	system	Ref.
Tablet	silica-gel 60 F_{254} plate	Chloroform: 2-propanol: 25% ammonia: ACN (10.8:1.2:0.3: 4 v/v)	UV at 282 nm	[35]
Tablet	silica-gel 60 F_{254} plate	Methanol: water: ammonium acetate, (4:1:0.5 v/v).	UV at 290 nm	[36]
Tablet	silica-gel 60 F_{254} plate	ethyl acetate: methanol (9:1v/v)	UV at 278 nm	[37]
Tablet	silica-gel 60 F_{254} plate	Methylene chloride: ethyl acetate: methanol: ammonia (25%) (12:2:0.8:0.2, v/v)	UV at 289 nm	[38]
Tablet, vials, and plasma	silica-gel 60 F_{254} plate	chloroform–methanol–ethyl acetate (6:2:2 v/v).	UV at 302 nm	[39]

2.3.3. Other methods:

Capillary electrophoresis [40], voltametry [41], potentiometry [42, 43].

Conclusion:

This literature review represents an up to date survey about all reported methods that have been developed for determination of ondansetron hydrochloride and pantoprazole in their pure form, combined form with other drugs, combined form with degradation products, and in biological samples such as liquid chromatography, spectrophotometry, spectroflourimetry, electrochemistry, etc...

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