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Review Article

MINI REVIEW: INSIGHTS ON INSTRUMENTAL ANALYSIS OF OMBITASVIR, PARITAPREVIR AND RITONAVIR

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ABSTRACT

In this literature review, we will introduce most of the up-to-date reported methods that have been developed for the determination of Ombitasvir, Paritaprevir and Ritonavir in their pure form, combined form with other drugs combined form with degradation products, and in biological samples. Most of reported methods includes spectrophotometric and chromatographic methods specially HPLC and HPTLC.

Keywords: HCV, Ombitasvir, Paritaprevir, Ritonavir, Degradation products, Biological samples

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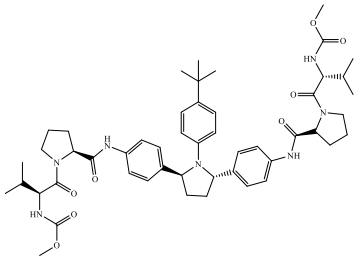
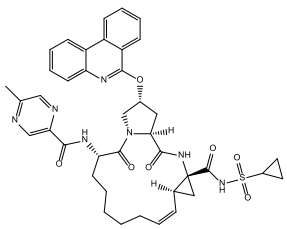
INTRODUCTION

Infection due to hepatitis C virus (HCV) is a leading cause for severe chronic liver disease, which can result in progressive liver damage such as cirrhosis and hepatocellular carcinoma. HCV is a single-stranded RNA virus that is categorized into nine distinct genotypes, with genotype 1 being the most common in the United States and affecting 72% of all chronic HCV patients [1]. Ombitasvir **(**OMB) is an inhibitor of NS5A, a protein essential for viral replication and virion assembly. The barrier for the development of resistance to NS5A inhibitors is lower than that of NS5B inhibitors, another class of DAAD [2]. In addition, the combination of OMB, the ritonavir-boosted PI paritaprevir, and the non-nucleoside polymerase inhibitor dasabuvir with or without ribavirin was approved for patients with HCV genotype 1 [3]. Treatment with direct acting antivirals such as OMB is associated with very minimal side effects, with the most common being headache and fatigue; Lack of significant side effects and short duration of therapy is a considerable advantage over older interferon-based regimens, which were limited by infusion site reactions, reduced blood count, and neuropsychiatric effects [4]. Paritaprevir (PAR) prevents viral replication by inhibiting the NS3/4A serine protease of HCV. Following viral replication of HCV genetic material and translation into a single polypeptide, Nonstructural Protein 3 and its activating cofactor Nonstructural Protein 4A are responsible for cleaving genetic material into the following structural and nonstructural proteins required for assembly into mature virus: NS3, NS4A, NS4B, NS5A, and NS5B [5].

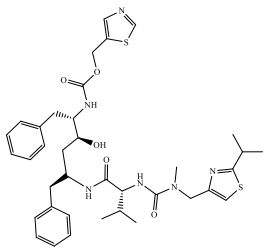
As such, in this literature review, we will introduce most of the up-to-date reported methods that have been developed for the determination of OMB, PAR and RIT in different matrices.



OMB



PAR



RIT

Fig. 1: Chemical structures of ombitasvir (OMB), paritaprevir (PAR), and ritonavir (RIT), Ombitasvir (OMB)

Review of analytical methods

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

Table 1: Chromatographic methods for determination of OMB

Matrix	Column	Mobile phase	System	Ref.
Plasma	UPLC BEH C_{18}	Ammonium acetate 5 mmol (pH 9.5): ACN (gradient elution).	UHPLC–MS/MS	[6]
Tablet	Hypersil BDS C_{18} column	0.01N % mmol phosphate buffer (pH 3) and acetonitrile (35:65, v/v).	HPLC-DAD 254 nm	[7]
plasma	Intersil ODS C_{18}	20% ACN: 20% Methanol, 60%1 mmol $NH_4H_2PO_4$ Buffer (PH 6.5).	HPLC-UV 230 nm	[8]
Liver	Waters Acquity BEH C_{18} column	A gradient elution with 0.1% FA in water and ACN.	UHPLC–MS/MS	[9]

Other methods

A novel micellar electrokinetic capillary chromatographic (MEKC) method was developed for the simultaneous determination of OMB, PAR, RIT and dasabuvir (DAS). The technique was based on the separation of all of the selected drugs in a deactivated fused silica capillary with a background electrolyte solution (BGE) composed of 25 mM phosphate buffer with 30 mM sodium dodecyl sulphate (SDS) (the pH of the aqueous phase was adjusted to 8) mixed with ethanol in a ratio of 65:35 (v/v). The capillary and sample temperature was maintained at 24 °C, and the detection was performed at 239 nm. The electrophoresis was performed by applying a high voltage (30 kV) to the capillary [10].

Paritaprevir (PAR)

Review of analytical methods

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

Table 2: Chromatographic methods for determination of PAR

Matrix	Column	Mobile phase	System	Ref.
Plasma	UPLC BEH C_{18}	Ammonium acetate 5 mmol (pH 9.5) and acetonitrile (gradient elution).	UHPLC–MS/MS	[6]
Tablet	Hypersil BDS C_{18} column	0.01N % mmol phosphate buffer (pH 3) and acetonitrile (35:65, v/v).	HPLC-DAD 254 nm	[7]
Rat liver	Acquity BEH C_{18}	A gradient elution with (95:5:0.1v/v/v), water: acetonitrile: formic acid and (acetonitrile containing 0.1% formic acid).	UPLC–MS/MS	[11]
plasma	Intersil ODS C_{18}	20% Acetonitrile, 20% Methanol, 60%1 mmol $NH_4H_2PO_4$ Buffer (PH 6.5).	HPLC-UV 230 nm	[8]
Liver	Waters Acquity BEH C_{18}	A gradient elution with 0.1% FA in water and ACN.	UHPLC–MS/MS	[9]

Ritonavir (RIT)

Review of analytical methods

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

Table 3: Spectrophotometric methods for determination of RIT

Drugs	Method or reagent	λ_{max}	Ref
RIT and Atazanavir (ATV)	Ratio spectra derivative method, Area under curve method.	280.01 nm(ATV), 286.12 nm(RIT), 246.97-252.03 nm (ATV): 240.78-244.16 nm(RIT)	[12]
RIT	First-order derivative method, under curve method.	253.2 nm (RIT) 237-242 nm (RIT)	[13]
RIT and lopinavir	First-order derivative method.	246.70 nm (RIT) and 278.10 nm (lipinavir)	[14]
Sofosbuvir, Lamivudine, and RIT	Silver nanoparticles synthesis.	421 nm for Sofosbuvir and RIT and at 425 nm for Lamivudine	[15]

Chromatographic methods for determination of RIT

Table 4: HPLC methods for determination of RIT

Matrix	Column	Mobile phase	System	Ref.
Plasma	UPLC BEH C_{18}	Ammonium acetate 5 mmol (pH 9.5) and acetonitrile (gradient elution).	UHPLC–MS/MS	[6]
Tablet	Hypersil BDS C_{18} column	0.01N % mmol phosphate buffer (pH 3) and acetonitrile (35:65, v/v).	HPLC-DAD 254 nm	[7]
Plasma	Aquasil® C_{18}	A gradiant elution with 0.05% formic acid in either water or methanol.	HPLC–MS/MS	[16]
Rat liver	Acquity BEH C_{18}	A gradient elution with (95:5:0.1v/v/v),water: acetonitrile: formic acid and (acetonitrile containing 0.1% formic acid).	UPLC–MS/MS	[11]
plasma	Intersil ODS C_{18}	20% Acetonitrile, 20% Methanol, 60%1 mmol $NH_4H_2PO_4$ Buffer (PH 6.5).	HPLC-UV 230 nm	[8]

Liver	Waters Acquity BEH C_{18} column	A gradient elution with 0.1% FA in water and ACN.	UHPLC–MS/MS	[9]
Plasma	OmniSpher C_{18} column	A gradient elution with ACN: 50 mmol/l potassium phosphate (pH 5.75).	HPLC-UV at 215 nm	[17]
Plasma	C_{18} column	ACN: 50 mmol phosphate buffer (pH 5.63) (40:60, v/v).	HPLC-UV at 215 nm	[18]
Plasma	C_{18} Column	Acetonitrile plus distilled water within25 mmol sodium acetate and 25 mmol hexane-1-sulfonic acid and adjusted to pH 6.0 (40.5:59.5, v/v).	HPLC-UV at 239 nm	[19]
Plasma	NovaPak C_{18} column	ACN, methanol and tetramethylammonium perchlorate in dilute aqueous TFA (45: 5: 50 v/v/v).	HPLC-UV at 205 nm	[20]
Plasma	C_{18} column	ACN, methanol and 0.01 M tetramethylammonium perchlorate in 0.1% aqueous TFA (40: 5: 55 v/v/v).	HPLC-UV at 205 nm	[21]
Plasma	Inertsil ODS column	ACN: 5 mmol ammonium acetate buffer (pH 3.5) (80: 20 v/v).	HPLC–MS/MS	[22]
Tablet	phenomenex-Luna C_{18}	Acetonitrile: 0.5% TEA (pH 5) (67:33 %, v/v).	HPLC-DAD at 205 nm	[23]
Plasma	Waters UPLC C_{18} column	10 mmol AF (pH 4.0) adjusted with FA: methanol (10:90 v/v).	UPLC–MS/MS	[24]
Tablet	A symmetry C_{18}	Phosphate buffer (pH 4): ACN (50:50).	HPLC-UV at 239 nm	[25]
Plasma	Acquity UPLC C_{18}	0.1% FA: methanol (40:60, v/v).	UPLC–MS/MS	[26]
Tablet	a Hypersil BDS-C_{18}	Phosphate buffer (pH3.4): ACN (50:50, v/v).	HPLC-UV at 250 nm	[27]
Tablet	Waters UPLC C_{18} column	A gradient elution with 0.01 M potassium dihydrogen phosphate (pH 3.5): ACN	UPLC–MS/MS	[28]
Tablet	a Waters Symmetry C_{18}	ACN: 2 mmol ammonium acetate containing 0.01% FA (v/v) (70:30 v/v).	HPLC–MS/MS	[29]
Tablet	An Agilent TC-C_{18}	Methanol: ACN: water in the (35:41.5:23.5 v/v/v).	HPLC-UV at 222 nm	[30]
Tablet	a Thermo Hypersil C_{18}	0.05M KH_2PO_4 buffer (pH3.0): ACN (45:55 v/v).	HPLC-UV at 254 nm	[31]
Tablet	An Agilent TC-C_{18}	ACN: 0.05 M phosphoric acid (55: 45, v/v).	HPLC-UV at 240 nm	[32]
Tablet	a C_{18} column	0.06 M SDS: 1-pentanol (pH 7) (97.5: 2.5 v/v).	HPLC-UV at 214 nm	[33]
Tablet	Symmetry C_{18}	phosphate buffer (pH 4.0): ACN (45:55 % v/v).	HPLC-UV at 237 nm	[34]
tablet	RP-C_{18} Kinetix core-shell column	(0.15 M sodium lauryl sulfate and 0.01 M sodium dihydrogen phosphate, pH 6.2) and ethanol (56:44).	HPLC-Uv at 254	[35]

Table 5: HPTLC methods for determination of RIT

Matrix	Column	Mobile phase	System	Ref.
Tablet, vials, and plasma	silica-gel 60 F_{254} plate	Chloroform–methanol–ethyl acetate (6:2:2 v/v).	UV-302 nm	[35]
Tablet	silica-gel 60 F_{254} plate	Ethyl acetate: ethanol: toluene: diethylamine (7:2.0:0.5:0.5, v/v/v/v).	UV-266 nm	[36]
Tablet	silica-gel 60 F_{254} plate	Ethyl acetate: Toluene: methanol (7.5: 2: 0.5 v/v/v).	UV-234 nm	[37]
Tablet	silica-gel 60 F_{254} plate	Chloroform: ethyl acetate: acetone (5:2:3, v/v/v).	UV-244 nm	[38]

CONCLUSION

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

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Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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