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Review Article

PIBRENTASVIR – A REVIEW

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ABSTRACT

Objective: The main purpose of the study to review the drug Pibrentasvir will come under Anti-viral drugs. It is a NS5A inhibitor formation of HCV particles. It will be available as Brand name – Mavyret (Combination of Pibrentasvir & Glecaprevir). It is indicated for the treatment of adult patients with chronic Hepatitis C virus (HCV). Mavyret is contraindicated to the Patients with severe hepatic impairment (Child-Pugh C) and to the drugs like Rifampin or Atazanavir. The common adverse effects are Headache and fatigue.**Methods:** In the present work, the developed method Chromatogram was run through Kinetics Phenyl Hexyl C8 (150×4.6) mm, 2.6µm. Mobile phase contains a mixture of Buffer: ACN (70:30) was pumped through a flow rate of 1.0mL/min. Buffer used in this method was 0.01M of Potassium Di hydrogen phosphate in 1L of Milli Q water, pH to 2.8 with diluted OPA. Temperature of column and sample was maintained at 300C & 250C respectively.**Results:** Optimized wavelength selected was 252nm.Retention time of pibrentasvir was found to be 38.454 min. % RSD of the pibrentasvir was found to be 0.9999%. Recovery was found to be 99.73 to 101.15 %.**Conclusion:** Pibrentasvir is an anti-viral agent that is useful in the treatment of hepatitis C. It is associated with the fewer adverse effects compared to others. It is an oral drug with normal biological half-life. Therefore, the pibrentasvir is an ideal drug for 'Hepatitis C'. % RSD of the pibrentasvir was found to be 0.9999%. Recovery was found to be 99.73 to 101.15%. LOD & LOQ values obtained from regression equations were 0.8557 & 2.593µg/mL. Regression equation of pibrentasvir is Y=31256.x + 8728.

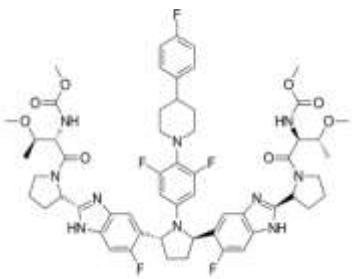
Keywords: Pibrentasvir, Anti-viral drugs, NS5A, HCV.

INTRODUCTION

Pibrentasvir is an NS5A inhibitor antiviral agent. It is approved for use with a combination like glecaprevir such as glecaprevir/Pibrentasvir with brand name Mavyret for treating hepatitis C and manufactured by Abbvie. Drug contains glecaprevir as 100 mg & Pibrentasvir as 40 mg. This fixed-dose combination therapy was FDA-approved in August 2017 to treat adults with chronic hepatitis C virus (HCV) genotypes 1-6 without cirrhosis (liver disease) or with mild cirrhosis, including patients with moderate to severe kidney disease and those who are on dialysis. Pibrentasvir is a direct acting antiviral agent and Hepatitis C virus (HCV) NS5A inhibitor that targets the viral RNA replication and viron assembly. Pibrentasvir is a useful therapy for patients who experienced therapeutic failure from other NS5A inhibitors. Hepatitis C viral infection often leads to decreased liver function and subsequent liver failure, causing a significantly negative impact on the patients' quality of life. The ultimate goal of the combination treatment is to achieve sustained virologic response (SVR) and cure the patients from the infection [1].

PHYSICOCHEMICAL PROPERTIES & ANALYSIS [2, 3]

Table 1: Physicochemical properties.

IUPAC	Methyl N-[(2S,3R)-¹-[(2S)-2-[6-[(2R,5R)-1-[3,5-difluoro-4-[4-(4 fluorophenyl)piperidin-1-yl]phenyl]-5-[6-fluoro-2-[(2S)-1-[(2S,3R)-3-methoxy-2-(methoxy carbonylamino) butanoyl]pyrrolidin-2-yl]-3H-benzimidazol-5-yl]pyrrolidin-2-yl]-5-fluoro-1H-benzimidazol-2-yl]pyrrolidin-1-yl]-3-methoxy-1-oxobutan-2-yl]carbamate
Molecular Wt	1113.201 gm/mol
Exact mass	1112.491 g/mol
Molar mass	1113.201 g/mol
Water solubility	<0.1 mg/Ml
Molecular formula	$C_{57}H_{65}F_5N_{10}$
Route of administration	Oral tablets
Structure	

DOSAGE & ADMINISTRATION [4]

Table 2: Duration for treatment.

Duration for treatment-naive patients	
Genotypes 1-6, no cirrhosis	8 Weeks
Genotypes 1-6, compensated cirrhosis (Child-Pugh A)	12 Weeks
Duration for treatment-experienced patients	
Genotype 1 and NS5A inhibitor prior treatment	16 Weeks
Genotype 1 and NS3/4A protease inhibitor prior treatment	12 Weeks

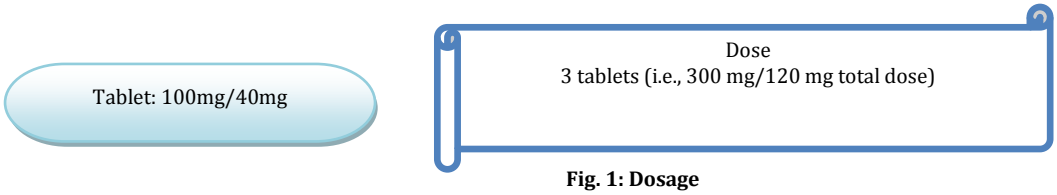


Fig. 1: Dosage

DOSAGE MODIFICATIONS

Table 3: Dosage modifications.

Renal impairment	Mild, moderate or severe, including patients on dialysis	No dosage adjustment required
Hepatic impairment	Mild (Child-Pugh A)	No dosage adjustment required
	Moderate (Child-Pugh B)	Not recommended
	Severe (Child Pugh C)	Contraindicated.

PHARMACOKINETIC & PHARMACODYNAMIC PROPERTIES [4,5]

Table 4: Pharmacokinetic and Pharmacodynamic Properties.

Protein binding	> 99.9 % & the blood-to-plasma ratio = 0.62
Elimination half-life	13 hours
Excretion	96.6%
Metabolism	Not metabolized
Route of administration	Biliary-fecal where 96.6% of administered drug is excreted in the urine.
Toxicity	Pibrentasvir is not shown to be genotoxic according to in vitro or in vivo studies.
Interactions	Abacavir metabolism get decreased when it gets combined with the pibrentasvir
Acebutolol	Serum concentration of Acebutolol can be increased when it is combined with pibrentasvir
Food interaction	Not applicable

MECHANISM OF ACTION [6]

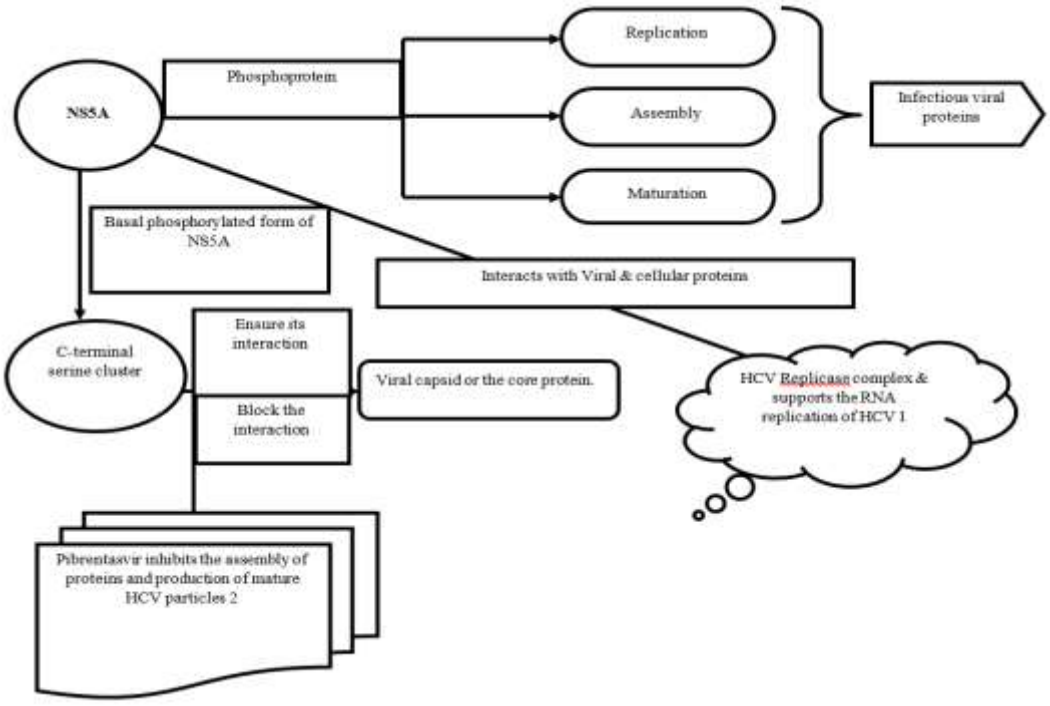


Fig. 2: Mechanism of action of Pibrentasvir

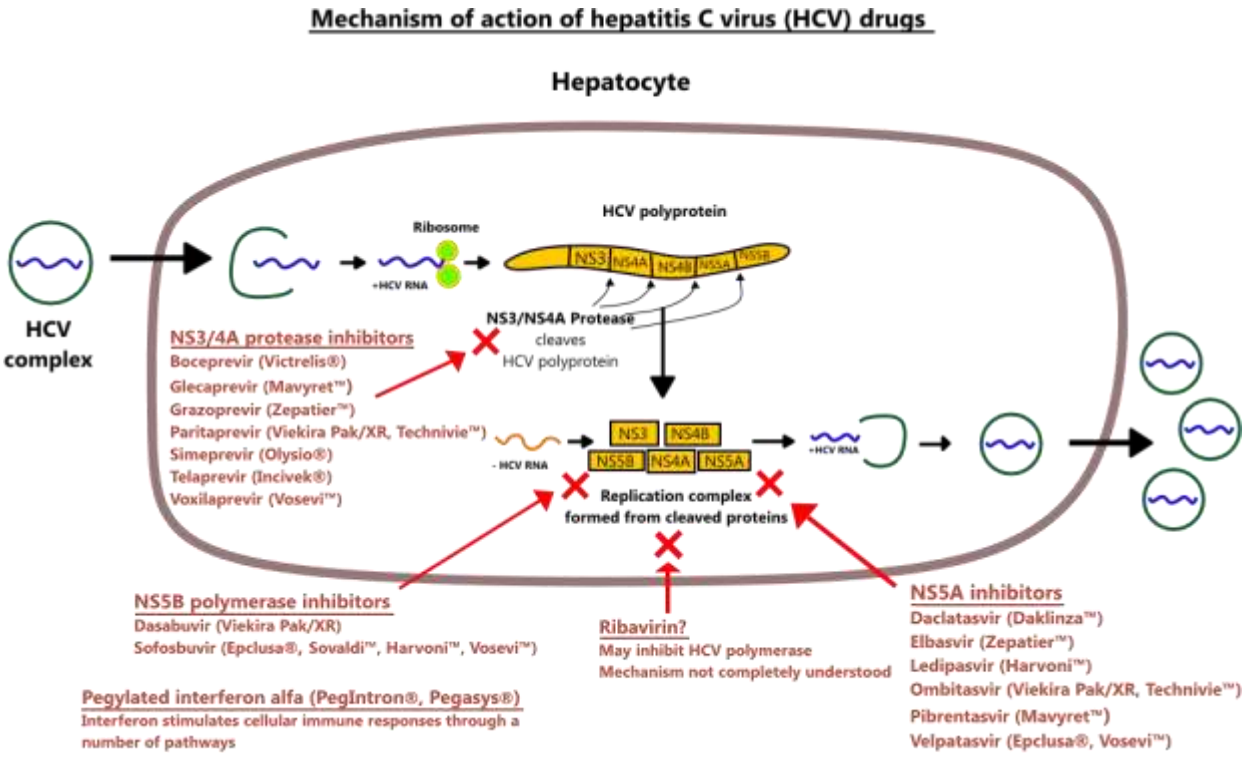


Fig. 3: Mechanism of action of Hepatitis C

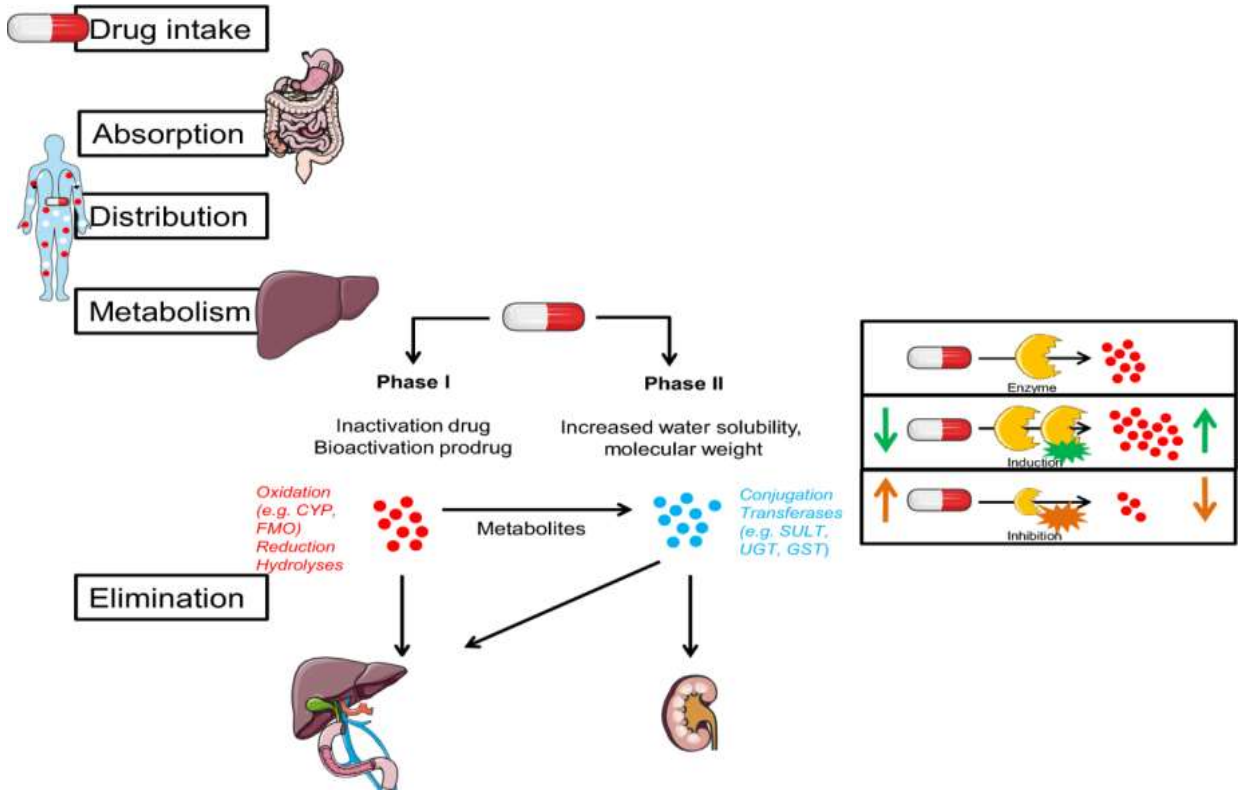


Fig. 4: Pharmacokinetics pathway.

ANALYSIS

An RP-HPLC method was choose for the method development and validation of pibrentasvir and its related substances as my project topic. Validation was done according to ICH guidelines. After so many trials, the pibrentasvir drug was eluted at 38.454 minutes with all its impurities according to the run time as 90 minutes and this was selected as the optimized trial as it was best of all and the acceptance criteria was met (Figure 5) and (Table 5). Validation parameters liken Accuracy, Precision, Linearity, LOD; LOQ & Robustness was chosen to validate my method. Accuracy was within the limit such as 98-101 %, Precision is 0.11%, Linearity is 0.9999, LOD is 0.8557 µg/mL, LOQ is 2.593 & Robustness was within limit (Table 6).

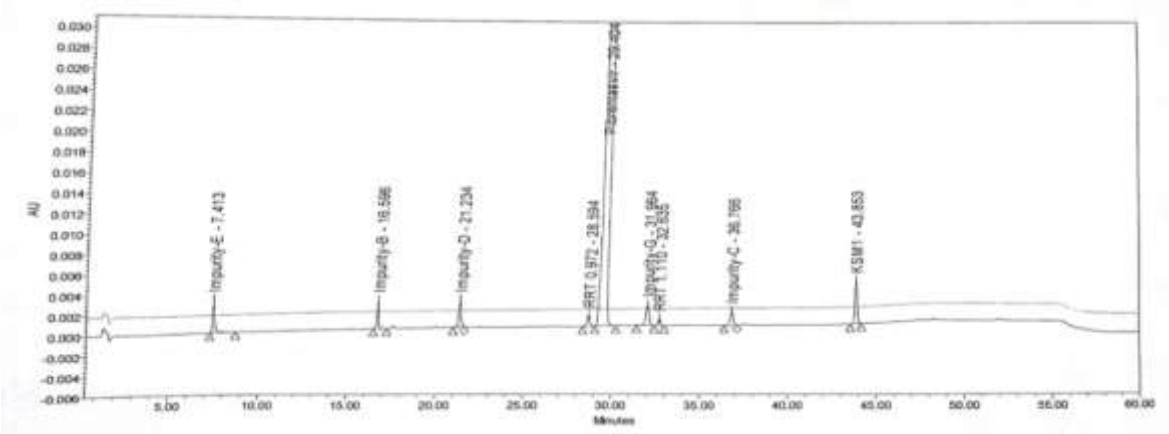


Fig. 5: Chromatogram of Pibrentasvir and its impurities

Table 5: Peak results of Pibrentasvir and its impurities.

S.No	Name	Retention time	Area	Height	USP Resolution	USP Tailing
1	Impurity-E	3.358	63531	9846	-	1.6
2	Impurity-D	13.328	57666	5291	26.4	1.3
3	Impurity-B	21.733	46055	3060	15.2	1.1
4	Pibrentasvir	38.454	9862273	462290	5	1.4
5	Impurity-G	42.151	49419	2345	6	1
6	Impurity-C	50.623	42130	1907	14.7	1
7	Ksm 1	65.162	56959	3523	28.3	1

Table 6: Peak results of Optimized chromatogram.

S.No	Parameters	Limit	Observations	Inference
1	Specificity	No Interferences at retention time of the analyte peak.	Within Limit	Passed
2	System Precision	% RSD=NMT 2	%RSD=0.11%	Passed
	Method Precision	% RSD NMT 2.0%	%RSD =0.18%	
3	Linearity	Correlation co-efficient= NLT 0.99	R^2= 0.9999	Passed
4	Accuracy	% Recovery = 98-102%	99.73-101.15%	Passed
6	Robustness	% RSD NMT 2.0%	Within limit	Passed
7	Limit of detection (LOD)	Signal noise ratio should be more than 3:1	0.8557µg/mL.	Passed
8	Limit of quantitation (LOQ)	Signal noise ratio should be more than 10:1	2.593µg/mL.	Passed

CONCLUSION

Pibrentasvir is an anti-viral agent that is useful in the treatment of hepatitis C. It is associated with the fewer adverse effects compared to others. It is an oral drug with normal biological half-life. Therefore, the pibrentasvir is an ideal drug for **'Hepatitis C'**. In the present work, the developed method has been validated according to ICH guidelines. Chromatogram was run through standard Kinetics Phenyl Hexyl C_8 (150×4.6) mm, 2.6µm. Mobile phase contains a mixture of Buffer: ACN (70:30) was pumped through a flow rate of 1.0mL/min. Buffer used in this method was 0.01M of Potassium Di hydrogen phosphate in 1L of Milli Q water, pH to 2.8 with diluted OPA. Temperature of column and sample was maintained at 30°C & 25°C respectively. Optimized wavelength selected was 252nm.Retention time of pibrentasvir was found to be 38.454 min. % RSD of the pibrentasvir was found to be 0.9999%. Recovery was found to be 99.73 to 101.15 %. LOD & LOQ values obtained from regression equations were 0.8557 & 2.593µg/mL. Regression equation of pibrentasvir is Y=31256.x + 8728.

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