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Review Article

Spectroscopic, Chromatographic and Electrochemical Determination of Ribavirin in Different Matrices

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Abstract

Ribavirin is a synthetic purine nucleoside analog with a broad spectrum of antiviral activity. It's critical to understand the pharmacokinetic characteristics and the mechanism of action of ribavirin. As such, it is crucial to focus on analytical methods that can allow specific, sensitive, and accurate measurement of ribavirin, so we introduce in this literature the last up to date of these methods in different matrices.

Key words: ribavirin; antiviral; pharmacokinetic; mechanism of action; analytical methods

Introduction

Ribavirin (RBV, Figure 1) is chemically nomenclated as ([(2*R*,3*R*,4*S*,5*R*)3,4-dihydroxy-5-(hydroxymethyl) oxolan-2-yl]-1,2,4-triazole-3 carboxamide). It is a nucleoside analogue and antiviral agent used in therapy of chronic hepatitis C in combination with other antiviral agents with the goal of achieving sustained virologic response (SVR). It's also been used to treat hemorrhagic fevers, Lassa fever, and SARS. RBV has some significant side effect with more than 10% of cases suffer from: dermatologic, endocrine & metabolic, anorexia, nausea, vomiting and anemia [1,2].

For the determination of RBV in various forms, a variety of analytical approaches have been used. As such, RBV has been explored in terms of chemical properties, mechanism of action, and the most reported analytical methods for determining this medication in various matrices in this review article.

Mechanism of Action

RBV is said to have several mechanisms of actions that lead to inhibition of viral RNA and protein synthesis. Ribavirin triphosphate (RTP) is the most common metabolite that inhibits viral mRNA polymerase directly by attaching to the enzyme's nucleotide binding site. This prevents the proper nucleotides from binding, resulting in reduced viral replication. RTP also has an inhibiting effect on dengue virus mRNA guanylyl transferase and mRNA 2′-O-methyltransferase. Inhibition of these enzymes causes RBV to be integrated at the 5′ end of viral mRNA instead of guanosine, disrupting posttranslational capping and preventing cap methylation [3].

Another method of RBV action is the inhibition of host inosine monophosphate dehydrogenase (IMPDH) and subsequent depletion of the GTP pool. IMPDH catalyzes the rate-limiting step in the formation of guanosine monophosphate (GMP) when inosine 5′-monophosphate is transformed to xanthine monophosphate. Later, GMP is transformed to guanosine triphosphate (GTP). RBV monophosphate is a competitive inhibitor of IMPDH that mimics inosine 5′-monophosphate. Reduced intracellular GTP pools and inhibited de novo guanine nucleotide synthesis reduce viral protein synthesis and limit viral genome replication [4].

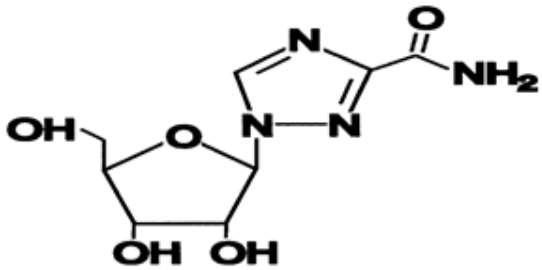

Figure 1: Chemical structure of Ribavirin.

Review of analytical methods

Various techniques were used for the analysis of Ribavirin in its pure forms, in pharmaceutical formulations and in biological fluids.

The available reported methods in the literature can be summarized as follows:

1.Spectroscopic methods

1.1. Spectrophotometric method

Drugs	Matrix	Method or Reagent	λ_{max} (nm)	Linearity range	LOD	Ref.
RBV, acyclovir	Pharmaceutical formulation	Method A:Cerium (IV) ammonium sulfate Method B: Potassium persulfate	630 630	10-60 µg/mL 20-50 µg/mL	0.63 µg/mL 1.40 µg/mL	[5]
RBV	Capsules	1,2-naphthoquinone-4-sulfonate (NQS) in alkaline medium	452	5-65 µg/mL	1.48 µg/mL	[6]
RBV	Capsules	Eriochrome black-T in acidic medium	576	2-120 µg/mL	0.87 µg/mL	[7]
RBV	Capsules	UV spectrophotometry	224	5-40 µg/mL	0.026 µg/mL	[8]
RBV	Spiked human urine, spiked human plasma	Ratio spectra Iso-absorptive Mean centering Constant center	226–210 239 224 216	6-42 µg/mL 6-42 µg/mL 6-42 µg/mL 6-42 µg/mL	0.9771 µg/mL 0.5853 µg/mL 1.0635 µg/mL 0.3317 µg/mL	[9]
RBV	Capsules	Inorganic oxidant (ammonium molybdate)	675	5-35 µg/mL	0.77 µg/mL	[10]
RBV	Pharmaceutical formulation	UV spectrophotometry	207	10-60 µg/mL	1.10 µg/mL	[11]

1.2. Spectrofluorimetric methods

Drugs	Matrix	Method or Reagent	λ_{ex} (nm)	λ_{em} (nm)	Linearity range	LOD	Ref.
RBV	plasma	1,2-naphthoquinone-4-sulfonate (NQS) in an alkaline medium	344	406	0.05-8.0 µg/mL	0.02 µg/mL	[6]
RBV	Capsule	Sodium dodecyl sulfate (SDS)	270	396	0.01-3.0 µg/mL	$5.02x10^3$ µg/mL	[12]
RBV	Capsule	Dansyl chloride in bicarbonate solution (pH 10.5)	382	529	200-900 ng/mL	30.49 ng/mL	[13]
RBV	Capsule	Cerium (IV) in presence of perchloric acid	255	355	50–1400 ng/mL	20-49 ng/mL	[14]

2. Chromatographic methods

Drugs	Matrix	Column	Mobile phase	Detector	Linearity range	LOD	Ref.
RBV	Human plasma	C_{18}-bonded silica column with 5-µm beads (3.9 by 300 mm; Novapak)	10 mM ammonium phosphate buffer (pH adjusted to 2.5)	UV at 207 nm	0.2-5 µg/mL	0.06 µg/mL	[15]
RBV	Serum	Phenylboronic acid columns	10 mM ammonium phosphate buffer	UV	1-64 µM	0.1 µM	[16]
RBV	Serum, urine	LiChrosorb RP C_{18} (25 x 0.5 cm, 7-µm, Merck),	Distilled water	UV at 207 nm	20-1000 ng/mL	------	[17]
RBV	Plasma	C_{18} RP (4.6 x 150 mm)	10 mM ammonium phosphate buffer (pH 2.5)	UV at 225 nm	5.3-1,024 µM	1.2 ng	[18]
RBV	CEMss cells	Phenomenex Luna C_{18} (100 mm x 1.1 mm, 3 µm)	5% MeOH, 10% of 100 mM ammonium acetate (pH 5.0)	MS	0.01–10 µg/mL	------	[19]
RBV	Rat plasma	Phenomenex Luna Hilic column (3 mm, 2 x 100 mm)	5mM ammonium acetate in 95% acetonitrile in water	MS	10-5000 ng/mL	------	[20]
RBV	Tablets	Zorbax 50 mm × 4.6 mm, 5 µm)	Ammonium formate (pH: 7.50): acetonitrile (30:70, v/v)	MS	2 - 100 ng/mL	0.7 ng/mL	[21]

3. Electro Chemical Method

Drug	Matrix	electrode	Linearity range	LOD	Ref.
RBV	Capsules, urine and serum	Hanging mercury drop electrode (HMDE)	1×10^{-10} - 2×10^{-7} mol/L	2.02×10^{-10} mol/L	[22]
RBV	Capsules	TiO2-CdTe glassy carbon electrode (GCE)	3.9×10^{-4} - 3.9 µmol/L	1.3×10^{-10} mol/L	[23]
RBV	Injections	Pt electrode	1.5×10^{-7} - 6.3×10^{-5} mol/L	3.20×10^{-8} mol/L	[24]

By the end of this literature review, we would like to emphasize that we continue in our current project to provide an updated reviews on diseases and drugs chemistry that help the humanity all over the world [25-60].

Conclusions

For a better understanding of Ribavirin, several analytical methods have been developed, and we have covered so many of them in this literature review, spectrophotometric, spectrofluorimetric, and chromatographic methods such as HPLC with UV-absorbance or MS detection, some of them offers adequate sensitivity and specificity for the analysis of different samples.

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