



Review Article

A concise review on analytical profile of risperidone

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ABSTRACT

Risperidone (RIS) is an atypical antipsychotic medication. This works by selectively antagonising serotonin 5HT₂ and dopamine D₂ receptors. It's used to treat schizophrenia and other mental illnesses. As per literature, RIS was first approved USA by Food and drug administration (FDA) in 1993. Therefore, the main objective of this analysis of RIS in pharmaceutical and biological formulation is in both qualitative and quantitative terms. In this review article, we have summarized UV/Vis spectroscopy, high-performance liquid chromatography (HPLC), High-performance thin-layer chromatography (HPTLC), Liquid chromatography-mass spectroscopy-mass spectroscopy (LC-MS/MS) etc. based methods for estimation of risperidone. In addition to that, we have discussed the bioanalytical methods for RIS analysis. In conclusion, this review article will help to research scholars for further method development for drug estimation in pharmaceutical dosage forms and biological fluids.

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1. Introduction

Risperidone is a second-generation antipsychotic (SGA) medicine that is used to treat a variety of mood and mental health disorders, such as schizophrenia and bipolar disorder. It's one of the most popular SGAs.¹ An excess of dopaminergic D₂ and serotonergic 5-HT_{2A} activity is hypothesised to induce schizophrenia and different mood disorders, resulting in over activity of central mesolimbic and mesocortical pathways, respectively. Risperidone inhibits dopaminergic D₂ receptors and serotonergic 5-HT_{2A} receptors in the brain, which is considered to lessen over activity.¹

Risperidone is a benzisoxazole derivative with antipsychotic property. Risperidone (RIS) chemically known as 3-[2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-

1-yl]ethyl]-2-methyl-6,7,8,9-tetrahydropyrido[1,2-a]pyrimidine-4-one.^{2,3} Figure 1 depicts the chemical structure of RIS.

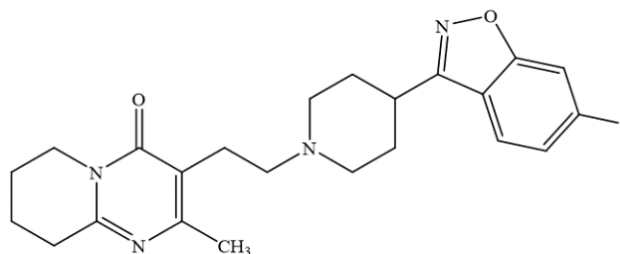


Fig. 1: Chemical structure of RIS

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1.1. Mechanism of action

Risperidone binds to a variety of receptors, including 5-HT_{2A/2C} serotonin receptors, D₂ dopamine receptors, and alpha 1 and H₁ receptors. It has no discernible effect on M₁ receptors. At D₂ and 5-HT_{2A} receptors, its major metabolite (9-hydroxyrisperidone) is almost equal to the parent molecule.²

1.2. Pharmacokinetics

1.2.1. Absorption

Well taken in. Risperidone has a 70% absolute oral bioavailability (CV=25%). When compared to a solution, the relative oral bioavailability of risperidone from a tablet is 94% (CV=10%).¹

1.2.2. Distribution

The volume of distribution of risperidone is approximately 1 to 2 L/kg.¹

1.2.3. Metabolism

Hepatic cytochrome P450 2D6 isozyme metabolises it to 9-hydroxyrisperidone, which has a similar receptor binding affinity as risperidone. N-dealkylation occurs to a lower amount in risperidone.²

1.2.4. Elimination

Risperidone is processed extensively in the liver. Renal clearance of both risperidone and 9-hydroxyrisperidone was reduced in healthy senior adults, and elimination half-lives were longer than in young healthy subjects.²

1.2.5. Pharmacodynamics

Risperidone's main effect is to reduce dopaminergic and serotonergic pathway activity in the brain, which helps to alleviate symptoms of schizophrenia and mood disorders.¹

2. Analytical Account of RIS

For the determination of RIS in bulk and pharmaceutical formulations, an exhaustive literature search found numerous analytical techniques such as UV/Visible Spectrophotometry, HPLC, HPTLC, LC-MS/MS, and bioanalytical approaches. RIS is measured as a single constituent and in combination with Fluoxetine, Olanzapine, Clozapine, Ziprasidone, Haloperidol in various dosage forms and 9-hydroxyrisperidone its active metabolites forms. Figure 2 shows different analytical methods implemented for the estimation of RIS.

2.1. Bio-analytical method for RIS

Bio-analysis is a sub-discipline of analytical chemistry covering the quantitative measurement of xenobiotics (drugs and their metabolites, and biological molecules

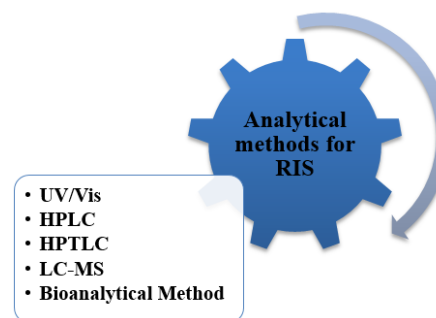


Fig. 2: Analytical methods of RIS

in unnatural locations or concentrations) and biotics (macromolecules, proteins, DNA, large molecule drugs, metabolites) in biological systems.⁴ The summary of the reported bioanalytical methods is shown in Table 1.

2.2. UV-Visible spectroscopy method for RIS

To date, lots of spectrophotometric methods have been accounted for the determination of RIS alone. This review compiles three papers describing spectrophotometric methods for determination of alone RIS. The details of Spectrophotometry determination of basic principle, sample matrix, lambda max, solvent linearity range and the correlation coefficient are summarized in Table 2.

2.3. HPLC method for RIS

The specificity of the HPLC method is excellent and simultaneously sufficient precision is also attainable. However, it has to be stated that the astonishing specificity, precision, and accuracy are attainable only if wide-ranging system suitability tests are carried before the HPLC analysis. For this reason, the expense to be paid for the high specificity, precision, and accuracy is also high.²⁵ The summary of the reported HPLC methods is shown in Table 3.

2.4. HPTLC method for RIS

Thin-layer chromatography is a popular technique for the analysis of a wide variety of organic and inorganic materials, because of its distinctive advantages such as minimal sample clean-up, a wide choice of mobile phases, flexibility in sample distinction, high sample loading capacity and low cost. *R. B. Patel et. al* established HPTLC method development and validation for analysis of risperidone in formulation and in-vitro release study. TLC was carried out by stationary phase silica gel 60 F₂₅₄ plates with methanol-ethyl acetate 8.0:2.0 (v/v) as mobile phase. The linearity range for risperidone was 100-600 ng per band. The developed method was successfully applied for determination of risperidone in formulation.³⁴

Table 1: Bio analytical determination of RIS

Sr. No.	Drug	Sample Matrix	Method	Column	Detection	Internal Standard	Ref.
1	RIS	Human plasma	HPLC	Nucleosil C8 column	280 nm	Diltiazem	5
2	RIS	Plasma	HPLC	Cyano column	***	Remoxipride	6
3	RIS	Human plasma	HPLC-DAD	C8 column	240 nm	Clozapine and Loxapine	7
4	RIS	Human plasma	HPLC-MS/MS	Alltima-C18 Column	***	Paroxetine	8
5	RIS	Human plasma	HPLC	Waters XTerra RP-18 column	278 nm	Clozapine	9
6	RIS	Human plasma & saliva	LC	Reversed phase C18 column	***	Pipamperone	10
7	RIS	Human plasma	LC/MS/MS	Betasil C18 column	***	Methyl risperidone	11
8	RIS	Human plasma	LC-MS/MS	Analytical column	***	Acetonitrile	12
9	RIS	Rat plasma	UPLC-MS/MS	BEH C18	***	Propranolol	13
10	RIS & 9-HRIS	Human Serum	HPLC	ODS Hypersil C18	285 nm	Clozapine	14
11	RIS & 9-HRIS	Human plasma	LC-MS-MS	Atlantis HILIC Silica C18 column	***	Clozapine	15
12	RIS & 9-HRIS	Human plasma & urine	LC-MS/MS	Chiralcel OJ column	***	Methanol	16
13	RIS & 9-HRIS	Human plasma, urine & saliva	MEPS-LC-UV	C8 reversed-phase column	238 nm	Diphenhydramine	17
14	RIS & 9-HRIS	Human plasma	DLLME-LC-MS/MS	Ascentis [®] Express C18 chromatographic column	***	Clozapine	18
15	RIS & 9-HRIS	Plasma	LC-MS/MS	C18 column	***	Clozapine	19
16	RIS, FLX & 9-HRIS	Rat plasma	UPLC-MS/MS	ACQUITY UPLC BEH C18 column	***	Olanzapine	20
17	OLZ, RIS, 9-HRIS, CLZ, HAL & ZIP	Rat plasma	LC/ESI-MS/MS	Waters Atlantis TM dC-18	***	Midazolam	21

***Not provided

Table 2: Spectrophotometric methods used for determination of RIS

Sr. No.	Drug	Matrix	Solvent	Lambda Max (nm)	Linearity ($\mu\text{g/mL}$)	Correlation coefficient (R^2)	Ref.
1.	RIS	Pure form & pharmaceutical dosage forms	Methanol	240 and 280 nm	20 to 60 $\mu\text{g/ml}$	0.99	22
2.	RIS	Bulk & Tablets Formulation	0.1N HCl	238 nm	2-12 $\mu\text{g/ml}$	0.999	23
3.	RIS	Bulk drug & Pharmaceutical formulation	0.1N HCL	280 nm	2 to 6 $\mu\text{g/ml}$	0.99	24

Table 3: Summary of HPLC methods for the determination of RIS in a single and combined dosage form

Sr. No.	Drug name	Column	Mobile phase	Lambda max (nm)	Linearity ($\mu\text{g/mL}$)	Retention time (min)	Flow rate (mL/min)	Detector	Ref.
1.	RIS	C18 column	Acetonitrile-potassium dihydrogen phosphate (45:55, v/v, pH 6.5; 0.05 M)	237 nm	1–100 $\mu\text{g/mL}$	6 min	1.0 mL/min	PDA	26
2.	RIS	C18 column	Methanol: acetonitrile (80 : 20, v/v)	280 nm	10–60 $\mu\text{g/mL}$	3.35 \pm 0.01	1 mL/min	PDA	27
3.	RIS	Hypersil ODS C-18 column	Methanol-acetonitrile-phosphate buffer (0.02 M) (65 : 20 : 15, v/v/v)	238 nm	1.0–10 mg/ml-1	6.16 min	1.0 ml/min-1	***	28
4.	RIS	Waters Xterra RP8 column	(10 mM potassium dihydrogen phosphate, pH 3.5 \pm 0.05): acetonitrile: methanol (65:20:15)	276 nm	5–45 $\mu\text{g/mL}$	12 min	1.0 mL/min	UV	29
5.	RIS	Gemini C-18	Methanol: acetonitrile: 50 mM potassium dihydrogen orthophosphate (80:10:10 v/v)	234 nm	1–11 $\mu\text{g/ml}$	2.5 min	1.3 ml/min	UV/VIS	30
6.	RIS	Lichrosorb RP C 18 column	Methanol:0.05M potassium dihydrogen phosphate pH 7 (65:35 (v/v))	280 nm	25–500 $\mu\text{g/ml-1}$	***	1 ml/min-1	DAD	31
7.	RIS	Purosphere STAR RP-18e	Water: glacial acetic acid 0.50 %: triethylamine 0.80 %: acetonitrile (65.00: 0.32: 0.52: 34.16, v/v)	294 nm	25.00 $\mu\text{g/mL}$ to 250.00 $\mu\text{g/mL}$	***	1 mL/min	DAD	32
8.	RIS & HPD	XBridge C18	Methanol: triethyl amine Buffer (60::40) and the pH of triethylamine adjusted to pH2.5 using orthophosphoric acid	260 nm	2-10 $\mu\text{g/ml}$ & 8-40 $\mu\text{g/ml}$	1.82 min & 4.42 min	1.0 ml/min	PDA	33

***Not provided

3. Conclusion

The present review article provides comprehensive data of various analytical and bioanalytical methods developed for RIS alone and in combinations. For analysis purpose, different analytical methods have been reported that includes HPLC, HPTLC, UV spectroscopy, LC-MS/MS etc. The method along with their details concerning the mobile phase, stationary phase, retention time, etc., have been summarized in tabular form that will more helpful for the researchers for further analytical method development for estimation of RIS in dosage form and pure form. In the future, enlisted data can be used for the development of analytical methods bio-analysis of RIS in pharmaceutical and biological formulations. Finally, it presents an opportunity for greater information on what has already been done and what new methods and changes can be developed to get a better estimation of RIS.

4. Abbreviations

1. RIS - Risperidone
2. USA — United states of America
3. DA — Food and drug administration
4. UV/VIS - Ultra violet/visible spectroscopy
5. HPLC — High-performance liquid chromatography
6. HPTLC — High-performance thin layer chromatography
7. LC-MS/MS — Liquid chromatography-mass spectroscopy-mass spectroscopy
8. SGA — Second-generation antipsychotic
9. DNA — Deoxyribonucleic acid
10. RP — Reverse phase
11. nm — Nanometer
12. $\mu\text{g/mL}$ — Micro gram per Milliliter
13. PDA - Photo diode array
14. TLC — Thin layer chromatography

5. Source of Funding

None.

6. Conflict of Interest

None.

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