REVIEW ARTICLE

Effect of Hydrotropic Solubilisation on Quantitative Determination of Ulipristal Acetate in Pharmaceutical Formulations

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ABSTRACT

Objective: The study's main objective was to solubilize poorly water-soluble drug ulipristal acetate, develop an analytical method for the quantitative estimation, and validate the analytical method developed. Validation parameters studied like range, linearity, and assay.

Methods: Ulipristal acetate is freely soluble in distilled water when 1.5 M Nicotinamide was used as a solubilising agent. Ulipristal Acetate shows an Absorption maximum at 298.55 nm in first order mode of measurement using Shimdzu UV Spectrophotometer 1800 spectronic model.

Result: At the absorption maximum 298.55 nm, ulipristal Acetate shows a linear response in the range between 5µg/mL to 25µg/mL concentration.

Conclusion: The current study is useful for the aqueous solubilization and quantitative determination of ulipristal acetate in pharmaceutical formulation thus avoiding toxic solvents.

Keywords: Hydrotropic solubilization, Linearity profile, Quantitative determination, Solubility profile, Ulipristal Acetate.

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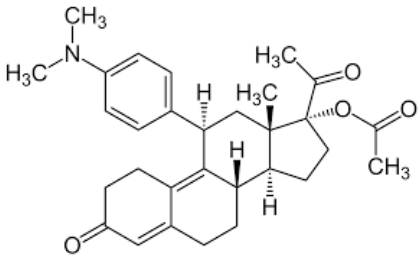
Conflict of interest: None

INTRODUCTION

Ulipristal acetate is poorly water-soluble drug and selective progesterone receptor used as emergency contraception and for the treatment of uterine fibroids. Ulirpistal acetate is a 19- nor progesterone derivative and has partial antagonist and agonist activity at the progesterone receptor.[1] Therapeutic efficacy and bioavailability of the drug is mainly dependent upon the solubility of the drug. As there are several methods have been developed for the enhancement of solubility of poorly water-soluble drugs. Among them one of the significant techniques is the Hydrotropic solubilization technique. Which involves the addition of large amount of second solute increases the aqueous solubility of other solutes. Hydrotropy enhances the drugs' solubility by using hydrotropes like Nicotinamide, Sodium benzoate, sodium salicylate, urea.[2-4] In this current study, an effort is made to improve the aqueous solubility of the selected drug ulipristal acetate by using niacinamide as a solubilizing agent, as there are no reported method is available so far to enhance water solubility and establish linearity of selected drug molecule by hydrotropic solubilization technique.



MATERIALS AND METHODS

Materials

The study was carried out by using Shimadzu UV spectrophotometer Spectronic model 1800 with 1 cm matched quartz sample cells. The reagents used were distilled water, sodium benzoate, sodium salicylate, urea, nicotinamide (niacinamide). The study was carried out on ulipristal acetate Marketed formulation.

Methodology

The procedure for solubility test is based on an effort to dissolve chemicals in water as a solvent with gradually more

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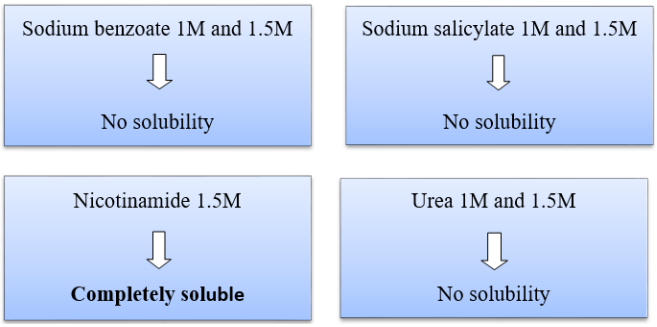
Table 1: Identification of the ideal solubilizing agent

Concentration	*Trial 1*	*Trail 2*	*Trail 3*	*Trial 4*
Drug	10mg	10mg	10mg	10mg
Solubilizing agent	1M, 1.5M	1M, 1.5M	1M, 1.5M	1M, 1.5M

Table 2: Linearity data table and range

Concentration (µg/mL)	*Absorbance*	*Derivative (A)*
5	0.642	0.800
10	0.523	0.610
15	0.438	0.510
20	0.346	0.420
25	0.253	0.300



Solubility flow chart

The results found were satisfactory and Ulipristal Acetate is completely soluble in 1.5M Nicotinamide

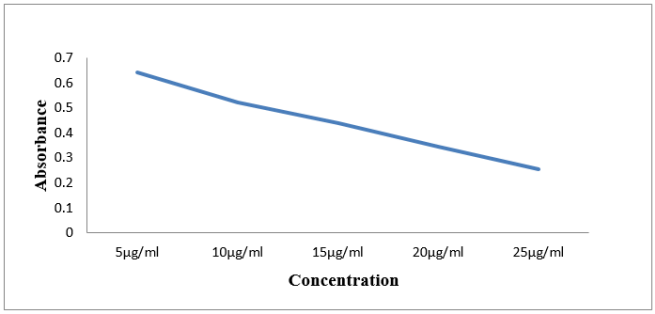


Figure 1: Linearity graph of experimental data for ulipristal acetate at N = 5

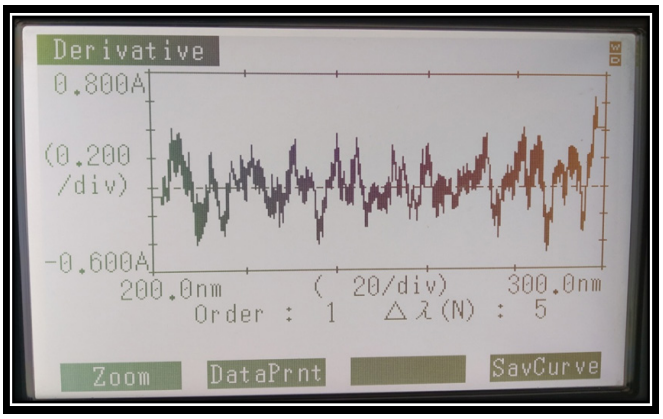


Figure 2: Instrumental response first order derivative spectrum 5 µg/mL

through mechanical methods. The solubilizing agents to be employed, in the preferential order, are sodium benzoate, sodium salicylate, urea, nicotinamide (niacinamide). Solubility shall be resolute in a step-by-step route that involves an effort to dissolve a chemical under test in selected solvents in the order of preference at reasonably high concentration using the series of mechanical procedures as cited in Table 1. In the condition where the test chemicals fails to dissolve, try to increase the volume of a solubilizing agent so as to decrease the drug concentration by a factor of 10, and then the array of mechanical trials are repeatedly made in an effort to increase the solubility of the chemical at a still lower concentration. To determine if the chemical has been dissolved depends entirely on visual examination. The chemical is dissolved if the solution is absolutely clear and there is no sign of precipitation observed.[5-7]

PROCEDURE

a. Trial 1 starts with solubility testing of the drug in 1 M solution of the solubilizing agent in Distilled water as per the order of preference. If complete solubility is accomplished, then further solubility trials are not required.
b. If the chemical under test is insoluble in either medium of dilution or medium of Treatment, then move on to trial 2 by adding up a sufficient amount of medium, just about 1.5 M to attempt to dissolve the drug. If the chemical under test gets dissolved in a medium at 1.5 M concentration, further steps are not required. If the drug does not dissolve in one medium or the other (if both agents are checked in this trial), stop the attempts to dissolve the chemical. If the drug is soluble in any of these solvents, no extra solubility measures are required.
c. If the drug is still insoluble in either of the media applied in trial 2, then go on with tier 2, 2.5, by increasing the concentration. If the drug is soluble, no further solubility trials are needed. The details are given in Table 1. If the chemical under test is not dissolving, drop the solubilizing agent and try another solubilizing agent in the preferential order as referred in the flow chart.

VALIDATION

The method was subjected to validation parameters like range, linearity, and assay using marketed formulation at 298.55 nm (at N = 5) UV first derivative absorption maximum to ascertain the experimental conditions. However, the present method should be revalidated according to ICH or USFDA guidelines.[8,9] Data provided in Table 2 and Figures 2 to 7.

RESULTS AND DISCUSSION

After following the above procedures, ulipristal acetate was freely soluble in 1.5 M Niacinamide (1.0 mg/mL) and not in other solubilizing agents. To check the reproducibility of the procedure, the serial dilutions of 5, 10, 15, 20, and 25 µg/mL

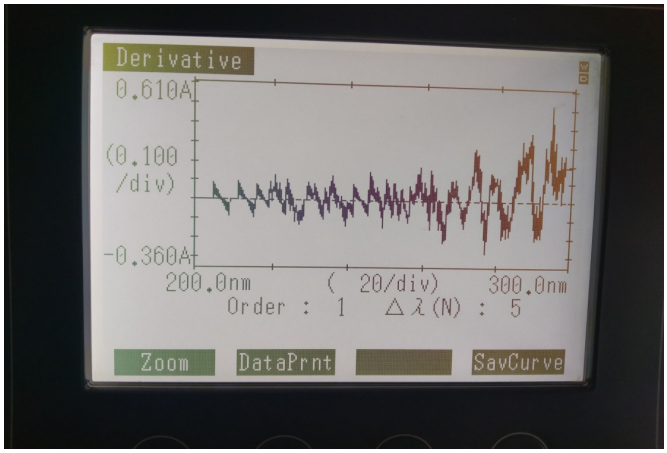


Figure 3: Instrumental response First order Derivative spectrum 10 µg/mL

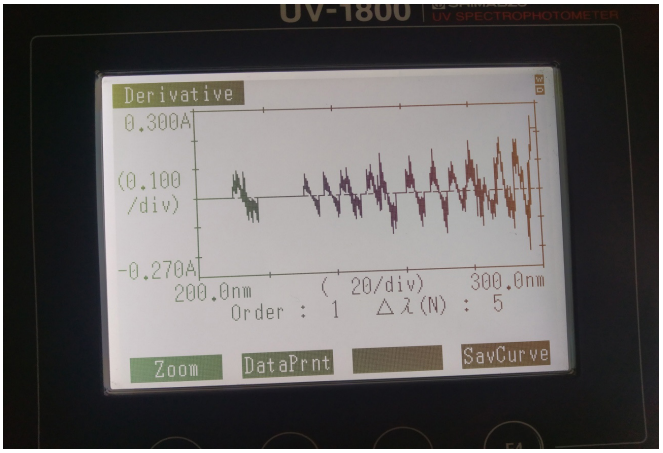


Figure 6: Instrumental response first-order derivative spectrum 25 µg/mL

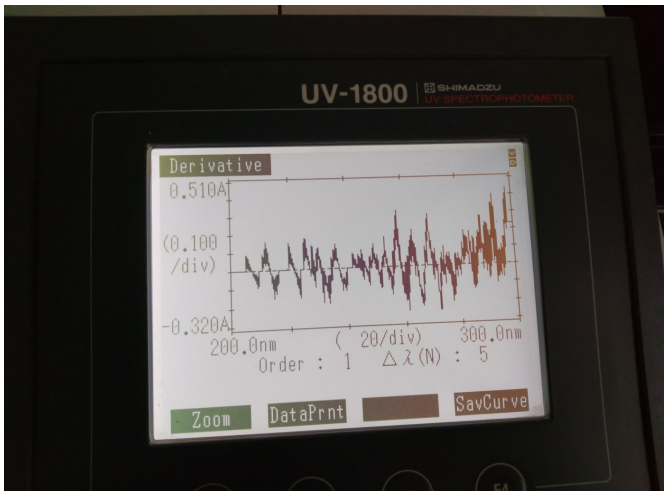


Figure 4: Instrumental response first order derivative spectrum 15 µg/mL

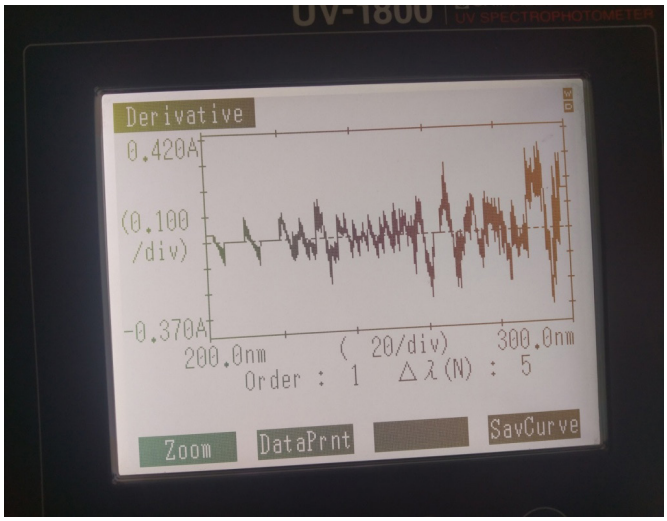


Figure 5: Instrumental response first order derivative spectrum 20 µg/mL

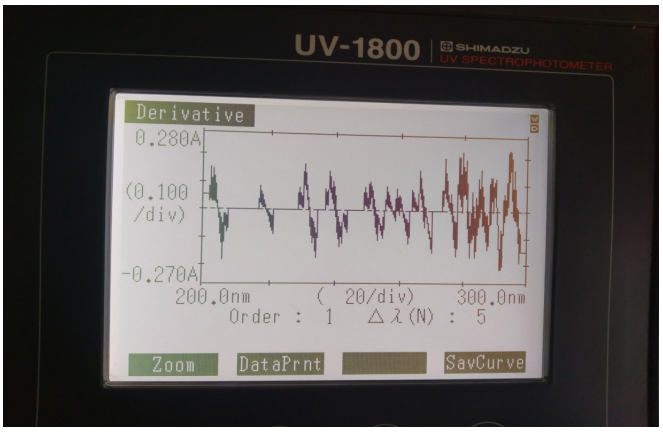


Figure 7: Instrumental response first-order derivative spectra for validation parameter assay

Table 3: Experimental data of validation parameter Assay

Concentration	*max*	*Absorbance*	*Derivative*
22 µg/mL	294.60	0.232	0.280A

Table 4: Optimum conditions for linear graph

Parameters	*Conditions*
Solubilizing agent	Nicotinamide
Concentration	1.5M
Solubility of Ulipristal Acetate	1.0 mg/mL
Range	5 to 25µg/mL
Regression Equation	y=0.04X+1.97
LOD	0.00934 µg/mL
LOQ	0.05439 µg/mL
Assay	99% (n = 5)
Assay	SD 0.9901
Assay	CoV 0.9995

solutions were prepared and subjected to linearity study. A graph of derivative values versus concentration was plotted and the results were found to be precise. The assay values were accurate with low standard deviation values and low values of coefficiency of variation. The details are given in Table 4.

CONCLUSION

The current newly developed method offers an accurate, reproducible, linear, economical, time-saving method with

a suitable concentration range for the determination of ulipristal acetate using an environment-friendly method that avoids the use of harmful and toxic solvents which are health hazardous. The report is also useful for the routine analysis of ulipristal acetate in pharmaceutical formulations. These studies are further applicable for dissolution, disintegration, pharmacological evaluations, pharmacokinetic and pharmacodynamic studies of ulipristal acetate. This report's future scope involves the complete validation profile according to internationally accepted guidelines like International Council for Harmonisation (ICH) and United States Food and Drug Administration (USFDA) etc.

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