

**Original Article**

**HYDROTROPIC SOLUBILIZATION AND LINEARITY PROFILE OF PAZOPANIB**

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**ABSTRACT**

**Objective:** A study on the hydrotropic solubility and linearity profile of Pazopanib was carried out by using Niacinamide as the solubilizing agent as Pazopanib is poorly soluble in water.

**Methods:** Pazopanib was freely soluble in water when 2.8M Niacinamide was used as a solubilizing agent. Pazopanib shows an absorption maximum at 282 nm in First derivative mode of measurement using Shimadzu UV Spectrophotometer 1800 spectronic model.

**Results:** At the absorption maximum of 282 nm, Pazopanib shows a linear response in the range of 5µg/ml to 15µg/ml concentration.

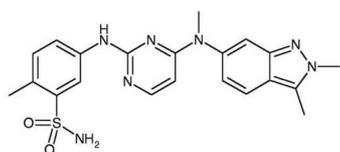
**Conclusion:** The present study is useful for the aqueous solubilization and quantitative determination of Pazopanib in bulk drug and in pharmaceutical formulations thus avoiding toxic solvents.

**Keywords:** Pazopanib, Hydrotropic, Solubilization, Solubility Profile, Linearity profile, Quantitative Determination

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**INTRODUCTION**

Pazopanib is a poorly water soluble drug used to treat kidney cancer. Water solubility is the greatest physicochemical parameter during drug development and research [1, 2]. Insolubility of any drug can hinder the improvement of parenteral products. Hydrotropic solubilization method development is the most convenient tool to enhance the aqueous solubility of such molecules to avoid harmful organic solvents like dimethyl sulphoxide, chloroform, carbon tetra chloride, methanol and ethanol etc [3-6]. In this present study, an effort is made to improve the aqueous solubility of the selected drug Pazopanib by using Niacinamide as the solubilizing agent, as there is no reported method is available so far to enhance water solubility and establish linearity of selected drug molecule by Hydrotropic Solubilization method.



**MATERIALS AND METHODS**

**Materials**

The study was carried out using Shimadzu UV Spectrophotometer Spectronic Model 1800 with 1 cm matched quartz sample cells. The reagents used were distilled water, Sodium Benzoate Sodium Salicylate, Sodium Ascorbate, Urea, Sodium Citrate and Niacinamide. The study was carried on Pazopanib API and Marketed formulation.

**Methodology**

**Test system**

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

mechanical methods. The solubilizing agents to be employed, in the preferential order, are Sodium Benzoate, Sodium Salicylate, Sodium Ascorbate, Sodium Citrate, Urea, Niacinamide, DENA and DMBA. Solubility shall be resolute in a step by step route that involves effort to dissolve a chemical under test in the 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 chemical fails to dissolve, try to increase the volume of 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 still lower concentrations. To determination if that chemical has been dissolved depends entirely on visual examination. The chemical is said to be dissolved if the solution is absolutely clear and there is no sign of precipitation or cloudiness is observed [7, 8].

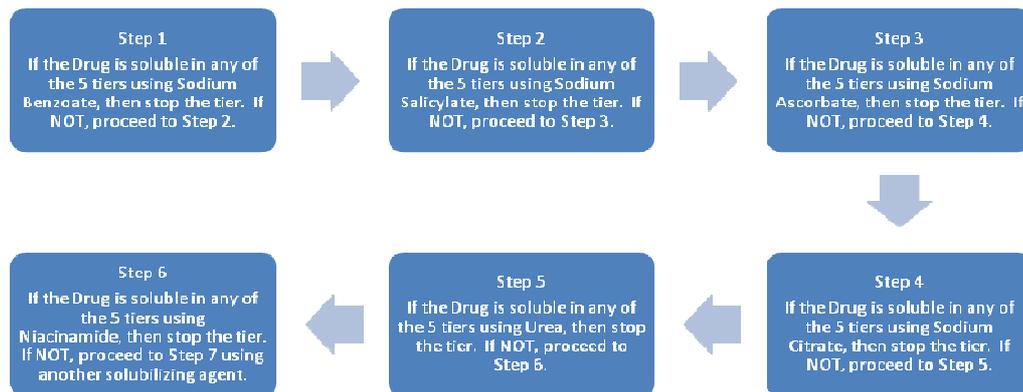
**Procedures**

- a) Tier 1 starts with solubility testing of the drug in 1M solution of the solubilizing agent in water as per 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 Tier 2 by adding up a sufficient amount of medium, just about 2M to attempt for dissolving the drug. If the chemical under test get dissolved in medium at 2M concentration, further steps are not required. If the drug not dissolves in one medium or the other (if both agents are checked in this tier), 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 Tier 2, then go on with Tier 3, 4 or 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.

**Table 1: 5 Tier systems**

Concentrations	Tier 1	Tier 2	Tier 3	Tier 4	Tier 5
Drug	1 mg	1 mg	1 mg	1 mg	1 mg
Solubilizing agent	1M, 1.5 M	2M, 2.5M	3M, 3.5M	4M, 4.5M	5M

**Solubility flow chart**



Steps 1 to Step 5 procedures were unsuccessful and step 6 was followed. The results here were found satisfactory in this step and pazopanib was completely soluble in 2.8M niacinamide

**Validation**

To ascertain the experimental conditions, the method was subjected to validation parameters like range, linearity (fig. 2 to 6) and assay

using marketed formulation compared with standard drug, at 282 nm (at N=4)UV first derivative absorption maximum. However, the present method should be revalidated according to ICH or USFDA guidelines [9, 10].

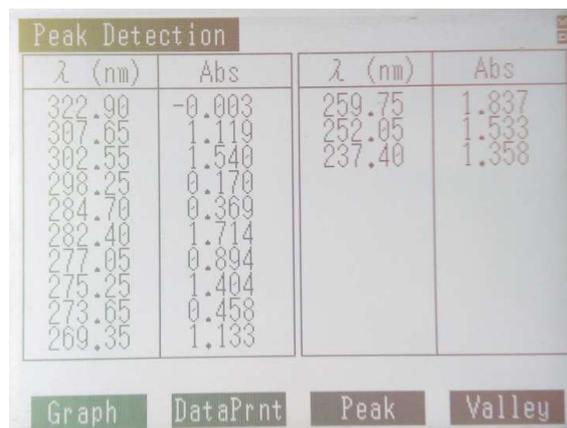


Fig. 1: Absorption peak at 282 nm

Table 2: Linearity and range

S. No.	Pazopanib concentration (µg/ml)	First derivative value
1	5 µg/ml	2.2
2	10 µg/ml	2.3
3	15 µg/ml	2.6

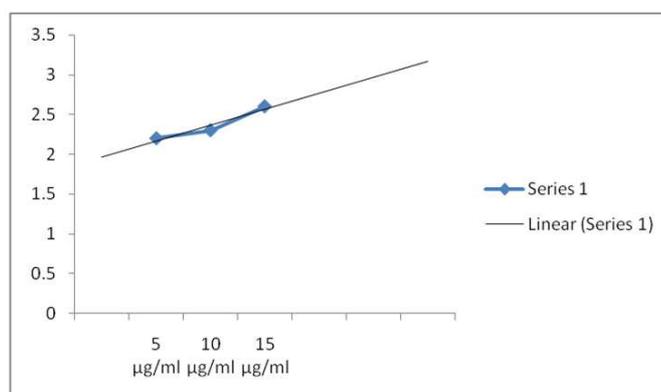


Fig. 2: Linearity graph  $y=0.04X+1.97$

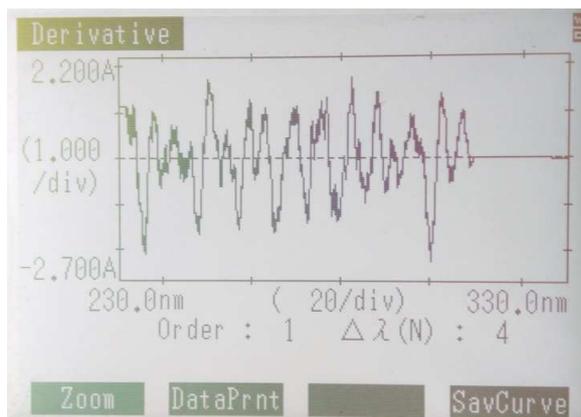


Fig. 3: Pazopanib concentration 5 µg/ml

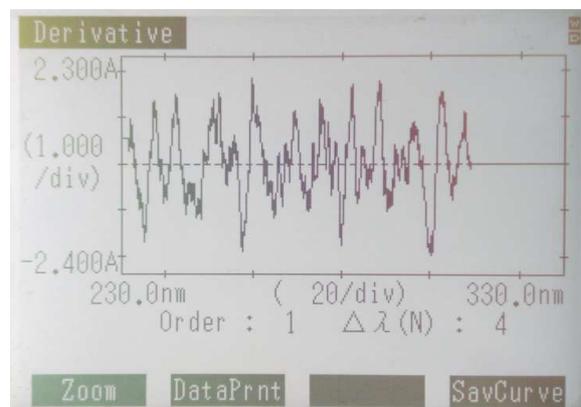


Fig. 4: Pazopanib concentration 10 µg/ml

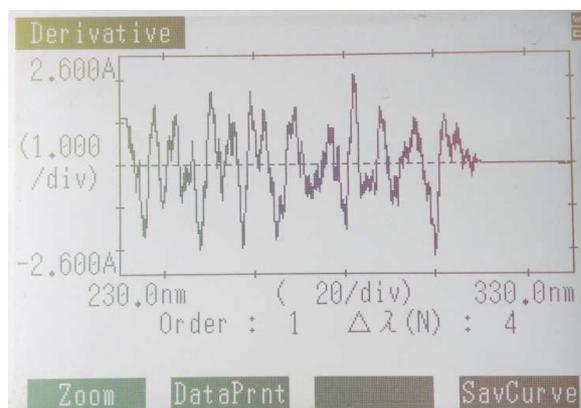


Fig. 5: Pazopanib concentration 15 µg/ml

Table 3: Optimum conditions for linear graph

Parameter	Condition
Solubilizing agent	Niacinamide
Concentration	2.8M
Solubility of Pazopanib	1 mg/ml
Range	5 to 15 µg/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

**RESULTS AND DISCUSSION**

After following above procedures, Pazopanib was found to be freely soluble in 2.8M Niacinamide (1 mg/ml) and not in other solubilizing agents. To check the reproducibility of the procedure, the serial dilutions of 5, 10 and 15 µg/ml 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 with equation for straight line slope 0.04 and intercept 1.97. The assay values were found to be accurate with low standard deviation values and low values of co efficient of variation. The details are given in the table 3.

**CONCLUSION**

The present newly developed method offers an accurate, reproducible, linear, economical, time saving method with a suitable concentration range for the determination of Pazopanib using an environment friendly method which avoids the use of harmful and toxic solvents which are health hazardous. The report is also useful for the routine analysis of Pazopanib in pharmaceutical formulations. These studies are further applicable for dissolution, disintegration, pharmacological evaluations, pharmacokinetic and pharmacodynamic studies of Pazopanib. Future scope of this report involves the complete validation profile according to internationally accepted guidelines like ICH and USFDA etc.

**ACKNOWLEDGEMENT**

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**AUTHORS CONTRIBUTIONS**

All the authors have contributed equally.

**CONFLICT OF INTERESTS**

Declared none

**REFERENCES**

1. Maheshwari RK, Moondra S. A novel method for the quantitative determination of aceclofenac in bulk drug and tablet using niacinamide as a hydrotropic solubilizing agent. *J Adv PharmTech Res* 2010;1:78-82.
2. Sherje AP, Desai KJ. Spectrophotometric determination of poorly water soluble drug rosiglitazone using hydrotropic solubilization technique. *Indian J Pharm Sci* 2011;73:579-82.
3. Ji Young Kim, Sungwon Kim, Michelle Papp, Kinam Park, Rodolfo Pinal. Hydrotropic solubilization of poorly water soluble drugs. *J Pharm Sci* 2010;99:3953-65.
4. Patidar A. Analytical application of hydrotropic solubilization in spectrophotometric determination of naproxen in tablet dosage form. *Int J Pharm Biol Archive* 2011;2:1479-80.
5. Sharma MC, Smita Sharma. Spectrophotometric determination and application of hydrotropic solubilization in the quantitative analysis of ranitidine hydrochloride in pharmaceutical dosage form. *Int J PharmTech Res* 2011;3:253-5.
6. Nidhi K, Singhvi I, Mehta K, Karwani G, Sen G. Hydrotropy: a promising tool for solubility enhancement. *Int J Drug Dev Res* 2011;3:26-33.
7. <https://www.epa.gov/> U. S. Environmental protection agency. [Last accessed on 27 Feb 2020]
8. <http://z8d6mv5klx.myhome.cx/537.html> DDG Meeting online: USP Proposed Solubility measurements. [Last accessed on 06 May 2020]
9. <https://www.ich.org/page/quality-guidelines> [Last accessed on 27 Feb 2020]
10. <https://www.fda.gov/media/71021/download> [Last accessed on 27 Feb 2020]