CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://zenodo.org/records/10442347

https://www.iajps.com/volumes/volume10-december-2023/55-issue-12-december-23/

Available online at: http://www.iajps.com *Research Article*

METHOD DEVELOPMENT AND VALIDATION FOR ESTIMATION OF APREPITANT USING HYDROTROPY

Nirasha[1]*, Mrs. Swarupa Ashok Wankhade[2], Dr. Avinash K Kondalkar[3], Mrs. Sapna Avinash Kondalkar, Mr. Muraree Lal, Mr. Jogendra Singh[4], Mr. Munesh Singh Bhadauria[5]

[1]Sun Institute of Pharmaceutical Education and Research, Lahar, Bhind, Madhya Pradesh
kushwahnirasha@gmail.com

Article Received: October 2023 Accepted: November 2023 Published: December 2023

Abstract:

Solubilization of poorly soluble pharmaceuticals is a recurring challenge in screening testing of novel chemical entities as well as formulation design and development. The most effective method for improving a drug's water solubility is the hydrotropic solubilization process. This study's main goal was to create a simple ecofriendly method development & validation for procedures for estimation of aprepitant using hydrotropy. The Solubility results showed that the drug aprepitant was freely soluble in 2M Sodium acetate: 2M Sodium Benzoate (1:1).). Also, remarkable 15-fold increase in solubility of aprepitant was seen with this combination. The maximum absorbance of Aprepitant was observed at 264 nm respectively. The linearity results indicate that aprepitant was entirely soluble in 2M Sodium acetate: 2M Sodium Benzoate (1:1) and the graph are linear. The rate of solubility increases as the graph becomes more linear. Further at recovery level of 120% the % recovery obtained was 99.32±0.704. The repeatability precision was noticed as 99.416±0.107. The precision in reproducibility of result was estimated to be 99.34±0.111. The % RSD in Day to day & analyst to analyst was estimated as 99.06±0.110 and 98.98±0.233 respectively. The analysis of aprepitant tablet with 80 mg label claim showed that actual drug amount as 79.45 mg. So, the % label claim becomes 99.31. Also, the S.D & 5 R.S.D value revealed to be 0.225 & 0.341 respectively. Thus, it can be concluded that newly developed eco-friendly Hydrotropic Solubilization process can be successfully used to improve the solubility of drug that is weakly aqueous soluble aprepitant is accurate and exact.

Keywords: *Hydrotropy, Method development, Validation, Aprepitant, Eco friendly, Solubalization*

Corresponding author:

Nirasha,

Sun Institute of Pharmaceutical Education and Research,
Lahar, Bhind, Madhya Pradesh
kushwahnirasha@gmail.com

QR code

Please cite this article in press ***Nirasha*** *et al* ***Method Development & Validation For Estimation Of Aprepitant Using Hydrotropy,*** *Indo Am. J. P. Sci, 2023; 10 (12).*

INTRODUCTION:

In screening tests of novel chemical entities as well as in the design and development of formulations, the solubilization of poorly soluble medicines is a recurrent difficulty. Solvents are an important part of each stage in the investigation of drugs using various techniques. The method's accuracy, sensitivity, cost, and outcome are all impacted by the solvent choice. The drug's solubility influences the choice of solvent. Numerous medications found in pharmacopoeias and novel chemical entities have poor water solubility. To increase the solubilization and bioavailability of a poorly water soluble medication, a variety of approaches can be modified. Only when a medicine is somewhat soluble in stomach fluid and has a decent bioavailability do oral medications entirely absorb. Drug permeability via lipophilic membranes and drug solubility in an aqueous environment are two major aspects that affect bioavailability (Kumar and Singh, 2013; Vemula *et al*., 2010).

The most effective method for improving a drug's water solubility and resolving issues with organic solvents is the hydrotropic solubilization process. The term hydrotropic agent was first introduced by Neuberg (1916) to designate anionic organic salts which, at high concentrations, considerably increase the aqueous solubility of poorly soluble solutes. Hydrotropy is a solubilization phenomenon whereby addition of a large amount of the second solute results in an increase in the aqueous solubility of another solute. However, the term has been used in the literature to designate non-micelle-forming substances, either liquids or solids, organic or inorganic, capable of solubilizing insoluble compounds (Patil *et al*., 2021; Dhapte and Mehta, 2015).

The most often utilised hydrotropic substances include sodium salicylate, sodium benzoate, nicotinamide, urea, sodium ascorbate, sodium ascorbate, sodium citrate, and sodium acetate. Thiourea has been used to enhance the solubility of medications that are poorly soluble in water. Other organic solvents like methanol, chloroform, and alcohol have also been used to solubilize drugs that are poorly soluble in water. Organic solvents have a number of drawbacks, including increased cost, toxicity, pollution, and mistake in analysis caused by volatility (Choudhary & Nayal, 2019; Maheshwari *et al*., 2010). This study's main goal was to create a simple ecofriendly method development & validation for procedures for estimation of aprepitant using hydrotropy.

MATERIALS & METHODS:

Chemicals:

Sodium acetate, Urea, Sodium Citrate, Sodium Benzoate, Ammonium Acetate was obtained from Loba Chemical Pvt Ltd (Mumbai, India). Ethanol, methanol and water obtained from Merck Ltd, Mumbai, India. All solvents and reagents were of analytical grade.

Solubility:

Solubility of Aprepitant was determined at 25±1°C. Accurately weighed 10 mg Aprepitant was added in different 10 ml volumetric flask containing different solvent and placed at mechanical shaker for 8 hrs. After 8 hrs filter both solution were filtered through whatman filter paper No. 41. The filtrates were diluted suitably and analyzed visually.

Determination of solubility enhancement by UV/ Vis. Spectroscopy:

Solubility studies were performed in distilled water 2M Sodium acetate, 8M Urea, 2M Sodium Citrate, 2M Sodium Benzoate, 2M Ammonium Acetate, 2M Sod. Citrate, 2M Sodium acetate: 2M Sodium Benzoate, 2M Urea: 2M Sodium acetate, 2M Sodium citrate: 8M Urea, 2M Sodium citrate: 8M Urea, 2M Ammonium Acetate: 2M Sod. Citrate at room temperature (25 ± 2^0C). An excess amount of drug was added to 100ml of solvent in screw-capped glass vials; these were mechanically shaken for 48 hours at 25°C until equilibrium was achieved. Aliquots were withdrawn, filtered through a membrane filter (0.45µ) and spectrophotometrically analyzed for solubility.

Selection of wavelength for linearity:

Solution of 10 µg/ml Aprepitant were prepared separately the solutions were scanned in the spectrum mode from 200 nm to 400 nm. The maximum absorbance of Aprepitant was observed at 264 nm respectively. Aprepitant showed linearity in the concentration range of 10-50 µg/ml Calibration curve was plotted, absorbance versus concentration.

RESULTS & DISCUSSION:

The Solubility results showed that the drug aprepitant was freely soluble in 2M Sodium acetate: 2M Sodium Benzoate (1:1). Also, remarkable 15-fold increase in solubility of aprepitant was seen with this combination.

The results of solubility enhancement of aprepitant using UV-VIS spectroscopy are as follows. 2M Sodium acetate: The solubility of aprepitant was enhanced 3-fold when dissolved in 2M sodium acetate solution. 8M Urea: Aprepitant showed a 4-fold increase in solubility when dissolved in 8M urea solution. 2M Sodium Citrate: The solubility of aprepitant was enhanced 3-fold when dissolved in

2M sodium citrate solution. 2M Sodium Benzoate: Aprepitant exhibited a 4-fold increase in solubility when dissolved in 2M sodium benzoate solution. 2M Ammonium Acetate: Aprepitant showed a significant 7-fold increase in solubility when dissolved in 2M ammonium acetate solution. 2M Sod. Citrate: Aprepitant exhibited an 8-fold increase in solubility when dissolved in 2M sodium citrate solution. 2M Sodium acetate: 2M Sodium Benzoate (1:1): The combination of 2M urea and 2M sodium acetate in equal proportions resulted in a 3-fold increase in solubility. 2M Sodium citrate: 8M Urea (1:1): The combination of 2M sodium citrate and 8M urea in equal proportions resulted in a 4-fold increase in solubility. 2M Sodium citrate: 8M Urea (1:1): The combination of 2M sodium citrate and 8M urea in equal proportions resulted in a 6-fold increase in solubility. 2M Ammonium Acetate: 2M Sod. Citrate (1:1): The combination of 2M ammonium acetate and 2M sodium citrate in equal proportions resulted in an 8-fold increase in solubility

The maximum absorbance of Aprepitant was observed at 264 nm respectively. The linearity results indicate that aprepitant was entirely soluble in 2M Sodium acetate: 2M Sodium Benzoate (1:1) and the graph is linear. The rate of solubility increases as the graph becomes more linear. Further at recovery level of 120% the % recovery obtained was 99.32±0.704. The repeatability precision was noticed as 99.416±0.107. The precision in reproducibility of result was estimated to be 99.34±0.111. The % RSD in Day to day & analyst to analyst was estimated as 99.06±0.110 and 98.98±0.233 respectively. The analysis of aprepitant tablet with 80 mg label claim showed that actual drug amount as 79.45 mg. So, the % label claim becomes 99.31. Also, the S.D & 5 R.S.D value revealed to be 0.225 &0.341 respectively.

Table 1: Solubility of drug in different solvents

S. No.	Solvents	Solubility
		Aprepitant
1	Water	-+
2	Hot water	-+
3	Cold water	-+
4	2M Sodium acetate	+
5	8M Urea	+
6	2M Sodium Citrate	+
7	2M Sodium Benzoate	+
8	2M Ammonium Acetate	++
9	2M Sod. Citrate	++
10	2M Sodium acetate: 2M Sodium Benzoate (1:1)	+++
11	2M Urea:2M Sodium acetate (1:1)	+
12	2M Sodium citrate:8M Urea (1:1)	+
13	2M Sodium citrate:8M Urea (1:1)	+
14	2M Ammonium Acetate: 2M Sod. Citrate (1:1)	+

(-) Insoluble, (-+) Slightly soluble, (+), Sparingly soluble (++) Soluble, (+++) Freely soluble

Table 2: Results of solubility enhancement by UV VIS. Spectroscopy

S. No.	Solvents	Solubility Enhancement (folds)
1	2M Sodium acetate	3
2	8M Urea	4
3	2M Sodium Citrate	3
4	2M Sodium Benzoate	4
5	2M Ammonium Acetate	7
6	2M Sod. Citrate	8
7	2M Sodium acetate: 2M Sodium Benzoate (1:1)	15
8	2M Urea:2M Sodium acetate (1:1)	3
9	2M Sodium citrate:8M Urea (1:1)	4
10	2M Sodium citrate:8M Urea (1:1)	6
11	2M Ammonium Acetate: 2M Sod. Citrate (1:1)	8

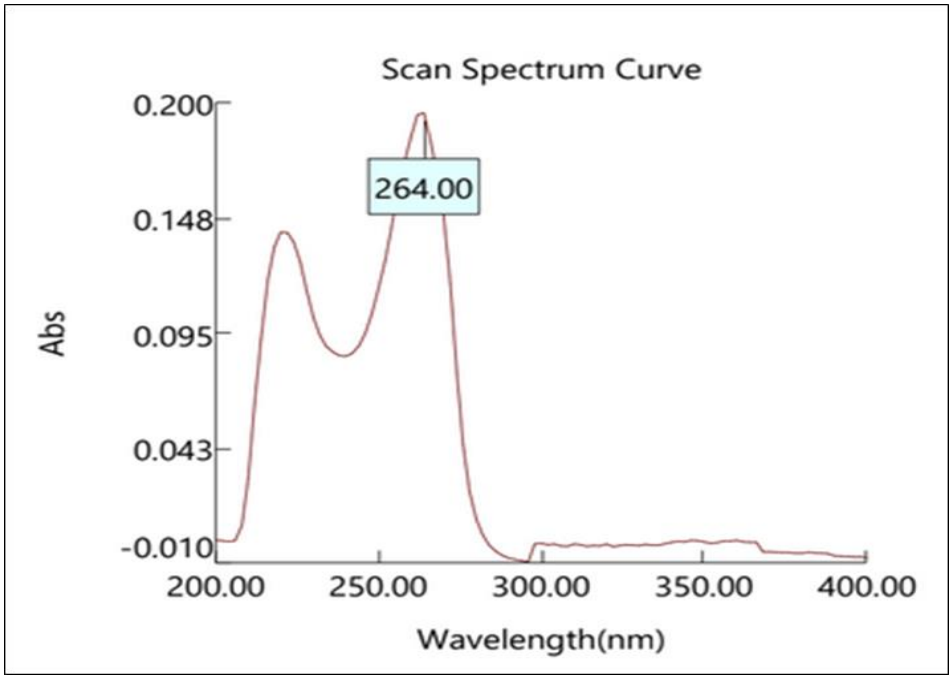

Figure: Determination of λ_{max} of Aprepitant

Table 3: Linearity of Aprepitantat λ_{max} = 264 nm

Standard Conc. (µg/ml)	Rep-1	Rep-2	Rep-3	Rep-4	Rep-5	Mean	S.D.	% RSD
10	0.158	0.157	0.156	0.157	0.156	0.157	0.001	0.005
20	0.312	0.311	0.312	0.312	0.311	0.312	0.001	0.002
30	0.458	0.457	0.456	0.457	0.457	0.457	0.001	0.002
40	0.612	0.614	0.613	0.613	0.612	0.613	0.001	0.001
50	0.758	0.757	0.756	0.756	0.758	0.757	0.001	0.001

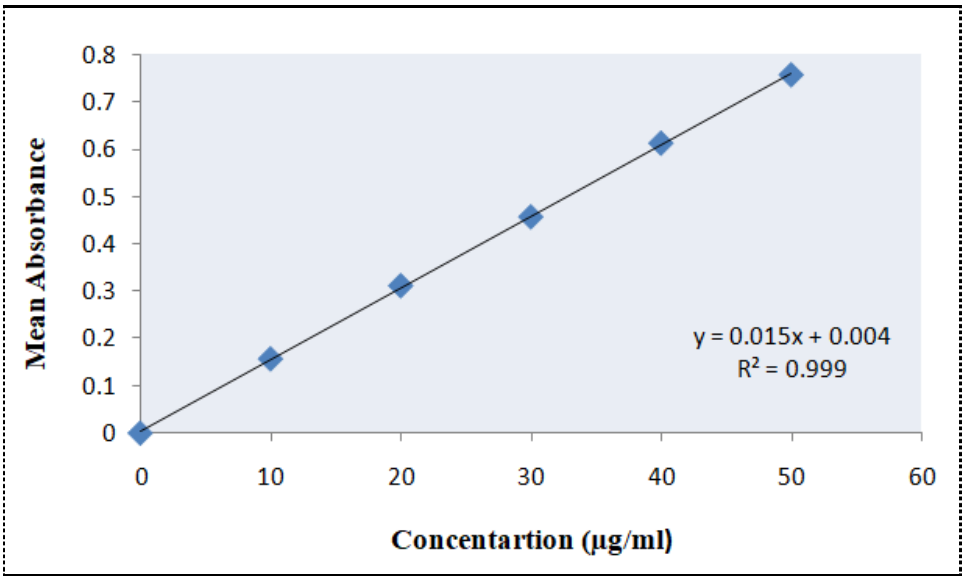

Figure: Calibration curve of Aprepitant

Validation of simultaneous equation method

Linearity

Table 4: Response Ratio of APT

S. No.	APT		
	Conc. (µg/ml)	ABS	Response Ratio
1.	10	0.157	0.016
2.	20	0.312	0.016
3.	30	0.457	0.015
4.	40	0.613	0.015
5.	50	0.757	0.015

Accuracy

Table 5: Results of recovery studies on marketed formulations

Recovery Level %	% Recovery (Mean±SD)*
	APT
80	98.95±0.547
100	99.12±0.404
120	99.32±0.704

Precision

Table 6: Results of validation

Parameter		
		APT (Mean±SD)*
Precision (%R.S.D.)*	Repeatability	99.416±0.107
	Day to Day	99.06±0.110
	Analyst to Analyst	98.98±0.233
	Reproducibility	99.34±0.111

*Average of five determination

Analysis of tablet sample

Table 7: Analysis of tablet sample

Drug	Label claim (mg)	Amount found (mg)	Label claim (%)	S.D.	% RSD
APT	80	79.45	99.31	0.225	0.341

CONCLUSION:

The newly developed Hydrotropic Solubilization process has been successfully used to improve the solubility of drug that is weakly aqueous soluble aprepitant is accurate and exact. The maximum enhancement in solubility was observed in 2M Sodium acetate: 2M Sodium Benzoate (1:1) Quantitative estimation is carried out by using UV Visible spectrophotometer. Validation parameters like Range, Linearity and Assay are carried out. As the solubility of a drug increases, so does its bioavailability, resulting in an increase in the medicine's efficiency. For a broader area of research, Accuracy, precision, repeatability, and reproducibility are some of the validation parameters can be used.

REFERENCES:

1. Kumar P, Singh C. A study on solubility enhancement methods for poorly water soluble drugs. American Journal of Pharmacological Sciences. 2013;1(4):67-73.
2. Vemula VR, Lagishetty V, Lingala S. Solubility enhancement techniques. International journal of pharmaceutical sciences review and research. 2010 Nov;5(1):41-51.
3. Patil MR, Ganorkar SB, Patil AS, Shirkhedkar AA, Surana SJ. Hydrotropic solubilization in pharmaceutical analysis: Origin, evolution, cumulative trend and precise applications. Critical reviews in analytical chemistry. 2021 May 7;51(3):278-88.
4. Dhapte V, Mehta P. Advances in hydrotropic solutions: An updated review. St. Petersburg Polytechnical University Journal: Physics and Mathematics. 2015 Dec 1;1(4):424-35.
5. Dhapte V, Mehta P. Advances in hydrotropic solutions: An updated review. St. Petersburg Polytechnical University Journal: Physics and Mathematics. 2015 Dec 1;1(4):424-35.
6. Choudhary AN, Nayal S. A review: Hydrotropy a solubility enhancing technique. Pharma Innovation J. 2019;8(4):1149-53.
7. Maheshwari RK, Rajput MS, Sharma S, Nair V. New spectrophotometric determination of hydrochlorothiazide in tablets using mixed hydrotropic solubilization technique. Der Pharmacia Lettre. 2010;2:70-4.