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A NOVEL QUANTITATIVE ESTIMATION OF POORLY WATER SOLUBLE DRUG ATORVASTATIN BY USING HYDROTROPIC SOLUBILIZATION TECHNIQUE

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ABSTRACT

In the present research, hydrotropic solubility enhancement has been done helpful for soluble poorly water soluble anti hypertensive drug is atorvastatin. The hydrotropic substance is urea. This technique is reliable and simple. In the present study more than 2 folds solubility enhanced when compared to distilled water alone. The urea was used in different concentrations 10, 20,30,40,50 and 60mg. The drug and hydrotropic substance ratios were 1:1, 1:2, 1:3, 1:4, 1:5 and 1:6. The hydrotropic substance (urea) did not interfered in the analysis. The hydrotropic substances are freely available, less cost, pollutant free method. The hydrotropic solubility enhancement technique is very accurate, the solubility enhancement further helpful for improve bioavialabity of drug.

Key words: Atorvastatin, Urea, Hydrotropic technique, Solubity enhancement.

INTRODUCTON

In the pharmaceutical analysis and formulation development areas solubility is most important criteria. Solubility is commonly related to bioavailability. The solubility is an important challenge in poorly water-soluble drugs[1]. Most of the newly developed drug

molecules are lipophilic in nature and poor solubility is one of the most difficult problems of these drugs. Only 8% of novel drug candidates have both highly solubility and highly permeability[2]. Various organic solvents like methanol, chloroform, alcohol, dimethyl formamide, and benzene have been used for the solubilization of poorly water soluble drugs for spectrophotometric estimations. Drawbacks of organic solvents include higher cost, toxicity, pollution, and error in analysis due to volatility.

There are various approaches for solubilization of insoluble and poorly aqueous soluble drugs. "**Hydrotropy**" is one of importent solubilization technique. Hydrotropy refers to ability of concentrated solution of compound to increase solubility of another compound[3]. The hydrotropic agents are defined as non-micelle-forming substances, either liquids or solids, organic or inorganic, capable of solubilizing insoluble compounds. Hydrotropic agents consist generally of two essential parts, an anionic group and a hydrophobic aromatic ring or ring system. The anionic group is obviously involved in bringing about high aqueous solubility, which is a prerequisite for a hydrotropic substance. On the other hand, planarity of the hydrophobic part has been emphasized as an important factor in the mechanism of hydrotropic solubilization[5, 8]. Sodium benzoate, sodium salicylate, sodium acetate, sodium ascorbate, niacinamide, sodium citrate, N,N-dimethylbenzamide (DMBA)[6], N,N-diethylnicotinamide (DENA)[6] and urea are the most popular examples of hydrotropic agents these are used for enhance the solubility of poorly aqueous soluble drugs[3]. The hydrotropic agents helpful for enhance bioavailability by improving solubility[4]. The mixed hydrotropic substances (N,N dimethyl urea and sodium citrate)[5] are effectively enhancing solubility of poorly soluble drugs. Hydrotropic solutions can be used to extract hydrophobic drugs without need of organic solvents[6, 7].

In this study, efforts were made to develop a simple, easy, safe and economic UV spectrophotometric method using hydrotropic solubilization technique for the determination of Atorvastatin in the bulk form.

MATERIALS AND METHODS

The model drug, Atorvastatin used in present study. Atorvastatin was obtained as gift sample from Suven pharmaceutical Pvt limited, Hyderabad. Methanol and other chemicals procured from Rankem industries. All chemicals were analytical grade.

Methodology

Selection of solvent

In this distilled water was used as a solvent since this technique is mainly employed to increase the solubility of poorly water soluble drugs.

Preparation of Standard stock solution

Standard atorvastatin of 10mg was accurately weighed and transferred to 10ml volumetric flask. It was dissolved properly by using 2ml of methanol and diluted to mark with distilled water to obtain concentration of 1mg/ml. This solution was used as standard stock solution.

Calibration graph

From the standard stock solution (1000 µg/ml) 0.5, 1, 1.5, 2, 2.5 ml was transferred into five 10 ml volumetric flask and make up to the volume with the distilled water. The absorbance of different concentration solutions were measured at 246 nm against blank. The calibration curve was plotted using concentration versus absorbance[9-11]. The curve obtained was linear with the concentration range of 50-250 µg/ml. The values were given in the following table 1.

Table-1 Linearity of Atorvastatin by UV

S.No.	Concentration (µg/ml)	Absorbance
1	50	0.309
2	100	0.459
3	150	0.604
4	200	0.773
5	250	0.923

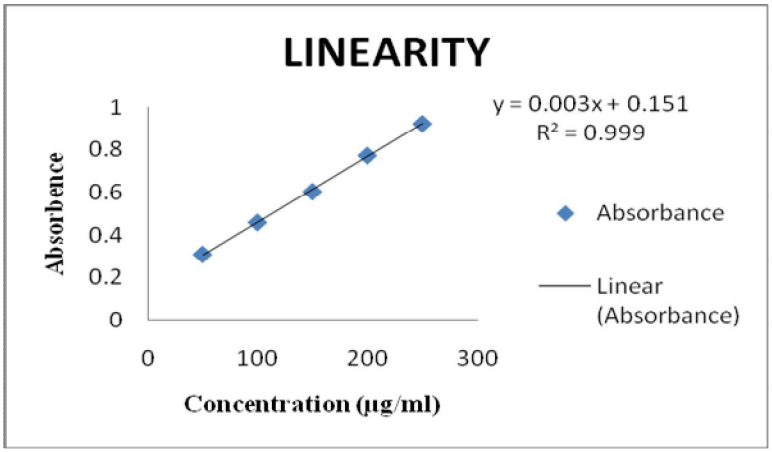

Fig-1 Linearity graph

Solubility analysis with variation amount of urea

The atorvastatin is poorly water soluble drug. Various methods are used for enhance solubility of atorvastatin. The solubility enhanced by methods like nanosuspension[11], microspheres[12], and self emulsifying substance[13]. The hydrotropic substance (urea) is enhancing solubility. This method is very simple convenient method. Solubility was determined with hydrotropic substance of different amounts (10, 20, 30, 40, 50 and 60mg of urea). 10 mg of Standard Atorvastatin was weighed into series of glass vials and increasing amounts of 10, 20, 30, 40, 50 and 60mg of urea was added and made the volume up to 10ml with distilled water. The samples were sonicated for 4 hrs and kept at 25°C for 24 hrs and passed through a 0.45 µm filter. Then clear solutions were analyzed spectrophotometrically at 246nm using UV-Vis Spectrophotometer (UV-201, Thermoscientific). Absorbance was extrapolated on the calibration curve to determine the unknown concentration and the solubility of each sample was calculated by using the following formula.

Drug solubility= unknown conc. from graph × Dilution factor

Then from obtained values % drug solubility was calculated.

The aqueous solubility of atorvastatin is 0.00116mg/ml at 25°C[9]. In the present investigation, solubility enhancement caused by urea was studied. The % drug solubility of at 25°C in atorvastatin presence of different amounts of urea was given in following Table-2

Table-2 Solubility study with increase in amount of urea

S.No	Amount of urea added (mg)	Drug solubility(mg)	%Drug Solubility
1	10	0.0153	0.153
2	20	0.0762	0.762
3	30	0.109	1.09
4	40	0.165	1.65
5	50	0.215	2.15
6	60	0.247	2.47

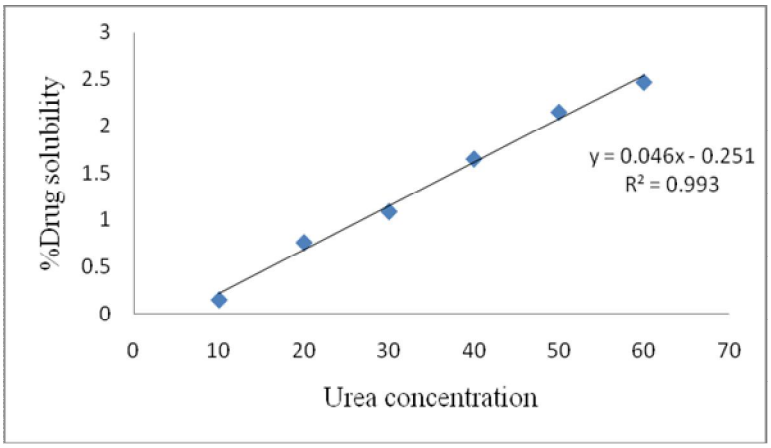

Fig-2 Linearity graph

RESULTS AND DISCUSSION

The present study indicates that the increase in Atorvastatin solubility was due to addition of Hydrotropes. Increase in amount of urea increased the solubility of the Atorvastatin in distilled water. This experimental method using a hydrotropic agent provides an alternative tool for increase in release of poorly soluble drugs in aqueous solution. Thus hydrotropic solubilization can be used for quantitative analysis, dissolution study and increase in bioavailability. Thus method provides the dynamics of the Hydrotropes in solubilization of atorvastatin. The solubility of atorvastatin was increased by increasing concentration of urea (Hydrotrope). Drug: Hydrotropic substance were taken as 1:1, 1:2, 1:3, 1:4, 1:5 and 1:6. The enhanced solubility was found to be 2.47% (0.247mg/l)

CONCLUSION

The present study was very simple and convenient method. Solubility can easily enhance by this technique. The urea is hydrotropic substance helpful for enhance aqueous solubility of poorly soluble drugs like Metronidazole, Norfloxacin, Gresiofulvin, Pioglitazone, and Riluzole etc. In all the solubility enhancement techniques Hydrotropic enhancement is very convenient, less cost effect, accurate method. The technique can also done with combination of hydrotropic substances for effective solubilization.

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