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Application of Hydrotrophy in HPLC; Hydrotrophic Solution, A Novel Cost Effective and Eco-Friendly Mobile Phase for Solubilization of Poorly Water Soluble Drugs

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ABSTRACT

Hydrotrophy is a unique molecular phenomenon that posses the ability to increase the solubility of sparingly soluble & poorly soluble drugs in water. A hydrotrophic solution can be defined as adding a solute, that is Hydrotrope, (eg: urea) to the primary one (solvent) and is used as mobile phase for HPLC. High solubility, easy availability, cost effectiveness, eco-friendly are the major advantages which makes the solubilization technique superior. Here we use paracatamol and diclofenac sodium as example to review and conclude this topic. The current review takes the readers throughout a brief summary and features of hydrotropic agents and their different advances towards HPLC technique. It provides an insight of the future perspectives concerned with HPLC and Hydrotropism.

KEYWORDS: *HPLC, Hydrotrophy, Hydrotropism, Hydrotrophic mobile phase, Solubility enhancement*

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INTRODUCTION

HPLC estimation is usually performed with the help of organic mobile phases which are volatile, harmful and expensive [1-4]. Here in the review and presently organic solvents was employed as mobile phase for the estimation of poorly water or aqueous soluble drugs (ie paracetamol & diclofenac sodium here). This is the only method reported till date by using HPLC [10-15]. Though literature surveys revealed that a few spectraphotometric[4-9], TLC[23, 24], HPTLC[16] methods were also reported for the estimation of the paracetamol & diclofenac sodium in various pharmaceutical dosage forms. But in all these reported methods volatile, expensive & toxic organic solvents are used as mobile phase. Hydrotrophy enlights the ability of a concentrated solution of a chemical compound to enhance the aqueous solubility of another compound which is usually poorly or sparingly soluble[26]. Each hydrotropic agent effectively increasing the water solubility of selected hydrotropic or aqueous insoluble drugs. Example for hydrotropic agents includes sodium salicylate, sodium caprylate, sodium citrate, sodium ibuprofen, sodium gluconate, lysine, urea, nicotinamade etc[17-20]. So here we study to develop and validate accurate, sensitive, simple, cost-effective, eco-friendly method for the estimation of poorly water soluble drugs taking paracetamol & diclofenac by using hydrotropic solution (5% urea solution) as mobile phase.

Advantages of Hydrotropic solubilisation

- Solvent character is independent of pH, has high selectivity and does not require emulsification. It only requires mixing the drug with hydrotrope in water. So hydrotrophy is known to be superior to other solubilisation methods such as micellor solubilization, miscibility, co-solvency, salting etc.
- Hydrotrophy does not require chemical modification of hydrophobic drugs, preparation of emulsion system or use of organic solvents.
- Safe, economic, user friendly & environment friendly method.

The present investigation enlights the application of hydrotrophy for HPLC estimation of selected sample or model drugs in comparison to normal Indian pharamacopoeial method (that is using specific organic solvents as mobile phase). Here paracetamol & diclofenac sodium are taking as model drugs for estimation by HPLC using 2% urea solution (Hydrotropic solution) as mobile phase.

Materials & Methods

Materials

- The bulk drug samples of paracetamol[RS] & diclofenac sodium[RS] to prepare standard samples of paracetamol & diclofenac for HPLC estimation.
- HPLC graded water
- Mobile phase suggested by Indian pharmaceutical method (eg :methanol)
- Hydrotrope (analytical from) for preparing hydrotropic mobile phase - 2% urea

Method

High performance liquid chromatography of the drugs were carried out on HPLC using methanol as mobile phase, followed by using 5% urea solution as mobile phase. Obtain the respective solubility curves on both cases for solubility studies and area under retension time (Rt) curve to findout the quanitity of each drug recovered in both cases, which also enlights the impact on solubilisation caused by hydrotrope urea.

1. Determination of Solubility

Solubility of paracetamol & diclofenac sodium were determined at 28 ± 1°C. An excess amount of drugs was added to a screw capped 30 ml glass vials containing increasing amount of urea (10, 20, 30, 40, 50, & 60 mg) and with distilled water made the voulme upto 10 ml. The vials were shaken mechanically for 12 hrs at 28 ± 1°C in a mechanical shaker. This solution were allowed to equilibrate for net 24 hrs, centrifused for 5 minute at 200 rpm, supernatant was filtered through what man filter paper #41 & analyzed spectrophoto metrically at 286 nm, Absorbance was extrapolated on the calibration curve to determine the unknown concentration and thereby the solubility of each sample was calculated. The same procedure was done using methanol as solvent, compare the solubilities in both cases using the following equation.

Solubility = unknown concentration from graph * dilution factor

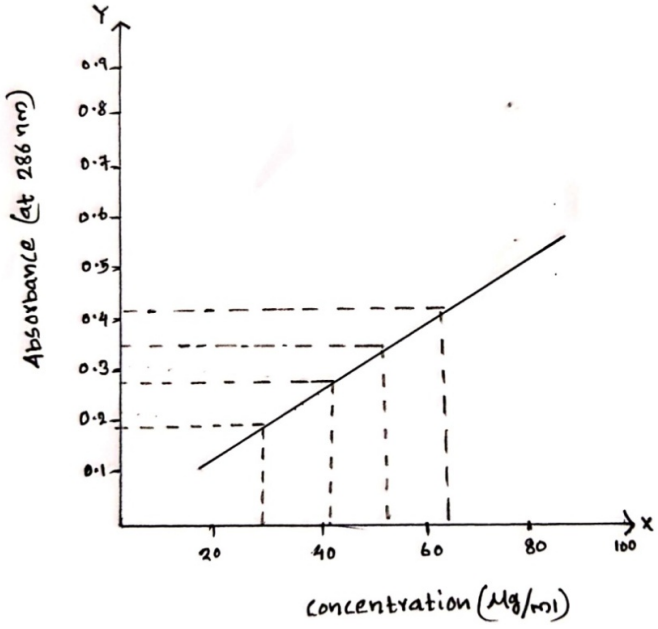

Fig (a): Calibration curve for paracetamol solubility in methanol as suggested by IP.

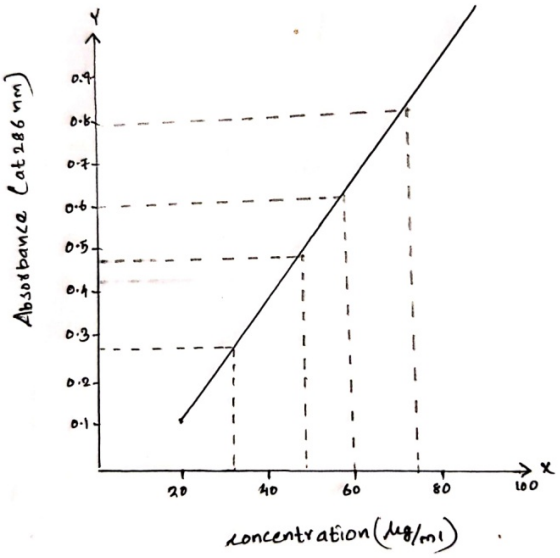

Fig (b): calibration curve for paracetamol solubility in urea solution as suggested by this article

Here from the fig (b) it clears that absorbance determined in using each dose of urea is greater than the corresponding absorbance while methanol is used in fig (a).It implies that the unknown concentrations determined by extrapolating the corresponding absorbance in fig (b) are also greater and thus it clearly seems that there were tremendous increase in solubility of paracetamol & likewise diclofenac sodium while using hydrotrope (urea) as solvent or solubilising agent as compared to solublisation using methanol solvent as suggested by Indian pharmacopoeia.

2. Determination of quantity recovered

Filled 5% urea solution in mobile phase reserviour, the detection wavelength was set at 268 nm, fixed volume of 20 micro litre. Sample drug mixture (325 mg Paracetamol+ 50 mg Diclofenac sodium) was injected to the HPLC column and the components eluted from the system were moniterd for a run time of 10 minute, repeat the same with methanol solution as mobile phase. Two sharp peaks for paracetamol & diclofenac sodium were appeared with retension time 3.272 and 1.772 minutes respectively, findout the area under curve in both cases, compared and identified that area under curve is greater when using urea solution as mobile phase than while using methanol solution as mobile phas, which confirms the highest percentage recovery and which is only due to solubility enhancement of the drug in urea solution.

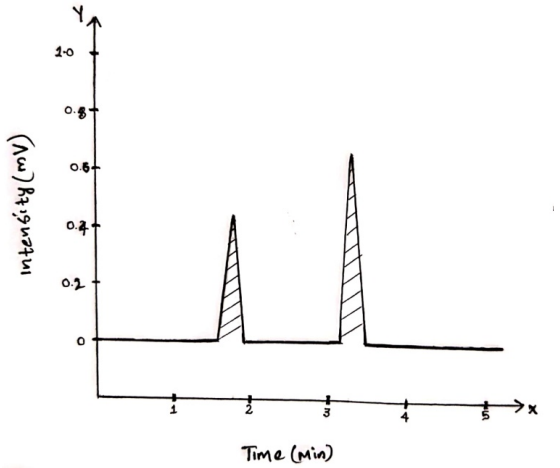

Fig (c): Chromatogram obtained using organic methanol as mobile phase (as suggested by IP)

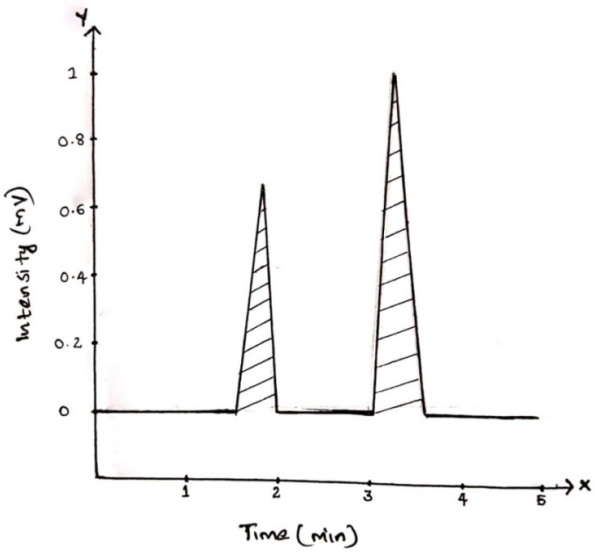

Fig (d): chromatogram obtained using urea 2% solution as mobile phase

SUMMARY OF RESULTS

The proposed method well confirms the effect of hydrotropic solution as mobile phase in HPLC, which is quite safe, cost effective and eco-friendly. 5% urea solution was found to be satisfactory in all wise and gives sharp and accurate peaks for paracetamol and diclofenac with retention time 3.272 & 1.772 minutes respectively. The Rt plot was given in figure (c) & figure (d) and percentage survey were also found in both cases confirms more recovery in using hydrotropic solution in HPLC study. It also found solubility difference between methanol and 2% urea solution as solvents & it confirms more solubility in urea solution.

CONCLUSION

It may thus concluded that the proposed method of HPLC using hydrotropic solution as mobile phase is new, cost effective, simple, safe & eco friendly. This method can be copied on other drugs as were using varieties of hydrotropes available in singule or mixed form. The proposed method already used in other analytical techniques like TLC, HPTLC, spectroscopy, etc. Thus it can be developed as a novel tool to eliminate the use of expensive, toxic, pollutant organic solvents in future.

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