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RESEARCH ARTICLE

Eco-friendly Spectrophotometric analysis of Mefenamic acid (poorly water-soluble drug) using the mixed solvency concept

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Abstract

Objectives: To investigate an eco-friendly method to enhance the solubility of Mefenamic acid. The present investigation was to employ these hydrotropic solutions to extract the drugs from their dosage forms, precluding the use of costlier and harmful organic solvents. **Methodology:** Mefenamic acid was analyzed by using UV Visible spectrophotometer (Model 1800, Shimadzu), and its solubility (poorly water-soluble drug) measured by mixed solvency method. Sodium caprylate solution was used as a hydrotropic solubilizing agent. **Findings:** The solubility of the Mefenamic acid drug in water was very low at about 0.2 mg/ml and the solubility of Mefenamic acid in the 20% sodium caprylate solution was 10 mg/ml. The value of percentage estimation obtained was from 98.6 (tablet II) to 98.8 (tablet I). This value is obtained near to 100% hence, we can say that the proposed method is correct. Standard deviation (0.173 to 0.346), percentage coefficient of variation (0.175 to 0.350) and the value of standard error (0.101 to 0.202) are also very low to validate the accuracy of the proposed method. **Novelty:** Mixed solvency concept can be utilized for spectrophotometric estimation of poorly water-soluble drugs from their bulk drug samples to avoid the use of organic solvents that provide a new, economical, environmentally friendly, safe, and reliable analytical mechanism.

Keywords: Mixed solvency; solubility; hydrotropic; mefenamic acid; sodium caprylate

1 Introduction

Solubility is an important parameter in drug formation. Many drugs have very low solubility in water. Hence, it is necessary to increase the solubility of these drugs [1,2]. Mefenamic acid is a non-steroidal anti-inflammatory drug and its solubility in water is very low at about 0.2 mg/ml [3]. The pollution and toxicity caused by most of the organic solvents are a big challenge hence researcher is doing work to give an eco-friendly solution for this challenge [4,5]. The mixed solvency concept is an effective technique for the enhancement of the solubility of poorly water-soluble drugs by using a solubilizing technique, we can preclude the use of organic solvents, which are more costly, toxic, and harmful to our environment [6–9]. The solubility of the drug can be

increased in many ways but most methods require chemical or physical changes in the drug structure hence this proposed method increases the solubility of the drug[10–12]. This method also does not require chemical and physical changes in the drug[13]. The mixed solvency concept is an eco-friendly method. In this method, hydrotropic agents are used[14]. Hydrotropic agents are ionic organic salts with the help of these the solubility of any solute can be improved. Sodium acetate, sodium benzoate, urea, sodium caprylate, etc. are some examples of hydrotropic agents[15]. According to the mixed solvency theory, all matters of hydrotropic agents, whether it is liquid, gas, or solid, will have the properties of solubility ability[16–18]. In drug analysis, some organic solvents like methyl alcohol, toluene, benzene, chloroform, etc. are used to dissolve the drug which is very expensive and toxic[19–23]. The organic solvent is divided into three classes Class I, Class II, and Class III. Class III organic solvents are less harmful than Class I and Class II[24]. These organic solvents are not employed in the mixed solvency concept thus, it is an eco-friendly technique[25]. The main objective of this study was to investigate an eco-friendly method to enhance the solubility of mefenamic acid. The present investigation was to employ these hydrotropic solutions to extract the drugs from their dosage forms, precluding the use of costlier and harmful organic solvents. In this study, we used sodium caprylate to increase the solubility of mefenamic acid. The mixed solvency concept can be utilized for spectrophotometric estimation of poorly water-soluble drugs from their bulk drug samples to avoid the use of organic solvents that provide a new, economical, environmentally friendly, and safe analytical mechanism.

2 Procedure

Mefenamic acid was collected from the Brawan Pharmaceuticals, Faridabad, India. Mefenamic acid tablets were obtained from Indore's local market from two separate firms (Alkem laboratory ltd. and Indchemie health specialties Pvt ltd.). Analytical-grade chemicals were utilized.

2.1 Instrumentation

For spectrophotometric estimation, the UV Visible spectrophotometer (Model 1800, Shimadzu) was utilized.

2.2 Investigations of preliminary solubility

Suitable quantities of the mefenamic acid (drug) were added in a 25 ml capacity bottle including 10 ml of 20% (w/v) sodium caprylate solution. After applying the aluminum seal, the bottle was shaken for twelve hours in an orbital flask shaker. After 24 hours, filtration was done with the help of Whatman filter paper. 1 ml of saturated filtrate was diluted to 1000 ml with distilled water and absorbance was noted at 319 nm against reagent blank. Solubility was measured by using the obtained absorbance and absorbance was given in Table 1.

2.3 Determination of Solubility improvement

The solubility improvement ratio was determined and given in Table 1.

The following formula was used for the determination of the solubility improvement ratio:

Solubility improvement ratio = solubility in hydrotropic solution/ solubility in distilled water

2.4 The preparation of the drug's calibration curve (mefenamic acid)

100 mg of mefenamic acid standard drug and 90 ml of 20% (w/v) of sodium caprylate solution were transferred to a 100 ml volumetric flask. The flask was shaken until the drug is completely soluble. After completely dissolving the drug, enough quantity of sodium caprylate solution was added to make up the volume up to 100 ml. Standard solutions of 5, 10, 15, 20, and 25 μg/ml were prepared from this stock solution. The absorbance of these solutions was noted at 319 nm against the reagent blank and given in Table 2. The statistical description of this absorbance is shown in Table 3. A standard curve must be done in triplicates.

2.5 Proposed Research Approach

50 mg drug equivalent tablet powder (I) and an aqueous solution of 90 ml sodium caprylate were transferred to a 100 ml volumetric flask. The flask was shaken rapidly for 10 minutes and an aqueous solution of sodium caprylate was added to make up the volume up to 100 ml. To extract tablet excipients the solution was filtered with the help of Whatman filter paper. The absorbance was noted at 319 nm against reagent blank, after dilution of filtrate with distilled water (2 ml to 100 ml). The same procedure was performed with the tablet (II) and results were reported in Table 4.

2.6 Recovery studies

For recovery studies, the drug content was determined by the proposed method by adding 20 mg and 40 mg of the standard mefenamic acid drug separately in the tablet powder equivalent to 50 mg of the drug. The same procedure was repeated for a tablet (II) and results were noted in Table 5.

3 Results and Discussion

Table 1. Solubility of mefenamic acid (drug) in hydrotropic solution

Solvent	Absorbance	Solubility in mg/ml	Solubility improvement ratio
Hydrotropic solution (20% of sodium caprylate solution)	0.377	10	10/0.2=50

Table 2. Data of analysis curve

1	5	0.172
2	10	0.374
3	15	0.587
4	20	0.788
5	25	0.976

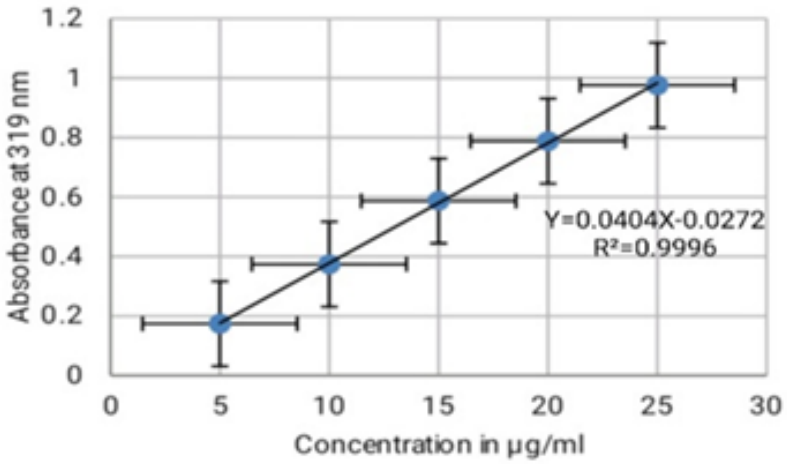

Fig 1. Calibration curve of Mefenamic acid with standard error bars

Table 3. Statistical description of Absorbance shown in table 2

Mean	0.5794
Standard deviation	0.319776172
Standard error	0.143008252

Table 4. Analysis of mefenamic acid tablet with statistical evaluation (n=3)

Tablet of mefenamic acid drug	Claimed amount of drug mg/tablet	% drug calculated (mean ± Standard Deviation)	% coefficient of variation	Standard error
I (Meftal P tab) Blue cross lab. PVT. Ltd.	100	98.8± 0.173	0.175	0.101
II (Mefacid) Floreat Medica Pvt. Ltd.	100	98.6± 0.346	0.350	0.202

Table 5. Statistically analyzed results of recovery experiments (n=3)

Tablet of mefenamic acid drug	Amount of drug in mg presented in preliminarily investigated tablet powder	Quantity in mg of the standard drug (spiked)	% drug calculated (mean ± Standard Deviation)	% coefficient of variation	Standard error
I (Meftal P tab) Blue cross lab. PVT. Ltd.	50	20	99.3±0.108	0.108	0.062
I (Meftal P tab) Blue cross lab. PVT. Ltd.	50	40	98.5±0.519	0.526	0.303
II (Mefacid) Floreat Medica Pvt. Ltd.	50	20	98.0±0.108	0.110	0.063
II (Mefacid) Floreat Medica Pvt. Ltd.	50	40	97.8±0.101	0.176	0.101

In the previous study done by Swathi et al.[3], the solubility of mefenamic acid (at the temperature of the room) was reported to be 0.2 mg/ml in the distilled water. In the present study, the solubility of mefenamic acid in the 20% of sodium caprylate solution was found to be 10 mg/ml. Table 4 shows the value of percentage estimation obtained from 98.6 (tablet II) to 98.8 (tablet I). This value is obtained by spectrophotometric analysis with the help of the mixed solvency technique. This value is obtained near 100% hence, we can say that the proposed method is correct. Standard deviation (0.173 to 0.346), percentage coefficient of variation (0.175 to 0.350) and the value of standard error (0.101 to 0.202) are also very low hence we can say that the proposed method is accurate.

Table 5 shows the value of the recovery studies that have been achieved from 97.8 to 99.3. This value is also close to 100 which shows the precision of the proposed method, as well as the standard deviation (0.101 to 0.519), percentage coefficient of variance (0.108 to 0.526), and the standard error (0.063 to 0.303) value also very low, which shows the validation of the proposed method.

In earlier research, the solubility of many drugs has been increased by this method, but this method has not yet been used to increase the solubility of the mefenamic acid drug. In previous research micellar solutions of several surfactants were used to increase the solubility of mefenamic acid. In this research, we used sodium caprylate solution to increase the solubility of mefenamic acid. In this research, we increased the solubility of mefenamic acid by about 50 times (shown in Table 1) with the help of the mixed solvency method. Also, this is an eco-friendly method because no organic solvent has been used in this method.

Currently, due to their unique characteristics such as fast availability, good recovery, absence of fire risks, and eco-friendly design, hydrotropic solutions have strong industrial needs. In the pharmaceutical sector, a mixed solvency technique can be assigned efficiently. It can be utilized for spectrophotometric estimation of poorly water-soluble drugs from their bulk drug samples to avoid the use of organic solvents that provide a quick, economical, environmentally friendly, safe, and reliable analytical mechanism.

4 Conclusion

Different technologies have been used for the enhancement of the solubility of poorly water-soluble drugs. It may be assumed that it is possible to use the mixed solvency technique to replace the use of an organic solvent that is more expensive and harmful for our atmosphere. The solubility enhancement for mefenamic acid in the hydrotropic solution was found to be more than 50 times as compared to the distilled water. The results concluded that the developed spectrophotometric method for the determination of mefenamic acid in bulk and formulations using 20% of sodium caprylate as a hydrotropic agent is reliable, accurate, precise, and eco-friendly. This method can be successfully utilized in the routine analysis of mefenamic acid in bulk drug and dosage formulations. For the spectrophotometric study of other poorly water-soluble drugs avoiding the use of organic solvents, there is a further scope of a sodium caprylate solution as a hydrotropic solubilizing agent.

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