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APPLICATION OF MIXED HYDROTROPY TO ANALYZE PIROXICAM TABLETS SPECTROPHOTOMETRICALLY

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ABSTRACT

A new, simple, safe, accurate and reproducible spectrophotometric analytical method was developed for the quantitative estimation of piroxicam in solid dosage form by mixed hydrotropic agents. The enhancement of solubility of piroxicam was more than 19 fold in mixed hydrotropic solution (20% N,N dimethyl urea and 20% sodium citrate solution) as compared to solubility in distilled water. Therefore, it was thought worthwhile to solubilize this poorly water soluble drug from fine powder of its tablets by this novel mixed hydrotropic solubilization technique and then carry out its spectrophotometric estimation at 254 nm (20% N,N dimethyl urea and 20% sodium citrate being non-interfering in the estimation). The results of the analysis were validated statistically and by recovery studies & its follows Beer's law in concentration range of 6-30 mcg/ml. The percent label claims and percent recoveries estimated were close to 100 with low values of standard deviation, percent coefficient of variation and standard error. Thus the statistical data proved the accuracy, reproducibility and precision of the proposed method providing additional advantage of being cost effective and environment friendly. The mixed hydrotropic agents used did not interfere in the analysis.

Keywords: Mixed hydrotropy, Piroxicam, Solubilization, N, N Dimethyl Urea, Sodium Citrate.

INTRODUCTION

Piroxicam is a member of the oxicam group of nonsteroidal anti-inflammatory drugs (NSAIDs). The chemical name for piroxicam is 4-hydroxyl-2-methyl-N-2-pyridinyl-2H-1, 2-benzothiazine-3-carboxamide 1,1-dioxide (Figure 1) [1]. It is indicated for acute or long-term use in the relief of signs and symptoms of osteoarthritis and rheumatoid arthritis. According to the Biopharmaceutic Drug Classification System (BCS) piroxicam is a class-II drug, characterized by low solubility–high permeability. Drug dissolution in vivo is the rate-controlling step in drug absorption [2, 3]].

A hydrotrope is a compound that solubilises hydrophobic compounds in aqueous solutions. Solubility enhancement is one of the advantages of hydrotropes, enhance in solubility is obtained by adding a second solute (hydrotropic agents) to increase the aqueous solubility of weakly soluble solutes and it is a molecular phenomenon [4, 5]. 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. Hydrotropic solubilization method involves cooperative intermolecular interaction with several balancing molecular forces, rather than either a specific complexation event or a process dominated by a medium effect, such as co-solvency or salting-in. Hydrotropic agents have been observed to enhance the aqueous solubility of poorly water-soluble drugs [6-10].

Mixed hydrotropic solubilization technique is the experience to increase the solubility of poorly water-soluble drugs, using blends of hydrotropic agents [10-13]. This technique can provide additive or synergistic enhancement effect on solubility of poorly water-soluble drugs. Utilization of this method in the formulation of dosage forms made of water insoluble drugs can also reduce the concentration of individual hydrotropic agents, in order to minimize the side effects (in place of using a

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large concentration of one hydrotrope, a blend of several hydrotropes can be employed in much smaller concentrations, reducing their individual toxicities). The objective of the present study is to explore the application of mixed hydrotropic solubilization technique to analyze piroxicam tablets spectrophotometrically [13-17]. In the present work, Piroxicam, a non-steroidal anti-inflammatory agent was selected as a model drug which is a BCS class II drug (highly permeable and low soluble).

EXPERIMENTAL WORK

Materials

All the chemicals and solvents used were of analytical grade. Piroxicam was procured from Sun Pharmaceuticals Ltd, Mumbai, India. N, N Dimethyl urea (Figure 2) and Sodium citrate (Figure 3) were obtained from LobaChemie Private Limited. The tablets of Piroxicam were purchased from the local market Modact 20mg **(**Merind pharmaceutical Ltd) and Dolokam DT 20 mg Cadila).

Apparatus

All absorbance measurements were performed using a Shimadzu UV-1800 UV-VIS spectrophotometer achieves a resolution of 1 nm, provided with 1cm matched quartz cells.

Preparation of calibration curve

50 mg of piroxicam bulk drug was solubilized with 80 ml mixed hydrotropic solution (20% N,N dimethyl urea and 20% sodium citrate) and then diluted to 100 ml with distilled water to obtain various dilutions (6, 12, 18, 24, 30 µg/ml). A linear relationship was observed, measuring their absorbances at 358 nm against respective reagent blanks.

Preliminary solubility studies of drug

Determination of solubilities of the drug in distilled water and mixed hydrotropic solution (20 % N, N dimethyl urea and 20% sodium citrate) were carried out at room temperature. Sufficient excess amount of drug was added to screw capped 30 ml glass vials containing hydrotropic. solutions and distilled water, separately. The vials were shaken mechanically for 12 hrs in orbital flask shaker. The solutions were allowed to equilibrate for next 24 hrs and then contrifuged for 5 minutes at 2000 rpm. The supernatant of each vial was filtered through Whatman filter paper # 41.Filtrates were diluted with distilled water suitably and absorbances of solutions were noted against respective reagent blanks to determine the solubilities. Enhancement in the solubility of piroxicam in mixed hydrotropic solution (20% N,N dimethyl urea and 20% sodium citrate) was more than 19-fold as compared to solubility in distilled water.

Analysis of piroxicam tablets using mixed hydrotropic solution (20% N,N dimethyl urea and 20% sodium citrate)

Twenty tablets of piroxicam (formulation-I) were weighed and ground to fine powder. Accurately weighed powder sample equivalent to 50 mg of piroxicam was transferred to 100 ml volumetric flask containing 80 ml of mixed hydrotropic solution (20% N, N dimethyl urea and 20% sodium citrate) . The flask was shaken for about 10 min & volume was made up to the mark with distilled water. The solution was filtered through Whatman filter paper # 41. The filtrate was diluted with distilled water and analyzed on UV spectrophotometer against reagent blank. Drug content of tablet formulation was then calculated. Same Procedure was followed for formulation-II.

Recovery studies

To evaluate the validity and reproducibility of the proposed method, recovery experiments was carried out. For recovery studies 10 & 20 mg of piroxicam pure drug was added to the pre-analyzed tablet powder equivalent to 50 mg piroxicam. Procedure of analysis were same using mixed hydrotropic solution (20% N, N dimethyl urea and 20% sodium citrate) . Percent recoveries were calculated.

Solubility determination studies indicated that enhancement in aqueous solubility of piroxicam in mixed hydrotropic solution (20% N,N dimethyl urea and 20% sodium citrate) was more than 19 fold as compared to solubility in distilled water. It is evident from Table-1 that the mean percent label claim estimated were 100.48 and 98.91 for formulation I & II respectively. The mean percent label claim are very close to 100 with low value of standard deviation, percent coefficient of variation and standard error showing the accuracy of the proposed method.

Accuracy, reproducibility and precision of proposed method were further confirmed by percent recovery values. As evident from Table-2, the mean percent recovery values ranged from 98.48 to 100.38, the values are very close to 100, indicating the accuracy of the proposed method.

The values of standard deviation, % coefficient variation and standard error were satisfactorily low which further validated the method.

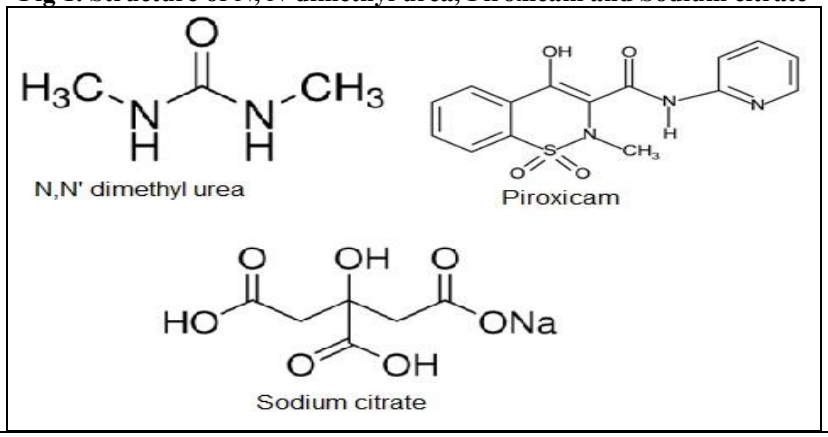
Table 1. Analysis data of commercial tablets of piroxicam with statistical evaluation (n=3).

Tablet formulation	Label claim (mg/tab)	% Label Claim estimated (mean ±SD)	% Coefficient of variation	Standard error
I	20	100.48±1.547	1.540	0.893
II	20	98.91±1.046	1.058	0.604

Table 2. Recovery studies for spiked concentration of drug added to preanalyzed tablet powder with stastical evaluation (n=3).

Tablet formulation	Drug present in preanalysed tablet powder (mg)	Pure drug added (spiked concentration) (mg)	%recovery estimated (mean)	% Coefficient of variation	Standard error
I	50	10	100.38±1.731	1.724	0.999
II	50	20	99.49±0.478	0.480	0.276
III	50	10	98.48±1.855	1.884	1.071
IV	50	20	99.28±0.859	0.865	0.496

Fig 1. Structure of N, N'dimethyl urea, Piroxicam and Sodium citrate



CONCLUSION

In pharmaceutical analysis generally organic solvents like ethanol, methanol, cyclohexane, toluene, DMSO, diethyl ether, chloroform, acetonitrile and haxane are used in spectrophotometic analysis of poorly water-soluble drugs, but these organic solvents are toxic in nature, costlier and responsible for pollution. Inaccuracy in spectrophotometric estimation due to volatility is another drawback of organic solvents. Mixed hydrotropic solution (20% N, N dimethyl urea and 20% sodium citrate) does not interfere in the method, therefore other poorly water-soluble drugs can also be estimated above 245 nm by similar mixed hydrotropy avoiding the use of organic solvents. It is, thus, concluded that the proposed method is new, simple, cost-effective and precise and can be employed in the routine analysis of piroxicam tablets. There is good scope for other poorly water-soluble drugs which may be tried to get solubilized by suitable hydrotropic agents to carry out their spectrophotometric analysis precluding the use of costlier and unsafe organic solvents.

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