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Short Communication

Analytical Application of Lignocaine Hydrochloride as Hydrotropic Solubilizing Agent

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Abstract: The term hydrotropy refers to solubilization process whereby addition of another solute results in increase in aqueous solubility of poorly soluble drug. There was more than 50 fold enhancement in aqueous solubility of hydrochlorothiazide in 1M lignocaine hydrochloride solution as compared to its solubility in water. Various organic solvents like methanol, chloroform, ethanol, acetonitrile hexane and toluene are widely used to conduct the spectrophotometric analysis. But higher cost and toxicity prevents their frequent use. In the present study 1M lignocaine hydrochloride solution was employed for the spectrophotometric estimation of hydrochlorothiazide at 272 nm. The results of the analysis were validated statistically and by recovery studies & its follows Beer's law in concentration range of 4-24 mcg/ml. The hydrotropic agent and excipients used in the manufacture of tablets did not interfere in the analysis. Statistical data proved the accuracy, reproducibility and precision of the proposed method. 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.
Keywords: Hydrotropy, Lignocain, Solubilization, hydrochlorothiazide.

INTRODUCTION

The present investigation illustrates the application of hydrotropy. There was miraculous synergistic effect on enhancement in solubility of a poorly water-soluble drug by hydrotropic agents. Increasing the aqueous solubility of insoluble and slightly soluble drug is of major importance. In hydrotropic solubilization phenomenon, addition of large amount of second solute results in an increase in aqueous solubility of poorly soluble compound. Concentrated aqueous hydrotropic solution of sodium benzoate, urea, nicotinamide, sodium salicylate, sodium gluconate and sodium glycinate have been observed to enhance the aqueous solubility of many poorly water-soluble drugs [1-4].

Melted (temperature less than 100°C) Poly-ethylene glycol (PEG)-4000, PEG-6000 and PEG-8000 dissolves diclofenac sodium (melting point: 283°C). This shows that melted PEGs act as solvent for diclofenac sodium. Melted urea (M.P.: 132-135°C) dissolves diclofenac sodium (M.P.: 283°C). This also shows that melted urea acts as solvent for diclofenac sodium. Melted ibuprofen (M.P.: 78°C) dissolves diclofenac sodium (M.P.: 283°C); salicylic acid (M.P.: 159°C) and niacinamide (M.P.: 132°C), which again shows that melted ibuprofen acts as solvent for diclofenac sodium, salicylic acid and niacinamide, respectively. In supercritical fluid technology, liquefied carbon dioxide acts as solvent for many insoluble substances. These points indicate that all types of substances possess some solvent character [5-6].

Maheshwari *et al.* [7-9] have developed new analytical methods based on the hydrotropic solubilization phenomenon for quantitative estimation of poorly water soluble drugs frusemide, cefixime, ketoprofen, salicylic acid, tinidazole, aceclofenac, ofloxacin, metronidazole and naldixic acid. Hydrochlorothiazide is a thiazide diuretics used in the treatment of hypertension however the lower aqueous solubility. Maheshwari [10-13] is of the opinion that all substances, whether liquid, gas or solid, possesses solubilizing power. Also, the author is of the opinion that hydrotropy is another type of co-solvency. A large number of poorly water-soluble drugs have been estimated quantitatively by titrimetry and ultra-violet (UV) spectrophotometry using a large number of hydrotropic solutions, thus, precluding the use of organic solvents [14-17]. There was considerable increase in the solubility of hydrochlorothiazide in 1M lignocaine hydrochloride solution as a hydrotropic

agent. Thus it was thought to solubilize the poorly water soluble hydrochlorothiazide (Fig-1) from fine powder of its tablets by lignocaine hydrochloride (Fig-2) solution to carryout spectrophotometric estimation, precluding the use of organic solvent.

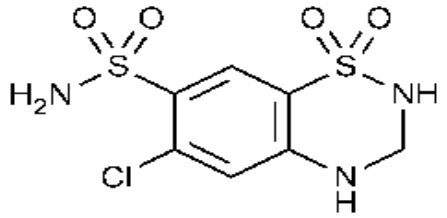

Fig-1: Structure of Hydrochlorothiazide

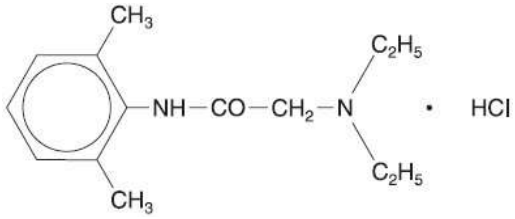

Fig-2:Structure of Lignocain HCl

MATERIAL AND MRTHOD

Materials

All the chemicals and solvents used were of analytical grade. Hydrochlorothiazide was procured from Ranbaxy Lab. Ltd, Dewas (India), Lignocain hydrochloride (Figure 2) was obtained from Modern Laboratories, Indore (India).

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 Hydrochlorothiazide bulk drug was solubilized with 10 ml of 1M lignocaine hydrochloride solution and then diluted to 50 ml with distilled water to obtain various dilution (4, 8, 12, 16, 20, 24 µg/ml). A Linear relationship was observed, measuring their absorbance at 272 nm against respective reagent blanks.

Preliminary solubility studies of drug

Determination of solubility of the drug in distilled water and 1 M lignocaine solution were carried out at room temperature. Sufficient excess amount of drug was added to screw capped 30 ml glass vials containing 1 M lignocaine 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 centrifuged for 5 minutes at 2000 rpm . The supernatant of each vial was filtered through Whatman filter paper # 41. Filtrates were diluted suitably and absorbances of solutions were noted against respective reagent blanks to determine the solubility.

Enhancement in the solubility of hydrochlorothiazide in 1 M lignocaine was more than 50-fold as compared to solubility in distilled water.

Analysis of hydrochlorthiazide tablets using 1M lignocaine hydrochloride solution

Twenty tablets of hydrochlorothiazide (formulation-I) were weighed and ground to fine powder. Accurately weighed powder sample equivalent to 50 mg of hydrochlorothiazide was transferred to 100 ml volumetric flask containing 10 ml of 1M lignocaine hydrochloride solution. The flask was shaken for about 10 min & volume was made up to the mark with distilled water. The solution was filtered through Whattman filter paper No.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 Study

To evaluate the validity and reproducibility of the proposed method, a recovery experiment was carried out. Procedure of analysis was same using 1M lignocaine hydrochloride solution. Percent recoveries were calculated.

Limit of detection (LOD) and Limit of quantitation (LOQ)

The LOD and LOQ of Hydrochlorothiazide by proposed method were determine using calibration standards. LOD and LOQ were calculated as 3.3 σ/S and 10 σ/S respectively, where S is the slope of calibration curve and σ is the mea standard deviation of response.

RESULTS

Solubility determination studies indicated that enhancement in aqueous solubility of hydrochlorthiazide in 1M lignocaine hydrochloride solution was more than 50-fold as compared to solubility in distilled water. It is evident from Table-1 that the mean percent label claim estimated were 99.28% ± 1.782 % and 98.61% ± 1.227 % for formulation I & II respectively. The mean percent label claim are very close to 100 with low value of standard deviation. The 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 value. As evident from Table-2, the mean percent recovery values ranged from 99.49% to 101.32%. The values are very close to 100%, indicating the accuracy of the proposed method. The low value of LOD (0.1639µg/ml) and LOQ (0.4967µg/ml) for

hydrochlorothiazide in 1 M lignocain indicated good sensitivity of proposed method (Table 3).

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

Table-1: Analysis of marketed tablets of Hydrochlorothiazide with statistical evaluation (n=3).

Tablet Formulation	Label Claim (mg/tablet)	% Label Claim estimated (mean ± SD)	% Coefficient of variation	Standard error
I	12.5	99.28 ±1.782	1.795	1.029
II	25	98.61 ± 1.227	1.244	0.708

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±SD)	% Coefficient of variation	Standard error
I	50	15	101.32 ±0.809	0.798	0.467
II	50	30	100.56 ±1.421	1.421	0.825
III	50	15	99.49 ±1.635	1.643	0.944
IV	50	30	99.81±0.899	0.901	0.519

Table 3: Optical characteristics data

Parameters	**Value of Hydrochlorothiazide in 1 M lignocain hydrochloride**
λ max (nm)	272
Beer's law limit (µg/ml)	4 – 24
Correlation coefficient	0.999
Regression equation (Y= mX + C)	0.061x (-0.018)
Intercept (C)	-0.018
Slope (m)	0.061
LOD (µg/ml)	0.1639
LOQ (µg/ml)	0.4967

DISCUSSION

The mean percent recovery values are very close to 100, indicating the accuracy of the proposed method. The low value of LOD and LOQ for hydrochlorothiazide in 1 M lignocain indicated good sensitivity of proposed method. All statistical data proves validity of the method and can be used for routine analysis of pharmaceutical formulations containing this drug by using hydrotropic agent. Use of hydrotropic agent in the analysis of drugs makes method eco-friendly and economic.

CONCLUSION

The proposed method is new, simple, cost-effective and precise and can be employed in the routine analysis of hydrochlorothiazide tablets. Lignocaine hydrochloride does not interfere in the spectrophotometric estimation above 270 nm. Thus the poorly water-soluble drugs can be checked for their solubilities in this hydrotropic solution. If there is sufficient solubility, the solution can be used to solubilize the drug for analysis. Just like hydrochlorthiazide other poorly water-soluble drugs may be tried to get solubilized by hydrotropy concept to carry out their spectrophotometric analysis, By proper choice of hydrotropic agents, the use of organic solvents in analysis may be discouraged to a large extent.

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