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Spectrophotometric methods for the determination of sulphathiourea

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Abstract: Three simple and sensitive spectrophotometric methods are described for the determination of sulphathiourea. The methods are based on the interaction of this thioamide with either iodine, tetracyanoethylene (TCNE) or copper nitrate to give the corresponding charge-transfer or metal-ion complexes, which can be measured at 363, 350 and 353 nm, respectively. In each case, a 1:1 complex was formed. Beer's law is obeyed for each procedure in a concentration range of 1–150 μg ml^{-1}. The proposed procedures can be applied to the determination of sulphathiourea in its pharmaceutical formulations.

Keywords: *Sulphathiourea; charge-transfer complexes; metal-ion complexes; spectrophotometry.*

Introduction

Sulphathiourea is a chemotherapeutic agent which is used in some countries for the treatment of urinary and biliary tract infections [1]. Quantitative methods for the determination of microgram amounts of sulphathiourea are few and lack both sensitivity and simplicity; they include acid–base titrimetric [2], argentometric [3, 4], iodometric [5–8], bromometric [9] and spectrophotometric methods [10–12].

Spectrophotometric studies of iodine with certain thioamides have been carried out. A new intense peak due to the charge-transfer band of a 1:1 molecular complex was observed [13]. The pharmacological activity of the thioamides is related to the facility to oxidize their thiol group to disulphide [14].

Tetracyanoethylene (TCNE) is known to yield charge-transfer complexes and radical ions with a variety of *n*- and π-electron donors [15–18]. In many of the systems studied, the presence of the TCNE anion radical (λ_{max}, 432 nm) has been detected by electron spin resonance spectroscopy. Radical formation was attributed to dissociation of the charge-transfer complex with complete one-electron transfer [19]. Broad bands which are formed in the region of 340–350 nm are attributed to the formation of a charge-transfer complex.

Thioamides form complexes with various metal ions; these complexes have been investigated by X-ray diffraction [20].

In the present study, the charge-transfer complexes formed between sulphathiourea and iodine or TCNE as well as the metal-ion complex of the drug with copper, have been used for the first time in spectrophotometric methods for the assay of sulphathiourea in the drug substance and in its dosage forms.

Experimental

Instrument

A Uvidec-320 spectrophotometer, Jasco (Tokyo, Japan) with matched 10-mm quartz cells and a Unicam SP 1025 IR spectrophotometer were used.

Reagents and materials

All chemicals were of analytical-reagent grade and solvents were of spectroscopic grade.

Sulphathiourea was obtained from Bayer Co. (FRG). Solutions of resublimed iodine, Riedel De-Haen (10^{-2} M) in 1,2-dichloroethane; tetracyanoethylene, Merck (0.1%, w/v) in acetonitrile; and copper nitrate, Merck (0.5% w/v) in methanol were prepared.

Preparation of sample solutions

Solutions (2 mg ml^{-1}) of the drug were prepared in the required solvent. For procedure A it was necessary to dissolve the drug in 0.5 ml of methanol per 100 ml of 1,2-dichloroethane.

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Procedure A

Accurately measured volumes of solutions of the drug in 1,2-dichloroethane, equivalent to 10–100 μg ml^{-1}, were transferred into a series of 10-ml flasks. Iodine solution (1 ml) was added to each flask. The contents of each flask were diluted to 10 ml with 1,2-dichloroethane and allowed to stand for 5 min at 25 ± 1°C. The absorbance of each solution was measured at 363 nm against a blank prepared similarly.

Procedure B

Accurately measured volumes of solutions of the drug in acetonitrile, equivalent to 0.04–0.15 mg ml^{-1}, were transferred into a series of 10-ml flasks. TCNE solution (1 ml) was added to each flask, and the solutions were mixed and heated for 15 min in a thermostatically controlled water-bath adjusted to 70° ± 1°C. The solutions were cooled, diluted to 10 ml with acetonitrile; the absorbance of each solution was measured at 350 nm against a reagent blank.

Procedure C

Accurately measured volumes of solutions of the drug in methanol, equivalent to 0.1–0.75 mg ml^{-1}, were transferred into a series of 10-ml flasks. Copper nitrate solution (2 ml) was added to each flask; the solutions were mixed, diluted to 10 ml with methanol and allowed to stand for 5 min at 25° ± 1°C. The absorbance of each solution was measured at 353 nm against a reagent blank.

Procedure for tablets

Twenty tablets were weighed and finely powdered. An accurately weighed amount of the powder, equivalent to 50 mg of the drug, was extracted with the appropriate solvent for each procedure and then treated in the same way as the drug substance.

Results and Discussion

When solutions of sulphathiourea and iodine in 1,2-dichloroethane (procedure A) were mixed the violet colour of iodine changed to yellow because of a charge-transfer complexation reaction between the *n*-donor sulphathiourea and the σ-acceptor iodine. The absorption spectrum of the reaction products (Fig. 1) shows two bands at 293 and 363 nm, characteristic of the *n*-donor charge-transfer complexes [21]. In 1,2-dichloroethane, iodine

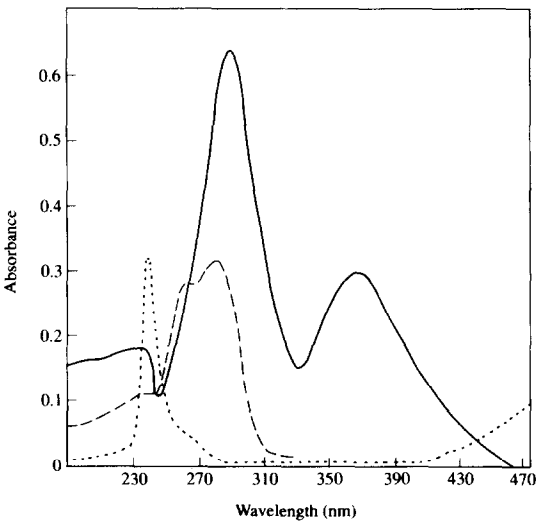

Figure 1
Absorption spectra of: sulphathiourea, 2 μg ml^{-1} (--); iodine, 1 × 10^{-2} M (···) and their charge-transfer complex in 1,2-dichloroethane (——).

itself has a maximum absorption at about 520 nm and sulphathiourea has an absorption peak at 280 nm; therefore measurements of the complex were carried out at 363 nm to avoid interference from the reactants.

Tetracyanoethylene in acetonitrile (procedure B) gives an absorption spectrum with a maximum at 285 nm. On the addition of sulphathiourea to TCNE solution, however, the characteristic absorption band of the TCNE anion radical with an absorption maximum [22] in acetonitrile at 432 nm was not formed. Instead, a band at 350 nm was obtained (Fig. 2) which corresponds to the *n*–π-charge-transfer complex.

The formation of such contact charge-transfer complexes has also been reported [23]; in addition their λ_{max} values were found to differ in accordance with the structure of the donor compound [13, 24].

The optimum temperature was 70°C and the reaction product was stable for at least 1 h. The effect of the solvent (acetonitrile, chloroform, dioxane and cyclohexane) on the formation of the charge-transfer complex was studied. No absorption band was observed in the electronic spectra at the concentration tested in dioxane or cyclohexane. Acetonitrile was preferred because of the high molar absorptivity of the complex formed in this solvent.

When the methanolic solution of copper(II) and sulphathiourea were mixed (procedure C),

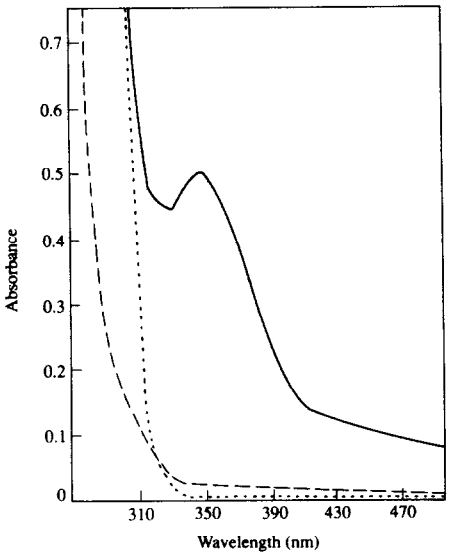

Figure 2
Absorption spectra of sulphathiourea, 130 μg ml^{-1} (--); TCNE, 1 mg ml^{-1} (···); and their charge-transfer complex in acetonitrile (——).

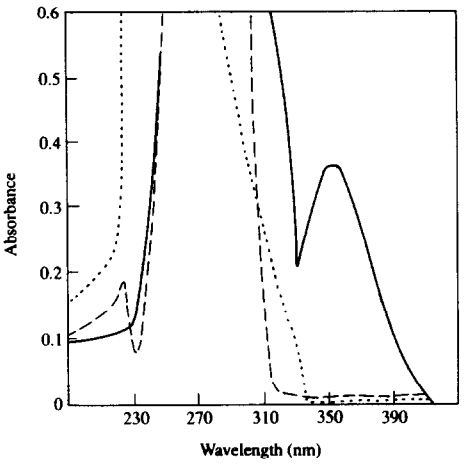

Figure 3
Absorption spectra of: sulphathiourea; 20 μg ml^{-1} (--); copper nitrate, 5 mg ml^{-1} (···) and their reaction product in methanol (——).

a greenish-yellow colour was observed. The absorption maximum was observed at 353 nm, whereas the absorbance of copper and sulphathiourea in this region was negligible (Fig. 3). The effect of the solvent (methanol, ethanol, acetone, chloroform and carbon tetrachloride) on the intensity colour was studied; methanol was found to be the solvent of choice.

Of the different salts of copper (sulphate, chloride, acetate and nitrate) tested, copper nitrate gave the most stable absorbance readings.

The molar absorptivities were 3.31×10^4, 8.51×10^2 and 3.81×10^3 l mol^{-1} cm^{-1} for procedures A, B and C, respectively. By application of Job's method of continuous variation [24], a molar ratio of 1:1 was obtained. Calibration graphs were constructed by plotting absorbance versus concentration of the drug (μg ml^{-1}) in the final dilution. Regression analysis indicated excellent conformity with Beer's law in concentration ranges of 1–10, 40–150 and 10–75 μg ml^{-1} for the iodine, TCNE and copper methods, respectively. The graphs are described by the following regression equations:

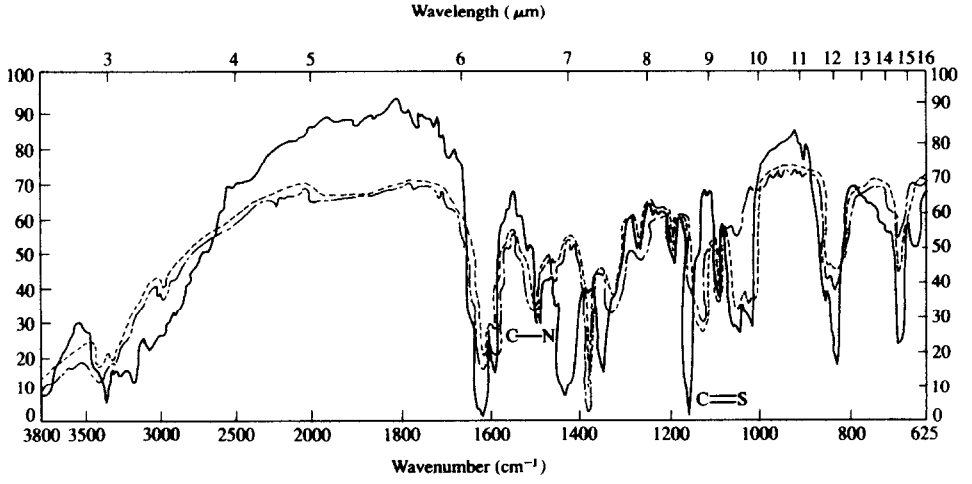

Figure 4
IR spectra of: sulphathiourea (——); the iodine (- · · ·); and the copper complexes (···).

$A_{363} = 0.044 + 0.144C$ ($r = 0.9969$) (Procedure A),
$A_{350} = 0.04 + 0.004C$ ($r = 0.9975$) (Procedure B),
$A_{353} = 0.012 + 0.017C$ ($r = 0.9998$) (Procedure C),

where A is the absorbance, C is the concentration of the measured solution ($\mu g\ ml^{-1}$) and r is the correlation coefficient.

The IR band of the C=S in either the iodine or the copper complex (Fig. 4) was shifted 20 cm^{-1} lower than the absorption of the free sulphathiourea. This indicates a decrease in the stretching force constant and favours coordination to the sulphur atom. Moreover, the absorption frequency assigned to the C—N stretch at 1430 cm^{-1} was shifted to high frequencies (about 1450 cm^{-1}). This shift is expected if the sulphur atom is the donor centre. Similar changes in the IR spectra of the donor upon coordination have been reported for several carbonyl compounds [26]. In addition, it can be deduced from thermodynamic data [20] of similar interactions that coordination, like protonation, occurs at the sulphur atom. Amides and thioamides were reported to bind the iodine by oxygen and sulphur, respectively [27]. In contrast, primary and sulphonyl amino groups do not seem to be responsible for such interactions since sulphanilamide failed to give a positive response with iodine.

Scheme 1 shows the possible reaction pathway, as predicted from the earlier discussion, where iodine or copper coordinate with the sulphur atom.

The proposed methods were applied to the determination of sulphathiourea in pharmaceutical dosage forms (Table 1). The results compared favourably with those obtained by the Bratton–Marshall method [25]. The proposed methods are simple, sensitive and time saving. In addition, the interaction between iodine and sulphathiourea can be considered to be specific for the analysis of sulphathiourea since other sulpha drugs do not interact under the specified reaction conditions.

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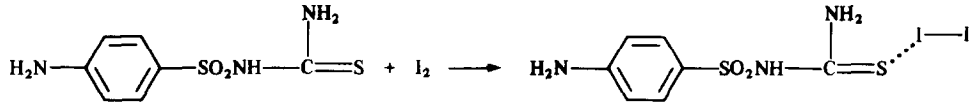

Scheme 1

Table 1
Assay of dosage forms using the proposed methods and the Bratton–Marshall method

	Procedure	% Recovery* ± SD Proposed	Bratton–Marshall
Badional tablets†	A	100.61 ± 0.75	
	B	99.60 ± 0.63	100.52 ± 0.52
	C	100.28 ± 1.10	
Bendonal tablets‡	A	98.15 ± 0.69	
	B	97.58 ± 0.34	97.10 ± 0.70
	C	97.70 ± 0.55	

*Mean of three determinations.
†Bayer Leverkusen (FRG) labelled to contain 0.5 g in each tablet.
‡The Alexandria Co. (Egypt) labelled to contain 0.5 g in each tablet.

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