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INDIRECT DETERMINATION OF SULPHAMERAZINE, SULPHADIAZINE AND SULPHATHIAZOLE BY ATOMIC ABSORPTION SPECTROPHOTOMETRY

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ABSTRACT

A systematic study for the determination of sulphamerazine, sulphadiazine and sulphathiazole applying atomic absorption spectrophotometry is undertaken.(The method is based on the precipitation of sulphamerazine by Cu (II), sulphadiazine by sulphadiazine by Cd (II) and sulphathiazole by Co (II) under optimum conditions followed by the determination of the unreacted metal ion as well as that in the precipitate. The conditions for a quantitative stoichiometric precipitation of the sulphonamides are discussed.

INTRODUCTION

Sulphmerazine (I). sulphadiazine (II) and sulphathiazole (III) are members of the group of sulphonamides, which are in general bacteriosstatic drugs [1]. The sulphonamides of pharmaceutical interest have the general molecular formula NH_2–C_6H_4–SO_2–NH–R, where R is a variable group essentially a heterocyclic nucleus[2]. The methods utilised for the analysis of sulphonamides are based on the properties conferred upon the molecule by the presence of the primary aromatic amino-group or the acidic hydrogen of the–SO_2–NH–group. These methods can be classified as direct or indirect titration [3], argentometric [4], complexometric [5] and precipitation with metal ions [6]. Sulphonamides can be precipitated by different cations such as Al (III), Hg(II), Ag(I), Cd(II), Co(II), Mg(II), Cu(II) and Sn (II) under proper experimantal conditions [7,8,9].

In the present investigation, it is aimed to determine the sulphonamides under investigation indirectly by atomic absorption spectrophotometry. The drugs are precipitated as their insoluble Cu(II), Cd(II) or

Co(II) complexes then the metal ion in solution and precipitate are dedetermined. The conditions favouring the complete precipitation of the sulpha drug and the stoichiometry of the precipitate are also considered.

EXPERIMENTAL

Materials:

All chemicals used in the present investigation were chemically pure grade products from BDH or Merck. The sulpha drugs used were A.R. products from BAYER.

Solutions:

Standard Cu(II), Cd(II) and Co(II) solutions were prepared by dissolving 0 .1964 g of copper sulphate, 0 .8150 g cadmium chloride or 0 .2468 g cobalt chloride in 500 ml of redistilled water. The concentrations of the prepared standard solutions were checked colourimetrically by recommended methods of analysis[10,11]. The standard sulphamerazine, sulphadiazine and sulphathiazole solutions were prepared by dissolving 0 .1 g of the dried sulphonamide in 50 ml of ammonia buffer solution of pH 10.

Procedure:

In a 25 ml centrifuge tube, a certain amount of the sulpha drug stock solution was mixed with another quantity of the metal ion, Cu(II) in case of (I), Cd(II) for (II) and Co(II) with(III).

The reaction mixture was then completed to 10 ml with the ammonia buffer of pH 10, well shaken and allowed to stand for at least 6 mins. in case of (I), 15 mins. in case of (II) and 10 mins. in case of (III). The mixture was then centrifuged and the precipitate was filtered off and washed with redistilled water. The residue was then disolved in 10 ml 0 .1 N HCl. The concentration of the metal ion, Cu(II), Cd(II) or Co(II) in the filterate and precipitate was determined by measuring the absorbance using atomic absorption spectrophotometry.

Procedure for tablets:

An accurate weight of the powdered sulpha drug, containing 0 .10–1 mg of sulpha, is shaken with another quantity of the metal ion. The reaction mixture was then completed to 10 ml with the ammonia buffer of pH 10, then proceed as mentioned above.

Apparatus:

The Beckman model 17900 atomic absorption spectrophotometer was utilised for measurements.

RESULTS AND DISCUSSION

The present work includes the development of an indirect method for the determination of sulphamerazine (I), sulphadizaine(II) and sulphatiazole (III) by atomic absorption spectrophotometry. The quantitative reaction between (I) and Cu (II)., between(II) and Cd (II) or between Co(II) and (III) is made the basis for the determination of the three sulphonamides.

The optimum conditions for the quantitative precipitation of the metal sulpha drug complex are first studied. The time of shaking the mixture and of allowing it to stand is found to be significant for the quantitative precipitation of the metal sulphonamide complex. It is found that 6, 15 and 10 mins. of shaking and allowing the reaction mixture to stand are the minimum times required for complete precipitation of the metal sulphonamide complexes for the medium is of important role for the quantitative precipitation of the metal sulphonamide with the appropriate stoichimetry. It is found that pH 10 is the most suitable pH for achieving a complete stoichiometric precipitation of the drugs by the appropriate metal ion.

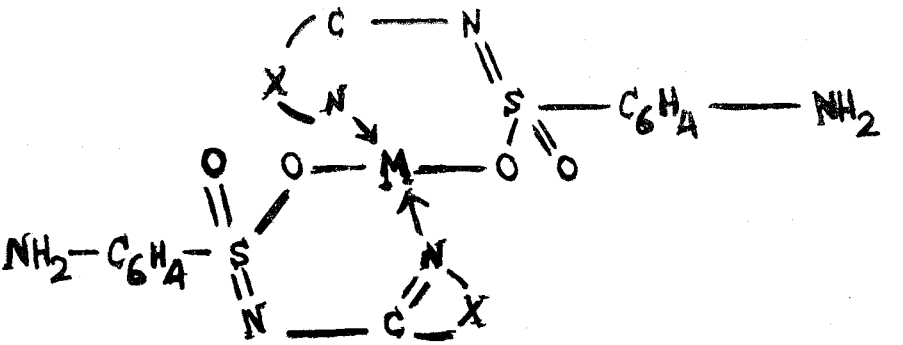
The recommended sequence for mixing the reactants and medium are found to be either, metal ion-buffers-sulphonamide or sulphonamide-metal ion - buffer. The results given in Table 1 show the effect of metal ion concentration on a constant of the sulpha drug to test the stoichio-

Table (I)

Effect of metal on the determination of sulphamerazine (I), sulphadiazine (II) and sulphathiazole (III) using 2 mg of the sulpha drug.

μgCu add	μgCu in Filtrate	μgCu reacted	μgCd add	μgCd in Filtrate	μgCd reacted	μgCO add	μgCO in Filtrate	μgCO reacted
Results for (I)			Results for (II)			Results for (III)		
100	—	100	80	—	80	100	—	100
200	—	200	150	—	150	200	—	200
300	80	220	300	—	300	300	80	220
500	280	220	500	52	448	500	270	230
1000	780	220	700	252	448	1000	770	230
1500	1280	220	800	352	449	1100	865	235
2000	1780	218	1000	550	450	1400	1166	234

metry of the precipitated complex. It is clear that the ratio of the ion to the sulphonamide in the precipitated complex is 1:2 . The precipitates are found also to be deprived of the metal salt anion. Based on the results obtained in the present investigation, the precipitates formed would have the following structural formula:



in which X is the rest of the heterocyclic ring, pyrimidine for (I), 4-methyl pyrimidine for (II) and thiazole for (III).

The enolisation of the sulphonamide linkage as given in the above formula is necessary to give a stable six membered ring structure since the bonding of the metal atom to the nitrogen of the sulphonamide would lead to a very strained unstable four membered chelate ring. The structure suggested is confirmed by examining their spectra of the solid complexes in comparison to those of the free sulphonamides. An identical behaviour was considered for aromatic acid amides and benzoylhydrazones.[12]

The reactions between the sulphonamides under investigation and the metal ions are applied under optimum conditions, favouring the formation of the stoichiometric insoluble complexes as quantitative reaction products, for the quantitative indirect determination of the drugs by atomic absorption spectrophotometry. This includes the determination of the metal ion concentration in both filterate and solution of the precipitated complex.

The results shown in Table II indicate that the proposed method is applicable for the accurate determination of the three sulpha drugs under investigation. The success of the method depends to a large extent upon the accuracy with which the sulphonamide is quantitatively pre-

Table (II)

Indirect determination of sulphamerazine (I), sulphadiazine (II) and sulphathiazole (III) by atomic absorption spectrophotometry

mg sulpha drug added	μg M^{2+} In filtrate	μg M^{2+} precipitore	mg sulpha found	error %
Results for (I) using 1000 μg Cu (II)				
1	841	109	0.99	— 1.0
2	780	220	2.00	—
4	551	449	4.08	+ 2.0
6	336	664	6.03	+ 0.5
8	123	877	7.97	— 0.3
Results for (II) using 1500 μg Cd (II)				
1	1237	227	1.01	+ 1.0
2	1055	445	1.98	— 1.0
4	611	889	3.97	— 0.7
6	140	1360	6.07	+ 1.1
8	18	1482	7.92	— 1.0
Results for III using 1500 μg Co (II):				
1	1389	116	1.01	+ 1.0
2	1272	228	1.98	— 1.0
4	1036	462	4.01	+ 0.2
6	810	690	6.005	+ 0.08
8	574	926	8.05	+ 0.6

cipitated and the accuracy with which the metal ion is determined by atomic absorption spectrophotometry. The present method has the advantage of being very suitable for the determination of very small amounts of the sulphonamides in pharmaceutical preparations with fair accuracy. Representative results are given in Table III. As been evident from this table, the results of atomic absorption method are in good agreement with the British Pharmacopoeia (B.P.) method[13].

Table (III)

Application of the proposed Methods to the Determination of the investigated Sulpha drug in Pharmaceutical Preparations.

Name of preparation	Name of Manufacture	Stated Concentration/mg per unit dose	Concentration found % of stated amount	
			British pharmacopoeia (B.P.) method	Atomic absorption met.
Sulphamerazine tablets	Kahira	0.5 gm	97.21	96.80
Sulphamerazine tablets	Angeli	0.5 gm	99.98	99.98
Sulphamerazine tablets	Specia	0.5 gm	98.97	99.79
Sulphamerazine tablets	Kahira	0.5 gm	95.22	96.80
Sulphamerazine tablets	Cid	0.5 gm	96.07	98.04
Sulphamerazine tablets	Nile	0.5 gm	102.52	97.02
Sulphamerazine tablets	Alex	0.5 gm	95.54	95.67
Sulphathiazole tablets	Kahira	0.5 gm	98.50	102.38

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