raphy and Mass Spectrometry. John Wiley and Sons, New York, 1976, 118.
10. Chialva, F., Monguzzi, F., Manitto, P. and Akgul, A., **J. Essent. Oil Res.**, 1993, 5, 105.
11. Ranade G.S., **Pafai J.**, 1997, 19, 61.

Determination of Milligram Amounts of Embramine and Hydroxyzine Hydrochlorides with Silver Nitrate

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Accepted 15 December 2001
Revised 24 November 2001
Received 5 February 2001

Three simple, accurate and rapid methods have been developed for the assay of two antihistamines, embramine and hydroxyzine hydrochlorides in pure sample and in pharmaceutical preparations. The methods depend on the titration of the chloride content of the drugs with silver nitrate, with visual, potentiometric and conductometric end-point detection.

Mebrophenhydramine hydrochloride (MPH) (embramine) and hydroxyzine hydrochloride (HDH) are antihistaminic drugs that belong to diphenylmethylene ether and diphenylmethylene amino groups, respectively. MPH is used in all allergies, and HDH, in addition to having anxiolytic, sedative and antihistaminic properties, also has muscle relaxation and analgesic effects[1]. Not many methods are available for the determination of MPH. Visible spectrophotometry[2], uv-spectrophotometry[3,4], potentiometry[5] and capillary isotachophoresis[6] are some of the methods reported for the determination of MPH. HDH has been assayed by conductometry[7], coulometry[8], uv-spectrophotometry[9], visible-spectrophotometry[10], gas chromatography[11], reversed phase HPLC[12], ion-exchange chromatography[13] and titrimetry[14].

Three titrimetric procedures for the determination of MPH and HDH in bulk samples and in pharmaceutical preparations are presented in this paper. The methods are based on the titration of the chloride content of the hydrochlorides of the studied drugs with $AgNO_3$ as the titrant and employing visual, potentiometric and conductometric end-point detection. The proposed methods offer the advantages of simplicity, good accuracy and precision.

Standard solutions of MPH and HDH (mg/ml) were prepared by dissolving requisite amount of drug in double distilled water. A stock solution of silver nitrate (0.05 M) was prepared in double distilled water and standardised by Mohr method[15]. The solutions of lower concentrations were obtained by appropriate dilution of the stock solution. The solutions were stored in amber coloured bottles and kept in dark when not in use. A 5% solution of potassium chromate and 1% solution of sodium tetraborate were prepared using analytical reagent-grade chemicals in double distilled water.

To a 10 ml aliquot solution containing 4-10 mg of MPH or 5-10 mg of HDH, 1% sodium tetraborate solution was added to adjust the pH to 6.5-7.0 followed by 1 ml of 5% potassium chromate and titrated with 0.01 M $AgNO_3$ to the first appearance of buff colour due to silver chromate. An indicator blank was determined by suspending about 100 mg of calcium carbonate in about 10 ml of double distilled water containing 1 ml of 5% potassium chromate. In potentiometric end-point detection, a 25 ml aliquot containing 5-25 mg of MPH or 5-20 mg of HDH was titrated with $AgNO_3$ (0.01 M), the latter being added in 0.1 ml increments near the equivalence point. The equivalence point was located by the graphical method. Alternatively, a 25 ml aliquot of solution containing 5-25 mg of either drug was titrated conductometrically by adding 0.25 ml increments of 0.01 or 0.02 M $AgNO_3$ solution.

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TABLE 1: REACTION STOICHIOMETRY AND RANGE OF DETERMINATION.

Method	Mebrophenhydramine hydrochloride				Hydroxyzine hydrochloride			
	Stoichiometry			Range (mg)	Stoichiometry			Range (mg)
	Amount taken (mg)	Amount found* (mg)	'n' value		Amount taken (mg)	Amount found* (mg)	'n' value	
Visual titration	5.00	5.10	1.02	3.0-10.0	5.00	5.15	2.06	3.0-10.0
	7.00	7.40	1.05		7.00	6.95	1.98	
	9.00	8.75	0.97		9.00	8.88	1.97	
Potentiometric titration	5.00	5.32	1.06	5.0-25.0	5.00	5.21	2.06	5.0-20.0
	10.00	10.83	1.08		15.00	15.61	2.07	
	25.00	24.39	0.97		20.00	19.61	1.95	
Conductometric titration	10.00	9.60	0.97	5.0-25.0	5.00	4.90	1.96	5.0-25.0
	15.00	14.82	0.98		15.00	15.53	2.06	
	25.00	24.17	0.96		25.00	23.93	1.90	

* Values obtained for three trials, 'n' is the number of moles of $AgNO_3$ reacting with one mole of drug.

Twenty tablets were weighed and powdered. An amount of powder equivalent to 250 mg of MPH or HDH was weighed accurately and was transferred into a 250 ml volumetric flask. It was shaken with 150 ml of double distilled water and then diluted to volume with double distilled water. The solution was filtered through a Whatman No. 1 filter paper. The first 10 ml of the filtrate were discarded and the remaining portion was used for assay as described above. The contents of twenty capsules were weighed and brought to a fine powder. The rest of the procedure is the same as the one used for analysing tablets. The contents of twenty injections was mixed and a volume equivalent to 250 mg of the active ingredient was quantitatively transferred into a 250 ml volumetric flask and diluted to mark with double distilled water. A suitable aliquot was then analysed.

TABLE 2: THE DETERMINATION OF MPH AND HDH IN PHARMACEUTICAL PREPARATIONS BY THE PROPOSED METHODS.

Drug and Formulation*	Label claim (mg)	FoundΨ, % recovery ± SD		
		Visual method	Potentiometric method	Conductometric method
MPH				
Mebryl tablet[a]	25	100.76±0.37	100.06±0.83	99.69±0.64
HDH				
Atarax tablet[b]	10	101.30±1.15	102.40±0.46	101.20±0.44
	25	98.94±0.64	100.11±0.29	98.44±0.76
Atarax injection[b]	25	99.13±0.31	100.11±0.38	98.44±0.76
Atarax syrup[b]	2	102.40±1.61	103.15±0.43	102.30±0.92
Atarax drops[b]	6	101.40±1.31	103.18±0.37	102.50±1.54

* Marketed by a: Smithkline Beecham; b: UCB Pharma; ψ Mean ± SD for 7 determinations with visual method and 3 trials with potentiometric and conductometric methods.

Since MPH and HDH ionise in aqueous solution into protonated drug moiety and chloride ions, both drugs could be titrated conveniently with $AgNO_3$. The results in Table 1 indicate that MPH reacts with $AgNO_3$ in 1:1 molar ratio, whereas HDH does so in 1:2 ratio. The titration methods were applied to the analysis of pharmaceutical preparations containing MPH and HDH. The percent recoveries with RSD values are shown in Table 2. The potentiometric method was found to be more precise and accurate compared to visual and conductometric end-point detection methods. Excipients such as lactose, starch, magnesium stearate and talc were found not to interfere in the determination. From the results compiled in Table 2, it can be concluded that the titrimetric methods described in this paper are suitable for the determination of MPH and HDH in various pharmaceutical preparations through the titration of chloride content. The analysis can be carried out within a few minutes and therefore be used for quick routine analysis.

ACKNOWLEDGEMENTS

Sincere thanks are due to M/s. Smithkline Beecham (India) Ltd., and UCB Pharm Ltd., India, for providing gift samples of drugs.

REFERENCES

1. Budavari, S., Eds., In; The Merck Index; An Encyclopedia of Chemicals, Drugs and Biologicals, 12th Edn., Merck Research Laboratories, White House Station, NJ, 1996, 600, 833.
2. Sastry, C.S.P., Tipirneni, A.S.R.P. and Suryanarayana, M.V., **Indian J. Pharm Sci.,** 1989, 51, 146.
3. Caddy, B., Fish, F. and Trantes, J., **Analyst,** 1975, 100, 563.
4. Caddy, B., Fish, F. and Trantes, J., **Analyst,** 1974, 99, 555.
5. Jancik, S., Korbl, J. and Buben, F., **Cesk. Farm.,** 1961, 10, 416.
6. Jokl, V., Kovbalikova, J. and Vitkovic, B., **Cesk. Farm.,** 1990, 39, 168.
7. Mikuhski, R. and Dembinski, B., **Anal. Chem. Acta,** 1993, 272, 233.
8. Szyszko, E. and Gawrgch, Z., **Acta Pol. Pharm.,** 1975, 32, 333.
9. Davidson, A.G., **Analyst,** 1983, 108, 728.
10. Nacea, V. and Murgu, L., **Rev. Chem** (Bucharest), 1978, 29, 577.
11. Kintz, P., Godelar, B. and Mauyin, P., **Forensic Sci. Int.,** 1990, 48, 139.
12. Roberts, S.E. and Delaney, M.F., **J. Chromatogr.,** 1982, 242, 364.
13. Blazek, J., Mares, V. and Stejskal, Z., **Cesk. Farm.,** 1957, 6, 150.
14. Dembinski, B., **Chem. Anal.** (Warsaw), 1993, 38, 183.
15. Vogel, A.I., In; Quantitative Inorganic Analysis, 3rd Edn., ELBS, London, 1961, 259.

Spectrophotometric Determination of Sildenafil Citrate in Pharmaceutical Dosage Forms

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Accepted 31 December 2001

Revised 30 October 2001

Received 14 May 2001

Two simple extractive spectrophotometric methods have been developed for the estimation of sildenafil citrate in both pure and pharmaceutical dosage forms. These methods are based on the formation of ion association-pair complexes of the drug with two acid dyes namely orange-II and erichrome black-T in acidic medium followed by their extraction in to chloroform. The absorbance of the chloroform layers was measured at their respective wavelength of maximum absorbance against the corresponding reagent blank. The method has been statistically evaluated and is found to be precise and accurate.

Sildenafil citrate (SLD) designated chemically as 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo-[4,3-d]-pyrimidin-5-yl)-4-ethoxyphenyl]sulfonyl]-4-methylpiperazine citrate, which is a selective inhibitor of cyclic guanosine

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