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Short Communication

Determination of cimetidine in pure form and in dosage forms using *N*-bromosuccinimide

K. GIRISH KUMAR* and R. JAYASHREE

Department of Chemistry, Gandhigram Rural Institute, Gandhigram 624 302, India

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Introduction

Cimetidine is a highly effective drug for the treatment of patients with duodenal ulcers and other hypersecretory conditions. Since the incidence of such clinical conditions is increasing the use of the drug is highly important. Few methods are available for the determination of cimetidine. The Kjeldhal [1] method is widely used for its assay; in addition, some spectrophotometric [2–5], chromatographic [6], and titrimetric [7–10] methods have also been proposed. All the available titrimetric methods have one or more drawbacks. *N*-haloimides have been used as effective oxidizing/brominating agents for the determination of different drugs [11–16], *N*-bromosuccinimide (NBS) being the most versatile; however, no attempt has been made to develop a method for the determination of cimetidine using this novel reagent. In the present paper, a direct titrimetric method with a visual end-point is reported for the quantitative analysis of cimetidine in different formulations using *N*-bromosuccinimide.

Experimental

Reagents

N-bromosuccinimide (NBS) was prepared by brominating succinimide. The standard solution (~0.02 N corresponding to 0.01 M) was prepared in water as reported previously [15]. The following cimetidine formulations were analysed: cimetin tablets (The Pharmaceutical Company of India, Bombay); cimetidine tablets (Cadila Chemicals Pvt. Ltd, Ahmedabad, India); Tacamed-200 tablets (Eskayef Ltd, Mysore, India); and laboratory-made tablets. Ten tablets of each type were weighed accurately. The tablets were finely powdered and a known mass (~0.15 g) of the powder was dissolved in 50 ml of aqueous acetic acid (15% v/v). The solution was filtered through a Whatman No. 41 filter-paper; the residue was washed five times with aqueous acetic acid (15% v/v) and the combined filtrate and washings were diluted to 250 ml. A solution of a sample of pure cimetidine (~0.15 g) was also prepared by the same method. Amaranth indicator solution (0.2% w/v) was prepared in water [17].

Procedure

To a measured volume (5–15 ml) of the sample solution, 10 ml of KBr solution (10% w/v) was added followed by 10 ml of hydrochloric acid solution (20% v/v). This was titrated with standard NBS solution using amaranth indicator solution (two drops). The end-point was the disappearance of the pink colour. From the titre value, the amount of cimetidine was calculated by the equation

$$\text{weight of cimetidine} = \frac{M \times V \times N}{n} \text{ mg},$$

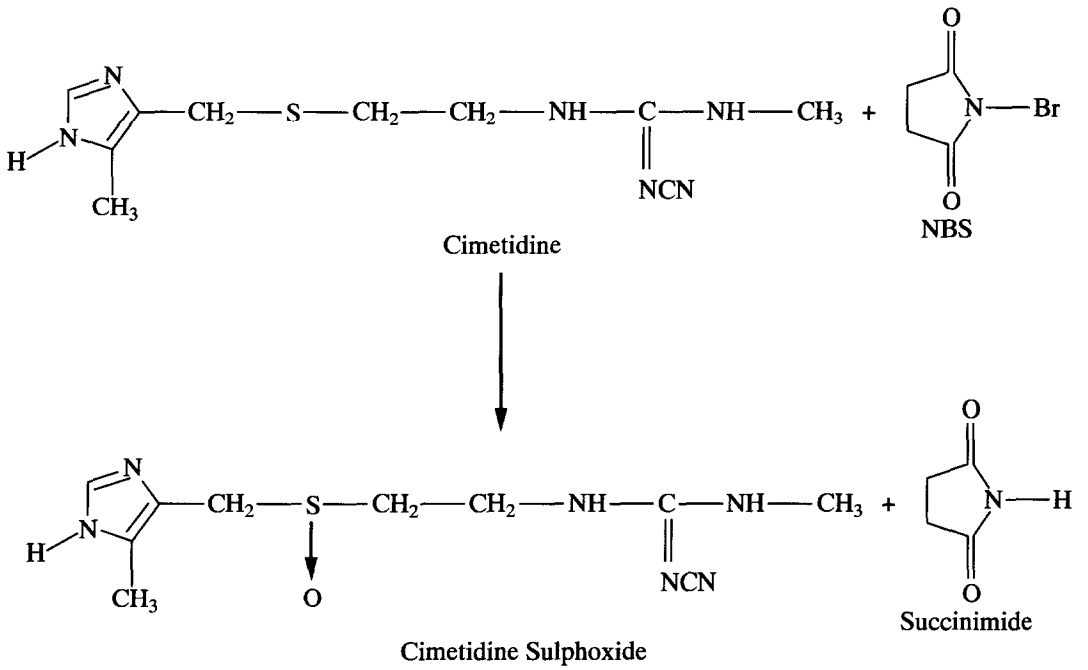
where M is the molecular weight of cimetidine (252), V is the volume (ml) of NBS solution of normality N and n is the equivalence number

* Author to whom correspondence should be addressed.

(the number of equivalents of NBS consumed per mole of cimetidine); in this method $n = 2$.

Results and Discussion

Results of the titration of pure cimetidine with NBS are presented in Table 1. This table shows that 1 mole of cimetidine consumes 1 mole of NBS (equivalence number = 2). Table 2 presents data on the analysis of different cimetidine formulations using NBS. This method was compared with the standard potassium bromate method [7] and the results are included in Table 2. To check the validity of the developed method, recovery studies were carried out by the standard addition



Scheme 1

Table 1
Determination of cimetidine (pure substance)

	Range (mg)	Equivalence number	Recovery* (%)	RSD (%)
NBS method	3.02–8.47	1.99	99	0.84
Potassium bromate method	3.62–8.84	1.99	98	1.10

*Mean of 10 replicates.

Table 2
Determination of cimetidine in dosage forms

		NBS method		Potassium bromate method		Recovery studies†		
Tablet	Maker's specification (mg tablet^{-1})	Cimetidine found* (mg tablet^{-1})	RSD (%)	Cimetidine found* (mg tablet^{-1})	RSD (%)	Cimetidine added (mg)	Recovery* (%)	RSD (%)
Cimetin	200	199	0.38	200	3.69	0.5–3	101	0.93
Cimetidine	200	200	1.04	210	1.40	0.5–3	98	0.62
Tacamed-200	200	200	1.37	203	4.16	0.5–3	99	1.02
Laboratory-made tablet	100	100	0.38	99	1.58	0.5–3	98	0.68

*Mean of 10 replicates.
†Amount of tablet powder taken = 3 mg.

method and the findings are presented in Table 2. Interference studies demonstrated that drug excipients like starch, magnesium stearate, talc and lactose do not interfere with the titrimetric method.

In the proposed method cimetidine is oxidized quantitatively by NBS to the corresponding sulphoxide as represented in the reaction scheme. Since the reaction takes place in an aqueous medium, the end-point is very clear with amaranth indicator solution. NBS is comparatively stable in the solid state and is soluble in water; therefore a solution of the reagent can be prepared in water from stocks of solid sample when required. The data in Tables 1 and 2 indicate that the proposed method using NBS is more precise than the potassium bromate method. In the potassium bromate method [7] the end-point is very difficult to detect because no indicator is present. In the perchloric acid method [8] the medium must be completely anhydrous whereas in the bromine method [9] the reagent is unstable. Since the proposed method is free from such drawbacks, it is superior to the other methods and can be suggested for the quality control of cimetidine in pure form and in dosage forms.

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