MICROCHEMICAL JOURNAL 41, 362–365 (1990)

Some Observations on a Simple Method for the Determination of Novalgin in Drug Formulations with Iron(III)–1,10-Phenanthroline

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Received October 11, 1989; accepted January 26, 1990

An accurate and simple spectrophotometric method for the determination of novalgin has been developed. The method is based on reduction of iron(III) with novalgin and subsequent complexation of iron(II) with 1,10-phenanthroline. The method has been applied to the determination of novalgin in drug formulations and interferences by excipients have been checked.

INTRODUCTION

Novalgin or dipyrone is an important analgesic and antipyretic drug and is found with paracetamol and acetylsalicylic acid in drug formulations. Spectrophotometric methods in visible and ultraviolet ranges are discussed in the literature (*1, 2, 4–6, 8*). Another titrimetric method is based on oxidative degradation of novalgin (*3*). The recommended method described in this communication is advantageous for the determination of novalgin in a lower pH range in microgram amounts.

It is well known that the iron(II)–1,10-phenanthroline complex shows an intense red color and is more stable than its corresponding ferric complex over a wide pH range. On the other hand, reducing agents have been shown to reduce the ferric complex to a ferrous complex. This fact is the basis for the present work. Because of the instability of colored solutions, no report has been described for the determination of novalgin using the ferric complex as a coloring agent. The instability of the colored solution seems to be caused by the photoreduction of the ferric complex.

The photoreduction of the ferric complex, however, can be avoided by adding a chelating agent such as ethylenediaminetetraacetic acid (EDTA) to mask excessive ferric ion after the color development.

EXPERIMENTAL

Apparatus

A Bausch and Lomb Spectronic-20 was used for absorption measurements.

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0026-265X/90 $1.50

Reagents

All reagents used were of analytical grade.

A 0.1% (w/v) ferric ammonium sulfate solution and a 0.01 *M* EDTA solution were prepared in 0.001 *M* sulfuric acid and conductivity water, respectively.

A 0.1 *M* 1,10-phenontroline solution was prepared in ethanol.

Buffer solution was prepared by mixing 1 *M* acetic acid and 1 *M* sodium acetate solutions in a ratio of 3:7.

Solutions of iron(III) and 1,10-phenanthroline were prepared fresh daily before use.

Analgin

Aqueous 0.1% (w/v) pure analgin solution was used for the preparation of the calibration curve. All drug samples of analgin were purchased from the local market. Analgin has the same structural formula as novalgin. It is a trade name assigned by different Indian pharmaceutical industries.

Procedure

Preparation of the calibration curve. Take 1 ml of buffer and 1 ml of iron(III) solution in a 10 ml measuring flask. Add a sample solution containing 0.01 to 0.07 ml of novalgin and then add 0.1 ml of the 1,10-phenanthroline. Leave the reaction mixture for about 30 min for complete development of color, then add 1 ml of the EDTA solution, dilute to the mark with water, and measure the absorbance of the colored solution against a reagent blank within one-half hour.

Application of the proposed method. The proposed method was employed for novalgin content estimation in drug formulations. A comparison of reference methods was also performed.

An accurately weighed amount equivalent to 100 mg of novalgin was stirred in 50 ml of conductivity water and the reaction mixture was allowed to stand for 10 min. The residual solid was filtered on Whatman No. 42 paper and washed with water. The filtrate was made up to 100 ml in a volumetric flask.

The determination was carried out simultaneously.

RESULTS AND DISCUSSION

Absorption Spectra

The absorption spectra of the blank iron(II) and iron(III) complexes are shown in Fig. 1. The maximum absorbance for both A and B in Fig. 1 is observed at 500 nm where the blank shows a slight absorption. The shapes of the absorption spectra are quite similar for A and B.

The reduction of iron(III) by novalgin and the formation of iron(II)–1,10-phenonthroline complex depend on pH. The development of color is almost instantaneous in acetic acid–sodium acetate buffer solution in the pH range 3 to 6.

Confirmation with Beer's law

Beer's law was obeyed in the concentration range 10–70 μg/10 ml with molar absorptivity of 4.27×10^4 liters mol^{-1} cm^{-1}.

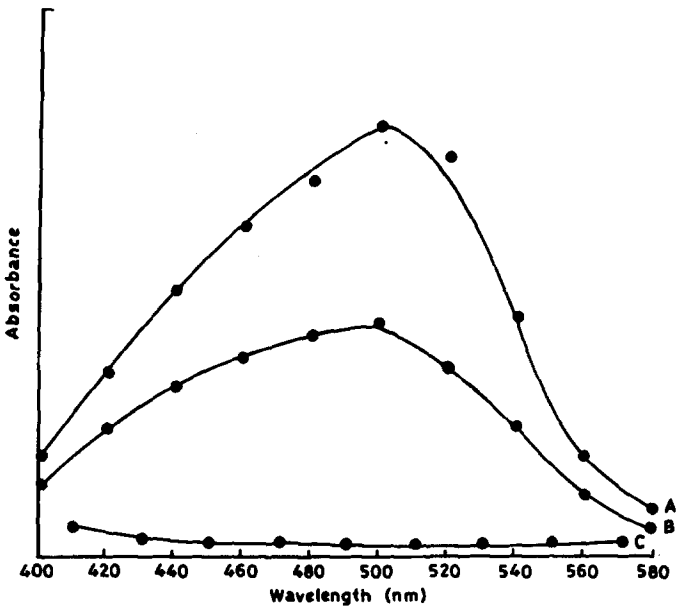

FIG. 1. Absorption spectra of (A) Fe(III)–novalgin-1,10-phenonthroline; (B) Fe(II)–1,10-phenonthroline; and (C) Fe(III)–1,10-phenonthroline.

TABLE 1
Determination of Novalgin (Analgin) in Pharmaceutical Preparations (Average and Coefficient of Variation, Five Replicates)

Drug and supplier	Nominal composition (mg)	Found by present method[a] (mg)	CV	Found by comparison method (mg)	Reference for comparison method
Baralgan (Hoechst)	500 Analgin 5 *p*-Piperidinoethoxy-*O*-carbomethoxy benzophenone hydrochloride 0.1 Diphenylpiperidinoethyl acetamidebrom-*O*-methylate	502	0.1	505	(*8*)
Ginox (Averest Chem. Lab)	500 Analgin 100 Oxyphenbutazone	509	0.2	515	(*7*)
Maxigon (Unichem)	500 Analgin 5 *p*-Piperidinoethoxy-*O*-carbomethoxy benzophenone hydrochloride	490	0.2	495	(*8*)
Algesin-O (Alembic)	300 Analgin 100 Oxyphenbutazone	303	0.2	293	(*8*)
Pamagin (Alkem)	500 Analgin 5 Diazepam	468	0.2	459	(*8*)
Ultragin (Manner)	250 Analgin 35 Orphenadrine hydrochloride 25 Caffeine	255	0.5	256	(*8*)
Oxalgin (Cadila)	500 Analgin 100 Oxyphenbutazone	513	0.4	510	(*6*)
Novalgin (Hoechst)	500 Analgin	499	0.1	495	(*7*)
Brugesic (Brawn)	500 Analgin 100 Oxyphenbutazone	494	0.1	498	(*6*)

Determination of Novalgin

The determination of novalgin was done in various pharmaceutical preparations and the results are presented in Table 1. Some excipients and other drugs commonly added to dosage forms were found not to interfere: these are acetylsalicylic acid, salicylamide, caffeine, phenylbutazone, chlorpheniramine maleate, and diazepam. Paracetamol, being an oxidant, interferes with the test, so the method cannot be used for the determination of novalgin in the presence of paracetamol. The interference of oxyphenbutazone can be removed by dissolving the drug in water, filtering the undissolved oxyphenbutazone, and using the filtrate for the determination.

The present method is more simple, accurate, and sensitive, with respect to the microgram range of determination and the higher molar absorptivity, than are earlier methods (*8*).

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