Indirect Determination of Mefenamic acid by Atomic Absorption Spectrometry

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Summary: A method is described based on the complexation of mefenamic acid with copper(II) amine sulpahte and extraction of complex in chloroform. The copper is back extracted with nitric acid. The copper content in aqueous phase is determined by flame atomic absorption spectrometry (FAAS). The concentration of copper is proportional to mefenamic acid. The linear calibration curve was obtained with 30-241 ug/ml, with detection limit 5 ug/ml.The method was applied for the determination of mefenamic acid in pharmaceutical preparations.

Introduction

Mefenamic acid 2-(2,3-dimethylphenylamino-benzoic acid) is potent non-steroidal analgesic and anti-inflammatory agent, extensively used for rheumatoid arthritis. A number of analytical methods are reported for the determination of mefenamic acid principally based on titrimetry [1,2], spectrophotometry [3-5], spectrofluorimetry [6-7], polarography [8], chromatography [9-12] and atomic absorption spectrometry (AAS) [13,14]. A wide range of chromato-graphic techniques have been reported for the determination of mefenamic acid in pharmaceutical preparations, blood and urine. Mefenamic acid being the derivative of anthranilic acid forms complexes with a number of metal ions [15-21]. Khier *et al* [22] have reported the formation of mefenamic acid complex with copper aminesulphate, which is extractable in chloroform for the spectrophotometric determination of mefenamic acid. In the present work complexation of mefenamic acid with copper amine has been examined for the determination of mefenamic acid using FAAS.

Results and Discussion

Mefenamic acid reacts with copper(II) in ammonical solution at pH 9 to form a complex in a metal ligand ratio 1:1, which is extractable in chloroform (Fig. 1). Copper was back extracted with nitric acid. Concentrated nitric acid added proved sufficient to back extract copper from organic phase. The copper was determined by air acetylene flame atomic absorption spectrometry (FAAS) using standard conditions recommended by the manufacturer.The effect of concentration on the FAAS response was examined and linear calibration curve was obtained within 30-241 ug/ml with coefficient of correlation (r) 0.983. Analysis of test solution of mefenamic acid indicated relative % error within + 4%.The effects of possible additive present alongwith mefenamic acid in pharmaceutical preparations were examined. Glucose, starch, lactose talcum, gum acaccia and magnesium nitrate were added ten times the concentration of mefenamic acid and it was observed that they did not effect the determination. The Mefenamic acid in pharmaceutical preparations is generally not present in combination with other analgesic, however the effect of paracetamol and indomethacin on the determination of mefenamic acid was also examined. It was observed that they did not effect the determination of mefenamic acid. Mefenamic acid in pharmaceutical preparation was investigated in tablets. The results obtained agreed to the expected value (Table 1). The pharmaceutical preparations were also analysed for mafenamic acid contents by using independent spectrophotometric method [23]. The absorbance was measured at 348 nm. (Table 1) and are in agreement with FAAS results.

Table-I Analysis of mefenamic acid in pharmaceutical preparations

	Name of drug	Weight of tablet	Amount of mefenamic acid found mg/tablet (RSD %) by AAS Spectrophotometer	Amount in mg/ tablet by spectrophotometric method
1.	Ponstan	0.592	246.6(0.3)	–
2.	Dolor	0.591	261.6(0.4)	248(1.5)
3.	Mefnac	0.584	236.6(0.6)	245(2.0)

Amount of mefenamic acid reported in each tablet by the manufacturer was 250 mg/tablet.

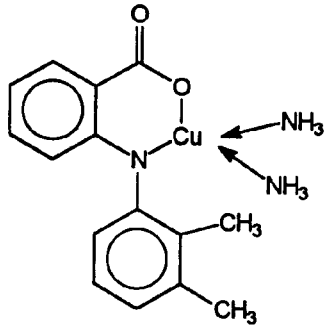

Fig.1: Structure diagram of diamine mefenamic acid copper(II) complex

Experimental

Analytical Procedure

To a separating funnel was added 4 ml of copper(II) containing 1 mg/ml and was adjusted to pH 9 with ammonia solution (25%). Mefenamic acid (Parke-Davis, Karachi) ethanolic solution (0.1-1.0 ml) containing (62.4 to 624 ug) and 4 ml of chloroform were then added. The contents were mixed well and layers were allowed to separate. The organic layer was collected and extraction was repeated with 2 ml of chloroform. The organic layer was added 0.5 ml of nitric acid (65%) and contents were mixed well for 5 min. Water 5-7 ml was added and contents were again well mixed. The aqueous layer was collected and volume was adjusted to 10 ml. The copper contents in solution was measured on Varian Spectr AA-20 atomic absorption spectrometer using air-acetylene flame atomization at 324 nm.The analysis was carried out in triplicate with delay time 3 second and integration time 3 sec.

Analysis of Mefenamic acid in Pharmaceutical Preparations

Tablets Ponston (Parke-Davis, Site Karachi) (0.595 g), Dolar(Adamjee, Korangi Karachi (0.591 g) or Mefenac tablet (Feroze Chemical Industries, Karachi (0.584 g) was ground and Powdered 0.6 g was dissolved in ethanol, filtered and volume was adjusted to 100 ml with ethanol. Solution 0.5 ml and 1.0 ml prepared from each of the pharmaceutical preparation was taken and the same procedure as above was followed. The spectrophotometric determination of mefenamic acid using reported procedure [23] was carried out with Hitachi 220 Spectrophotometer.

Conclusions

The method examine the use of flame atomic absorption for the determination of mefenamic acid in pharmaceutical product. The results indicated RSD within 0.3 to 0.6% and indicated comparable results with spectrophotometric method and expected values.

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