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Separation of Ibuprofen Enantiomers by HPLC-Mass Spectrometry

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Ibuprofen and its enantiomers separation from tablets using HPLC-MASS spectrometry has been carried out. In this work, a separation of ibuprofen enantiomers using HPLC-mass spectrometry method has been used. An achiral ODS column (150 × 4.6 mm id)) with the mobile phase consisting of CH_3CN-H_2O (35-65) was used for the extraction of the ibuprofen racemate and a chiralcel OJ-R column (150 × 4.6 mm id) with the mobile phase consisting of CH_3CN-H_2O (35/65) to separate the ibuprofen enantiomers from tablets. The separation is stereoselective and the enantiomers are well resolved with reasonable retention times and the drug purity was confirmed.

Key Words: Ibuprofen, Enantiomers, HPLC, Mass spectrometry.

INTRODUCTION

Ibuprofen belongs to NSAID drugs. Its analgesic and antiinflammatory activities have been achieved principally through S-form. Whereas the R-form is responsible for its undesired effects. Ibuprofen (Fig. 1) appears to have the lowest incident of gastrointestinal adverse drug reactions of all the non-selective NSAIDs, however this only at low doses of it[1-3]. Indeed it was found that the s-form was the active form both *in vitro* and *in vivo*. It was logical then, that there was the potential for improving the selectivity and potency of ibuprofen formulation by marketing ibuprofen as single enantiomer product. Due to the expense that might be involved in marketing single dose, most ibuprofen formulations currently marked are racemate mixtures.

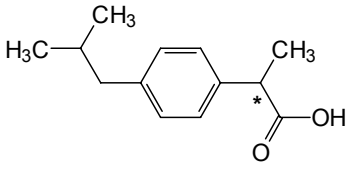

Fig. 1. Structural formula of ibuprofen

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Several assays for measurment of ibuprofen as racemate and its enantiomers has been reported in the literature. These include direct and indirect liquid chromatographic method[4-6].

In this paper, we report a method of separation of ibuprofen and its enantiomers from tablet, using HPLC-mass spectrometry. The method is selective and stereoselective and can be used to determine the total concentration of ibuprofen racemate and ibuprofen enantiomers with a reasonable retention times.

EXPERIMENTAL

An initial purification was carried out before HPLC and mass spectrometry. Separation of ibuprofen and its enantiomers RP-HPLC purification was carried out on ODS C18 column (50 × 4.6 mm id) connected to a Beckman Coulter System, Gold LC-168 diode array detector (Beckman Coulter, Fullerton, CA, USA). The mobile phase was CH_3CN-H_2O (35:65) The ibuprofen enantiomers were separated using a chiralcel OJ-R column (150 × 4.6 mm id) with the mobile phase consisting of CH_3CN-H_2O (35:65).

Ibuprofen tablets were SAIDAL company, Algiers and ibuprofen racemate and enantiomers were a kind of gift from laboratory of aminoacides, peptides and proteines of university Montpellier2, France.

Mass spectrometry was carried out on a Tofspec 2E matrix-assisted laser desorption ionization-time of flight mass spectrometer. The HPLC-mass separations were carried out with a system consisting of a pump (system gold LC-126) solvent module Beckman and a reodyne (Cotati, CA) with 50 μL sample loop.

Sample treatment procedures

Tablet formulation assay: A tablet (200 mg) was crushed and triturated in a mortar until a fine powder was obtained. An amount of the powder was dissolved in the mobile phase consisting of CH_3CN-H_2O and then filtered under vacuum through 0.45 Millipore filter using an all glass apparatus and degassed by ultrason.

RESULTS AND DISCUSSION

Optimization of mobile phase was required to achieve resolution of ibuprofen enantiomers using a Chiralcel OJ-R column and mobile phase using achiral ODS column to extract ibuprofen racemate until peak symmetry and reasonable analysis time were achieved. This was accomplished by percentage organic modifier, CH_3CN-H_2O (35:65 % v/v) without buffer.

Fig. 1 and 2 show the chromatograms of racemate and enantiomers of ibuprofen, respectively. As can be seen from these figures, the optimum

conditions were obtained and the method can be used for the determination of both racemate and enantiomers of ibuprofen with reasonable retention time (Table-1). Fig. 3 shows mass spectrum of ibuprofen and confirms its purity and hardly any fragmentation occurs with good signal-to-noise ratios.

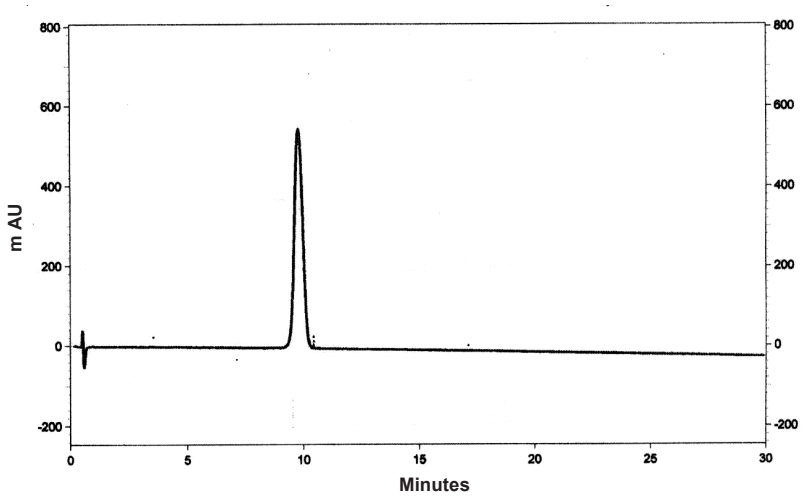

Fig. 2 . Chromatogram of Ibuprofen racemate

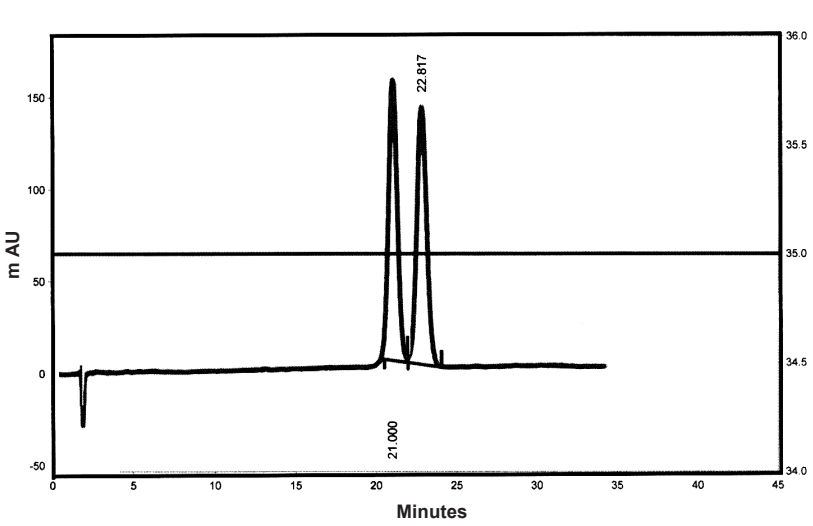

Fig. 3. Chromatogram of Ibuprofen enantiomers

TABLE-1

PK	Retention Time	Area	Area Percent
1	21.000	5847486.00	49.241
2	22.817	6027762.00	50.759
Total		11875248.00	100.000

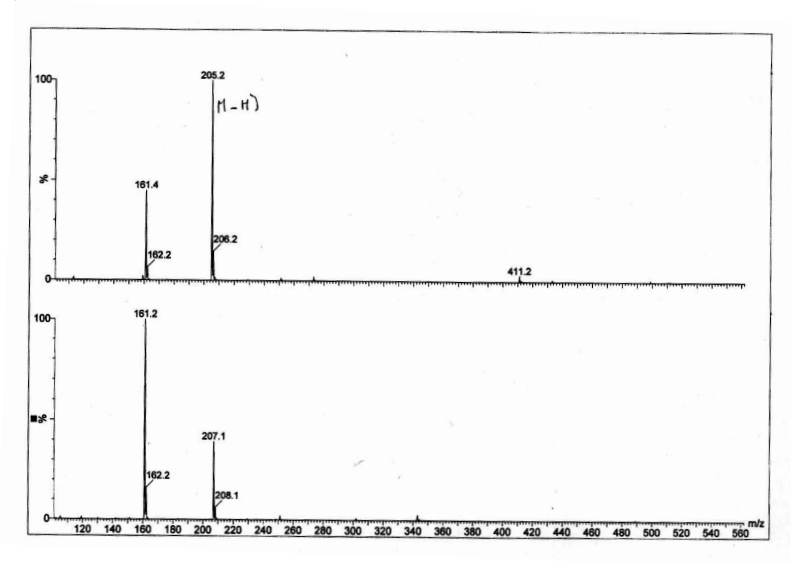

Fig. 4. Mass-spectrometry of ibuprofen

Conclusion

HPLC-MS method was used to extract ibuprofen and to separate its enantiomers from tablets. The same mobile phase was used for both racemate and enantiomers without any buffers and coupled column which causes base line disturbance. Therefore the method is selective, sensitive and simple and presents a compatible chromatographic system to be used for qualitative and quantitative analysis in different matrix. Enhanced selectivity can be achieved by coupling HPLC-MS.

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