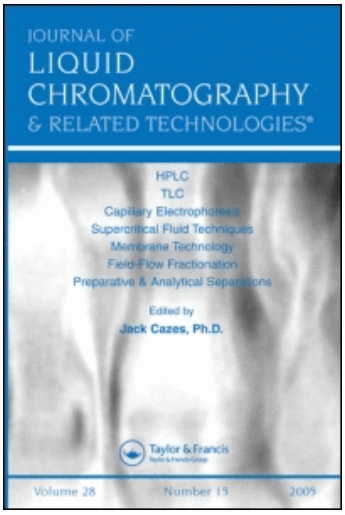

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A GPC Method for Analysis of Low Molecular Weight Drugs

K. Sreenivasan[a]; Prabha D. Nair[a]; K. Rathinam[b]
[a] Laboratory for Technical Evaluation of Biomaterials, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum [b] Division of Toxicology Sree Chitra Tirunal, Institute for Medical Sciences and Technology, Trivandrum

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A GPC METHOD FOR ANALYSIS OF LOW MOLECULAR WEIGHT DRUGS

K. Sreenivasan, Prabha D. Nair and K. Rathinam*
Laboratory for Technical Evaluation of Biomaterials
and
*Division of Toxicology
Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Trivandrum - 695 012.

ABSTRACT

Gel permeation chromatography has been shown as a versatile method for the analysis of low molecular weight drugs. Aspirin and its hydrolysis product, salicylic acid, which differ in a molecular weight of 42 units have been efficiently separated by a retention time difference of 3.25 minutes. Qualitative idea of other impurities is also obtained.

INTRODUCTION

Gel permeation chromatography (GPC) separates sample molecules by differences in effective molecular size in solution. This technique has been widely used for the determination of weight average molecular weight M_w molecular weight distribution and dispersity of polymeric materials. GPC is used

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primarily for high molecular weight (> 1000) components and its application in routine drug analysis is limited. We report here the use of GPC for the analysis of low molecular weight drugs. As a representative example we chose to analyse the amount of salicylic acid in commercially available aspirin samples.

Aspirin (acetyl salicylic acid) is widely used for its analgesic, anti-inflammatory and antipyretic effects. Aspirin has been found to interfere with platelet aggregation (1,2) reduce venous thrombosis (3) and is also associated with secondary prevention of myocardial infarction (4,5). Salicylic acid, the major decomposition product of aspirin, irritates the digestive system. The limit of salicylic acid content in aspirin powder is prescribed to be 0.1% by pharmacopoeias (6,7). But the assay for aspirin powder described in them is qualitative. There have been reports on the assay of salicylic acid in aspirin by HPLC (8,9) and GLC (10). However, these methods are time consuming, require chromatographic conditioning and even chemical derivatization for the GLC method (10). Reverse phase methods are not desirable as aspirin is not stable in the mixed

aqueous organic eluents in that form of LC. Gel permeation chromatography has been used to an advantage for the analysis of salicylic acid in aspirin. This method can also be used for other low molecular weight xenobiotics.

EXPERIMENTAL

Apparatus

The chromatographic system was a Waters Associates Model 6000A solvent delivery pump equipped with a U6K injector. A μStyragel column (30x0.78cm I.D. Pore size 100A°) and a model 440 absorbance detector. Chromatograms were obtained in a Houston Instruments Omniscribe recorder and peak absorbance values were directly read from the digital display of the Model 440 system.

Chromatographic Conditions

A flow of 1 ml/min of the mobile phase was used and absorbance monitored at 280nm.

Reagents

Aspirin AR (Sigma Chemicals, USA) and Salicylic acid (Wilson Laboratories, India) were used

for preparing the standard samples. Aspirin was used after recrystallization in acetone. Freshly distilled Dichloromethane Analar (Glaxo Laboratories, India) was used for preparing the solution and as the mobile phase.

Calibration curve

The calibration curve for salicylic acid was prepared by noting the peak absorbance values for salicylic acid solutions at varied concentrations (10 to 100 μg/ml)

Aspirin samples

Standard aspirin sample consisted of a dichloromethane stock solution containing 1.2 mg/ml of standard aspirin.

Other samples were 1-2 mg/ml solution of 6 commercially available aspirin samples in dichloromethane. Samples were injected as soon as they were prepared and the injection volume for all samples was 100 μl.

RESULTS AND DISCUSSION

Under the experimental conditions described above, aspirin and salicylic acid had a retention

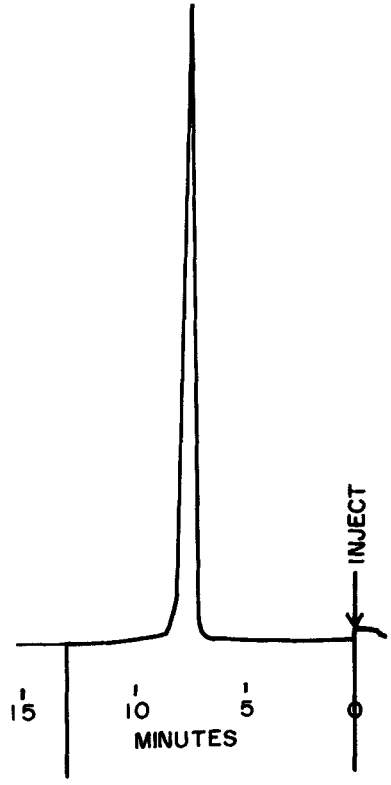

FIGURE 1 - Chromatogram of aspirin (1.2 μg/ml) in the mobile phase.

time of 7.5 ± 0.1 and 10.75 ± 0.1 minutes respectively.

Fig.1 is a chromatogram of standard aspirin (1.2mg/ml) in the mobile phase. Fig.2 is a chromatogram of standard salicylic acid (70 μg/ml) Fig.3 is a chromatogram of one of the commercial samples of aspirin, peak 1 corresponds to aspirin,

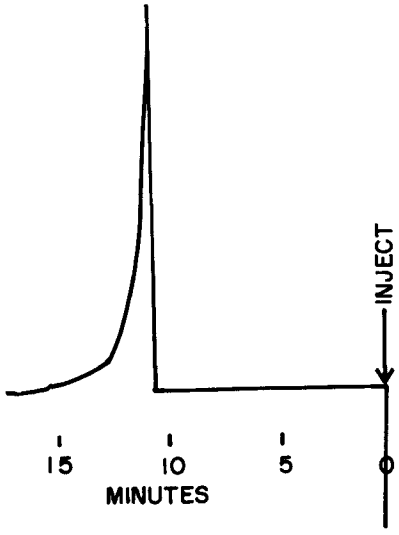

FIGURE 2 - Chromatogram of salicylic acid (70 μg/ml) in the mobile phase.

Peak 2 corresponds to salicylic acid (37.5 μg/ml), other peaks correspond to unidentified impurities. Salicylic acid concentrations in commercial aspirin samples ranged from 3-37.5 μg/ml. The minimum limit of detection for salicylic acid is 0.6 μg.

Adsorption techniques such as normal phase and reverse-phase liquid chromatography require extensive methods development time. However, in GPC analysis time is reduced considerably in additon to the simplicity of operating conditions. Salicylic acid and aspirin differ only in a molecular

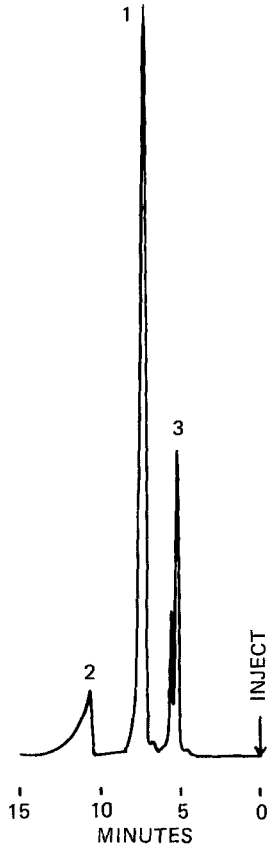

FIGURE 3 - Chromatogram of one commercial aspirin sample. Peak 1 corresponds to pure aspirin. Peak 2 corresponds to salicylic acid (37.5 µg/ml).

weight of 42 units, but are separated by a retension time of 3.25 minutes. Further, a qualitative idea of the nature of other impurities in aspirin can be obtained e.g. Peak 3 in Fig.3 corresponds to an impurity having higher molecular weight than aspirin.

In conclusion, Gel permeation chromatography has clearly been shown as a versatile technique for analysis of low molecular weight drugs.

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