Gas Chromatographic Determination of Clopidogrel from Tablet Dosage Forms

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A gas chromatographic method was developed for the determination of clopidogrel in its tablet form. The method involves use of a DB-17 capillary column. Column is of 30 m length, 0.25 mm i.d. and 0.25 μ film thickness, and hydrogen as a carrier gas with the flow rate of 2.0 ml/min. Oven temperature was maintained at 250° for 8 min. Split type of injector and flame ionization detector was used. The retention time of clopidogrel and dioctyl phthalate (internal standard) was 4.1 min and 3.2 min, respectively. Linearity for the clopidogrel was in the range of 0.5 to 5.0 mg/ml. Percentage recovery obtained was 99.89. The proposed method is accurate, precise and rapid for the estimation of clopidogrel.

Clopidogrel inhibits ADP-induced platelet aggregation[1] and is used therapeutically as an antithrombotic[2-3]. Chemically, clopidogrel is (αS)-α-{2-chlorophenyl}-6,7-dihydrothieno-(3,2-C) pyridine-5-(4H)-acetic acid methyl ester. Clopidogrel is available in tablet form for clinical use. However there is no gas chromatographic method reported for the determination of clopidogrel from tablets. In this communication, we report a gas chromatographic method for the determination of clopidogrel from tablet dosage forms, which is simple, rapid and precise.

Working standard clopidogrel hydrogen sulphate of purity 99.7% was procured from Hetero Drugs Hyderabad . Clopilet® tablets of Sun Pharmaceuticals Industries Ltd., Mumbai were procured from a local pharmacy store. Label claim of clopilet® tablet is clopidogrel hydrogen sulphate equivalent to clopidogrel 75mg per tablet. Other reagents and solvents such as dichloromethane, dioctyl phthalate, sodium hydroxide used were of analytical grade and were procured from S. D. Fine Chemicals, Tarapur.

Perkin Elmer (Autosys-XL) gas chromatograph was used and this is equipped with a split injector port and a flame ionization detector. Turbo chrom navigator software was used for gc analysis. In this method the stationary phase containing a mixture of 50% phenyl and 50% dimethyl polysiloxane and mobile phase (carrier gas) used was hydrogen with the flow rate of 2.0 ml/min. During analysis, the oven, injector and detector port temperature were kept at 250, 230 and 250°, respectively. Split type of injector was used with a split ratio of 1:50. The typical retention times observed for dioctyl phthalate (internal standard) and clopidogrel were 3.2 and 4.1 min, respectively as shown in fig. 1.

Accurately weighed (652.5 mg) clopidogrel hydrogen sulphate was taken in a separating funnel containing a mixture of water (5 ml) and 5 N sodium hydroxide solution (10 ml). This mixture was extracted four times with dichloromethane (10 ml each extraction). The extracted dichloromethane layer was dried using anhydrous sodium sulphate. Dried dichloromethane layer carefully collected into a 50 ml volumetric flask, and then diluted to the mark with dichloromethane. A final concentration of 10 mg/ml of clopidogrel, was thus obtained. One gram of dioctyl phthalate was weighed accurately and transferred into the 100 ml volumetric flask and diluted up to mark with dichloromethane to get the internal standard solution. Standard drug solution (3 ml) and 2 ml of internal standard solution were diluted to 10 ml with dichloromethane.

Twenty tablets were weighed accurately and finely powdered. The powder equivalent to 150 mg of clopidogrel was taken in a separating funnel. Water (5 ml) and 5 N sodium hydroxide solution (10 ml) was added into a separating funnel and the mixture was extracted four times with dichloromethane (10 ml each extraction). The extracted dichloromethane layer was dried using anhydrous sodium sulphate. Dried dichloromethane layer collected into a 50

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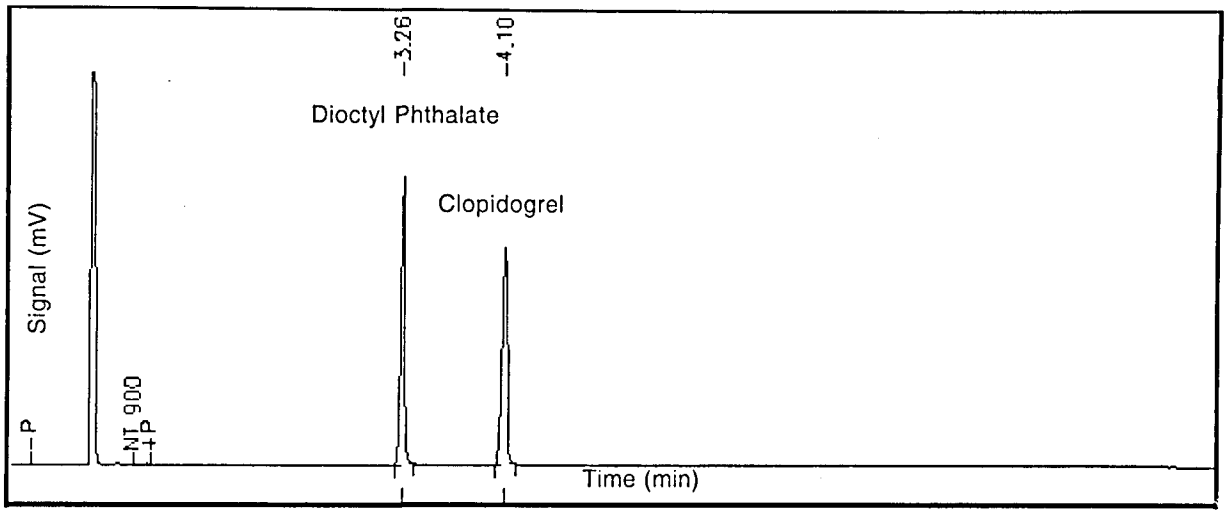

Fig. 1: Typical chromatogram of standard solution of clopidogrel and dioctyl phthalate.

ml volumetric flask, 2 ml of internal standard solution was added and then diluted to the mark with dichloromethane.

Aliquots of standard solutions were taken in 10 ml volumetric flasks and 2 ml of internal standard solution was added and diluted to the mark with dichloromethane such that the final concentration of clopidogrel obtained was in the range of 0.5 to 5 mg/ml. Peak area ratios were recorded for that of clopidogrel and dioctyl phthalate. To study the accuracy and precision of the proposed method, recovery experiments were carried out with fixed amount of pre-analyzed sample and standard solution at 3 different levels. Each level was repeated 3 times. Analysis of clopidogrel by proposed method was carried out. The results obtained by the proposed method were close to the label claim of clopidogrel, indicating that method is precise and accurate. The plot of peak area ratio versus the respective concentrations was found to be linear in the range 0.5 to 5 mg/ml with coefficient of correlation (r=0.9999).

TABLE 1: RECOVERY STUDY FOR SPIKED CONCENTRATIONS OF CLOPIDOGREL

Amount added (mg)	Amount found (mg)	Amount* recovered (%)
7.5	74.55+7.53=82.08	100.04 (0.38)
15	74.55+5.39=89.94	100.44 (0.44)
22.5	74.55+22.45=97.00	99.95 (0.25)

*Each value is average of three determinations. Values in parenthesis refer to relative standard deviation.

The contents of clopidogrel found by proposed method during recovery studies were shown in Table 1 .The mean recovery was 99.89%. High percent recovery suggested that the method was free from interference from excipients used in tabletting. The proposed method gave good resolution between clopidogrel and dioctyl phthalate within short analysis time of less than 10 min. The method was found to be very simple and rapid.. Therefore this method can be used for routine quality control analysis of clopidogrel.

REFERENCES

1. The Merck Index, 13th Edn., Merck & Co., Inc., Whitehouse Station, NJ, 2001, 420.
2. Feuerstern, G., **Exp. Opin. Invest. Drugs**, 1995, 4, 425
3. Mills, D.C.B., **Arterioscler. Thromb.**, 1992, 12, 430.