RESEARCH PAPER

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Simultaneous Determination of Paracetamol, Diclofenac Sodium and Chlorzoxazone by HPLC from Tablet.

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A simple, reverse phase high performance liquid chromatographic method was developed for the simultaneous determination of Paracetamol, Diclofenac Sodium and Chlorzoxazone from tablets. The method described is precise, accurate reproducible and rapid.

PARACETAMOL, Chlorzoxazone and Diclofenac Sodium with their dosage forms, including combination with other drugs have been listed in various pharmacopoeias.[1-4]

HPLC method has been described for the simultaneous determination of Paracetamol and Diclofenac Sodium from tablets, Chlorzoxazone in combination with Paracetamol in tablet and capsule forms is official in U.S.P XXII[1], which reported HPLC method for the simultaneous determination of both the drugs. Besides this, simultaneous determination of Paracetamol and Chlorzoxazone has been carried out by spectrophotometric[6-7] methods. HPLC[8-9], Fluorimetric[10] methods have also been reported for Chlorzoxazone in analgesic mixtures as well as in biological fluids.

A simple, precise and rapid reverse phase HPLC method is proposed for the simultaneous determination of Paracetamol, Diclofenac Sodium and Chlorzoxazone in tablet dosage forms.

EXPERIMENTAL

Instrumentation : The HPLC system consisted of PERKIN-ELMER isocratic LC 250 pump, LC 290 UV detector and PE Nelson 1020 computing integrator. Injections were made through an injector equipped with a 20 ul sample loop (Rheodyne model 7125) using Hamilton 50 ul syringe. Shodex C_{18} (5 micron, 15 cm) column was used. The flow rate of the mobile phase was 1.0 ml/min with an average operating pressure of 2200 psi. Detection was monitored at 275 nm.

*For Correspondence.

Reagents

Chromatographic grade water, methanol, triethylamine, phosphoric acid (E.Merck, India) were used.

Materials

Standard Paracetamol, Diclofenac Sodium and Chlorzoxazone were procured from IPCA Laboratories (I) Ltd.

Paracetamol-Diclofenac Sodium-Chlorzoxazone tablets (Mobizox) were procured from market.

Mobile Phase

The mobile phase consisted of methanol : water: triethylamine (55:45:0.1 v/v) pH adjusted to 6.8 with dilute orthophosphoric acid. This solution was filtered through 0.45 micron filter paper and then was de-

Table 1: Results of the replicate analysis of tablets.

DAY	Paracetamol Labelled Amount (500 mg/tab)			Chlorzoxazone Lebelled Amount (500 mg/tab)			Diclofenac Sodium Labelled Amount (50 mg/tab)		
	Amount Found* mg/tab	RSD (%)	% Labelled Amount	Amount Found* mg/tab	RSD (%)	% Labelled Amount	Amount Found* mg/tab	RSD (%)	% Labelled Amount
I	495.7	1.14	99.14	499.8	0.91	99.64	49.73	1.19	99.47
II	497.3	0.99	99.46	500.2	1.17	100.04	50.02	1.36	100.04
III	496.3	1.08	99.26	499.4	1.23	99.88	49.76	1.22	99.52

*:-Average of three experiments.

aerated by sonication for 5 min. Before injections, column was stabilised with the eluent for 30 min.

Preparation of standard curves

Standard stock solution of Paracetamol, Diclofenac Sodium and Chlorzoxazone was prepared in methanol in the concentration range 5 mg/ml, 0.5 mg/ml and 5 mg/ml respectively.

Varying volumes of the above standard stock solution (0.1-0.7 ml) were taken in seven 50 ml standard volumetric flasks and diluted with mobile phase. 20 microlitres of each solution was injected into the column three times and peak were integrated.

Calibration curves were constructed by plotting mean peak areas against the corresponding drug concentrations.

Sample Preparation

Twenty tablets each of combined dosage were accurately weighed and powdered to a fine composite. A quantity of composite equivalent to 500 mg of Paracetamol was weighed and transferred into a 100 ml flask, to which 50 ml of methanol was added and kept for sonication for 10 minutes and finally diluted upto the mark with the same. This was filtered through 0.5 micron whatman paper using filtration kit. 0.5 ml of the filtered solution was diluted to 100 ml with mobile phase. 20 microlitres of this solution was injected in triplicate and chromatograms were recorded.

Calculations

Amount of Paracetamol, Diclofenac Sodium and Chlorzoxazone were calculated using regression equations from corresponding standard curves prepared each day.

Recovery Studies

To study the accuracy, reproducibility and precision of the above method, recovery experiment was carried out at five levels. Each level was repeated three times. The percentage recovery was calculated from the amount of drug found at each level.

RESULTS AND DISCUSSION

Various mobile phase systems were prepared and used for chromatographic separation. methanol: water: triethylamine (55:45:0.1 v/v) adjusted to pH=6.8 with dilute phosphoric acid gave a better

resolution and sensitivity. All final solutions were prepared in mobile phase to prevent interference in baseline. The order of elution was Paracetamol (2.0 min), Chlorzoxazone (6.04 min)and Diclofenac Sodium (11.6 min)

A linear relationship was obtained for Paracetamol and Chlorzoxazone in the concentration range of 10-70 mcg/ml and for Diclofenac Sodium in the concentration range 1-7 mcg/ml.

The calibration curves could be represented by the following regression equations

Y(Paracetamol) = 22.3043 X + 11.614 (r=0.999)

Y(Chlorzoxazone) = 29.4105 X + 11.2857 (r=0.999)

Y(Diclofenac Sodium) = 47.3775 X - 6.64 (r=0.999)

The results of the replicate analysis (n=7) of the tablets carried out on three different days are tabulated in **table1.** The mean recoveries obtained for Paracetamol, Diclofenac Sodium and Chlorzoxazone were 99.58%, 99.85% and 99.58% respectively.

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