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Note

Quantitative gas chromatographic determination of tamoxifen citrate in pharmaceuticals

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Tamoxifen citrate is a non-steroidal triphenylethylene antioestrogen that is used in the treatment of breast cancer and in basic laboratory endocrinology studies[1,2]. Although various pharmaceutical formulations are commercially available, none of the pharmacopoeias mentions a suitable method for the determination of tamoxifen citrate in dosage form. A number of high-performance liquid chromatographic (HPLC) methods for the determination of tamoxifen in blood plasma have been reported[3-7].

In this paper we report a gas chromatographic method for the determination of tamoxifen citrate in pharmaceuticals.

EXPERIMENTAL

Reagents and materials

Preparation of standard solution. A 1:1 (v/v) mixture of methanol and chloroform (both of chromatographic grade) was used as the solvent and solutions of tamoxifen citrate and dicyclohexyl phthalate of concentration 5 mg/ml were prepared in this solvent. A mixture of 3 ml of the tamoxifen citrate solution and 2 ml of the dicyclohexyl phthalate solution was used as a working standard solution.

Preparation of the sample: Fifty tablets were powdered and transferred into a 100-ml beaker, 25 ml of the above solvent were added and the solution was filtered into a 100-ml volumetric flask. The volume, after two to three washings, was made up to the mark to give a concentration of one tablet per 2 ml. A mixture of 2 ml of the sample solution and 2 ml of dicyclohexyl phthalate solution was used as a working sample solution.

Gas chromatography

A Hewlett-Packard HP 3800 gas chromatograph equipped with dual flame ionization detectors and a Spectra-Physics integrator was used. A stainless-steel column (3 ft. × 0.2 cm I.D.) packed with 3% Dexsil 300 on Chromosorb W HP (100–120 mesh) was used.

The oven temperature was set at 235°C (isothermal) and the injection port and detector were set at 250°C. The gas flow-rates were maintained at 35 ml/min for nitrogen (carrier gas), 35 ml/min for hydrogen and 400 ml/min for air. After the gas

CHANNEL A   INJECT   23/12/84 74:45:27

		23/12/84 71:15:27	CH = "A"	PS = 1.	
FILE 1.	METHOD 2.	RUN 10	INDEX 7		
SAMPLE 1	TAB + 6 mg				
SA 100.	IS 10.	XF 100.			

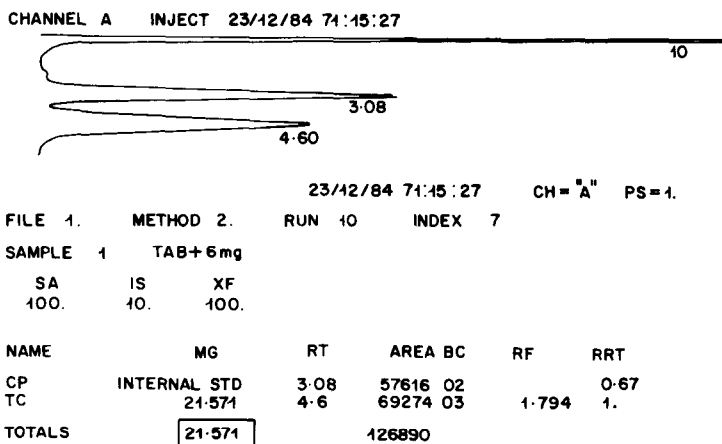| NAME		MG	RT	AREA BC	RF	RRT
CP	INTERNAL STD	3·08	57616 02			0·67
TC		21·571	4·6	69274 03	1·794	1.
TOTALS		21·571		126890		

Fig. 1. Chromatogram for a standard sample. Method 2 = internal standard method; Run = injection number; SA = sample amount; XF = factor; Name = name of component; MG = mg; RT = retention time; RF = relative factors; RRT = relative retention time; BC = baseline code.

chromatographic conditions had been attained, 1 μl each of the working sample and working standard solutions were injected separately. By comparing the peak-area ratios of tamoxifen citrate in the sample and standard tamoxifen citrate, the amount of tamoxifen citrate present per tablet could be calculated. A typical chromatogram is shown in Fig. 1.

RESULTS

The recovery of added tamoxifen citrate was studied at four different levels. From the amount of tamoxifen citrate found, the percentage recovery was calculated using the equation

$$\text{Recovery (\%)} = \frac{N(\Sigma XY) - (\Sigma X)(\Sigma Y)}{N(\Sigma X^2) - (\Sigma X)^2} \cdot 100$$

where A = amount of standard tamoxifen citrate added, Y = amount of tamoxifen citrate found by the proposed method and N = number of observations.

A plot of the amount of tamoxifen citrate found against the amount of standard tamoxifen citrate added is shown in Fig. 2. The intercept on the ordinate indicates the amount of tamoxifen citrate present per tablet. From this graph the recovery can also be calculated using the equation

$$\text{Recovery (\%)} = \text{slope} \cdot 100$$

A set of observations and calculations is shown in Tables I and II. The coefficient of variation and the relative mean deviation, based on the data in Tables I and II, are given in Table III.
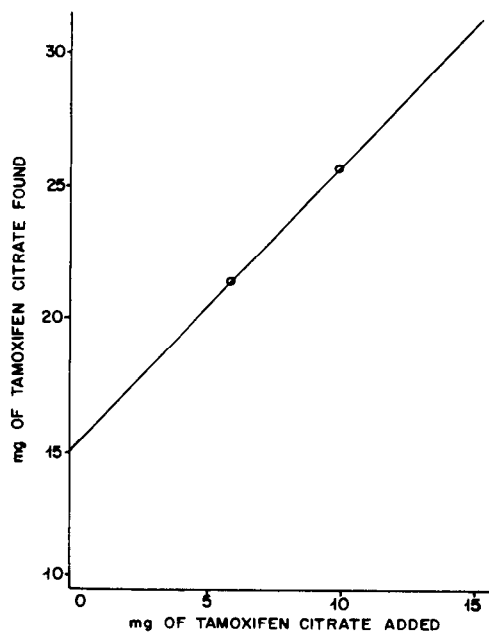
Fig. 2. Graph for standard additions method.

TABLE I

RESULTS OF REPLICATE ANALYSES OF TAMOXIFEN CITRATE AT FOUR DIFFERENT LEVELS OF ADDITION

Level of addition	Standard drug added per tablet (mg)	Tamoxifen citrate found by the proposed method (mg per tablet)							
		1	2	3	4	5	6	7	Average
Zero	0	15.095	15.064	15.742	15.539	15.495	15.134	15.113	15.311
1	4	19.531	18.679	19.114	19.434	19.667	20.089	20.189	19.529
2	6	21.571	21.258	21.205	20.912	20.959	20.935	20.873	21.102
3	12	27.966	27.396	27.938	27.840	27.305	27.348	26.852	27.521

TABLE II

CALCULATIONS OF PERCENTAGE RECOVERY (SEE FIG. 2)

Recovery = 101.33% ($N = 28$).

Level of addition	X	Y	X^2	XY
0	7×0	7×15.31	7×0	7×0
1	7×4	7×19.53	7×15	7×78.12
2	7×6	7×21.10	7×36	7×126.61
3	7×12	7×27.52	7×144	7×330.25
	$\Sigma X = 154$	$\Sigma Y = 584.24$	$\Sigma X^2 = 1372$	$\Sigma XY = 3744.86$

TABLE III

PRECISION OF THE PROPOSED METHOD AT DIFFERENT LEVELS OF ADDITION

Level of addition	Coefficient of variation (%)	Relative mean deviation (%)
0	1.79	1.57
1	2.70	1.99
2	1.21	0.99
3	1.49	1.23

DISCUSSION

We believe that the porposed assay method is the first gas chromatographic procedure developed for the determination of tamoxifen citrate in pharmaceutical formulations. Previous reported methods involve the HPLC determination of tamoxifen citrate in blood plasma. The proposed method was devised with the purpose of developing a fast and accurate technique, devoid of any interferences from common excipients, thereby eliminating any elaborate sample treatment. This technique is economical (cost of reagents compared with the previous HPLC methods). The proposed method also does not involve any derivatization.
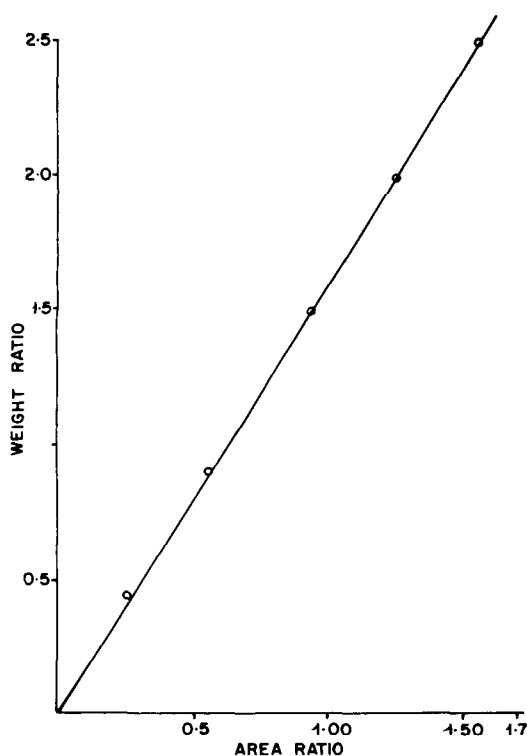

Fig. 3. Calibration graph for tamoxifen citrate using dicyclohexyl phthalate as an internal standard.

The proposed assay method was carried out by the internal standard ratioing method in order to eliminate any errors that may occur during injection. A calibration of peak-area ratio of tamoxifen citrate to dicyclohexyl phthalate against the weight ratio of tamoxifen citrate is shown in Fig. 3. The regression equation is

$$Y = 0.7344 + 0.6302 \, X$$

where X = weight ratio and Y = area ratio. The graph was found to be linear from 0.45 to 2.5 mg/ml.

The amount of tamoxifen citrate found per tablet was calculated using the equation

$$\text{Amount per tablet} = A \cdot \frac{R_{\text{samp}}}{R_{\text{std}}} \cdot \frac{D}{W}$$

where A = concentration of standard tamoxifen citrate (mg/ml), R_{samp} = peak-area ratio of tamoxifen citrate to dicyclohexyl phthalate in the sample, R_{std} = peak-area ratio of tamoxifen citrate to dicyclohexyl phthalate in the standard, D = dilution factor, W = weight of sample taken.

The amount of tamoxifen citrate found was 15.31 mg per tablet compared with the labelled claim of 15.2 mg per tablet. The recovery of the added standard was 101.33%, indicating that there was no interference from excipients present in the tablet. The coefficient of variation and relative mean deviation values are low, indicating that the proposed method is precise and reproducible.

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