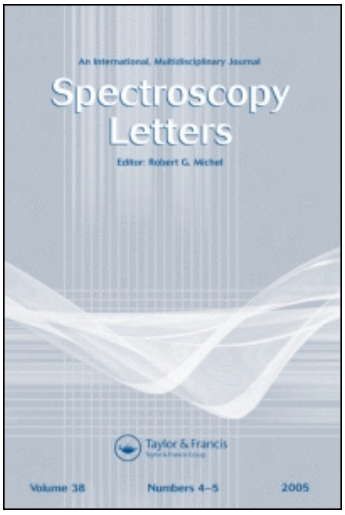

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Flow Injection Analysis of Pharmaceutical Compounds. VI. Determination of Some Central Nervous System Acting Drugs by UV-Spectrophotometric Detection

A. E. El-Gendy[a]; M. G. El-Bardicyy[a]; H. M. Loutfy[a]; M. F. El-Tarras[a]
[a] Analytical Chemistry Department, Faculty of Pharmacy, Cairo University, Cairo, Egypt

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FLOW INJECTION ANALYSIS OF PHARMACEUTICAL COMPOUNDS. VI. DETERMINATION OF SOME CENTRAL NERVOUS SYSTEM ACTING DRUGS BY UV-SPECTROPHOTOMETRIC DETECTION

Key words: Flow Injection Analysis, Spectrophotometry, Amitriptyline hydrochloride, Carbamazepine, Clomipramine hydrochloride, Fluphenazine hydrochloride, Imipramine hydrochloride.

A.E. El-Gendy, M.G. El-Bardicy, H.M. Loutfy and M.F. El-Tarras
Analytical Chemistry Department,
Faculty of Pharmacy, Cairo University,
Kasr El-Aini, ET-11562 Cairo, Egypt.

ABSTRACT

The Present work describes a direct flow injection analysis (FIA) of five commonly used central nervous system (CNS) acting drugs namely amitriptyline hydrochloride, carbamazepine, clomipramine hydrochloride, fluphenazine hydrochloride and imipramine hydrochloride. The characteristics of the system and the conditions of the spectrophotometric determination are evaluated. The proposed technique can be applied for pharmaceutical quality control of the pure material and pharmaceutical dosage forms containing the drug. Amount ranging from 16 to 80 $\mu g.ml^{-1}$ of amitriptyline hydrochloride,

carbamazepine and fluphenazine hydrochloride and from 32 to 160 $\mu g.ml^{-1}$ of clomipramine hydrochloride and imipramine hydrochloride dissolved and/or extracted in ethanol could be accurately analyzed. Standard addition (0.5 to 3 times of the claimed amounts) of authentic samples to powdered tablets gave good mean percent recoveries with low standard deviations. Samples can be introduced at rates of about 180 per hour or even more. The results obtained by applying the proposed FIA method are statistically analyzed and compared with those obtained from applying pharmacopoeial procedures.

INTRODUCTION

Central nervous system acting drugs have either antidepressant, antipsychotic or anticonvulsant activity. They are available in dosage forms mainly tablets. Many procedures are known for their quantitative determination.

Among the several analytical methods of analysis are spectrophotometric[1-3], flurometric[4], nuclear magnetic resonance[5], atomic absorption spectroscopy[6] and polarographic [7] methods. Chromatographic methods[8-12] can be recommended for estimation of these drugs in raw materials and in dosage forms. Recently, attention has been given to repetitive, rapid determination of drugs in samples injected into flowing streams. Flow injection analysis (FIA) can be applied for several groups of pharmaceuticals to develop simple, reproducible and rapid procedures to find applications in pharmaceutical research and quality control laboratories. The present work investigates a direct flow injection determination of some CNS acting drugs in pure and in its dosage forms.

EXPERIMENTAL

Apparatus

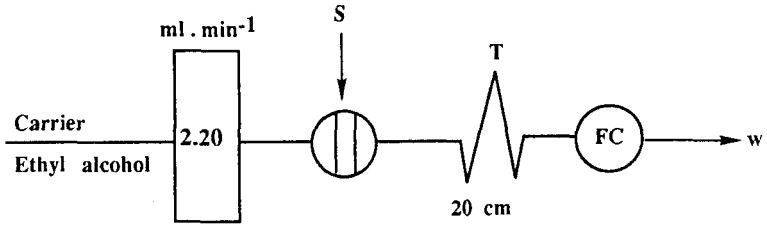
The flow diagram obtained by using a small Flow Injection Analyzer (5001 Fiastar-Tecator AB, Hoganas, Sweden) is shown in figure 1. The fluids were impelled with a peristaltic pump and tygon pumping tubes were employed. The volume of sample depends on the length of tubing Ls (0.5 mm i.d. x 12 cm, i.e. equivalent to 24 μl). The spectrophotometric measurement was performed by the use of a flow cell (volume of 80 μl) with a light path of 1 cm, installed in a spectrophotometer (SP 6-500 UV- spectrophotometer, Pye-Unicam, U.K.) connected to a strip chart linear recorder (Unicam AR 25, Pye-Unicam, U.K.) with a chart speed of 1 cm.min^{-1} at a normal sensitivity of 10 mV. The incubation coil was a polyethylene tube (0.5 mm i.d. x 20 cm). Spectroscopic-grade ethanol (E.Merck) was used as a carrier at a rate of 2.2 ml. min^{-1}.

Materials

The central nervous system acting drugs used were carbamazepine, clomipramine hydrochloride and imipramine hydrochloride, kindly supplied by Ciba-Geigy, Egypt; fluphenazine hydrochloride, kindly supplied by Squibb-Egypt and amitriptyline hydrochloride, kindly supplied by Kahira-Pharm. and Chem.Ind.Co., Cairo, Egypt.

Their purities were established by the British Pharmacopoeia method[13]. All compounds had a purity of not less than 99.99%. of the active ingredients present.

The Pharmaceutical Preparations studied were Tegretol 200, Tegretol CR 200 and, Tegretol CR 400 tablets; Anafranil 25 and Anafranil 75 tablets; Tofranil 10 and Tofranil 25 tablets, Produced by Ciba-Geigy,



uv - spectrophotometer at 230 nm , 285 nm 252 nm, 259 nm and 251 nm

Figure (1) Diagam of the flow injection analyzer .

FC , denotes the flow cell where detections are made at indicated wavelengths ; T , is the incubation coil ; S , means sampling ; and W, indicates waste .

Egypt; Moditin tablets Produced by Squibb-Egypt; Tryptizol 10 and Tryptizol 25 tablets Produced by Kahira-Pharm. and Chem. Ind., Co., Cairo, Egypt.

Analytical Techniques

Preparation of Calibration Graphs

Calibrated curves were prepared by taking aliquots from a stock solution (0.8 $mg.ml^{-1}$) of amitriptyline hydrochloride, carbamazepine and fluphenazine hydrochloride and from stock solution (1.6 $mg.ml^{-1}$) of clomipramine hydrochloride and imipramine hydrochloride in ethanol and diluting with the same solvent. The absorbance and Peak height of diluted solutions were scanned at 238 nm, 285 nm, 259 nm, 252 nm and 251 nm respectively and plotted versus concentration.

Preparation of Samples

To determine the concentration of the studied drugs, weigh accurately not less than twenty tablets and

calculate the average weight of each tablet. Take an aliquot of the powdered tablets and extract with absolute ethanol to get the proper dilution, filter through dry filter paper into a dry volumetric flask. Proceed as mentioned before for preparing calibration graphs, starting from "the absorbance and peak height...." and calculate the concentration referring to the prepared calibration curves.

Standard Addition

An accurately weighed amount of pure drug equivalent to 0.5 to 3 times of the labelled amount in tablets was added to an accurately weighed amount of powdered tablets followed by the above procedure for preparing samples.

RESULTS AND DISCUSSION

The FIA system used is a single-line manifold consisting of one tube through which the carrier stream (abs.ethanol) moves towards the flow-through detector. A system with limited dispersion, i.e. no sample treatment, has been used where the original composition of the sample solution is to be assayed. Therefore, the connecting tube between the detector and the injection valve has to be made as short as physically possible and the sample volume is then relatively large. Performance of the system, in the absence of reaction, was evaluated. The dependence on sensitivity, sampling rate, and residence time were also studied. Sensitivity was correlated to the dispersion coefficient, represented as: $D = C^{o}/C^{max}$, where C^{o} is the original concentration of the injected sample solution and C^{max} is the concentration within that imaginary element of fluid that corresponds to the maximum of the recorded curve. The sampling rate V (samples per hour) is given by $V = 3600/t_b$ (seconds), where t_b is defined as the time interval between the

appearance of the signal and its return to the base line. The residence time t_1 (seconds) is defined as the time interval elapsed between the time of sample introduction and the appearance of the signal. Table 1 shows the results obtained from such evaluation. The sample volume was 24 μl and flow rate (Q) was 2.20 ml min^{-1}. The results show that sampling rates of about 180 samples per hour can be obtained with good sensitivities, for the sample volume and the flow rate indicated.

After the performance of the proposed system had been established, it was applied to the spectrophotometric determination of the studied CNS acting drugs.

The absorption spectra of amitriptyline hydrochloride, carbamazepine, clomipramine hydrochloride, fluphenazine hydrochloride and imipramine hydrochloride exhibits absorption maxima at about 238 nm, 285 nm, 252 nm, 259 nm and 251 nm respectively.

Linearity was obtained in concentration range 16-80 $\mu g.ml^{-1}$ in case of amitriptyline hydrochloride, carbamazepine, fluphenazine hydrochloride and 32-160 $\mu g.ml^{-1}$ in case of clomipramine hydrochloride and imipramine hydrochloride.

The regression equations and correlation coefficient derived using the least square method are shown in table 2.

Table 3 represents the results obtained from the FIA determination of the studied drugs in raw materials compared with those obtained by applying the official BP 1988 procedures. Similary, table 4 demonstrates the

TABLE 1

Appropriate analytical conditions for the flow injection determination of some central nervous system acting drugs.

Introduced volume (μl)	Q ($ml.min^{-1}$)	D*	Incubation Coil (cm)	t_b sec	V sample h^{-1}	t_I sec.
24	2.20	2.84	20	20	180	5.75 5.70**

*(D) for limited dispersion = 1-3

** Calculated residence time t_I (seconds).

TABLE 2

Assay parameter for the FIA determination of some central nervous system acting drugs

Compound	Concentration range ($\mu g.ml^{-1}$)	λ_{max} (nm)	Regression Parameter*		
			a	b	r
Amitriptyline hydrochloride	16-80	238	0.10000	0.12375	0.9999
Carbamazepine	16-80	285	0.02000	0.11875	0.9999
Fluphenazine hydrochloride	16-80	259	0.16000	0.13875	0.9998
Clomipramine hydrochloride	32-160	252	0.01024	0.03406	0.9998
Imipramine hydrochloride	32-160	251	0.01024	0.04031	0.9998

*$A = bc + a$

where

A is the peak height in cm

a,b and c are the intercept, slope and the concentration ($\mu g.ml^{-1}$),

and r is the correlation coefficient

TABLE 3

Results of FIA determination of some central nervous system acting drugs in raw materials compared with those obtained by applying the official BP 1988 methods

Compound	FIA. Technique			Official Method Found (%) ± C.V
	Found (%) ± C.V	F*	Student's t**	
Amitriptyline hydrochloride	100.05 ± 1.04	1.31	0.097	99.99 ± 0.91
Carbamazepine	99.87 ± 0.92	5.56	0.336	100.02 ± 0.39
Clomipramine hydrochloride	100.04 ± 0.96	2.11	0.652	100.38 ± 0.66
Fluphenazine hydrochloride	100.21 ±0.21	3.81	0.329	100.01 ± 0.62
Imipramine hydrochloride	100.04 ± 0.81	2.97	1.003	100.46 ± 0.47

* Tabulated F (n_1, n_2 = 5) for (4,4) df and P (0.05) is 6.39

** Tabulated t (n_1, n_2 = 5) for (8) df and p (0.05) is 2.306

TABLE 4

Analysis of pharmaceutical preparations containing central nervous system acting drugs by FIA technique compared with those obtained by applying the official BP 1988 methods

Compound	Pharmaceutical Preparation	FIA-Technique				Official Method Found (%) ± C.V
		Found (%) ± C.V	F*	Student's t**	Standard Addition Recovery % ± C.V	
Amitriptyline hydrochloride	Tryptizol 10 tab. B.N 110651	100.04 ± 0.80	1.67	0.421	98.90 ± 1.03	99.62 ± 0.62
	Tryptizol 25 tab. B.N 210410	98.74 ± 0.91	1.44	0.888	98.64 ± 0.93	99.28 ± 1.09
Carbamazepine	Tegretol 200 tab. B.N 192	98.89 ± 0.41	1.29	2.154	98.78 ± 0.99	99.39 ± 0.36
	Tegretol CR 200 tab. B.N. 011	99.20 ± 0.48	2.74	0.901	98.97 ± 0.85	98.99 ± 0.29
	Tegretol CR 400 tab. B.N 009	99.17 ± 0.64	1.47	0.260	99.02 ± 0.63	99.26 ± 0.52
Clomipramine hydrochloride	Anafranil 25 tab. B.N. 020	99.28 ± 0.46	0.31	1.591	99.29 ± 1.50	99.63 ± 0.26
	Anafranil 75 tab. B.N. 004	100.01 ± 0.40	1.05	1.047	99.53 ± 0.98	99.76 ± 0.39
Fluphenazine hydrochloride	Moditen tab. B.N 1D0316	99.66 ± 0.22	1.50	0.668	98.90 ±1.03	99.58 ± 0.18
Imipramine hydrochloride	Tofranil 10 tab. B.N 046	100.23 ± 0.61	4.13	0.819	99.11 ± 1.01	100.00 ± 0.30
	Tofranil 25 tab. B.N 080	99.40 ± 0.46	1.75	1.776	99.60 ± 1.23	99.99 ± 0.61

* Tabulated F ($n_1 = 5$, $n_2 = 6$) for (4,5) df and P (0.05) is 5.19 & 6.26

** Tabulated t ($n_1 = 5$, $n_2 = 6$) for (9) df and p (0.05) is 2.262

results obtained from the analysis of some pharmaceutical preparations available in the market containing the studied CNS acting drugs at their absorption maxima using the proposed FIA technique, compared with those obtained by applying the official B.P 1988 methods. Precision and reproducibility of the adopted FIA-system was assessed by applying the standard addition technique. Varying amounts (0.5-3.0 times) of the labelled claim of the drug to its formulation, gave good mean percent recoveries with relatively low standard deviations. The results obtained with the proposed method and its favourable characteristics seem to permit the conclusion that FIA can advantageously substitute the classical methods of amitriptyline hydrochloride, carbamazepine, clomipramine hydrochloride, fluphenazine hydrochloride and imipramine hydrochloride assay in the routine work for pharmaceutical quality control.

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