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SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF TRAZODONE HYDROCHLORIDE IN PHARMACEUTICAL FORMULATIONS

Yasser A. Z. *[1], Rabie S. Farag [2], M. Elnawawy [3] Ahmed M. A. [4], Sayde R. Abd Alsalam [5]

Medico-Legal Department Ministry of Justice [1, 4, 5], Faculty of Science Al-Azhar University [2, 3], Cairo, Egypt

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Correspondence to Author:

Yasser Abd Elaziz

Medico-Legal Department Ministry of Justice, Cairo, Egypt

ABSTRACT

Spectrophotometric methods have been developed for the assay of trazodone hydrochloride (TRH) in pure and pharmaceutical formulations. These method based on the formation of chloroform soluble ion-association complexes of TRH with bromphenol blue (BPB) and with chlorophenol red (CPR) in buffer of pH 2.0 (for BPB) and buffer of pH of 4 (for CPR) with absorption maximum at 420 nm and at 410 nm for BPB and CPR, respectively. Reaction conditions were optimized to obtain the maximum color intensity. The absorbance was found to increase linearly with increase in concentration of TRH, which was corroborated by the calculated correlation coefficient values (0.9996, 0.9945). The systems obeyed Beer's law in the range of 0.2-14.5 and 0.2-14.1m g/ml for (BPB) and (CPR), respectively. Various analytical parameters have been evaluated and the results have been validated by statistical data. No interference was observed from common excipients present in pharmaceutical formulations. The proposed methods are simple, accurate and suitable for quality control applications.

INTRODUCTION: Trazodone hydrochloride, 2-{3-[4-(3-chlorophenyl)-1-piperazinyl]propyl}-1, 2, 4-triazolo [4, 3-a]pyridin-3-(2H)-onemonohydrochloride, is a anti-depressant. It has been shown to be effective in patients with major depressive disorders and other subsets of depressive disorders. It is generally more useful in depressive disorders associated with insomnia and anxiety. This drug does not aggravate psychotic symptoms in patients with schizophrenia or schizoaffective disorders.

The official method for the determination of trazodone hydrochloride (TRH) is potentiometric non-aqueous titration with perchloric acid [1] and HPLC using octadecyl silane column and methanol-0.01 M ammonium phosphate buffer pH6.0 (60 : 40) as mobile phase [2]. Analytical methods that are reported for the determination of TRH in pharmaceutical formulations include UV absorption measurement at 246 nm [3] ion-selective electrode [4, 5] voltammetry [6, 7] and HPLC [2, 8]. Various chromatographic methods have been reported for the determination of TRH in biological fluids including HPLC [9, 10], capillary gas chromatography [11], gas chromatography, mass spectrometry [12] and instrumental thin layer chromatography [13]. Though modern methods of analysis (HPLC, GLC, NMR and Mass) for purity assay of any drug afford simplicity, speed, good specificity and excellent precision and accuracy, they involve sophisticated equipments, which are not in the reach of most laboratories and small-scale industries. Moreover, they pose problems of maintenance.

TRH is relatively weak UV absorbing compound and hence the direct UV absorbance measurements at low concentration will be unreliable.

Recently, spectrophotometric, spectrofluorimetric and LC determination of TRH has been reported [14]. The reported spectrophotometric method does not discuss about the sensitivity, detection limits and stability of the method.

More over, the effect of common excipients has not been investigated by spectrophotometric method. This prompted us to develop simple, sensitive and accurate spectrophotometric methods for the determination of TRH in pure and pharmaceutical formulations. These methods are sensitive and based on the formation of chloroform soluble ion-association complexes of TRH with BPB and with (CPR) in KCl-HCl buffer of pH 2.0 for (BPB) and in NaOAc-HCl buffer of pH 3.6 for (BCP).

Experimental:

Apparatus: The spectral measurements were carried out by using UV-Visible spectrophotometer (Helios Alpha) with quartz cell of 1 Cm optical path length was used. The pH adjustment was carried out by using Jenway pH meter. Doubly distilled water was used.

Reagents and Chemicals: All chemicals used were of analytical or pharmaceutical grade and quartz processed high-purity water was used throughout. TRH was obtained as a gift sample from EPICO, EGYPT. Aqueous solutions of BPB (0.05%) and CPR (0.1%) were prepared separately in high purity water. Series of buffer solutions of KCl-HCl (pH- 1.0-2.2), NaOAc-HCl (pH- 1.99-4.92), NaOAc-AcOH (pH- 3.6-5.6) and potassium hydrogen phthalate-HCl (pH- 2.2-3.6) were prepared by following the standard methods.

A stock solution of TRH containing 250m g/ml was prepared in distilled water. The solution is stable at room temperature. Commercial tablets of TRH were obtained from different firms.

Assay Procedure for Pure Drug: An aliquot of the solution containing 2-145m g (for BPB) or 2-141m g (for CPR) of TRH were transferred into a series of 125 ml separating funnels. A volume of 3 ml of KCl-HCl buffer of pH 2.0 for(BPB) or 4 ml of NaOAc-AcOH buffer of pH 3.6 (for BCP),and 5 ml of (BPB) or 3 ml(CPR) were added. Chloroform 10 ml was added to each of the separating funnels, the contents were shaken well and left at room temperature for a minute. The two phases were allowed to separate and the chloroform layer was passed through anhydrous sodium sulphate. The absorbances of the yellow colored complexes were measured at 420 and 410nm for (BPB) and (CPR), respectively, against corresponding reagent blank. A calibration graph was plotted.

Assay Procedure for Tablets: Six tablets were weighed and powdered. An amount of the powder equivalent to 100 mg of TRH was weighed into a 100 ml volumetric flask containing about 75 ml of distilled water. It was shaken thoroughly for about 15-20 min, filtered through a Whatmann filter paper No. 12.5to remove the insoluble matter and diluted to the mark with distilled water. A volume of 25 ml of the filtrate was diluted to 100 ml and a suitable aliquot was analyzed using the procedure given above.

RESULT AND DISCUSSION: Spectrophotometric procedures are popular for their sensitivity in the assay of drugs and hence, ion-pair extractive spectrophotometry has received a considerable attention for the quantitative determination of many pharmaceutical compounds [15-18]. TRH reacts with (BPB) and with (CPR) in acidic buffer to give chloroform soluble ion-association complexes, which exhibit absorption maxima at 420 and at 410 nm for (BPB) and (CPR), respectively. Under the experimental conditions, the reagents blank showed negligible absorbance thereby permitting good analytical conditions for quantitative determination of TRH. The drug to dye stoichiometric ratio was determined by Job's method of continuous variation [19] and was found to be 1:1 with (BPB) as well as with (CPR).

TABLE 1: OPTICAL CHARACTERISTICS, PRECISION AND ACCURACY DATA

Parameter	BPB	CPR
l max (nm)	420	410
Beer's law limits (m g/ml)	0.2-14.5	0.2-14.1
Molar absorptivity (l mol_1 cm_1)	2.11_104	2.92_104
Sandell's sensitivity (ng cm_2)	19.315	13.982
Stability (h)	6	6.5
Correlation coefficient (*R*)	0.9996	0.9989
Regression equation (*Y*)*a*)		
Slope, *b*	0.0434	0.0459
Intercept, *c*	0.0641	0.0679
Relative standard deviation (%)*b*)	1.0526	0.8267
% Range of error *b*) (95% confidence limit)	0.87	0.98
Limit of detection (mgml_1)	0.066	0.071
Limit of quantification (mgml_1)	0.219	0.236

a. *Y*=_*Bx*+_*c*, where *X* is the concentration of drug in m g/ml. Average of six determinations

TABLE 2: ANALYSIS OF TABLET, RECOVERY AND RUGGEDNESS OF ASSAY OF TRH BY THE PROPOSED METHODS AND THEIR COMPARISON WITH THE OFFICIAL METHOD 2

Sample	Drug present (mg)	Official method	BPB method	CP R method
Commercial tablet	100	100.4_0.78	99.56_0.69 *F*_1.27 *t*_1.49	99.24_0.84 *F*_1.16 *t*_1.97
Recovery	100	—	99.38_0.46	99.23_0.55
Between-day analysis	100	—	99.12_0.87	100.11_0.59
Within-day analysis	100	—	99.66_0.67	99.84_0.98

CONCLUSIONS: Unlike the gas chromatographic and HPLC procedures, the spectrophotometer is simple and is not of high cost. The importance lies in the chemical reactions upon which the procedures are based rather than upon the sophistication of the instrument. This aspect of spectrophotometric analysis is of major interest in analytical pharmacy since it offers distinct possibility in the assay of a particular component in complex dosage formulation. The reagents utilized in the proposed methods are cheaper, readily available and the procedures do not involve any critical reaction conditions ortedious sample preparation.

The method is unaffected by slight variations in experimental conditions such as pH and reagent concentration. Moreover, the methods are free from interference by common additives and excipients. The wide applicability of the new procedures for routine quality control is well established by the assay of TRH in pure form and in pharmaceutical preparations.

REFERENCES:

1. "British Pharmacopoeia," Her Majesty's Stationery Office London, 1998, 1318.
2. "The United States Pharmacopeia," 24 revision, Asian Edition, UnitedStates Pharmacopoeial Convention, Inc., Twinbrook Parkway, Rockville,MD, 2000, 1681-1682, 2149-2152.
3. Dhumal S. N., Dikshit P. M., Ubharay I. I., Mascarenhas B. M., Gaitonde C. D., *Indian Drugs*, 1991; 28, 565-567.
4. Khalil S., *Analyst* (London), 1991;124, 139-142.
5. Suzuki H., Akimoto K., Nakagawa H., Sugimoto I., *J. Pharmacol. Sci989;* 78, 62-65.
6. Dogrukol-Ak D., Zaimoglu V., Tuncel M., Eur. J. Pharmacol. Sci., 1999; 7,215-220.
7. Kauffmann J. M., Vire J. C., Patriarche G. J., Nunez-Vergara L. J.,Squella J. A., Electrochim. Acta, 1987; 32, 1159-1162.
8. Sane R. T., Nerurkar V. R., Tendolkar R. V., Gangal D. P., Mainkar P.S., Dhumal S. N., Indian Drugs, 1990; 27, 251-254.
9. Ohkubo T., Osanai T., Sugawara K., Ishida M., Otani K., Mihara K.,Yasui N., J. Pharm. Pharmacol.,1995; 47, 340-344.
10. Vatassery G. T., Holden L. A., Hazel D. K., Dysken M. W., Clin.Biochem.,1997 30, 149-153.
11. Andriollo O., Lartigue-Mattei C., Chabard J. L., Bargnoux H., Petit J.,Berger J. A., Pognat J. F., J. Chromatogr.,1992; 575, 301305.
12. Gammans R. E., Kerns E. H., Bullen W. W., Covington R. R., RussellJ. W., J. Chromatogr.,1985; 339, 303-312.
13. Siek T. J., J. Anal. Toxicol, 1987; 11, 225-227.
14. El-Gindy A., El-Zeany B., Awad T., Shabana M. M., J. Pharm. Biomed.Anal., 2001; 26, 211-217.
15. Milano J., Cardoso S. G., J. Pharm. Biomed. Anal., 37, 639-642(2005).
16. Nafisur R., Khan N. A., Azmi S. N. H., Il Farmaco., 59, 47-54(2004).
17. Ashour S., Al-Khalil R., Il Farmaco. 2005; 60, 771-775.
18. Gowda B. G., Melwanki M. B., Seetharamappa J., J. Pharm. Biomed.Anal., 2001; 25, 1021-1026.
19. Job P., Ann. Chim. (France), 1928; 9, 113-203.
20. Analytical Methods committee, Analyst (London), 1987; 112, 199-204.

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