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Ion-Pair Extraction Spectrophotometric Determination of Trace Amounts of Imipramine

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A simple, sensitive and selective extraction-spectrophotometric method for the determination of trace amounts of imipramine is reported. The imipramine-orange II ion-pair in acidic media is quantitatively extracted into chloroform and its absorbance is measured at 487 nm at room temperature. The effect of different variables such as solvent, volume of extracting solvent, volume of anionic reagent, pH, ionic strength (NaCl 0.1 M) and shaking time is investigated and optimum conditions for quantitative extraction of imipramine is obtained. Linear calibration graph over the imipramine concentration range of 0.03-7.00 μg mL^{-1} and regression coefficient of 0.9999 is obtained. The relative standard deviation of 10 replicate determination of 2 μg mL^{-1} of imipramine is 1.945 %. Limit of detection of the method is 0.022 μg mL^{-1}. The method is used for determination of imipramine in 10 mg, 25 mg, 50 mg tablets.

Key Words: Imipramine, Extraction, Orange II, Determination.

INTRODUCTION

Imipramine is an antidepressant medication of the tricyclic class. Medications in this class are often referred to as tricyclic antidepressants (TCAs). Depression is defined as an all-pervasive sense of sadness and gloom[1] (Fig. 1).

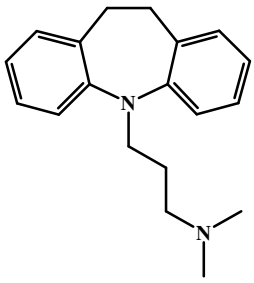

Fig. 1. Structure of imipramine

Various analytical techniques have been reported for the determination of imipramine including UV spectrophotometric, HPLC, mass spectroscopy and LC/MS/MS[2-5]. These methods are either insensitive or inconvenient for topical formulation development with imipramine.

A scientillation counting[6] using radiolabeled imipramine formulation is very sensitive and is widely used in the pharmaceutical industry for imipramine formulation development.

Solvent extraction is perhaps the most versatile of analytical techniques, in that it has an extremely wide range of application and invokes most of the physical and chemical principles used generally in analytical chemistry[7-9]. It therefore has pedagogic as well as practical value. Extraction methods using ions associated with a large ionic dye or counter ions, forming an ion-associated complex with large molar absorptivities are still limited[10-11]. Many quantitative pharmaceutical determination methods such HPLC suffer from large solvent consumption[12-18]. More investigation in this field could lead to sensitive methods for trace pharmaceutical determinations. In this paper we intend to examine a simple, sensitive and low cost method for the quantitative extraction of imipramine H^+-Orange II ion pair from an acidic solution into carbon tetrachloride organic solvent followed by spectrophotometric measurements at 487 nm.

EXPERIMENTAL

All the chemicals were of the highest purity available and used without further purification. Double distilled deionized water was used throughout. 20 μg mL^{-1} stock solution of imipramine was prepared by dissolving 0.1 g of imipramine powder in water and diluting to the mark in a 500 mL volumetric flask with distilled water. Working solution were prepared by appropriate dilution of the stock solution with water. OrangeII, stock solution (10×10^{-4} M) was prepared by dissolving proper amount of the dyestuff (Merck) in water and diluting to the mark in a 100 mL volumetric flask. 4 M solution of hydrochloric acid was prepared by diluting 195.5 mL of the concentrated acid to 250 mL in a volumetric flask.

The absorption spectra were recorded on a Shimadzu Model 160A UV-VIS recording spectrophotometer was used for absorbance measurements. All pH measurements were made by a metrohm digital pH meter equipped with a combined glass electrode.

Recommended procedure: An aliquot of sample solution containing 0.03-7.0 µg of imipramine was placed in a 10 mL volumetric flask. 2 mL of orangeII solution (2×10^{-4} M), 0.6 mL of 0.1 M of NaCl solution and 2.0 mL of bufferic solution (pH = 6) were added and the solution was diluted to mark with distilled water. The solution was transferred into a 50 mL separatory funnel and 5 mL of chloroform was added. The solution was shaken vigorously for 2 min. The phases were allowed to separate and its absorbance was measured at 487 nm against a reagent blank.

RESULTS AND DISCUSSION

Since imipramine H^+ ion forms a fairly stable ion-pair with orange II anionic dyestuff as counter ion in aqueous acidic solution, it is expected to result in a sensitive and useful spectroscopic method for trace imipramine determination.

In preliminary experiments it was found that the counter anion plays an important role in the formation of a stable ion-pair and among the dyestuffs examined such as methyl orange, orange II and alizarine yellow, best results were obtained with orange II dyestuff.

Choice of organic solvent: The extraction process was performed with some common organic solvents such as dichloromethane, dichloroethane, chloroform and carbon tetrachloride. It was found that the ion-pair is readily extractable in chloroform, while in other solvents used, the coloured complex could not be extracted into the organic phase as completely as chloroform.

Effect of buffer solution: The effect of bufferic solution on the extraction process of imipramine H^+-orangeII ion-pair was studied using bufferic solutions 3-10. On the basis of results presented in Table-1, 2 mL of buffer solution (pH = 6) gives the best results.

TABLE-1
EFFECT OF BUFFER SOLUTION ON THE EXTRACTION OF IMIPRAMINE H^+-ORANGE II ION-PAIR

Buffer solution	Absorbance of extracted ion-pair	Buffer solution	Absorbance of extracted ion-pair
3.0	0.298	7.0	0.321
4.0	0.312	8.0	0.140
5.0	0.378	9.0	0.122
6.0	0.566	10.0	0.096

Effect of orange-II concentration: The effect of orange II concentration on the extraction of imipramine H^+-orange II ion-pair was investigated and the results the shown in Fig. 2. It is seen that the absorbance of the organic phase increases with increasing orange II concentration in the aqueous phase. The concentration 2×10^{-4} M of orange II in the final solution was chosen as the optimum concentration of orange II.

Effect of solvent volume: It must be mentioned that quantitative extraction of imipramine H^+-orange II ion-pair is complete by 5 mL of chloroform in a single stage extraction process.

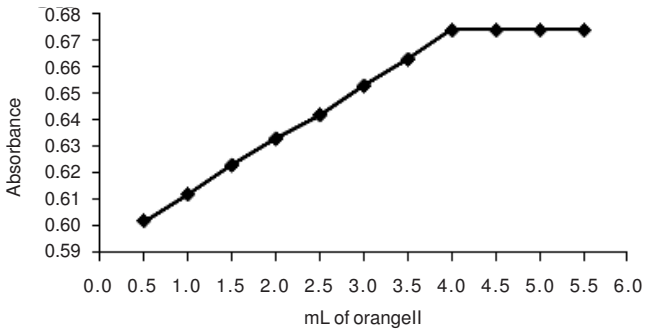

Fig. 2. Effect of orangeII concentration on the absorbance of extracted imipramine H^+-orange II ion-pair

This was confirmed by observing further enhancement in the absorption of complex in the mixture of two 5 mL portions of the organic phase obtained from two successive extraction of an aqueous imipramine H^+-orange II ion-pair solution, compared with that of an 10 mL organic phase obtained from a single stage extraction of the same complex solution under optimal experimental conditions. The absorbance reading for 10 mL organic phase containing the imipramine H^+- orange II ion-pair is half of the absorbance from 5 mL chloroform from the first stage of extraction.

Effect of shaking time: The effect of shaking time on the extraction of imipramine H^+-orange II ion-pair was studied. A shaking time of 2 min was found to be sufficient for the extraction of ion-pair. By increasing the shaking time, the absorbance of related blank will have no difference.

Analytical performance: Under the optimum conditions described above. Linear calibration graph for imipramine was obtained in the concentration range of 0.03-7.0 µg mL^{-1}. The regression equation for imipramine is $A_{imipramine} = 0.273\ C_{imipramine} + 0.00367$ (where $A_{imipramine}$ is the absorbance of the sample against a blank solutions and $C_{imipramine}$ is the concentration of imipramine in µg mL^{-1}) with a correlation coefficient of 0.9999. The relative standard deviation (RSD) of 10 replicate determination of 2.0 µg mL^{-1} of imipramine is 1.945 %, respectively and the limit of detection (LOD)[19] of the method is 22 ng mL^{-1}.

Effect of interferences: In order to study the influence of various cations and anions on the determination of imipramine, a fixed concentration of imipramine, 2 µg mL^{-1}, was taken with different amounts of foreign ions and the recommend procedure was followed. A relative error of ± 5 % with respect to the absorbance difference for the imipramine solution was considered tolerable. Tolerance limits are as follows: Cu^{2+}, Li^+, NH_4^+, I^- (1200 folds), NO_3^-, Fe^{2+}, Fe^{3+}, Na^+, Ca^{2+}, K^+, SCN^-, CO_3^{2-}, SO_4^{2-}, PO_4^{3-} (1000 folds), Mn^{2+} (900 folds), Pb^{2+}, Ni^+, Co^{2+}, Mg^{2+}, Cl^- (800 folds). The results show that most of the cations and anions used have no considerable effect on the determination of imipramine.

Application: The proposed method was applied to the determination of imipramine of 10, 25, 50 mg tablets, (from Chemi Daruo Co).The results of tablets are shown in Table-2. As it is seen, there is a satisfactory agreement between the results of the proposed method and the reference value of imipramine content of the formulations.

TABLE-2
DETERMINATION OF THE IMIPRAMINE CONTENT OF 10, 25, 50 mg FORMULATION TABLETS BY THE PROPOSED METHODS

Sample	Reference amount (mg)	Obtained (mg)	Recovery (%)
1 (tablet)	2.0	1.961	98.05
2 (tablet)	2.0	1.999	99.95
3 (tablet)	2.0	1.978	98.90

Conclusion

The method described, provides a simple and reliable means of determination of trace amounts of imipramine in formulation samples. The limit of detection of the proposed method seems to be good. The method compares favourably in sensitivity and selectivity with most of the published methods[20-23] for the determination of imipramine and it can certainly be placed among the most sensitive ones.

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