"Development of New Spectrophotometric Methods for the Determination of Some Ions"

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List of Abbreviations

Name	Abbreviation
Clomipramine hydrochloride	CPH
Imipramine hydrochloride	IPH
Desipramine hydrochloride	DPH
Trimipramine	TMP
Bromo cresol green	BCG
Bromo cresol purple	BCP
Bromo thymol blue	BTB
Bromo phenol blue	BPB

EXPERIMENTAL

2.1.Apparatus:-

Absorbance measurements were made a calibrated UV - 1601 Shimadzu double beam spectrophotometer (Kyoto, Japan). Eppendorf vary pipettes (Westbury, NY, USA), 10-100 µl and 100 - 1000 µl were used to deliver accurate volumes, the pH values of buffer solutions were measured using Jenway instrument pH-meter (combined electrode).

2.2.Materials and reagents:-

All chemical used of ACS or equivalent products were purchased from Merck (Dormstadt, Germany) or Fluka (Buchs, Swizerland) and were used without further purifications.

Clomipramine (is 3-chloro-5-{3-(dimethyl amino) propyl}-10,11-dihydro-5H-dibenz[b.f] azepine mono hydro-chloride, [CPH] and imipramine,11- dihydro-5H -5-{3-(dimethyl amino) propyl}-5-dibenz[b.f]azepine mono hydrochloride, [IMP], from J.A.E. Cairo under license from Novarts pharma AG., Basle, Switzerland.

Stock solutions (100 $\mu g ml^{-1}$) of pure drugs were prepared by dissolving 0.025 gm of pure samples in the

least amount of deionized water in 100 ml volumetric flask then diluted with deionized water to the mark. Further dilutions were carried out with deionized water to obtain solutions of required concentration for studied drugs.

A solution of 5 x 10^{-4} bromo cresol purple (BCP), bromo phenol blue (BPB), bromo cresol green (BCG) and bromo thymol blue (BTB) (Aldrich products) were prepared by dissolving an accurately of the acid dyes in a few drops of acetone and then diluted to the mark with distilled water in a 100 ml calibrated flasks separately. A series solutions of NaOAc - HCl (pH 2.2 - 5.2) were prepared by standard methods.

2.2.A.British pharmacopoeia method for determination of clomipramine hydrochloride :-

Dissolve 0.25 g of clomipramine hydrochloride in 50 ml of alcohol and add 1 ml of 0.1 M HCl, potential titration using 0.1 M NaOH, read value between two points of inflection. 1 ml of 0.1 M of sodium hydroxide equivalent to 351.3 gm of $C_{19}H_{24}Cl_2N_2$ (**British Pharmacopoeia, 1998).**

Calculations:

Assay = $(V-V_b) \times 35.15 \times 100 / (Wt \times (100 - L))$

Where

V : Volume of 0.1 M NaOH consumed for the sample.

V_b : Volume of 0.1 M NaOH consumed for the blank.

Wt : Weight of the sample.

L : Loss on drying.

2.2.B.British pharmacopoeia's method for determination of imipramine hydrochloride:-

Dissolve 0.3 g of imipramine in 50 ml of chloroform and add 10ml of mercuric acetate solution (1%) titrate with 0.1M perchloric acid using 0.5 ml of metanil yellow solution as indicator (**British Pharmacopoeia, 1998)**.

Calculations:

Assay = $(V-V_b) \times 31.69 \times 100 / (Wt \times (100-L))$

Where

V: Volume of 0.1 M $HClO_4$ consumed for the sample.

$V_{b:}$ Volume of 0.1 M $HClO_4$ consumed for the blank .

Wt: Weight of the sample.

L: Loss on drying.

2.2.1.Working procedures:-

2.2.1.A. Effect of pH:-

In order to investigate the optimum pH value favoring the ion-pair complex formation between drug and bromo phenol blue, bromo cresol green, bromo thymol blue and bromo cresol purple. A series of solutions containing 0.5 ml (100 µg ml^{-1}) from drug, 1 ml (5 x 10^{-4} M) dyes, 1 ml buffer solutions of different pH values and 5 ml carbon tetrachloride each solution was completed to 10 ml with bi-distilled water. The content of each flask was mixed well to 2 min, and then the extracting aqueous layer was measured in the visible region against blank solution prepared by the same way without the examined substance.

2.2.1.B.Determination of λ_{max} of complex species :-

For the determination the value of λ_{max} at which each ion-pair complex species absorbed, the following spectra are recorded:

A. A spectrum of pure examined substance (5.0 x 10^{-4}M) using water as blank.
B. A spectrum of pure reagent (5.0 x 10^{-4} M) using water as a blank.

C. A spectrum of solution mixture of 1.0 ml pure examined substance (100 ppm) + 2 ml of buffer + 2 ml dyes extracted with 5ml of carbon tetrachloride against blank treated with same way.

2.2.1.C.Effect of time :-

The effect of time on the ion-pair complexes formed with examined substance in pure forms was studied by measuring the absorbance of a sample solution prepared by the same way without the examined substance at various time intervals. The highest absorbance value is obtained at the optimum time giving highest absorbance.

2.2.1.D.Effect of reagent concentration :-

To evaluate the effect of reagent concentration the drugs concentration was kept constant while that of reagent was regularly varied. The absorbance was measured at recommended wavelengths. The best reagent concentration gave the highest absorbance value.

2.2.1.E.Effect of extracting solvent :-

The effect of extracting solvent by measuring the absorbance of solutions prepared using different solvents

(chloroform, carbon tetra chloride, xylene, benzene, toluene, 1,2-dichloroethane). The best solvent gave the highest concentration.

2.2.1.F.The molar Ratio method :-

It was described by **Yoe and Jones** where the concentration of drug is kept constant (0.5 ml of 5 $x10^{-4}$ M) while that of reagent is regularly varied. The absorbance of the prepared solutions was measured at the optimum wave length for each complex. The absorbance was plotted versus the molar ratio (reagent/drug). The intersection of the obtained straight lines shows the molar ratio of the most stable complexes.

2.2.1.G.The continuous variation method :-

A modification of (**Job's, 1928**) continuous variation method preformed by (**Vesbourgh and Cooper, 1941)** was utilized for investigating the stoichiometric ratio of the reaction between drug and reagent.

A series of solutions were prepared by mixing equimolar solutions of the drug and reagent in different proportions (0.1- 0.9 ml of 5 x 10^{-4} M). While keeping the total molar concentration constant (1.0 ml of 5x 10^{-4} M).