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Colorimetric determination of amitriptyline hydrochloride in bulk and some dosage forms.

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Abstract : Colorimetric method was established to determination of amitriptyline hydrochloride (AMT-HCl) in bulk and pharmaceutical dosage forms. The method depend on the simple chromogenic oxidative coupling reaction between AMT-HCl and 1,2-diamino benzene (DAB) reagent using sodium periodate as oxidizing agent in acidic media. Beers law is obeyed in the range (2-32) ppm at wavelength 464 nm with molar absorptivity 1.36×10^4 $L.mol^{-1}.cm^{-1}$. Optimum conditions for the chromogenic reaction was studied. The method had high sensitivity, good selectivity and reproducibility. This method was applied to determine AMT-HCl in pure and some dosage forms.

Keywords : Colorimetric**,** chromogenic oxidative coupling, amitriptyline HCl, 1,2-diamino benzene.

Introduction

Amitriptyline hydrochloride IUPAC name 3-(10,11-Dihydro-5*H*-dibenzo[*a*,*d*][7]annulen-5-ylidene)-*N*,*N*-dimethylpropan-1-amine hydrochloride (Fig.1) is monoamine reuptake inhibitor; tricyclic antidepressant.[1] For many years amitriptyline has been considered one of the reference compounds for the pharmacological treatment of depression.[2] Also amitriptyline used in the tretament of chronic daily headache.[3]Amitriptyline also could be used in the treatment of interstitial cystitis.[4]

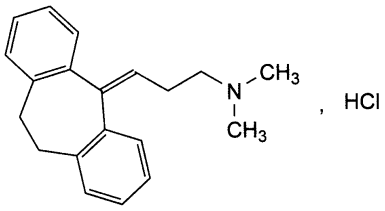

Fig.1 Amitriptyline hydrochloride (AMT-HCl)

Many methods have been used for the determination of AMT-HCl in different samples. Chromotographic methods[5-9], electroanalytical methods[10-12], spectrophotometric methods[13-20], and nanotechnology based methods[21-23]. In our work we developed a colorimetric procedure for assay of AMT-HCl as standard form and in some formulatins depending on the chromogenic oxidative coupling reaction between AMT-HCl and 1,2-diamino benzene in acidic medium.

Experimental

Apparatus :

Spectrum scan and absorbance readings were done using UV-Visible 160 digital double-beam recording spectrometer.

Material and reagents :

Chemicals used were of analytical reagent grade purity. Standard amitriptyline hydrochloride was obtained from (State Company for Drug Industries and Medical Appliance, SDI, Samara, Iraq). Pharmaceutical preparations containing AMT-HCl obtained from the commercial market.

The standard stock solution of(AMT-HCl) (500) ppm is prepared by dissolving (0.05)gm of (AMT-HCl) in(100)Ml deionized water. Sodium periodate $NaIO_4$(BDH company)(0.01) M, prepared by dissolving (0.214)gm of pure material in(100)mL deionized water. Hydrochloric acid (GCC company).1,2-diamino benzene(BDH company)(DAB)(0.01) M by dissolving (0.054)gm of pure material in(50 ml) absolute ethanol from(BDH Chemicals Ltd,%99.9).

Recommended Procedure and calibration graph.

Take increasing volumes of working AMT-HCl solution covering the range (2-32 ppm) add to 25-mLvolumetric flasks, followed by addition of (2ml) (DAB) (0.01) M and 5 ml of sodium periodate(0.01) M, then add(2mL)of HCl acid (1M) The solutions were left for20 minutes in a water bath adjusted at 30°C and the absorbance was measured at (464) nm against reagent blank prepared in the same manner but containing no AMT-HCl using 1-cm cells.

Procedure for dosage formsTablet[24]

Five tablets (10 mg /tablet) were weighed and finely powdered. A portion of the powder equivalent to 0.05 g of the drug was weighed and dissolved in water then transferred into 100 mL volumetric flask shaken well and completed to the mark with the deionized water. The solution shaken well, filtered and an aliquot of the filtered drug solution was then treated as done in the recommended procedure.

Results and Discussion

The effects of the various conditions on the absorption value of the color product were examined and the reaction conditions are optimized.

Effect of volume of the reagent

Volume of reagent effect was studied, by taken from (0.5 – 4) mL of the reagent DAB (0.01M) with (2mL)of the $NaIO_4$ and (2 mL)HCl solution (1 M). The result found is(2 mL) is the best volume, which was used in the next experiments

Effect of the volume of oxidizing agent

0.5–6mL of $NaIO_4$at concentration (0.01M) with (2 mL)of the reagent and (2mL)HCl solution. (5 mL) is the best volume.

Effect of acid types

Different types of acids such as HCl, CH_3COOH,H_2SO and HNO_3 are examined. It was found that all these acids give absorbance, so we use HCl which was found that (2mL) of this acid give best results and used in the subsequent experiments.

Effect of order of addition

Best order of addition is (R+D+O+A)where(R= Reagent, D=Drug, O= oxidizing agent and A=acid solution) which selected in next experiments.

Effect of Temperature

Different temperatures were examined the results indicate that the absorbance reading remain nearly stable in the temperature range (0-70ºC),at higher temperatures the absorbance decrease. The temperature (30ºC) which was selected for next experiments.

Effect of reaction time

After 20 minutes the color intensity reach its maximum. Therefore,20 minutes development time was selected in the recommended procedure. The color obtained was stay stable to100 minutes.

Spectral characteristics

Fig.2 show the absorption spectrum of the orange product with maximum absorption at 464 nm. The reagent blank solution give negligible absorption at this wavelength. So that all measurements was made at 464 nm against reagent blank solution.

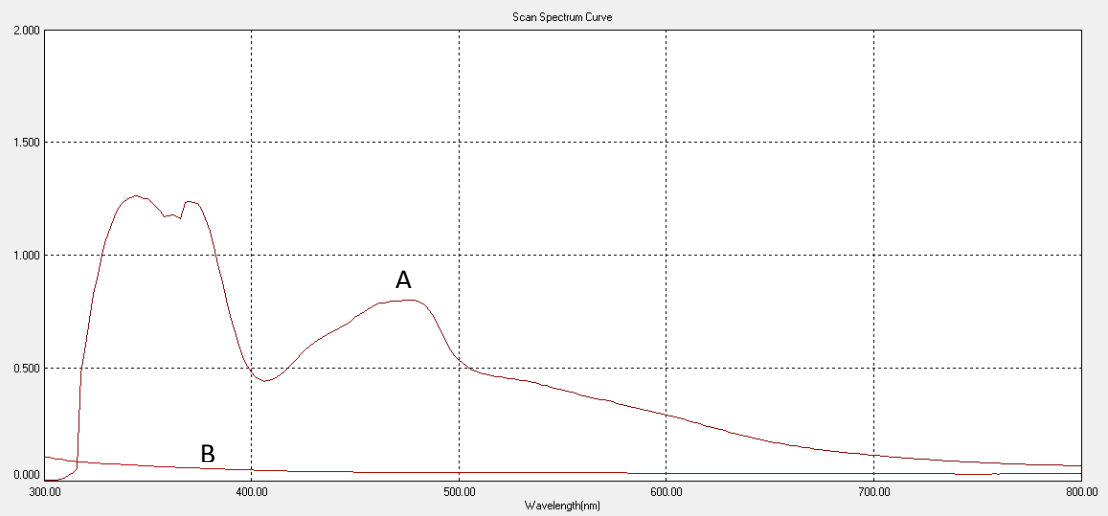

Fig.2 Absorption spectra of A: AMT-HCl-DAB color product B: the DAB reagent blank measured against deionized water.

Calibration Curve and Sensitivity

By applying the optimum parameters studied above, standard calibration curves for AMT-HCl-DAB color product were constructed Fig.3, and some analytical parameters of the proposed method are summarized in Table(1)

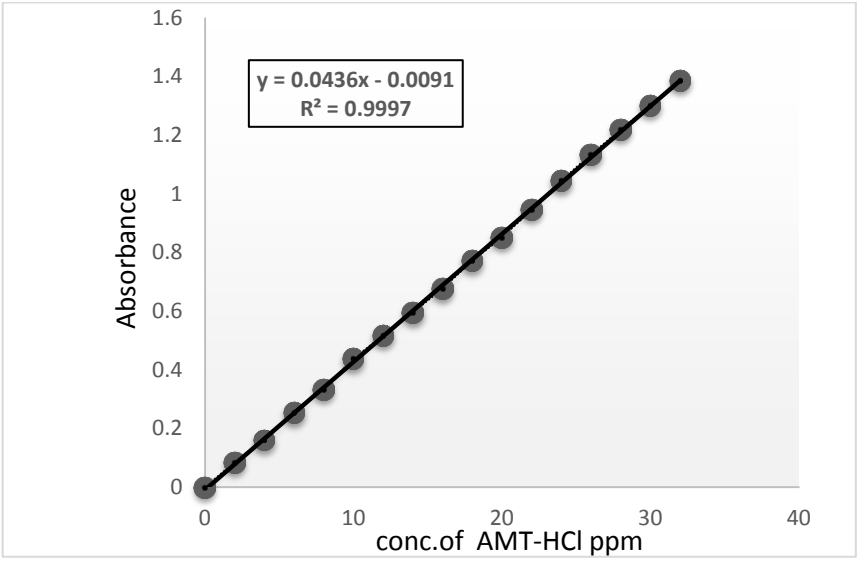

Fig.3 Calibration graph for AMT-HCl determination using DAB.

Table 1: Analytical features of the procedure developed for the determination ofAMT-HCl

Analytical parameter	Proposed method
Regression equation	Y=0.0436X-0.0091
Slope	0.0436
Correlation coefficient	0.9997
Linear Range (ppm)	2-32
Molar absorptivity ($L.mol^{-1}.cm^{-1}$)	1.36×10^4
Limit of detection (LOD) (ppm	*0. 626*
Limit of quantification (LOQ) (ppm)	*2.088*
Sandell's sensitivity, S (µg cm^{-2})	0.022

Accuracy and precision

Three different concentrations of AMT–HCl were used to examine the accuracy and precision of proposed method. The results in Table (2) indicate that the method have high accuracy and precision.

Table (2) Accuracy and precision of the proposed method.

No	Conc. AMT-HCl (ppm)		Error%	Recovery%	R.S.D%
	Present	Found			
1	4	3.912	- 2.200	97.800	0.635
2	18	17.943	- 0.316	99.684	0.542
3	30	30.231	+ 0.770	100.770	0.438

Effect of organic solvents

Various organic solvents are given in Table (3) were examined to find the best solvent depend on sensitivity.

Table (3): Spectrophotometric characteristics of the color product in various organic solvents

Solvent	λ_{max} ,nm	ε ,L.mol^{-1}.cm^{-1}
Acetone	310	2.410×10^3
Chloroform		1.225×10^3
2- propanol	290	1.002×10^3
Acetic acid	470	2.165×10^3
Dimethyl sulphoxide	332	1.121×10^3
CCl_4		1.653×10^3
Dioxane		Turbid
Dimethyl formamide		Turbid
Ethanol	456	1.122×10^3
Benzene		Two layers
Methanol	448	2.432×10^3
Teri butyl alcohol		3.129×10^3
Formic acid	410	1.229×10^3
Pyridine		Turbid
Di ethyl ether		1.318×10^3

Interference study

Interference from some common excipients frequently found with AMT-HCl pharmaceutical formulations were determined. These excipients include PVP, acacia, mennitol, Tween 80, lactose, sucrose, benzoic acid, talc, aspartate, microcrystalline cellulose, starch, and magnesium stearate. The study done by measuring the absorption of a synthetic sample solutions containing 1 mL of 500 ppm of AMT-HCl and 1 mL of 5000 ppm of each excipient solution and apply the recommended procedure. The results of this study in Table (4).

Table (4) The effect of interference.

Interference	Con of AMT-HCl Found (ppm)	% Error	% Recovery
Lactose	19.976	- 0.120	99.880
Talc	20.100	+ 0.500	100.500
Starch	19.945	- 0.275	99.725
Acacia	19.935	- 0.325	99.675
Sucrose	20.129	+ 0.645	100.645
Glucose	19.894	- 0.530	99.470
magnesium stearate	19.933	- 0.335	99.665
PVP	19.842	- 0.790	99.210
Benzoic acid	20.045	+ 0.225	100.225
Aspartame	19.954	- 0.230	99.770
Manetol	20.072	+ 0.360	100.360
Cross povidone	20.034	+ 0.170	100.170
Twin 80	19.968	- 0.160	99.840
Titanium di oxide	19.945	- 0.275	99.725
Micro crystal cellulose	19.982	- 0.090	99.910

Pharmaceutical applications

To know the analytical usefulness of the proposed colorimetric method, it was applied to analysis three tablet dosage forms containing AMT-HCl from different commercial companies. The results indicate that it applied successfully to the analysis. Which give good results with good recoveries and reproducibility's. This is done by three determinations for three different concentrations of each pharmaceutical preparation Table (5).

Table (5) Pharmaceutical applications of the proposed method.

Pharmaceutical preparations containing AMT-HCl)	Conc. of AMT-HCl (ppm)		Error%	Recovery%	R.S.D%
	Present	Found			
Amitriptyline Tablets (10) mg Actavis, Bamstaple, UK	4	3.909	- 2.275	97.725	0.713
	18	17.917	- 0.415	99.585	0.596
	30	30.126	+ 0.420	100.420	0.324
Amitriptyline Tablets (25) mg Actavis, Bamstaple, UK	4	3.918	- 2.050	97.950	0.801
	18	17.922	- 0.433	99.567	0.641
	30	30.143	+ 0.476	100.476	0.426
Deprezol Tablets (25)mg (SDI)Iraq	4	3.904	- 2.400	97.600	0.865
	18	17.955	- 0.250	99.750	0.604
	30	30.274	+ 0.913	100.913	0.345

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