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DETERMINATION OF DILTIAZEM HCl AND DOTHIEPIN HCl THROUGH COMPLEX FORMATION

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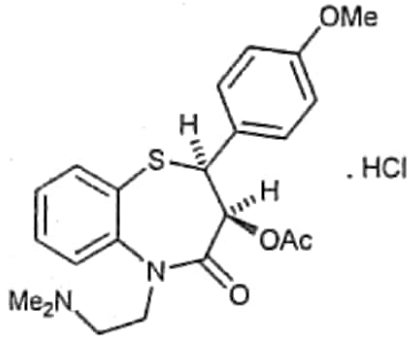
ABSTRACT:

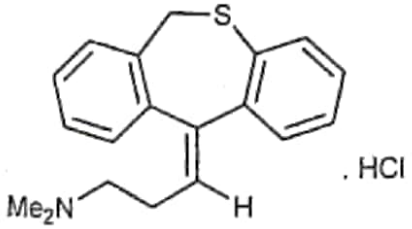
Simple, sensitive and accurate spectrophotometric and atomic absorption spectrometric procedures were developed for the determination of both diltiazem and dothiepin hydrochlorides in pure forms and in pharmaceutical preparations. The first method was based on the formation of ion-pair complexes between the two drugs and tropeolin oo using extractive procedures. The complex showed absorption maxima at 477 nm. Beer's Law was obeyed in the concentration range of (4-20) and (1.6-16) $\mu g ml^{-1}$ for diltiazem and dothiepin hydrochlorides respectively.

The second method was based on formation of a ternary complex between (copper(II), rose bengal and drug). This complex was extracted with methylene chloride and measured at 555 nm. Beer's Law was obeyed in concentration range (24-80) and (16-32) $\mu g ml^{-1}$ for diltiazem and dothiepin hydrochlorides, respectively. The third method depends on determination of copper content of the formed complex using atomic absorption procedure, Beer's Law was obeyed in concentration range (16-24) and (32-68) $\mu g\ ml^{-1}$ for dothiepin and diltiazem hydrochlorides respectively. The proposed methods hold their accuracy and precision well when applied to the determination of diltiazem and dothiepin in their dosage forms.

INTRODUCTION:



Diltiazem HCl



Dothiepin HCl

Diltiazem HCl (2,5-cis)-3-(acetyl-oxy)-5[2-(dimethylamino)ethyl-2,3-dihydro-2-(4-methoxyphynel)-1,5-benzothiazepin-4-(5H)-one hydrochloride is used as anti-anginal, antihypertensive and antiarrhythmic drug.

Several procedures were reported in the literature for the analysis of diltiazem HCl. These methods were spectrophotometric using eriochrome black[1], alizarine Red [2]S, bromocresolgreen[3], rose bengal[4], cobaltthio-cyanate[5], chromotrope 2R and rose bengal[6], potentiometric and chromotographic methods[13-21].

Dothiepin HCl, 3(6H)-dibenzo-[b,e]thiepin II ylidene) propyldimethyl amine hydro-chloride, is indicated in the treatment of depression and anxiety, the few reported methods in the literature for the determination of this drug were spectrophotometric determination using chromazurol S[33], chro-motrope 2R and rose bengal, flurimetric[34] and liquid chromatographic determination HPLC technique[35-36].

The aim of the present work is to develop accurate easy and sensitive procedures for the analysis of the cited drugs in bulk form and pharmaceutical preparations.

EXPERIMENTAL

*** Instrumentation:**

A shimadzu UV and visible recording spectrophotomer (UV 260) with matched 10-20 quartz cells was employed for all absorbance measurements. Shimadzu atomic absorption spectrophotometer model AA-640-B was used.

Materials and reagents:

Chemicals used were of the highest purity available from their source:

1- Troeoplin oo (Prolabo), 0.1% aqueous solution.

2- Acetate buffer (pH 2.7, 3.6 and 5) were prepared according to BP[37] by dissolving the calculated amounts of sodium acetate in distilled water ands adjusted to the specific pH by acetic acid.

3- Copper (II) chloride solution 0.4% w/v solution in distilled water.

4- Rose bengal (Aldrich) 0.25% w/v solution in distilled water.

5- Diltiazem HCl pure drug and diltiazem SR capsules containing 120 mg diltiazem HCl per capsule, (Egyptian International Pharmaceuticals Industries Company, EIPICo), Batch No. 199933301A.

6- Dothiepin HCl pure drug and prothiaden® capsules containing 25 mg dothiepin HCl per capsule. (KAHIRA Pharm. & Chem IND. Co.), Batch No. AH-9-01584.

Standard solutions:

Solution of 0.4 $mg ml^{-1}$ of diltiazem HCl and dothiepin HCl were prepared by dissolving 10 mg drug in distilled water and completed to 25 ml.

General procedures:

I- Spectrophotmetric method using tropeolin oo (method A):

Aliquots of each standard drug were transferred into 100 ml separating funnel, then the appropriate volumes of dye and buffer were added, extracted twice with 5 ml organic solvent complete to volume with the solvent in 10 ml volumetric flasks and measuring the absorbance at the suitable wavelength against blank solution omitting the drug. (Table I).

II- Spectrophotometric method using (copper – rose bengal) (Method B):

Appropriate volumes of the standard solution were pipetted into 100 ml separating funnel, then appropriate volumes of copper chloride, rose bengal and buffer were added, extracted twice with 5 ml organic solvent, complete to volume with the same solvent in volumetric flasks, measuring the absorbance at suitable wavelength against blank. (Table I).

III- Atomic absorption spectrometric method (method C):

The procedure applied as was mentioned under method B, the organic layer for dothiepin and diltiazem hydrochlorides were extracted twice with 5 ml 1N HCl. The volume was completed to 10 ml with distilled water and the absorption was measured for both drugs at the following condition:

Analysis wave length 3247Å
Lamp current 7 m A
Slit width 3.8 A
Burner height 4 mm
Burner slot, flame 1 cm, air C_2H_2
Fuel gas flow 2.3/min^{-1}
Absorption sensitivity 0.13 ppm

The concentration of the consumed copper was calculated from calibration graph of standard copper chloride solution.

Assay of pharmaceutical preparations:

The contents of ten capsules were weighed, pulverized into fine powder, then a specific quantity of powdered capsules equivalent to 10 mg drug were dissolved in 20 ml distilled water, solutions were filtered and diluted to 25 ml.

Aliquots from this final solutions were used for application of proposed methods by using standard addition technique for methods I and II. Also method III was applied for the analysis of the two drugs in their commercial capsules and was found to be almost quantitative (table 3A,B).

RESULTS AND DISCUSSION

The dye-salt separation technique was employed to estimate different drugs in pure dosage forms[38-40] the cited drugs being cationic in nature can interact easily and quantitatively with the anionic dye under favourable conditions forming coloured ion pairs extractable with organic solvent. (Fig. 1)

Also ternary complexes of general formula $L_NM_xS_y$ was widely used in spectrophotmetric analysis[41-46] L is the cited drugs, S is rose bengal and M is copper (II). These triple complexes were extracted with organic solvent, whereas the binary systems (metal – drug and metal – dye) cannot be extracted in that way. (Fig. 2)

Optimum conditions affecting the reaction were studied.

*** Method I (drug – tropeolin oo):**

- Effect of reagent volume:

2-3 ml of 0.1% dye were sufficient to give maximum absorbance with diltiazem and dothiepin hydro-chlorides res-pectively (Fig. 8).

- Effect of solvent:

Many organic solvents e.g. toluene, chloroform, mythylene chloride and benzene were tried, it was found that chloroform, methylene chloride give maxi-mum absorbance with dothiepin and diltiazem hydrochlorides respectively.

- Effect of buffer:

3 ml buffer of pH 2.7 and 2 ml buffer of pH 3.7 were sufficient to give best results with diltiazem HCl, and dothiepin HCl respect-ively (Fig. 9).

- Effect of number of extrac-tion:

There was no difference in results between single, double or triple extraction with organic solvent, the absorbances was stable in the three cases for at least 2 hours. So double extraction was done.

*** Method (II) (Drug – $CuCl_2$ – rose bengal)**

- **Effect of reagents concentra-tions:**

1 ml $CuCl_2$ 0.4% was sufficient to give maximum absorbance with both drugs 1, 1.5 ml dye were sufficient to give best results with dothiepin and diltiazeme hydro-chlorides respectively (Fig. 10, 11).

- **Effect of buffer:**

Many buffers were tried at the pH, range (1.1 – 9.7), the highest absorbance values were obtained using 0.5 and 1 ml buffer of pH 5 for diltiazem HCl and dothiepin HCl, respectively (Fig. 12).

- **Effect of solvent:**

Methylene chloride gave best results with both drugs.

- **Effect of number of extraction:**

double extraction was sufficient to give best and stable results.

- **Effect of order of addition:**

It was found that adding drug, metal, dye then buffer was the best order of addition in case of diltiazem HCl, while in case of dothiepin HCl drug, buffer, metal, then dye gave the best result.

In case of atomic absorption procedure, it was not practical to aspirate the organic solvent of the ternary complex in the atomic absorption spectrometer, the high chlorine/ carbon ratio would lead to the

formation of a large quantity of HCl in the flame which would damage the instrument[47-48]. To avoid that, ternary complex was extracted with organic solvent, and then with 1NHCl and aspirated directly. The effect of reagents, pH, time, order of addition, solvents with respect to maximum sensitivity was found to be the same as the extractive procedure.

Composition of the complex:

In order to ascertain the stoichiometry of the reaction, Job's method of continuous variation[49] and molar ratio were carried out, results indicated that the stoichiometry ratio of drug: tropeolin oo was (1:1) (Fig.4).

The results of applying this method for ternary complex can be summarized as follow: the [Cu(II): drug] ratio in presence of excess rose bengal was (1:1) (Fig. 5), while the [rose bengal: drug] ratio in presence of excess Cu(II) chloride was (2:1) (Fig. 6), and the [rose bengal: Cu II] ratio in presence of excess drug was (2:1) (Fig. 7). Hence the composition of the ternary complex formed may be expressed as: drug : Cu (II): rose bengal (1:1:2).

Quantitation, accuracy and precision:

A linear correlation was found between absorbance and concentration in the range given in table (2). The correlation co-efficient, intercept and slope for the calibration data for each, ion pair were calculated using the same table containing the detection and quantification limits obtained by applying the proposed method. Also the relative standard deviation and the analytical error were calculated. Results of application of the cited technique on pharmaceutical preparations were incorporated in table (3 A,B).

The proposed methods were compared with official non-aqueous titration methods[37] using non-aqueous titration method. The results obtained showed that the calculated t and F values didn't exceed the theoretical values, (Table 4) from which we can conclude that the proposed methods don't differ significantly from the official methods.

CONCLUSION

The data given reveal that the proposed methods are simple, accurate and sensitive, method A is more preferable as it is more sensitive, gives precision and accurate results.

Table (1): Analytical parameters for determination of diltiazem and dothiepin hydrochlorides using tropeolin oo (method A) and $CuCl_2$, rose bengal (method B)

Parameters	Method (A)		Method (B)	
	Diltiazem HCl	Dothiepin HCl	Diltiazem HCl	Dothiepin HCl
Dye concentration	2ml 0.1%	3ml 0.1%	1.5ml 0.25%	1ml 0.25%
Metal concentration	–	–	1ml 0.4% $CuCl_2$	1ml 0.4% $CuCl_2$
Buffer	2 ml pH 3.7	3 ml pH 2.7	0.5 ml pH 5	1 ml pH 5
Solvent	CH_2Cl_2	$CHCl_3$	CH_2Cl_2	CH_2Cl_2
Wave length	477	477	555	555
Beer's Law limit	4-20 μg ml^{-1}	1.6–16 μg ml^{-1}	24-80μgml^{-1}	16–32 μgml^{-1}

The development methods are suitable for analysis of the cited drugs in pure and dosage forms in control laboratories.

Table (2): Optical characteristics and statistical data of the regression equations for method (A) using tropeolin oo, method (B) using $CuCl_2$, rose bengal in spectrophotometric determination and method (C) atomic absorption method.

Parameters	Method (A)		Method (B)		Method (C)	
	Diltiazem HCl	Dothiepin HCl	Diltiazem HCl	Dothiepin HCl	Diltiazem HCl	Dothiepin HCl
Beer's Law (μg ml^{-1})	4 - 20	1.6 - 16	24 - 80	16 - 32	32 - 68	16 - 24
Molar absorptivity (1mol cm^{-1})	1.8×10^4	2.1×10^4	3.4×10^3	6.7×10^3	1.8×10^6	1.6×10^6
Sandell's sensitivity (□g cm^{-2})	402×10^{-3}	6.5×10^{-3}	7.59×10^{-4}	2.02×10^{-3}	0.40	0.50
Regression equation:						
Intercept (a)	0.04	- 0.001	- 0.22	- 0.57	102.94	- 62.57
Slope (b)	0.04	0.06	0.01	0.04	1.72	8.28
Correlation coefficient (r)	0.99	0.99	0.99	0.99	0.99	0.99
Variance	0.26	0 21	0.96	0.07	0.11	0.14
Standard deviation	0.51	0.46	0.98	0.27	0.33	0.38
Relative standard deviation	0.51	0.46	0.97	0.27	0.33	0.37
Standard analytical error	0.21	0.17	0.34	0.11	0.16	0.19
Detection limit (□g ml^{-1})	0.25	0.19	0.36	0.13	0.25	0.28
Confidence limit	100.01±0.199	100.07±0.147	100.56±0.27	100.12±0.102	100.02±0.20	100.06±0.23
m. (Mean)	100.01	100.07	100.56	100.12	100.02	100.06
n. (No. of experiments)	6	7	8	6	4	4

Table (3-A): Application of standard addition technique for the determination of diltiazem and dothiepin hydrochlorides in pharmaceutical preparations using spectrophotometric methods

Commercial product	Diltiazem HCl						Commercial product	Dothiepin HCl					
	Tropeolin oo method			$CuCl_2$ – rose bengal method				Tropeolin oo method			$CuCl_2$ – rose bengal method		
	Claimed amount (mg µl^{-1})	Authentic added (µg ml^{-1})	Recovery %	Claimed amount (mg µl^{-1})	Authentic added (µg ml^{-1})	Recovery %		Claimed amount (mg µl^{-1})	Authentic added (µg ml^{-1})	Recovery %	Claimed amount (mg µl – 1)	Authentic added (µg ml – 1)	Recovery %
Ditliazem capsules Containing 120 mg diltiazem HCl per capsule (EIPICO). Batch No.: 199933301A	4	--	98.68	32	--	99.38	Prothiaden® capsules Containing 25 mg dothiepin HCl per capsule (KAHIRA Pharm & Chem Ind. Co.). Batch No.: AH-9-01584	1.6	--	96 12	16	--	100 37
		4	97.58	--	32	99.33			1.6	98 98	--	16	100 64
		6	99.04		40	100 40			2	98 97	--	18	101 11
		8	98.68		48	98.18			4	99.71	--	20	100 42
		12	97.22		56	99.67			6	100.46	--	22	100 25
		14	97.58		68	100 53			14	100 89	--	24	99.48
Mean ± SD	98 02 ± 0.79			99.62 ± 0.948			99 80±0.86				100 38±0 597		
n	5			5			5				5		
V	0.62			0.89			0.74				0.35		
SD	0.79			0.94			0.86				0.59		
RSD	0.80			0.951			0 86				0.59		
SE	0.35			0 42			0 38				0.26		

Table (3-B): Determination of diltiazem and dothiepin hydrochlorides in their pharmaceutical preparations by using atomic absorption

Diltiazem HCl			Dothiepin HCl		
Commercial product	Label claim µg ml^{-1}	Found %	Commercial product	Label claim µg ml^{-1}	Found %
Diltiazem capsules containing 120 mg diltiazem HCl per capsule (EIPICo.) Batch No.: 1999333 01A	32	98.00	Prothiaden ® capsules containing 25 mg dothiepin HCl per capsule (KAHIRA Pharm & Chem. Ind. Co.) Batch No.: AH-9-01584	18	97.00
	40	99.90		20	96.30
	72	98.50		24	97.30
	80	99.50		32	96.90
Mean ± SD	98.97		96.87		
n	4		4		
SD	0.87		0.41		
RSD	0.88		0.43		
V	0.76		0.17		
SE	0.43		0.20		

Table (4): Determination of diltiazem and dothiepin hydrochlorides through the proposed methods compared with official methods

Statistical data	Diltiazem HCl				Dothiepin HCl			
	Official method	Method (A)	Method (B)	Method (C)	Official method	Method (A)	Method (B)	Method (C)
Mean * (p=0.05)	99.69±0.48	100.01±0.51	100.56±0.98	100.02±0.33	99.84±0.50	100.07±0.46	100.12±0.27	100.06±0.38
n	4	6	8	4	5	7	6	4
V	0.23	0.26	0.96	0.11	0.25	0.21	0.07	0.14
SD	0.48	0.51	0.98	0.33	0.50	0.46	0.27	0.38
F-test	--	1.13 (5.41)	4.17 (4.35)	2.05 (9.28)	--	1.15 (4.53)	0.25 (2.26)	1.78 (9.28)
t-test	--	0.99 (2,30)	1.64 (2.22)	1.13 (2.44)	--	0.82 (2.22)	3.35 (5.19)	0.705 (2.44)

* Mean ± SD (Mean of three different experiments)

** Theoretical values for t and F at p = 0.05

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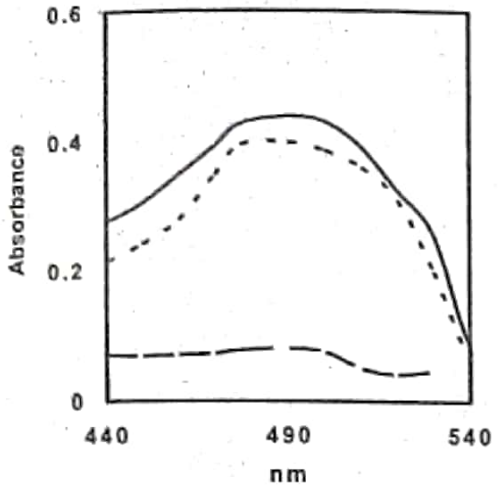

Fig. (1): Absorption spectra of the ion pair formed through reaction of tropeolin oo with 10 μg ml^{-1} diltiazem HCl (—), 15 μg ml^{-1} dothiepin HCl (.....), Blank solution (-.-.-.).

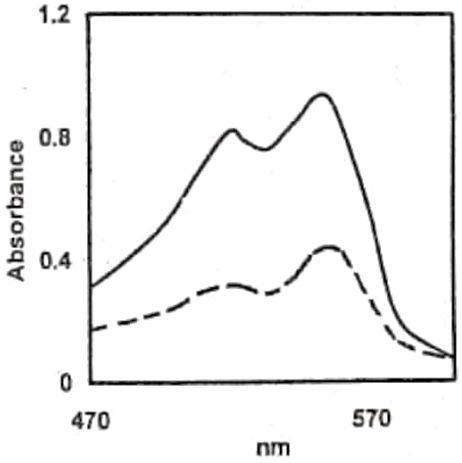

Fig. (2): Absorption spectra of the terneray complex formed through reaction of 32 μg ml^{-1} dothiepin HCl with Cu (II)-chloride and rose bengal (—), blank solution (.....).

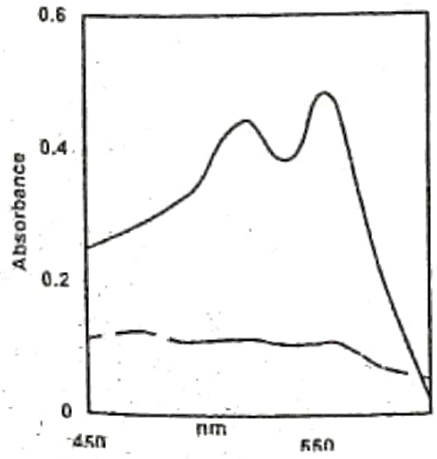

Fig. (3): Absorption spectra of the terneray complex formed through reaction of 56 μg ml^{-1} deltiazem HCl with Cu (II)-chloride and rose bengal (—), blank solution (.....)

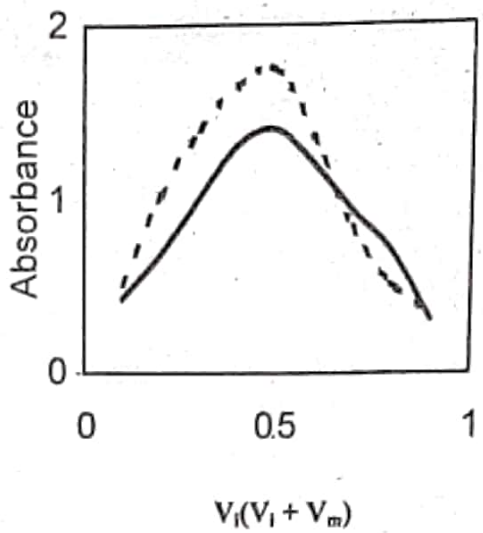

Fig. (4): Continuous variation plot for deltiazem HCl, (—) dothiepin HCl (.....) and tropeolin oo (2×10^{-4}) complex ratio (Vi, Vm =Ligand and metal volume respectively)

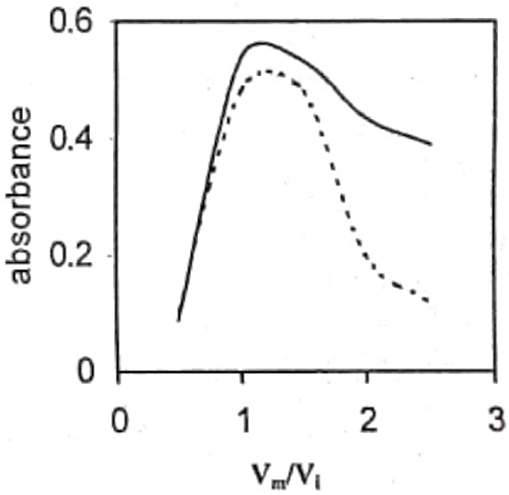

Fig. (5): Mole-ratio plot for drug: Cu(II) (1×10^{-3} M) complex ratio (Vi , Vm = drug and Cu (II) volume respectively) in presence of constant dye volume: diltiazem HCl (—) and dothiepin HCl (.....).

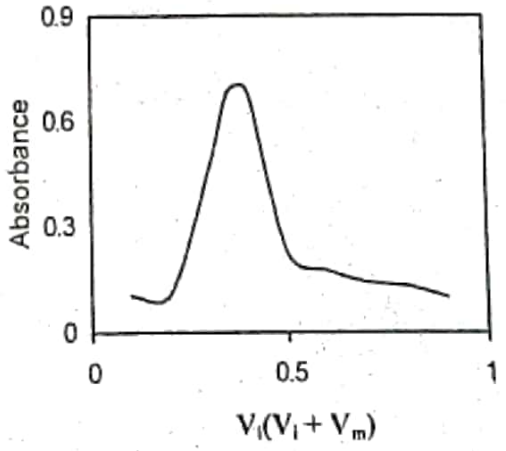

Fig. (6a): Continuous variation plots for diltiazem: rose bengal (1×10^{-3} M) complex ratio in presence of constant volume of Cu(II) (Vi, Vm = drug and rose bengal volume respectively):

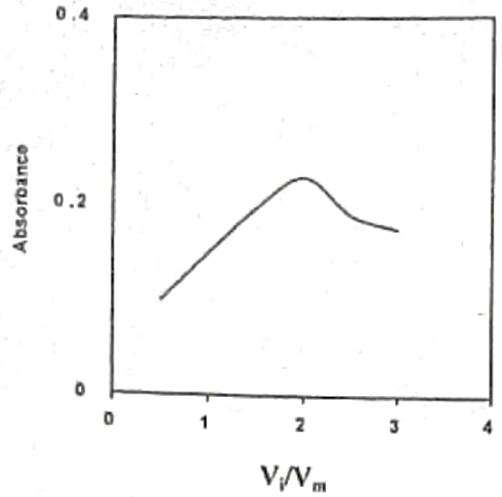

Fig. (6b): Mole-ratio plot for dothiepin HCl: rose bengal (1×10^{-3} M) complex ratio (Vi, Vm = rose bengal and dothiepin HCl volume respectively) in presence of constant Cu(II) volume.

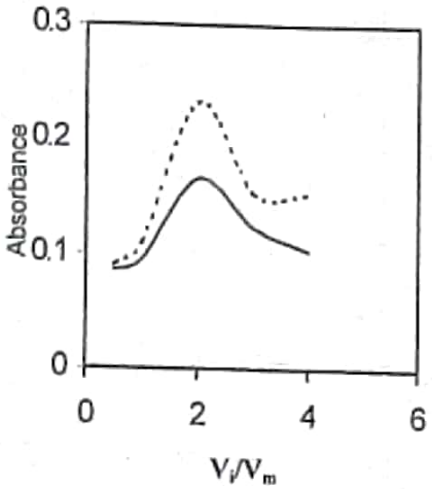

Fig. (7): Mole-ratio plot for Cu(II): rose bengal (1×10^{-3} M) complex ratio (vi , Vm = rosebengal and Cu (II) volume respectively) in presence of constant drug volume. diiltiazem HCl (—) and dothiepin HCl (.....).

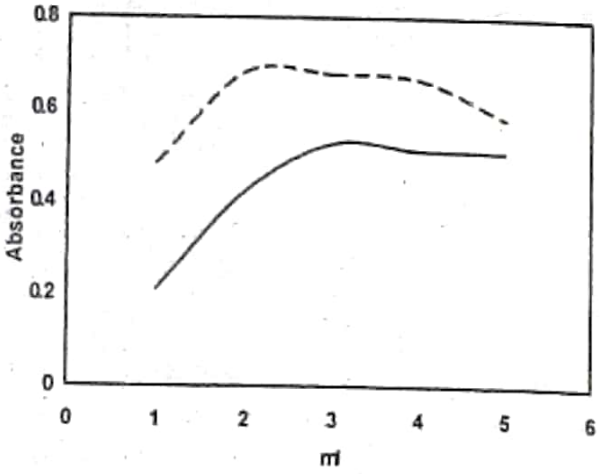

Fig. (8): Effect of tropeolin oo volume on the absorbance of the ion pair formed through reaction with16 μgml^{-1} diltiazem HCl (.....), 8 $\mu g\ ml^{-1}$ dothiepin HCl (—)

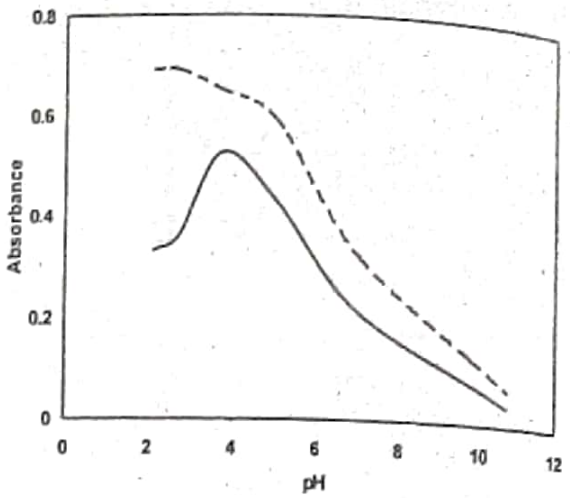

Fig. (9): Effect of pH on the absorbance of the ion pair formed through reaction of 16 μgml^{-1} diltiazem HCl (.....), 8 $\mu g\ ml^{-1}$ dothiepin HCl (—) with tropeolin oo.

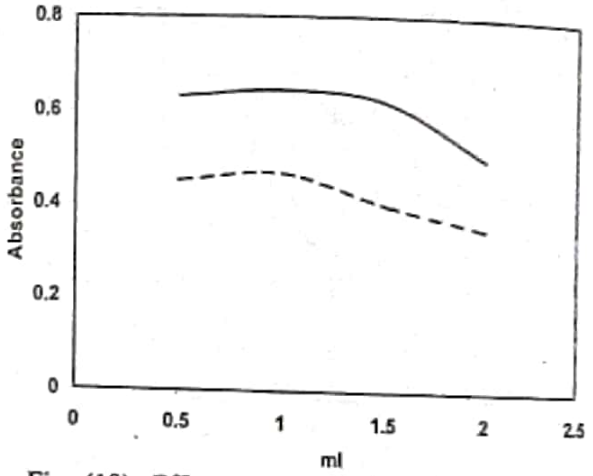

Fig. (10): Effect of Cu (II) chloride volume on the absorbance of the ternary complex formed with 56 μgml^{-1} diltiazem HCl (.....), 26 $\mu g\ ml^{-1}$ dothiepin HCl (—) in presence of rose bengal..

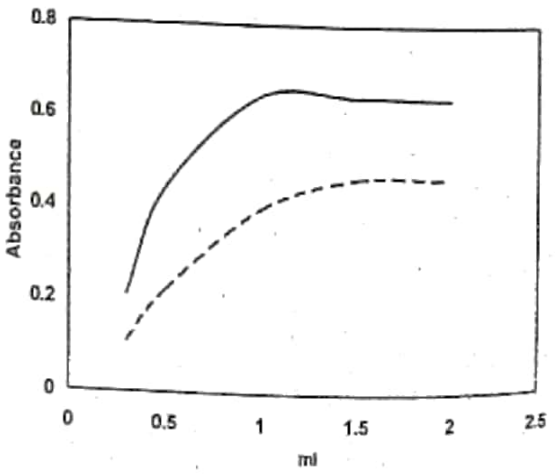

Fig. (11): Effect of rose bengal volume on the absorbance of the ternary complex through reaction of 56 μgml^{-1} diltiazem HCl (.....), 26$\mu g\ ml^{-1}$ dothiepin HCl (—) with Cu(II) chloride.

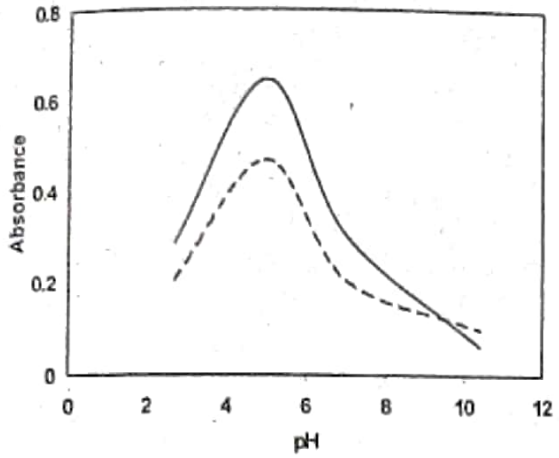

Fig. (12): Effect of pH on the absorbance of the ternary complex formed through reaction of 56 $\mu g ml^{-1}$ diltiazem HCl (.....), 26 $\mu g\ ml^{-1}$ dothiepin HCl (—) with Cu(II) chloride rose bengal.

REFERENCES

1- Kamath B.V. and Shivram K.; **Indian Drugs**, 29 (1) 50(1991). Through anal. Abst. 54(5), 5G 129 (1992).

2- Sreedhar K., Sastry C.S.P., Reddy M.N. and Sankar D.G .; **Indian Drugs**, 32(2)90(1995). Through Anal. Abst. 57(8),8G91,(1995).

3- Rahman N. and Hejaz-Azmi S.N.; **J.Pharm. Biomed.Anal**, 24(1) 33 (2000).

4- Hosny M., "Thesis of Doctor Philosophy on Pharmaceutical Sciences "Department of Analytical Chemistry, Faculty of Pharmacy, Zagazig University, 117(2003).

5- Bindu R. and Chandra-sekharan A.K.; **Indian Drugs**, 31 (4) 168 (1994). Through Anal. Abst. 56 (10) 10G 80 (1994).

6- Hosny M.; **Mansoura Journal of Pharm. Sci.**, 20(1), 64 (2004).

7- Cunningham L. and Freiser H.; **Anal. Chim. Acta**, 157 (1) 157 (1984).

8- Wang J., Farias P.A.M. and Mahmoud J.S.; **Analyst**, 111 (7) 837 (1986).

9- Leng Z., Hu X., Feng P. and Bai W.; **Fenxi , YI qi** ,3 ,15 (1993) . Through Anal. Abst. 56 (7) 7G 69, (1994).

10- Leng Z.Z., Hu X.Y., Jiang X. M. and Yu R.J.; **Fenxi-Huaxue**, 23 (3) 332 (1995). Through Anal. Abst. 57 (9) 9G 66 (1995).

11- Ivanov Skaya E.A., Bobleva Y. V. and Karpov R.S.; **J. Anal. Chim.**, 55(11) 1077 (2000).

12- Ghandour M.A., Aboul-Kasim E., Ali A.N.M., El-Haty M.T. and Ahmed M.M.; **J. Pharm. Biomed. Anal.**, 25(3-4) 443(2001).

13- Shimizu R., Ishii K., Tsumagari N., Tanigawa M., Matsumoto M. and Harrison I.T.; **J. Chromatogr.**, 253(1), 101 (1982).

14- Alebic-Kolbah T. and Palvasic F.; **J. Pharm. Biomed. Anal.** 8 (8-12) 915. (1990).

15- Nishi H., Fujimura N., Yamaguchi H. and T. Fukuyama; **J. Chromatogr.** 663 (1-2), 89 (1993).

16- Ishii K., Wakamoto S., Nakai H. and Sato T.; **Chromatographia**, 43 (7-8) 413, (1996)

17- Garcia M.A., Solans C ., Aramayone J.J., Fraile L.J., Bregante M.A. and Castillo J.R.; **Talanta**, 47(5) 1245 - 1254, (1998).

18- Gil-Agusti M., Carda-Broch S. and Garcia-Romero J.; **J. Chro-matogr. Sci.**, 38 (12) 521, (2000).

19- **British Pharmacopiea**; Her Majesty's Stationary Office, London 605, (2002).

20- Aboul-Enein H.Y.; **J. Chromatogr.** A., 906 (1-2) 185 (2001).

21- Gil-Agusti M., Cardar Broch S., Capella-Peiro M.E. and Esteve-Romero J.; **J. Pharm. Biomed. Anal.**, 41 (4)1235, (2006).

22- Ramappa P. G., Gowda H.S. and Nayak A. N.; **Micro Chem. J.**, 28 (4) 586, (1983).

23- Hackmann E.R.M., Santoro M.I.R.M., Magalhaes J.F. and Martins J.L.S.; **Pharmazie**, 39 (10) 718, (1984).

24- Ramappa P.G., Nayak A.N. and Basavaiah K.; **Indian Drugs**, 21 (10) 448, (1984).

25- Mahrous M.S. and Abdel-Khalek M.M.; **Talanta**, 31(4) 289, (1984).

26- Ramappa P.G. and Rao N.R.R.; **Indian Drugs**, 24(9) 441, (1987).

27- Jayarama D., Souza M.V., Yathirajan H.S. and Rangaswamy; **Talanta**, 33 (4) 352, (1986).

28- Rychlovsky P. and Nemcova I.; **Cesk. Farm**, 38 (6) 241, (1989).

29- Nagaraja P., Dinesh N.D., Made Gowda N.M. and Rangappa K.S.; **Anal. Sci**, 16 (11) 1127, (2000).

30- Kojlo A., Karpinska J., Kuzmicka L., Misiuk W., Puzanowska H. and Tarasiewicz M.; **Journal of Trace and Micropro-betechniques** , 19 (1) 45, (2001).

31- Takamura K., Inoue S., Ito K., and Kusu F.; **Bunseki Kagaku**, 35 (3) 161, (1986).

32- Peng T., Yang Z. and Lu R.; **Zhongguo Yaoxue Zazhi**, 25 (4) 277, (1990).

33- Popelkova-Mala Z. and Malat M., **Cesk. Farm.**, 34 (10) 422, (1985).

34- Abdellatef H.E., El-Henawee M.M., El-Sayed H.M. and Ayad M.M.; **Spectrochim. Acta**, 20, (2006).

35- Po A.L.W. and Irwin W.J.; **J. Pharm. Pharmaceutical**, 31 (8) 512, (1979).

36- Sauvage F.L., Gaulier J.M., Lachatre G. and Marquet P.; **Ther. Drug Monit**, 28 (1) 123 (2006).

37- British Pharmacopiea; Her Majesty's Stationary Office; London, 402,509,510,76 A, (1998)

38- Foster R.J.; Phys. Chem, 84, 213, (1980).

39- DasGupta V ; Ind.J.Pharm, 35,77, (1973).

40- Sirdhar K., Sastry C.S.P., Reddy M.N., Sankar D.G. and Rama K.; Anal. Lett. 30 (1) 121. (1997)

41- Ayad M. M., Abdellatef H.E., Taha E. A. and Soliman S.M.; Zagazig J. Pharm. Sci., 8 (2) 7. (1999).

42- El-Walily A.M., Belal S.F. and Bakry R.S.; J. Pharm. Biomed. Anal., 14, 561, (1996).

43- Issopouls P.B., Economou P.T. and Fresenius J.; Anal. Chem., 343, 515 (1992).

44- Issopouls P.B., Economou P.T. and Fresenius J. Anal. Chem., 345, 595, (1993).

45- Fujita Y., Mori I., Fujita K., Tanaka T. Koshiyama Y. and Kawabe H., Chem. Pharm Bull., 34, 2236, (1986)

46- Rose J.; Advanced Physico Chemical Experiments, Pitman, London, 54, (1964)

47- Cristine N. and Agustin G.; Anal. Chem., 57, 36 (1985).

48- Nerin C., Cacho J. and Garanis A., Anal. Lett. 18 (B15), 1887, (1985).

49- Inczedy J.; "Analytical Applications of Complex Equilibria" Ellis Horwood Ltd., England, 17, (1976).

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تعيين هيدروكلوريدات الدلتيازيم والدوثيبين من خلال مركبات معقدة

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تم استخدام طرق التحليل الطيفى والذرى لتعيين كل من هيدروكلوريدات الدلتيازيم والدوثيبين فى كل من المواد الخام والمستحضرات الصيدلية.

الطريقة الأولى: تعتمد على تكوين مركب معقد بين الدواء وصبغة التروبيولين باستخدام مذيب عضوى وكان الامتصاص عند طول موجى ٤٧٧.

الطريقة الثانية: تعتمد على تكوين مركب معقد ثلاثى بين الدواء والنحاس وصبغة الروزبنجال ويستخلص الناتج باستخدام مذيب عضوى ويتم القياس عند طول موجى ٥٥٥. وتعتبر هذه الطرق سهلة وبسيطة ودقيقة.

الطريقة الثالثة: فى هذه الطريقة تم تعيين الأدوية باستخدام النحاس لتكوين معقد ثلاثى يتم استخلاصه بالمذيب العضوى ثم يتم تقديره بطريقة الامتصاص الذرى. وتم تطبيق هذه الطريقة على المستحضرات الصيدلية وثبت فاعليتها.