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Analysis of Pharmaceuticals Containing Antihistamines by Ultraviolet Spectrophotometry

Antihistaminik Madde İhtiva Eden İlâçların Ultraviyole Spektrofotometrik Analizleri

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In a previous study(1), a thin layer chromatographic procedure was developed for the quantitative determination of some antihistamines in the pharmaceuticals. This paper describes the development of ultraviolet spectrophotometric method for the quantitative analysis of the same antihistamines.

The utility of UV absorption spectrograms for identification and assay of some antihistamines is well known and some data of this nature have been reported for pyrilamine maleate by Anderson et al. (2), for thenylpyramine in aqueous-acid solution by Harrison and Martin(3). Biglino and Ferrato(4) analysed Neo-antergan in the mixture with fargan and teforin. Neuhoff and Auterhoff(5) described the UV characteristic of nilistin, allercur, sandosten and omeril; Kleckner and Osol(6) determined the position of maximum and minimum absorbances and calculated $E^{\%\,1}_{1\,cm}$ for antazolin, chlorcyclizine, methapyrilene, thenyldiamine and tripellenamine hydrochlorides, pyrilamine maleate, phenindamine tartarate and chlorothen citrate. Gendi et al.(7) determined the UV absorption maxima of 11 antihistamines and calculated the extinction of a solution containing 10 mg in 100 ml ethanol.

In this investigation an ultraviolet spectrophotometric assay for pheniramine, chlorpheniramine, brompheniramine and pyrilamine maleates, thonzylamine and diphenhydramine hydrochlorides, phenyltoloxamine citrate, Allercur, antazoline methanesulfonate and hydrochloride, cyproheptadine hydrochloride and oxomemazine is described and the method is applied to the tablets, coated tablets and solutions.

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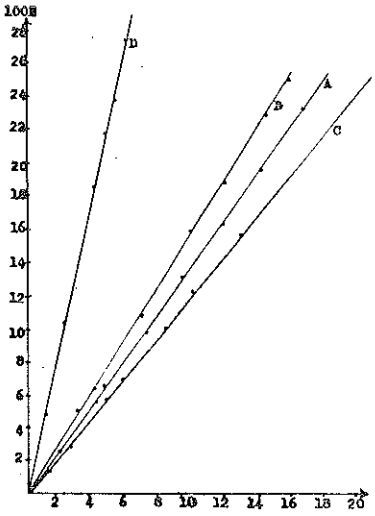
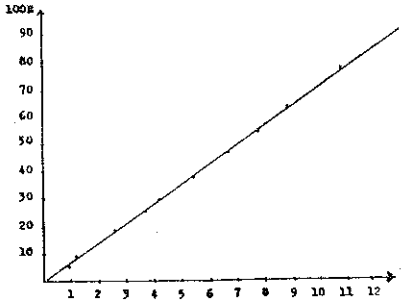


Concentration mcg/ml

Fig. 1. Calibration curves of A : pheniramine meleate at 263 mμ, B : chlorpheniramine maleate at 262 mμ, C : brompheniramine maleate at 262 mμ, D : pyrilamine maleate at 250 mμ.



Concentration mcg/ml

Fig. 2. Calibration curve of thonzylamine hydrochloride at 243 mμ.

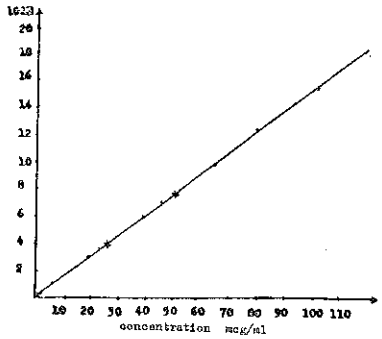
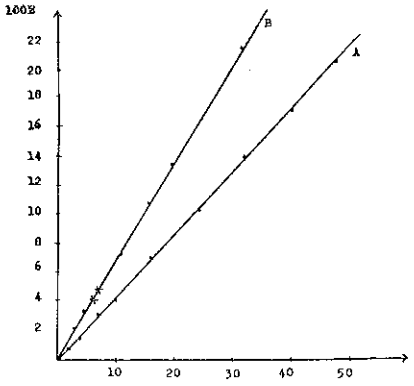


Fig. 3. Calibration curve of diphenhydramine hydrochloride at 258 mμ, x : Benadryl capsul.



Concentration mcg/ml

Fig. 4. Calibration curves of A: phenyltoloxamine citrate at 243 mμ, B: omeril at 282 mμ, x: Incidal tablet.

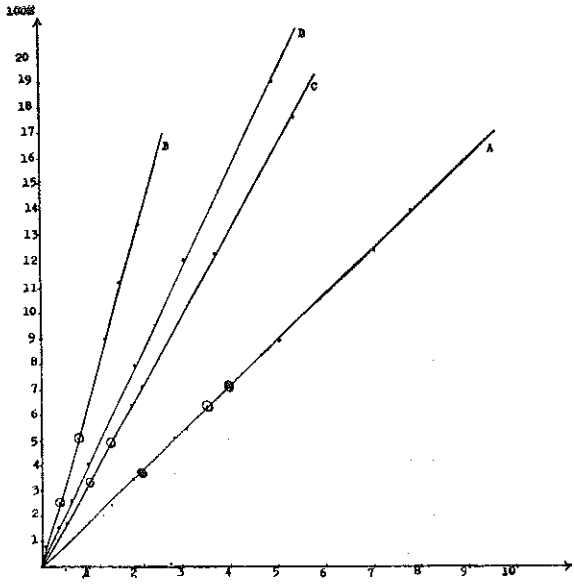
EXPERIMENTAL

All of the antihistaminic agents were purified by recrystallization and maximum absorbance were determined in ethanolic solutions. Various solutions of standard for each substances were prepared to study their conformance to Beer's law.

Absorption data were obtained with Zeiss-Spectrophotometer model VSU 1. Figures 1-6 show the standard curves prepared with the ethanolic solution of antihistamines; $E^{\%\,1}_{1\,cm}$ and ε max. were calculated.

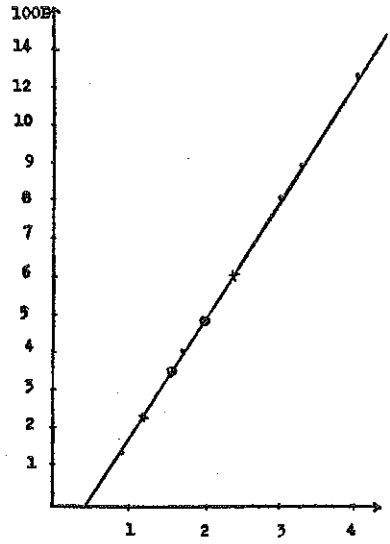
TABLE I. Spectral data of some antihistamines.

Substances	$\lambda^{EtOH}_{max.}$	ε max	$E^{\%\,1}_{1\,cm}$
Pheniramine maleate	263	4800	135
Chlorpheniramine maleate	263	6073	155
Brompheniramine maleate	262	5580	125
Pyrilamine maleate	250	18330	456
	310	4500	112
Thonzylamine hydrochloride	243	23000	712
	304	3050	
Diphenhydramine hydrochloride	258	450	15.3
Phenyltoloxamine citrate	270	2000	42.9
	277	1730	
Allercur (as HCl salt)	254	6300	177
Antazoline hydrochloride	239	19800	655
	295	2850	
Antazoline methanesulfonate	242	11300	312
	293	1400	
Omeril	285	1700	61.4
Cyproheptadine hydrochloride	286	8690	240
Oxomemazine	271	13400	400
	296	2375	
	335	1630	



Concentration mcg/ml

Fig. 5. Calibration curves of A: Allercur at 254 mμ, ●: Allercur tablet, O: Allercur injection, B: antazolin HCl at 238 mμ, O: Antistin tablet, C: antazoline methanesulfonate at 242 mμ, O: Antistin injection, D: oxomemazine at 271 mμ.



Concentration mcg/ml

Fig. 6. Calibration curve of cyproheptadine HCl at 286 mμ, x : Perideca tablet, o : Periactin tablet.

Determination of antihistamines in pharmaceuticals

Benadryl capsules: Weighed quantities of pulverized powder from 5 capsules, representing about 25 mg and 12.5 mg of declared diphenhydramine hydrochloride were extracted with ethanol and diluted to 100 ml, 20 ml aliquots were diluted again to 100 ml. The absorbance of each solution is measured at 258 mμ. Using the mean absorptivity value of 15.3, recoveries of 5.03 mg and 2.61 mg of diphenhydramine hydrochloride were obtained, which represent 100.6 and 104.4 % of the declared amount. From the calibration curve 5 mg and 2.55 mg were obtained, which represent 100 and 102 %.

Allercur tablets. 36 mg and 18 mg weighed powder from 5 coated tablets were extracted with ethanol, the extracts were filtered and diluted to 100 ml. Aliquots of 10 ml were diluted to 100 ml. The absorbance of the solutions representing about 400 mcg and 200 mcg of declared 1-p-chlorobenzyl-2-(pyrrolidinomethyl) benzimidazol hydrochloride in 100 ml, were measured at 254 mμ. Using the mean absorptivity value 177, recoveries of 406 mcg and 209 mcg of Allercur were obtained, which represent 101.5 and 104.5 % of declared amounts. From the calibration curve 400 mcg and 210 mcg were obtained which represent 100 and 105 %.

Allercur injection. The content of 5 ampuls each representing 10 mg 1-p-chlorobenzyl-2-(pyrrolidinomethyl) benzimidazol hydrochloride per ml were diluted to 100 ml with ethanol. 5 ml aliquot was diluted to 25 ml (sol. A). Two different solutions were prepared from the solution A by diluting 4 ml and 3.5 ml to 100 ml (all dilutions were made with ethanol). The absorbance of the solutions representing 400 mcg and 350 mcg were measured. Using the mean absorptivity value 177, recoveries of 406 mcg and 355 mcg of Allercur were obtained which represent 101.5 and 101.4 % of the declared amount. From the calibration curve 400 mcg and 356 mcg were obtained which represent 100 and 101.7 %.

Antistin tablets. 5 antistin tablets were weighed and reduced to a fine powder. Two aliquots portions of this powder, containing approximately 80 mg and 40 mg antazoline hydrochloride were weighed and extracted with ethanol, filtered and diluted to 100 ml. 1 ml of each solution was diluted with ethanol to 100 ml. The absorbance of solutions were measured at 242 mμ. Using the mean absorptivity value, 655, recoveries of 790 mcg and 390 mcg of antazoline hydrochloride were obtained which represent 98.75 and 97.5 % of declared amounts. From the calibration curve 800 mcg and 405 mcg were obtained, representing 100 and 101.25 %.

Antistin injection. 10 ml from the content of 5 ampuls were diluted to 1000 ml. 10 ml of this solution were diluted to 100 ml. 3 ml and 2 ml from this solution were diluted again to 100 ml. Each solution corresponds to 150 mcg and 100 mcg of antazoline methanesulfonate in 100 ml. Using the mean absorptivity value 312, recoveries of 157 mcg and 105 mcg, and from the calibration curve 152 mcg and 100 mcg of antazoline methanesulfonate were obtained which represent 104.6, 105, 101.3 and 100 % respectively.

Incidal tablets. Solutions corresponding to 804 mcg and 670 mcg of

5-benzyl-1,2,3,4-tetrahydro-2-methyl-γ-carboline (Omeril) in 100 ml were prepared by extracting coated tablets with ethanol. Absorbance was measured at 285 mμ, and calculation made using the mean absorptivity value 61.4. Recoveries of 797 mcg and 667 mcg and from the calibration curve 790 mcg and 670 mcg of Incidal were obtained which represent 99.1, 99.5, 98.25 and 100% respectively.

Periactin tablets. Solutions representing about 200 mcg and 160 mcg of declared cyproheptadine hydrochloride in 100 ml were prepared by extracting powdered tablets with ethanol and absorbance was measured at 286 mμ. Using the mean absorptivity value, recoveries of 204 mcg and 159 mcg, and from the calibration curve 201 mcg and 159 mcg of cyproheptadine hydrochloride were obtained which represent 102, 99.37, 100.5 and 99.37% of the declared amount.

Perideca tablets. With the solutions representing 240 and 120 mcg/100 ml of cyproheptadine hydrochloride, recoveries were 240 mcg and 124 mcg which represent 100 and 103.3%.

RESULTS

Table I summarizes the spectral data of 12 antihistamines as their salts. All antihistamines, except cyproheptadine hydrochloride, obey the Beer's law for the solutions containing approximately 1-10 or 20 mcg/ml; (for diphenhydramine hydrochloride the concentration range is 6.5 - 100 mcg/ml). The absorbance was plotted against the concentrations; in subsequent works, this lines served as the standard reference graph in determining the antihistamine contents of various pharmaceuticals. $E^{\%\,1}_{1\,cm}$ were calculated for each substance and the mean absorptivity values were used in calculation of the results.

Ethanol was found to be a convenient solvent for extraction of antihistaminic agents from tablet, coated tablet and capsul forms for subsequent spectrophotometric assay of the solutions.

The proposed method can be adapted readily for the determination of antihistamines in injections, tablets and capsuls. Sugar, dye substances and other ingredients which dissolve easily in ethanol, interfer the antihistamines assay in pharmaceuticals.

Cyproheptadine hydrochloride and oxomemazine in solution or in syrups are not stable and the results of analysis of stored samples showed significant loss of antihistamines.

SUMMARY

12 antihistaminic agents were determined spectrophotometrically. The standard curves were traced and $E^{\%\,1}_{1\,cm}$ were calculated. Antihistamines were extracted from tablets, coated tablets and capsuls with ethanol, injections were diluted with the same solvent and the results were calculated according to $E^{\%\,1}_{1\,cm}$ or from the calibration curves.

ÖZET

12 antihistaminik ilâçta spektrofotometrik çalışma yapılmış, her bir madde için standart eğriler çizilmiş, $E^{\%\,1}_{1\,cm}$ hesaplanmıştır. Tablet, draje ve kapsül gibi müstahzarlarda antihistaminik madde miktar tayini için etanolle ekstraksiyon maddeyi kantitatif olarak almayı sağlamış, enjeksiyonluk solüsyonlarda miktar tayini etanolle dilüsyondan sonra yapılmıştır; standart eğri ve $E^{\%\,1}_{1\,cm}$ yardımıyla bulunan sonuçlar metodun bahis konusu antihistaminiklerin miktar tayini için elverişli olduğunu göstermiştir.

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