Spectrophotometric Determination of Diphenhydramine hydrochloride and Application to Pharmaceutical Preparations

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Abstract

The research involves the use of analytical method for determination of the diphenhydramine hydrochloride (DPH) drug in some pharmaceutical preparations using molecular absorption technique (UV-Vis.) in addition to the investigating of complexes obtained. The optimum analytical data obtained throughout of study could be summarized as follows: order of addition (DPH + 2% CS_2 in $CHCl_3$+Ag(I), pH(11),volume of ammonia solution (1ml), concentration of Ag(I) (8µg/ml), aqueous : organic phase ratio 1:1, reaction time (4 minutes), extraction time (8minutes), reaction temperature 25^oC, one extraction process, extraction ratio (E%=99.82) chloroform proved to be the best solvent for extraction of DPH-Ag complex without interferences, λmax.=363nm. The analytical figures obtained were: linear dynamic range (0.25-80µg/ml)for DPH , RSD% (0.396), D.L (0.29µg/ml), Erel% (0.125), recovery (99.87%).This method was applied for determination of DPH in pharmaceutical preparation (syrup) using direct and standard addition methods, recovery's was found to be (97.8%, 98.2 %).

التقدير الطيفي للمركب الدوائي (داي فين هدرامين هيدروكلوريد) وتطبيقاته على المستحضرات الصيدلانية

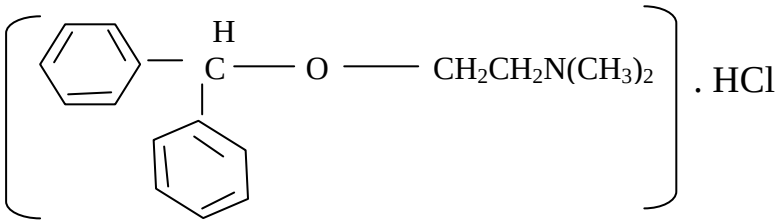
قبس ناجي رشيد

الملخص

يتضمن البحث إيجاد طريقة تحليلية لتقدير المركب الدوائي Diphenhydramine Hydrochloride (DPH) في بعض المستحضرات الصيدلانية بطريقة الامتصاص الجزيئي UV-Visible مع إجراء دراسات تحليلية لبعض المعقدات المحضرة، وتم التوصل في هذا البحث الى النتائج الآتية: تم تقدير الـDPH بهيئة DPH-Ag بعد استخلاصه بالكلوروفورم ولأجل تقديره في المستحضرات الصيدلاني ة تم تطبيق الظروف التجريبية والآ ليق المثلى وأمكن الحصول على المعلومات الآتية: تسلسل الإضافات هو(محلول DPH + محلول الكلوروفورم الحاوي (CS_2 2%) + محلول عنصر الفضة)، الأس الهيدروجيني (pH) كان (11)، حجم محلول الامونيا كان (1) مل، تركيز الايون (Ag) كان(8 مايكروغرام/مل)، نسبة الطور المائي الى العضوي (1:1)، ومدة اكتمال التفاعل قبل الاستخلاص كان (4) دقائق، أما أفضل مدة للاستخلاص هي (8) دقائق، درجة الحرارة 25 درجة مئوية، وكانت عملية الاستخلاص مرة واحدة كافية تقريباً لاستخلاص المعقد، النسبة المئوية للاستخلاص (E%= 99.82)، وجد أن الكلوروفورم هو أفضل مذيب لاستخلاص معقد DPH-Ag بدون تداخلات منشأ، والتقدير عند الطول الموجي λmax.= 363nm ، فيما يخص المعطيات الإحصائية كانت خطية التركيز لتعيين DPH هي (0.25-80) مايكروغرام/مل، وكان الانحراف القياسي النسبي المئوي (RSD% = 0.396) وحد الكشف (D.L = 0.29) مايكروغرام/مل، أما الخطأ النسبي المئوي فكان (Erel% = 0.125)، والاسترداد (Rec.% = 99.87). وتم تعيين المركب الدوائي DPH في مستحضره الصيدلاني بهيئة الشراب (الألرمين) بطريقتين المباشرة، وطريقة إضافة القياس وكانت مقاربة للكمية المثبتة أصلاً على عبوة المستحضر الصيدلاني اذ بلغت النسبة المئوية للاسترداد (98.2% , 97.8%).

Introduction

Chemically Diphenhydramine Hydrochloride is 2- (diphenylmethoxy) – N, N-dimethylethanamine hydrochloride[1], the literature survey reveals that (DPH) was analyzed by capillary gas chromatography[2], LC-MS[3], which has developed and successfully used in pharmacokinetic study of (DPH) in Rabbit plasma[4], chemiluminescence method[5] and by HPLC[6]. The FT-Raman spectroscopy and HPLC method[7] were also used. Diphenhydramine Hydrochloride (DPH), is an antihistamine drug[8], It occurs as a white, crystalline powder, is freely soluble in water and alcohol and has a molecular weight of 291.82. The molecular formula is $C_{17}H_{21}NO.HCl$, M.P.=$(166\text{-}170)^0$C, the structural formula is as follows[9] :



Diphenhydramine Hydrochloride (DPH), is a histamine H_1-receptor antagonist, it is widely used as antiallergic, antimetic and antitussive drug in many pharmaceutical preparations. It is usually administered orally and may be used by intramuscular or intravenous injection in severe allergies and applied topically for local allergic reactions[10]. Also,(DPH) works by blocking the effect of histamine at H_1- receptor sites. It induce an increase of vascular smooth muscle contraction, thus reducing the redness, hyperthermia and edema that occur during an inflammatory reaction. In addition, by blocking the H_1-receptor on peripheral nociceptors. DPH decrease their sensitization and consequently reduce itching i.e., associated with an allergic reaction. Bromhexine supports the body's own natural mechanism for clearing mucus from the respiratory tract[11]. Antihistaminic substance are act by blocking the chemical messenger of histamine, the main trigger of allergic symptoms in the nose, airways, and skin. Histamine is a part of the body's natural defense mechanisms. It works in part by widening blood vessels. That action causes congestion, sneezing, redness, itchy hives on the skin after, a bug bite[12], and it acts on Central Nervous System cause depression and sedative properties[13]. Antihistamine is present in a low concentrations in plasma, and such drug levels are generally not determined on a routine basis. From the pharmacokinetic perspective, the assay methods used have improved in recent years with the introduction of new techniques such as gas-liquid chromatography and high performance liquid chromatography with mass spectrometry (HPLC-MS), which allow the detection of minimal concentrations in plasma and tissues, and the identification of components and their metabolites. Antihistamine acts upon histamine receptors at the surface of the different cell types that express them. There are four histamine receptor subtypes: H_1, H_2, H_3 and H_4, of which H_1 and H_2 are extensively expressed by many cells within the body[14]. Diphenhydramine Hydrochloride (DPH) and Codeine Phosphate (COP) are commonly used in preparation of cough mixtures either in single or combined dosage forms as cough expectorants or suppressants. They are known to act synergistically to produce the desired therapeutic effect[15]. The aim of the study is to determine Diphenhydramine hydrochloride and application to Pharmaceutical preparations.

Materials and Apparatus

1- Standard solution of DPH (1000 µg/ml), prepared by dissolving (0.1 ml) of pure substance in distilled water.

2- Standard solution of Silver (1000 µg/ml), prepared the discharge of the contents of the container is made of company (Fixanal)

containing (1.0 gm) of Silver in the volumetric capacity of bottle of (1000 ml).

3- Chloroform solution containing (2%) carbon disulphide, prepared by mixing certain volumes of organic solvent carbon disulfide and chloroform.

4- Ammonium solution NH_4OH. (28% in water ~16M).

The following apparatus were used: molecular absorption spectrometry: JASCO V – 530, (Japan), pH meter: Orion Research Microprocessor Analyzer 90, (Germany), Electronic balance: Thermo Orion, (Switzer land).

Procedure

Diphenhydramine Hydrochloride (DPH) has been appointed in the manner spectral molecular ion and interaction with the silver, convey a certain size in terms of a solution of compound (drug) to separatory funnel, and added to the volume of (5 ml) of chloroform solution containing (2% CS_2), then (0.8 ml) of the mixture solution of Silver ion (100 µg/ml), were added the pH was adjusted to about (pH = 11) by adding (1 ml) of ammonia solution, stand time is approximately (4 min.), then complete the volume to (10 ml) with deionised water, The solution was shaked for (8 min.) and then the two phases was left to separate, the organic layer was withdrawed and collected and measured spectrophotometrically at λmax. = 363 nm.

Results and Discussion

- The spectrum of DPH (1000µg/ml) and silver solution (100 µg /ml) in the wavelengths of (190-1100 nm), are shown on figure (1) and (2) respectively.
- Figure (3), shows the absorption spectrum of the complex (DPH-Ag), and found to absorbs at (363)nm. The position and shape of the peak of the complex allow the possibility of investment of this interaction to estimate the DPH without overlapping with the peaks of (DPH), and Ag solutions.

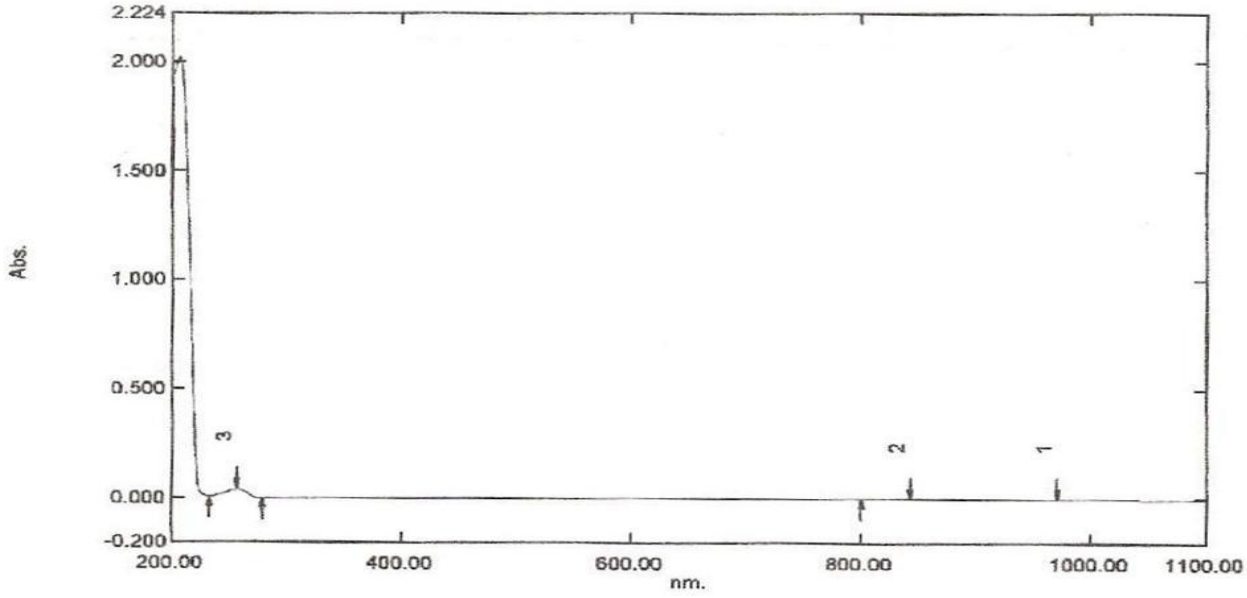


Fig.(1): Molecular absorption spectrum of (DPH) solution

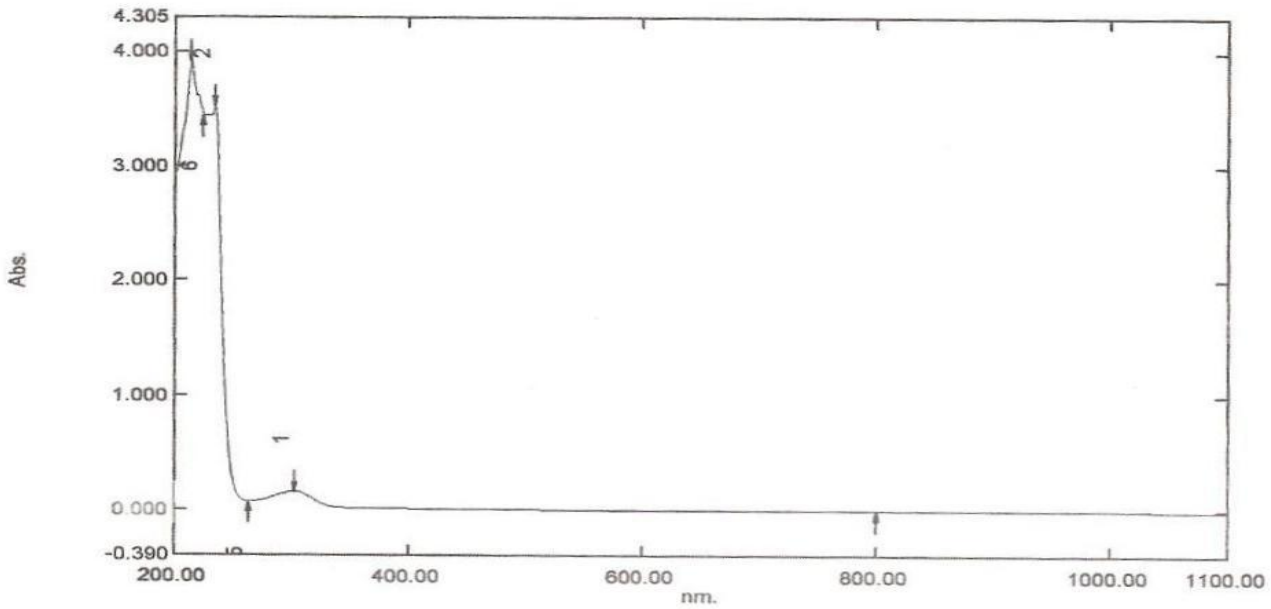


Fig.(2): Molecular absorption spectrum of the standard solution of Silver

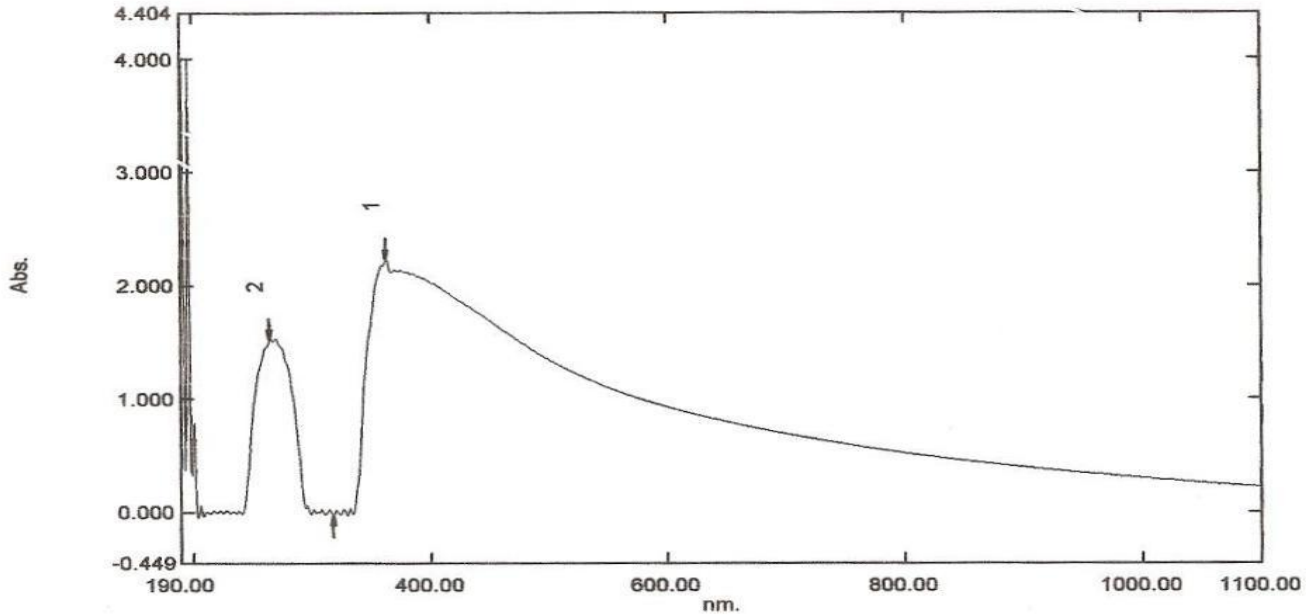


Fig.(3): Molecular absorption spectrum of DPH-Ag complex

Study the optimum conditions for determination of (DPH)

- The optimum conditions for the complex formation and its extraction were investigated. The order of addition was found to be: (DPH) solution + Chloroform solution containing 2% CS_2 + Silver solution.
- The effects of pH in the range 8-12.5 and the volume of ammonia solution were also studied. The optimum pH was (11) and the volume of ammonia solution was (1ml).

To form the DPH-Ag complex in the presence of 2% CS_2, the best concentration of Ag was 8µg /ml with optimum reaction time of 4 minutes.

Extract ion of the complex

Several experiments were conducted to find the optimum conditions for extraction of the complex formed and the following results were found.

Table (1) shows the type of phase & time of extraction

Type of phase	Ratio of phase	Time of extraction	Degree Celsius	Volume (ml)	Number of extractions
$CHCl_3$	1:1	8	20-30	5:5	One batch

Determination of the drug compound (DPH)

By applying the optimum conditions of the developed method, a series of solutions (0.25-80 µg/ml) of (DPH) were prepared and absorbance was measured at a wavelength of maximum absorption of the complex (DPH-Ag). Figure (4) shows the calibration curve with a linear of 0.25-80 µg /ml of DPH and r = 0.9999.

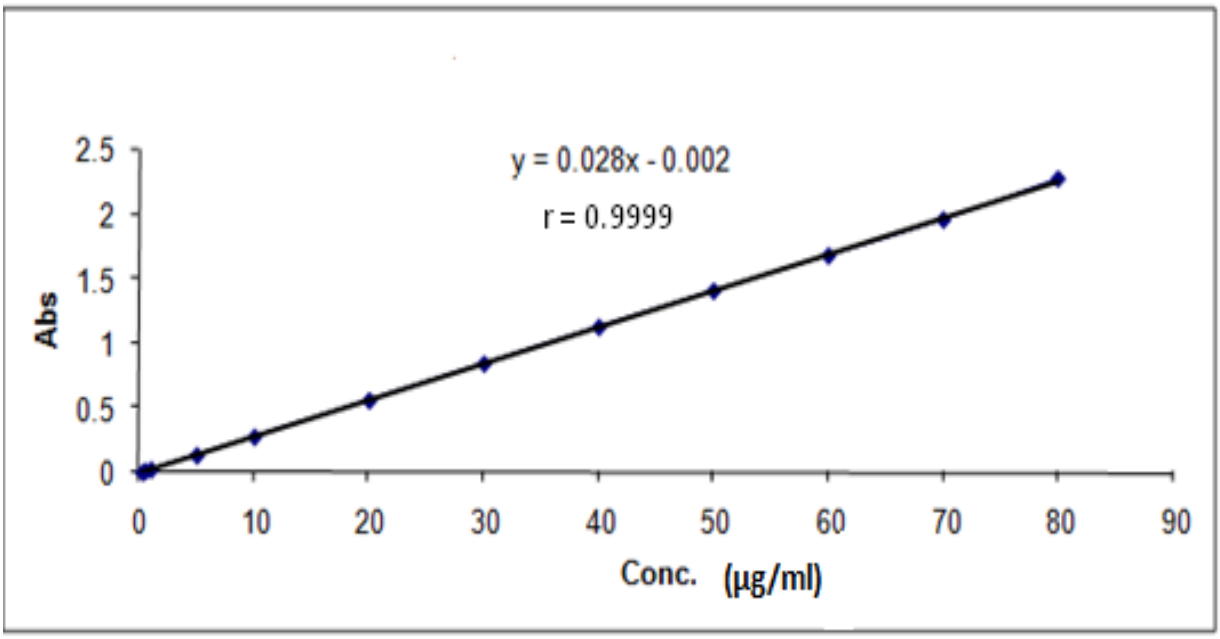


Fig.(4): Calibration curve of (DPH-Ag) complex

- The concentration of DPH in (Allermine Syrup: in SDI-Iraq) was determined by direct method (calibration curve in fig.4) and by (standard addition methods in fig.5). The results are shown on table (2).

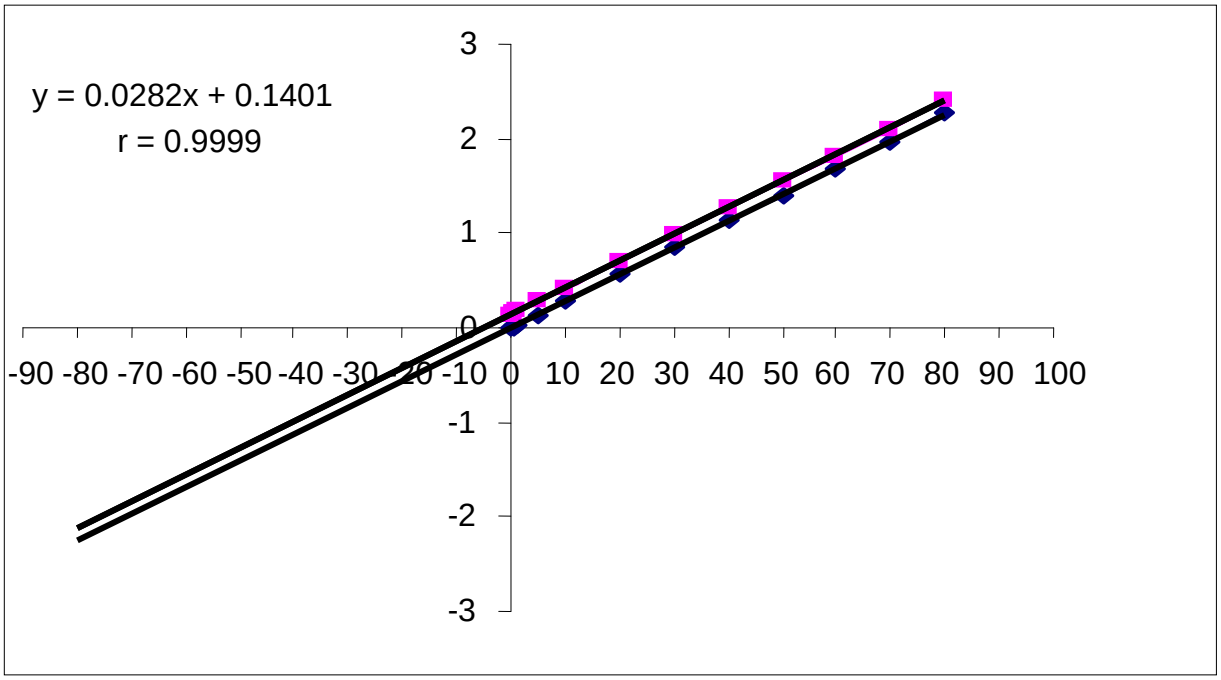


Fig.(5): Curve of the standard addition method of determination of DPH

From the results obtained, the DPH drug can be determined by both methods direct and standard addition methods. The following is a comparison of the results obtained using the present developed method with the literature methods.

Table (2): Results of determination of (DPH)

max.λ (nm)	Pharmaceutical name	manufacturer	Stated concentration ($\mu g.ml^{-1}$)	Found (direct calb.) ($\mu g.ml^{-1}$)	Found (St.add.) ($\mu g.ml^{-1}$)	Rec.% (St.add.)	Rec.% (direct calb.)
363	**Allermine syrup**	**SDI-Iraq**	**5**	**4.89**	**4.91**	**98,2**	**97.8**

Table (3):- Comparison of the results for the method used with the results of other methods

Reference	pH	Time	^{o}C	λmax. (nm)	%RSD	D.L	%Rec.	(r)	Linear range
Present method	11	4 min.	25	363	0.396	0.29 µg/ml	99.87	0.9999	0.25-80 µg/ml
[8]	7.2	10 min.	30	263	0.87	0.03 µg/ml	99.07	0.9998	7.5-120 µg/ml
[10]	6.3-6.8	1.5 h	70	258	0.26	1.16 µg/ml	-	0.998	-
[11]	3.0	25 min.	-	258	0.53	4.1 µg/ml	-	0.9904	64-96 µg/ml
[15]	4.7	-	25	258	0.24	0.001 mg/ml	98.07	0.9963	0.050-0.45 µg/ml
[16]	7.4	60 min.	50	258	0.2989	3.130 µg/ml	98.97	0.9934	10-100 µg/ml

Conclusions

The present method showed the possibility of determination of DPH drug (secondary amine) in the measurement when the availability of appropriate technical. The results obtained showed the success of this method in according to the analytical results and statistical data obtained. It also showed that the method is of high precision, good linearity, sensitivity and detection limit. This method was successfully applied for the determination of DPH in its pharmaceutical preparation (Allermine syrup).

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