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SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF FEXONFENDINE HYDROCHLORIDE IN PHARMACEUTICAL FORMULATIONS

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Abstract

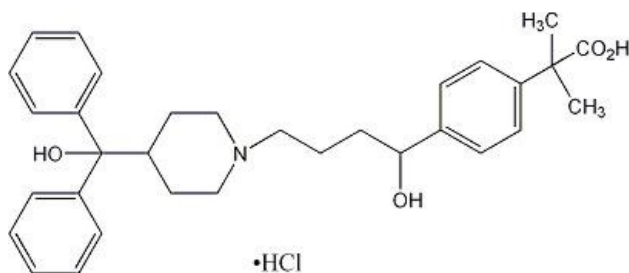
Spectrophotometric method have been developed for the assay of Fexonfendine hydrochloride (FEX) in pure and pharmaceutical formulations. This method is based on the formation of chloroform soluble ion-association complexes of (FEX) with picric acid(PIC), bromphenol blue (BPB) and with chlorophenol red (CPR) with absorption maximum at 403 nm , at 429 nm and 418 nm for PIC ,BPB and CPR, respectively. Reaction conditions were optimized to obtain the maximum color intensity. The absorbance was found to increase linearly with increasing in concentration of FEX,. Effect of the extracting solvents, effect of pH and effect of temperature on the stability of ion-associates have been investigated for studying the ion-associates of the cited drugs with the reagents under consideration

Key words spectrophotometric determination; Fexonfendine hydrochloride

Introduction

Antihistamines are H1-receptor antagonists widely used in human and veterinary medicine to provide symptomatic relief of allergic signs caused by histamine release, including pruritus and anaphylactic reactions. They are also commonly used as sedative and antiemetics [1]. Antihistamines can be divided in to first and second generation (also called non-sedating) agents. First generation antihistamines are small lipophilic molecules, so they may cause adverse effects because of their cholinergic activity and their ability to cross the blood-brain barrier. Second generation antihistamines are more lipophobic than first generation antihistamines and are thought to lack central nervous system and cholinergic effects when given at therapeutic doses [2]. Fexofenadine hydrochloride, the active ingredient of Allegra and Telfast, is a second-generation histamine H1- -dimethyl-4-[1-hydroxy-4-[4-(hydroxydiphenyl- methyl)-1-piperidinyl] butyl]-benzene acetic acid. Fexofenadine is used as the hydrochloride salt in the symptomatic relief of allergic conditions including seasonal

allergic rhinitis and urticaria [3, 4]. The probability that cardiotoxic side effects occur in connection with fexofenadine is assessed as being extremely low. Since metabolism is not effected by cytochrome P-450 no interaction with other drug is assumed. Fexofenadine does not have a negative effect on the psychomotor efficiency and it shows a high degree of daily-life suitability. The substance has anti-inflammatory characteristics which presents a modern approach to allergy therapy. Besides, fexofenadine may prove a safer alternative in the treatment of asthma [5] and atopic dermatitis [6] and is rapidly absorbed with a long duration of action, making it suitable for once daily administration. Thus, fexofenadine fulfils the essential and desirable characteristics of an ideal antihistamine, being responsible for the improvement in quality of life of the patients with allergic diseases [7]. Fexofenadine hydrochloride is rapidly absorbed after oral administration with peak plasma concentrations being reached in 2-3 h. It is about 60-70% bound to plasma proteins. Elimination half-life is about 14 h [3,4]. It is having the capability to exist in zwitter-ionic form, it cannot pass through blood-brain barrier and therefore does not cause sedation [8,9].



Experimental

Apparatus

The spectral measurements were carried out by using UV-Visible Diode Array spectrophotometer (Hewlett Packard-Model 8452A) with quartz cell of 1 cm optical path length used. The pH adjustment was carried out by using Orion pH-meter

Reagents and Chemicals

All chemicals used were of analytical reagents grade and solutions were prepared using doubly distilled water. The reagent included hydrochloric acid, anhydrous sodium sulphate (BDH);

highly purified solvents as chloroform (lab-scan), methanol (BDH), methylene chloride (BDH), carbon tetrachloride, benzene (Prolabo), petroleum ether, diethyl ether, toluene, n-hexane, cyclohexane, ethyl acetate (Merck), picric acid, bromophenol blue and chlorophenolred (Merck).

Stock solution (10⁻² M) of (FEX) was freshly prepared by dissolving 0.269 g in the least amount of methanol then the solution is completed to 100 mL with bidistilled water and successive dilutions were prepared for further studies.

Stock solutions (10⁻² M) of picric acid (Pic), bromophenol blue (BPB) and chlorophenolred (CPR) were freshly prepared by dissolving 0.114, 0.334 and 0.211g, respectively in the least amount of water then the solutions are completed to 100 mL with bidistilled water and Buffer solutions.

(FEX) was obtained as a gift sample from HI Pharm, EGYPT. Commercial tablets of (FEX) were obtained from different firms.

Fexone tablets (120 mg/tablets), ten tablets were weighed and finally powdered. A portion of the powder corresponding to prepare 10⁻³ M of the drug was weighed and dissolved in less amount of methanol and completed by bidistilled water. The slurry was filtered off; in which 10 ml was taken from the filtrate and subjected to UV-VIS. Analysis.

Assay Procedure for Pure Drug

Using 50 mL separating funnel, 5 mL of either different amount of (Pic, BPB or CPR) were added by a pipette, then a volume of FEX solution up to 2 mg/mL according to the above reagents, respectively. The volume was completed to 10 mL with bidistilled water. The formed ion-associate was extracted with 20 mL chloroform and was shaken for two minutes and allowed to separate into two phases. The organic layer was collected and dried with anhydrous sodium sulphate and completed to 25 mL with chloroform. The absorbance spectra of the extracts were measured at 403, 429 and 418 nm for Pic, BPB and CPR, respectively against a reagent blank prepared similarly in the same manner without the addition of (FEX), linear curves are obtained by plotting absorbance versus concentration. The calibration

graphs are constructed and the concentrations of unknown samples were determined using such calibration curves.

Assay Procedure for Tablets

Six tablets were weighed and powdered. An amount of the powder equivalent 100 mg of (FEX) was weighed into a 100 ml volumetric flask containing about 75 ml of distilled water. It was shaken thoroughly for about 2-5 min, filtered through a Whatman filter paper No. 12.5 to remove the insoluble matter and diluted to the mark with distilled water. A volume of 25 ml of the filtrate was diluted to 100 ml and a suitable aliquot was analyzed using the procedure given above.

Results And Discussion

The absorption spectra of the formed ion-associates were recorded in the visible region within the wavelength range 300-700 nm against reagent blank prepared in the same manner without the addition of the drug. The wavelengths corresponding to the maximum absorption were determined and found to be 413, 425 and 418 nm for RAN with Pic, BPB, and CPR reagents, respectively as shown in Fig. 1, 2 and 3 .

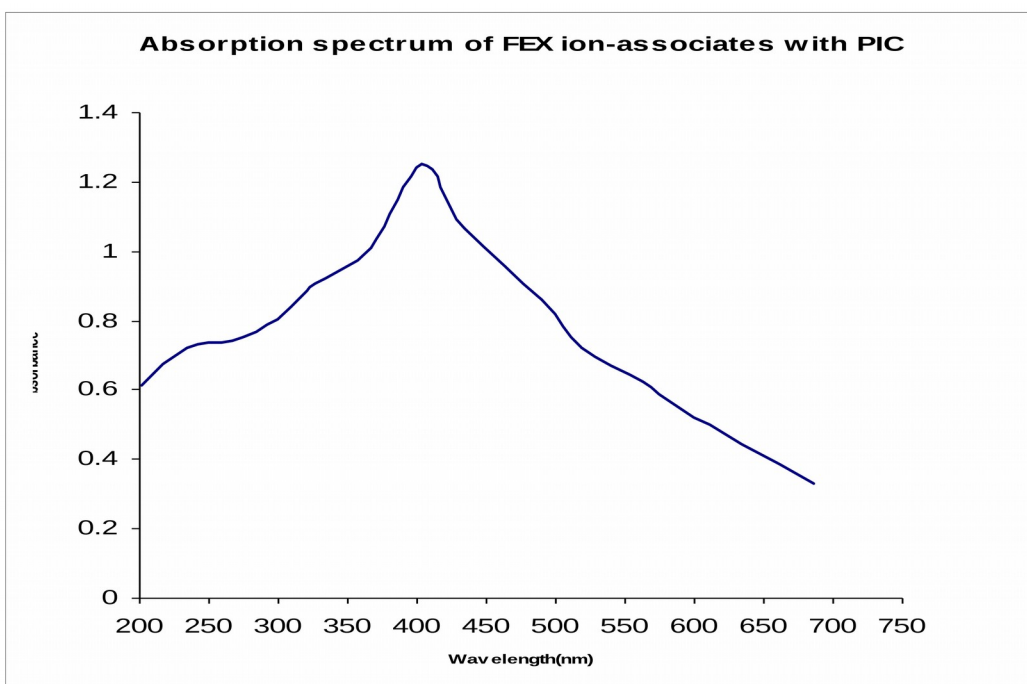


Fig. 1:Absorption spectra of (FEX)ion-associates with (PIC)

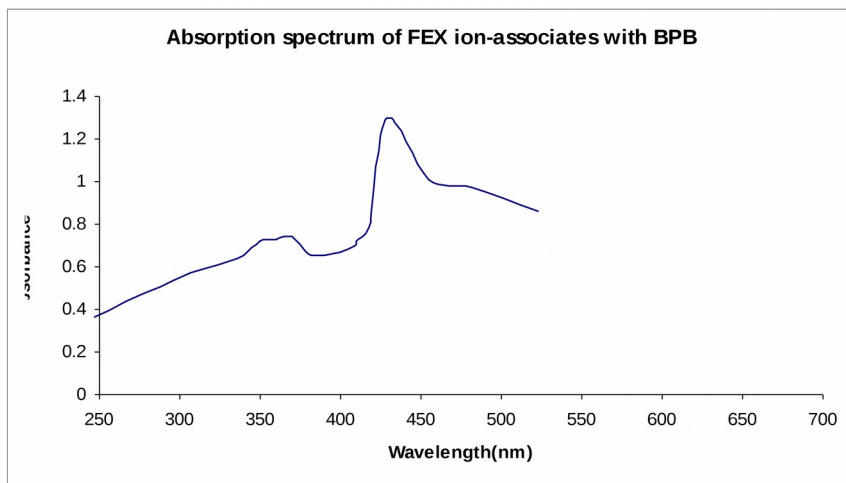


Fig 2:Absorption spectra of (FEX)ion-associates with (BPB)

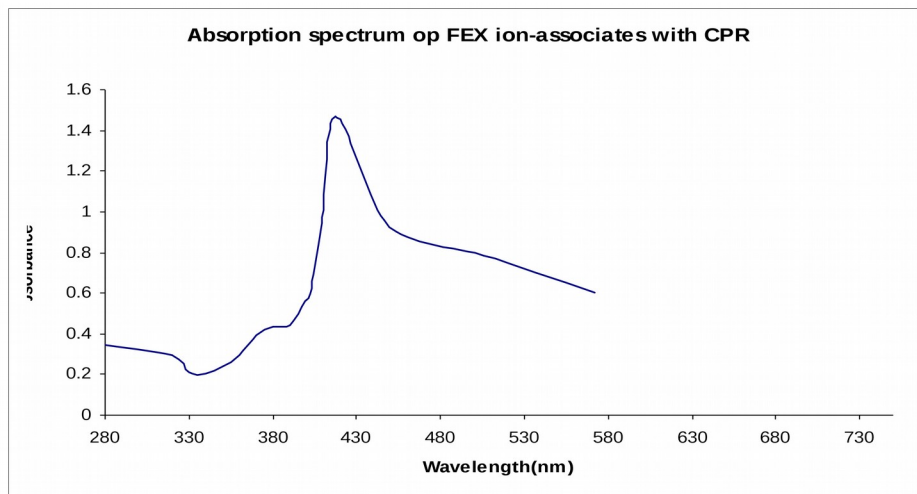


Fig 3:Absorption spectra of (FEX)ion-associates with (CPR)

The most convenient solvents found to produce the highest absorbance, extraction power and stability of colour of the formed ion-associates were chloroform in the case of Pic and CPR and chloroform and Methylene chloride in the case of BpB. The effects of extracting solvents on both extraction efficiency and absorptivity of the ion-associates in the case of Pic, BPB and CPR are represented graphically in Fig. 4 ,5and 6 respectively.

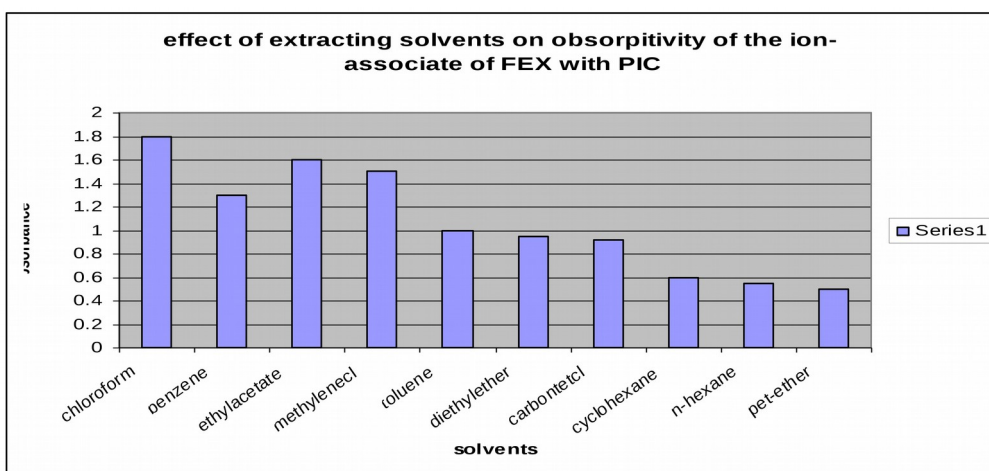
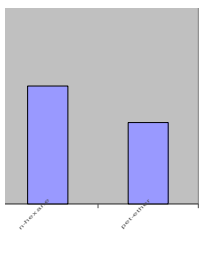


Fig. 4:Effect of extracting solvents on absorbance of the ion-associate of (FEX)with(PIC)

Fig. 5:Effect of extracting solvents on absorbance of the ion-associate of(FEX)with(BPB)**Fig. 6:Effect of extracting solvents on absorbance of the ion-associate of(FEX)with(CPR)**

The effect of pH is studied to reach to the optimum pH for the best colour obtained for the ion-associates. The optimum pH range for complete formation of the ion-associates was found to be in the range 2-6, 3-5 and 3-6, for Pic, BPB and CPR respectively as shown in Fig. 7. It was noticed that the absorbance of the ion-associate decreases at $\text{pH} < 2$ for Pic, and at $\text{pH} < 3$ For BPB and CPR due to formation of diprotonated species of the drug. However the absorbance decreases at $\text{pH} > 5$ For BPB and CPR and at $\text{pH} > 6$ for Pic due to the formation of free base of drug which insoluble in water using λ_{max} of each ion-associates and the selected organic solvent the effect of temperature on the formation of the ion-associates was studied by measuring absorbance of the extracted ion-associates at increased temperature intervals. The results showed that the ion-associates are formed almost instantaneously in all cases at room temperature $25 \pm 5^\circ\text{C}$. The effect of temperature

on the stability of ion-associates on Pic, BPB and CPR is shown graphically in Fig 8. It is showed that the thermal stability of ion-associate is stable up to 50°C, 60°C and 70°C for PIC, BPB and CPR respectively. It is showed that the thermal stability of ion-associate is stable up to 50°C, 60°C and 70°C for Pic, BPB and CPR respectively.

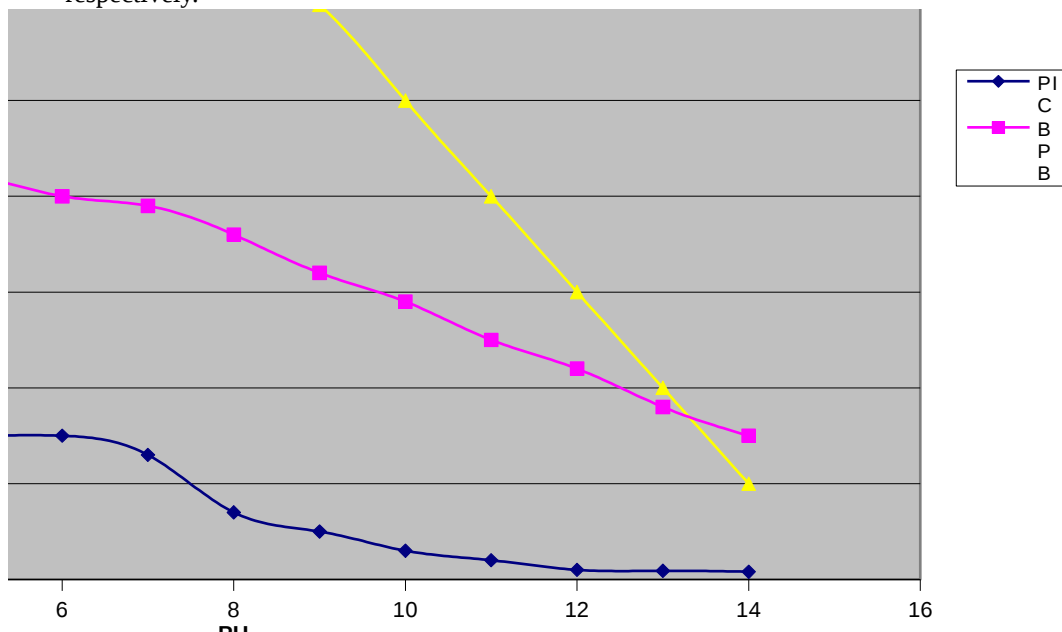


Fig. 7: Effect of pH on (FEX) ion-associates with (PIC, BPB and CPR)

Effect of temperature on FEX ion-associates with PIC, BPB and CPR

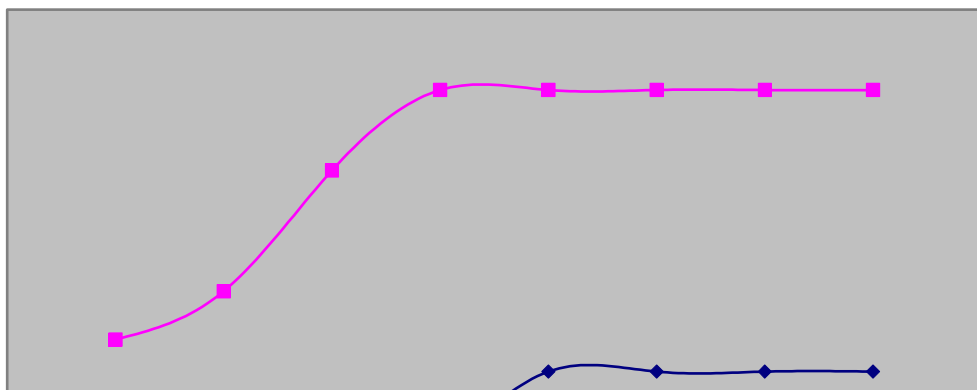


Fig. 8:Effect of temperature on (FEX)ion-associates with (PIC,BPB andCPR)**Conclusions**

Unlike the gas chromatographic and HPLC procedures, the spectrophotometer is simple and is not of high cost. The importance lies in the chemical reactions upon which the procedures are based rather than upon the sophistication of the instrument. This aspect of spectrophotometric analysis is of major interest in analytical pharmacy since it offers distinct method possibility in the assay of a particular component in complex dosage formulation.

The reagents utilized in the proposed methods are cheaper, readily available and the procedures do not involve any critical reaction conditions or tedious sample preparation. The method is unaffected by slight variations in experimental conditions such as pH and reagent concentration. Moreover, the methods are free from interference by common additives and excipients. The wide applicability of the new procedures for routine quality control is well established by the assay of (FEX) in pure form and in pharmaceutical preparations.

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