

STABILITY OF CHLORPHENIRAMINE MALEATE IN COUGH SYRUPS

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Experiments were performed to investigate the effects of temperature, pH, sunlight and other ingredients of cough syrups on the stability of chlorpheniramine maleate. There was no significant difference between the samples containing only chlorpheniramine maleate (sample A) and the samples of chlorpheniramine maleate compounded with other ingredients of cough syrups (sample B&C). However, the sample C containing ephedrine hydrochloride deteriorated more as compared to samples A & B.

Keywords : Chlorpheniramine maleate; Stability; Cough syrup

Introduction

Chlorpheniramine maleate is one of the most potent antihistaminic agents having short duration of action. It is being used in many formulations due to its antihistaminic properties in human as well as in veterinary practice. The preparations of chlorpheniramine maleate are available in the market in the form of oral, parenteral, injectable, nasal and ophthalmic preparations. The stability of a pharmaceutical is extremely significant. A drug product should retain its chemical, physical, microbiological, therapeutic and toxicological properties until administered to the patient. The United States Pharmacopoeia defines drug stability as the extent to which a drug product retains within specified limits, throughout its period of storage and use i.e., its shelf-life, the same properties and characteristics that it possessed at the time of manufacture (1). The stability of a drug product is affected by its external factors such as temperature, light, humidity and gases & internal factors such as pH, solvent, excipients and microbial growth & by the characteristics of container resulting in physical and chemical alterations. The present project was therefore conducted to study the effects of different parameters like tem-

perature, pH, sunlight and other ingredients of cough syrups such as ammonium chloride and ephedrine hydrochloride on the concentrations of chlorpheniramine maleate in cough syrups.

Materials and Methods

The commercial samples of cough syrups used for the analysis of chlorpheniramine maleate in this study are given in Table 1. The samples A, B and C were exposed to temperatures 25°C, 45°C and 60°C for 336 hours. Different pH values were maintained i.e., 3.6, 7 and 8 with hydrochloric acid and sodium hydroxide solutions. The samples were also exposed to sunlight in colourless glass bottles for 336 hours. Samples were taken at 0, 48, 96, 144, 192, 240, 288 and 336 hours and analysed for chlorpheniramine maleate content.

Different methods for the estimation of chlorpheniramine maleate are described in the British Pharmacopoeia (2-5) and British Pharmaceutical Codex (6-9), but the method best used for the determination of chlorpheniramine maleate with other drugs is of BP 1980 (10) and BPC 1973 (11). This method was suitably modified for the extraction of chlorpheniramine maleate. Instead of anesthetic ether, n-hexane was used on the basis of better distribution ratio of nitrogenous base between water and n-hexane which favours complete extraction by organic the phase. The percentage recovery of chlorpheniramine maleate was determined spectrophotometrically at 265 nm by preparing the 0.001%

Table 1. Commercial samples of cough syrups used for the analysis of Chlorpheniramine maleate.

S. No	Sample	Batch No	Formulation (Each 5 ml contains)
1	A	340891	Chlorpheniramine maleate.....2 mg
2	B	5391	Chlorpheniramine maleate.....2.5 mg Ammonium chloride.....125 mg Sodium citrate.....55 mg Glycerine.....750 mg
3	C	122213	Chlorpheniramine maleate..... 2 mg Ephedrine hydrochloride.....7 mg Ammonium chloride.....100 mg Sodium citrate......60 mg Menthol.....1 mg

dilution of each sample (A,B & C) with 0.2 N sulphuric acid. The percentage recoveries were computed by applying the following formula:
Absorption X 100/Concentration of sample E (212)

Results and Discussion

Effect of temperature: The results obtained are presented in table 2 and shown graphically in fig.1. At 25°C, the decomposition rate is 1% in each sample while at 45°C, the degradation of chlorpheniramine maleate in samples A, B & C is 2.4%, 2.5% & 2.8%, respectively. The deterioration rate at 60°C is 4.3%, 4.5% & 5.2% in samples A, B & C respectively. It has been noted that loss in potency is more in sample C (which contains ephedrine HCl) as compared to sample A (containing only chlorpheniramine maleate) and sample B (containing ammonium chloride also).

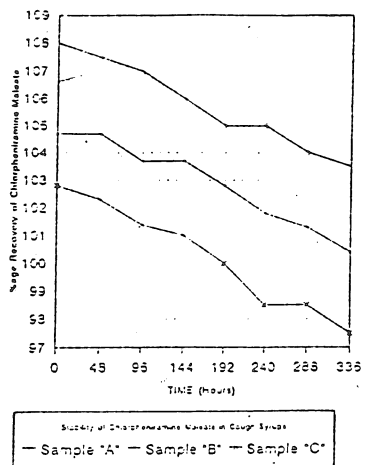
Effect of pH : Table 3 shows a summary of results obtained from the effect of pH and Fig.2 presents these results graphically. At pH 3.6, very low rate of decomposition was observed as 1%, 1.5% and 2% in samples A, B and C, respec-

tively. At pH value of 7.0 the degradation rate in samples A, B, & C was 3.0%, 3.5% and 3.5%, respectively. Furthermore, the loss in quantity of chlorpheniramine maleate was 3.3%, 4.7% & 5.7% in samples A, B & C respectively at pH value of 8.0. These results demonstrate that chlorpheniramine maleate is highly stable in acidic values.

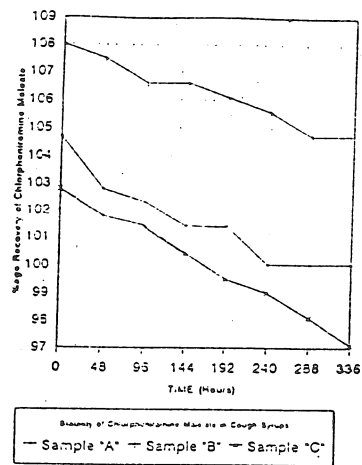
Effect of sunlight

The sunlight also affects the concentration of chlorpheniramine maleate to some extent. The decrease recorded in the quantity of chlorpheniramine maleate was 1.0%, 1.4% & 1.86% in samples A, B & C respectively. These results are presented in table 4 and fig.3. The effect of different factors i.e., temperature, pH, sunlight and other ingredients of cough syrups on the stability of chlorpheniramine maleate shows no significant difference between the samples containing only chlorpheniramine maleate (A) and the samples of chlorpheniramine maleate compounded with other ingredients of cough syrups (B & C). However, sample C containing

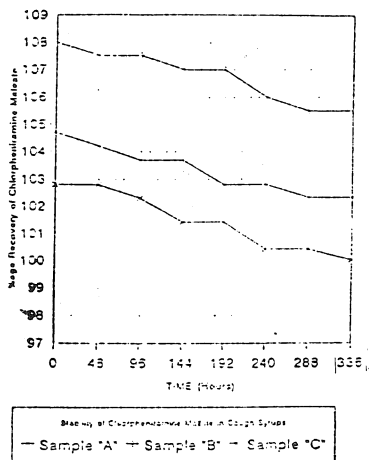
1. Graph between Time & %age Recovery at Temp. 60°C



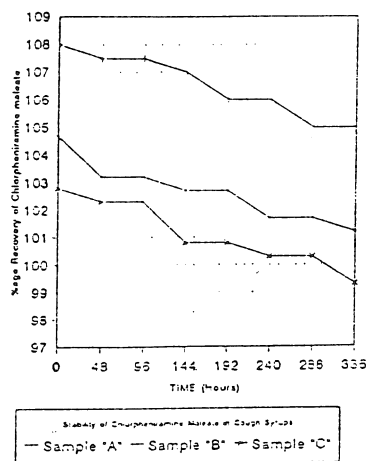
Graph between Time & %age Recovery at pH 8.0



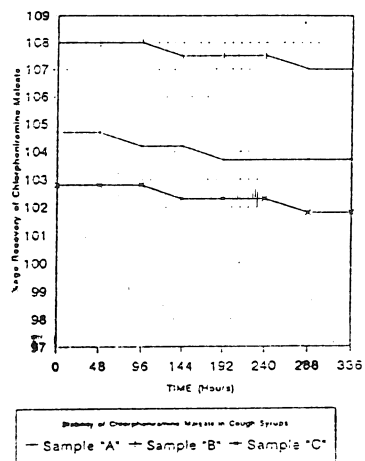
2. Graph between Time & %age Recovery at Temp. 45°C



Graph between Time & %age Recovery at pH 7.0



3. Graph between Time & %age Recovery at Temp. 25°C



Graph between Time & %age Recovery at pH 3.6

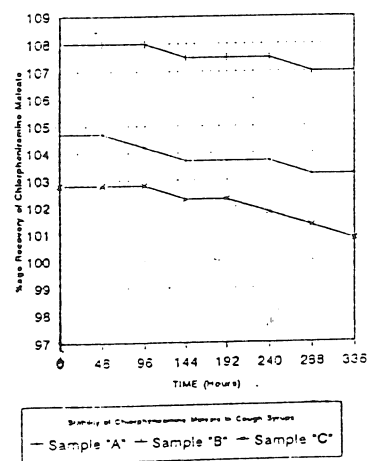


Fig.1. Graph between time and %age recovery at 60°C

Fig.2. Graph between time & %age recovery at 45°C

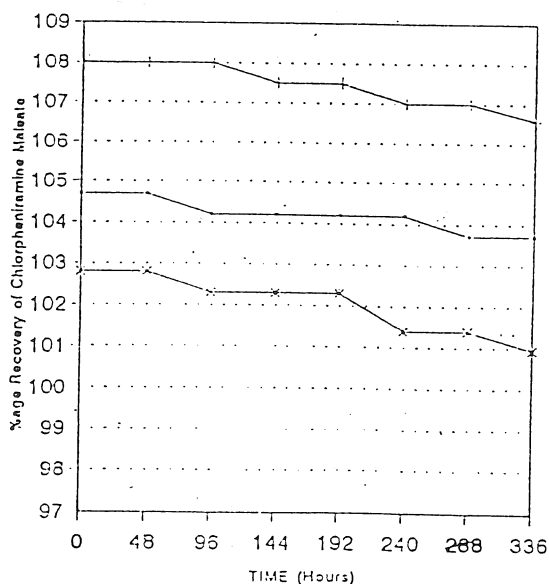
Table 2. Effect of different temperatures on the stability of chlorpheniramine maleate in cough syrups

No. of observations	Time interval (Hours)	Sample A %age recovery at			Sample B %age recovery at			Sample C %age recovery at		
		25°C	45°C	60°C	25°C	45°C	60°C	25°C	45°C	60°C
1	0	104.70	104.70	104.70	108.00	108.00	108.00	102.80	102.80	102.80
2	48	104.70	104.20	104.70	108.00	107.50	107.50	102.80	102.80	102.30
3	96	104.20	103.70	103.70	108.00	107.50	107.00	102.80	102.30	101.40
4	144	104.20	103.70	103.70	107.50	107.00	106.00	102.30	101.40	101.40
5	192	103.70	102.80	102.80	107.50	107.00	105.00	102.30	101.40	100.00
6	240	103.70	102.80	101.80	107.50	106.00	105.00	102.30	100.40	98.50
7	288	103.70	102.30	101.30	107.00	105.50	104.20	101.80	100.40	98.05
8	336	103.70	102.30	100.40	107.00	105.50	103.70	101.80	100.00	97.60

Table 3. Effect of different pH values on the stability of chlorpheniramine maleate in cough syrups

No. of Observations	Time interval (Hours)	Sample A %age recovery at			Sample B %age recovery at			Sample C %age recovery at		
		3.6°C	7.0°C	8.0°C	3.6°C	7.0°C	8.0°C	3.6°C	7.0°C	8.0°C
1	0	104.70	104.70	104.70	108.00	108.00	108.00	102.80	102.80	102.80
2	48	104.70	103.70	103.70	108.00	107.50	107.50	102.80	102.30	101.80
3	96	104.20	103.30	102.30	108.00	107.50	106.60	102.80	102.30	101.40
4	144	103.70	102.80	101.40	107.50	107.00	106.60	102.30	101.80	100.40
5	192	103.70	102.80	101.40	107.50	106.00	106.10	102.30	100.80	99.50
6	240	103.70	101.80	100.00	107.50	106.00	105.60	101.80	100.40	99.00
7	288	103.20	101.40	100.00	107.00	105.50	104.70	101.40	100.40	98.10
8	336	103.20	101.40	100.00	107.00	105.00	104.70	100.90	99.50	97.10

Graph between Time & %age Recovery at Sunlight



Stability of Chlorpheniramine Maleate in Cough Syrups
 — Sample "A" - - - Sample "B" ···· Sample "C"

ephedrine HCl deteriorated more as compared with samples A & B. recovery at sunlight

Table 4. Effect of sunlight on the stability of chlorpheniramine maleate in cough syrups at sunlight

No. of observations	Time interval (Hours)	Sample A %age recovery	Sample B %age recovery	Sample C %age recovery
1	0	104.70	108.00	102.80
2	48	104.70	108.00	102.80
3	96	104.20	108.00	102.30
4	144	104.20	107.50	102.30
5	192	104.20	107.50	102.30
6	240	104.20	107.00	101.40
7	288	103.70	107.00	101.40
8	336	103.70	106.60	100.94

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Fig. 3. Graph between time & %percentage

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