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Simultaneous spectrophotometric analysis of a ternary mixture of pharmaceuticals — assay for meclozine hydrochloride, pyridoxine hydrochloride and caffeine

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Abstract Based on an extension of Vierordt's method and in continuation of earlier work, the simultaneous analysis of a ternary mixture of meclozine hydrochloride, pyridoxine hydrochloride and caffeine is discussed Using 0 01 M methanolic sodium hydroxide as the solvent, the absorbance of the solution of the mixture is recorded at 230, 273 and 307 nm The concentration of each component is determined by the solution of three simultaneous equations

Keywords *Simultaneous spectrophotometry, ternary mixture, extension of Vierordt's method, meclozine hydrochloride, pyridoxine hydrochloride, caffeine*

Introduction

In earlier work [1], the authors of the present work have discussed the simultaneous determination of aspirin, paracetamol and caffeine in mixtures The equations derived for a ternary mixture in the earlier work have been successfully used in the analysis of a mixture of meclozine hydrochloride, pyridoxine hydrochloride and caffeine

Meclozine hydrochloride (meclizine hydrochloride) has potent anticholinergic activity although its sedative effects are not marked This drug in combination with pyridoxine hydrochloride and caffeine is used in the treatment of nausea and vomiting associated with the early stages of pregnancy

Meclozine hydrochloride, pyridoxine hydrochloride and caffeine together with their dosage forms, including combinations with other drugs, have been listed in various pharmacopoeias [2–4] The official compendia describe non-aqueous titrimetry for the estimation of meclozine hydrochloride as the bulk drug and in dosage forms Caffeine has been assayed in various pharmacopoeias gravimetrically, titrimetrically and spectrophotometrically Colorimetric and titrimetric procedures are described in pharmacopoeias for pyridoxine hydrochloride as the bulk drug and in dosage forms In

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addition, meclozine hydrochloride has been determined titrimetrically [5] spectrophotometrically [6] and by HPLC [7] Pyridoxine hydrochloride has been determined by spectrophotometry [6, 8], fluorimetry [9], GLC [10], TLC [11], HPLC [7, 12–14] colorimetry [15], titrimetry [16] and PMR [17] Caffeine in combination with other drugs has been determined by titrimetry [18] non-aqueous titration [19], UV spectrophotometry [20, 21], IR spectrophotometry [22], NMR [23] and HPLC [24–28] The analysis of mixtures of meclozine hydrochloride and pyridoxine hydrochloride has been reported [6, 7] but no work has been reported on the analysis of a ternary mixture of meclozine hydrochloride, pyridoxine hydrochloride and caffeine

The present work was prompted by the need for developing a rapid and reliable method for the routine analysis of such a combination Instruments are now commercially available that can collect spectra from individual components and their mixtures and then solve the simultaneous equations to yield the contents of each compound

Experimental

Reagent and equipment

Reference standards of meclozine hydrochloride, pyridoxine hydrochloride and caffeine were obtained from the Central Drugs Laboratory (Calcutta, India) All inorganic and organic chemicals were of analytical reagent grade

A Beckman UV-visible spectrophotometer Model 24 equipped with a recorder was used

Commercial samples of the mixtures were obtained locally

Method

An accurately weighed quantity of powdered tablets equivalent to about 5 mg of meclozine hydrochloride was placed in a 100-ml volumetric flask and 40 ml of methanol was added, the contents were shaken for 5 min and diluted to 100 ml with water The resulting suspension was filtered and the first few millilitres of the filtrate were discarded, 5 ml of the filtrate was diluted to 50 ml with 0 01 M methanolic sodium hydroxide The absorbance of the final solution was measured at 230, 273 and 307 nm using 0 01 M methanolic sodium hydroxide as the blank

Calculations were carried out using the following equations

$$\text{weight (mg, of meclozine hydrochloride} = 34\ 35\ E_1 - 16\ 75\ E_2 - 14\ 21\ E_3, \quad (1)$$

$$\text{weight (mg) of pyridoxine hydrochloride} = 29\ 85\ E_3, \quad (2)$$

$$\text{weight (mg, of caffeine} = 21\ 02\ E_2 - 2\ 613\ E_3 - 0\ 57\ E_1, \quad (3)$$

where E_1, E_2 and E_3 are the absorbance values of the sample solution at 307, 273 and 230 nm, respectively

The marketed mixture contains meclozine hydrochloride, pyridoxine hydrochloride and caffeine in the ratio of 2 5 5·2 (m/m/m) It was, however, felt desirable to determine the ratios within which one of the compounds can be accurately determined in the presence of the other two In Table 1 the results for three sets of experiments are reported with different ratios of the mixture In set 1, the concentration of meclozine

Table 1
Experiments on authentic samples of meclozine hydrochloride (M), pyridoxine hydrochloride (P) and caffeine (C) in different ratios

Sample no	Ratio M	P	C	Recovery mean* ±SD (%) M	P	C
Set 1†						
1	1 5	5 0	2 0	102 2 ±0 68	100 5 ±0 31	101 8 ±0 52
2	2 0	5 0	2 0	100 2 ±0 56	99 7 ±0 26	101 6 ±0 42
3	2 5	5 0	2 0	101 6 ±0 49	100 5 ±0 27	100 8 ±0 41
4	3 0	5 0	2 0	101 7 ±0 54	99 7 ±0 21	100 2 ±0 39
5	3 5	5 0	2 0	102 0 ±0 38	100 3 ±0 35	100 7 ±0 52
Set 2‡						
6	2 5	4 0	2 0	100 1 ±0 72	100 0 ±0 41	101 0 ±0 46
7	2 5	4 5	2 0	99 9 ±0 69	100 0 ±0 35	102 0 ±0 38
8	2 5	5 0	2 0	101 6 ±0 49	100 5 ±0 27	100 8 ±0 41
9	2 5	5 5	2 0	102 1 ±0 59	100 2 ±0 23	100 6 ±0 39
10	2 5	6 0	2 0	100 9 ±0 54	100 4 ±0 17	101 1 ±0 42
Set 3§						
11	2 5	5 0	1 0	100 5 ±0 62	100 5 ±0 27	102 6 ±0 58
12	2 5	5 0	1 5	101 7 ±0 58	101 4 ±0 17	101 9 ±0 65
13	2 5	5 0	2 0	101 6 ±0 49	100 5 ±0 27	100 8 ±0 41
14	2 5	5 0	2 5	102 0 ±0 68	100 8 ±0 21	100 7 ±0 53
15	2 5	5 0	3 0	101 9 ±0 71	100 0 ±0 11	101 3 ±0 44

*$n = 3$
†Set 1 — P and C kept constant and M changed
‡Set 2 — M and C kept constant and P changed
§Set 3 — M and P kept constant and C changed

hydrochloride was changed but concentrations of pyridoxine hydrochloride and caffeine were kept constant In set 2, the concentration of pyridoxine hydrochloride was changed but concentrations of meclozine hydrochloride and caffeine were kept constant In set 3, concentrations of meclozine hydrochloride and pyridoxine hydrochloride were kept constant but the concentration of caffeine was changed The recoveries in all the three sets were found to be 99 7–102 1%

Experiments were also conducted with standard additions to one of the commercial samples Table 2 shows that the recoveries are fairly satisfactory

The method was also applied to some commercial samples The results are tabulated in Table 3

Results and Discussion

The principles governing the absorptiometric measurements for the analysis of binary mixtures, initially discussed by Vierordt [29] and extended to cover ternary mixtures [1],

Table 2
Recovery experiments on standard additions to a commercial sample of tablets containing meclozine hydrochloride (M), pyridoxine hydrochloride (P) and caffeine (C)

Sample no *	Added (mg)			Recovered (mg)			% Recovery		
	M	P	C	M	P	C	M	P	C
1	0 100	—	—	0 102	—	—	102 0	—	—
2	0 200	—	—	0 203	—	—	101 5	—	—
3	0 300	—	—	0 301	—	—	100 3	—	—
4	—	0 1056	—	—	0 105	—	—	99 5	—
5	—	0 2112	—	—	0 213	—	—	100 8	—
6	—	0 3168	—	—	0 318	—	—	100 3	—
7	—	—	0 1007	—	—	0 0996	—	—	98 9
8	—	—	0 2014	—	—	0 199	—	—	98 8
9	—	—	0 3021	—	—	0 296	—	—	98 0

Mean recovery (% ± SD) M, 101 267 ± 071, P, 100 2 ± 0 53, C, 98 56 ± 0 40

*Sample was Pregnidoxin tablets of declared content pyridoxine hydrochloride 50 mg, caffeine 20 mg and meclozine hydrochloride 25 mg Contents found pyridoxine hydrochloride 48 8 mg, caffeine 19 76 mg and meclozine hydrochloride 26 35 mg

Table 3
Results obtained with commercial samples of tablets containing meclozine hydrochloride (M), pyridoxine hydrochloride (P) and caffeine (C)

Sample no	Declared content (mg/tablet)			Found (mg/tablet)			Found % of the declared content ± SD*		
	M	P	C	M	P	C	M	P	C
1	25 0	50 0	20 0	26 35	48 8	19 8	105 4 ±0 82	97 6 ±0 27	99 0 ±0 71
2	25 0	50 0	20 0	25 4	48 2	20 4	101 6 ±0 60	96 4 ±0 32	102 0 ±0 59
3	25 0	50 0	20 0	25 6	48 1	20 2	102 4 ±0 43	96 2 ±0 28	101 0 ±0 56
4	25 0	50 0	20 0	24 8	49 2	20 6	99 2 ±0 75	98 4 ±0 36	103 0 ±0 49
5	25 0	50 0	20 0	25 3	48 9	19 4	101 2 ±0 68	97 8 ±0 40	97 0 ±0 39

*$n = 5$

have been successfully applied to the analysis of a mixture containing meclozine hydrochloride, pyridoxine hydrochloride and caffeine In all such cases, the accuracy in spectral measurements, spectral pattern and the nature of the individual components are key factors for obtaining reliable results in the simultaneous spectrophotometric analysis of multicomponent mixtures Another important factor contributing towards the precision of the analysis of a mixture is the relative composition of the individual components Nevertheless, a higher absorbance in the case of a minor component will improve the precision The selection of wavelengths in a ternary mixture may pose a little difficulty but it is always preferable to select such wavelengths which may fall at a maximum and where there is least slope of the other two compounds

In the case of meclozine hydrochloride, pyridoxine hydrochloride and caffeine, the most suitable wavelengths would be 230, 307 and 273 nm, respectively (Fig 1) At the 230 nm wavelength chosen for meclozine hydrochloride, other compounds absorb In the case of pyridoxine hydrochloride, the maximum at 307 nm was preferred to that at 244 nm, as both meclozine hydrochloride and caffeine do not absorb at 307 nm, and 244 nm corresponds with the rising curve of caffeine The measured absorptivities (E 1%, 1 cm) of meclozine hydrochloride at 230, 273 and 307 nm are 295, 8 and 0, respectively, those of pyridoxine hydrochloride are 161, 46 and 335, respectively, those of caffeine are 235, 482 and 0, respectively These values were obtained from standard solutions of meclozine hydrochloride, pyridoxine hydrochloride and caffeine in 0 01 M methanolic sodium hydroxide The figures given in equations (1), (2) and (3) were obtained by numerical substitution for the absorptivity values in equations (4), (5) and (6) taking into consideration the dilution factors given in the procedure

Concentration of meclozine hydrochloride (C_m)

$$C_m = \frac{E_1(\beta_2\nu_3 - \beta_3\nu_2) + E_2(\beta_3\nu_1 - \beta_1\nu_3) + E_3(\beta_1\nu_2 - \beta_2\nu_1)}{\alpha_1(\beta_2\nu_3 - \beta_3\nu_2) + \alpha_2(\beta_3\nu_1 - \beta_1\nu_3) + \alpha_3(\beta_1\nu_2 - \beta_2\nu_1)}$$

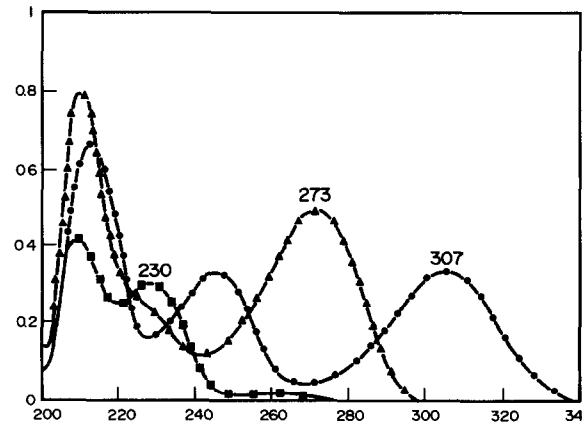

Figure 1
UV spectra of pyridoxine hydrochloride (●), caffeine (▲) and meclozine hydrochloride (■) in 0 01 M methanolic sodium hydroxide

Since β_3 and $\alpha_3 = 0$, the equation can be reduced to

$$C_m = \frac{E_1\beta_2\nu_3 - E_2\beta_1\nu_3 + E_3(\beta_1\nu_2 + \beta_2\nu_1)}{\alpha_1\beta_2\nu_3 - \alpha_2\beta_1\nu_3} \tag{4}$$

Concentration of caffeine (C_c)

$$C_c = \frac{E_1(\alpha_3\nu_2 - \alpha_2\nu_3) + E_2(\alpha_1\nu_3 - \alpha_3\nu_1) + E_3(\alpha_2\nu_1 - \alpha_1\nu_2)}{\alpha_1(\beta_2\nu_3 - \beta_3\nu_2) + \alpha_2(\beta_3\nu_1 - \beta_1\nu_3) + \alpha_3(\beta_1\nu_2 - \beta_2\nu_1)},$$

$$C_c = \frac{E_2\alpha_1\nu_3 - E_1\alpha_2\nu_3 + E_3(\alpha_2\nu_1 - \alpha_1\nu_2)}{\alpha_1\beta_2\nu_3 - \alpha_2\beta_1\nu_3} \tag{5}$$

Concentration of pyridoxine hydrochloride (C_p)

$$C_p = \frac{E_1(\alpha_2\beta_3 - \alpha_3\beta_2) + E_2(\alpha_3\beta_1 - \alpha_1\beta_3) + E_3(\alpha_1\beta_2 - \alpha_2\beta_1)}{\alpha_1(\beta_2\nu_3 - \beta_3\nu_2) + \alpha_2(\beta_3\nu_1 - \beta_1\nu_3) + \alpha_3(\beta_1\nu_2 - \beta_2\nu_1)},$$

$$C_p = \frac{E_3}{\gamma_3}, \tag{6}$$

where α, β and γ are the absorptivity values of meclozine hydrochloride, caffeine and pyridoxine hydrochloride Suffixes 1, 2 and 3 indicate the wavelengths, i e 230, 273 and 307 nm, respectively

Perusal of Tables 1–3 indicate that the results are fairly satisfactory, thereby demonstrating the utility of the proposed method for the analysis of the mixture in dosage forms, particularly for different batches

The validity of the method for pharmaceutical preparations as well as the effect of possible causes of interference was studied by assaying authentic samples containing the drugs together with common additives and excipients, e g lactose, dicalcium phosphate, starch, talc and magnesium stearate The recovery (%) was satisfactory

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