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ANALYSIS OF PARACETAMOL AND OXYPHENBUTAZONE IN TANDALGESIC CAPSULE PREPARATION BY DIFFERENCE SPECTROSCOPY

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ABSTRACT

The technique of difference spectrophotometry was applied to the rapid analysis of Tandalgesic capsule preparation without prior separation from other materials. Factors like the variation of pH and reactions such as hydrolysis were utilized to produce spectral shifts. It was found that the absorption of the individual components at the wave-length of isosbestic points i.e. 285 nm of the difference spectra was due solely to the individual drugs with no interference from the other. The individual concentrations of paracetamol and oxyphenbutazone were not

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less than 84.08 ± 1.90% and 18.66 ± 1.39% respectively and on the whole from 101 - 103%.

INTRODUCTION

The formulation of paracetamol (N-acetyl-p-amino-phenol) and ooxyphen butazone (Hydroxyphenyl butazone as a single preparation, "Tandalgesic"* has resulted in a drug combination with marked analgesic, antipyretic and anti-inflammatory properties by virtue of which it prevents or rapidly reduces post-operative or post-traumatic swelling [1,2].

Tandalgesic is relatively a new drug preparation and has been popular as one medication for three common symptoms.

Although some assay procedures have been established on paracetamol and oxyphenbutazone individually the published work is scanty and indeed none is on the determination of one of the components in the presence of the other.[3] Therefore, the analysis of the individual drugs in the presence of each other in such a dosage form was undertaken in this study.

EXPERIMENTAL

Substances and Equipment:

Pure paracetamol was obtained from the Department of Pharmaceutics and Pharmaceutical Technology, University of

*Ciba-Geigy Ltd., Basle, Switzerland is the marketer of this preparation in this region of the globe.

Benin, Benin City. (Nigeria). Pure oxyphenbutazone was received as gift sample from Messers Sarabai International, Barada, India. The absorbance data was obtained on a Pye-Unicam UV/Vis SP - 500 Spectrophotometer.

All reagents and chemicals used in this study were obtained from BDH chemicals Ltd., Poole, England and were of analytical grade.

Methods:

Difference Spectrophotometry (General Procedure):

The experimental procedures described by Doyle and Fazari[4] and Shane and Routh were adopted in this study.[5,6] The whole content of the Tandalgesic Capsule (470 mg) was dissolved directly in some quantity of methanol and made up to 100 ml with the same solvent.

Duplicate aliquot of the stock solution were prepared by adding acid to one aliquot, base or buffer to the other. Both aliquotes were then diluted to an identical final concentration (i.e. 0.001% w/v) giving two solutions 'A' and 'B'. Duplicate aliquotes of the pure paracetamol and pure oxyphenbutazone were similarly treated. Blank solutions 'A' and 'B' were also prepared since buffer was used. The sample solutions were then scanned in standard cells in a spectrophotometer by placing sample solution 'A' in the sample compartment and sample solution 'B' in the reference

compartment (and vice cersa) and the absorbance determined in the range of 220 - 335 nm.

The standard solutions were similarly treated. The difference spectra obtained from the absorbances were superimposed on the sample spectra to facilitate the observance of isosbestic points.

Ultraviolet Spectroscopy:

Conventional spectra of pure paracetamol, pure oxyphenbutazone and the mixture in Tandalgesic Capsule preparation were obtained by employing the standard procedure for the determination of organic drug mixture described by Williams.[7]

Three hundred milligrams (300 mg) of pure paracetamol powder was transfered into a 100 ml Volumetric flask, dissoved and made up to 100 ml volume with methanol Aliquots of this solution was taken and further diluted with enough 0.1N sodium hydroxide solution to obtain a concentration of 0.001% w/v of the pure paracetamol in alkali.

The solution was then scanned in 1 cm quartz cells in a spectrophotometer and the absorbance determined in the wave length range of 230 - 300 nm. A solution of 0.1N sodium hydroxide was used as the reference solution in this determination.

Similarly, a 0.001% w/v solution of pure oxyphenbutazone and a 0.001% w/v solution of Tandalgesic Capsule powder

was prepared and the absorbance determined over the same wave length range, using 0.01N sodium hydroxide solution as a reference.

The entire procedure was performed using 0.1N hydrochloric acid solution and buffer solutions of pH 5,7,9 and 11 as the solvent medium for the powdered drug samples and as reference solutions.

The values for the absorbance of a 1% solution of each drug in a 1 cm cell (i.e. A 1%, cm) were calculated using the formula described in B.P.[3] $A\ (1\%, cm) = \frac{A}{C.B.}$

where A = absorbance of the solution

C = concentration of the drug in solution

B = path length.

Also, the molar absorbance, E, has been computed according to the formular used in Beckett and Stenlake[7].

$$E = A\ (1\%, 1cm) \times \frac{N.wt}{10}$$

where N.wt = molecular weight of the drug in solution.

The formula is used provided the concentrations of oxyphenbutazone and paracetamol in Tandalgesic were also determined using the method outlined in Beckett and Stenlake for a drug in a mixture.[7]

The formula is as follows:

$$\%\ Sample = \frac{A\ Sample \times 100}{C\ Sample \times A\ (1\%, 1cm)\ Standard}$$

pure oxyphenbutazone powder and pure paracetamol powder were used as the standard.

RESULTS AND DISCUSSION

In practice, when analyzing pharmaceutical samples, there is always uncertainty concerning interfering materials which hace accompanied the sample and which remain uncompensated for by the reference solution. Therefore, the difference spectrophotomatric method which provides an approximation of ideal reference solution by employing an aliquot of the sample solution itself as reference, adjusted by change in pH or other parameters but containing both the substances being analysed and all extraneous substances at exactly the same concentrations as the sample was applied.

When the pH or other variations cause an alteration in the spectrum the instrument records this as a characteristic difference spectrum. It other materials present are unaffected by the change in conditions, their contribution to the total absorbance of each solution will be identical and their effect will be exactly cancelled out.[4]

The conventional spectra of the pure drugs - paracetamol and oxyphenbutazone and their mixture Tandalgesic in acid and base have been shown in fig. 1 and 2. The maxima for pure paracetamol shifted by only 10nm i.e. from 245 nm

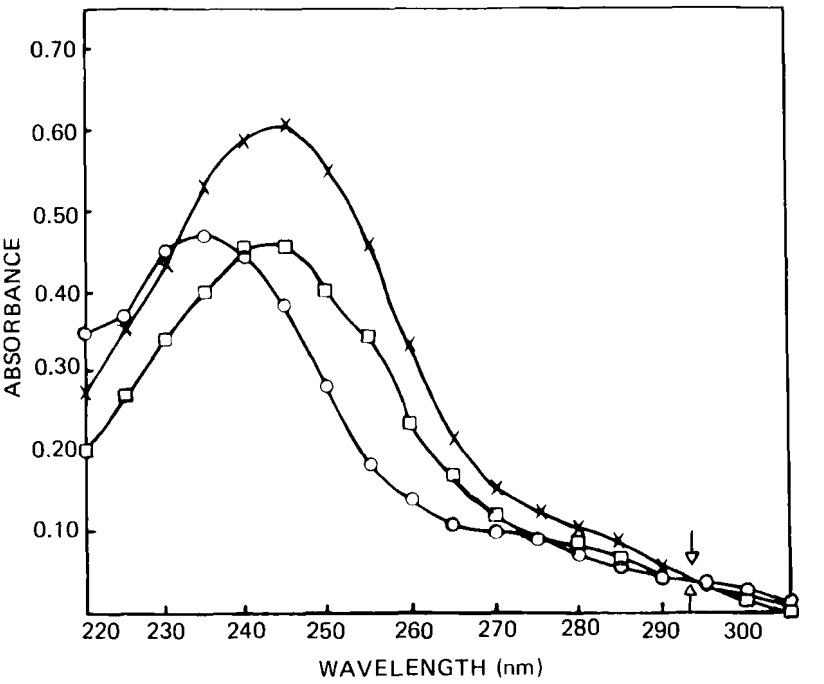

FIG.1: ABSORBANCE SPECTRA IN 0·1N HCL

Paracetamol 0·001 % w/v
Oxyphenbutazone 0·001 % w/v
Tandalgesic 0·001 % w/v

in acid to 255 nm in base and absorbances at these maxima differed by 5.5%.

However, the difference spectrum when superimposed on the conventional spectra, and determined at the concentration of 0.00% w/v, gave an amplitude that was 64% as sensitive as the base spectrum.

In the case of pure oxyphenbutazone the maxima was shifted by 19 nm i.e. from 235 nm in acid to 254 nm in base and the absorbances at these maxima differed by

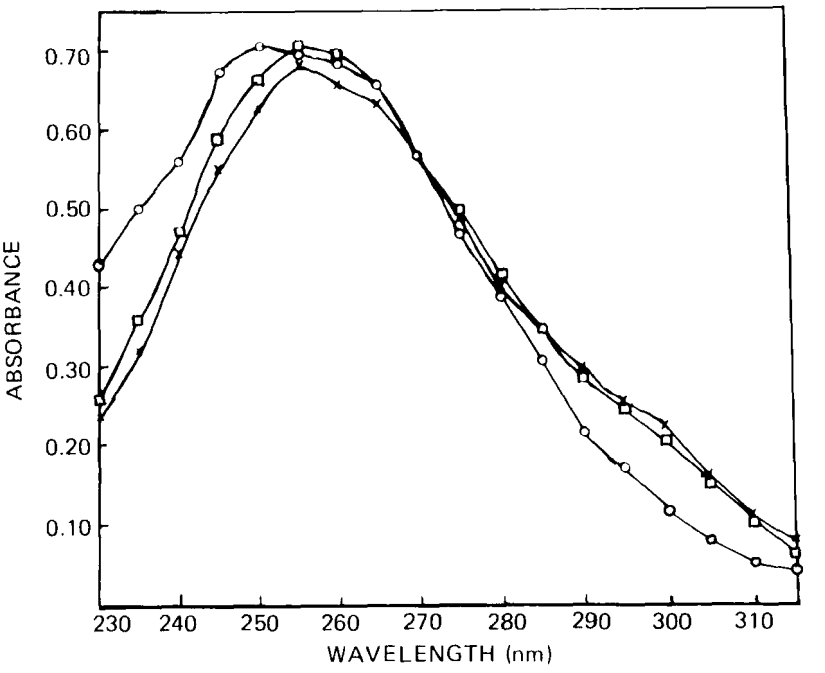

FIG 2: ABSORPTION SPECTRA IN 0·1N NaoH
Paracetamol 0·001% w/v
Oxyphenbutazone 0·001% w/v
Tandalgesic 0·001 % w/v

32.9%. On superimposing the difference spectrum on the conventional spectrum and determined at the same concentration the amplitude was 92.9% as sensitive as the base spectrum. For the sample i.e. Tandalgesic the maxima as recorded in Fig. No. 10 was shifted by 11 nm and the absorbances at these maxima differed by 32.9%. However, in the differences spectrum a maxima was obtained at 265 nm and a minimum at 230 nm. This gave an amplitude that was fully 64% as sensitive as the base spectrum and 67% as sensitive at 250 nm and 265 nm respectively.

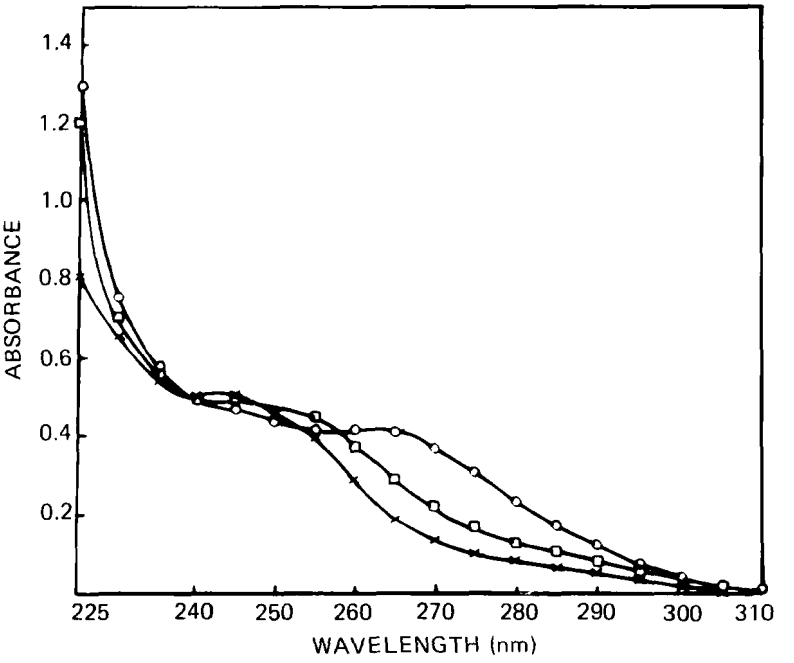

FIG.3: ABSORPTION SPECTRA IN P.H.S. BUFFER SOLUTION

Paracetamol 0.001% w/v
Oxyphenbutazone 0.001% w/v
Tandalgesic 0.001% w/v

Isobestic points:

In the Fig. Nos. 8, 9 and 10 pure paracetamol pure oxyphenbutazone and their mixture Tandalgesic, the conventional acidic and basic spectra intersect at 247, 233 and 240 nm respectively, indicating that the two forms in each of the figures have identical absorbances at these wavelengths. When the standard and the sample curves were superimposed as shown in Fig. No. 7 the isosbestic points were observed at 223 and 285 nm respectively which indicated that any form of interferences at these points have been cancelled out.

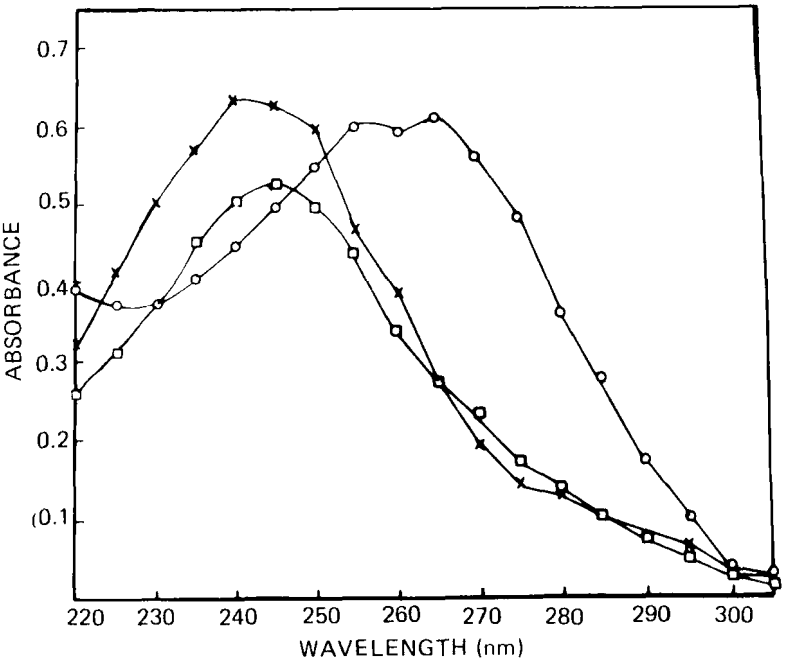

FIG.4: ABSORPTION SPECTRA IN NEUTRAL SOLUTION

Paracetamol 0·001% w/v
Oxyphenbutazone 0·001% w/v
Tandalgesic 0·001% w/v

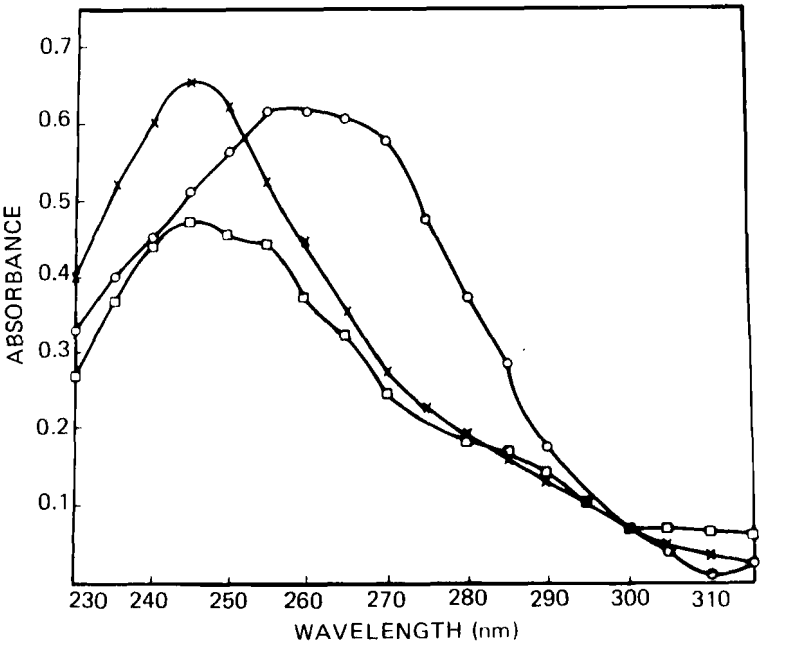

FIG.5: ABSORPTION SPECTRA IN PH 9 BUFFER SOLUTION

Paracetamol 0·001% w/v
Oxyphenbutazone 0·001% w/v
Tandalgesic 0·001% w/v

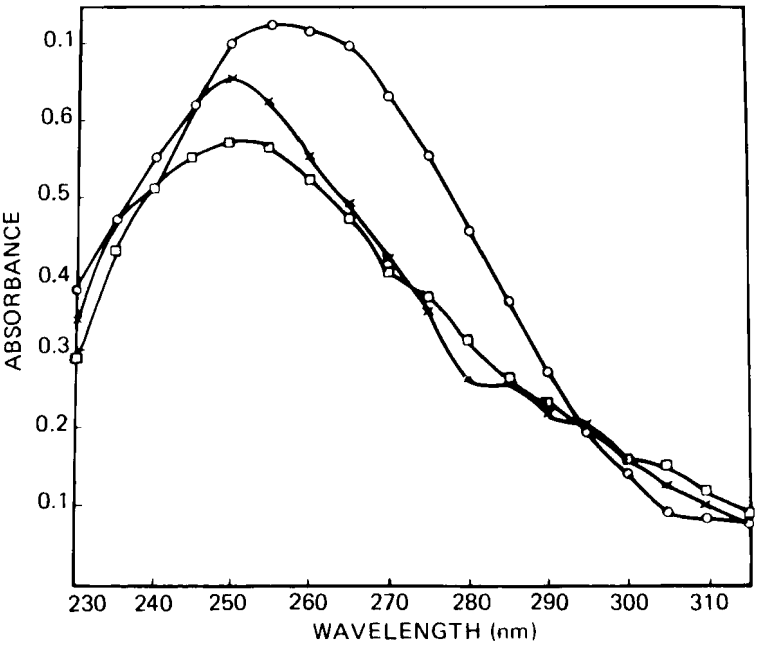

FIG. 6: ABSORPTION SPECTRA IN PH II BUFFER SOLUTION

× × Paracetamol 0.001% w/v
○ ○ Oxyphenbutazone 0.001% w/v
△ △ Tandalgesic 0.001% w/v

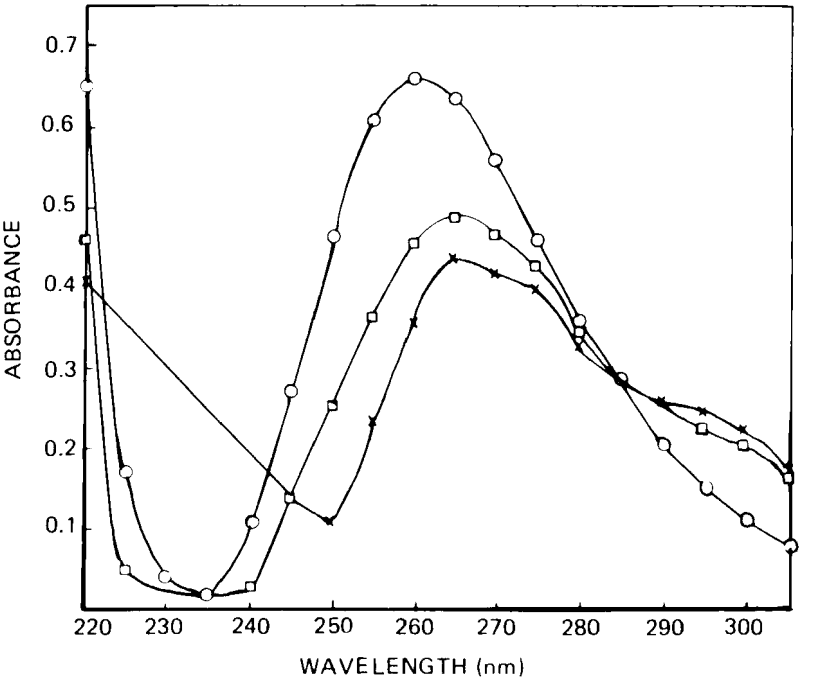

FIG.7: DIFFERENCE SPECTRA (ACID Vs BASE)

Paracetamol 0.001% w/v
Oxyphenbutazone 0.001% w/v
Tandalgesic 0.001% w/v

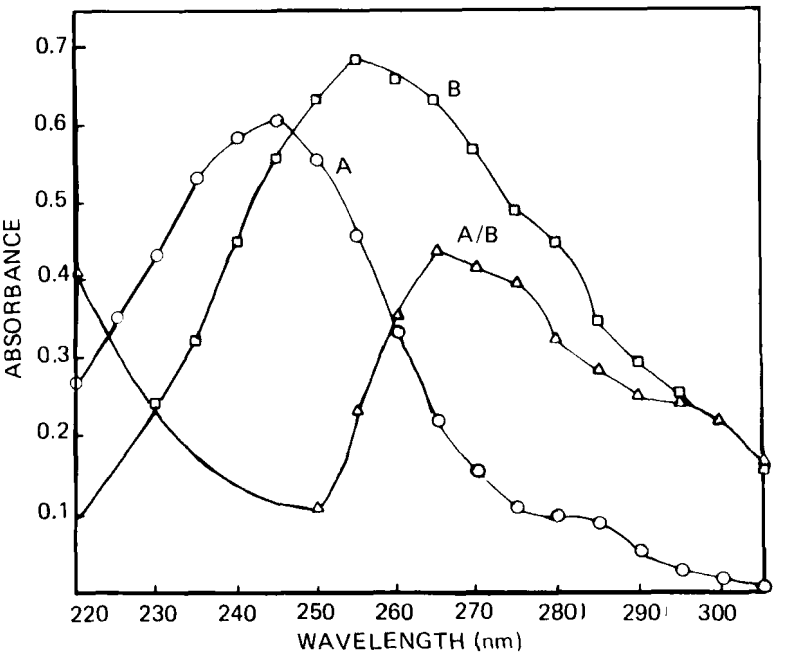

FIG.8: CONVENTIONAL SPECTRA SUPERIMPOSED WITH DIFFERENCE SPECTRUM

—o— Paracetamol 0·001% w/v in acid
—o— Paracetamol 0·001% w/v in Base
—Δ— Difference spectrum (Acid vs Base)

Effect of pH:

In the analysis of organic compounds by ultraviolet absorption spectrophotometry, considerable inroads into the solution of problems can be achieved from a study of the wavelength and the intensity of absorption and the effect of these on changing the solvent or its pH.

In the present case of study consisting of drugs - paracetamol and oxyphenbutazone both of which carry phenolic groups, shifts in the wavelengths of absorption

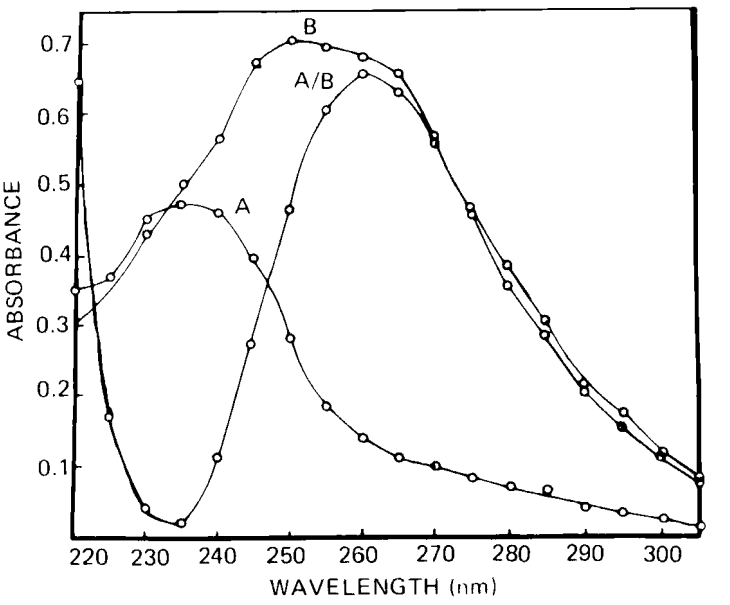

FIG 9 CONVENTIONAL SPECTRA SUPERIMPOSED WITH DIFFERENCE SPECTRUM

A = Conventional spectrum of oxyphenbutazone in acid

B = Conventional spectrum of oxyphenbutazone in Base

A/B = Difference spectrum (Acid vs Base)

and their intensity can be expected on making the solutions alkaline.

In the fig. No. 3,4,5and 6 the effects of pH 5, 7, 9 and 11 respectively have been presented.

In fig, No. 3 the absorption was almost linear except for the appearance of isosbestic point at 240 nm. In fig. No. 4 the maxima were observed at 240 nm for pure paracetamol, 255 and 265 nm for pure oxyphenbutazone and 245 nm for tandalgesic respectively. But these shifted to 255, 254, 235 and 244 nm respectively on acidification.

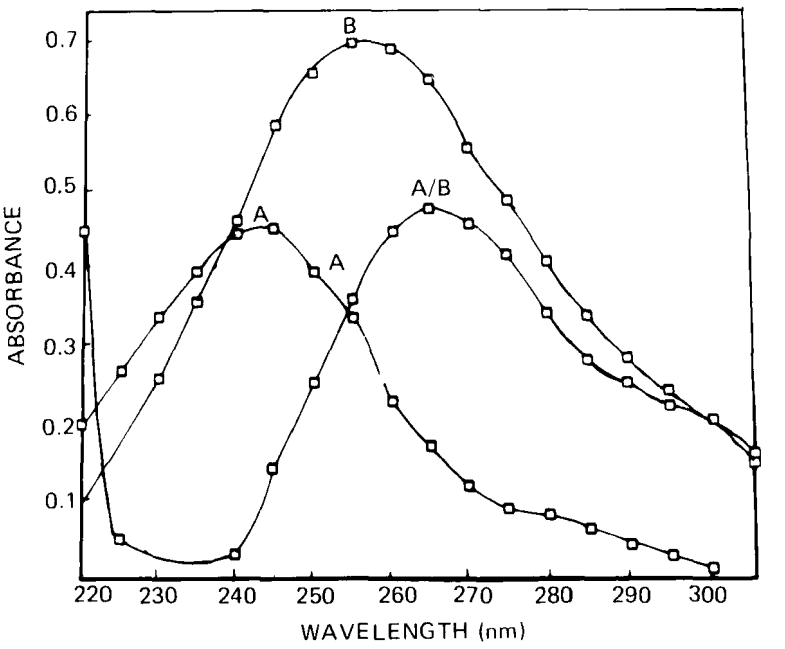

FIG.10 CONVENTIONAL SPECTRA SUPERIMPOSED WITH DIFFERENCE SPECTRUM

A = Tandalgesic in acid
B = Tandalgesic in base
A/B = Difference spectrum (Acid Vs Base)

In Fig. N. 5 the maxima observed in Fig. No. 4 were shifted to 245 nm and 258 nm for pure paracetamol and the mixture but maintained at 255 nm for pure oxyphenbutazone. All these effects indicated that the phenolic groups present in the drug solutions were affected by the change in pH to alkaline one and these effects were exhibited by the shifts in absorption mixima to longer wavelengths as the solution was made more alkaline as seen in Fig. No. 6. Further, the intensity of absorption increased accordingly.

Isosbestic points were also observed in Fig. Nos. 5 and 6 since the absorption changed smoothly from that of undissonated molecule to that of the ion with the change in pH. At these points both the wavelength and intensity were independent of pH. As such it was a further means of indentification of the constituents.

CALCULATIONS:

Calculation of concentration of paracetamol and oxyphenbutazone at wavelengths 235 nm 0.1N sodium hydroxide:

The method described in Beckett and Stenlake was adopted for the determination of concentrations as % w/v of paracetamol and oxyphenbutazone in Tandalgesic capsules[7]. The formulas used were as follows:

$$X = \frac{100(b_1 s_2 - b_2 s_1)}{(b_1 a_2 - b_2 a_1)}$$

$$Y = \frac{100(a_1 s_1 - a_2 a_1)}{(a_1 b_2 - a_2 b_1)}$$

a_1 and a = E(1%, 1 xm) value of paracetamol at wave lengths λ_1 and λ_2.

b_1 and b_2= E(1%, 1 cm) value of oxyphenbutazone at wave lengths λ_1 and λ_2.

s_1 and s_2= E(1%, 1 cm) value of mixture Tandalgesic solution at λ_1 and λ_2.

X = concentration of paracetamol

Y = concentration of oxyphenbutazone.

The results obtained are shown in table No. 1

Calculation of concentrations of paracetamol and oxyphenbutazone using data from their difference spectra:

The method of calculation described by Williams was used for the determination of concentrations of paracetamol and oxyphenbutazone as single entity in Tandalgesic capsules[7]. The use of this method is based on the fact that provided other materials present in the mixture are unaffected by the change in conditions their contributions to the total absorbance of each solution will be identical and their effect will be exactly cancelled.

Also, at the isosbestic points the absorption will be entirely due to the individual components and hence the concentration of each component at these points should be 100%. The formula used for the calculation is as follows:

$$\% \text{ Sample} = \frac{A_{(\text{Sample})} \times 100}{C_{(\text{Sample}} \times A\ (1\%, 1\text{cm Standard}}$$

Pure samples of paracetamol and oxyphenbutazone were used as the standard and the results obtained have been presented in table 2. It can be seen that the values obtained at 285 nm i.e. wave length at which isosbestic points appear is 100% in both the tables.

TABLE 1

Calculation of concentrations of paracetamol and Oxyphenbutazone at wave lengths 235nm in 0.1N NaOH

Wavelength and E(1% cm) Values	Number of Determinations*		
	1	2	3
λ_1	235	245	250
λ_2	240	250	255
a1	320	550	625
a2	440	625	675
b1	500	670	700
b2	560	700	690
s1	360	590	660
s2	470	660	700
X	81.86%	86.52%	83.87%
Y	19.61%	17.00%	19.39%
Total	101.47%	103.52%	103.26%

Mean of X = 84.08%
Standard Deviation = ±1.908
Mean of Y = 18.66%
Standard Deviation = ±1.395
Mean of Sample = 102.75%
Standard Deviation = ±0.91%

*In all five determinations were performed and similar data was obtained.

TABLE 2

Caculation of concentrations of paracetamol and oxyphenbutazone using data from their difference spectra

Wave length (nm)	Paracetamol		
	A (Sample)	A (1%, 1 cm	% Sample
275	0.42	390	107
280	0.34	320	106
285	0.28	280	100
295	0.22	240	91.66

Mean of Sample = 100.93%

Standard deviation = ±5.48%

Wave length (nm)	Oxyphenbutazone		
	A (Sample)	A (1%, 1cm)	% Sample
270	0.46	550	84
275	0.42	450	93.33
280	0.34	350	97.14
285	0.28	280	100

Mean of Sample = 93.62%

Standard deviation = ±6.04%

CONCLUSION

Difference spectroscopy has the special advantage of cancellation of interference and is very suitable for the analysis of drugs in combination though it is slightly elaborate than the direct dissolve and read method. The method is sensitive, accurate and the results show that Tandalgesic capsules satisfy the B.P. requirements for the concentration of paracetamol and oxyphenbutazone in the preparation.

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