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SIMULTANEOUS ESTIMATION OF NABUMETONE AND PARACETAMOL BY VIERODT'S METHOD IN COMBINED TABLET DOSAGE FORM

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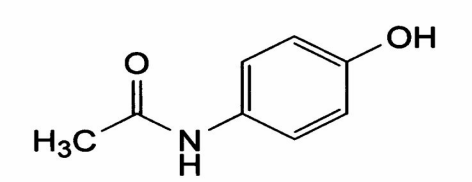
ABSTRACT: The simple, accurate, rapid and economical Vierodt's spectrophotometric method have been developed for the simultaneous determination of nabumetone (NAB) and paracetamol (PCM) in combined tablet dosage form. The method developed employs formation and solving simultaneous equations using 229.2 nm (λ max of nabumetone) and 248 (λ max of paracetamol) nm as two wavelengths for formation of equations. Both the drugs and their mixtures obey Beer-Lamberts law at selected wavelengths in the range 2 µg/ml to 8µg/ml for Nabumetone and for Paracetamol 2 µg/ml to 20µg/ml.

Keywords: Vierodt's spectrophotometric method, Nabumetone, Paracetamol.

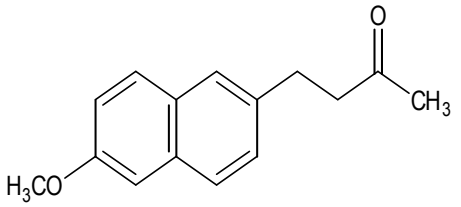
INTRODUCTION

Nabumetone, 4-(6-methoxynaphthalen-2-yl) butan-2-one, is a non-steroidal anti-inflammatory drug (NSAID) of naphtylalkanone class. The drug has proved to be effective in the treatment of rheumatoid arthritis, osteoarthritis and acute soft tissue injuries. Nabumetone is a prodrug which undergoes extensive first pass metabolism to 6-methoxy-2-naphthylacetic acid (6-MNA), the major circulating metabolite. 6-MNA is largely responsible for the therapeutic efficacy of nabumetone [1,2,3]. Paracetamol is chemically N-(4-hydroxyphenyl) acetamide. It is used mainly as analgesic and antipyretic [1,4]. The combination offers faster as well as prolonged relief from pain and inflammation. Literature survey reveals that many RP-HPLC methods [5-7] have been reported for the determination of Nabumetone and its metabolite in tablet dosage form & also in human plasma. Simultaneous estimation of Naproxen and Nabumetone was also reported by RP-HPLC in human plasma, human urine and in pharmaceutical. Paracetamol [8-15] individually and in combination with other drugs like Valdecoxib, Aceclofenac, Chlorpheniramine maleate, Dipyrone, Caffeine and Cetrizine in human plasma and pharmaceuticals were reported to be estimated by UV Spectroscopy and RP-HPLC. But no method is available for simultaneous estimation of Nabumetone and Paracetamol in tablet dosage form.

This paper describes simple, rapid, accurate, reproducible and economical method for the simultaneous determination of nabumetone and paracetamol in tablet dosage form.



A: Nabumetone



B: Paracetamol

Figure 1: Structure of Nabumetone and Paracetamol [2, 4]

EXPERIMENTAL

The reference standard of Nabumetone and Paracetamol were obtained as gift samples from Ipca laboratory and Torrent Pharmaceuticals, respectively. Methanol having analytical grade of Ranchem Laboratory. Tablet dosage form available was NILTIS-P manufactured by Ipca laboratory, each tablet containing 500mg of Nabumetone and 500mg of Paracetamol were used for the study. A SHIMAZDU UV-Visible double beam spectrophotometer with matched quartz cells (1cm), Model: 1700 was used.

Nabumetone (10 mg) and Paracetamol (10 mg) were accurately weighed and dissolved in methanol to give stock solution having concentration of 100 µg/ml. From these stock solutions, working standard solutions of drugs (5 µg/ml) was prepared by appropriate dilutions.

Working standard solutions were scanned in the entire UV range to determine the λ-max. [Figure 1] represents the overlain spectra of both the drugs. The λ-max of Nabumetone and Paracetamol were found to be 229.2 nm and 248.0 nm respectively. Standard solutions were prepared having concentrations 2, 4, 6, 8, µg/ml for Nabumetone and 2, 4, 6, 8, 10, 12, 16 and 20 µg/ml for Paracetamol using the working standard solution. For simultaneous study according to Vierodt's method, the absorbance values were recorded at the both wavelength 229.2 nm and at 248.0 nm for.

For determining the concentration of drugs by Vierodt's method, following equation was used. $C_X = (A_2\, a_{y1} - A_1\, a_{y2}) / (a_{X2}\, a_{y1} - a_{x1}\, a_{y2})$, $C_Y = (A_1\, a_{X2} - A_2\, a_{X1}) / (a_{X2}\, a_{y1} - a_{x1}\, a_{y2})$, where C_X and C_Y are concentration of nabumetone and paracetamol, respectively, a_{X1} and a_{X2} are the absorptivity values of nabumetone at 229.2 nm and at 248 nm, respectively. a_{y1} and a_{y2} are the absorptivity values of paracetamol at 229.2 nm and at 248 nm, respectively. A_1 and A_2 are the absorbances of the diluted mixture sample at 229.2 nm and 248 nm respectively. equations were used $Cx = 477.26\ A_2 - 1052.54\ A_1 / -3453165.8$ (1) and $Cy = 123.98\ A_1 - 333.07\ A_2 / -3453165.8$ (2), where, Molar absorptivities determined for nabumetone at 229.2 nm and 248 nm are 477.26 and 1052.54, respectively, and molar absorptivities determined for paracetamol at 248 nm and 229.2 nm are 123.98 and 333.07, respectively.

Drug concentrations of 5µg/ml (nabumetone), 5 µg/ml (paracetamol) and a mixture containing the same concentration of both the drugs were analyzed by Vierodt's method.

Twenty tablets containing 500 mg nabumetone and 500 mg paracetamol (Niltis-p, Ipca Labs Ltd), were weighed and finely powdered. A quantity of powder equivalent to 10 mg nabumetone or 10 mg Paracetamol was accurately weighed and transferred to a 100 ml volumetric flask, dissolved in 70 ml methanol, filtered through Whatman filter paper No. 1 and the volume was made up to 100 ml with the same solvent. Aliquots of this solution were diluted with methanol to get the working standards of 5 µg/ml Nabumetone (~ 5 µg/ml Paracetamol). Absorbance of the sample solutions at 229.2 nm and 248 nm and at 229.2 nm and 248 nm (overlain spectra) were measured and from the absorbance values, the concentration of drugs in the sample solution was determined by Vierodt's method and result of tablet formulation are shown in [Table 1].

RESULTS AND DISCUSSION

To study the linearity, accuracy and precision of the proposed method, the recovery studies were carried out by adding a known quantity of standard to the pre analyzed sample and the % recovery was calculated and shown in [Table 2]. The regression analysis of the calibration curves and the optical characteristics such as Beer's law limits, molar absorptivities and sandell's sensitivities are presented in [Table 3].

The proposed Vierodt's method is simple, accurate and economical for routine analysis of two drugs without prior separation. The amount found was in good agreement with the label claim of the formulation. The value of the standard deviation was satisfactorily low indicating the reproducibility and accuracy of the proposed method.

Table 1: Statistical analysis for Niltis- P Tablet

(For NAB 5 µg/ml; PCM 5 µg/ml respectively)

S. No.	Absorbance Data		Conc. Found in µg/ml		Labelled amount in tablet (mg/tablet)		Amount found in (mg/tablet)	
	229.2 nm	248.0 nm	NAB	PCM	NAB	PCM	NAB	PCM
1	1.897	0.5869	4.97	4.99			497.09	499.04
2	1.889	0.5794	4.95	4.92			495.69	492.08
3	1.896	0.5895	4.96	5.01	500	500	496.43	501.59
4	1.902	0.5791	4.99	4.91			499.70	491.33
5	1.893	0.5819	4.96	4.94			496.57	494.36
Mean			**4.97**	**4.95**			**497.10**	**495.68**

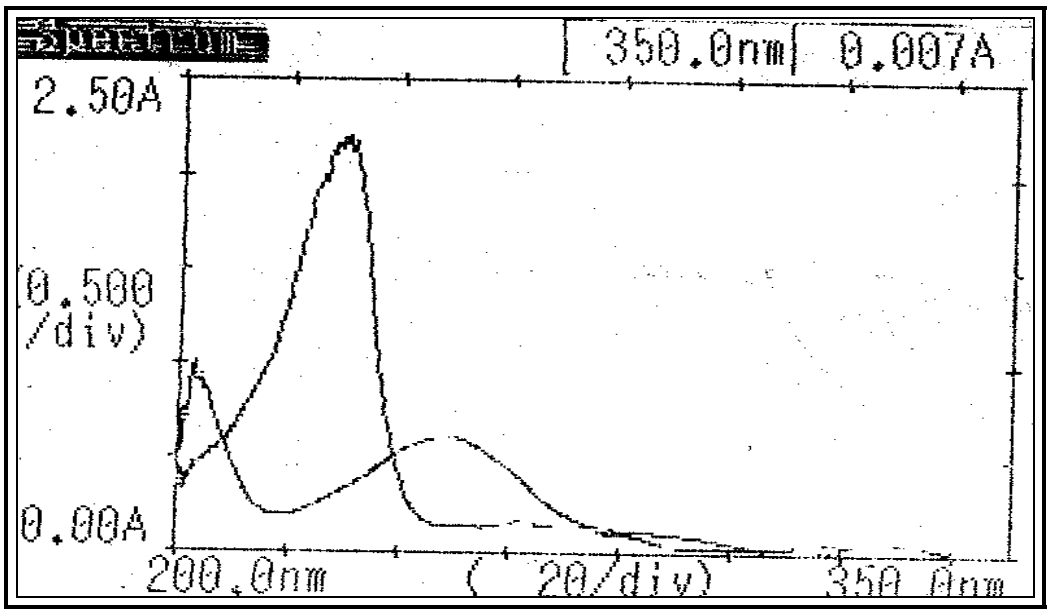
Table 2: Data showing Recovery study

Mix.	WL. (nm)	Conc. (ppm)	Std. Added (ppm)	Abs.	Amt. Found (mg)	% Recovery	Mean Recovery ± S.D.	% C.V.
1	229.2	2.07	2	1.507	3.956	98.90	**NAB**	**NAB**
	248.0	2.08	2	0.461	3.913	97.84	100.27 ± 0.890	0.889
	229.2	2.07	2	1.511	3.971	99.28		
	248.0	2.08	2	0.459	3.893	97.32		
	229.2	2.07	2	1.513	3.966	99.15	**PCM**	**PCM**
	248.0	2.08	2	0.467	3.969	99.24	100.09 ± 1.826	1.824
2	229.2	2.07	4	2.312	6.050	100.84		
	248.0	2.08	4	0.721	6.137	102.28		
	229.2	2.07	4	2.311	6.046	100.76		
	248.0	2.08	4	0.722	6.114	102.45		
	229.2	2.07	4	2.314	6.067	101.12		
	248.0	2.08	6	0.713	6.059	100.98		
3	229.2	2.07	6	3.079	8.073	100.91		
	248.0	2.08	6	0.949	8.065	100.81		
	229.2	2.07	6	3.071	8.044	100.55		
	248.0	2.08	6	0.952	8.097	101.21		
	229.2	2.07	6	3.082	8.076	100.95		
	248.0	2.08	6	0.951	8.083	101.04		

Table 3: Optical parameters & regression characteristic for Nabumetone and Paracetamol

Parameters	Nabumetone		Paracetamol	
	229.2 nm	248.0 nm	248.0 nm	229.2 nm
Beers's law limit (μg/ml)	2-8	2-8	2-20	2-20
Molar absorptivity (l mole^{-1}cm^{-1})	7.6 x 10^4	2.8 x 10^3	1.5 x 10^4	7.2 x 10^3
Sandell's sensitivity (mg/cm^2/.001absorbance unit)	0.0806	0.0029	0.0095	0.0209
Regression equation (y= a + bc)				
slope (b)	0.0374	0.0200	0.0926	0.0486
intercept (a)	- 0.0332	- 0.0303	0.0912	-0.0065
Correlation coefficient (r$^{2)}$	0.9991	0.9988	0.9993	0.999

Figure 1: Overlain spectra showing λ max. of Nabumetone (229.2 nm) and Paracetamol (248 nm)



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