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Simultaneous Estimation Of Paracetamol, Aceclofenac And Chlorzoxazone In Oral Dosage Form Using Spectrophotometric Method

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ABSTRACT

A simple, fast and precise multicomponent mode analysis method has been developed for the simultaneous determination of paracetamol, aceclofenac and chlorzoxazone in combined tablet dosage form. Shimadzu UV-1700 instrument was used and the λmax of paracetamol, aceclofenac and chlorzoxazone was found to be 247nm, 275nm and 282nm using methanol as a solvent and linearity lies between 1-12μg/ml for paracetamol, 1-28 μcg/ml for aceclofenac and 1-30μg/ml for chlorzoxazone at their respective wavelengths. Amount found for paracetamol, aceclofenac and chlorzoxazone were found to be 519.95, 100.80 and 498.57μg/tablet respectively. Percentage recovery range was found to be within 99.74-101.30% for paracetamol, 99.52-101.80% for aceclofenac, 99.23-101.35% for chlorzoxazone.

KEYWORDS

Paracetamol;
Aceclofenac;
Chlorzoxazone;
Multicomponent mode;
Tablets.

INTRODUCTION

Paracetamol[1-2,4-5] is a non-opiate, non-salicylate analgesic and antipyretic. It acts by inhibiting prostaglandin synthetase centrally. Specifically, it is a potent inhibitor of cyclo-oxygenase in the CNS.

Aceclofenac[2,4-5] is an orally administered phenyl acetic acid derivative with effects on a variety of inflammatory mediators. It is from the class of non-steroidal anti-inflammatory drug(NSAID). The mode of action of aceclofenac is largely based on the inhibition of prostaglandin synthesis. Acelofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins.

Chlorzoxazone[3-5] is 5-chloro-3H-benzooxazol-2-one, is inhibits antigen-induced bronchospasm and hence, is used to treat asthma and allergic rhinitis. Chlorzoxazone is also a centrally acting agent for

painful musculoskeletal conditions. It also has sedative property.

The earlier literature survey[10-15] reveals the analytical methods like UV, HPLC and HPTLC are available for determination of these drugs individually and other combinations in pharmaceuticals and biological preparations. There is no method has been reported for the estimation of paracetamol, aeclofenac and chlorzoxazone simultaneously. In the present investigation an attempt was made to develop a simple and economical spectrophotometric method with greater precision, accuracy and sensitivity for the simultaneous estimation of paracetamol, aceclofenac and chlorzoxazone in pure and tablet dosage forms.

EXPERIMENTAL

The solvent methanol used was analytical grade. Spectral absorbance measurements were made on Shimadzu UV-1700 with 10mm matched quartz cell. The commercially available tablets were procured from the local market.

Preparation of standard stock

Standard stock solutions of paracetamol, acelofenac and chlorzoxazone were prepared separately by dissolving about 50mg of each standard individually in methanol and made up to 100ml volume with methanol. Then, 5ml of three individual solutions diluted to 100ml with methanol, which were used for establishing the various parameters.

Preparation of mixed standard solution

The stock solution containing 100mcg/ml of paracetamol, aceclofenac and chlorzoxazone were prepared for mixed standard solution. Five dilutions were made from mixed stock solution containing varying concentrations ranging from 2µcg/ml, 4µcg /ml, 5µcg/ml, 10µcg/ml, 20µcg/ml of paraceta-mol, aceclofenac and chlorzoxazone. Mixed standards were then scanned over the range of 200-400nm in the multicomponent mode using three sampling points 247nm, 275nm and 282nm.

Preparation of sample solution

Twenty tablets were weighed accurately and grounded to fine powder. An accurately weighed quantity of powder equivalent to 50mg of paracetamol was transferred to 100ml volumetric flask. The contents in the flask was dissolved with minimum amount of methanol, sonicated for 15 minutes and then diluted to 100ml with methanol. The resultant was filtered with Whatmann filter no:4. The filterate was further diluted to made concentrations of 5µg/ml, 10µg/ml, 20µg/ml of paracetamol and chlorzoxazone and 1µcg/ml, 2µcg/ml, 4µcg/ml of aceclofenac respectively.

Assay

Mixed standards and sample solutions were scanned over the range of 200 nm-400nm in the multicomponent mode using three sampling points 247 nm, 275nm and 282nm. The concentration of each component was obtained by analysis of the spectral data of sample solution with reference to that of five mixed standard dilutions in the multicomponent mode of analysis.

Assay results

The quantitative estimation was carried out on marketed tablets and percentage purity values were obtained ranging from 102.28-104.8% for paracetamol, 99.81-101.38% for aceclofenac, and 99.02-100.59% for chlorzoxazone. The values were presented in TABLE 3.

Linearity and calibration

The stock solutions were suitably diluted with methanol to provide varying concentrations of 2µcg /ml, 4µcg/ml, 5µcg/ml, 10µcg/ml, 20µcg/ml of

TABLE 1: Optical characteristics and statistical data of the regression equation

Parameters	Paracetamol	Aceclofenac	Chlorzoxazone
Abs Maximum (nm)	247	275	282
Beer' Law limit (mcg/ml)	1-12	1-28	1-30
Correlation coefficient	0.9997	0.9994	0.9999
Regression equation	0.0754x-0.0105	0.034x +0.0057	0.0316x +0.0085
Intercept (A)	-0.0105	0.0057	0.0085
Slope (B)	0.0754	0.034	0.031

Full Paper

paracetamol, aceclofenac and chlorzoxazone which were scanned at their respective absorption maxima and absorbances were plotted against respective concentrations. The observed values were shown in TABLE 2. From the graph it was found that the Beer's law limit lies between 1-12µcg/ml for paracetamol, 1-28µcg/ml for aceclofenac an 1-30µcg/ml for chlorzoxazone. The regression analysis was carried out for calibration graph to find out correlation coefficient that was found out to be 0.9997 for paracetamol, 0.9994 for aceclofenac and 0.9999 for chlorzo-xazone and the values were depicted in TABLE 1.

Recovery studies

Conducting recovery studies satisfied accuracy. Recovery studies were carried out by mixing a known quantity of standard drug in three levels to preanalysed sample solution and the contents were reanalyzed by the proposed method. The values were presented in TABLE 4.

TABLE 2: Calibration data of paracetamol, aceclofenac and chlorzoxazone

Drug	Concentration (mcg/ml)	Absorption maxima		
		247nm	275nm	282nm
Paracetamol, Aceclofenac and Chlorzoxazone	2	0.139	0.080	0.061
	4	0.286	0.141	0.132
	5	0.360	0.176	0.519
	10	0.286	0.347	0.318
	20	0.139	0.685	0.637

Repeatability studies

Repeatability was given by inter-day and intra-day precision. Intra-day precision was determined by analyzing, the three different concentration of drug for three times in the same day. Inter-day precision was determined by analyzing the three different concentration of the drug for three days in a week. The values were presented in TABLE 5.

Method validation

As per ICH guidelines the method is validated and following parameters were evaluated.

Accuracy of the method was checked by recovery studies. Precision of the method was studied by inter-day and intra-day analysis of multiple samplings of homogenous sample and expressed as %RSD.

RESULTS AND DISCUSSION

The λmax of the paracetamol, aceclofenac and chlorzoxazone was found to be 247nm, 275nm and 282nm respectively. Paracetamol, aceclofenac and chlorzoxazone follows linearity in the concentration range of 1-12mcg/ml, 1-30mcg/ml for and 1-28 mcg/ml respectively. Marketed tablets were analyzed

TABLE 3: Statistical validation

Drug	Label claim (mg/tablet)	Amount estimated (mg/tablet)*	%Amount estimated*	% RSD	S.E.
Paracetamol	500	519.95	103.95	1.51	0.89
Aceclofenac	100	100.80	100.80	0.85	0.49
Chlorzoxazone	500	498.57	99.71	0.80	0.46

*** Mean of three determinations**
RSD-Relative Standard Deviation; SE-Standard Error

TABLE 4: Recovery data

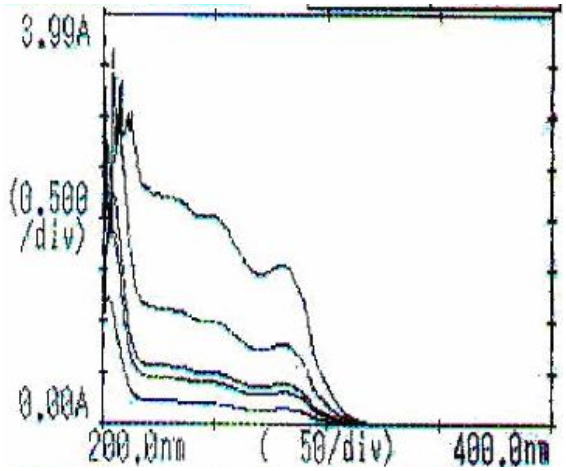
Drug	Amount Added(mcg)	Amount RecovereD*(mcg)	% Recovery*	Average Recovery(%)	% RSD
Paracetamol -500mg	5	4.98	99.74	100.33	0.84
	10	10.13	101.30		
	20	19.99	99.96		
Aceclofenac -100mg	5	4.97	99.52	100.79	1.15
	10	10.18	101.80		
	20	20.21	101.05		
Chlorzoxazone -500mg	5	5.04	100.8	100.46	1.09
	10	9.92	99.23		
	20	20.27	101.35		

Mean of three determinations at each level

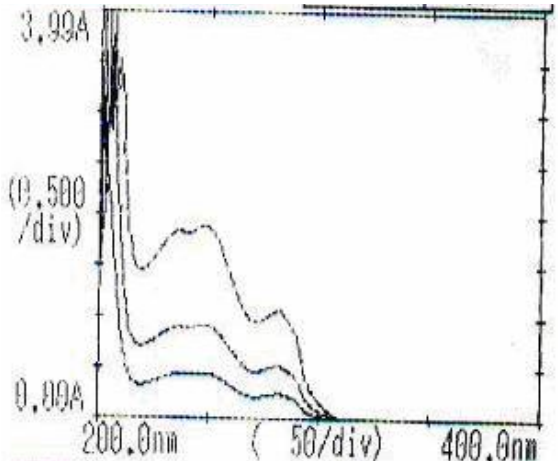
TABLE 5: Repeatability studies

Drug	Amount taken (Mcg/Ml)	Inter-day		Intra-day	
		Amount found* (µcg/Ml)	%Rsd	Amount found* (Mcg/Ml)	%Rsd
Paracetamol	5	5.1170	0.69	5.129	0.64
	10	10.489	0.36	10.224	0.48
	20	21.006	0.98	20.002	1.12
Aceclofenac	1	0.9987	0.85	1.024	0.72
	2	2.0259	0.63	2.002	0.66
	4	4.0578	0.89	4.112	0.82
Chlorzoxazone	5	4.8854	0.62	5.012	0.54
	10	9.9084	0.71	9.952	0.60
	20	20.331	0.92	20.114	0.93

***Mean of three determinations**



Overlain spectra of mixed standards by multicomponent mode



Spectra of sample formulation by multicomponent mode

and amount of drug were determined by proposed method; it was in good agreement with the label claim. The proposed method was validated as per the ICH guidelines[6]. The recovery of drug was determined at 50, 100 and 150% level. The recovery ranges from 99.74-101.30% for paracetamol, 99.52-101.80% for aceclofenac, and 99.23-101.35% for chlorzoxazone, which shows the accuracy of the method. Inter-day and intra-day precision of the assay was determined by analyzing the drug sample at three different concentrations. The intra-day and inter-day % RSD values were found to be less than 2 indicates hat the proposed method is precise.

These methods are limited to a spectrophotometer equipped with facilities like multicomponent mode of analysis.

CONCLUSION

It is concluded that the proposed methods can be successfully employed for routine simultaneous estimation of paracetamol, aceclofenac and chlorzoxazone in three-component tablet formulation.

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REFERENCES

[1] Indian Pharmacopoeia, **I**, 554-555, **(1996)**.
[2] British Pharmacopoeia, **I**, 38-40, **II**, 1417-1418, **(2003)**.
[3] United States Pharmacopoeia, **25**, (NF-20), 410-411.

Full Paper

[4] Martindale, 'The Complete Drug Reference', **32**, 1313.1, 12.1, and 72.2.
[5] The Merck Index, **13**, 10(48), 6(22), 379(2214).
[6] Text on Validation of Analytical Procedures, ICH Hormonised tripartite guidelines, adoption on 27 Oct **(1994)**.
[7] H.Willard; 'Instrumental Methods of Analysis', 7, CBs Publishers and Distributors, New Delhi, 580-600.
[8] A.H.Beckett, Eds., In; 'Practical Pharmaceutical Chemistry', 4, CBS Publishers and Distributors, New Delhi, 157-167, 276-296, **(2001)**.
[9] Current Index of Medical Specialities, 15, 16 and 40, **(2006)**.
[10] Hasan, M.Abdel-Elkawy, B.Elzeany, N.E.Wagieh; Farmaco, **58**, 91-9, **(2003)**.
[11] N.H.Zawilla, N.M.Abdul Azim Mohammad, El Kousy, S.M.El-Moghazy Aly; Journal of Pharmaceutical and Biomedical Analysis, **27**, 243-251, **(2002)**.
[12] Chang Kyun Jeong, Hye Suk Lee, Sung Jin Choi, Sang Beom Kim, Mi Hyun Lee, Geon II Ko, Dong Hwan Sohn; Journal of Pharmaceutical and Biomedical Analysis, **23**, 775-781, **(2002)**.
[13] K.V.Gowda, D.S.Rajan, U.Mandal, P.S.Selvan, W.D.Sam Solomon, A.Bose, A.K.Sarkar, T.K.Pal, T.K.Chattaraj; Drug Dev Ind Pharm., **32**, 1219-25, **(2006)**.
[14] B.Hinz, D.Auge, T.Rau, S.Rietbrock, K.Brune, U.Werner; Biomed Chromatogr., **17**, 268-75, **(2003)**.
[15] K.Rajanarayana, S.R.Mada, J.Vidyasagar, P.Kishore, D.R.Krishna; Pharmazie, **57**, 811-3, **(2002)**.