The results reveal the suitability of the proposed methods for estimation of pioglitazone.

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Spectrophotometric Determination of Tranexamic acid in Pharmaceutical Dosage Forms

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A simple, rapid, precise, highly specific and economical spectrophotometric method has been developed for the determination of tranexamic acid in its pharmaceutical dosage forms. The method is based on the reaction of the drug with sodium 1,2-napthoquinone-4-sulphonate forming reddish orange coloured chromogen with absorption maximum at 474 nm. The chromogen obeyed linearity in the concentration range of 10-70 μg/ml.

Tranexamic acid is (*trans*-4-aminomethyl cyclohexane carboxylic acid) is used in haemophilic patients to prevent haemorrhage and to reduce the need for replacement of blood factors[1,2]. Its most interesting use has been in the treatment of malignant ovarian tumors, to promote formation of a fibrin capsule to wall off and inhibit growth of the tumor[3]. The drug is official in BP[4]. A few spectrophotometric methods are reported in literature for the estimation of tranexamic acid in formulations[5-8]. In addition, HPLC method is reported for the estimation of tranexamic acid in formulation and in plasma and serum[9]. Other methods of estimation include gas-chromatography[10] and spectrofluorometric[11] determination in pharmaceutical dosage forms. In the present communication we report yet another very simple colorimetric estimation procedure.

A GBC Cintra 10 UV/vis spectrophotometer with 10 mm matched quartz cells was used in the present study. The chemicals used were of analytical grade. Sodium 1,2-napthoquinone-4-sulphonate (Merck, 0.5% w/v in distilled water, NQS) was prepared. The commercially available tablets (TX, Ochoa Labs New Delhi and T Clot, Tidal Labs Mumbai), capsules (Cymin, Wockhardt, Mumbai) and injections (Clip, FDC Ltd, Mumbai) of tranexamic acid were procured from a local pharmacy. Tranexamic acid (analyzed sample) as provided by Aristo Pharma Pvt. Ltd. was used as such without further purification.

A solution of tranexamic acid was prepared by dissolving 10 mg (accurately weighed) of the standard tranexamic acid in 10 ml of distilled water. This stock solution was further diluted to get a working standard solution of 100 μg/ml for colorimetric estimation. Aliquots (1, 2, 3.....7 ml) of working standard solution were transferred into a series of 10 ml volumetric flasks. To that 0.5 ml solution of NQS was added. The volumetric flasks were kept on boiling water bath for 30 min. The volumes were made up after cooling with distilled water. The absorbance of the reddish orange chromogen was measured at 474 nm against reagent blank, and the calibration curve plotted.

Average weight of twenty tablets was determined and

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these were then finely powdered (separately for each of the two formulations tested). The powdered amount equivalent to 100 mg (accurately weighed) was dissolved in 50 ml of distilled water and the insoluble excipients were separated by centrifugation at 3000 rpm for 10 min. The supernatant liquid was transferred to 100 ml volumetric flask quantitatively with distilled water and volume made up and drug content was determined from the calibration curve.

Average weight of twenty capsules was determined. The capsules were opened and contents mixed. The empty shells were weighed and average content of each capsule determined. The powdered amount equivalent to 100 mg (accurately weighed) was dissolved in 50 ml of distilled water. The insoluble excipients were separated by centrifugation at 3000 rpm for 10minutes. The supernatant liquid was transferred to 100 ml volumetric flask quantitatively with the help of distilled water and volume made up. The aliquots were made and diluted accordingly with distilled water and estimated using the calibration curve.

One milliliter of the injection solution (100 mg/ml) was transferred to 100 ml volumetric flask. The volume was made up with distilled water. After diluting the solution with distilled water the content of the drug was determined from the calibration curve.

In the present work, a colorimetric method has been developed for the estimation of tranexamic acid in pharmaceutical dosage forms. The method uses the reaction of aliphatic primary amine and NQS to give reddish orange coloured complex with λ_{max} at 474 nm, soluble in distilled water. The colour was found to be stable for 1 h.

Optimum operating conditions used in the procedures were established adopting variation of one variable at a time. The absorption maxima of the chromogen was found to be 474 nm. The Beer's law was found to obey in the concentration range of 10-70 µg/ml. The molar absorptivity was found to be 1.432×10^{-3} l/mol/cm and Sandell's sensitivity was found to be 0.1097 µg/cm^{2}x0.001. The regression equation gave a slope of 0.0066 with an intercept at 0.0653. The correlation co-efficient was found to be 0.9905=1.0000. The precision and accuracy of the method was established by measuring six replicate samples of the drug in commercial formulations. None of the excipients of the formulations interfered in the analysis of tranexamic acid by this proposed method. The results obtained by the proposed method were in good agreement with the labeled amounts. The accuracy of the proposed method was checked by performing recovery experiments using standard addition method. In this, known amount of pure drug was added to previously analyzed samples, and these samples were re-analyzed. The percentage recovery was close to 100% (Table 1). The proposed method is simple convenient, accurate, sensitive and reproducible. Hence this can be employed for routine analysis of tranexamic acid in formulations.

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TABLE 1: RESULTS OF ANALYSIS OF COMMERCIAL FORMULATIONS

Formulation	Amount labelled (5ml)	Amount found* mg/tab	SD*	% RSD*	SE*	't' cal.*	't' theo	% Recovery
Tablets TX	500	496.9	0.3091	0.0008	0.1951	1.9825	2.571	100.1
T-KLOT	500	492.8	0.7690	0.0195	0.3138	1.8478	2.571	100.9
Capsules CYMIN	500	495.8	0.3513	0.0088	0.1434	2.3711	2.571	100.3
Injection CLIP	500	497.8	0.6101	0.0153	0.2490	0.7228	2.571	100.0

*Average of six determinations. Theoretical 't' values are at 95% confidence level for (n-1) degrees of freedom. 't' (0.05,5)=2.571. SD is standard deviation, % RSD is percent relative standard deviation and SE is standard error.

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Spectrophotometric Methods for Determination of Clopidogrel in Tablets

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Two simple, rapid, precise, highly specific and economical spectrophotometric methods have been developed for the determination of clopidogrel bisulphate in its pharmaceutical dosage forms. Method A is based on the reduction of ferric ions to ferrous ions which produce blue colour with potassium ferricyanide with absorption maximum at 760 nm. The chromogen obeyed linearity over 18-32 μg/ml. Method B is based on the hydrolysis of ester linkage of drug into acid form by heating with sulphuric acid. This acid form of drug has absorption maximum at 217 nm. Beer's law is obeyed in the concentration range of 4-18 μg/ml.

Clopidogrel hydrogen sulphate [S(α)-(2-chlorophenyl)-6,7-dihydrothieno(3,2-c)pyridine-5(4H)-acetic acid methyl ester], is a new thienopyridine derivative chemically related to ticlopidine[1-2]. It prevents ischaemic stroke, myocardial infarction and vascular disease and is indicated for the reduction of athesclerotic events and demonstrated clinical efficacy superior to that of aspirin, in a large phase 3 trial[3-4]. Only HPLC methods are reported for estimation of clopidogrel bisulphate in formulation[5] and its metabolite in plasma and serum[6]. As no spectrophotometric method is reported in the literature, and more over as clopidogrel bisulphate as such gives no absorption maximum in workable UV range, therefore this work was undertaken.

A GBC Cintra 10 UV/Vis spectrophotometer with 10 mm matched quartz cells was used for experiments. The chemicals used were of analytical grade. Ammonium ferric sulphate (CDH, Mumbai, 0.17 M in 0.1 N H2SO4), potassium ferricyanide (CDH, Mumbai, 0.17 M in distilled water) and sulphuric acid (Qualigens, Mumbai, 1 N) were used. The commercially available tablets of clopidogrel bisulphate used for estimation were procured from a local pharmacy store. Clopidogrel bisulphate (analysed sample) as provided by Dr. Reddy's Laboratories was used as such without further purification.

A solution of clopidogrel bisulphate was prepared by dissolving 10 mg (accurately weighed) of standard clopidogrel bisulphate in 10 ml of methanol. This stock solution was further suitably diluted to get a working standard solution (A) of 100 μg/ml for colorimetric method. (Method A). Similarly working standard solution (B) was separately prepared by heating appropriate volume of stock solution with 1 ml H_2SO_4.(1 N) for 30 min (Method B).

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