ABSTRACT
A simple, sensitive, rapid, economic and accurate first order derivative spectrophotometric method has been developed for estimation of Telmisartan (TMS), Metoprolol succinate (MPS) and Chlorthalidone (CTD) in bulk and in tablet dosage form. The wavelengths selected for quantitation were 315 nm for TMS (zero cross for Telmisartan and Metoprolol succinate). Beer’s law was obeyed in the concentration range of 16-80 μg/ml, 9.5- 47.5 μg/ml and 2-12.4 μg/ml for TMS, MPS and CTD. The methods were validated as per ICH guidelines. Statistical analysis proved that the methods were accurate, precise, and reproducible for analysis of TMS, MPS and CTD in tablet dosage form. The wide linearity range, sensitivity, accuracy and simple procedure imply that the proposed technique demonstrated to be appropriate for routine analysis and quality control assay of tablet.

KEYWORDS: Telmisartan, Metoprolol succinate, Chlorthalidone, First Order Derivative Spectroscopy.

INTRODUCTION
Telmisartan chemically known as 2-[4-[[4-methyl-6-[(1-methylbenzimidazol-2-yl) propyl benzimidazol-1-yl][methyl] phenyl][benzoic acid. Telmisartan is a benzimidazole derivative and a non-peptide angiotensin II receptor antagonist with antihypertensive property. Telmisartan selectively antagonizes angiotensin II binding to the AT1 subtype receptor, located in vascular smooth muscle and adrenal gland. The antagonism results in vasodilation and inhibits the angiotensin II-mediated aldosterone production, which in turn leading to a decrease in sodium and water as well as an increase in potassium excretion leading to a subsequent reduction in blood pressure.

Metoprolol succinate is chemically called as (±)-1-(isopropylamino)-3-[p-(2-methoxyethyl) phenoxo]-2-propanol succinate. Metoprolol Succinate is the succinate salt form of metoprolol, a cardioselective competitive beta-1 adrenergic receptor antagonist with antihypertensive properties and devoid of intrinsic sympathomimetic activity. Metoprolol succinate antagonizes beta 1-adrenergic receptors in the myocardium, thereby reducing the rate and force of myocardial contraction, and consequently a diminished cardiac output. This agent may also reduce the secretion of renin with subsequent reduction in levels of angiotensin II thus decreasing sympathetic activation, including vasoconstriction, aldosterone secretion. Chlorthalidone is chemically called as racemic mixture of 2-chloro-5 (1-hydroxy-3-oxo-1-isooindolinyl) benzene-sulfonamide.

MATERIALS AND METHODS
Instrumentation
The instrument used in the present study was Shimadzu double beam UV/Visiblespectrophotometer (Model UV-1700) with spectral band width of 1 nm. All weighing was done on electronic balance (Model Shimadzu AUX-220).

Reagents and chemicals
Analytically pure sample of TDF, LAM and EFV was kindly supplied by Madras pharmaceuticals. The pharmaceutical dosage form used in this study was a MET XL 3D tablets manufactured by Ajanta pharma Ltd (Chennai, India) labeled to contain 40 mg of Telmisartan,23.75 mg of Metoprolol succinate and 6.25

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mg of Chlorthalidone I.P and methanol used as a solvent.

**Preparation of standard stock solution**
Standard stock solution of Telmisartan were prepared by dissolving 40 mg was weighed and transferred into 25 ml volumetric flask, dissolved in methanol and made up to the volume with methanol to get a concentration of 1000μg/ml. Standard stock solution of Metoprolol succinate were prepared by dissolving 23.75 mg was weighed and transferred into 25 ml volumetric flask, dissolved in methanol and made up to the volume with methanol to get a concentration of 1000μg/ml. Standard stock solution of Chlorthalidone were prepared by dissolving 6.25 mg was weighed and transferred into 25 ml volumetric flask, dissolved in methanol and made up to the volume with methanol to get a concentration of 1000μg/ml.

**Study of spectra and selection of wavelength**
In this method, solutions of TMS, MPS and CTD (10μg/ml), each were prepared separately by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. The absorption spectra thus obtained were derivatized for first order. From the overlay spectra of these drugs, wavelength selected for quantification were 351 nm for TMS (zero cross for MPS and CTD shows absorbance), to estimate the amount of Telmisartan at 351 nm the absorbance corrected for interference method was applied. The absorbance of Metoprolol succinate was corrected for interference at 231 nm. Thus, the amount of Metoprolol succinate was found out, 231 nm for MPS (No zero cross for Telmisartan and Chlorthalidone) and 250 nm for CTD (zero cross for Telmisartan and Metoprolol succinate and). The overlay first order derivative spectra of TMS, MPS and CTD is shown in Fig.No.1.

**Analysis of Tablet Formulation**
For the estimation of drugs in the commercial formulation, twenty tablets were weighed accurately. The average weight was calculated and then crushed to obtain fine powder. A quantity of tablet powder equivalent to about 40 mg of tablet was transferred to 25 ml volumetric flask and make up with methanol and sonicated for 15min, volume was then made up to the mark with methanol. The resulting solution was mixed and filtered through Whatmann filter paper no 41 and filtrate was appropriately diluted to get approximate concentration of 32μg/ml of TMS, 19μg/ml of MPS and 4.96μg/ml of CTD, the concentration of TMS, MTS and CTD were determined by measuring absorbance of sample solution in first order derivative mode at 351 nm, 231 nm and 250 nm. Concentration of TMS, MTS and CTD in the diluted solution was obtained from calibration curves. Amount of in mg/tab was then TMS, MTS and CTD calculated, by multiplying the concentration obtained with dilution factor. Results of tablet analysis are shown in Table No.1.

**Validation**
The proposed method was validated as per ICH guidelines.

**Accuracy**
To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels (50%, 100% &150%). The results of recovery studies, expressed as percent recovery, were satisfactory and are presented in Table2.

**Precision**
The reproducibility of this method was determined by analyzing tablets at different time intervals on three different days (Inter-day assay precision). Inter-day assay precision %RSD was found to be 0.3807 (for TMS), 0.4801 (for MPS) and 1.4349 (for CTD). The recovery studies was shown in Table2.

**RESULTS AND DISCUSSION**
The method discussed in the present work provide a convenient and reliable way for quantitative determination of TMS, MPS and CTD in combined dose tablet formulation. The quantitative determination was carried out at wavelength range and 315 nm (for TMS), 231nm (for MPS) and 250 nm (for CTD). Linearity for TMS was observed in the concentration range of 16-80 μg/ml, MPS was observed in the concentration range of 9.5-47.5 μg/ml, and CTD was found to be linear in the concentration range of 2.48-12.4 μg/ml. Percent label claim for TMS, MPS and CTD in tablet analysis was found in the range of 99.08 to 99.69 %. Percent recovery for TMS, MPS and CTD was found in the range of 99.81% to 91.99 % with standard deviation well below 2 indicating accuracy of the method.
Overlay Spectrum of TMS, MPS, CTD.

Table 1. Results of analysis of tablet.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Label claim</th>
<th>% Label claim (mean ± S.D)</th>
<th>% RSD</th>
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<tbody>
<tr>
<td>TMS</td>
<td>40mg</td>
<td>99.6950±0.3795</td>
<td>0.3807</td>
</tr>
<tr>
<td>MPS</td>
<td>23.75mg</td>
<td>99.6415±0.4801</td>
<td>0.4818</td>
</tr>
<tr>
<td>CTD</td>
<td>6.25mg</td>
<td>99.0833±1.4217</td>
<td>1.4349</td>
</tr>
</tbody>
</table>

Table 2. Recovery studies.

<table>
<thead>
<tr>
<th>Parameter</th>
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<th>MPS</th>
<th>CTD</th>
</tr>
</thead>
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<tr>
<td>Recovery</td>
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<td></td>
</tr>
<tr>
<td>50%</td>
<td>99.5063</td>
<td>99.9333</td>
<td>99.4252</td>
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<td>100.0677</td>
<td>99.9244</td>
<td>100.0249</td>
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<tr>
<td>150%</td>
<td>100.0626</td>
<td>99.9002</td>
<td>99.9999</td>
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<tr>
<td>Mean</td>
<td>99.8668</td>
<td>99.9199</td>
<td>99.8163</td>
</tr>
<tr>
<td>% RSD</td>
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<tr>
<td>50%</td>
<td>0.6246</td>
<td>0.1523</td>
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</tr>
<tr>
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<td>0.1997</td>
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<tr>
<td>150%</td>
<td>0.1670</td>
<td>0.2500</td>
<td>0.6587</td>
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</table>

CONCLUSION
The validated First order derivative method employed here proved to be simple, economical, rapid, precise and accurate. Thus these can be used for routine estimation of TDF, LAM and EFV in tablet dosage form instead of processing and analyzing each drug separately.

REFERENCE