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Article

Analytical Applications of Iron(III) and Ortho Phenanthroline In the Determination of Eletriptan Hydrobromide

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ABSTRACT

Two simple and sensitive extractive visible spectrophotometric methods (A and B) were developed for the assay of eletriptan hydro bromide (EHB) in pure and pharmaceutical formulations based on oxidation of the EHB. When treated with known excess of Fe(III), EHB undergoes oxidation, giving products of oxidation inclusive of reduced form of oxidant, Fe (II) from Fe(III) besides unreacted oxidant and estimating EHB colorimetrically, which is equivalent to either reacted oxidant or reduced form of oxidant formed. The reduced form of Fe (II) has a tendency to give a colored complex on treatment with either [Fe (CN)6]-3 in method-A, or with O-Phenanthroline(O-Phen) in method-B. The colored products exhibit absorption λ_{max} at 767 nm and 480 nm, Beer-Lambert limits are in the concentration ranges (4-24) µg/ml, (4–28) µg/ml, and correlation coefficients are 0.9999 and 0.9985. The Sandell's sensitivities are 1.561 × 10–3, 2.462 × 10–3 (1 mole cm^{-1}) and molar absorptivity values are 2.9688 × 105, 1.8827 × 105 (µg cm^{-2}), for methods A and B, respectively The proposed methods are applied to commercial available formulations and the results are statistically compared with those obtained by the ultraviolet reference method and validated by recovery studies. These methods offer the advantages of rapidity, simplicity, and sensitivity and low cost without the need for expensive instrumentation and reagents.

Key words: Ferric Iron, Oxidation, O-Phen, Amino group, Regression analysis.

1. INTRODUCTION

Eletriptan hydrobromide (EHB) is a second generation triptan drug and it intended for treatment of migraine headache [1,2]. It is used as an abortive medication, and blocks migraine attack which is already in progress. EHB chemically known to be 3-[(-1-methylpyrrolidin-2-yl) methyl]-5-(2-phenylsulfonylethyl)-1H-indole [Figure 1]. It is selective at 5-HT1B/1D receptor agonist; thought to be due to the agonist effects at the 5-HT1B/1D receptors located on intracranial blood vessels (including arteriovenous anastomoses) and sensory nerves of the trigeminal system that results in cranial vessel constriction and inhibition of pro inflammatory neuropeptide release[3].

Literature survey reveals few chromatographic methods to determine the EHB by high-performance liquid chromatography (HPLC) [4-10], thin-layer chromatography (TLC) [11] and liquid chromatography coupled with tandem mass spectroscopy [12], simultaneous determination of EHB with other anti-migraine drugs [13,14], determination of EHB in plasma using forced degradation studies, development of stability indicating method [15], spectrophotometric method [16,17], determination of process related impurities in Eletriptan using UPLC method [18], TLC-Densitometric method [19], fluorimetric and colorimetric method [20][243], capillary electrophoresis [21], and thermal diffractometric studies [22,23]. The authors have also found some ultraviolet (UV) methods [24-26], reversed-phase-HPLC [27,28] methods and some applications of the reagents chosen for the determination of EHB [29,30].

The analytical useful functional groups in EHB have not been fully exploited for designing suitable visible spectrophotometric methods and so still offer a scope to develop more visible spectrophotometric methods with better sensitivity, precision, and accuracy. The author has made some attempts in this direction and succeeded two methods for determination and validation of EHB in pharmaceutical dosage forms.

2. EXPERIMENTAL

2.1. Instruments Used

A Shimadzu UV-Visible spectrophotometer 1801 with 1 cm matched quartz cells was used for all spectral and absorbance measurements. A Systronics digital pH meter 361 was used for pH measurements.

2.2. Preparation of Standard Drug Solution

The stock solution (1 mg/ml) of EHB was prepared by dissolving 100 mg of it in 100 ml of Millipore-distilled water. A portion of this stock solution was diluted stepwise with the distilled water to obtain the working standard EHB solution of 24 µg/ml for the proposed methods M_1, M_4, M_5 ,M_6, and M_9, respectively.

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2.3. Procedure of Assay of EHB in Formulations

An accurately weighed amount of formulation (tablets) equivalent to 100 mg of drug was dissolved in 20 ml of distilled water, shaken well, and filtered. The filtrate was further diluted to 100 ml with distilled water to get 1 mg/ml solution of drug in formulations.

1 ml of this solution was furthered diluted to 25 ml to get 40 µg/ml solutions. The absorbance of the solution was determined λ_{max} 223 nm (Figure 2). The quantity of the drug was computed from the Beer's law plot (Figure 3) of the standard drug in distilled water.

2.4. Recommended Procedures

After systematic and detailed study of the various parameters involved, as described under results and discussion in this chapter, the following procedures were recommended for the determination of EHB in bulk samples.

- Method-A

Into a series of 25 ml calibrated tubes, aliquots of standard EHB solution (0.1–0.6 ml and 24 µg/ml) were transferred and 1 ml of 3.32×10^{-3}M $FeCl_3$ solution was added. The tubes were stoppered immediately and shaken well for 5 min. Then 2.5 ml of 3.02×10^{-3} M potassium Ferri cyanide solution was added into each tube and was closed with lids immediately. After 5 min, 1 ml of 1.0N HCl was added and final volume was made up to 25 ml with distilled water. The absorbance of the solution in each tube was measured immediately at λ_{max} 767 nm (Figure 4) against the similar reagent blank. The amount of EHB was calculated from its calibration graph (Figure 5).

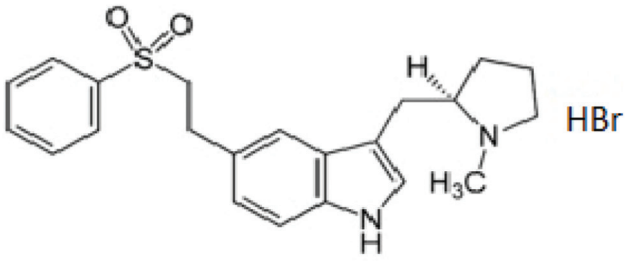
- Method-B

Into a series of 25 ml calibrated tubes, aliquots of standard EHB solution (0.1–0.6 ml and 24 µg/ml) were transferred and then 1.5 ml of Fe(III) and 2.0 ml O-Phen were added successively. The total volume in each flask was brought to 10.0 ml with distilled water and heated for 30 min in a boiling water bath. After cooling at room temperature, 2.0 ml of ortho-phosphoric acid was added, the volume in each flask was made up to the mark with distilled water. The absorbance of the colored complex solution was measured after 5 min at λ_{max} 480 nm (Figure 6). Against a reagent blank prepared similarly. The amount of the EHB was calculated from its calibration graph (Figure 7).

Chemistry of the colored species in the present investigation:

EHB possesses different functional moieties such as tertiary amino group and indole of varied reactivity. The reducing property due to the presence of functional moieties (one or more) vulnerable to oxidation selectively with excess oxidizing agents Fe(III) in the methods A and B and the color development of unreacted oxidant with the appropriate reagent under experimental conditions is the basis for its determination.

When treated with known excess of Fe(III), EHB undergoes oxidation, giving products of oxidation inclusive of reduced form of oxidant, Fe (II) from Fe(III) besides unreacted oxidant. It is possible to estimate the drug content colorimetrically, which is equivalent to either reacted oxidant or reduced form of oxidant formed. The reduced form of Fe (II) has a tendency to give a colored complex on treatment with either $[Fe(CN)_6]^{-3}$ in method-A, or with O-phen in method-B. The reactions are described in the Schemes 1 and 2.



AQ5 **Figure 1:** Structure of eletriptan hydrobromide.

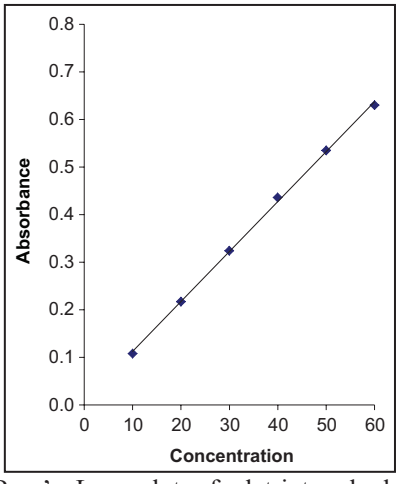


Figure 3: Beer's Law plot of eletriptan hydrobromide in methanol (UV reference method).

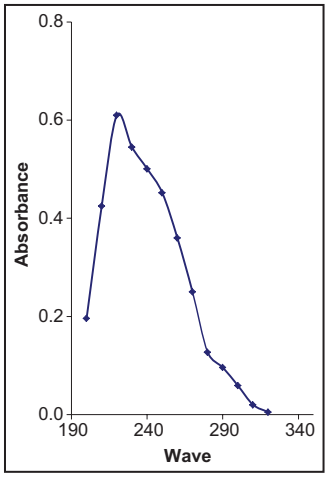


Figure 2: Absorption spectra of eletriptan hydrobromide in methanol (UV Reference method).

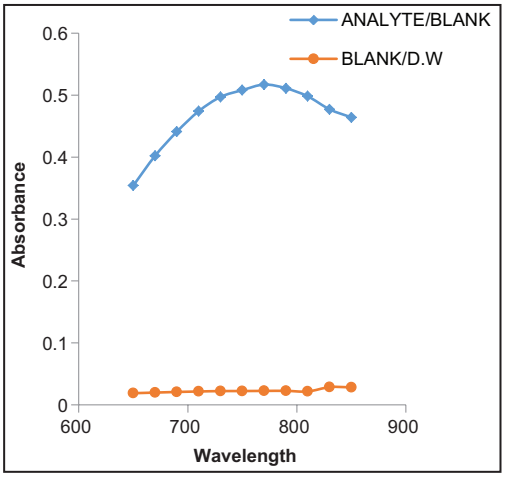


Figure 4: Absorption spectra of eletriptan hydrobromide: FeIII/ $K_3[Fe(CN)_6]$.

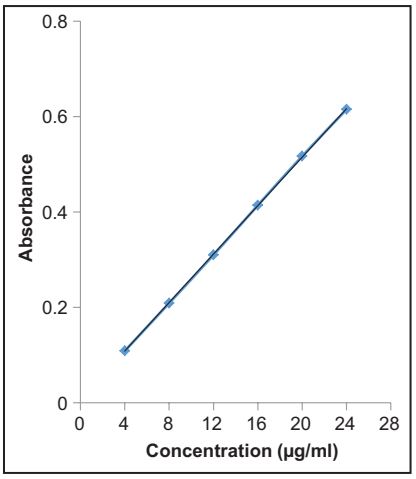


Figure 5: Beer's plot of eletriptan hydrobromide: FeIII/ $K_3[Fe(CN)_6]$.

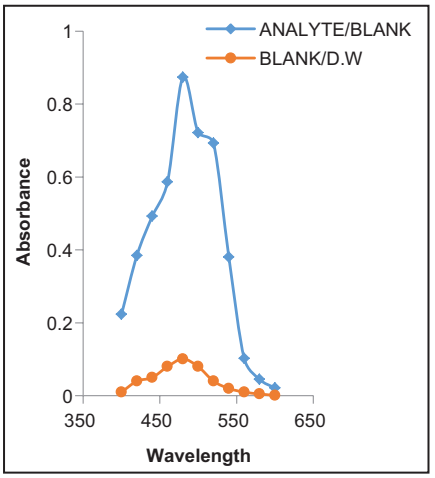


Figure 6: Absorption spectra of eletriptan hydrobromide: FeIII/ O-Phen.

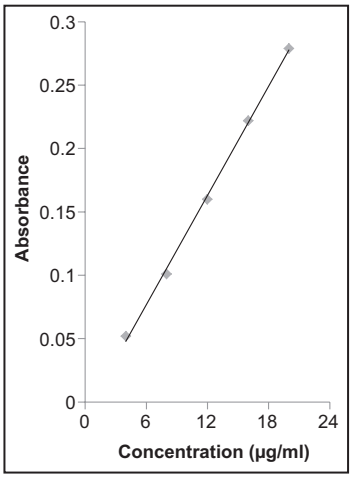


Figure 7: Beer's plot of eletriptan hydrobromide: FeIII/O-Phen.

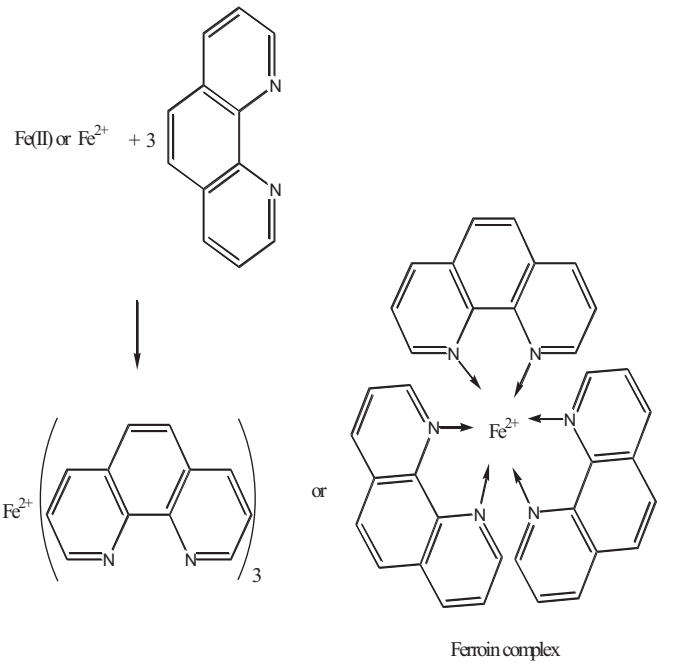
3. RESULTS AND DISCUSSION

Optimum operating conditions used in the procedure were established adopting variation of one variable at a time method. The effect of various parameters such as was studied. Effect of volume of Iron(III) required for oxidation, Potassium Ferri cyanide on color development,

EHB + Fe(III) ⟶ oxidation product + Fe II + unreacted Fe(III)

$3\ Fe^{2+} + 2[Fe(CN)_6]^{-3} \longrightarrow Fe_3[Fe(CN)_6]_2$

Scheme 1



Scheme 2

Table 1: Optical and regression characteristics, precision, and accuracy of the proposed methods for eletriptan hydrobromide.

S. No.	Parameter	Method-A	Method-B
1	Wave length λ_{max} (nm)	767	480
2	Beer's law limits (µg ml^{-1})	4-24	4-28
3	Detection limits (µg ml^{-1})	0.6021	2.1373
4	Molar absorptivity (1 mole cm^{-1})	2.9688×10^{5}	1.8827×105
5	Sandell's sensitivity (µgcm^{-2}/0.001 absorbance unit)	1.561×10^{-3}	2.462×10-3
6	Regression equation (Y=a + bC) Slope (b)	0.0254	0.0144
7	Standard deviation of slope (S_b)	1.0351×10^{-4}	6.5813×10^{-4}
8	Intercept (a)	0.0065	−0.0097
9	Standard deviation of intercept (S_a)	1.6124×10^{-3}	1.0261×10^{-1}
10	Standard error of estimation (S_e)	1.7320×10^{-3}	1.1022×10^{-2}
11	Correlation coefficient (r^2)	0.9999	0.9985
12	Relative standard deviation (%)*	1.0743	2.2422
13	% Range of error (confidence limits) 0.05 level*	1.1276	2.3534
14	% Range of error (confidence limits) 0.01 level	1.7683	3.6908
15	% Error in bulk samples**	0.412	0.511

Table 2: Assay and recovery of eletriptan hydrobromide in pharmaceutical formulations.

Sample	Amount taken (mg)	Amount found by proposed methods		Reference Methods	Percentage recovery by proposed methods	
		Method-A	Method-B		Method-A	Method-B
Tablet I	40	39.85±0.017 F=1.12 t=0.78	39.75±0.021 F=1.72 t=1.91	39.92±0.016	99.800±0.284	99.812±0.044
Tablet II	40	39.75±0.025 F=1.25 t=0.48	39.80±0.024 F=1.36 t=0.54	39.88±0.028	99.772±0.068	99.749±0.110

*: Average±standard deviation of six determinations; the t- and F- values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limit t=2.57, F=5.05. **: After adding two different amounts of the pure labeled to the pharmaceutical formulations, each value is an average of three determinations

temperature, volume of hydrochloric acid, order of addition of reagents, and nature of solvent for final dilution were studied for method-A. Similarly volume of O-Phen, Fe(III) solution on color development, heating time, volume of phosphoric acid, and order of addition of reagents on color development were studied for method-B.

The optical characteristics such as Beer's law limit, Sandell's sensitivity, molar absorptivity, percent relative standard deviation, calculated from the six measurements, regression characteristics such as standard deviation of slope (S_b), standard deviation of intercept (Sa), standard error of estimation (S_e), and % range of error (0.05 and 0.01 confidence limits) were calculated and the results are summarized in Table 1. Commercial formulations containing EHB were successfully analyzed by the proposed methods. The values obtained by the proposed and reference methods for formulations were compared statistically by the *t*-test and F-test and found not to differ significantly. As an additional demonstration of accuracy, recovery experiments were performed by adding a fixed amount of the drug to the pure analyzed formulations at three different concentration levels. These results are summarized in Table 2.

4. CONCLUSION

The results presented above indicate that the proposed methods have good sensitivity, selectivity, precision, and accuracy. Results of analysis in bulk form and in formulations reveal that the proposed methods are suitable for the estimation of EHB, as impurities and excipients present in them cause no interference virtually.

5. REFERENCES

1. L. R. Snyder, J. J. Kirkland, (2009) ***Introduction to Modern Liquid Chromatography***, 2nd ed. New York: John Wiley and Sons, Inc., p.292.
2. S. C. Sweetman, (2005) Martindale, the Complete Drug Reference. 34th ed. London, Chicago: Pharmaceutical Press.
3. Available from: http://www.en.wikipedia.org/wiki/eletriptan. [Last accessed on 2019 Nov 04].
4. J. E. Macor, M. J. Wythes, (1996) ***Indole Derivates, U.S. Patent No. 5545644***.
5. D. Suneetha, A. L. Rao, (2010), RP-HPLC method for the estimation of Eletriptan in pharmaceutical dosage forms, ***International Journal of Chemical, Environmental and Pharmaceutical Research***, **1**: 95-99.
6. G. R. R. Raju, R. V. K. Vegesna, G. S. Prasad, (2013), Method development and estimation of eletriptan hydrbromide in tablet dosage form by RP-HPLC, ***Indo American Journal Pharmaceutical Research***,**3**: 7299-7306.
7. D. S. Naik, K. Ramadevi, D. Bhagawan, (2013), Method development and validation of eletriptan hydrobromide pharmaceutical dosage form by RP-HPLC, ***International Journal of Engineering Research and Applications***, **3**: 1-5.
8. S. S. Chandra, T. Priyanka, N. Sowjanya, A. Ajitha, U. M. Rao, (2014), A new method development and validation for estimation of eletriptan by using RP-HPLC, ***International Journal of Pharmacy and Analytical Research***, **4**: 344-347.
9. C. Babu, B. S. Rao, K. V. N. Suresh Reddy, B. Naganjaneyulu, (2013) Development and validation of HPLC assay method for the acamprosate ca in commercial tablets, ***Indian Journal of Advances in Chemical Science***, **2**: 46-49.
10. D. R. Rao, V. Sreenivasulu, B. U. Maheswari, M. V. Narayana, N. S. Reddy, A. Krishnaiah, (2015) Method development and validation for quantitative determination of para chloroaniline, an impurity, in efavirenz active pharmaceutical ingredient by liquid chromatography-electrospray ionization-mass spectrometry/mass spectrometry, ***Indian Journal of Advances in Chemical Science***, **3**: 267-273.
11. R. I. El-Bagary, N. G. Mohammed and H. A. Nasr, (2012), Two chromatographic methods for the determination of some anti-migraine drugs, ***Analytical Chemistry Insights***, 7: 13-21.
12. V. S. Ponnuru, B. R. Challa, R. Nadendla, (2011), Quantitative analysis of eletriptan in human plasma by HPLC-MS/MS and its application to pharmacokinetic study, ***Analytical and Bioanalytical Chemistry***, **401**: 2539-2548.
13. N. U. Rani, R. S. Rao, K. Saraswathi, T. E. G. Murthy, (2012), RP-HPLC method for simultaneous estimation of avitriptan and eletriptan in pharmaceutical dosage forms. ***Novus International Journal of Analytical Innovatons***, **1**: 19-29.
14. M. Zrcevic, B. Jocic, S. Agatonovic-Kustrin, L. Zvanoic, (2006), Validation of an HPLC method for the simultaneous determination of eletriptan and UK 120.413, ***Journal of the Serbian Chemical Society***, **71**: 1195-1205.
15. B. Jocia, M. Zecevia, L. Zivanovia, A. Protia, M. Jadranin, (2009), Study of forced degradation behavior of eletriptan hydrobromide by LC and LC-MS and development of stability-indicating method, ***Journal of Pharmaceutical and Biomedical Analysis***, **50**: 622-629.
16. P. Sunitha, C. H. Jhansirani, B. Kavitha, N. Sirisha, A. Pavan, (2012), Method development and validaton of eletriptan hydrobromide tablets by UV-Visible spectrophotometric method, ***International Journal of Pharmaceutical, Chemical and Biological Sciences***, **2**: 427-430.
17. K. G. Swamy, J. M. R. Kumar, J. V. L. Sheshagiri Rao, U. A. Kumar, E. V. Snehalatha, (2011), Spectrophotometric method for the estimation of eletriptan hydrobromide in pure and tablet dosage forms, ***International Journal of Chemical and Analytical***

Science, **2**: 123-125.
18. N. Balaji, V. R. Sivaraman, P. Neeraja, (2013), A validated UPLC method for the determination of process related impurities in Anti-migraine bulk drug, ***Journal of Applied Chemistry***, **3**: 20-28.
19. A. Suneetha, R. N. Pradeep, A. Pratyusha, (2014), TLC-Densitometric method for estimation of eletriptan hydrobromide in bulk and pharmaceutical dosage forms, ***International Journal of Pharmaceutical and Chemical Sciences***, **3**: 66-70.
20. R. I. El-Bagary, N. G. Mohammed, H. A. Nasr, (2011), Fluorimetric and colorimetric methods for the determination of some antimigraine drugs, ***Journal of Chemical and Pharmaceutical Research***, **3**: 340-314.
21. W. J. David, S. Kenneth, L. E. Craig, (2001), PH-Mediated field-amplified sample stacking of pharmaceutical cations in high-ionic strength samples, ***International Journal of Research in Pharmaceutical and Biomedical Sciences***, **22**: 59-65.
22. N. Rajendraprasad, K. Basavaiah (2016) Modified spectrophotometric methods for determination of Iron (III) in leaves and pharmaceuticals using salicylic acid. ***Indian Journal of Advances in Chemical Science***, **4**: 302-307.
23. S. V. Babu, K. H. Reddy. (2012) Direct spectrophotometric determination of mercury (II) using 2-acetylpyridine thiosemicarbazone in environmental samples, ***Indian Journal of Advances in Chemical Science***, **1**: 65-72.
24. G. K. Swamy, J. M. R. Kumar, J. V. L. Sheshagiri Rao, U. A. Kumar, E. V. Snehalath, (2011) Spectrophotometric method for the estimation of eletriptan hydrobromide in pure and tablet dosage forms, ***International Journal of Chemical and Analytical Science***, **2**: 123-125.
25. S. Annasaheb, I. Gaikwad, (2019) Development and validation of UV spectrophotometric area under curve method for estimation of eletriptan hydrobromide, ***International Journal of Pharmacy and Pharmaceutical Research***, **15**: 1-9.
26. A. Ayman, E. Gouda, I. R. Sheikh, M. E. A. Rham. (2013) Utility of charge transfer and ion-pair complexation for spectrophotometric determination of eletriptan hydrobromide in pure and dosage forms, ***Journal of Chemistry***, **2013**: 402164.
27. K. P. Kumar, S. Rawat, D. Bhikshapathi, (2015) Estimation of eletriptan hydrobromide in oral film dosage form by RP-HPLC, ***International Journal of Pharmaceutical Sciences and Drug Research***, **7**: 484-488.
28. K. P. Kumar, (2015) Estimation of eletriptan hydrobromide in oral film dosage form by RP-HPLC, ***International Journal of Pharmaceutical Sciences and Drug Research***, **7**: 484-488.
29. U. N. Rani, S. R. Rao, K. Saraswathi, (2014) New spectrophotometric methods for the quantitative estimation of eletriptan in drug formulation, ***Indian Drugs***, **51**: 18-26.
30. V. R. Myrthy, M. L. N. Acharyulu, B. V. Srinivas, T. S. Reddy, G. V. S. Sarma, (2013) Spectrophotometric determination of mycophenolic acid in bulk and dosage forms using 1,10 ortho phenanthroline, ***European Journal of Applied Engineering and Scientific Research***, **2**: 9-13.

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- Conferences:14
- Paper presentations:14

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Session Chair: Chaired the session during International Conference, in Chemistry during ICMSEA-2019 held at Parlakhimundi,Odisha on 21.12.2019
National level WEBINAR Talk- "Role of Composites in Modern Industrialisation Era"-28.05.2020, conducted by Tirumala Engineering College, Narasarao peta, Andhra pradesh.