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Krishnasis Chakraborty
Department of Quality Assurance, Al-Ameen College of Pharmacy, Opposite to Lalbagh Main Gate, Hosur road, Bangalore-27, India.

Mubeen G
Department of Quality Assurance, Al-Ameen College of Pharmacy, Opposite to Lalbagh Main Gate, Hosur road, Bangalore-27, India.

Ritu Kimbahune
Department of Quality Assurance, Al-Ameen College of Pharmacy, Opposite to Lalbagh Main Gate, Hosur road, Bangalore-27, India.

Lalitha N
Department of Quality Assurance, Al-Ameen College of Pharmacy, Opposite to Lalbagh Main Gate, Hosur road, Bangalore-27, India.

Yajnesh Pai
Department of Quality Assurance, Al-Ameen College of Pharmacy, Opposite to Lalbagh Main Gate, Hosur road, Bangalore-27, India.

Correspondence:
Ritu Kimbahune,
Asst. Professor, Department of Quality Assurance, Al-Ameen College of Pharmacy, Opposite to Lalbagh Main Gate, Hosur road, Bangalore-27 , India.

Photometric method for estimation of Magaldrate

Krishnasis Chakraborty, Mubeen G, Ritu Kimbahune, Lalitha N, Yajnesh Pai

Abstract
The complex formation between Magaldrate, Magnesium and Aluminium hydroxide salt, and Eriochrome Black T at pH10 has been proposed for photometric estimation of Magaldrate. The absorbance of stable violet colored complex of Eriochrome Black T and Magnesium and Aluminium ions of Magaldrate was measured at 527 nm and used for quantitation by single point method. The method has been successfully employed for Magaldrate tablets and the obtained results were found complying with official specification. The method has been validated as per ICH guidelines and the results for all the parameters were found in the recommended limits.

Keywords: Magaldrate, Eriochrome Balck T, Chemical derivatization.

Introduction
Current life style and diet regime have increased the use of Antacids which are available in different dosage forms. Magaldrate is one of the commonly prescribed antacid which provides fast and long lasting acid neutralization, long term stability and distinct adsorption capability with respect to pepsin, bile acid and lysolecithin [1, 2].
Magaldrate (MG), $Al_5Mg_{10}(OH)_{31}(SO_4)_2.X\ H_2O$, a Magnesium and Aluminium hydroxide salt[3] is converted rapidly in gastric acid to $Mg(OH)_2$ and $Al(OH)_3$, which are absorbed poorly and thus provide a sustained antacid effect.

$$\left[Al^{3+}\right]\ \left[Mg^{2+}\right]_2\ \left[HO^-\right]_7\ \left[H_2O\right]$$

Chemical formula of Magaldrate
Indian Pharmacopoeia 2010 describes a Potentiometric titration [4] method for quantification of Magaldrate in pharmaceutical dosage forms. Literature survey reveals that no spectrophotometric procedures have been reported so far for Magaldrate in formulation. Hence it was found essential to develop a simple and suitable photometric method for estimation of MG in pharmaceutical formulations for routine quality control analysis. The objective of the present study was to develop and validate a photometric method for estimation of Magaldrate in formulations.

Materials and Methods
Instrument
A Shimadzu UV-Visible double beam spectrophotometer model 1700 (Japan) with 1 cm matched quartz cells connected to a PC computer running UV- Probe processor software was used for absorbance measurements and treatment of data. Acculab digital balance and Mark ultra sonicator were also used during the studies.

Materials and Methods
Analytical grade chemicals, reagents and double distilled water were used throughout the study. Magaldrate was procured from SPI Pharma, Bangalore in the form of gift sample. Boric acid (Thomas Baker), Hydrochloric acid (SDFCL, Mumbai), Potassium chloride (SDFCL, Mumbai) and Sodium hydroxide (Finar) were used for the preparation of buffer. Eriochrome Black T (HIMEDIA) was used as a complexing agent.

Preparation of Alkaline Phosphate buffer pH10
Boric acid 3.09 gm and potassium chloride 3.7 gm were dissolved and made up the volume to250 mL double distilled water. Accurately 62.5 mL of this solution and54.6 mL of 0.2 N sodium hydroxide were mixed and diluted to 250 mL to prepare alkaline phosphate buffer pH 10.

Preparation of 0.5 mM Eriochrome black T
Accurately 0.023 gm of EBT was weighed and transferred to 50mL volumetric flask and sonicated for 2-3 min in few mL of alkaline buffer pH 10 to dissolve. The volume was made to the mark with alkaline buffer and used as a complexing agent.

Pre-treatment of Drug Sample
Considering hygroscopic nature of MG, standard and sample were dried at 70˚ C for 15 min in hot air oven, and then cooled to room temperature in the desiccator.

Preparation of Standard Solution
Accurately 0.250 g of MG was dissolved with 6 mL of dilute hydrochloric acid, sonicated for 2 to 3 min. Final volume was made up to100 mL with double distilled water to get a concentration of 2500 µg/mL. Further this solution was diluted with double distilled water to obtain a working standard solution 100 µg/mL.

Preparation of Calibration Curve
Aliquots from the working standard solutions 100 µg/mL were suitably diluted with buffer to get concentrations 1 to 15 µg/mL after addition 5 mL of 0.5mM EBT indicator in 25mL volumetric flask. The absorbance was measured at 527nmagainst blank. The blank was prepared by diluting 5 mL of 0.5 mM of EBT with buffer to 25 mL. Calibration curve was constructed by plotting absorbance *vs* concentration.

Analysis of Tablet formulation
Ten MG tablets were weighed, powdered; powdered equivalent to 0.250 gm was transferred to 100mL volumetric flask and dissolved in 6 mL of dilute hydrochloric acid by sonication. The final volume was made up with double distilled water. This solution was filtered through whatmann filter paper No 41 and filtrate was further diluted to get a concentration 100 µg/mL with buffer pH 10.

Procedure for colorimetric estimation
To 4 mL each of sample and standard solutions, 5 mL 0.5 mM EBT indicator was mixed and diluted to 25mL with buffer pH10. The absorbances of both solutions were measured at 527 nm against the blank. The single point analysis method was followed to estimate MG as given below,

$$C_{test} = \frac{A_{test}}{A_{std}} \times C_{std}$$

Method Validation
The proposed method for the Quantitation of Magaldrate was validated as per ICH Guidelines [5, 6]. Q2 (R1) for parameters like accuracy, precision, linearity, range, limit of detection and limit of quantification.

Accuracy
Accuracy of the method was performed by standard addition method at three different levels. A known amount of standard MG was added to the sample solution and percent recoveries were determined and results are presented in table 1.

Precision
Precision of the method was carried out by measuring the % RSD of sample solutions (n=3) at different time intervals (0, 2, 4 hours) on the same day (Intraday) and three consecutive days (Interday).

Reproducibility
Sample solutions of MG was prepared (n=3) by Analyst 1 and Analyst 2 and measured at 527nm. The values obtained were evaluated using F-test and t-test to verify their reproducibility.

Linearity and Range
Linearity of the method was evaluated by analyzing the serial concentrations of standard solutions. The linearity was decided from correlation coefficient (R^2) and range was obtained between the upper and lower level of analyte from the calibration curve as shown in figure no 1 and table no 1.

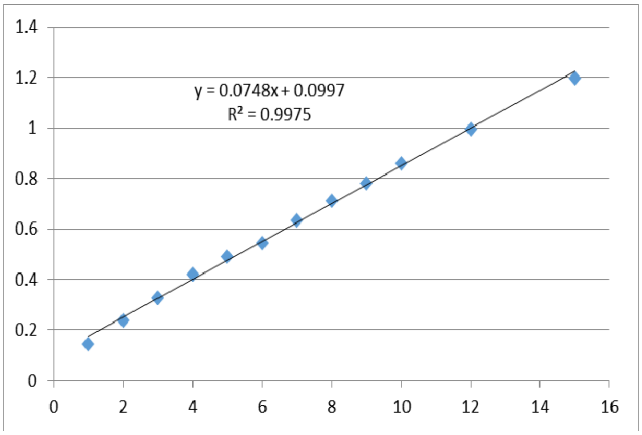

Fig 1: Calibration curve of EBT-MG complex

Sensitivity
Sensitivity was determined by Sendell's Sensitivity, detection limit (LOD) and quantitation limit (LOQ).
Sandell's sensitivity (µg/cm^2/0.001 Abs unit) is defined as smallest weight of substance that can be detected in column of unit cross section and determined by following formula[7].

$$\text{Sensitivity}(S) = \frac{\text{Mole Wt} \times \text{No of atoms in the element}}{\text{Molar absorbitivity of colored species}}$$

Detection limit and quantitation limit were determined from the standard deviation of y – intercepts of six calibration curves and average slope of six calibration curves.

$$LOD = 3.3 \times \frac{\text{Standard Deviation of yIntercepts of Six Calibration Curves}}{\text{Average Slope of Six Calibration Curves}}$$

$$LOQ = 10 \times \frac{\text{Standard Deviation of y Intercepts of Six Calibration Curves}}{\text{Average Slope of Six Calibration Curves}}$$

Discussion
Magaldrate is a combination of inorganic hydroxide salts of Aluminium and Magnesium. It is soluble only in dilute mineral acids; hence the mixture of dilute hydrochloric acid and double distilled water was used to prepare the standard stock solution of MG.
As MG does not exhibit any absorbance in the region of 200 to 800 nm, the chemical derivatization of MG was carried out. Eriochrome Black T (EBT), a commonly used indicator in complexometric titration, was selected as a derivatizing agent.

Aluminium and Magnesium ions of MG formed the violet colour complex with EBT and the proposed reactions between Aluminium and Magnesium with EBT are as shown in figure 2.

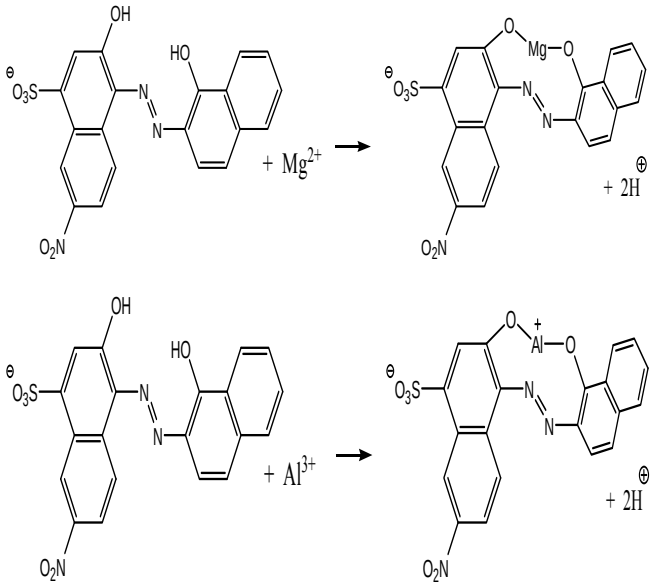

Fig 2: Reaction between Aluminium and Magnesium ions of MG with EBT

The EBT- MG complex was found to be stable in alkaline buffer pH 10 as reported [8]; hence all the dilutions for colorimetric method were made with alkaline buffer pH 10.
Initially MG – EBT complex and EBT solutions were scanned in the range of 400 to 800 nm against alkaline buffer pH 10 to differentiate absorbance maxima. To identify the wavelength for photometric estimation, the EBT spectrum was subtracted from MG-EBT complexes spectra using UV-Probe software and absorbance maxima was found at 527 nm as shown in figure 3.

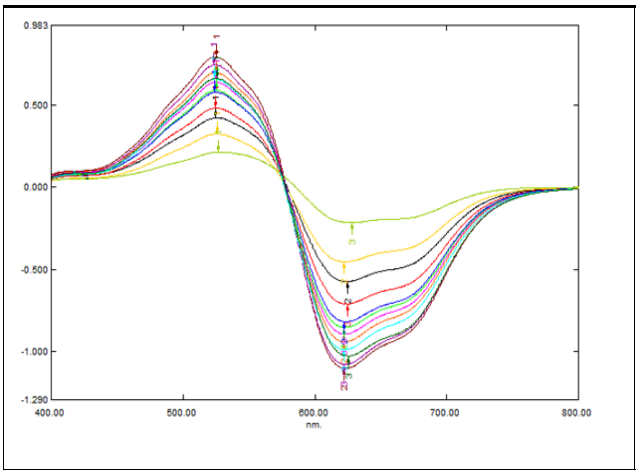

Fig 3: Overlain Spectra of serial dilutions of MG-EBT complexes after subtracting

EBT scan

The strength of the indicator was selected based on the number of Aluminium and Magnesium ions present in MG. Different strengths like 1, 0.5, 0.05, 0.005 and 0.0005mM of EBT were tried and the strength 0.5 mM showed optimum absorbance for EBT-MG complex at 527nm against buffer as shown in figure 4.

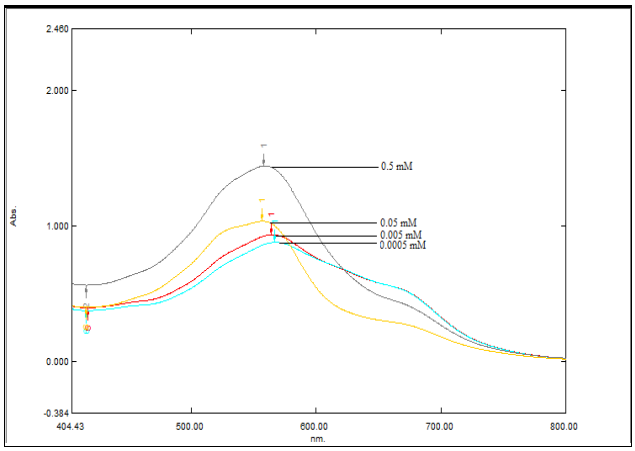

Fig 4: Overlain spectra of MG-EBT complex against buffer

Magaldrate tablets of 0.500 gm strength were directly compressed using excipients starch, lactose, stearic acid and talc in our lab and analysed by the proposed method. The percentage assay of MG in formulated tablets was found to be 104.93 with % RSD 1.00.
The developed photometric method was validated in accordance with ICH guidelines. Accuracy was determined by standard addition method at three different levels 50%, 100% and 150% and percentage recoveries of MG was found to be 102.20, 101.90 and 100.70 With % RSD less than 2. Precision of the methods, intra-day and inter-day were determined by % RSD and found to be less than 3. Reproducibility was determined by preparing and measuring the standard solutions of MG by Analyst 1 and Analyst 2, separately. The obtained data showed no significant difference between the results and precision of two analysts.
The linearity for MG was found to be in the concentration range of 1-15 µg/mL with coefficient of correlation (R^2) 0.9975 as shown in figure 1. The Sandell's sensitivity, LOD and LOQ for MG were calculated from calibration curve and found to be 1.176, 0.850 and 2.910 µg/mL respectively. All the validation parameters results are summarized in table 1.

Table 1: Summary of the validation parameters results of MG

Parameters	Results
Linearity Range (µg/mL)	1-15
Regression Equation (y = mx+c)	0.074x+0.099
Correlation Coefficient (R^2)	0.9975
Assay (n=6) (% ±%RSD)	104.90 ± 1.00
Accuracy at 50% (n=3) (% ±%RSD)	101.3± 0.560
Accuracy at 100% (n=3) (% ±%RSD)	101.6± 0.745
Accuracy at 150% (n=3) (% ±%RSD)	100.7± 0.500
Intra Day Precision (%RSD)	2.728 ± 0.200
Inter Day Precision (%RSD)	2.850 ± 0.200
Sandell's sensitivity (µg/mL)	1.176
LOD (µg/mL)	0.850
LOQ (µg/mL)	2.910

Potentiometric titration was carried out as per IP for the formulated MG tablets and results were found within the specified limits. The statistical analysis [9], F and t tests were carried out to compare official method with developed colorimetric method. There is no significant difference found in the results and precision of the methods at P=0.10 and degree of freedom 2, 2.
Due to hygroscopic nature, MG was required to dry at 70˚ C for 15 min in hot air oven and cooled to room temperature in

desiccators to improve the results. Deionised water can be favoured to avoid the interference of ions which can forms a stable complex with EBT at pH 10. The proposed photometric method can be successfully used for analysis of MG using EBT as a complexing agent.

Conclusion

A new simple and sensitive colorimetric method has been developed and validated for quantitative estimation of MG and the method could be used for routine analysis of MG for bulk and formulations containing non-ionic excipients.

Acknowledgements

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