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MBTH: A CHROMOGENIC REAGENT FOR ESTIMATION OF PHARMACEUTICALS

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ABSTRACT

3-methylbenzthiazolinone-2(3H)-hydrazone is a chromogenic reagent used in spectrophotometric determination of pharmaceuticals. This review explains the work done by different researchers so far for estimation of the drugs by spectrometric analysis. Therefore, this review gives compiled data on utilisation of MBTH reagent in spectrometric analysis

Key Words: Spectrophotometry, MBTH, Chromogen.

INTRODUCTION

MBTH is chemically 3-METHYL-2-BENZOTHIAZOLINE HYDRAZONE (Figure 1) having molecular weight 215.7 & chemical formula $C_8H_9N_3S.HCl$. MBTH was synthesised by Besthron in1910. MBTH is originally introduced as a reagent for aldehyde. Later its use was extended to a variety of organic compound (example: Phenols, aryl amines and different N- and S-heterocyclic compound) to form highly coloured products, MBTH was introduced into analytical chemistry as a sensitive reagent for the detection and photometric determination of carbonyl compounds. The reagent is used in the form of an aqueous solution and the reaction products can be extracted into chloroform, if desired. MBTH reacts with aldehyde first to form an azine. Only if there is remaining MBTH, it is oxidized to another species which combines with the azine to form formazan. However, if there is enough aldehyde, all the MBTH is converted to azine and there is no formation of blue colour. Thus, by using the limiting agent MBTH to test the amount

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of aldehyde around the point of interest, then less aldehyde would produce bluer colour and more aldehyde would produce less blue colour.

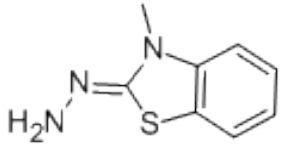

Figure1: Structure of MBTH

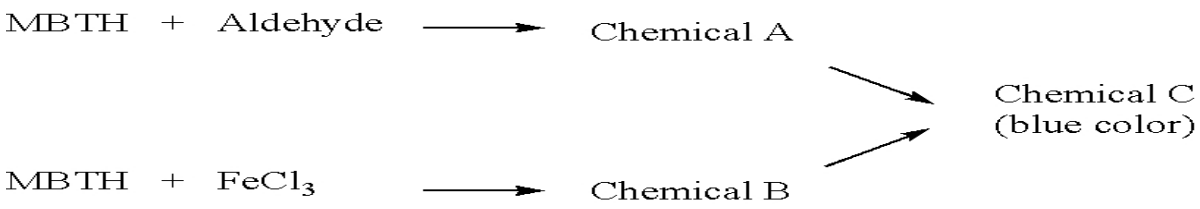

Figure 2: Reaction of MBTH with aldehyde and $FeCl_3$

The end colour may be different depending upon the order of addition of the reactants. For example, if an oxidizing agent and MBTH are mixed before adding the aldehyde, a light green to green/blue colour results. This method could be used for solution test or for tests on a solid phase such as on nylon membrane. The latter also could be used for measurements with a device or instrument such as a colour reader and used in combination with a second aldehyde tester and a pH tester (Figure 2). With Phenols under reaction condition MBTH loses two electrons and one proton to form the electrophilic intermediate, which has been identified as the active coupling species that undergoes electrophilic substitution with phenol and other groups to form the coloured product.

Spectrophotometric Determination of Dobutamine Hydrochloride Using 3-Methylbenzothiazolin-2-One Hydrazone

A simple and sensitive validated spectrophotometric method has been described by *Michael et al (1987)*[1] for the assay of dobutamine hydrochloride. The proposed method uses 3-methylbenzothiazolin-2-one hydrazone as the chromogenic reagent. A mixture of aqueous solutions of the drug and reagent is treated with cerium (IV) ammonium sulphate in an acidic medium. Dobutamine reacts to give a pink colour with a $\lambda_{max.}$ at 510 nm (Molar absorption E1% 1.5×10^4 l mol^{-1} cm^{-1}). Beer's law is obeyed in the concentration range 4–20 µg ml^{-1} of dobutamine in the final assay solution. The method was successfully applied to the determination of the bulk drug and its dosage form (Dobutrex vials).

Selective and Validated Spectrophotometric Methods for the Determination of Nicorandil in Pharmaceutical Formulations

One of the simple and sensitive validated spectrophotometric methods have been described by *Nafisur et al (2004)*[2] for the assay of nicorandil in drug formulations. This uses the oxidative coupling of 3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) with DL-3, 4-dihydroxyphenylalanine (DL-dopa) in the presence of nicorandil as oxidant in sulfuric acid medium to form an intensely colored product having maximum absorbance at 530 nm. Beer's law is obeyed in the concentration range 1.0 to 15.0 μg mL^{-1}. The method has been successfully applied for the analysis of drug in pharmaceutical formulations. The reliability and the performance of the proposed method is established by point and interval hypothesis and through recovery studies. The experimental true bias of all samples is smaller than ±2%.

A Novel Use of Oxidative Coupling Reactions for Determination of Antibiotic and Anti-Inflammatory Drugs in Pharmaceutical Formulations

A new spectrophotometeric method by *Srinivasa Rao Narala et al (2011)*[3] for the assay of four drugs namely Meropenem (MPN), Cefditoren Pivoxil (CTP), Mesalamine (MSL) and Cefdinir (CDN) in both pure form and Pharmaceutical formulations. All methods involve the oxidative coupling reaction of MPN, CTP, MSL and CDN with 3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) in presence of Fe (III) in an acidic medium to form coloured products with absorption maxima at 620, 630, 500 and 620 nm respectively. Beer's law was obeyed in the ranges of 5-25, 5-40, 5-25 and 2-12 μg/ml for MPN-MBTH, CTP-MBTH, MSL-MBTH and CDN-MBTH respectively. Statistical treatment of the experimental results indicates that the methods are precise and accurate. The proposed methods have been applied to the determination of the active components in commercial formulations with no interference from excipients. A comparative study between the suggested procedures and reference procedure for these compounds in the commercial formulations showed no significant difference between two procedures

Development of New Visible Spectrophotometric Methods for Determination of Benidipine Hydrochloride in Bulk and Formulations Based On Oxidative Coupling and Diazo Coupling Reactions

One of the simple and sensitive visible spectrophotometric methods (A-C) have been developed by *Kalyanaramu et al (2011)*[4] for the estimation of Benidipine hydrochloride [BEN] from its bulk drug and dosage forms. It was based on the reduction of the nitro group to amino group of

the drug. This can be achieved by heating a mixture of an alcoholic solution of BEN, zinc powder and dilute hydrochloride in a water bath at 90^0c ±5 for 15 minutes. The cold and clear filtrate reacts with 3-methyl-2-benzothiazolinonehydrazone hydrochloride in the presence of ferric chloride to form coloured species with wavelength maximum at 620nm. Beer's law obeyed in the concentration range of 10-30µg/ml. Commercial formulations were analyzed, the results obtained by the proposed methods were in good agreement with the labeled amounts. Recovery in all the methods is found to be close to 99-100%.

Use of 3-Methyl-2-Benzothiazolonehydrazone in an Automated Colorimetric method for Determination of Triglycerides in Plasma or Serum

A new automated colorimetric method is described by *Neeley et al (1972)*[5] for the determination of serum or plasma triglycerides. The samples are extracted with 2- propanol containing activated alumina. An Auto-Analyzer Sampler II and Proportioning Pump II are used in combination with a Gilford Model 300 N spectrophotometer and Model 3091-A debubbler flow cell. Following on-line saponification, glycerol is oxidatively cleaved with sodium metaperiodate. The resulting formaldehyde is reacted with 3- methyl-2-benzothiazolone hydrazone (MBTH) under mild conditions to produce the corresponding azine. Further reaction of MBTH with the azine in the presence of an oxidizing agent results in the formation of a blue cationic adduct. Beer's law is obeyed, at 670 nm, to a triglyceride concentration of 400 mg/100 ml. Because of the high sensitivity of the MBTH reaction, short incubation periods, high sampling rates (60/h), and low flow rates can be used. The results correlate well with those obtained by the Kessler-Lederer method and by a totally enzymatic method.

Application of MBTH and Sulphanilic Acid for the Quantitative Spectrophotometric Determination of Diacerein in Bulk and Formulations

One of the simple, rapid and sensitive spectrophotometric methods have been proposed by *G. Vijaya Raja et al (2009)*[6] for the determination of diacerein in bulk and pharmaceutical formulations. Method *A* was based on the oxidation of 3-methylbenzothiazolin-2-one hydrazone (MBTH) by ferric chloride followed by its coupling with the drug in acidic medium. The colored complexes produced in the method shows maximum absorbance at 670 nm. Under optimized experimental conditions, Beer's law is obeyed over concentration ranges of 1-5 µg/ml. The methods have been applied to the determination of diacerein in pharmaceutical dosage forms. Results of analysis are validated statistically (Figure 3).

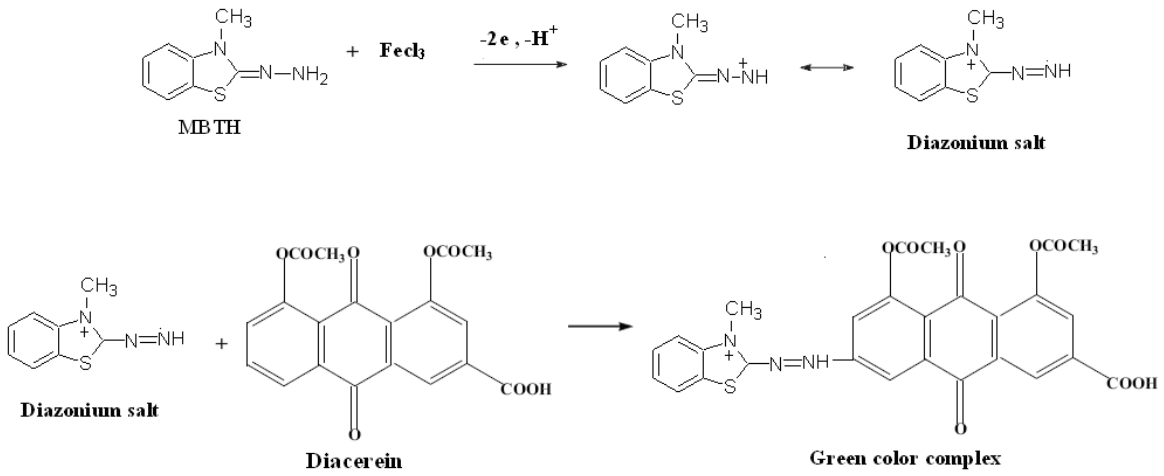

Figure 3: Tentative reaction scheme for oxidative coupling of MBTH with Diacerein

Visible Spectrophotometric Estimation of Pemetrexed Disodium in Pharmaceutical Formulations

One of the simple, accurate, rapid and sensitive methods has been developed by *P. Janaki Pathi et al (2011)*[7] for the estimation of Pemetrexed Disodium in its pharmaceutical dosage form. Method is based on the reaction of Pemetrexed Disodium with 3-methyl-2- benzothiazolinone hydrazone (MBTH) in the presence of Ferric Chloride to form a bluish green colored chromogen, which shows maximum absorbance at 735 nm. The absorbance-concentration plot is linear over the range of 0-80 µg /mL. Results of analysis for all the method was validated statistically and by recovery studies. The proposed method is economical and sensitive for the estimation of Pemetrexed Disodium in bulk drug and in its formulations (Figure 4).

Colorimetric Determination of Ethamsylate in Bulk and Its Pharmaceutical Formulations

One of the simple and economical spectrophotometric methods has been developed by *M. D. Arshad et al (2011)*[8] for the quantitative determination of Ethamsylate in bulk drug and pharmaceutical form has been developed. Method is based on oxidative coupling reaction of Ethamsylate with 3-methyl benzothiazolinone hydrazone (MBTH) reagent under alkaline conditions forming a green colored chromogen and exhibits absorption maxima at 580 nm. Beer's law was obeyed in the concentration range of 4-20 µg/ml. These method was extended to pharmaceutical formulations and there was no interference from any common excipients. The results of analysis have been validated statistically and by recovery method.

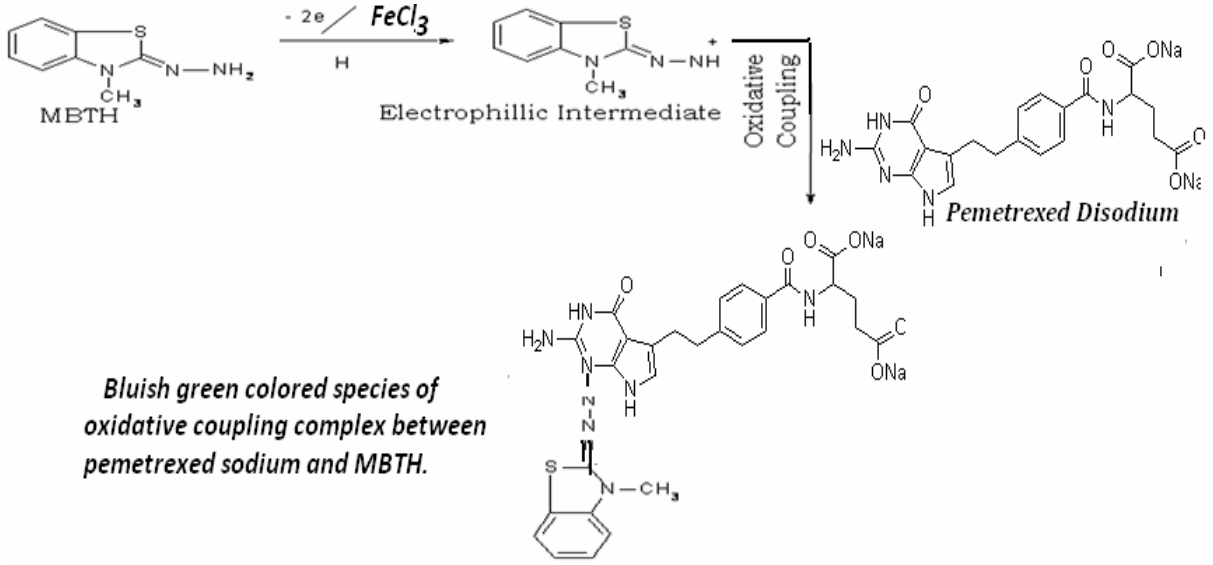

Figure 4: Tentative reaction scheme for oxidative coupling of MBTH with Pemetrexed Disodium

Spectrophotometric Determination of Oseltamivir Phosphate in Bulk Drug and in Pharmaceutical Formulation

One of the simple and sensitive spectrophotometric methods has been developed by *Jahan et al (2010)*[9] for the quantitative determination of oseltamivir phosphate in bulk as well as pharmaceutical formulation. It is based on oxidation followed by coupling reaction. In which oseltamivir phosphate formed a green coloured chromogen when treated with MBTH in the presence of ferric chloride. The chromogen exhibit absorption maxima at 666 nm and obeyed Beer's Law in concentration range 10-50 µg/ml. The results of the method have been validated statistically and by recovery studies. It is simple, sensitive, economical and accurate for quantitative determination of oseltamivir phosphate in bulk drug and pharmaceutical formulation.

Spectrophotometric Determination of Lamotrigine Using Gibb's and MBTH Reagent in Pharmaceutical Dosage Form

One of the simple, extractions free spectrophotometric method by *R. S. Chandan et al (2011)*[10] for the quantitative estimation of lamotrigine (LTG) in bulk drugs and pharmaceutical formulations (tablets) have been developed. It is based on reaction of oxidative coupling of lamotrigine with 3-methyl-2-benzthiazolinone hydrochloride (MBTH) to form green colored product. Lamotrigine at its absorption maxima 662 nm shows linearity in the concentration range of 15-350 µg/ml. The relative standard deviation is 0.23% was obtained. Linear relationships with good correlation coefficients (0.996-0.998) were found between absorbance and the

corresponding concentrations of the drug. The reliability and performance of the proposed method was validated statistically the percentage recovery ranged from 100.06%. The results of analysis for the two methods have been validated statistically and by recovery studies.

Spectrophotometric Methods for the Estimation of Duloxetine

One of the simple, sensitive, rapid and accurate colorimetric methods has been developed by *Jane et al (2011)*[11] for the estimation of Duloxetine in bulk and pharmaceutical dosage forms. This was based on the formation of pink coloured complex between duloxetine and 3- methyl-2 benzothiazolinone hydrazone hydrocholoride (MBTH) in presence of cerric ammonium sulphate, which shows maximum absorbance at 524nm. The linearity was found to be 10-60 µg/ml. The proposed method was validated statistically and the recovery studies were carried out by standard addition method.

Selective Visible Spectrophotometric Estimation of Ambroxol Hydrochloride in Presence of Cetirizine Hydrochloride in Tablets

a simple, accurate, rapid and sensitive method by *V. H. Potdar et al (2009)*[12] for the estimation of Ambroxol hydrochloride in presence of cetirizine hydrochloride in tablets. The estimation is based on the reduction of ferric from ferric nitrate to ferrous ions by the drug (ambroxol hydrochloride),which further in presence of 3-Methyl- 2-Benzothiazolinone Hydrazone Hydrochloride (MBTH), to produce red colored complex, measured at 568 nm. The chromogen obeyed linearity over 6-54 µg/ml (r=0.9988) with percent relative standard deviation (% RSD) of 0.16, showing that method has good accuracy and precision.

Development and Validation of Spectrophotometric Methods for Determination of Ceftazidime in Pharmaceutical Dosage Forms

One of the spectrophotometric methods for the determination of ceftazidime (CFZM) in either pure form or in its pharmaceutical formulations are described by *Mruthyunjayaswamy et al (2008)*[13]. The method is based on the reaction of 3-methylbenzothiazolin-2-one hydrazone (MBTH) with ceftazidime in the presence of ferric chloride in acidic medium. The resulting blue complex absorbs at 628 nm. The absorbance was found to increase linearly with increasing the concentration of CFZM; the systems obeyed the Beer's law in the range 2–10 µg mL–1 for MBTH. *LOD*, *LOQ* and correlation coefficient values were 0.15, 0.79 and 0.50, 2.61. No interference was observed from common excipients present in pharmaceutical formulations. The proposed method is simple, sensitive, accurate and suitable for quality control applications.

CONCLUSION

This review complies various estimation methods of pharmaceuticals by utilizing MBTH as a chromogenic reagent for spectrophotometric determination which would be very useful information as a whole in future research field of analysis.

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