Indirect spectrophotometric determination of Metoclopramide-hydrochloride using potassium hydrogen peroxymonosulfate

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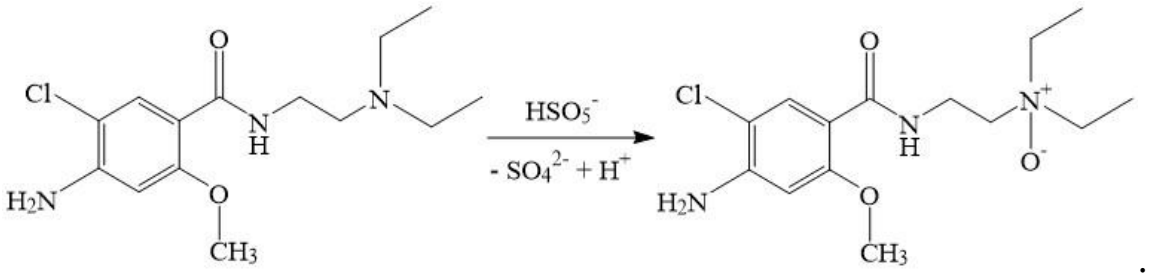
Metoclopramide-hydrochloride (MCP) chemically is 4-amino-5-chloro-N-(2-diethylaminoethyl)-2 methoxybenzamidemonohydrochloride monohydrate. MCP was used as a treatment of nausea and vomiting in association with migraine and severe headache. The drug was used for the control of sickness due to radiation therapy and chemotherapy, and for the prevention and treatment of post operative nausea and vomiting.

Liquid chromatography (HPLC) is the official method for assay of MCP in BP and USP; further, literature survey revealed HPLC and spectrophometric methods for estimation of MCP in pharmaceutical formulations. Direct spectrophotometric determination possible considering the pharmacophoric groups in the molecule of MCP which absorb in UV range. The wave length of 270 nm recorded to have the maximum absorbance in the using 0.1 M HCl as solvent. On the contrary to common pharmaceutical dosage forms such as tablets and suspensions, injectable dosage forms are almost excipients-free; consequently fewer interference will be encountered. Some of the reported procedures are not simple for routine analysis and required expensive or sophisticated instruments. Literature survey revealed that no simple spectrophotometric assay of MCP has ever been reported.

Its application in therapy requires methods for the determination in pharmaceutical dosage forms. The stoichiometric oxidation of MCP to its corresponding *N*-oxide by means of potassium hydrogen peroxymonosulfate, $KHSO_5$ (also known as the trade names Caroat and Oxone) was used to develop a new spectrophotometric method for determination of the drug. The proposed procedure is based on oxidation of MCP by $KHSO_5$ and the determination excess oxidant

spectrophotometrically by reaction with iodide to form tri-iodide. The determination of tri-iodide in the aqueous phase proved to be equally sensitive (ε_{350} = 2.3 $\times 10^4$) and reproducible and was preferred because of its simplicity. Conditions have been established for the determination of MCP by $KHSO_5$ oxidation. The rate of the reaction is pH-dependent, for instance, MCP oxidation is most rapid at pH pH 8.6-9.9. A probable mechanism involving a rate-determining attack of monoanoin Caro's acid (HSO_5^-) molecule on free amine (R_3N) was proposed and discussed:



Experiments with MCP showed that the reaction, consuming 1 mole of $KHSO_5$ per mole of mepivacaine, was complete within 10-15 min and no further reaction occurred within 30 min. Neither of the reaction products (K_2SO_4) interfered in any way with the $KHSO_5$ determination.

The possibility of application of $KHSO_5$ as reagent for indirect determination of MCP by spectrophotometric method in Metoclopramide 10 mg tablets was investigated. The required amount of MCP was dissolved in water, pH 9.9 buffer solution and $KHSO_5$ solution was added. After 10 min, the solution was acidified. The $KHSO_5$ unconsumed was determined spectrophotometrically by reaction with iodide to form tri-iodide. the determination of tri-iodide in the aqueous phase proved to be equally sensitive (ε_{350} = 2.35 $\times 10^4$ $L \cdot mol^{-1} \cdot cm^{-1}$.) and reproducible and was preferred because of its simplicity.

The advantages of the applied analytical techniques in the determination of Metoclopramide Hydrochloride in tablets «Metoclopramide 10 mg» was presented. The recovery of this analyte in preparation sample ranged from 98.35 to 101.65%. A paired *t*-test showed that all results obtained for bulk drug and in tablets «Metoclopramide 10 mg», using the proposed procedure and the official procedure respectively, agreed at the 95% confidence level.