Determination of Metoclopramide in Pharmaceutical Commercial using Flow Injection– Chemiluminescence Technique

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ABSTRACT
A new method used for determination of Metoclopramide by flow injection–chemiluminescence method using luminal and H2O2 for luminescence and Ni2+ as activator has been introduced. The method used to determine Metoclopramide in commercial Pharmaceutical. Locally produced flow injection-chemiluminescence was used in this experiment and good results were obtained. The linear range was (5-30) µgm.ml-1, detection limit was (1.2 ppm) and the relative standard deviation was 0.87 % (n = 5) for the system.

INTRODUCTION
Luminescent reactions has been observed since ancient time, luminous animals are known in the Greek civilization, however the first report of artificial chemiluminescence occurred in 1669 (1). Chemiluminescence is a term used to describe the emission light, which occurs when a molecule in an excited state relaxes to its ground state the energy which is produced by a chemical reaction (2). The term chemiluminescence was first used in 1888 by Elhardt Weidemann, later; Albrecht reported in 1928 the luminescent properties of luminol (3). Early research on chemiluminescence was focused on the observation of a reaction and investigation of the mechanism and the analytical applications of the phenomenon appeared in the literature in 1960s (4). The benefits of chemiluminescent methods include ultra-sensitive detection limits (attomole–zeptomole), rapid assays, (5) and have a diverse range of analytical application (6).

Two probes may be used with chemiluminescence assay: luminol and lucigenin. The luminol-mediated chemiluminescence assay is more advantageous, it can measure H2O2, O2- and OH- levels (7). Luminol based chemiluminescence probe is extremely sensitive and convenient for diagnostic purposes the data they generate have to be interpreted with care (8). The CL reaction of luminol with oxidizing agents was first reported in 1928. Since then, the reaction has mainly found use in the determination of hydrogen peroxide, other oxidants, and metal ions such as Cr(III), Cu(II), Fe(II),... (9). Metoclopramide hydrochloride (MCP-HCl), artificially known as 4-amino-5-chloro-N-(2-diethylaminoethyl)-2-methoxy benzamine hydrochloride, is a antiemetic and gastroprokinetic operator. Its activity and use is dopamine receptor antagonist and antiemetic, it is essential used to treat nausea and retching, to encourage gastric exhausting in patients with gastro paresis. It is additionally utilized for the counteraction of malignant growth chemotherapy-actuated emesis at a lot higher dosages and utilized in pregnancy as a subsequent option for treatment of hyperemesis (heaving of pregnancy) (8-9).

Metoclopramide can be utilized to treat stomach upset including acid reflux, wind, torment, heartburn, infection and bile disgorging, to stop nausea and spewing. Numerous strategies have been accounted for the assurance of metoclopramide hydrochloride in pharmaceutical definitions or potentially organic liquids. These strategies incorporate, stream infusion analysis, spectrophotometry, potentiometry, and titritymetry.

MATERIALS AND METHODS
A locally synthesized flow injection conjugated chemiluminescence system used in this experiment (fig. 1) , the system consist of peristaltic pump, injection unit, silicon pipes (0.5mm in diameter and 2.5 mm length), peroxide cell, flow cell and detector.
Chemicals
a. All chemicals used were analytically grade; [Luminol (98%), fluka], [Metoclopramide (99%)], [Nickel chloride (97%), fluka], [Sodium carbonate (99%), fluka], [Hydrogen peroxide (48%), fluka], [Sulfuric acid (98%), BDH]

b. Sample preparation
Thirteen tablets weight, crushed and grinded. Tablets containing 10 mg of metoclopramide hydrochloride for (Sanofi-aventis France, Actavis UK) and 5mg of SDI Iraq (were weight (1.336, 1.384, 2.432 g) equivalent to 106.29 mg of active ingredient 3 mMol.L$^{-1}$ respectively. The powder was dissolved in distilled water followed by filtration to remove any undissolved residue affecting on the response and complete the volume to 50 mL with distilled water.

Preparation of Ion exchange column
These columns used for elimination of ions from chemiluminescence system, two types of columns were prepared:

A-Cation exchange column: were prepared by using resin (Dowex 50, fluka) as Na+ KSO$_3$ with 20-100 µm diameter and 1.8 meq/gm. as 25 ml of the resin in 200 ml beaker and filled with D.W to half and leave for 24 hrs. The mixture was mixed and washed many times until D.W become clear. A column (15*15 cm) sealed from one end and filled with glass wall and then filled with the resin, the other side of the column closed to prevent moving of the resin by the steam of buffer and H$_2$O$_2$.

B-Anion exchange column:
All steps of cation exchange column were repeated except in the resin type (Dowex 30, fluka), 10-50 µm diameters and 1.2 meq/gm. as K$^+$Cl$^-$ capacity on H$_2$O$_2$ line.

Effect of the catalytic ion concentration
A series of concentrations of the catalytic ion was prepared, which works to oxidize the reagent by the hydrogen peroxide oxidizing agent. A series of concentrations was 10-40 ppm where the best concentration was 40 ppm, without deformation peaks, very clear, and identical.

Study the effect of luminal concentration (reagent)
A series of concentrations was prepared for the reagent, starting with 0.1 M to 0.01 M concentration, where the concentration 10$^{-4}$ M that gave the highest peaks strength was the concentration. Because in high ion concentrations, a complex works with the detector, thereby reducing the intensity of the resulting signal.
Study the effect of hydrogen peroxide concentration
Several concentrations of peroxide were prepared (10⁻¹, 10⁻³, 10⁻⁵ M) and it was found that the best concentration that gives the best intensity is 0.001 molar concentration where the peaks were sharp and regular.

Effect of flow velocity on the signal
The studied speed was as follows (1, 2, 3, 4, 5) ml/min, since it was found that the best flow velocity is 3 ml/min gives the best signal, because high speed does not give sufficient time to obtain the interaction between the sample and the reagent. Slowly, the recorder is noisy and thus leads to beam width and slackness, which shows the effect of velocity on the peaks Study the effect of sample size

The effect of sample volume
We also studied sample volume by injection valve And the sizes that have been studied (50, 125, 175, 180) micro liter

RESULTS AND DISCUSSION
the system used is suitable for chemiluminesces depended estimations as the system provides a rapid mixing for reagents and all chemical reactions occur in closed system in fixed factors such as concentration, flow rate, retention time, and speed of reagent entre to flow cell, all these factors provide accurate results with many application. Also this system is simple, rapid sample feeding and low cost.

After measurement of luminescence signal of all concentrations vis absorbance were plotted, a linear regression obtained with R² value (0.97) as shown in figure 8.
The method applied on the commercial sample by standard addition method and via plotting luminescence vies volume (figure 3), the unknown concentration were calculated. The following results were obtained ($r = 0.99$, detection limit $=1.2$ ppm, recovery $98\%$ and $RSD = 0.87$). This regression value makes the probe used reliable and the detection limit is making it sensitive and good for trace detections.

![Figure 8: plot of the standard curve of Metoclopramide](image1)

![Figure 9: plot of standard addition of unknown sample](image2)

REFERENCES