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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 H_2O_2 for luminescence and Ni^{+2} 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.

Key words: flow injection, chemiluminescence, Metoclopramide, luminal
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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 Eilhardt Weidemann, later; Albrecht reported in 1928 the luminescent properties of luminol [(1)].
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 [(1)]. The benefits of chemiluminescent methods include ultra-sensitive detection limits (attomole–zeptomole), rapid assays, [(3)] and have a diverse range of analytical application [(4)].

Two probes may be used with chemiluminescence assay: luminol and lucigenin. The luminol-mediated chemiluminescence assay is more advantageous, it can measure H_2O_2, O_2 and OH^{-} levels [(5)]. Luminol based chemiluminescence probe is extremely sensitive and convenient for diagnostic purposes the data they generate have to be interpreted with care [(6)]. 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),. [(7)]. Metoclopramide hydrochloride (MCP-HCl), artificially known as 4-amino-5-chloro-N-(2-diethylaminoethyl)- 2-methoxy benzamine hydrochloride, is an antiemetic and gastroprokinetic operator. Its activity and use is dopamine receptor opponent and antiemetic, it is essential used to treat queasiness 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 queasiness 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[(10-11)], spectrophotometry[(12-13)], potentiometry[(14)], and titrimetry[(15)].

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.

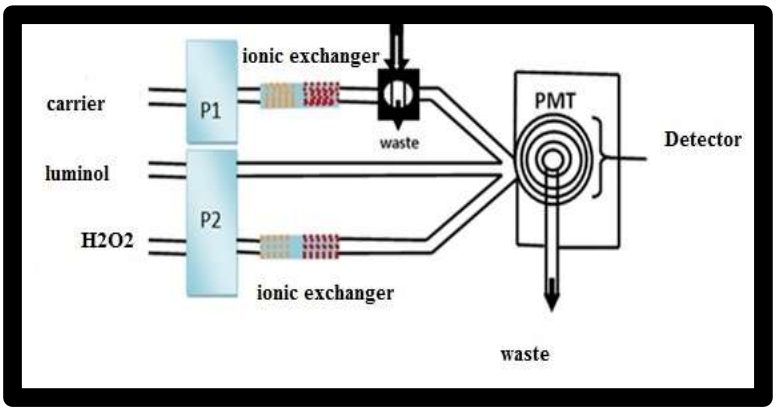

Figure1: scheme of chemiluminescence detection system

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 106.29mg 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_2O_2.

B-Anion exchange column;

Al steps of cataion exchange column were repeated except in the resin type (Dowex30, fluka), 10-50 µm diameters and 1.2 meq/gm. as K^+Cl^- capacity on H_2O_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

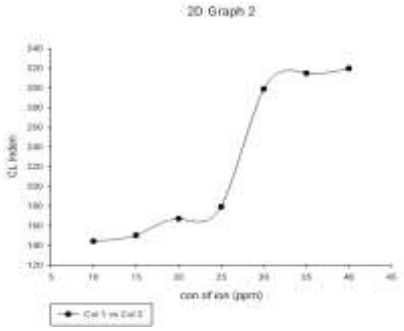

Figure2: Effect of the catalytic ion concentration

Study the effect of removing air bubbles

Practically he found that the bullous bubbles Toothier on the signal resulting from the process of chemical luster where it was found that with the presence of an ion exchanger, the resulting signal is distorted, unclear and noise, but when the ion exchanger is present and the figure below shows the indication of the presence of the ion exchanger and the absence of an ion exchanger

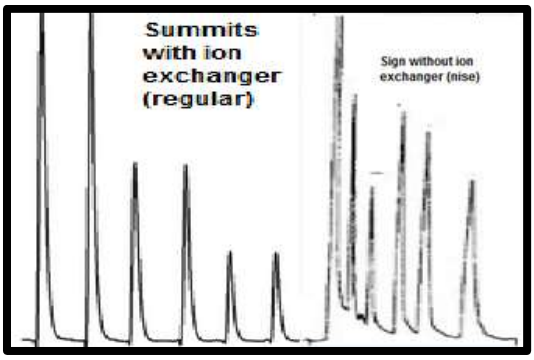

Figure3: The effect of ion exchangers on the peaks

Study the effect of luminal concentration (reagent)

A series of concentrations was prepared for the reagent, starting with0.1 M-10^{-6}M concentration, where the concentration10^{-3}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.

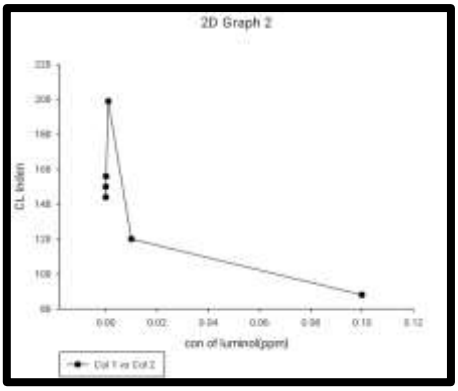

Figure4: Effect of luminal concentration

Study the effect of hydrogen peroxide concentration
Several concentrations of peroxide were prepared (10^{-1}_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

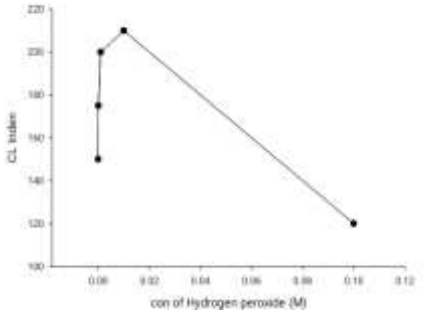

Figure5: Effect of H_2O_2 concentration

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

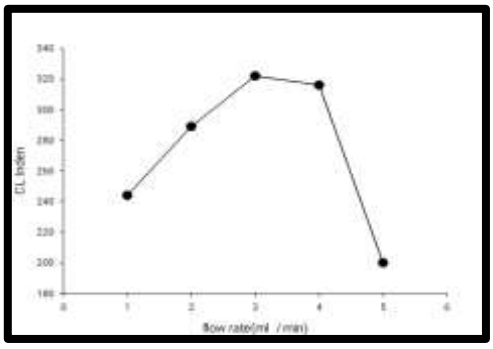

Figure6: Effect of Flow rate concentration

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 litter

Where he found the best volume that gives the best signal is 125 micro liters.

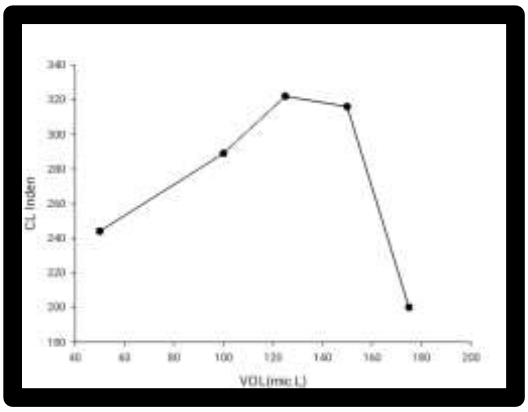

Figure7: The effect of sample volume

Table 1: Optimal conditions for the determination of the drug

Con of ion	40 ppm
Con of luminal	10^{-3}M
Con of H_2O_2	10^{-3}M
FLOW Rate	3Ml min $^{-1}$
Volume of sample	125 mic .litter

Application
This method applied on commercial Metoclopramide (10mg) from using standard addition method, unknown samples were injected in the sample injector and luminescence were measured and expressed as mV .Results were explained in results discussion.

Calibration curve
A series of concentrations of standard Metoclopramide (5 – 40 mg/ml) were prepared using the standard conditions in the following table , the chemiluminesce were measured and expressed as mV, five measures were taken for each concentration, the result were analyzed using (sigma plot) software and the equation of linear regression expressed as y=ax+b.

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 R^2 value (0.97) as shown in figure(8).

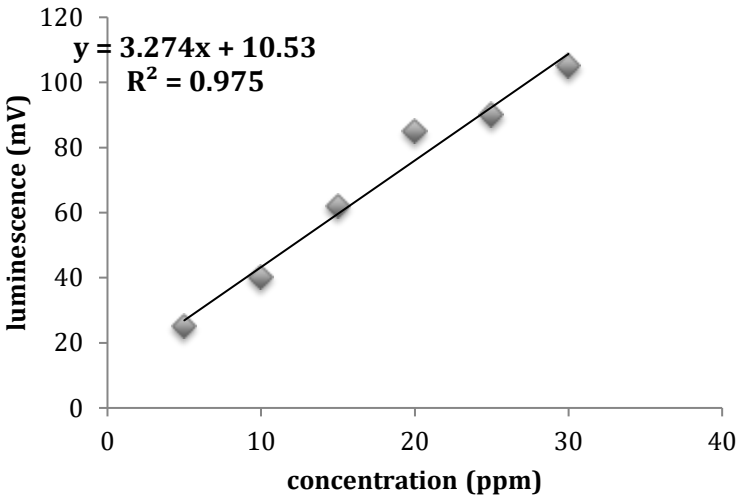

Figure 8: plot of the standard curve of Metoclopramide

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.

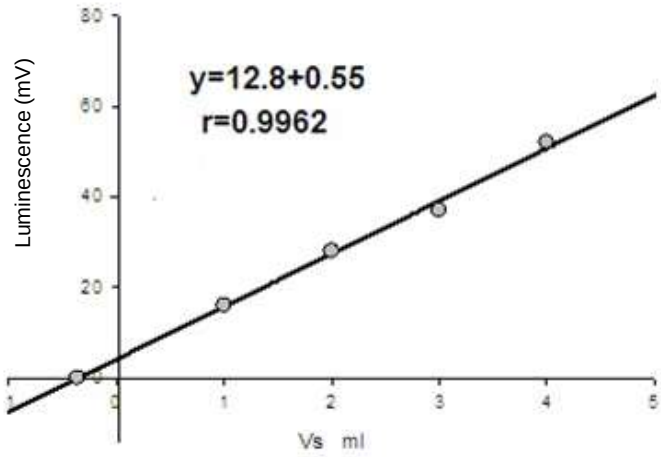

Figure 9: plot of standard addition of unknown sample

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