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A Novel Coated Pencil-Shaped Graphite Electrode for Potentiometric Determination of Metoclopramide-HCl in Pure and Pharmaceutical Commercial Products

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Abstract

The present article aims to determine metoclopramide hydrochloride (MCP) drug by the construction of a coated pencil graphite(CPG) electrode using phosphomolybdic acid (PMA) as an active substance to produce MCP-phosphomolybdate ion-pair (MCP-PMA), tributyl phosphate (TBP) as a plasticizer and polyvinyl chloride (PVC) as a matrix. The results showed good linearity (1.0×10^{-2} - 1.0×10^{-7}) $mol.L^{-1}$, the slope was 58.486 $mV.decade^{-1}$ at pH range between 2.8 - 4.7. The detection and quantification limits were 2.1×10^{-7} and 6.9×10^{-7} $mol.L^{-1}$, the response time was 21 Sec., and the lifetime was 43 days for MCP electrodes. The selectivity coefficient (K_{pot}) was also studied for the present electrode in the presence of molecules and other ions with mono, di and tri charges that achieved K_{pot} values of less than 1 for all investigated species. The MCP fabricated electrode was applied for determination of the active ingredient in pharmaceutical dosage forms. The recovery percentage range was (99.41-101.39)%.

Keywords: Metoclopramide-HCl, Coared pencil graphite, PVC electrodes, TBP, PMA..

Introduction:

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Metoclopramide, which is also called (4-amino-5-chloro-[N]-[2-(diethylamino) ethyl]- 2-methoxybenzamide[1], and is used as an antiemetic and gastrointestinal prokinetic drug in both children and adults[2]. It is also prescribed for gastroparesis in diabetic patients. It helps with nausea, vomiting, loss of appetite, and satiety[3,4]. Many studies have focused on determining its dose forms due to its extensive use and excellent therapeutic value in empirical and clinical medicine. High-performance liquid chromatography (HPLC)[5], spectrofluorimetric analysis[6], spectrophotometric technique[7], chemiluminescence[8], tandem mass spectrophotometry[9], and electrochemical methods are among the analytical approaches suggested for the measurement of MCP in pharmaceutical forms and biological fluids[10-12]. MCP is "white or almost white, crystalline powder or crystals, very soluble in water, freely soluble in alcohol, and sparingly soluble in methylene chloride. It melts at about 183 °C with decomposition"[13] **Figure 1**.

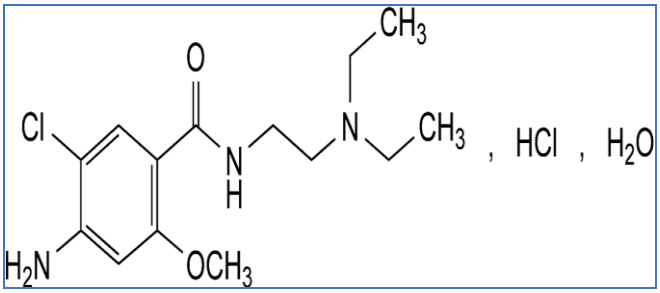

Figure1: Chemical structure of metoclopramide-HCl

Experimental:

Apparatus:

The potentiometric measurements were done by JENWAY pH Meter 3310(Germany) and attached with Calomel Electrode. Sartorius BL 210S was used to weigh all solid materials. Hot Plate with Stirrer-Germany and Ultrasonic bath were also used.

Materials and Chemicals:

Sigma-Aldrich supplied the pure metoclopramide hydrochloride, while graphite pencils were purchased from nearby shops. MERCK provided the tetrahydrofuran solvent and tributyl phosphate. SABC of KSA was used for the production of the high molecular weight PVC.

Standard drug solutions

A 100 mL volumetric flask was completed to the mark with deionized water to create the MCP stock solution prepared by dissolving 0.3543g in the same solvent.

Working solutions

The stock solutions were diluted individually using deionized water to create a series of working solutions with concentrations ranging "from 1.0×10^{-7} to 1.0×10^{-3} mol L^{-1}."

Procedure

Preparation of the ion-pair MCP-PMA

By mixing 0.01 mol.L^{-1} of MCP with the same concentration of PMA, the ion pair of MCP cation and PMA anion was created. After the formation of a greenish-yellow precipitate, it was filtered and rinsed many times with deionized water.

The removal of all obstructive ions was validated when the filtrate's conductivity was found to be less than or equal to 1-2 µs.cm^{-1} [14].

Constructing an MCP-PMA pencil graphite-coated electrode

In order to make the coating solution, 0.45 grams of PVC were combined with 0.6 grams of TBP, and then 0.1 grams of ion-pair MCP-PMA were added. In a small amount of THF, all the ingredients were dissolved. A pencil-graphite rod was immersed in this solution many times to get a uniform coating on the rod. To activate the coated pencil-graphite electrode, it was submerged in a 0.01 mol.L^{-1} MCP solution for 24 hours prior to potential measurement [15].

Potentiometric measurements of metoclopramide hydrochloride

The optimal preparation of a standard series of MCP (10^{-7} to 10^{-2}) mol.L^{-1} was carried out. The calomel reference electrode was used in conjunction with the proposed electrodes made of pencil-graphite to conduct potentiometric measurements [16]. For each concentration, the constructed-electrode potential was recorded to obtain the straight-lone equation that was utilized to determine the pure drug and pharmaceutical products (Figure 2).

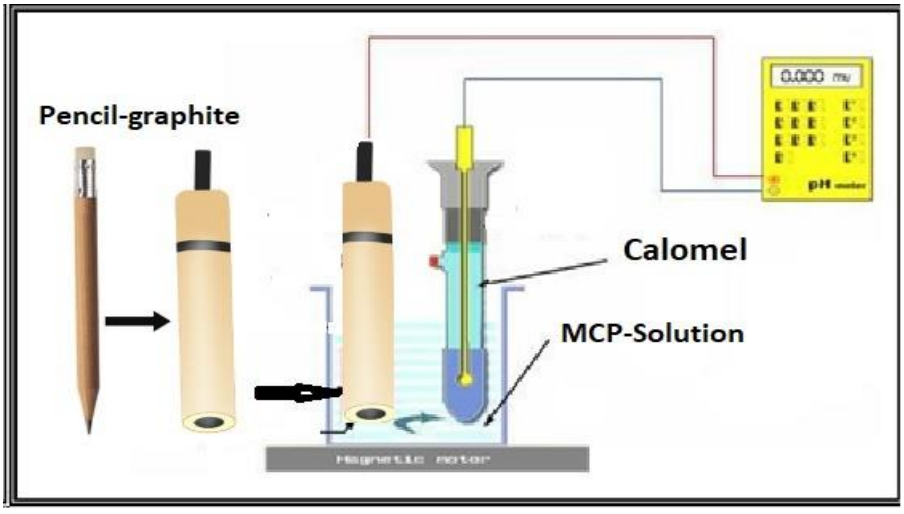

Figure2: The constructed electrode bonded with pH-mV cell

Optimal conditions

pH Effect

"The effect of pH on the potential response of the fabricated sensor was studied over the pH ranges" of [2–5] for MCP-PMA. This was "obtained by adding diluted aliquots of (0.1 mol.L^{-1}) hydrochloric acid or sodium hydroxide solutions" to the (10^{-2} and 10^{-3}) mol.L^{-1} drug solutions. The potential obtained at each pH value was recorded, and the optimal pH was 2.8 to 4.7 **Figure3**.

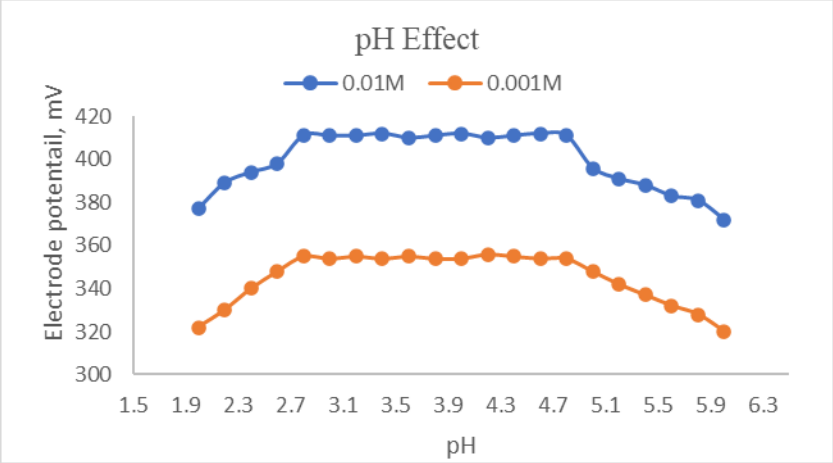

Figure3: The effect of pH on the proposed electrode

The selectivity coefficient (K_{pot})

Various obstructive ions and excipients, which might be present in the medicinal substance, were tested to determine how sensitive the existing sensors were examined the selectivity by means of the matched potential technique. According to this technique, the selectivity coefficient is defined as the ratio of the necessary ion's activity to that of the interfering ion, when both exhibit the same potential change [17].

Table1: Selectivity coefficients (Kpot) for the proposed electrodes

Interferings	Kpot for the constructed electrode MCP-PMA pencil electrode
Ca ions	2.1×10^{-4}
K ions	2.9×10^{-4}
NH4 ions	4.1×10^{-4}
Cl ions	2.5×10^{-3}
Mg stearate	6.2×10^{-3}
Na ions	3.5×10^{-4}
Glucose	5.8×10^{-4}
TiO_2	7.1×10^{-3}
Starch	2.2×10^{-3}
SO_4 ions	1.8×10^{-4}

Calibration curve of MCP-PMA pencil electrode

The constructed electrode was immersed in a standard series of drug solutions ranging from 1.0×10^{-7} to 1.0×10^{-2} mol.L−1. The potential of each solution was recorded, and a calibration graph was created by plotting the potential against the minus logarithm of MCP concentration, as illustrated in Figure 4. The findings are displayed in **Table 2**, which shows that the validation standards were implemented according to the suggestions made by the ICH. It took 43 days for the sensor to start working. The slope of the regression equation remained nearly constant for these days; however, it clearly declined beyond this length.

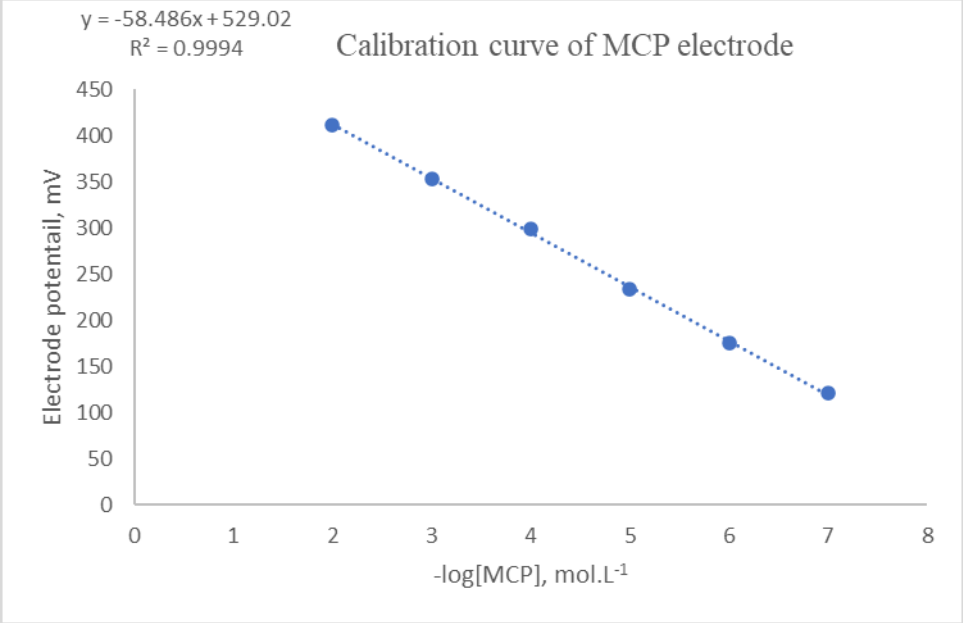

Table 2: Response characteristics and the validation data of the constructed MCP-PMA electrode

parameter	Value
Regression line equation	Emv= -58.486[MCP]+529.02
Slope ± SD (mV.decade^{-1})	-58.486±0.21
Intercept (mV)	529.02
Correlation coefficient	0.9997
Response time (seconds)	21
pH range	2.8-4.7
Linearity range (mol L^{-1})	1.0×10^{-2}–1.0×10^{-7}
Life time (days)	43
Recovery range %	99.41-101.39
Repeatability	1.91
Reproducibility	1.62
Lod (M)	2.1×10^{-7}
Loq (M)	6.9×10^{-7}

Determination of MCP in various samples solution

The fabricated electrode and the double junction calomel reference electrode were immersed separately in the sample solution after its pH reached within the suggested electrode's effective pH range. We determined the relevant concentration using the electrode's regression equations and recorded the corresponding potential. Without prior separation, we could correctly identify the medication in its combined form. The additional excipients did not affect the possible reaction. Table 3 indicates that the proposed approach can accurately determine MCP in its quantitative dose form.

Table 3: Determination of MCP in various pharmaceutical formulations via proposed constructed electrode

Commercial product name	Dosage	Amount found	Recovery%±SD
Metoclopramide tablets Actavis	MCP 10mg	9.95mg	99.5±0.3
Plasil tablets	MCP 10mg	9.98mg	99.9±0.7
Primperan	MCP 10mg	10.02mg	100.2±0.9
PLAZIMIDE injection	MCP 10mg/2mL	9.99mg	99.9±1.5

Conclusion:

A novel method was suggested for electrochemical determination of Metoclopramide hydrochloride. The findings of the developed pencil graphite sensor appear to be significant in terms of detection limit, extended life-time, and selectivity, as demonstrated in this work. Since several published methods exist to identify this combination, it might compete with them. For the determination of the drug in its pure form, laboratory-created combinations, and pharmaceutical formulation, the constructed technique was found to be accurate, exact, and sensitive according to the validation outcomes. Based on the results, it is recommended to use coated pencil graphite electrodes for drug analysis since they provide a strong and adaptable analytical approach, a wide linear dynamic range, and reasonably inexpensive equipment.

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Date Availability

“The datasets used and analysed during the current study are available from the corresponding author on reasonable request.”

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