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Original Research Article

Modified Coated Graphite Electrodes and PVC Membrane Sensor for Potentiometric Determination of Ranitidine Hydrochloride

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Abstract:

Two relatively selective electrodes were fabricated for determination Ranitidine hydrochloride (RNH); first was modified coated graphite electrode (MCGE) and second one was polyvinyl chloride electrode (PVC). Both MCGE and PVC electrodes were based on Ranitidine hydrochloride-phosphomolybdic (RNH-PMA) ion pair and plasticized with di-butyl phthalate (DBP). Both electrodes experience satisfactory sensitivity towards RNH within concentration range of (1.0×10^{-6} - 1.0×10^{-1} and 1.0×10^{-5} - 1.0×10^{-1} M), pH range (3-6 and 3-5) and detection limit (4.6920×10^{-7} and 4.8044×10^{-6} M), Nernstian slope (57.48 and 55.158) mV/decade for MCGE and PVC electrode, respectively. The electrodes can be applied for the determination of RNH in pure solution, pharmaceutical preparation and human fluids (serum and urine) with high accuracy and precision. The methodology (using two electrodes) was fast, simple and economical compared to the rest of the established methods.

Keywords: Modified coated graphite electrode, PVC Membrane Sensor, Ranitidine hydrochloride, Histac.

Introduction

Ranitidine hydrochloride (RNH) is a pale yellow crystalline powder of molecular weight of 350.9 g/mol and chemically it is ((N-[2-[[[5-[(Dimethyl amino)methyl]furan-2- yl] methyl] sulfanyl]ethyl]-N′′-methyl-2- nitroethene-1,1-diamine hydro chlo ride)). The chemical formula is $C_{13}H_{23}N_4O_3SCl$ and its chemical structure is showed in figure (1) [1]. The RNH drug has widely be used for the short-term treatment of duodenal ulcers and for the management of hyperacidity conditions [2]. It can be taken by several ways; such as mouth, muscle injection and vein injection.

It involves; however, side effects, such as pain or burning, headaches, liver problems and a slow heart rate, RNH have been found to be safe when in use at the usual recommend dose [3]. It is official in both BP and USP [1,4]. There have been numerous ways reported for the determination of RNH drug in pharmaceutical and biological samples, such as spectrophotometry [5-7], x-ray [8,9], high- pressure liquid chromatography (HPLC) [10-12], electrochemical method using glass carbon [13], voltammetry [14], conductmetry [15], flow injection [16], differential pulse polarography [17], liquid chromatography [18] and thin layer chromatography [19]. This research characterizes construction, characterizations and applications of PVC and MCGE sensors for determination of RNH in pure, pharmaceutical preparations and biological fluids.

Performance characteristics of both (PVC and MCGE) electrodes have low detection limit, satisfactory selectivity, high sensitivity and fast response.

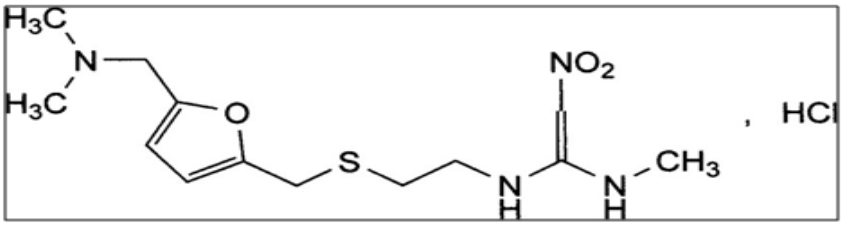

Figure 1: Ranitidine hydrochloride chemical Structure

Experimental

Instrument: Laboratory potentiometric measurements by applying HANNA instruments213 pH- meter, Jenway3310 pH-meter, calomel electrodes Swiss source. Perkin Elmer USA 2400 series II was used for elemental analysis CHN.

Reagents and Materials:

Deionized distilled water was utilized to prepare the stock solutions. The following chemical materials were used in this work: Ranitidine hydrochloride (RNH) (SDI) poly vinylchloride (PVC) (BDH), Dibutyl phthalate (Fluka), Graphite rod (Sony corporation), Tetra hydro furan.(THF) (BDH), phosphomolybdic acid (PMA) (BDH). Histac tablets (150 mg RNH) Sun Pharmaceutical Industries ltd- India was purchased from local pharmacies.

Standard Solution of RNH Drug

A stock solution of RNH drug 0.1 M of was prepared by dissolving 3.509 g in deionized distilled water till 100 mL. By appropriately diluting the drug with deionized distilled water, diluted solutions from 1.0×10^{-7} to 1.0×10^{-1} M of the drug were created.

Pharmaceutical Sample Preparation (Histac 150 mg)

Ten tablets of Histac 150 mg/tablet the total weight of the tablets is 3.084 g were evenly combined after being finely pulverized, (0.7214) g of Histac powder was dissolved in (100) ml of deionised distilled water to obtain 1.0×10^{-2} M.

The volume was then brought up to the mark of volumetric flask with deionised distilled water after the solution had been filtered via filter paper. By using the proper dilution of deionized distilled water, more diluted solutions for Histac were created.

Interfering Ion Stock Solutions

A series of solutions of 1.0×10^{-3} M of each of NaCl, KCl, NaBr, $CaCl_2$, $MgCl_2$, $NaNO_3$, NH_4Cl, Na_2SO_4, and Na_2CO_3 were made by dissolving a portion of these components in 100 ml volumetric flasks using deionized distilled water.

Determination of Drug in Biological Fluids

Pharmaceutical preparation of RNH was determination in biological fluids (urine and serum) using constructed electrodes. In test tube with a tight cover 4.5 ml of serum or urine was added, then 0.5 ml (0.1 M) of the pharmaceutical preparation drug was added, then the tube was shaken for one minute. More diluted solutions can be prepared using deionized distilled water [20].

Preparation of Ion-Pair (RNH-PMA)

The ion-pair RNH-PMA was made by adding 50 mL (1.0×10^{-2}) M of RNH to 50 mL (1.0×10^{-2}) M of PMA, light green precipitate was formed. The product was filtered, rinsed several times with deionized distilled water and allowed to dry for a few days at room temperature.

Construction of Modified Coated Graphite Electrode (MCGE)

MCGE electrode was construction utilizing a pure graphite rod 5.5 cm length and 8.0 mm diameter using a tightly-fitting polyethylene tube. The electrode surface was coated with the active membrane by dunking one end of graphite rod in this mixture [[55 % plasticizer di butyl phthalate (DBP), 30 % poly vinyl chloride (PVC), 10 % ion-pair (RNH-PMA), 5 % zinc oxide nano particle (ZnO) and 10 mL THF]] for several times, letting each time's drying in the air. The other end of the rod was joined with insulated copper wire and connected to pH- meter [21].

Construction of PVC membrane sensor

The first step: The PVC-membrane prepared by [45% of PVC dissolve in a mixture of (5 ml THF + 5 ml butanone), 10% of the ion pair (RNH-PMA) and 45% of the plasticizer DBP] and mixed until a homogenous mixture was formed, followed by pouring into a glass petri dish and left to evaporate for some days to dry at room temperature. A thin layer membrane was formed, then the membrane was carefully raise with special tongs and then cut a circular partlarger diameter than the PVC tube.

The second step: A PVC tube of 5 cm length and 1.5 cm diameter was used, dipping one end in THF solvent, and a circular part formed membrane in the first step was carefully glued to this end.

The third step: Fill the PVC tube with an internal solution with a standard solution of the drug RNH

and dipping it in the RNH drug solution for a period of time with the same concentration of the internal filling solution until it is saturated and the ion exchange process is completed [22].

Results and Discussion

Elementary Analysis (C.H.N)

RNH-PMA is an electro active compounds was used to preparation new electrode. Elemental analysis was carried out to confirm the composition of the ion-pair (RNH-PMA). The obtained results revealed 1:1 composition for [RNH:PMA] ion pair as indicated in table 1.

Table 1: Elemental analysis of the (RNH-PMA) ion pair

Elementanalysis	RNH-PMA		
	% C	% H	% N
Found	5.99	2.80	2.17
Calculated	5.97	2.86	2.15
Formula	$[C_{13}H_{22}N_4O_3SCl][H_3PO_{40}Mo_{12}].\ 24H_2O$		

Calibration Curve and Limit of Detection

The constructed electrodes (PVC) and (MCGE) were calibrated by soaked them with Calomel reference electrode in solutions of RNH drug in the concentration range (1.0×10^{-7} - 1.0×10^{-1})

M. The E (mV) was recorded for each solution, E (mv) versus –log [RNH] was plotted as seen in figure (2). Over the concentration range, the best liner response lies between 1.0×10^{-5} and 1.0×10^{-1}) and (1.0×10^{-6}-1.0×10^{-1}) M with Nernstian slopes of 55.158 and 57.48 mV/decade for PVC and MCGE electrodes, respectively. The values of low detection limit and upper detection limit are 4.8044×10^{-6} and 0.2103, respectively for PVC electrode and 4.6920×10^{-7} and 0.2033 for MCGE electrode demonstrating the excellent sensitivity of the investigational sensors and their use in the of determination of traces RNH and the (table 2) shows the comparison between the detection limit of the prepared electrodes with other electrodes.

Table 2: Detection limit of prepared electrodes with another electrode

Electrode type	detection limit
MCGE	4.6920×10^{-7}
PVC	4.8044×10^{-6}
MCPE [23]	1.0×10^{-6}
Ra-TPB [24]	1.26×10^{-5}

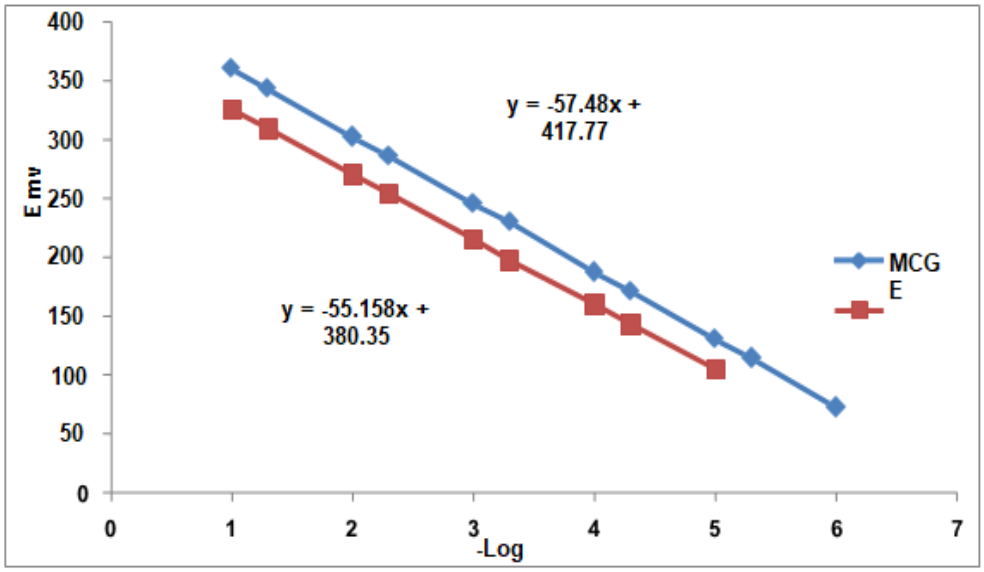

Figure 2: Calibration curve of RNH using PVC and MCGE electrodes

pH Effect

The pH effect of fabricated electrodes was studied by immersing the electrodes in a certain concentration of RNH (1.0×10^{-4}) M drug at various pH values (1-8).

The pH value was gradually decreases or increases upon addition of tiny portion of diluted HCl and/or

NaOH solutions and the potential was recorded. It is shown in figure (3) that the optimum pH range lies (3-5) for PVC electrode and the pH range of (3-6) was applied for MCGE electrode. It should be noted that the electrodes response decreases when pH values exceeds 5 or 6, indicating that the membrane has responded to hydroxyl ions (OH [25]. The electrode response decreases when pH is less than 3, seeming that the membrane respond tohydrogen ions (H^+) [26].

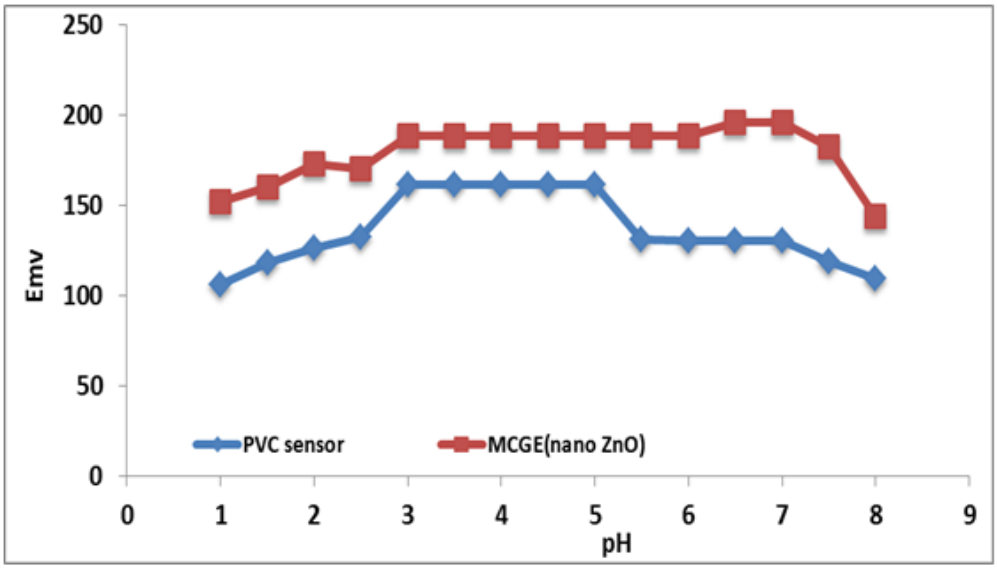

Figure 3: Effect of pH for PVC and MCGE electrodes

Temperature Effect: By altering the temperature of the pure drug solution from 5 to 70°C for a concentration of (1.0×10^{-4}) M RNH, the change in potential was recorded. Plots were made showing the relation between temperature and reported potential. According to the findings in figure 4, the ideal working temperature for both electrodes is between 10 and 50°C. These values demonstrate stability thermally of both electrodes without any change in the Nernstian slope.

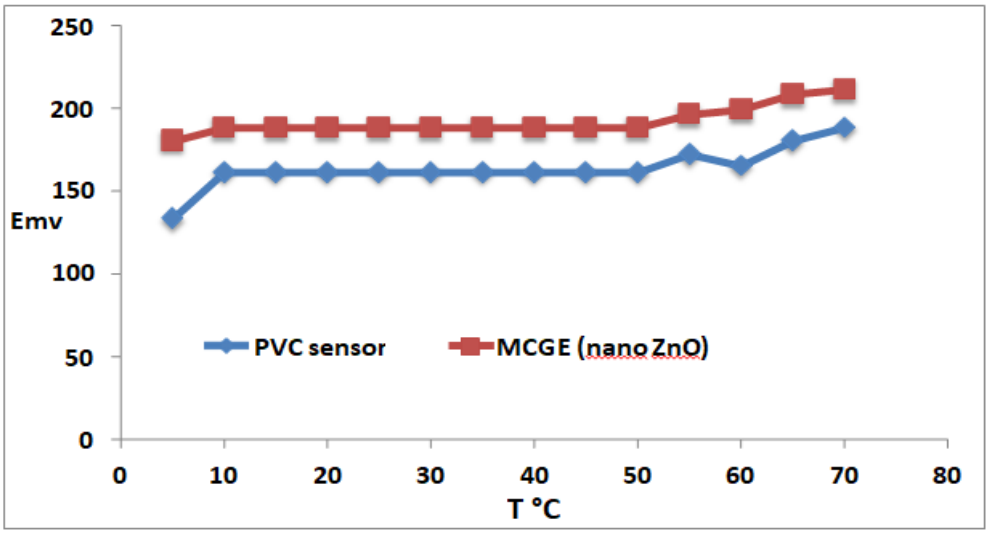

Figure 4: Effect of temperature on the response of PVC and MCGE electrodes

Selectivity of the Studied Sensors

Selectivity coefficients of the MCGE and PVC electrodes were determined by the separate solution method [27].

This method involves measuring the potential of a newly fabricated electrode in two separate solutions with the same concentrations of (RNH) and an interfering ion (1.0×10^{-3}) M. where the following equation was used: log K= (E_2– E_1)/S where E_1 is the electrode potential of RNH solution E_2 the

electrode potential of the interfering ion, S is the calibration curve's slope. This demonstrated that the constructed electrodes respond weakly to the interfering ions when the K value is less than 1. Table (3) presents the findings from the electrodes (MCGE and PVC) where both possess high degree of selectivity for the RNH.

Table 3: K value of both PVC and MCGE sensors

Interferingion	$K^{pot\ i,\ j}$	
	PVC sensor	**MCGE**
Na^{1+}	7.165×10^{-1}	5.900×10^{-1}
K^{1+}	7.001×10^{-1}	6.009×10^{-1}
NH_4^{1+}	1.098×10^{-1}	2.222×10^{-1}
Ca^{2+}	9.97×10^{-2}	1.734×10^{-1}
Mg^{2+}	9.22×10^{-2}	7.90×10^{-3}
Cl^{1-}	3.211×10^{-1}	1.911×10^{-1}
Br^{1-}	2.900×10^{-1}	2.055×10^{-1}
NO_3^{1-}	4.542×10^{-1}	3.000×10^{-1}
CO_3^{2-}	3.777×10^{-1}	4.0103×10^{-1}
SO_4^{2-}	1.089×10^{-1}	9.44×10^{-2}

Life Time

Potentiometric measurements were taken several times weekly to determine the stability of the (PVC) and (MCGE) electrodes. Utilizing RNH standard solutions for potentiometric calibration on various days, the electrodes' performance was evaluated. The findings indicate that the potential value of the (PVC) electrode can be used for 21 days without experiencing a remarkable change. While there is a change in Nernstian slope after 45 days for (MCGE) electrode. It is clear that the (ZnO nano particles) in (MCGE) electrode increases the life time of the electrodes when compared with the unmodified electrode (PVC) electrode [28].

Response Time

It is the time needed to attain the steady state with a potential alter of ±1 mV starting at the time when the constructed electrodes make contact with the reference electrode for the RNH solutions. For (1.0×10-1 - 1.0×10-5) M RNH solutions, the electrodes' response times were acquired. It is found that the shortest and longest response times of (MCGE) electrode was 22 s and 50 s for 1.0×10-5 and 1.0×10-1 M and for (PVC) electrode was 26 and 56 s for 1.0×10-5 M and 1.0×10-1 M, respectively as shown in figure 5. The findings indicate that the response times increases as concentration increases; thereby, this is explained that the more time lasts to attain equilibrium between the RNH-PMA in the membrane and the external drug solution when that concentration was high [29].

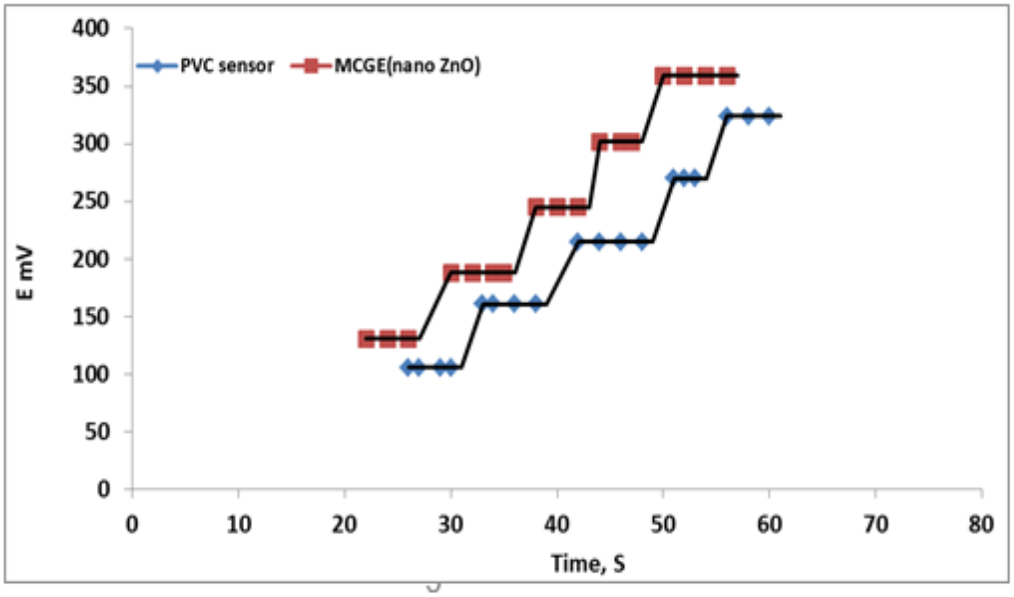

Figure 5: Response time of PVC and MCGE electrodes

Precision and Accuracy: Pure drug was evaluated, and each solution was repeated five or six times in order to assess the accuracy and precision of the suggested approach. The relative standard deviation (RSD%) and relative error (RE%) percentages were used to calculate precision and accuracy. RE% and RSD% have values that are not greater than (-2.3303) and (1.1498), respectively. These methods have acceptable precision and accuracy, according to the results (table 4).

Table 4: Statistical data for determinations of RNH in pureusing (PVC) and (MCGE) electrodes

Sample (pure drug)	Taken [RNH]M	Found [RNH] M	%Recovery	%RE
PVC	1×10^{-1}	9.9201×10^{-2}	99.20	-0.79
	1×10^{-2}	9.9858×10^{-3}	99.85	-0.14
	1×10^{-3}	1.0052×10^{-3}	100.51	0.51
	1×10^{-4}	1.0118×10^{-4}	101.18	1.18
	1×10^{-5}	1.0185×10^{-5}	101.85	1.85
%Mean ± SD	100.52 ± 1.0483			
n	5			
Variance	1.0989			
%RE	0.5234			
%RSD	1.0428			
MCGE	1×10^{-1}	9.8845×10^{-2}	98.84	-1.15
	1×10^{-2}	9.6807×10^{-3}	96.80	-3.19
	1×10^{-3}	9.8686×10^{-4}	98.68	-1.31
	1×10^{-4}	9.6652×10^{-5}	96.65	-3.34
	1×10^{-5}	9.8528×10^{-6}	98.52	-1.47
	1×10^{-6}	9.6497×10^{-7}	96.49	-3.50
%Mean ± SD	97.66± 1.1230			
n	6			
Variance				
%RE				
%RSD	1.1498			

Analytical Applications: In order to determine the presence of Ranitidine hydrochloride in human fluids (urine and serum) and in pharmaceutical tablets (Histac), a direct and standard addition method is used. Table 5 demonstrates that the constructed selective electrodes were successful in evaluating the amount of RNH in tablet pharmaceutical and biological fluid.

Table 5: Statistical Data for RNH measurements in pharmaceutical andbiological samples utilizing (PVC) and (MCGE) electrodes

Sample	Taken [RNH] M	Found [RNH]M	%Recovery	%RE
	Histac 150 mg (Direct method)			
PVC	5×10^{-2} 5×10^{-3}	5.0868×10^{-2} 5.1204×10^{-3}	101.74 102.41	1.73 2.41
MCGE	5×10^{-2} 5×10^{-3}	5.0026×10^{-2} 5.0998×10^{-3}	100.05 101.99	0.05 1.99
Sample	Histac 150 mg (standard Addition)			
PVC	2×10^{-4}	2.0268×10^{-2}	101.39	1.39
MCGE	2×10^{-4}	3.0444×10^{-2}	102.21	2.21
Sample	Urine			
MCGE	2×10^{-3}	2.0296×10^{-3}	101.48	1.48
PVC	2×10^{-3}	2.0438×10^{-3}	102.19	2.19
Sample	Serum			
MCGE	2×10^{-3}	1.9893×10^{-3}	99.46	- 0.54
PVC	2×10^{-3}	1.9603×10^{-3}	98.01	- 1.99

Robustness and Ruggedness: By switching the aqueous solution to ethanol, the (MCGE) and (PVC) robustness methods were examined. Using a different pH-meter model (HANNA instruments 213), the robustness was evaluated. The results are shown in figure (6 and 7) [20,21].

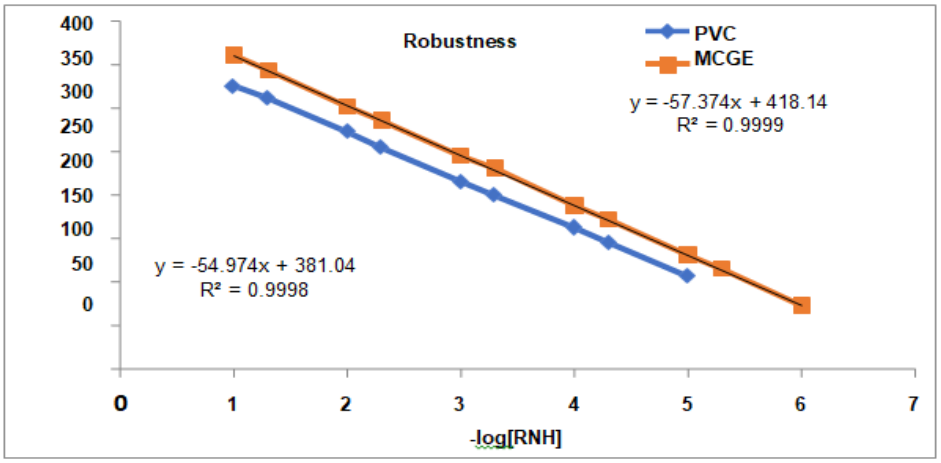

Figure 6: The impact of ethanol on the performance of the PVC and MCGE electrodes

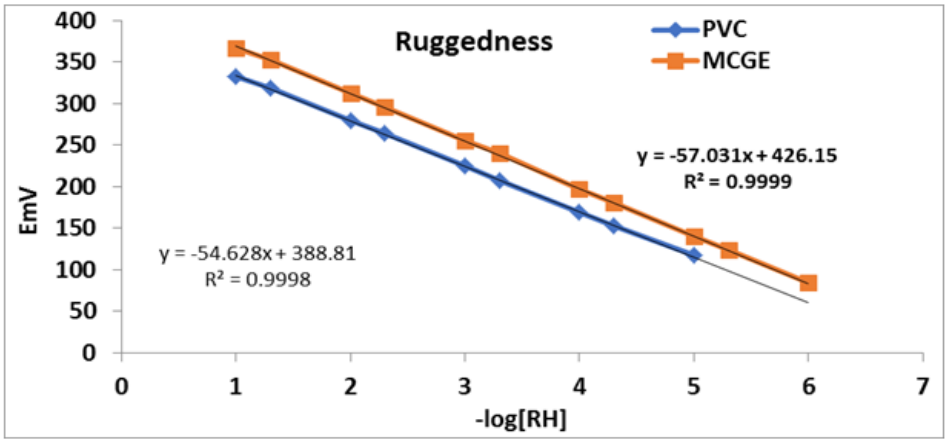

Figure 7: The effect of ruggedness of PVC and MCGE electrodesby using another model of pH-meter

Evaluation of the Results: The t-test and F-test is used to find out the validity and success of applying the constructed electrodes for determination pharmaceutical preparations, the result in (table 6) indicate success of the constructed electrodes and there were no significantly different between standard and suggested method.

Table 6: F-test and t-test for fabricated electrodes

Electrode type	%Mean ±SD	n	Calculated t-test	Tabulated t-test for %95	Calculated F-test	Tabulated F-test for %95
MCPE	100.68 ± 1.1678	6	-0.0335	2.57	1.0960	5.19
PVC	100.52 ± 1.0483	5	0. 5862	2.78	1.2267	6.39
Standard method* (HPLC)	99.32± 0.7114	5	0.00	0.00	0.00	0.00

Conclusions

- Ion selective electrodes were utilized in the present method for determining RNH in pharmaceutical formulations.
- The constructed electrodes are eligible for quantifying RNH in the pure form, pharmaceutical preparations and biological fluids.
- This is based on the fact that several common electro analytical parameters of the constructed electrodes are satisfactory.
- The statistical evaluations indicate that both electrodes are qualified for implementing in medicine field.

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