Innovative transducers based on molecular imprinting for selective potentiometric determination of trazodone hydrochloride in pure and pharmaceutical preparations

Abstract
Solid contact potentiometric sensors for trazodone hydrochloride based on host-guest interactions and potentiometric transduction has been designed and characterized. The sensors are produced via preparation of trazodone hydrochloride imprinted polymer particles using methacrylic acid and acrylonitrile as functional monomers. Subsequently, the leached molecularly imprinted polymer (MIP) particles were dispersed in dioctylphthalate and embedded in polyvinyl chloride matrix. The results of the MIP sensors show that they offered an improved electrode slope, pH wide range and an extremely prolonged life time reaching 4 months in comparison to conventional ion-exchangers reported in literature. Significantly, these simple and cost-effective potentiometric sensors promote accuracy, precision, good reproducibility, selectivity, sensitivity and long-term stability. There is no interference from any common excipients and additives present in pharmaceutical preparation so the proposed methods promote the global use of appropriate quality, safety assaying of pharmaceutical dosage form in tablets.

Keywords: molecularly imprinted polymer, methacrylic acid, acrylonitrile, trazodone hydrochloride

Introduction
Trazodone hydrochloride (TZ), (2-[[3-[(4-(3-chlorophenyl)piperazin-1-yl)propyl]-2H,3H-[1,2,4]triazolo[4,3-a]pyridin-3-one]), is a well-known chemical compound that is used for treatment of anxiety disorders and depression that belongs to a selective serotonin reuptake inhibitors. TZ dissolves in methanol at 25 mg/mL to yield a clear, colorless solution. Solubility in water was found to be 50 mg/mL, with heating to yield colorless solution. British Pharmacopoeia recommended potentiometric non-aqueous titration for the determination of trazodone hydrochloride using perchloric acid as a titrant where the United States Pharmacopeiamethod was HPLC. Literature survey revealed that several techniques have been developed for the quantitative determination of trazodone hydrochloride in pharmaceutical formulations include spectrophotometric methods and different chromatographic methods including; HPLC, capillary gas chromatography, high-performance liquid chromatography–tandem mass spectrometry, high performance thin layer chromatography, and only two spectrofluorimetric methods have been reported.

Charged carriers (membrane-active recognition) containing the target ion had been an important role over the past decades greatly effect on potentiometric transduction, also neutral macrocyclic compounds host drug had the same role, but the design of MIPS as sensing materials under optimized condition which are complementary and in harmonization manner to the charge and size of a template and after removal of the particular ion and persist thus enhancing the selectivity of the sensing unit due to its ability to rebind template or target by more selective interactions binding sites.

Molecular recognition is depending on many biological mechanism processes for example, enzymes binding substrates, and hormone receptors with their selective hormones or antibodies with their recognized antigens. Hence, the development of synthetic, tailor-made receptors capable of mimicking the template of interest with extremely exclusive selectivity and high affinity continues to be one of these synthetic receptors is molecularly imprinted polymer; these materials referred to as biomimetic.

Besides their strong positive impressive molecular recognition properties, they are resistance to many chemical environments, use in both aqueous and non-aqueous media, good shelf-life, inexpensive and can be used again without momentous deterioration to their properties.

The self-assembly of monomeric species around the template using noncovalent interactions in the recognition of the imprinting species, ensure the MIPS the simplest method of producing selective polymers. The interaction between the analyte and the monomers through the macro-porous network of polymer can be single or multiple points in nature. It involves host-guest complexes such as electrostatic, hydrophobic, dipole-dipole, π-π and hydrogen bonding. The most important interaction is electrostatic followed by hydrogen-bond formation. The formation of multiple bonds between the template and the macro-porous network of the monomers has the advantage of highly selective and excellent ligand recognition that mimics biological interactions. Furthermore, the comparison of the selectivity of MIPS in related tononimprinted polymers (NIPs) is higher due to the multiple interaction or contact between the analyte and the polymer.

In the present work, we prepare simple and sensitive molecularly imprinted polymer (MIP) membranes to quantify trazodone...
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hydrochloride in pure and pharmaceutical preparations where highly selective separation and excellent ligand recognition are obtained by macro-porous network of polymers that imitate closely to biological interactions by forming multiple bonds between the template and the monomers. The advantages of molecularly imprinted polymer include the diverse range of host-tailed polymer modifications available and the convenience in handling.

Experimental

Apparatus

pH-meter Jenway 3510 (Engand) containing Ag/AgCl reference electrode connected with the drug imprinted sensor, Bandelinononorox, Rx 510 S, magnetic stirrer (Hungarian). Shimadzu UV-Vis. 1650 Spectrophotometer (Japan). Centrifuge (TDL-60B) with max speed 6000 r/min. Bench top (Hunan, China, Mainland). The MIPs and NIPs electrodes surface morphology were examined by scanning electron microscopy (SEM) (JEOL JSM-5500LV). Shimadzu UV-Vis (Japan). Shimadzu UV-Vis. 1650 Electrode connected with the drug imprinted sensor, Bandeliononorox, Rx 510 S, magnetic stirrer (Hungarian).

Reagents and materials

All reagents were of the analytical grade and double distilled water was used throughout the experiments. Trazadone hydrochloride powder was kindly supplied by Egyptian International Pharmaceutical Industries Company (EIPICO) 10th of Ramadan City, Egypt. Its purity was 100.45±0.25 % (Batch No. A0967913). Trittico® tablets, labeled to contain 100 mg of trazodone hydrochloride per tablet manufactured by Egyptian International Pharmaceutical Industries Company (EIPICO) 10th of Ramadan City, Batch No. 1602039 and purchased from the local market. Dioctylphthalate (DOP) and Polyvinylchloride (PVC, relative high molecular weight) (Fluka, Germany). Methacrylic acid (MAA), acrylonitrile (AN), ethyleneglycoldimethacrylate (EGDMA) and azobis-isobutynitrilite (AIBN) were obtained from (Sigma-Aldrich, Germany). calcium chloride, ammonium chloride, sodium chloride, nickel chloride hexahydrate, magnesium chloride, citric acid, urea, glucose, glycine and sucrose (Prolabo, Paris, France).

Standard drug solutions

Stock standard drug solution (10⁻²mol L⁻¹) was prepared by dissolving 408.32 mg of trazodone hydrochloride in double distilled water and the volume was completed to 100 mL with the same solvent. Other solutions (1.0 x10⁻¹-1 x10⁻²mol L⁻¹) were prepared by serial dilution from the stock solution.

Preparation of molecularly imprinted polymers

TZ-imprinted polymers were made by thermal initiated polymerization within a 25 mL thick-walled glass tube. The polymerization mixture composed of 190 mg of TZ as a template, 0.45 mL of the monomer, 4.7 mL of EGDMA and 35 mg of AIBN were dissolved in 5 mL of water (as porogenic solvent). The solution was sonicated for 10 min and degassed with nitrogen for 5 min. The polymerization was performed under 70°C for 120 min. Non-imprinted polymer beads (NIPs) were prepared similarly but without the template. The resulting MIPs were ground using a mortar and pestle, the particles were sieved to obtain particles size less than 45 mm. Finally the particles were washed with methanol: acetic acid (9:1) several times to remove interfering compounds arising from the synthesis (templates and unreacted monomers). The removal of template was confirmed by UV/Vis measurements at 247 nm. All polymers either imprinted or non-imprinted were left to dry at ambient temperature prior to use. Scheme 1 (supplied in supplementary materials as Scheme 1) represents the mechanism of polymers preparation.

Scheme 1 Protocols for preparation of the molecularly imprinted polymer and its recognition towards Trazodone hydrochloride.

Electrode fabrication

190 mg of PVC powder, 350 mg of DOP as plasticizer and 30 mg of each polymer were used to prepare several polymeric membranes. The mixtures were separately stirred and dispersed till homogeneity in 5.0 mL THF in a 5-cm glass Petri-dish covered with a filter paper and left to stand overnight at room temperature allowing the evaporation of the solvent. 12 mm-discs were cut with a cork borer and glued to the end of 10mm tygon tubes using THF. Then, filled with equal volumes of 1.0x10⁻³mol-¹TZ and 1.0x10⁻³mol-¹KCl as an internal solution. Conditioning of these sensors was done by soaking in 1.0x10⁻³mol-¹TZ solutions for 24 hours before use. Storage of sensors was done in the previous solutions when not in use but in distilled water in between measurements.

Procedure

A series of TZ solutions covering the concentration range of 10⁻¹-10⁻¹⁰mol L⁻¹ were prepared under optimum conditions. The sensor and the reference electrode were immersed in the solution and the electro motive force (e.m.f) value was recorded at 25±1°C, after each addition. The values were plotted versus negative logarithmic value of the drug concentration (p drug).

Analytical applications

Pharmaceutical sample analysis

Ten Trittico® tablets were accurately weighed and finely powdered, then a quantity equivalent to 408.32 mg of trazodone hydrochloride was shaken four times with 15 mL of water for 20 minutes then filtered into 100- mL volumetric flask and the volume was adjusted to the mark with water to obtain a concentration of (10⁻⁴mol L⁻¹). The
solution was analyzed using the proposed procedure mentioned above. The standard additions technique was applied by adding certain known volumes (10^{-3} mol L^{-1}) of pure drug solution to 25 mL aliquot samples (10^{-3} mol L^{-1}) of pharmaceutical sample.\textsuperscript{35–38} The change in mV reading was registered for each regular addition and used to estimate the concentration of the drug in sample solution, using Equation 1.

\[
c_n = c_s \left( \frac{V_n}{V_n + V_0} \right) \left( \frac{(\Delta E)}{10^5} - \left( \frac{V_0}{V_n + V_0} \right) \right)
\]

where, \(c_n\) and \(V_n\) are the concentration and volume of solution to be determined, \(V_0\) and \(C_s\) are the volume and concentration of the standard solution added to the sample under test, respectively. \(\Delta E = (E_x - E_s)\) is the change in potential caused by the addition of each increment where \(E_s\) = electrode potential (mV) in the pure sample solution and \(E_x\) = electrode potential after the addition of standard and \(S\) is the slope of the calibration graph.

**Binding experiments**

Binding experiments were performed by addition of 20.0 mg of MIP and NIP free from a template and grinded particles in contact to 10.0 mL TZ aqueous solutions ranging from 5 to 80 μg/mL. The solid phase was precipitated and separated by centrifugation (4000 rpm, 25 min.) after standing the solutions overnight at room temperature. The supernatant clear solution was used to analyze the concentrations of free TZ by UV spectrophotometry at \(\lambda_{max} = 247\) nm\textsuperscript{39, 40} using calibration graph with TZ standard solutions. The concentration of free TZ was subtracted from the initial TZ concentration in order to obtain the amount of TZ bound to the polymers. The binding capacity (Q, μmol g^{-1}) for MIP and NIP are calculated according to the following equation:\textsuperscript{41}

\[
Q = \frac{\text{μmol(TZ bound)}}{g_{\text{MIP}}} = \frac{(c_i-c_f)V_s}{M_{\text{MIP}}} \times 1000
\]

Where Q is binding capacity of MIPs or NIPs (μmol g^{-1}), \(C_i\) the initial TZ concentration (μmol mL^{-1}), \(C_f\) the final TZ concentration (μmol mL^{-1}), \(V_s\) the volume of tested solution (mL) and \(M_{\text{MIP}}\) the mass of dried polymer (mg). The calculated Binding capacities were used to plot the binding isotherms. The scatchard analysis was subsequently used to evaluate the binding characteristics using the scatchard equation:\textsuperscript{42–44}

\[
\frac{Q}{C_f} = \frac{Q_{max} - Q}{K_d}
\]

Where Q is the binding capacity, \(C_f\) is the free analytical concentration at equilibrium (μmol/ml), Qmax is the maximum apparent binding capacity, and \(K_d\) is the dissociation constant at binding site. The equilibrium dissociation constant is calculated from the slopes and the apparent maximum binding capacity from the y-intercepts in the linear plot of Q/Cf versus Q.

**Results and discussion**

**Characterization of the MIP particles**

**Fourier Transform Infrared (FTIR) analysis**

FTIR spectra give the fundamental analytical base for rationalizing the mechanism of recognition during the imprinting process and study the types of interaction between the monomer and template molecule during pre-polymerization complex formation and the template incorporation into the imprinted polymer during rebinding.\textsuperscript{45, 46} Therefore, FTIR spectra analysis has been used in our study for polymer characterization. FTIR spectra of TZ has characteristic bands at 753, 1352, 1704, 2942 and 3076 cm\(^{-1}\) which are assigned to C-Cl, C-N, C=O, C-H\textsuperscript{39–41} and C-H aromatic, MAA has characteristic bands at 1639, 1729, 2989 and 3474 cm\(^{-1}\) which related to stretching vibration bands of C=C, C=O, C-H\textsuperscript{39–41} and weak broad of OH group. The AN has characteristic peaks at 960 cm\(^{-1}\) which related to C-H stretching (out of plane) of the butadiene double bond, nitrile stretching band (C≡N) at 2278 cm\(^{-1}\) and aliphatic –CH\textsubscript{2} stretching at 2997 cm\(^{-1}\). Fortunately, the interaction between TZ and all monomers (MAA or AN) has shifting in characteristic bands for example, in case of the interaction between TZ and MAA monomer, the weak-OH band becomes a very weak broad bonded OH peak and shifted to 3513 cm\(^{-1}\), C-H stretching at 2990 cm\(^{-1}\), shifting in aromatic ring to 1468 cm\(^{-1}\) and shifting in C=O to 1730 cm\(^{-1}\), where in case of AN, an appearance of stretching C=O at 1277 cm\(^{-1}\) and stretched C-Cl band at 761 cm\(^{-1}\) (supplied in supplementary materials as Figure S 1 & Figure S 2).

\[\text{Figure S1 FTIR spectra of TZ (A), NIP-MAA (B), MIP-MAA before template removal (C).}\]
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SEM analysis

The scanning electron microscopy (SEM) can analyze the surface morphology for all prepared polymer beads. Appreciable differences in the morphology of MIPs and NIPs were noticed as shown in Figure 1. The shape and morphology of polymer beads had great impact on the adsorption efficiency. The MIPs had rough morphology with small pores. The NIPs had identical, regular shape and smooth macro-porous network, which is probably attributed to the absence of specific binding sites in the polymers. The high percent of pores in the imprinted polymers were probably due to the imprinting process or the introduction of TZ during polymerization and removal of the template.

Equilibrium adsorption experiment

The calculated Binding capacities were used to plot the binding isotherms Figure 2. It can be seen from the adsorption data that the binding capacity of MIPs and NIPs increased with the increasing of the initial concentration of TZ, reaching to saturation at higher concentrations. All the binding capacity data of MIPs were always clearly higher than those of NIPs under the same conditions. This suggests the higher binding ability of MIPs to TZ than that of NIPs probably due to large number of binding sites in MIPs thus increasing its sensing properties over NIPs.

Sensor analytical features

Featuring of the prepared MIPs and NIPs were tested as sensing materials for their main analytical characters according to IUPAC recommendations. The potential response obtained with the sensors prepared with TZ-MIPs membranes and their blank membranes were given in Figure 4. Sensors based on MIP/MAA and MIP/AN membranes displayed cationic responses of 57.95±1.3 and 59.35±0.8 mV/decade with lower detection limits of 8.6×10⁻⁶ and 5.82×10⁻⁶ mol L⁻¹, respectively. NIPs membrane based sensors didn’t show linear response in all range of work concentration. These results suggested that TZ recognition was made solely on the tailored-cavities of each polymer, so that, from equilibrium adsorption experiment and linearity range results, the only MIPs were chosen for further study.

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Activation of the surface membrane of freshly prepared electrodes is very important to form an infinitesimal thin gel layer at which ion exchange occurs, and that happened by soaking them into stock solution at different times depending on diffusion and equilibration at the interface to obtain the best preconditioning process. Establishment of fast equilibrium is certainly a sufficient condition to get a fast potential response. For the present electrodes, the presoak times were 0, 0.5, 12, 24, 36 and 40 hours with optimum slopes 57.95 and 59.35 mV/concentration decade for sensor MIP-MAA and MIP-AN sensors respectively, and usable concentration ranges from $1 \times 10^{-5}$ to $1 \times 10^{-2}$ at 24 hours presoaking time. Figure 5 represents the effect of soaking on MIPs electrodes.

Effect of pH

The effect of pH of the test solution, $(10^{-4}$ and $10^{-3}$ mol L$^{-1}$ TZ) for MIPs on the electrodes potentials was investigated. The variation in potential with pH change was followed by addition of small volumes of hydrochloric acid and sodium hydroxide (0.1 mol L$^{-1}$) to the test solutions. Figure 6 shows the variation in the potential with pH using a test solution $(10^4$ and $10^3$ mol L$^{-1}$ TZ) as representative curves. At pH values lower than 4.0 the potential readings increase slightly, the increase in emf is most apparently accounted for the diffusion of the hydronium ions into the membrane surface. At pH values higher than 8.0, the decline in potential readings is attributed either to the diffusion of hydroxyl ions into the gel layer of the membrane or to the deprotonation of TZ in the solution leading to a continuous decline in its concentration so it is evident that the electrode does not respond to pH changes in the range 4.0-8.0.

Selectivity

The influence of some inorganic cations, sugars and amino acids on the TZ-electrodes was studied. The selectivity coefficients can be estimated by the $K^{separate}$ solution method for inorganic cations species using the following equation:

$$K^{separate} = \frac{[TZ]_{solution}}{[TZ]_{membrane}}$$

**Figure 3 (A)** The results of scatchard analysis for NIP-MAA and NIP-AN and (B) for MIP-MAA and MIP-AN.

**Figure 4** Potentiometric response of TZ membrane sensors (EMF) vs. -log ([TZ]).

**Figure 5** Effect of soaking time on the response of different MIPs.

**Figure 6** Effect of pH on the response of different MIPs.

Selectivity

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Linearly

The calibration graphs under the described experimental conditions for the method were constructed by plotting the potential reading versus negative logarithmic drug concentrations in mole per liter. The regression plots were found to be linear over the range of $10^{-5} - 10^{-2}$ mol L$^{-1}$ the linear regression equations for the graphs were:

$$E = -57.95 log[c] + 214.5 \quad (r = 0.9993), MIPs-MAA$$

$$E = -59.35 log[c] + 226.15 \quad (r = 0.9998), MIP-AN$$

Where $E$ is the potential difference, $C$ is the drug concentration in mole per liter and $r$ is the correlation coefficients. Linearity ranges, regression equations, intercepts, slopes and correlation coefficients for the calibration data were summarized in Table 2.

**Table 2** Electrochemical response characteristics of the proposed MIPs sensors

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MIP-MAA</th>
<th>MIP-AN</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLOPE(mV/decade)</td>
<td>-57.95</td>
<td>-59.35</td>
</tr>
<tr>
<td>Intercept(mV)</td>
<td>214.5</td>
<td>226.15</td>
</tr>
<tr>
<td>Correlation coefficient ($r$)</td>
<td>0.9993</td>
<td>0.9998</td>
</tr>
<tr>
<td>LOD(M)</td>
<td>$7.3 \times 10^4$</td>
<td>$6.4 \times 10^4$</td>
</tr>
<tr>
<td>Response time(sec.)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Isotonic coefficient (V/°C)</td>
<td>0.0016</td>
<td>0.00165</td>
</tr>
<tr>
<td>Working pH range</td>
<td>4-8</td>
<td>4-8</td>
</tr>
<tr>
<td>Concentration range (mol L$^{-1}$)</td>
<td>$10^{-5} \text{ to } 10^{-2}$</td>
<td>$10^{-2} \text{ to } 10^{-1}$</td>
</tr>
<tr>
<td>Stability(months)</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Accuracy (%R)</td>
<td>98.12</td>
<td>99.62</td>
</tr>
<tr>
<td>Precision (%RSD)</td>
<td>0.943</td>
<td>0.656</td>
</tr>
<tr>
<td>Robustness ($\text{Mean} \pm \text{RSD}$)</td>
<td>99.33±1.112</td>
<td>100.32±0.764</td>
</tr>
</tbody>
</table>

Limit of detection (LOD)

The limit of detection and quantification were estimated and expressed by LOD = 3 $\sigma$ / S, where $\sigma$ is the standard deviation of the response of the intercepts of regression lines and S is the slope of the calibration curve. The values listed previously in Table2, indicate that the proposed MIPs sensors were sensitive to detection of low concentrations of TZ.

Accuracy

The accuracy of the proposed potentiometric method for the determination of TZ was investigated. The results summarized in Tables 2 show that the proposed method is an accurate one, as indicated by the percentage recovery values. Accuracy was also determined by application of standard addition technique, where the mean percent recoveries of pure TZ±% RSD were 99.20±1.672 and 99.97±1.415 for MIP-MAA and MIP-AN sensors respectively, as shown in Table 3 which indicates no matrix interference.
Table 3 Recovery study of TZ by standard addition technique using the proposed sensors

<table>
<thead>
<tr>
<th>Pure added x10^4</th>
<th>Tablet taken x10^3</th>
<th>Pure found x10^4</th>
<th>% Recovery</th>
<th>Pure added x10^4</th>
<th>Tablet taken x10^3</th>
<th>Pure found x10^4</th>
<th>Recovery %</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIP-MAA</td>
<td></td>
<td></td>
<td></td>
<td>MIP-AN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.5</td>
<td>0.98</td>
<td>98</td>
<td>1</td>
<td>0.5</td>
<td>0.99</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>1.94</td>
<td>97</td>
<td>100.67</td>
<td>2</td>
<td>1.96</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3.02</td>
<td>99.5</td>
<td>100.83</td>
<td>3</td>
<td>3.04</td>
<td>101.33</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3.98</td>
<td>100</td>
<td>100.86</td>
<td>4</td>
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<td></td>
</tr>
<tr>
<td>6</td>
<td>6.05</td>
<td>100.83</td>
<td>100.5</td>
<td>6</td>
<td>6.06</td>
<td>101</td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>99.2</td>
<td>99.97</td>
<td></td>
<td>%RSD</td>
<td>1.672</td>
<td>1.415</td>
<td></td>
</tr>
</tbody>
</table>

Table 4 Statistical comparison for the results obtained by the proposed MIPs sensors and the official method

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MIP-MAA</th>
<th>MIP-AN</th>
<th>Official method*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Mean (%R)</td>
<td>99.4</td>
<td>99.69</td>
<td>99.14</td>
</tr>
<tr>
<td>SD</td>
<td>0.673</td>
<td>1.048</td>
<td>0.736</td>
</tr>
<tr>
<td>Variance</td>
<td>0.453</td>
<td>1.098</td>
<td>0.541</td>
</tr>
<tr>
<td>Student's t-test</td>
<td>0.283</td>
<td>1.529</td>
<td>(2.306)**</td>
</tr>
<tr>
<td>F-value</td>
<td>1.194</td>
<td>2.029</td>
<td>(6.338)**</td>
</tr>
</tbody>
</table>

*official method (HPLC method using octadeicylsilane column and water=0.01 M Ammonium phosphate buffer pH 6.0 (60:40) as mobile phase).

**The values in parenthesis are the corresponding tabulated t and F values at P= 0.05.

Precision

The intra- and inter-day precision was estimated by assaying freshly prepared solutions of analyte in three different concentrations in triplicate on the same day and on three different days, respectively using the proposed potentiometric method. The repeatability (intra-day) and intermediate precision (inter-day) of the results obtained by means of the proposed procedures were studied and the results indicated high precision of the proposed procedure and confirmed the suitability for quality control of TZ Table 2.

Table 4 Statistical comparison for the results obtained by the proposed sensors.

<table>
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Robustness

The robustness of the proposed method give us an indication about analytical procedure trusty worth can be investigated by measuring the capacity of the method keeps unaffected by even a small change in method parameters conditions such as pH (±0.1) and soaking time (±2 min.), only one parameter had been changed where the other conditions were kept constant, no defined changes were noticed in the obtained results, assuring robustness of the procedure.

Application

The proposed method was applied to the quantitative analysis of TZ in pharmaceutical preparation. These results explain that the proposed methods had acceptable precision and accuracy and therefore can be utilized for the determination of TZ in pure and pharmaceutical preparations without any interference. Statistical evaluation of the results of analysis of TZ in trittico tablets by the proposed sensors and the USP official method showed that there is no significant difference between the proposed and official method in terms of F- and t-test values as shown in Table 4.

Conclusion

The optimized proposed potentiometric sensors using molecularly imprinted polymers (MIPs) used for determination of trazodone hydrochloride in pure and dosage form without prior separation or derivatization steps. MIPs increase the selectivity and sensitivity of the polymeric membrane sensors by increase the number of conjugation and interaction sites. The results showed that the method is a simple, sensitive, easy-to-handle, and rapid for the determination of TZ in pure and pharmaceutical preparations with good precision, accuracy, selectivity and very low detection limit which indicate that these methods are suitable for the routine determination of the drug in quality control laboratories without interference from other ingredients.

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Conflict of interest

None.

References


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