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# ANALYTICAL STUDY OF SOME ANTI-HISTAMINIC DRUGS

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**Aim of the work** The aim of the present work is to develop analytical methods (potentiometric and spectrophotometric methods) for study and quantitative determinations of some anti-histaminic drugs [hydroxyzine hydrochloride (HYZ), meclizine hydrochloride (MOZ) and cinnarizine (CIZ)]. The present thesis comprises of three chapters: Chapter (1) Contains two parts: The first part includes general introduction concerning theoretical bases of the general properties of different types of ion selective electrodes and great attention was given to the applications of ion selective electrodes in pharmaceutical analysis. Also include basic spectrophotometry, theory, concepts and applications. The second part gives a literature survey of the previous studies for the analysis of the studied drugs including spectrophotometric, potentiometric, chromatographic, and electrophoresis methods. Chapter (2) Contains two parts: The first part is experimental part for ion selective electrode which dealing with the materials, reagents and instruments used as well as the experimental techniques applied. Full details are given for the preparation of the electrodes, construction of the calibration graphs and investigation of the effect of response time, and pH on the performance characteristics of the electrodes, also methods for evaluation of the electrode selectivity and determination of the studied drug in pure solutions and in its pharmaceutical formulations. The second part deals with experimental part for spectrophotometric technique which includes apparatus used for measurements and procedures for preparation of drug and reagent solutions. It is also contains the proposed spectrophotometric methods for determination of the studied drugs in pure and in dosage forms. Chapter (3) Contains two parts: The first part: deals with the results and discussion for potentiometric technique used ion selective electrodes for the determination of the studied drugs in which sodium 12-tungstophosphate (TP), ammonium reineckate (AR) and ammonium molybdate (AM) anions were tested as ion-pair agents for the preparation of electroactive ion association complexes of studied drugs. Sensors incorporating membranes with PVC as a plastic matrix, dioctyl phthalate as a solvent mediator and studied drug ion-pair were prepared and electrochemically evaluated. The following experimental variables were investigated. 1. Effect of acidity. 2. Study of response time. 3. Interference. The performance characteristics and uses of the proposed electrodes were fully discussed in terms of. • The usable concentration ranges of the studied drugs  $1 \times 10^{-2}$  -  $1 \times 10^{-7}$  M with (sodium 12-tungstophosphate, ammonium reineckate and

ammonium molbydate) and  $1 \times 10^{-2}$  -  $\times 10^{-6}$  M in case of ammonium reineckate with meclozinehydrochloride and cinnarizine. • The effect of soaking life time of the electrodes. • The effect of pH changes on the electrodes performance. The potential variations due to pH changes are considered acceptable in the pH ranges of (2.5-6.5, 3.0-6.5 and 2.5-7.0) for hydroxyzine HCl, (4.0-7.0, 4.0-6.0 and 3.0-7.0) for meclozine HCl and (3.0-7.0, 2.5-6.5 and 3.0-7.0) for cinnarizine with (sodium 12-tungstophosphate, ammonium reineckate and ammonium molbydate), respectively. • The response time of the electrode, which is the time required to achieve a steady state potential (within  $\pm 1$  mV) after successive immersion of the electrodes in a series of the drug solution, each having a 10-fold increase in concentration. The electrodes yielded steady potential within 10-20 s. • The selectivity of the electrodes towards different substances and ionic species was checked and the values of the selectivity coefficient were calculated to evaluate their degree of interferences. The obtained values indicating that the present electrodes have high ability to discriminate between the tested drug cation and interfering substances. • Analytical applications which involve determination of the studied drug using their selective electrodes in different samples applying standard addition method and potentiometric titration. • The results are in high agreement with those obtained using the official methods as clear from the statistical treatment of the results obtained from the analytical applications using F-test and t-test. The second part: contain the results and discussion for spectrophotometric procedures for the determination of the studied drugs using acid dyes reagents bromocresol green (BCG), bromocresol purple (BCP), bromophenol blue (BPB) and rose Bengal (RB). The proposed method are based on colored ion-pair complex formation between the acid dyes and drugs which is extracted with organic solvent except for rose bengal, (chloroform, carbon tetrachloride, methylene chloride, hexane and benzene) and determination of the concentration by measuring the absorbance of the extracted complex against a blank prepared by the same way except addition of the drug. The following experimental variables were investigated. 1. Effect of acidity. 2. Effect of time. 3. Effect of the extracting solvent. 4. Effect of reagent concentration. 5. Suggested mechanism. 6. Interference. 7. Validity of the method. Beer's law is obeyed within the concentration ranges (2.5-40.0, 2.5-37.5, 5.0-62.5 and 2.0-15.0  $\mu\text{g ml}^{-1}$ ) for hydroxyzine HCl, (5.0-45.0, 2.5-45.0, 2.5-37.5 and 2.0-20.0  $\mu\text{g ml}^{-1}$ ) for meclozine HCl and (2.5-30.0, 5.0-45.0, 2.5-25.0 and 2.0-25.0  $\mu\text{g ml}^{-1}$ ) for cinnarizine, in case of (BCG, BCP, BPB and RB) respectively. For more accurate results, ringbom optimum concentration ranges are determined. Molar absorptivity, sandell sensitivity, detection and quantification limits are calculated. In order to determine the accuracy and precision of the proposed methods, solutions containing three different concentrations of the studied drugs are prepared and analysed in six replicates. The recovery, relative standard deviations, relative error and confidence limits are calculated. The proposed methods can successfully applied to determine the pure form of the studied drugs and their dosage forms. The results obtained from studied drugs are compared statistically with their dosage forms. The results obtained are compared statistically by student's t-value and variance ratio F-test with the official methods at 95% confidence level. The results

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show that  $t$ - and  $F$ -values are less than the critical value indicating that there is no significant difference between the proposed and official methods. Thus, the proposed spectrophotometric method can be applied in determination of the studied drugs in pure form and in dosage forms.