physicohemical and anylytical studies of the micro determination of muscant drugs in pure and its pharmaceutical prepations

mohamed soltan mohamed

The aim of the work is to develop simple, accurate and sensitive methods for the determination of some skeletal muscle relaxant drugs in pure forms and in pharmaceutical preparations. The thesis consisting ofthe following.Chapter I contains the introduction which include five parts:The first part gives an idea for the analysis of drugs while the second part contains the definition, mode of action and chemical classification of skeletal muscle relaxant drugs. The third part contains trade name, chemical name, structure and characteristics of skeletal muscle relaxant drugs. The forth part gives literature survey on previous methods reported for the analysis of skeletal muscle relaxant drugs. The fifth part contains the spectrophotometric determination of some drugs by using binary complex with acid dyes, ternary complex with ammonium molybdate-thiocyanate complex or TLC/UV spectrodensitometric determination in pure forms and in dosage forms.Chapter II contains the experimental part which includes apparatus that were used for measurement and procedures for the preparation of the solutions of drugs and reagents. It contains also the proposed methods of spectrophotometric determination of the investigated drugs in pure and in dosage forms. Also contains Pharmacopoeial and official methods foranalysis of the studied drugs.Chapter III contains the results and discussions, which are included three parts:The first part includes spectrophotometric procedures for the determination of orphenadrine -citrate, tizanidine hydrochloride and pancuronoum bromide using four acid dyes.A -Bromothymol blue (BTB)B-Bromophenol blue (BPB)C-Bromocresol purple (BCP)D Bromocresol green (BCG)The four methods are based on allowing the drug which has a basic cationic nitrogen atom to react with the anionic dye at the optimum reaction conditions for formation a highly colored binary complex is formed which is extracted with an organic solvent to be measured spectrophotometrically at its Aimax The following points are investigated:1-Effect of pH.2-Effect of time.3-Effect of the extracting solvent.4-Effect of reagent concentration.5-Molecular ratio of complexes.6-Interferences.7-Suggested mechanism.8-Evaluation of the stability constants for the complexes.9-Spectrophotometric determination of the drugs in pure and dosage forms. Beer’s law is obeyed in the concentration range for orphenadrine citrate [2.5-25 µg/ml in case of BPB and BCP and 5-25 µg/ml in case of BTB and BCG], for tizanidine hydrochloride [2.5-20[ig/m in case of BTB and BCG and 5-20n/m1 in case of BPB and BCG] and for pancuronium bromide [2.5-25 vg/m1 in

case of BPB, BCP and BCG and 5- 25 µg/ml in case of BTB]. The stoichiometric ratios for binary complexes were established using the molar ratio and continuous variation methods and found to be 1:1 for all studied drugs. The accuracy and the precision of the proposed procedures were determined by statistical analysis of standard deviation, the relative standard deviation was found to - be 1.357 for orphenadrine citrate, 0.996 for tizanidine hydrochloride and 1.41 for pancuronium bromide standard error and confidence limits. The mean percent recovery ranged between 99.8-100.075 for orphenadrine citrate, 99.8-100.42 for tizanidine hydrochloride and 99.925-100.083 for pancuronium bromide. Determining the drugs in dosage form and applying standard addition technique tested the validity of the proposed procedures. The results are compared with those obtained by applying the official methods.The second part includes spectrophotometric determination of orphenadrine citrate, tizanidine hydrochloride and pancuronium bromide through ternary complex formation with molybdenium(VI) and thiocyanate. This method is based on ion-pair formation with molybdenium (V) thiocyanate complex in an acidic medium. The optimum reaction conditions for complete color formation of ternary complex formed were studied Dichloromethane is used for the extraction of the orange red ion-pair and its absorbance is measured at Xmax 470 nm.The following points are investigated.1-Effect of acidity.2-Effect of reagent concentration.3-Effect of shaking time.4-Effect of extracting solvent.5-Effect of time and temperature.6-Interferences.7-Stoichiometry of the formed ternary complex.8-Spectrophotometric determination of the drugs in pure and dosage forms. Abeyance to Beer’s law lies in concentration range of 5-35 µg/ml for orphenadrine citrate, 2.5-30 µg/ml for tizanidine hydrochloride and 2.5-25 µg/ml for pancuronium bromide. The nature of the molybdenum-thiocyanate-orphenadrine citrate, tizanidine hydrochloride or pancuronium bromide ternary complex in dichloromethane was determined by Bent and French’s method . The stoichiometric ratios were found to be 1:4:2 for (orphenadrine citrate and tizanidine hydrochloride) and 1:4:1 for pancurconium bromide. The proposed method is applied successfully for the analysis of samples of bulk powder and dosage forms with recoveries in the range of 99-101%, 99.8-101.4% and 98.9-101.2%, respectively. The accuracy and the precision of the proposed procedure was determined by statistical analysis of standard deviation, relative standard deviation, Standard error and confidence limits. Determining the drugs in dosage form and applying standard addition technique tested the validity of the proposed procedures. The results are compared with those obtained by applying the official methods.3. Densitometric method for the determination of orphenadrine citrate and tizanidine hydrochloride. Thin layer chromatographic procedures are quantitative methods of analysis that depend on either measuring spot (size and intensity) or elution of compounds from thin layer chromatographic plates. TLC is carried out on silica gel 60 F254 plates and chloroform: methanol 90 : 10 is used as mobile phase. Scanning of the developed chhromatograms is carried out under UV radiation’s at130wavelength 264 nm for orphenadrine citrate and 319 nm for tizanidine hydrochloride. Linear relationship between concentration and area under the peak is obtained in the range 5-25 µg/spot for orphenadrine citrate and 10-40 gg/spot for tizanidine hydrochloride. The proposed method was applied successfully for the analysis of samples of bulk

powder with percent recovery in the range 98.00-99.85 for orphenadrine citrate and98.98-100 for tizanidine hydrochloride.