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# SPECTROPHOTOMETRIC DETERMINATION OF TRAMADOL HCl, AMBROXOL HCl AND CLIDINIUM BROMIDE IN PHARMACEUTICAL FORMULATIONS

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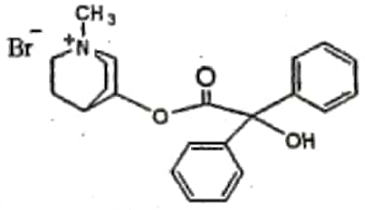
## ABSTRACT

Two simple, sensitive and accurate spectrophotometric methods have been established for the determinaton of clidinium bromide (CBr), ambroxol hydrochloride (AX) and tramadol hydrochloride (TD) using methyl orange (MO) and bromocresol purple (BCP). The proposed methods consist of extracting the formed ion-associates into methylene chloride in the case of (CBr and AX) using MO or of (TD) using BCP and into chloroform in case of (TD) using MO or of (CBr and AX) using BCP. The ion-associates exhibit absorption maxima at 425, 424 and 427 nm for MO and 415, 412, 410 nm using BCP with CBr, AX and TD, respectively. Beer's law was obeyed in the concentration ranges 2.0-34 μg $ml^{-1}$. The molar absorptivity, Sandell sensitivity of the reaction products were calculated. detection and quantification limits were also calculated. The correlation coefficient was ≥0.9987 with a relative standard deviation (R.S.D.) of ≤1.054 of six determinations for 10 μg $ml^{-1}$. The method was applied to the determination of the drugs in their pure state or pharmaceutical preparations and compared statistically using the Official methods.

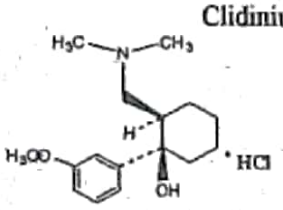
## INTRODUCTION

Tramadol [(±) trans-2-(dimethylaminomethyl)-1-(3-methoxy-phenyl)-cyclohexanol hydrochloride] is analgesic used for moderate to sever pain[1]. Tramadol contains a weakly absorbing chromophore in its molecule and it was determined by HPLC with UV detection or fluorescence detection in pharmaceutical, urine or blood plasma[2]. GC[3], LC-mass spectrometry[4], capillary electrophoresis[5], potentiometry[6] or UV-spectrophotometry[7-11] were also used for determining tramadol.

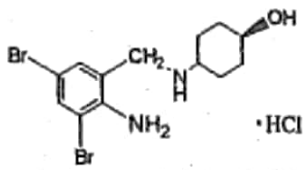
Ambroxol hydrochloride *trans*-4-(2-Amino-3,5-dibrombenzylamino)-cyclohexanol is reported[12] as mucolytic in acute and chronic bronchopulmonary diseases associated with abnormal mucous secretion and impaired mucous transport. Ambroxol hydrochloride was determined in human plasma and pharmaceutical preparation by HPLC[13] capillary gas isotachophoresis[14], HPLC and UV detection[15], automatic extraction spectrophotometric method[16], spectrophotometry[17-23], ion selective electrode[24] and GC with electron capture detector[25].



Clidinium bromide



Tramadol hydrochloride



Ambroxol hydrochloride

**Scheme 1.** Chemical structure of the studied drugs

Clidinium bromide (1-methyl-1-azoniabicyclo[2.2.2]-octan-8-yl) 2-hydroxy-2,2-diphenylacetate bromide, is a quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine [26]. Different analytical methods were used for determination of clidinium bromide e.g. spectrophotometry[27,28], capillary electrophoresis[29] and LC[30].

The present work aims to develop a simple, accurate, sensitive, more convenient and less time-consuming spectrophotomeric method for the determination of the drugs under investigation in pure form and in their pharmaceutical preparations. The method is based on the formation of ion-associates between the cited drugs (CBr, AX and TD) and methyl orange (MO) or bromocresol purple (BCP). The results obtained by applying the proposed methods are compared with those obtained by the official method.

## EXPERIMENTAL

### Apparatus

Kontron 930 (UV-Visible) spectrophotometer (German) equipped with 10 mm matched quartz cells was used for all spectral measurements and an Orion research model 601A/digital ionalyzer pH meter.

### Materials and regents

All chemicals, ragents and solvents were used of analytical reagent grade. Doubly distilled water was used to prepare all solutions in all experiments. Methyl orange (MO) and bromocresol purple (BCP) were Aldrich products and were used without further purification.

All pure drug (pharmaceutical grade) and dosage forms were obtained from the following sources:

1- Tramadol capsules (50 mg/cap.) and ampoules (100 mg) from October Pharma Company for Pharmaceutical Industries, Six of October City, Egypt
2- Mucosolvan tablets (30 mg/tab.), Cid Company for Pharmaceutical Industries, Egypt.
3- Amroxol syrup (15 mg / 5 ml), Glaxo Wellcom Misr Company for Pharmaceutical Industries, Egypt.

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4- Librax tablets (2.5 mg/tab.), Egyptian International Pharmaceutical Industries Company (EIPICO), Tenth of Ramadan City, Egypt.

**Standard Solutions**

A 200 μg $mL^{-1}$ standard solution of the studied drugs TD, AX and CBr were prepared by dissolving 20 mg of pure drug in bidistilled water and made up to 100 ml with bidistilled water. The solutions remained stable for one month when kept refrigerated.

**Reagents**

i- Methyl orange (MO) 0.1% (w/v) stock solution prepared by dissolving the appropriate weights in 30% aqueous methanol (v/v).

ii- Bromocresol purple (BCP) (1 x $10^{-3}$ M) stock solution prepared by dissolving the appropriate weights in least amount of methanol and completed to 100 ml with bidistilled water. The reagent solutions were stable for several months.

iii- Acetate buffer solutions of pH (2.0-8.0) were prepared by dissolving the appropriate weight of sodium acetate in glacial acetic acid and adjust the pH by 0.2 M NaOH as the recommended method[31].

**General procedures**

An aliquot volume containing (20-340 μg $mL^{-1}$) using MO or (20-200 μg $mL^{-1}$) using BCP of TD, AX and CBr were transferred into 25 ml separating funnels, 2.0 ml 0.1% of MO or (1 x $10^{-3}$M) of BCP for TD, AX and CBr, 4 ml of acetate buffer solution pH 3.0, 2.8 and 2.6 for TD, AX and CBr, respectively using MO and pH 3.2 and 3.0 for TD and (AX or CBr), respectively. The volume was made up to 10 ml with bidistilled water. The formed ion-associate was extracted with two portions each of 5 ml chloroform for TD, AX and CBr using MO or BCP. The mixture was extracted by shaking for 3.0 min after the addition of organic solvent. The reaction mixtures were allowed to separate into two phases. The organic layer was dried by running through anhydrous sodium sulfate and filtered then collected into 10 ml calibrated flask and the volume was made up to the mark with the same solvent. The absorbance of the extracts was measured for each system at the optimum wavelength (Table 1), against a reagent blank prepared in the same way without addition of the examined drug. All measurements were made at room temperature (25 ± 2°C).

**Application to various dosage forms**

***For tablets and capsules***

The contents of 20 tablets or capsules of the drugs (2.5 mg CBr per tab., 30 mg AX per tab. and 50 mg TD per cap.) were weighed into a small dish, powdered and mixed well. A portion equivalent to the nominal content of the tablets or capsules was weighed and dissolved in 100 ml water, shaken well and filtered through a sintered glass crucible $G_4$. The clear solution was diluted to 250 ml with water in a 250 ml calibrated flask. The drug content of this solution was obtained by applying the general procedures to aliquot containing 100 μg $ml^{-1}$ of the drug as described above.

***For injection and syrup***

The contents of five ampoules (100 mg of TD) or an aliquot volume of syrup equivalent to (15 mg of AX per 5 ml) were quantitatively transferred into 250 ml calibrated flasks and then completed to the mark with distilled water and the same procedures were followed.

**Stoichiometric relationship**

The continuous variation attributable to Job and modified by Vosburgh and Cooper[32] and the molar ratio[33] methods were employed. A ($1\times10^{-3}$ M) standard solution of TD, AX and CBr and ($1\times10^{-3}$ M) solution of MO or BCP were used. A series of solutions were prepared in which the total volume of drug and reagent was kept at 2.0 ml. The reagents were mixed in various proportions and diluted to volume in a 10 ml calibrated flask with the appropriate solvent for extraction following the above mentioned procedures.

## RESULTS AND DISCUSSION

**Optimization**

Careful investigations were carried out to establish the most favourable conditions to achieve maximum colour intensity for the quantitative determination of the examined drugs (CBr, AX and TD). The absorption spectra of CBr, AX and TD and their complexes with MO or BCP under the optimum conditions were obtained and shown in Figures 1 and 2. The influence of each of the following variables on the reaction was tested.

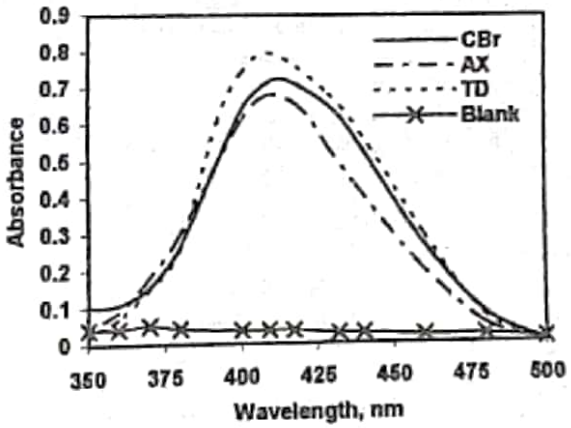



**Fig. (1).** Absorption spectra of (10 μg $mL^{-1}$) CBr, AX or TD with 2.0 mL of (1 x $10^{-3}$ M) BCP.

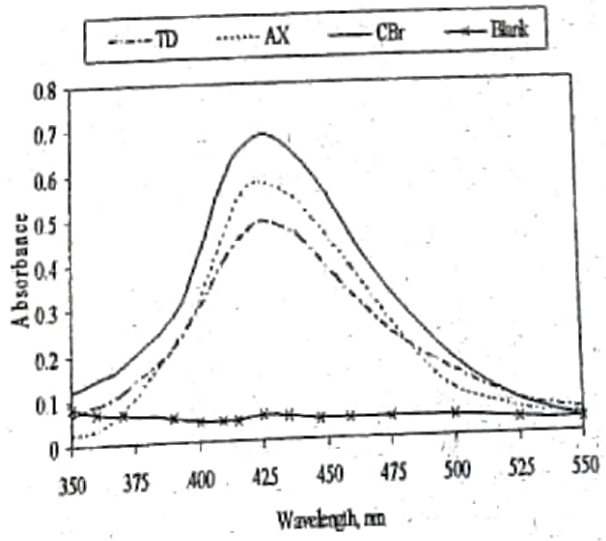



**Fig. (2).** Absorption spectra of (10 μg $mL^{-1}$) CBr, AX or TD with 2.0 mL of (1 x $10^{-3}$ M) MO.

**Effect of pH on the ion-pair formation**

In order to establish the optimum pH range, each reagent under consideration was allowed to react with the examined drugs in acetate buffer solutions of pH 2.0-8.0. The results showed that the most efficient extraction of the ion-associates was obtained at pH 3.0, 2.8 and 2.6 for TD, AX and CBr, respectively using MO and pH 3.2 and 3.0 for TD and (AX or CBr), respectively using BCP (Fig. 3), where maximum absorbance and high stability were achieved. The optimum amount of buffer solution added was also investigated and found to be 4.0 ml using MO and BCP.

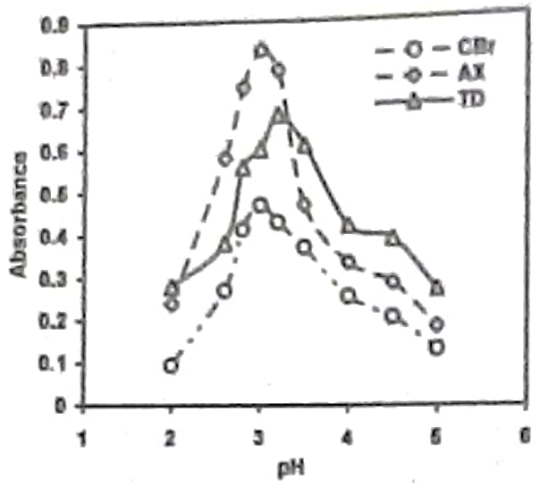



Fig. (3): Effect of pH on the absorbance of (10 μg mL$^{-1}$) CBr, AX and TD with ( 1.0 × 10$^{-3}$M) BCP.

**Choice of organic solvent**

The polarity of the solvents affects both extraction efficiency and absorptivity of the ion-associates. Several water-immiscible organic solvents, including benzene, toluene, carbon tetrachloride, chloroform, methylene chloride, 1,2-dichloroethane and ether were tried. The most convenient solvents found to produce the highest absorbance, extraction power and stability of colour was two portions each of 5 ml chloroform for for TD, AX and CBr using MO or BCP. The study reveals that a volume ratio of 1 : 1 (aqueous : organic) was the most suitable for ion-associate extraction.

**Effect of shaking time and temperature**

The optimum reaction time was studied by monitoring the colour development at ambient temperature (25 ± 2°C). The extraction was studied by varying the shaking time from 0.5 to 5.0 min for the complexes based on 10 μg ml$^{-1}$ of the examined drugs. A shaking times of 3.0 min for MO and BCP were adopted for all extractions. It was further observed that the developed yellow colour remained stable for at least 24 hours using MO and BCP.

**Effect of the reagent concentration**

The effect of the reagent concentration was tested by using varying amounts (0.2–5 ml) of (0.1%) MO or (1 × 10$^{-3}$M) BCP solution with 10 μg ml$^{-1}$ of the examined drugs. The results showed that 2.0 ml (0.1%) of MO or (1 × 10$^{-3}$M) of BCP solution were sufficient to produce maximum and reproducible colour intensity for all the examined drugs (Fig. 4).

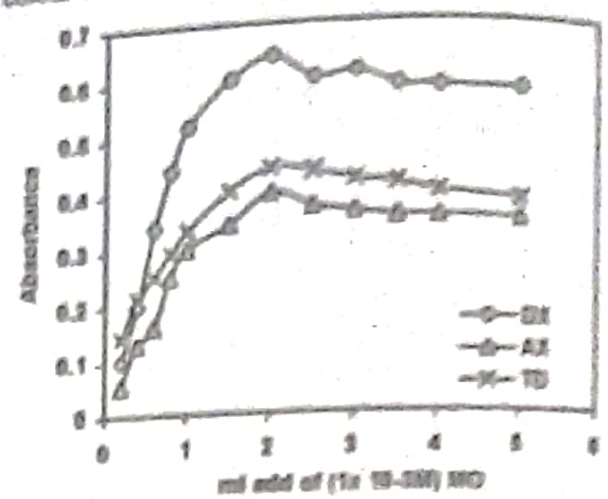



Fig. (4): Effect of reagent concentration on the reaction with (10 μg mL$^{-1}$) CBr, AX and TD with (1.0 × 10$^{-3}$ M) MO.

**Effect of sequence of mixing**

The most favourable sequence was reagent - drug -buffer for the highest colour intensity and the shortest time for developing maximum absorbance, while the other sequences require longer time and produce lower absorbance values.

**The stoichiometric ratio of the complex**

Job's method of continuous variation of equimolar solutions was employed: a 1.0 × 10$^{-3}$ M standard solution of drug base and 1.0 × 10$^{-3}$ M solution of MO and BCP were used. A series of solutions was prepared in which the total volume of drug and reagent was kept at 10 mL for MO and BCP, respectively. The molar ratio of the (drug : dye) in the ion-pair complexes was determined formed to be 1 : 1(Job's method) (Fig. 5). The ion-pairs are formed through the electrostatic attraction between positive protonated D$^+$ and negative MO$^-$ or BCP$^-$. A proposal for the reaction mechanism taking TD and BCP as an example is presented in Scheme II.

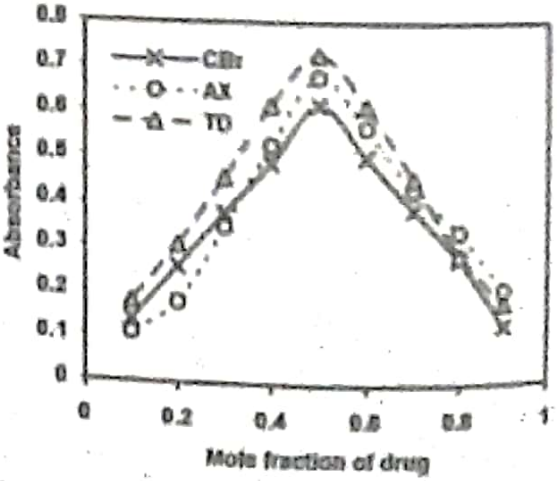
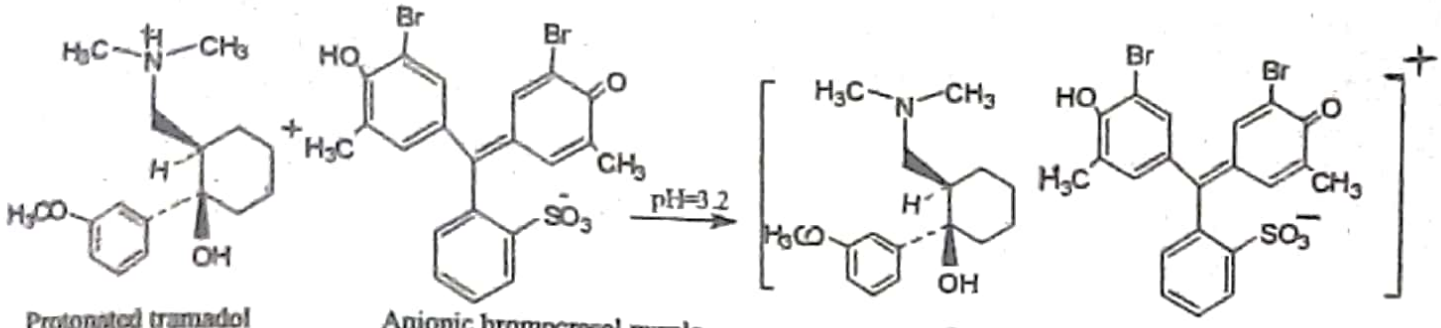



Fig. (5): Continuous variation plots for the ion-association complexes of the studied drugs CBr, AX and TD with BCP. [drug]=[dye]=(1.0 x 10$^{-3}$ M).




Protonated tramadol Anionic bromocresol purple TD-BCP ion pair complex

**Scheme (II):** Proposed mechanism for the formation of tramadol-BCP complex (1 : 1).

### 3.2. Method Validation

#### 3.2.1. Linearity

Under the above mentioned experimental conditions, standard calibration graphs were constructed for the reaction of TD, AX and CBr using MO and BCP, respectively. Beer's law was obeyed for drugs analyzed in concentration range of (2.0-34 or 2.0-20 μg ml$^{-1}$) with MO or BCP. For more accurate results, Ringbom [34] concentration range was determined by plotting log [drug] in μg ml$^{-1}$ against %T from which the linear portion of the curve give accurate range for microdetermination of the drugs under investigation as presented in Table 1. The linear regression equations, standard deviation, slopes and intercepts, correlation coefficients, relative standard deviation of response factors, and linearity ranges were given in (Table 1) for each proposed spectrophotometric method. The molar absorptivities and Sandell's sensitivities of each methods was calculated.

#### 3.2.2. Sensitivity

The detection limit (LOD) for the proposed methods were calculated using the following equation[34],

$$LOD = 3s / k$$

where $s$ is the standard deviation of replicate determination values under the same conditions as for the sample analysis in the absence of the analyte and $k$ is the sensitivity, namely the slope of the calibration graph.

The limits of quantitation, LOQ, defined as[34];

$$LOQ = 10\,s / k$$

#### 3.2.3. Precision and accuracy

In order to determine the accuracy and precision of the proposed method, solutions containing four different concentrations of each drug were prepared and six replicate determinations were carried out for the pure form and the pharmaceutical preparation of the drugs under investigation. The analytical results obtained from this investigation are summarized in Table 2. The relative standard deviation (RSD%) as precision and percentage relative error (Er %) as accuracy of the suggested method were calculated. Precision was carried out by six determinations at four different concentrations in these spectrophotometric methods. The percentage relative error calculated using the following equation:

$$Er\,\% = [(found - added) / added] \times 100$$

The inter-day and intra-day precision and accuracy results are shown in (Tables 2, 3). These results of accuracy and precision show that the proposed methods have good repeatability and reproducibility.

**Table (1):** Spectral characteristics of the colored products of CBr, AX and TD with MO or BCP.

| Parameters | MO | | | BCP | | |
|---|---|---|---|---|---|---|
| | TD | AX | CBr | TD | AX | CBr |
| pH | 2.6 | 2.8 | 3.0 | 3.0 | 3.0 | 3.2 |
| $\lambda_{max}$ (nm) | 425 | 424 | 420 | 415 | 412 | 410 |
| Beer's law limits, μg ml$^{-1}$ | 3.0-30 | 4.0-32 | 2.0-28 | 2.0-20 | 2.0-18 | 2.0-16 |
| Ringbom optimum range, μg ml$^{-1}$ | 5.0-28 | 5.5-30 | 4.0-26.5 | 4.0-18 | 4.0 -16 | 3.0-14 |
| Detection limits, μg ml$^{-1}$ | 0.135 | 0.092 | 0.11 | 0.161 | 0.176 | 0.125 |
| Quantification limits, μg ml$^{-1}$ | 0.45 | 0.307 | 0.367 | 0.538 | 0.587 | 0.417 |
| Regression equation [a] | | | | | | |
| Slop (b) | 0.0167 | 0.0169 | 0.0148 | 0.0899 | 0.0179 | 0.0381 |
| Intercept (a) | 0.001 | 0.0003 | 0.0009 | -0.00845 | 0.0007 | - 0.0046 |
| Correlation coefficient (r) | 0.9987 | 0.9989 | 0.9996 | 0.9995 | 0.9991 | 0.9992 |
| Molar absorptivity x10$^4$ (L mol$^{-1}$ cm$^{-1}$) | 3.131 | 1.61 | 1.50 | 3.887 | 1.653 | 1.481 |
| Sandell's Sensitivity, μg cm$^{-2}$ | 0.0138 | 0.0275 | 0.020 | 0.011 | 0.0280 | 0.0181 |
| RSD [b] % | 0.937 | 0.750 | 0.884 | 0.691 | 0.975 | 1.054 |
| RE % | 0.984 | 0.787 | 0.937 | 0.726 | 1.023 | 1.106 |

[a] A = a + b C, where A is the absorbance, a is the intercept, b is the slope and C is the concentration of drug in μg ml$^{-1}$.
[b] Relative standard deviation for six determinations (10 μg ml$^{-1}$).

Table (2): The intra-day and inter-day precision and accuracy data for the studied drugs obtained by MO method

| Drug | Intra-day | | | | | Inter-day | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Added (μg ml.$^{-1}$) | Recovery % | Precision RSD % [a] | Accuracy Er % | Confidence [b] limits | Recovery (%) | Precision RSD % [a] | Accuracy Er % | Confidence [b] limits |
| TD | 5.0 | 99.70 | 1.0159 | -0.30 | 4.985±0.0551 | 100.10 | 0.7784 | 0.10 | 5.005 ± 0.0775 |
| | 10 | 100.10 | 0.7762 | 0.10 | 10.01±0.0818 | 100.40 | 0.6318 | 0.40 | 10.040 ± 0.0646 |
| | 15 | 99.90 | 0.5921 | -0.10 | 14.985±0.0930 | 99.70 | 0.5445 | -0.30 | 14.955 ± 0.0764 |
| | 20 | 99.75 | 0.6461 | -0.25 | 19.95±0.1352 | 99.45 | 0.9272 | -0.55 | 19.890 ± 0.0854 |
| | 25 | 100.30 | 0.8420 | 0.30 | 25.075±0.2211 | 99.85 | 0.4089 | -0.15 | 24.963 ± 0.0775 |
| | 30 | 99.55 | 0.7281 | -0.45 | 29.865±0.2282 | 100.05 | 0.3870 | 0.05 | 30.015 ± 0.0763 |
| AX | 5 | 100.20 | 0.8927 | 0.20 | 5.01±0.0469 | 99.60 | 0.8615 | -0.40 | 4.980 ± 0.0619 |
| | 10 | 99.50 | 1.0249 | -0.90 | 9.91±0.1066 | 99.80 | 0.7821 | -0.20 | 9.980 ± 0.0919 |
| | 15 | 100.13 | 0.6628 | 0.40 | 15.06±0.1047 | 100.30 | 0.4440 | 0.30 | 15.045 ± 0.0781 |
| | 20 | 99.45 | 0.5491 | -0.85 | 19.83±0.1143 | 99.90 | 0.3670 | -0.50 | 19.900 ± 0.0760 |
| | 25 | 99.90 | 0.5170 | -0.1 | 24.975±0.1355 | 99.75 | 0.3117 | -0.25 | 24.938 ± 0.0811 |
| | 30 | 99.65 | 0.6083 | -0.35 | 29.895±0.1908 | 100.15 | 0.3846 | 0.15 | 30.045 ± 0.0963 |
| CBr | 3.0 | 100.28 | 1.1625 | 0.28 | 3.008±0.0367 | 99.75 | 1.074 | -0.233 | 2.993 ± 0.0337 |
| | 6.0 | 99.95 | 0.8892 | -0.05 | 5.997±0.0560 | 100.25 | 0.6972 | 0.25 | 6.015 ± 0.0486 |
| | 12 | 99.76 | 0.7922 | -0.24 | 11.97±0.0995 | 99.65 | 0.3624 | -0.35 | 11.958 ± 0.0492 |
| | 18 | 99.93 | 0.5184 | -0.07 | 17.987±0.0979 | 100.10 | 0.3021 | 0.10 | 18.018 ± 0.0577 |
| | 24 | 100.15 | 0.5006 | 0.15 | 24.036±0.1263 | 99.90 | 0.2876 | -0.10 | 23.976 ± 0.0724 |
| | 28 | 100.05 | 0.4920 | 0.05 | 28.014±0.1446 | 99.85 | 0.3004 | -0.15 | 27.958 ± 0.0881 |

[a] Relative standard deviation for six determinations. [b] 95% confidence limits and five degrees of freedom.

Table (3): The intra-day and inter-day precision and accuracy data for the studied drugs obtained by BCP method

| Drug | Intra-day | | | | | Inter-day | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Added (μg mL$^{-1}$) | Recovery % | Precision RSD % [a] | Accuracy Er % | Confidence limit [b] | Recovery % | Precision RSD % [a] | Accuracy Er % | Confidence limit [b] |
| TD | 4.0 | 100.06 | 0.84 | 0.06 | 4.002±0.0353 | 100.35 | 0.46 | 0.35 | 4.014±0.0184 |
| | 8.0 | 99.59 | 0.92 | -0.41 | 7.967±0.0769 | 100.25 | 0.83 | 0.25 | 8.020±0.0664 |
| | 12 | 99.90 | 0.77 | -0.1 | 11.988±0.0969 | 99.77 | 0.64 | -0.23 | 11.97±0.0766 |
| | 16 | 100.25 | 1.08 | 0.25 | 16.04±0.1818 | 99.68 | 0.91 | -0.938 | 15.85±0.1454 |
| AX | 4.0 | 99.82 | 0.99 | -0.275 | 3.989± 0.041 | 99.40 | 0.76 | -0.60 | 3.976±0.0303 |
| | 8.0 | 99.35 | 0.85 | -0.85 | 7.932± 0.071 | 100.10 | 0.57 | 0.10 | 8.008±0.0456 |
| | 12 | 98.95 | 1.12 | -1.06 | 11.873± 0.140 | 99.95 | 0.66 | -0.05 | 11.994±0.0793 |
| | 16 | 99.65 | 0.88 | -0.55 | 15.912± 0.147 | 100.30 | 0.39 | 0.30 | 16.048±0.0624 |
| CBr | 3.0 | 100.10 | 0.76 | 0.133 | 3.004± 0.024 | 99.75 | 1.08 | -0.25 | 2.993±0.0323 |
| | 6.0 | 99.95 | 0.79 | -0.15 | 5.991± 0.050 | 99.40 | 0.54 | -0.60 | 5.964±0.0324 |
| | 9 | 99.80 | 0.81 | -0.078 | 8.993± 0.076 | 99.50 | 0.45 | -0.50 | 8.955±0.0403 |
| | 12 | 100.15 | 1.23 | 0.15 | 12.018± 0.155 | 100.04 | 0.61 | 0.04 | 12.005±0.0732 |

[a] Mean of six determinations. RSD%, percentage relative standard deviation, Er%, percentage relative error.
[b] Confidence limit at 95% confidence level and five degrees of freedom ($t$ = 2.571)

### 3.2.4. Robustness and Ruggedness

For the evaluation of the method robustness, some parameters were interchanged, pH, dye concentration, wavelength range, and shaking time. The capacity remain unaffected by small deliberate variations. Method ruggedness was expressed as RSD% of the same procedure applied by two analysts using two different instruments on different days. The results showed no statistical differences between different analysts and instruments suggesting that the developed methods were robust and rugged.

### Interference

A systematic quantitative study was undertaken by measuring the absorbances of solutions containing 1 ml of $1\times10^{-3}$ M drug together with varying excess of different additives and excipients which may be present in the pharmaceutical preparations using the recommended methods of such reagents for TD, AX and CBr. No significant interference was observed from the excipients commonly used such as glucose, lactose, starch, fructose and magnesium stearate. This shows that the method is applicable in case of pharmaceutical preparations of the investigated drugs.

### Analytical applications

The validity of the proposed method was checked by determining the examined drugs in various dosage forms, viz. ampoules, tablets or capsules and syrup. The results obtained are recorded in (Table 4) and compared statistically with the official methods for TD (non-aqueous detecting the end-point potentiometrically)[11], AX (potentiometric titration)[12] and CBr (non-aqueous detecting the end-point potentiometrically with perchloric acid)[9&6]. The students t- and F-values obtained at 95% confidence level did not exceed the theoretical tabulated value

indicating no significant difference between the proposed and official method.

**Table (4) :** Application of the proposed methods to the determination of CBr, AX and TD in dosage forms

| Samples | Official methods | % Recovery ± SD | |
|---|---|---|---|
| | | MO | BCP |
| Tramadol Capsules (2.5 mg CBr/ tab ) | 100.40 ± 0.49 | 99.96 ± 0.51 | 100.20 ± 0.38 |
| t** | | 1.52 | 0.79 |
| F** | | 1.083 | 1.663 |
| Tramadol ampoules (50 mg AX / tab ) | 99.83 ± 0.29 | 99.67 ± 0.35 | 99.33 ± 0.41 |
| t** | | 0.863 | 1.220 |
| F** | | 1.457 | 2.00 |
| Mucosolvan tablets (15 mg AX / 5 ml) | 99.67 ± 0.52 | 99.92 ± 0.69 | 99.50 ± 0.57 |
| t** | | 0.709 | 0.540 |
| F** | | 1.761 | 1.202 |
| Amrexol syrup (50 mg TD / Cap.) | 100.24 ± 0.35 | 100.50 ± 0.47 | 100.45 ± 0.39 |
| t** | | 1.083 | 0.981 |
| F** | | 1.803 | 1.242 |
| Librax tablets (100 mg TD / amp.) | 100.25 ± 0.44 | 100.05 ± 0.71 | 99.90 ± 0.54 |
| t** | | 0.587 | 1.231 |
| F** | | 2.604 | 1.506 |

* Mean of six determinations.

** Theoretical vlues for t- and F- value for five degrees of freedom and 95% confidence limits are 2.57 and 5.05, respectively.

## CONCLUSION

The proposed method for the estimation of CBr, AX and TD using methyl orange and bromocresol purple are advantageous over many of the reported methods due to its sensitivity, rapidity and good agreement with the pharmacopoeial methods. The high recovery percentage and low relative standard deviation reflect the high accuracy and precision of the proposed methods, moreover, the methods are easy, applicable to a wide range of concentration, beside being less time consuming and depend on simple reagents which are available, thus offering economic and acceptable methods for the routine determination of the cited drugs.

## REFERENCES


1. **British Pharmacopoeia**, Her Majesty's, Stationary Office and Queen, London, , Volume II (2004).
2. Ceccato A., Chiap P., Hubert P., Crommen J., **J. Chromatogr., B.**, 698, 161 (1997)
3. Becker R., Lintz W., **J. Chromatogr. B**, 337, 213 (1986).
4. Ceccato A., Vanderbist F., Pabst J.Y., Streel B., **J. Chromatogr. B Biomed. Sci. Appl.**, 748, 65 (2000)
5. Soetebeer U.B., Schierenberg M.O., Schulz H., Grunefeld G., Andresen P., Blaschke G., **J. Chromatogr. B Biomed. Sci. Appl.**, 745, 271 (2000)
6. Hopkala H., Misztal G., Wieczorek A., **Pharmazie**, 53, 869 (1998)
7. Yang Y.Z., Lu Y.B., **Yaowu-Fenxi-Zazhi**., 16, 132 (1996), [Anal. Abstr.]
8. Rajput Sadhana J., Trivedi Priti D., **Indian Drugs.**, 38, 100 (2001).
9. Abdellatef H.E., **J. Pharm. Biomed. Anal.**, 29, 835 (2002).
10. Rama Subba Reddy T., Murali Mohan Rao S.V., Viplava Prasad U., Sastry C.S.P., **Asian J. Chem.**, 15(3-4), 1471, (2003), [Anal. Abstr.].
11. Abdellatef H.E., El-Henawee M.M., El-Sayed H.M., Ayad M.M., **Spectrochim. Acta. A.**, Accepted manuscript, (2006).
12. **European pharmacopoeia**, 417-418 (2001).
13. Wang W.H., Deng S.H., Huang G.H., Sun G.F., Qin Q. M., **Yaowu Fenxi-Zazhi.**, 21, 23 (2001). [Anal. Abstr.]
14. Pospisilova M., Polasek M., Jokl V., **J. Pharm. Biomed. Anal.**, 24, 421 (2001).
15. Dalmadi Kiss B., Balogh Nemes K., Urmos L., Szunyog J., Klebovich I., **Chromatographia.**, 51, 217 (2000).
16. Prezo-Ruiz T., Martinez-Lozano C., Sanz A., Bravo E., **J. Chromatogr. B: Biomed. Appl.**, 742, 205 (2000)
17. Indrayanto G., Handajani R., **J. Pharm. Biomed. Anal.**, 11, 781 (1993).
18. Sagar V., Shastry B. S., **Antiseptic**, 100, 8 (2003).
19. Kuchekar B. S.; Shinde G. S., Naikawadi I. T., Todkar K. J.; Kharade S. V., **Ind. J. Pharm. Sci.**, 65, 193 (2003).
20. Naryana Reddy M.; Kanna Rao K. V., Swapna M., Sarkar D. G.; Reddy N. M.; Rao KKV., **Ind. J. Pharm. Sci.**, 60, 249 (1998).
21. Sathish T., Kiran Babu U., Kishore Kumar K., Sujatha S., Balasekhar Reddy CH., **Biosci. Biotechnol.Res. Asia.**, 3(2), 383, (2005). [Anal. Abstr.].
22. Goyal A., Singhvi I., **Asian J. Chem.**, 17(4), 2836, (2005), [Anal. Abstr.].
23. Pai P.N.S., Lalitha N., Balakrishna B., Rao G.K., **Ind. J. Pharm. Sci.**, 68(4), 501, (2006).
24. Abdel-Ghani N. T., Hussein S. H., **IL Farmaco.**, 58, 581 (2003).
25. Colombo L., Marcucci F., Marini M.G., Pierfederici P., Mussini E., **J. Chromatogr., Biomed. Appl.**, 95, 141 (1990).
26. **United States Pharmacopoeia**, 25th Review, The National Formulary Convention, Rockville: MD, (2002).
27. Ozkan S. A., Erk N., Senturk Z., **Anal. Lett.**, 32, 497 (1999)
28. Inés Toral M., Pablo Richter, Nelson Lara, Pablo Jaque, Cesar Soto, Marcela Saavedra, **Inter. J. Pharm.**, 189, 67 (1999).
29. Nickerson B., **J. Pharm. Biomed. Anal.**, 15, 965 (1997)

Zagazig J. Pharm. Sci., June 2006
Vol. 15, No. 1, pp. 16-22

30. Yuen S. M., lehr G., **J. Assoc. Off. Anal. Chem.**, 74, 461 (1991).
31. Perrin, D.D.; Dempsey, B. **Buffers for pH and Metal Ion Control**, Chapman and Hall: London, p. 135 and 138 (1979).
32. Vosburgh W.C., Cooper G.R., **J. Am. Chem. Soc.**, 63, 437 (1941).
33. Yoe J.H., Jones A.L., **Ind. Eng. Chem., Anal. Edn.**, 16, 111–114 (1944).
34. Miller J. C., Miller J. N., **Statistics in analytical Chemistry**, third ed., Ellis Horwood, Chichester, UK, (1993).

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# تعيين الترامادول هيدروكلوريد ، الامبروكسول هيدروكلوريد والكليدينيوم بروميد باستخدام طرق طيفية ضوئية

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في هذا البحث تم استحداث طريقتان لتقدير الكليدينيوم بروميد ، الامبروكسول هيدروكلوريد و الترامادول هيدروكلوريد سواء في البودرة النقية أو في المستحضرات الصيدلية باستخدام الميثيل البرتقالي والبروموكريزول البنفسجي.

الطريقة المقدمة تعتمد على تكوين معقدات أيونية ازدواجية ملونة بين الميثيل البرتقالي والبروموكريزول البنفسجي مع العقاقير المذكورة، وقد تم قياس المعقدات المستخلصة عند طول موجه ٤٢٥ ، ٤٢٤ ، ٤٢٧ نانومتر بالنسبة لصبغة الميثيل البرتقالي وعند طول موجه ٤١٥ ، ٤١٢ ، ٤١٠ نانومتر بالنسبة لصبغة البروموكريزول البنفسجي مع الكليدنيوم بروميد ، الامبروكسول هيدروكلوريد، الترامادول هيدروكلوريد على التوالي.

وقد أمكن تطبيق هذه الطرق بنجاح في تحليل المستحضرات الصيدلية المحتوية على هذه العقاقير وتمت مقارنة النتائج مع دستور الأدوية وقد أثبتت أن الطرق المقترحة متقاربة مع الطرق الدستورية بالدرجات التي تسمح بها المقارنة الإحصائية.