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Chromotropic Acid Azo Dyes; Friends in Our Laboratory for Four Decades. An Overview.

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Summary. Chromotropic acid azo dyes, very famous analytical reagents in the fields of spectrophotometry and chelatimetry, have been used in our laboratory for four decades in the determination of several metal ions, and pharmaceutical compounds. The chemical and physical properties were the subject of many investigations. This article describes the history of continuous interest (for four decades) of the analytical chemistry group, at Chemistry Department, Faculty of Science, Cairo University in using such reagents in analytical chemistry.

Introduction

Chromotropic acid, was firstly known as 1,8-dihydroxynaphthalein-3,6-disulphonic acid, however, it was recommended by IUPAC to be named as 2,7-naphthalenedisulphonic acid 4,5-dihydroxy.

Since the preparation of chromotropic acid azo dyes, and their complexes with chromium in 1951 by Zollinger[(1)], there have been a very large interest for the new compounds being promising candidates to analytical chemistry. They are water soluble and exhibit very high stability in solution. Also, chromotropic acid azo dyes can be prepared in three types, mono-, bis- and di- azo dyes which impart diversity to this class of compounds.

These azo dyes have been enormously used in analytical chemistry as chromophoric indicators in spectrophotometric determination of several metal ions[(2)] and as metallochromic indicators using ethylenediaminetetraacetic acid (EDTA) and cyclohexanediaminetetraacetic acid (CDTA)[(3)].

Many of the chromotropic acid azo dyes are commercially available by several chemical producing companies and thus have commercial names (Tables 1 and 2).

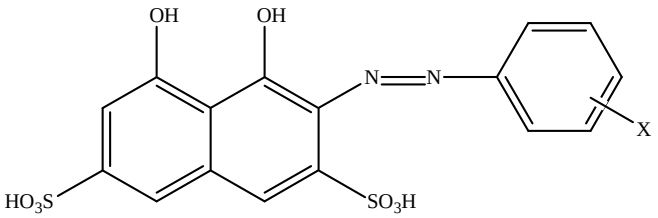

Table (1). Chromotropic acid mono azo dyes

X	Commercial name	Abbriviation
H	Chromotrope 2R	C2R
p-NO_2	Chromotrope 2B	C2B
o-COOH	Chromotrope 2C	C2C
o-$AsO(OH)_2$	Arsenazo I	AI
p-SO_3H	Spadns	
4- SO_3H (naph)	Snadns	

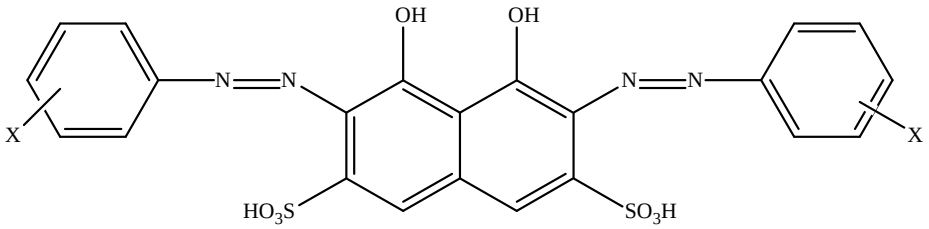

Table (2) Chromotropic acid bis-azo dyes

X	Commercial name	Abbriviation
o-$AsO(OH)_2$	Arsenazo III	AIII
p-SO_3H	Dispadns	
p-SO_3H(naph)	Disnadns	

The acid dissociation constants

The acid dissociation constants of chromotropic acid azo dyes were the subject of investigations by several authors.[4-8] Their was two contradicting views where several authors suggest the ionization of only one hydroxyl group of the chromotropic acid moiety, while the other group does not or may ionize above pH 14 that can not be achieved in aqueous media. The other opinion suggests the ionization of both hydroxyl groups of chromotropic acid. Which was confirmed by the studies carried

out in our laboratory as indicated by the variation of absorption spectra in buffer solutions of different pH values and the existence of isosbestic point within certain pH range and deviation from this point in other range cofirming the shift of the first acid-base equilibrium. The results reported by Toei[7] and Katayama[8] may be attributed to the use of 2.5 ml buffer solution in 25-ml measuring flask, i.e. 10 times dilution for the buffer mixture which affect the original pH value.

The acid dissociation constants of the hydroxyl groups of four chromotropic acid azo dyes (chromotrope 2R (C2R), chromotrope 2B (C2B), arsenazo I (AI) and arsenazo III (AIII)) were determined spectrophoto-metrically.[9] The ionization constants of the other acidic functional groups were determined potentiometrically by titration with sodium hydroxide. The results confirm the ionization of the two naphthalenic hydroxyl groups. The results were discussed in relation to molecular structure and substituent effect.

Carboxphenylazo-chromotropic acid derivatives, (o-, m- and p-carboxy), were prepared by coupling of the diazotized carboxyaniline derivatives with chromotropic acid in carbonate medium. The acid dissociation constants of the naphthalinic hydroxyl groups were determined spectrophotometrically. The absorption spectra were obtained in Britton-Robinson universal buffer solutions (pH 2-12). The absorption spectra and the absorbance-pH curves indicated the ionization of both naphthalenic OH groups of chromotropic acid. The ionization values were 7.6, 9.8; 7.1, 9.5; and 7.6, 9.8 for o-, m-, and p- derivatives respectively.[10]

The acid dissociation constants of some halogenated phenylazo-chromotropic acid derivatives were determined spectrophotometrically. The absorption spectra were recorded in universal buffer solutions within the pH range 2.0-12.0. The absorbance-pH curves were used to calculate the pK values. The ionization of the sulphonic acid groups, $pK_{1\&2}$, were determined by titration with NaOH. The $pK_{1\&2}$, pK_3 and pK_4 values are as follows; 3.55, 7.46, 9.68 (o-Cl); 3.50, 7.11, 9.67 (m-Cl); 3.57, 7.11, 9.92 (p-Cl); 4.08, 7.41, 9.50 (o,p-di-Cl); 3.42, 7.65, 9.84 (p-Br) and 3.34, 7.61, 9.77 (p-I). The relation between the Hammett constants and ionization constants was investigated and discussed.[11]

The acid dissociation constants of seven chromotropic acid azo dyes derivatives were determined spectrophotometrically. The spectra were obtained in Britton and Robinson universal buffers covering the range 2.0-12.0. The variation of spectra and the absorbance-pH curves indicated the existence of two ionization steps corresponding to the ionization of the two hydroxyl groups of chromotropic acid. The ionization of the sulphonic acid groups was determined potentiometrically.[12]

The electronic absorption spectra of some bis-azo dyes derived from chromotropic acid were investigated in within the pH range 2-12.[13] The ionization constants of the naphthalenic hydroxyl groups were determined from the variation of the absorbance with pH at several wavelengths. The values were in the ranges 8.25-8.50 and 10.05-10.50 for the two groups. The values were correlated with substitution effect and molecular structure. The ionization of the sulphonic acid groups was determined using potentiometric titration of the acid form of the dyes against sodium hydroxide.

The proton-ligand ionization constants of nine halogenated derivatives of mono- and bis-phenylazo-chromotropic acid dyes were determined potentiometrically using Sarin and Munshi technique[14]. The results confirmed the ionization of the two naphthalinic hydroxyl groups of the chromotropic acid moiety, as indicated by the proton-ligand formation constant curves. The formation constants of Ru(III) and V(IV) chelates were determined in 40% ethanolic solutions.

The acid dissociation constants of chromotropic acid azo dyes were critically discussed in the light of the data presented in literature[15]. Two opinions have been presented. The first stated that only one OH-group of the chromotropic acid moiety is ionizable while the other ionization is higher than 14. The second stated that both OH-groups are ionizable. The two opinions were critically evaluated.

Spectrophotometric determination of metal ions using chromotropic acid azo Dyes

Chromotropic acid azo dyes are considered to be excellent reagents for the spectrophotometric determination of metal ions considering their structure (existence

of two hydroxyl groups one of which is ortho to azo group). Also the stability of their aqueous solutions is a privilege over other reagents applied in this field. Several articles were published dealing with the determination of metal ions making use of chromotropic acid azo dyes. These publications are listed and discussed in this section:

Chromotrope 2R (C2R) was used for the spectrophotometric micro-determination of palladium at pH 2. The optimum conditions for the quantitation of Pd(II) were investigated. It was stated that Pd forms 1:1 and 1:2 (M:L) complexes and their log stability constants amount to 3.10 and 4.95 respectively. Beer's law is obeyed in the range 1-11.7 μg ml^{-1}. Several ions do not interfere [16]

Arsenazo I was used for the spectrophotometric microdeterminatiom of Ru(III) in hexamine or acetate buffer of pH 6. The reaction conditions were investigated extensively and the optimum conditions elucidated. The log stability of the 1:1 and 1:2 complexes were found to be 3.86 and 5.97, respectively. Beer's law was obeyed in the range 1-7 μg ml^{-1}, measuring the absorbance at 580 nm. The method was selective for the determination of Ru(III) towards several metal ions.[17]

Arsenazo I was used for the spectrophotometric determination of Pd(II). The optimum conditions fovouring the formation of the violet complexes were extensively investigated.[18] Arsenazo I forms 1:1 complexes with Pd(II) at pH values 2 and 12 absorbing maximally at 565 and 585 nm, respectively. The log stability constants amounted to 3.49 and 3.63 at pH 2 and 12, respectively. Beer's law was obeyed in the concentration ranges 1.0-10.6 and 0.64-6.39 μg ml^{-1}, respectively. The method was selective towards many ions, this was attributed mainly to the use of Britton and Robinson Universal buffers.

Palladium (II) was determined spectrophotometrically using chromotrope 2B (C2B).[19] The optimum conditions for the microdetermination of Pd(II) were critically investigated. Pd(II) forms 1:1 and 1:2 complexes with C2B at pH values 3, 6 and 11. The absorbance values were measured at 610 nm (pH 3), 610 and 650 nm (pH 6) and 650 nm (pH 11). Beer's law was obeyed up to 5.85 μg ml^{-1} and the molar absorptivities amount to $1.233x10^4$, $1.333X10^4$, and $1.666x10^4$ at pH 3, 6, and 11

respectively. The use of pH 3 buffer was favorably recommended rendering the method more selective.

A spectrophotometric titration method for the determination of palladium (II) ions with EDTA and CDTA, in Britton and Robinson universal buffers was suggested using chromotrope 2R (C2R) (pH 2), chromotrope 2B (C2B) (pH 3, 6, and 11), and arsenazo I (AI) (pH 2) as indicators. Also AI was used as indicator for the titration of ruthenium (III) (pH 2 hexamine or acetate buffers). The optimum concentration ranges for determination of Pd(II) were 1.0-11.7, 4.0-8.5, and 3.0-10.6 μg ml^{-1} using C2R, C2B and AI, respectively. Also, the optimum concentration range in determination of Ru(III) using AI was 3.0-20.2 μg ml^{-1}.[20]

Uranium (VI) was determined spectrophotometrically using m- (mC2C) and p-carboxyphenylazo-chromotropic acid (pC2C) in hexamine buffer of pH 5.5.[21] The absorbances were measured at 590 and 595 nm using mC2C and pC2C, respectively. Uranium forms 1:1 and 1:2 complexes with the two reagents, the log stability constants were 4.77 and 5.26 using mC2C and 5.18 and 5.35 using pC2C. Beer's law was obeyed in the ranges 2-16 (ε = 13,694±425) and 2-18 μg ml^{-1} (ε = 11,288±136) using the two reagents, respectively.

Thorium and zirconium were determined by spectrophotometric titration with EDTA using some halogenated derivatives of phenylazo-chromotropic acid as indicators. The used reagents were m-Cl, p-Cl, o,p-di-Cl, p-Br, and p-I. The quantification limits (μg ml^{-1}), pH values are as follows; for thorium 4.6-16.24, 3.5 using o,p-di-Cl; 4.6-16.24, 4.0 using p-Br; and 4.6-13.92, 3.5 using p-I, while for zirconium the data were, 3.6-10.32, 4.0 using m-Cl; 3.6-9.12, 4.0 using p-Cl, and 3.6-8.2, 4.5 using p-I.[22]

Thorium was determined spectrophotometrically using some halogen derivatives of phenylazo-chromotropic acid, (o,p-di-Cl, p-Br and p-I).[23] The optimum conditions for the determination of Th were critically investigated. Two complexes were detected having the stoichiometric ratios 1:1 and 1:2 (M:L). Beer's law was obeyed satisfactorily up to 16.24 ($\varepsilon=5.9x10^3$), 18.56 ($\varepsilon=6.00x10^3$) and 11.60 ($\varepsilon=1.73x10^4$) μg ml^{-1} using the three reagents, respectively. The absorbance values

were measured in hexamine buffers at 595 (pH 3.5), 585 (pH 4.0) and 590 (pH 3.5) nm, using the three reagents, respectively.

A spectrophotometric method was described for the determination of zirconium using m-Cl, p-Cl and p-I-phenylazo-chromotropic acid. The absorbance values were measured at 585, 590 and 590 nm (hexamine buffers).[24] Beer's law is obeyed up to 10.03 (pH 4.0), 9.12 (pH 4.0) and 8.20 (pH 4.5) μg ml^{-1} using the three reagents, respectively. Zirconium forms 1:1 complexes having log stability constants of 6.09, 5.86 and 5.80 using the three reagents, respectively.

A comparative study on the reaction of o-Cl, m-Cl, p-Cl, o,p-di-Cl, p-Br, and p-I substituted phenylazo-chromotropic acid with palladium (II) ions have shown that two (1:2) complexes are formed at two different pH values (acidic and alkaline). The p-derivatives were the most suitable reagents for the spectrophotometric determination of Pd(II) ions. The complexes absorb maximally at 580-620 nm (ε= 0.48-1.67x10^4). Beer's law was obeyed up to 6.38-8.51 μg ml^{-1}. Other parameters were listed and the optimum experimental conditions given. A spectrophotometric titration method for determination of Pd(II) was also described using EDTA as titrant.[25]

A spectrophotometric method for the determination of dioxovanadium (V) have been described using o-Cl, m-Cl, p-Cl, p-Br and p-I phenylazo-chromotropic acid derivatives.[26] Violet water soluble 1:1 and 1:2 complexes are formed at pH 4.5 (hexamine buffer). Beer's law is obeyed up to 7.80, 7.60, 7.60, 7.20 and 8.3 μg ml^{-1} using the mentioned reagents, respectively. The method is extended to the use of these reagents as indicators in spectrophotometric titration of V(V) using EDTA as titrant.

The halogen derivatives (o-Cl, m-Cl, p-Cl, and o,p-di-Cl) of phenylazo-chromotropic acid were used successfully for the determination of Iron (III) ions spectrophotometrically. The optimum experimental conditions were verified. The 1:1 and 1:2 (M:L) complexes were formed at pH 3.25 (acetate-acetic acid), the molar absorptivities were in the range 2.8-5.2 x 10^3 l mol^{-1} cm^{-1}. The equilibrium constants of the formed complexes are of the order 10^9. Beer's law is obeyed up to 4.5 μg ml^{-1} measuring at 590, 575, 585 and 610 using the four reagents, respectively. Iron (III) was also determined by titration with EDTA spectrophotometrically.[27]

Thorium content in thorium chelates with 3-acetyle- and 3-cyano-1,5-diarylformazans was determined using Kjeldahl flask digestion.[28] 5-15 mg was digested in 50 ml-flask using concentrated hydrochloric acid (5 ml) boiled for 2-3 h. Thorium in the concentration range 1-5 μg ml^{-1} was determined spectrophotometrically using Arsenazo III as chromophoric indicator measuring at 660 nm (average standard deviation = 0.123). the results were in good agreement with those theoretically calculated fron the tentative formula of the complexes as confirmed by microanalysis for C,H, and N.

Chemical Structure of Chromotropic Acid Azo Dyes and Their complexes

The relation between chemical structure and infrared absorption spectra of 17 substituted arylazo-chromotropic acid derivatives was investigated. The ir-spectra were obtained as KBr discs in the wave number range 4000-400 cm^{-1}. The different absorption bands were assigned to their corresponding groups. The relation between the stretching frequency of the azo group and Hammett substituent constant was discussed.[29]

The absorption spectra of 20 mono-phenylazo-, and 3 bis-phenylazo-chromotropic acid derivatives were obtained in organic solvents of different polarities. The absorption bands in ethanol were assigned to their electronic transitions. The first band observed in the range 235-245 nm was attributed to the local π-π* transition within the phenyl ring (^1L_a-1_A), the second band obtained in the range 270-370 nm was assigned to the ^1L_b-1_A + π-π* transition in the chromotropic acid moiety. The third band observed in the wavelength range 362-404 nm is assigned to the π-π* within the azo group. The fourth and fifth bands observed in the ranges 514-546 and 511-594 nm, respectively were attributed to the charge transfer as a result of hydrazone-azo tautomerism. The effect of substituents on the absorption maxima of the last three bands was investigated and discussed. The solvent effect on absorption spectra was also discussed.[30]

The complex formation reaction between Ti(IV), Zr(IV), and Th(IV) with 14 substituted phenylazo-chromotropic acid derivatives have been investigated using

potentiometric titrations.[31] The results reveal the formation of 1:1 and 1:2 (M:L) complexes (also confirmed by conductance titrations). The proton-, and metal ion-formation constants were reported and their values correlated to substitution Hammett constant. The modes of chelation between the metal ions and the investigated reagents have been elucidated using IR-spectroscopy.

The polarographic reduction of eleven substituted arylazo-chromotropic acid dyes was investigated at dropping mercury electrode. The reduction was performed at several conditions to determine the electrode kinetic reactions. The relation between the Hammett substituent constants and half-wave potential was linear.[32]

The solid complexes of some mono- and bis-arylazo-chromotropic acid with vanadium (IV) were prepared and subjected to elemental and thermogravimetric (TG) analyses, the structural formula of the complexes were proposed in accordance with the results of elemental analysis. Infrared spectroscopy was used to show the type and site of bonding in the complexes. The number of water molecules in the complexes was confirmed by TG. The complexes were found to undergo dehydration (drying), partial decomposition and final decomposition steps.[33]

Some chromotropic acid azo- (chromortope 2R (C2R), chromotrope 2B (2B), arsenazo I (AI), and spadns) complexes with Cr(III), Mn(II), Co(II), Ni(II) and Cu(II) were prepared and their structure investigated. The structure of the prepared complexes was elucidated using elemental analysis, thermogravimetric analysis, infrared spectroscopy, and magnetic susceptibility measurements. The formation of 1:1 and 1:2 (M:L) complexes was confirmed and their structure was elucidated.[34]

Spectrophotometric determination of pharmaceutical compounds using chromotropic acid azo dyes

The use of chromotropic acid in pharmaceutical analysis was firstly described by our group based on the fact that such azo dyes can form ion-pairs with bulky basic compounds which are soluble in water immiscible organic solvents contrary to azo compounds.

A spectrophotometric method is proposed for the determination of cephadroxil, cephlexine and cephadrine.[35] The method is based on the formation of ion-pair

complexes of the mentioned compounds with chromotrope 2B (C2B) and chromotrope 2R (C2R) to give a highly coloured radical anion. The coloured products are quantified spectrophotometrically at 542 and 564 nm for C2B and C2R, respectively. The optimization of the experimental conditions is described. The method has been used for the determination of 0.4-15, 0.4-14 and 0.4-18 μg ml^{-1} of the three drugs respectively. The accuracy of the method is indicated by the excellent recovery (100±1.7%) and the precision is supported by the low relative standard deviations ≤ 1.5%. The sensitivity of the method is discussed and the results are compared with the official method (BP 1993).[36] The interference from common degradation products and excipients was studied. The proposed method was applied successfully to the determination of the different cephalosporins in dosage forms with good precision and accuracy.

A sensitive and rapid extraction-spectrophotometric method for the determination of betamethasone, based on the formation of charge transfer complexes with benzocaprol red (BR) and acid ethyl blue (AEB) is described. The calibration graphs resulting from the measurement of the absorbance of the chloroform and benzene extracts (10 ml) at 588 and 677 nm using BR and AEB, respectively, are linear over the range 0-16 and 0-20 μg ml^{-1} of betamethasone with relative standard deviations (RSD) of 1.6 and 1.3% for 5 μg ml^{-1} betamethasone, Ringbom optimum concentration ranges were found to be 2-14 and 2-17.5 μg ml^{-1} using the two reagents respectively. The method was satisfactorily applied to the determination of betamethasone and its esters in pure form and pharmaceutical preparations and found in good agreement with the British Pharmacopoeia (1993) method.[37]

Two new spectrophotometric procedures for the determination of verapamil hydrochloride in pure form as well as in pharmaceutical preparations were suggested. The methods were based on the formation of C.T. complexes with chromotrope 2B or chromotrope 2R azo dyes followed by extraction in chloroform and measuring the absorbances at 530 and 546 nm, respectively. Linear calibration graphs were obtained in the ranges 4.91-58.93 μg ml^{-1} verapamil HCl. Variance coefficients of 1.07-3.85 and 1.09-4.10 were obtained for the verapamil tablets using C2R and C2B,

respectively, whereas for the Isoptin tablets, the C.V. values were 1.66-5.08 and 1.89-4.6 using C2R and C2B, respectively. Recoveries of 98-108 and 101-109% using C2R and C2B, respectively were recorded.[38]

A spectrophotometric method is proposed for determination of dipyridamole in pure form and in pharmaceutical preparations. Chromotrope 2B was used as charge-transfer complex forming agent with absorption maximum ≅ 40 nm red shifted relative to the chromotrope 2B itself.[39] The variables affecting the formation of the C.T. complex were studied and optimized. Linear calibration graphs were obtained up to 60 μg ml^{-1} at room temperature. The method was found to be accurate, precise and can be successfully used for authentic and pharmaceutical preparations in the working range up to 600 μg.

A spectrophotometric procedure[40] for the determination of terfenadine and a number of its pharmaceutical preparations has been developed that offers advantages of simplicity, rapidity, sensitivity and stability indication over the official USP(1995) method.[41] The proposed method is based on the formation of ion-pairs by the reaction of terfenadine with some chromotropic acid mono- and bis-azo dyes. At the maximum absorption of 557, 521, 592 and 543 nm, Beer's law was obeyed in the range 0.2-18.6, 0.2-16.4, 0.2-25.0 and 0.2-22.2 μg ml^{-1} using p-I, p-Br mono azo, p-I and p-Br bis azo dyes respectively. The stoichiometric ratio and stability of each ion-pair were estimated and the mechanism of the reaction is discussed. The molar absorptivity and Sandell sensitivity of the produced ion-pairs were calculated in addition to Ringbom optimum concentration ranges. Statistical treatment of the results indicates that the procedures are precise and accurate. Excipients used as additives in pharmaceutical formulations did not interfere in the proposed procedure. The reliability of the methods was established by parallel determination against the official USP method. The procedures described were successfully applied to the determination of the bulk drug and its pharmaceutical formulations by applying the standard addition technique.

Erythromycin and its esters were determined colorimetrically bsed on the formation of the ion-pairs with chromotropic acid (CA), chromotrope 2B (C2B), Chromotrope 2R (C2R), arsenazo I (AI), arsenazo III (AIII), benzcaprol red (BCR),

and acid ethyle blue (AEB).[42] The calibration resulting from the measurements of absorbance-concentration relations (at the optimum reaction conditions) of the extracted ion-pairs are linear over the concentration range 0.4-56 μg ml^{-1} erythromycin with a relative standard deviation (RSD) of 1.3% for 25 μg ml^{-1}. The detection limit, quantification limit, the molar absorptivity and Sandell sensitivity were evaluated. The interference from excipients commonly present in dosage forms and common degradation products was studied. The method was proved to be highly specific for the determination of erythromycin stearate and succinate esters in dosage forms. The method has been compared with the official method and found to be simple, accurate, and reproducible.

A spectrophotometric method for the rapid determination of dipyrimadole using p-chlorophenylazo-chromotropic acid (p-Cl) and p-nitrophenylazo-chromotropic acid (C2B) was proposed. Also, determination of chlorpheniramine maleate using (p-Cl), p-iodophenylazo-chromotropic acid, (p-I), C2B, and phenylazo-chromotropic acid (C2R) was suggested. The method consists of extracting the ion-associates into methylene chloride. The ion associates exhibit absorption maxima at 544 and 524 nm for p-Cl and C2B with dipyridamole, and at 540, 524, 536 and 524 nm for p-Cl, p-I, C2B and C2R with chlorpheniramine maleate, respectively. Dipyridamole was determined up to 3.50 and 3.78 mg ml^{-1} using p-Cl and C2B respectively. While Chlorpheniramine maleate was determined up to 3.10, 2.36, 1.90, and 1.70 mg ml^{-1} using p-Cl, p-I, C2B and C2R respectively. The drugs under investigation were found to react with the proposed reagents in the ratio 1:2 drug:reagent. The molar absorptivities and Sandell sensitivities were calculated. Statistical treatment of the results indicated that the procedure is precise, accurate and easily applied for the determination of the drugs under investigation in pure form and pharmaceutical formulations.[43]

A simple, accurate and highly sensitive spectrophotometric method was proposed for the rapid determination of meclozine and papaverine hydrochlorides using chromotrope 2B (C2B), and chromotrope 2R (C2R). The method consisted of extraction of the formed ion-associates into chloroform in case of meclozine HCl and into methylene chloride in case of papaverine HCl. The ionassociates exhibited

absorption maxima at 536 and 524 nm using C2B and C2R with meclozine HCl, and 540 and 528 nm with papaverine HCl respectively. Meclozine was determined up to 4.0 and 2.6 mg ml^{-1} using C2B and C2R, respectively, while papaverine was determined up to 1.68 and 1.37 mg ml^{-1}, respectively. The effects of acidity, reagent concentration, time, solvent and stoichiometric ratios of the ion associates were studied. The molar absorptivities and the Sandell sensitivities of the ion associates were calculated. The proposed method was applied to the determination of the drugs in their pure state and pharmaceutical preparations (Navidoxine tablets, 25 mg/tablet for meclozine HCl and vasorin ampoules, 60 mg/2 ml) with mean recovery values of 99.63-100.80 and 99.75-100.08% and coefficients of variation 0.945-2.210 and 1.020-1.268 for meclozine HCl and papaverine HCl respectively.[44]

Chromotropic acid was applied for the spectrophotometric determination of some sulphonamides (sulphadiazine, sulphadimidine, sulphamerazine, sulphapyridine and sulphasomidine) through its coupling with diazotized sulphonamides in sodium carbonate medium. The study revealed the formation of mono azo dye between the two reactants. The absorbance of the formed azo dyes was measured at 510 nm, with a high molar absorptivity (ε=2.87-3.29x10^4 l mol^{-1} cm^{-1}) Beers law was obeyed over the concentration range 0.5-9.0 μg ml^{-1}. The assay results of pharmaceutical formulations (sulphadiazine tablets, argiderm cream (sulphadiazine) and sulphadimidine sodium vials) showed good accuracy and precision over the recommended concentration range.[45]

A simple, fairly rapid, sensitive and accurate method is described for the colorimetric determination of neomycin sulphate (NMS), based on the measurement of the absorbance of the extracted the organic soluble ion-associate complex formed between NMS and chromotropic acid azo dyes. Several mono- and bis-chromotropic acid azo dyes were used as counter ions.[46] The effect of pH, the counter ion concentration, sequence of addition, and solvent used for extraction was critically tested. The most suitable system was based on the bis-p-iodo derivative at pH 7, using chloroform as the extraction solvent. The use of other derivatives was though successful yet less sensitive. The recommended reagent shows high selectivity towards several drug excipients. Determination of NMS up to 58 μg ml^{-1} was

achieved with good recovery (99.8±1.5%), and high precision as supported by the low relative standard deviation ≤1.3%. The proposed method was applied successfully to the determination of NMS in pure and dosage forms, with good precision and accuracy compared to the official method.

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