Extractive Spectrophotometric Determination of some Drugs Through Ion-Pair Complex Formation with Thiocyanate wnd Cobalt (II) or Molybdenum (V)

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Abstract: Two rapid, simple and sensitive extractive specrophotometric methods has been developed for the assay of Hyoscine butyle bromide (HBB), losartan potassium (LSR) and Sertaline HCl (SER) in bulk and in their pharmaceutical formulations. The proposed methods depend upon the reaction of cobalt(II)–thiocyanate (method A) and molybdenum(V)–thiocyanate ions (method B) with the cited drugs to form stable ion-pair complexes which is extractable with an n-butnol–dichloromethane solvent mixture (3.5:6.5) and methylene chloride for methods A and B, respectively. The blue and orange red color complexes are determined either colorimetrically at λmax 625,627 and 630 nm for HBB,SER and LSR respectively (using method A) and 478 , 465 and 468 nm for HBB,SER and LSR respectively (using method B). The concentration range is 20–400 and 5–50 gmL^{-1} for methods A and B, respectively. The proposed method was successfully applied for the determination of the studied drugs in pure and pharmaceutical formulations applying the standard additions technique and the results obtained were in good agreement with those obtained by the official method.

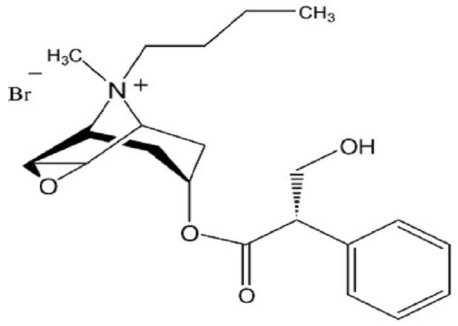
[Ragaa El-Shiekh, Magda Akl, Ayman Gouda and Wael Ali. **Extractive Spectrophotometric Determination of some Drugs Through Ion-Pair Complex Formation with Thiocyanate wnd Cobalt (II) or Molybdenum (V).** Journal of American Science 2011;7(4):794-807]. (ISSN: 1545-1003). http://www.americanscience.org.

Keywords: Hyoscine butyle bromide; losartan potassium ;Sertaline HCl ; Ion-pair complexes; Specrophotometry; Pharmaceutical formulations

1. Introduction:

Hyoscine butylbromide (HBB), (1S, 3s, 5R, 7S, 8r)-6,7-epoxy-3-[(*S*)-(3-hydroxy-2-phenylpropiony)oxy]-8-butyl-8- methyl-8-azoniabicyclol [3.2.1] octane bromide is used as an antispasmodic in treating peptic ulcer, gastritis and various disorders of the gastrointestinal tract which are characterized by spam.(Structure 1) It has also been found an employment for the relief of spasmodic conditions of the bile duct and urinary tract and for the treatment of dysmenorrhoea [10]. Famciclovir (FCV) is an antiviral drug and is chemically [2-(acetyloxymethyl)- 4-(2-aminopurin-9-yl)-butyl] acetate. **HBB** has been determined in pharmaceutical preparations including titrimetric methods spectrophotometric [11,12], high-performance liquid chromatographic [13], capillary electrophoresis [14,15] and electrochemical methods [16].

Losartanpotassium (LSR), 2-butyl-4-chloro-1-[[2′-(1H-tetrazol 5-yl)[1,1′-biphenyl]-4-yl]methyl]-1H-imidazole-5-methanol monopotassium salt, is the first member of a new class of nonpeptide angiotensin II receptor antagonist (Structure 2). It acts effectively at its receptors, thereby blocking the rennin-angiotensin system.[17,18] several analytical procedures have been reported for the determination of losartan potassium products in tablets, individually or in combination with other drugs; these include flow injection [19], high performance liquid chromatography (HPLC) [20,21,22], capillary zone electrophoresis [23], spectrophotometry [24–26], and electrochemical techniques [25].

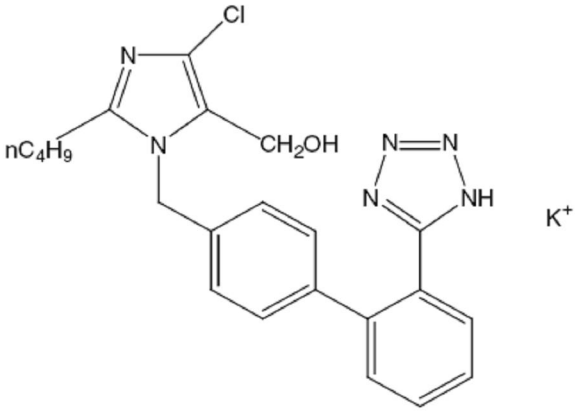


hyoscine butylbromide (HBB)

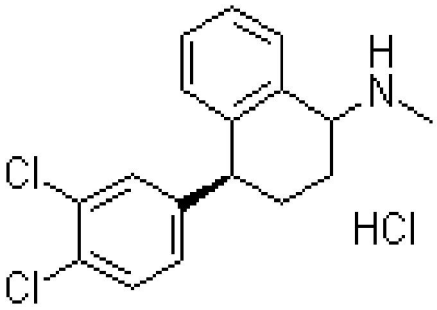
Structure (1)

Sertraline hydrochloride (Sert), (1S,4S)-4-(3,4-dichlorophenyl) -N-methyl-1,2,3,4-tetrahydronaphthalen-1-amine hydrochloride, is a selective serotonin reuptake inhibitor (SSRI) with

actions and uses similar to those of fluoxetine (Structure 3). Sertraline is slowly absorbed from the gastrointestinal tract with peak plasma concentrations occurring from about 4.5 hours to 8.5 hours after ingestion. It undergoes extensive first-pass metabolism in liver. The main pathway is demethylation to N-desmethylsertraline, which is inactive; further etabolism and glucuronide conjugation occurs [26]. Sertraline is widely distributed throughout body tissues and is highly bound (about98 %) to plasma proteins. various methods have been used for the determination of sertraline hydrochloride, its metabolites in human plasma and in pharmaceutical dosage forms, including HPLC method [27] gaschromatography-ass spectrometry [28,29] spectrophotometric method [30].



Losartan K (LSR)
Structre(2)



(Structure 3)

2. Expermental Section:

2.1. Apparatus:

ATI UNICAM (UV/Vis) Ver. 3.20 with scanning speed 200 nm/min, lamp change 325 nm, and band width 2.0 nm, equipped with 10 mm matched quartz cells.

Jenway pH meter 3310 for pH measurements.

2.2 Materials and reagents:

All chemicals and reagents were of analytical grade and water was always bidistilled water

2.2.1 Standard solution of drugs:

Stock solutions (100 μg mL^{-1}) of the studied drugs were freshly prepared by dissolving 10 mg of the drug in distilled water and then, completed to the mark in a 100 mL calibrated flask with distilled water. Working standard solutions were prepared by suitable dilution of the stock. These solutions are stable for at least 1 week if kept in the refrigerator.

2.2.2. Pharmaceutical formulations:

All the drugs in the pure form and formulations are provided by the Egyptian pharmaceutical companies in the local markets.

2.2.2.1 Hyoscine butylbromide (HBB) was supplied by Chemical Industries Development (CID), Egypt.
Pharmaceutical preparations:
1- Buscopan tablets (10 mg Hyoscine -N-Butylbromide per tab.)
2- Buscopan ampoules (20 mg Hyoscine -N-Butylbromide per amp.

2.2.2.2 Losartanpotassium (LSR) was supplied by the Universal Industrial Pharmaceutical Company (Unipharma), Egypt & Amriya Pharmaceutical Industries, Alexandria, Egypt.
Pharmaceutical preparations:
1-Losar 50 tablets (50 mg Losartanpotassium per tab.) (Unipharma)
2- Losartan 50 tablets (50 mg Losartanpotassium per tab.) (Amriya)

2.2.2. 3 Sertraline hydrochloride (SER) was supplied by Apex pharma, Egypt& Pharco Pharmaceuticals Co. Alexandria, Egypt.
Pharmaceutical preparations:
1-Moodapex 50 tablets (50 mg Sertraline hydrochloride per tab.) (Apex pharma)
2- Sertral 50 tablets (50 mg Sertraline hydrochloride per tab.) (Pharco)

2.2.3 Reagents:

Cobalt(II)–thiocyanate solution (method A) [5×10^{-3} M] was prepared by dissolving 11.9 g of cobalt chloride hexahydrate and 28.13 g of ammonium–thiocyanate in 100mL of water [38].

Molybdenum (VI) solutions (method B), 1×10^{-3}M aq. solution was also prepared by dissolving an appropriate weight of ammonium molybdate tetrahydrate in bidistilled water containing a fewdrops of ammonia and standardized gravimetrically using 8-hydroxyquinoline [31]. Ammonium–thiocyanate and ascorbic acid 10% aqueous solutions were prepared in distilled water. Citrate buffer, 0.4 M, was prepared by mixing various volumes of 0.4M citric acid and 0.4M sodium citrate solutions to the required pH values (2.0–6.0) as recommended [32].

2.3. General procedures for drugs in pure form

2.3.1. Method A (using cobalt(II)–thiocyanate)

Accurately measure aliquots of HBB, LSR or SER in the concentration ranges shown, were transferred into a 50 ml separating funnel, 5.0 ml of 5×10^{-3} M Co (II) thiocyanate solution and 5 ml of citrate buffer solution of the optimum pH 2.8, and 0.5 ml acetone were added successively. The volume of aqueous phase was adjusted to 20 ml with bidistilled water. Equilibrate the solution with 20 ml of n-butanol-dichloromethane mixture (3.5:6.5) by shaking for 1.0 min. The organic layer was separated and dried over anhydrous sodium sulfate. Into a 25 ml calibrated flask, the upper layer solution was filtrated through a Whatman No. 41 filter paper moistened with n-butanol-dichloromethane mixture, washed, if necessary, and adjust to the mark with the same solvent. The absorbance was then measured at 627 nm for SER, 630 nm for LSR and 625 nm for HBB versus a reagent blank prepared and treated similarly.

2.3.2. Method B (using molybdenum (V) thiocyanate)

In 50 mL separating funnel, 2.0 mL of (1×10^{-3} M) ammonium molybdate is added, 3.0 mL of HCl (4.0 M), 3.0 and 4.0 mL (10%) each of ammonium thiocyanate and ascorbic acid were mixed and left for 15 min at room temperature (20±5°C). Appropriate volumes of standard solutions in the concentration range stated were added and diluted with bidistilled water up to 20 ml. After another 10 min, 10 ml of methylene chloride was added twice with 5-ml portions, the mixture was shaken well for 1 min and allowed to separate into two phases. The organic layer was collected and dried over anhydrous sodium sulfate and its absorbance of the extract was measured at 465 nm for SER, 468 nm for LSR and 478 nm for HBB versus a reagent blank prepared similarly without the drugs.

2.4. Procedures for dosage form:

2.4.1. Procedures for tablets

At least 10 tablets of the investigated drugs were weighted into a small dish and the contents of five drops bottles (1.0 g Dextromethorphan hydrobromide per 15 mL) and five ampoules (Buscopan amp, 20 mg HBB per ampoule) are mixed well. A portion equivalent to 100 mg was weight and dissolved in 100 ml water, shaken well and filtered through a sintered glass crucible G4 and washed with distilled water. Then, the filtrate and washings were diluted to 100 mL with distilled water in a 100 mL calibrated flask. An aliquot portion of the solutions was used for the determination of each drug according to the procedure mentioned above.

2.4.2. Procedures for ampoules

The contents of five ampoules (20 mg HBB)were mixed and the average volume for one bottle or one ampoule was determined and quantitatively transferred into 100mLcalibrated flasks completed to the mark with water.An aliquot portion of the solutions was used for the determination of each drug according to the procedure mentioned above.

3. Results and discussion:

3.1. Method A (Using Cobalt (II) Thiocyanate)

The formation of the ion-pairs between the tertiary amine group of the drug and Co(II) thiocyanate binary complex occurs via the protonated nitrogen atom of the drug. Cobalt (II) thiocyanate complex is a classical reagent in pharmaceutical analysis. Several colorimetric methods for the determination of some drugs in pharmaceutical preparations use Co(II)-thiocyanate solution as a reagent forming blue-colored extractable ion-pairs.

In this work the investigated drugs were found to react with the cobalt (II) tetrathiocyanate ions to form ion-pair complexes. This interaction and subsequent formation of the ion-pairs occurred in acidic medium via the protonated nitrogen atom of the drugs. Although, the weak $[Co(SCN)_4]^{-2}$ ion complex became stabilized through the formation of the ion-pairs with the studied drugs, those produced ion-pair complexes were still highly labile and needed a large excess of $[Co(SCN)_4]^{-2}$ ions to be stabilized in the aqueous phase. Therefore, the produced ion-pairs were further satisfactorily stabilized by extraction into organic solvents [33]. and thus were determined accurately without interference from the excess unreacted metal complex in the aqueous phase. Concerning our investigated drugs, the common non-polar organic solvents such as chloroform, dichloromethane, 1,2-dichloroethane, benzene, and nitrobenzene failed to extract the ion-pairs due to their insolubility while solvents with more polarity, such as n-butanol and isobutylmethylketone, lacked selectivity. Therefore solvent mixture of

dichloromethane and n-butanol were tried. Better results regarding selectivity and accuracy were achieved using 35% n-butanol in dichloromethane in which the ion-pairs exhibited a greenish blue color with maximum absorbance at 625 nm for HBB,630 nm for LSR,and 627nm for SER against a reagent blank .

The different experimental parameters affecting the formation of the ion-pair complexes were extensively studied to determine the optimal conditions for the assay procedure.

3.1.1. Effect of pH

The results were obtained by varying the pH for the aqueous phase within the range of 1.5-5.0 using 0.4 M citrate buffer.A maximum absorption was clearly detected between 2.5-3.2 pH values at which the studied drugs were found to be maximally protonated thus helping the ion-pair formation

3.1.2. Effect of solvent mixture ratio

Dichloromethane was used as a solvent mixture with n-butanol to enhance the extraction selectivity of the latter toward the formed ion-pairs and considerably lower its extraction ability of the reagent blank. The study revealed that a volume ratio of 35% (regarding n-butanol/total volume of the organic phase) was the most suitable for the ion-pair extraction with minimal blank reading

3.1.3 Effect of reagents concentration

The Co(II) thiocyanate concentration suitable for ion pair formation and extraction, was found to be 5.0 ml of 5×10^{-3} M reagent in an aqueous solution of 20 ml proved to be required for maximum stabilization of the ion-pair associates as indicated by attainment of maximum absorbance .

3.1.4. Effect of number of extractions, shaking time and stability

Reproducible absorbance readings were obtained after a single extraction with 20 mL of the solvent mixture and a 1 min shaking time. Acetone was considered to be an ideal diluent for the extraction process, because it increases the extraction efficiency. The studied ion-pairs were stable for more than 24 hours at 25 °C in the organic solvent.

3.1.5. Reaction mechanism

A proposal for the reaction mechanism taking DEX as an example is presented in (Scheme 1). The shapes of the curves of the cobalt thiocyanate ion-pairs also indicated that the associates are too labile, as further indicated by the need for a large excess of the reagent to enhance stability of the ion-pairs.

3.2. Method B (Using Molybdenum(V) Thiocyanate)

Molybdenum (V) formed by the reduction of molybdenum(VI) with ascorbic acid combines with ammonium thiocyanate to form a red binary molybdenum (V) thiocyanate complex in 0.8-3.2 M hydrochloric acid is non-extractable with methylene chloride [34]On adding of the investigated drugs solution, an orange red ion-pair complex is formed and extractable with methylene chloride and had an absorption maximum at 478 , 465 and 468 nm for HBB,SER and LSR respectively against a reagent blank (Fig.6).

It was found that, the reduction probability of Mo(VI) to Mo(V) may occur by ascorbic acid or SCN^- in acidic media must be considered. It was also found that the rapidity, sensitivity and stability of Mo(V)-thiocyanate ion-pairs were depended on using ascorbic acid. Ascorbic acid gave reproducible values and masked many interfering ions.

3.2.1. Effect of ammonium molybdate

The effect of ammonium molybdate on the formation of the ion-pair complex and their extraction in methylene chloride was studied (Fig. 22). It was found that 1.5 and 2.0 mL of 1 x 10^{-3} M ammonium molybdate in a final aqueous solution of 20 mL. Also, it was found that 3.0 mL of the studied drugs (10 % each) of ammonium thiocynate and ascorbic acid in a final solution of 20 mL gave the maximum pronounced effect.

3.2.2. Effect of Acidity

It was found that the ion-pair were formed only in hydrochloric, sulfuric, nitric or phosphoric acid medium.The optimum acidity concentration range for maximum absorbance values and for extraction, was found to be between 1.0-5.0 M hydrochloric acid. It was found that 3.0 mL of 4.0 M hydrochloric acid was sufficient for maximum absorbance and the formation of Mo(V) thiocyanate-drug ion-pairs.

3.2.3. Effect of solvent

The common organic solvents such as methylene chloride, ethanol, methanol, chloroform, and benzene were examined. Methanol and other oxygenated solvents were found to extract both binary and ternary complex. Using slightly polar or non-polar solvents, such as dichloromethane and chloroform, the ternary complex could be extracted. Moreover, dichloromethane have high solubility of the ternary complex in this solvent. A double extraction was necessary to extract the complexes into the organic phase. An organic aqueous ratio of 1:2 was suitable for complex extraction of the ternary

complex. The organic red color in dichloromethane was quit stable for at least 24 hours. From the results an equation representing the reaction of Mo(VI) with ammonium thiocyanate in 4.0 M HCl and in the presence of ascorbic acid was suggested to be as follows:

$$Mo(VI) \xrightarrow{\text{ascorbic acid}} Mo(V) \xrightarrow{6SCN^-} Mo(SCN)^-_6$$

In this method, the complete formations of the ion-pairs needs 10 min before extraction with methylene chloride at room temperature (25 °C). the absorbance of Mo(V)-thiocyante binary complex was stable after 15 min while Mo(V)-thiocyanate-drugs ion-pairs need another 15 min for their complete formation.

3.3. Composition of the ion-pair associates

The composition of the ion-pair associates was established by Job's method of continuous variation [35]and molar ratio methods [36] using equimolar solutions of the drugs and reagents Mo(V) and Co(II) thioyanate. The results obtained are shown in (Fig 5 and 8) and indicated that the composition of the associates was (2:1) (drug: reagent). This stoichiometric ratio supported that the interaction between the studied drugs and the reagent used took place at only one site which was the more sterically free terminal basic aliphatic amino group.

3.4. Method of Validation

Under the experimental conditions described above, the calibration graphs for the four drugs were constructed for both methods over the concentration ranges cite in (Table 1). the molar absorptivities, the Sandell sensitivities and the regression equations, intercepts, slopes, and correlation coefficients for the calibration data for each drug are tabulated. The results obtained were compared with those of the official methods. Detection limits (3σ) and statistical analysis of the obtained results revealed that there is no significant difference between both as shown in (Table 1). Six replicate determinations at different concentration levels were carried out to test the precision of the methods. The relative standard deviations were found to be less than 1.4 %, indicating reasonable repeatability of the selected methods. The results obtained for each drug using the proposed Co(II) or Mo(V) thiocyanate methods are sensitive. The performance of the proposed methods was assessed by comparison with the official method. Mean values were obtained with a Student's *t*- and *F*-tests at 95% confidence limits for five degrees of freedom. The results showed comparable accuracy (*t*-test) and precision (*F*-test), since the calculated values of *t*- and *F*-tests were less than the theoretical data (Table 1).

3.4.5.Analytical Applications

The proposed methods were applied to the determination of Hyoscine n-Butylbromide and ,Sertraline hydrochloride (SER) and Losartan potassium (LSR) in pure and dosage forms using the standard additions method. The obtained results are given in (Tables 2-4) for the analysis of commercial preparations. The proposed methods has the advantage of being virtually free from interference (either from excipients such as lactose, fructose and starch or from common degradation products). Therefore, the standard addition principle was used to evaluate the accuracy of the proposed methods and to test interferences (Tables 2-4). The recoveries% of the drugs in their commercial preparations compared with that of the reference methods are given in (Table 5).

4. Conclusions

The proposed methods described in this paper are simple, rapid, and applicable for routine analysis of some drugs, e.g., Hyoscine butyle bromide (HBB), losartan potassium (LSR) and Sertaline HCl (SER) in bulk and in their pharmaceutical formulations through the formation of ion-pairs by the reaction of the studied drugs and cobalt (II) or molybdenum (V) and thiocyanate over a wide concentration range without interference from common excipients. Moreover, it exhibits the advantage of being convenient at low cost without losing accuracy.

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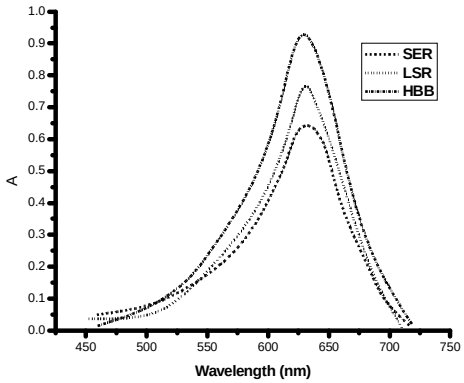


Figure (1) Absorption spectra of the ion-pair associates formed between (5.0 x 10^{-3} M) cobalt (II) thiocyanate complex and the studied drugs, SER at λ = 627 nm , LSR at λ =630 nm and HBB at λ =625 nm in n-butanol- dichloromethane.

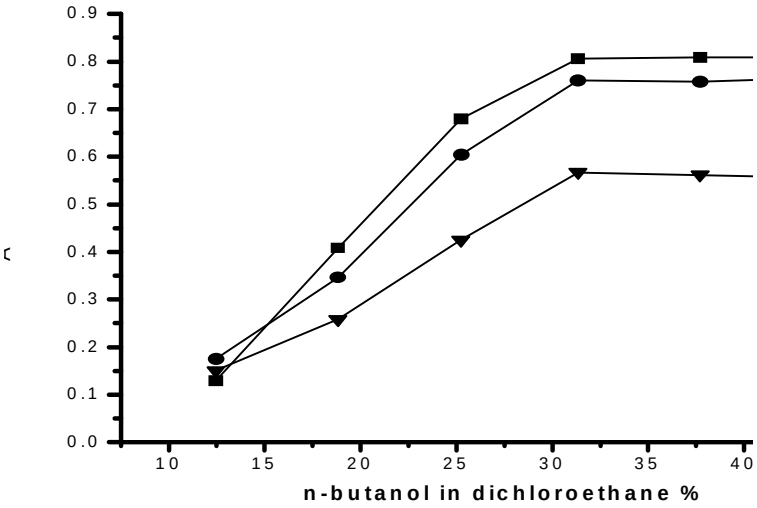


Figure (2) Effect of n-butanol concentration on the extraction efficiency of the formed ion-associates of the studied drugs with cobalt (II) thiocyanate complex.

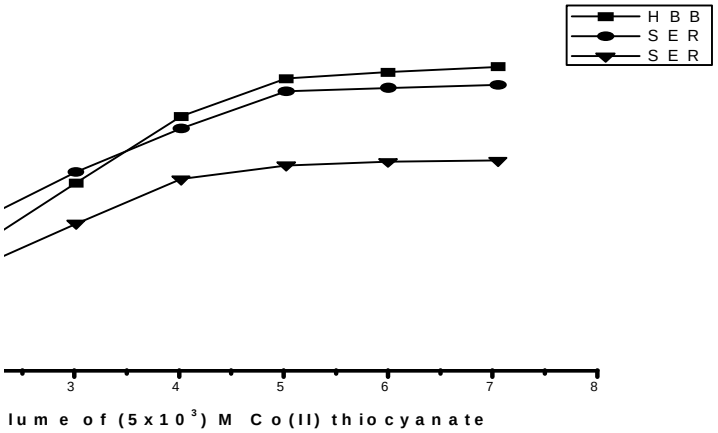


Figure (3) Effect of cobalt (II) thiocyanate concentration on the development of the ion-associates of the studied drugs .

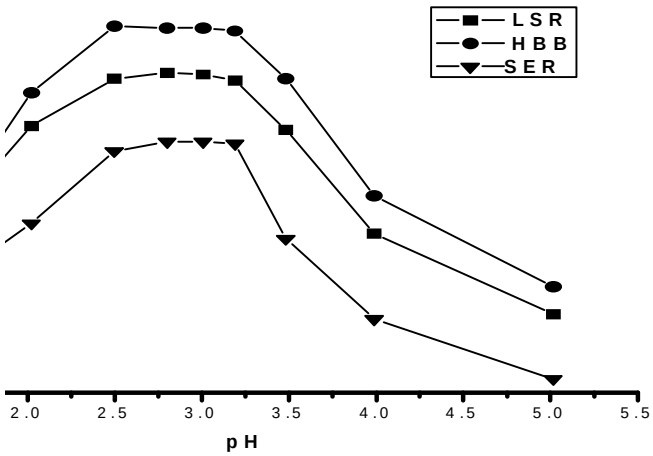


Figure (4) Effect of pH on the development of the ion associates of the studied drugs with cobalt (II) thiocyanate complex .

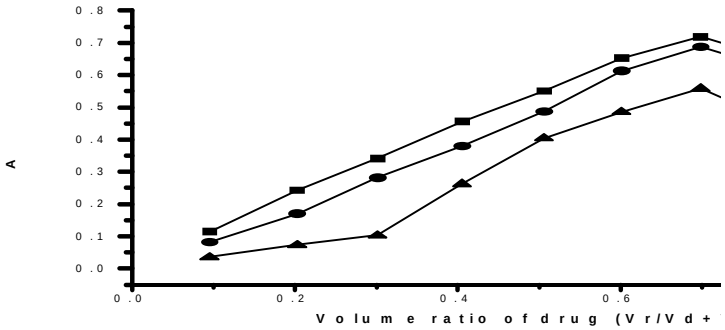


Figure (5) Continuous variation plots for the ion-association complexes of the studied drugs with (5 x 10^{-3} M) with cobalt (II) thiocyanate complex Where, Vd and Vr are the volumes of added drug and reagent, respectively; (Vd + Vr) = 1 mL.

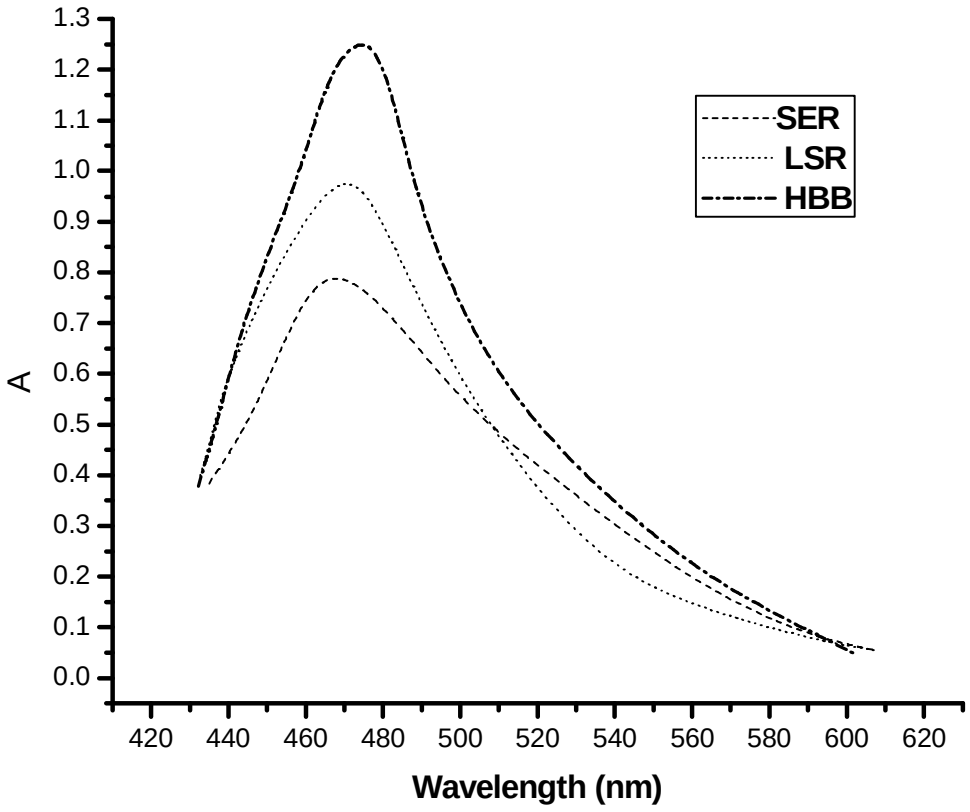
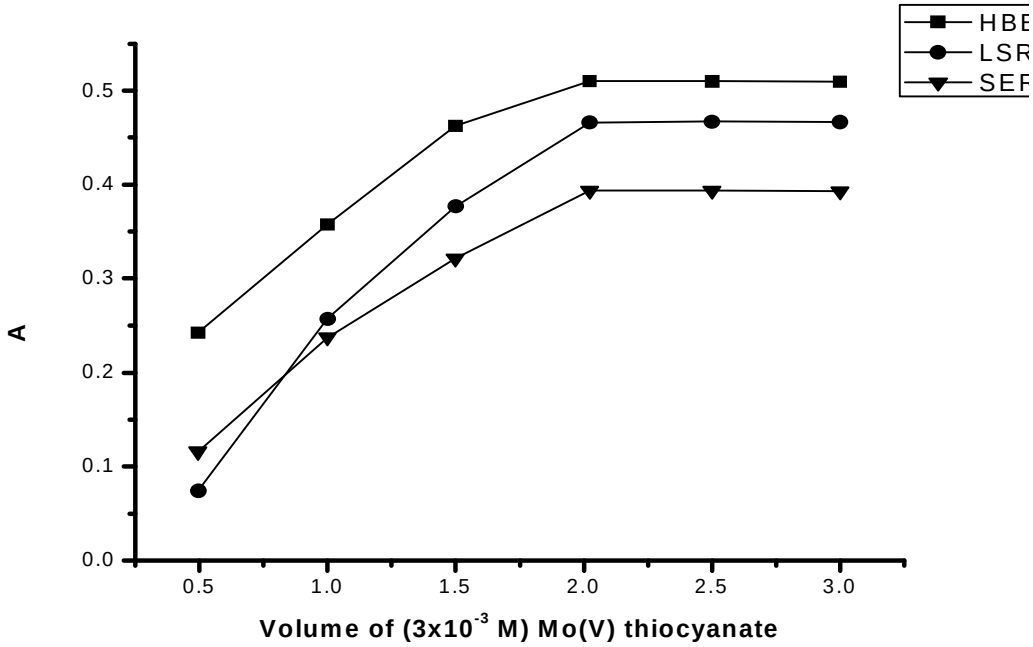


Figure (6) Absorption spectra of Mo(V) ion-pairs in methylene chloride vs. Reagen blank. 1:SER 465 nm, 2: LSR468 nm and 3:HBB 478 nm



Figure(7) Effect of Mo (V) thiocyanate concentration on the development of the ion-associates of the studied drugs.

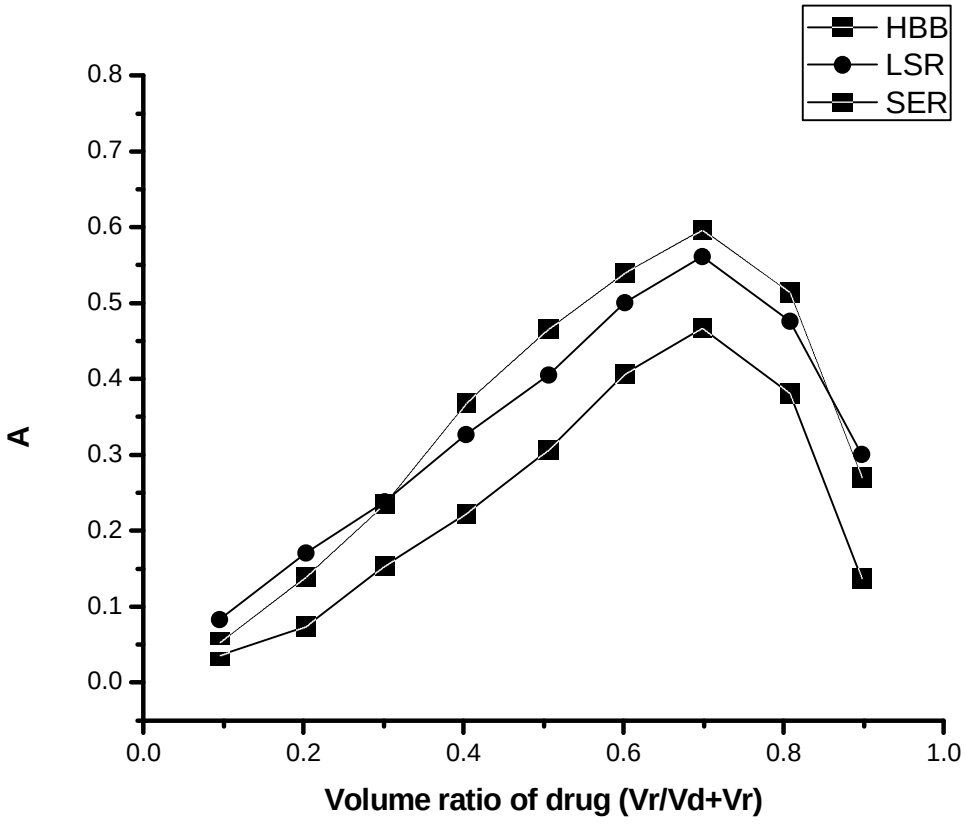


Figure (8) Continuous variation plots for the ion-association complexes of the studied drugs with (1 x 10^{-3} M) with Mo (V) thiocyanate complex. Where, Vd and Vr are the volumes of added drug and reagent, respectively; (Vd + Vr) = 1 mL.

Table (1). Analytical Parameters for The determination of The studied Drugs by The proposed Methods.

* A=a + bC, where C is the concentration in (µg mL^{-1}), A is the absorbance, a is the intercept and b is the slope.

Parameters	Co(II) thiocyanate			Mo(V) thiocyanate		
	SER	LSR	HBB	SER	LSR	HBB
λmax	627	630	625	465	468	478
Conc. Range(µg mL^{-1})	20-300	35-350	50-400	5-30	4-50	5-45
Molar absorpitivity ε, (L mol^{-1} cm^{-1}) x 10^4	0.231	0.1229	0.1782	1.155	1.745	1.332
Sandel sensitivity, (µg cm^{-2})	0.318	0.258	0.511	0.054	0.027	0.043
Regression equation *						
Intercept	0.052	0.0172	0.0312	0.025	0.198	0.014
Slope	0.0036	0.0014	0.0022	0.0244	0.0155	0.017
Correlation coefficient (*r*)	0.9997	0.9990	0.9998	0.9997	0.9998	0.9998
RSD%	1.64	1.23	1.44	1.3	0.8812	1.291
Detection limits (µg mL^{-1})	0.59	0.84	0.77	0.52	0.26	0.18
SE	0.442	0.563	0.37	0.71	0.32	0.44
V	1.947	1.44	1.62	1.39	1.91	1.93
Mean ± SD	100.16±1.64	99.18±1.23	100.11±1.44	100.36 ±1.31	100.45±0.64	99.82±1.291
Reference method	99.53 ± 1.47	100.08± 1.06	99.22 ±1.39	99.53 ± 1.47	100.08± 1.06	99.22 ±1.39
Calculated t-value (2.57)**	0.63	1.21	1.07	0.85	0.67	0.68
Calculated F-value (5.05)**	1.31	1.46	1.11	1.20	2.74	1.00

** Theoretical values for five degrees of freedom and 95 % confidence level at p = 0.05 **Miller (1993)**.

Table (2). Application of The standard Addition Technique for The Determination of SER in Pharmaceutical Preparations Using The Proposed Methods.

Sample	Co(II)-thiocyanate			Mo(V)-thiocyanate		
	Taken (µg mL^{-1})	Added (µg mL^{-1})	Recovery* (%)	Taken (µg mL^{-1})	Added (µg mL^{-1})	Recovery* (%)
Moodapex 50 Tablets	100	-	100.08	10	-	99.65
(50 mg SER / tab)		40	99.97		4	100.30
		80	99.5		10	98.93
		120	98.88		16	99.45
		150	99.75		22	100.50
		180	100.2		26	99.70
Mean ± SD			99.73± 0.49			99.76±0.57
N			5			5
V			0.235			0.33
R.S.D			0.49			0.57
S.E			0.198			0.234
Sertral 50 Tablets	100	-	99.98	10	-	100.15
(50 mg SER / tab)		40	100.08		4	99.85
		80	100.25		10	98.95
		120	99.91		16	99.97
		150	100.4		22	100.5
		180	99.87		26	100.3
Mean ± SD			100.08±0.21			99.95±0.54
N			5			5
V			0.043			0.295
R.S.D			0.21			0.54
S.E			0.085			0.222

* The average of at least three determinations.

Table (3). Application of The standard Addition Technique for The determination of HBB in Pharmaceutical Preparations Using The ProposedMethod

Sample	Co(II)-thiocyanate			Mo(V)-thiocyanate		
	Taken (µg mL^{-1})	Added (µg mL^{-1})	Recovery* (%)	Taken (µg mL^{-1})	Added (µg mL^{-1})	Recovery* (%)
Buscopan Tablets	**100**	**-**	**100.7**	**10**	**-**	**99.56**
(10 mg HBB / tab.)		**50**	**100.27**		**5**	**99.41**
		100	**99.91**		**10**	**98.39**
		150	**99.48**		**15**	**101.56**
		200	**98.71**		**20**	**100.34**
		250	**99.64**		**25**	**99.52**
Mean ± SD			**99.79±0.69**			**99.80±1.06**
N			**5**			**5**
V			**0.472**			**1.133**
R.S.D			**0.69**			**1.06**
S.E			**0.28**			**0.435**
Buscopan Ampoules	**100**	**-**	**100.12**	**10**	**-**	**100.32**
(20 HBB/amp.)		**50**	**101.03**		**5**	**99.47**
		100	**99.74**		**10**	**100.55**
		150	**99.71**		**15**	**99.59**
		200	**98.96**		**20**	**100.27**
		250	**99.88**		**25**	**99.93**
Mean ± SD			**99.91±0.674**			**100.02±0.43**
N			**5**			**5**
V			**0.454**			**0.186**
R.S.D			**0.674**			**0.43**
S.E			**0.275**			**0.176**

* The average of at least three determinations.

Table (4). Application of The standard Addition Technique for The determination of LSR in Pharmaceutical Preparations Using The Proposed Methods.

Samples	Official methods	Co(II)-thiocyanate	Mo(V)-thiocyanate
Buscopan Tablets			
X ± SD	**99.70 ± 1.163**	**100.02±1.24**	**99.94±0.975**
t-value (2.57)*		**0.42**	**0.35**
F*-value (5.05)		**1.14**	**1.43**
Buscopan Drops			
X ± SD	**100.50 ± 1.364**	**100.06±1.18**	**99.84 ± 1.57**
t-value (2.57)*		**0.55**	**0.71**
F*-value (5.05)		**1.34**	**1.32**
Losartan 50 Tablets			
X ± SD	**98.92 ± 0.852**	**99.37 ± 0.624**	**99.60 ± 1.03**
t-value (2.57)*		**0.96**	**1.13**
F*-value (5.05)		**1.86**	**1.46**
Losar 50 Tablets			
X ± SD	**99.22 ±1.39**	**99.72 ± 1.08**	**99.93 ± 1.25**
t-value (2.57)*		**0.63**	**0.85**
F*-value (5.05)		**1.66**	**1.24**
Sertral 50 Tablets			
X ± SD	**99.90 ± 0.51**	**100.07 ± 0.477**	**99.48 ± 0.63**
t-value (2.57)*		**0.54**	**1.16**
F*-value (5.05)		**1.14**	**1.53**
Moodapex 50 Tablets			
X ± SD	**98.97± 0.52**	**99.18 ± 0.39**	**98.60 ± 0.46**
t-value (2.57)*		**0.72**	**1.19**
F*-value (5.05)		**1.78**	**1.28**

*The average of at least three determinations

Table (5). Application of The proposed Methods to The determination of the studied Drugs in Pharmaceutical Preparations

Sample	Co(II)-thiocyanate			Mo(V)-thiocyanate		
	Taken (µg mL^{-1})	Added (µg mL^{-1})	Recovery* (%)	Taken (µg mL^{-1})	Added (µg mL^{-1})	Recovery* (%)
Losartan 50 Tablets	**100**	**-**	**100.16**	**10**	**-**	**99.98**
(50 mgLSR / tab.)		**50**	**101.17**		**5**	**100.15**
		100	**99.27**		**10**	**101.24**
		150	**98.65**		**20**	**99.95**
		200	**99.59**		**30**	**99.84**
		300	**100.09**		**40**	**100.39**
Mean ± SD			**99.82±0.864**			**100.26±0.52**
N			**5**			**5**
V			**0.747**			**0.268**
R.S.D			**0.864**			**0.52**
S.E			**0.353**			**0.211**
Losar 50 Tablets	**100**	**-**	**99.96**	**10**	**-**	**100.40**
(50 mg LSR / tab)		**50**	**100.05**		**5**	**99.67**
		100	**98.75**		**10**	**101.2**
		150	**99.19**		**20**	**100.35**
		200	**99.94**		**30**	**99.60**
		300	**100.18**		**40**	**98.95**
Mean ± SD			**99.68±0.57**			**100.03±0.79**
N			**5**			**5**
V			**0.328**			**0.62**
R.S.D			**0.57**			**0.79**
S.E			**0.234**			**0.321**

* theoretical values at P= 0.05 at 95 % level.
** average of six determinations.

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