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QUANTITATIVE ANALYSIS OF SOME PHARMACEUTICAL FORMULATIONS THROUGH CHARGE TRANSFERCOMPLEXATION REACTION

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ABSTRACT

Three accurate, rapid and simple spectrophotometric procedures were developed for the analysis of Aripirazole (I), Sumatriptan succinate (II), Lamivuidine (III) and Rabeprazole sodium (IV) in pure form as well as in their pharmaceutical formulations. The methods were based on formation of charge transfer complexes between the studied drugs as n-electron donors with three different reagents acting as electron acceptor either π-acceptor such as p-chloranilic acid (PCA) and 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) or σ-acceptor as iodine. The different experimental parametrs affecting the development and stability of the color including reagent concentration, reaction solvent, time and temperature, were carefully studied and optimized. The obtained charge transfer complexes (CTC) were measured generally at 520nm (for PCA), 460nm (for DDQ) and 290nm (for iodine). Beer's law limits, molar absorbitivity,Sandell's sensitivity, detection and quantifications limits were also investigated. The proposed methods were validated and successfully applied for determination of the studied drugs in pure form and in pharmaceutical preparations. The obtained results were statistically compared with reference methods and no significant differences were found.

INTRODUCTION

Charge transfer complexes are known as electron donor-acceptor complexes in which one electron was transfered from the donor to the acceptor component of the complex. Acceptors may be of the σ or of the π-type. In this study we use iodine as σ-acceptor and (PCA and DDQ) as π-acceptor. These acceptors form complexes with a variety of aromatic, aliphatic and heterocyclic compounds containing lone pair of electrons on oxygen, sulfur and nitrogen atoms.

As the investigated drugs contain these atoms in their structures, they are considered good electron-donors which can strongly react with these acceptors. In this work PCA and DDQ react with the four cited drugs but in case of iodine it reacts with the drugs except lamivuidine. Hence the reaction of PCA with the four cited drugs, DDQ with I [1a], II [1b] and III [1c] and iodine with I, II and IV [1d] will be studied.

Aripirazole, 7-{4- (4- (2, 3-dichlorophenyl)-1-piprazinyl) butoxy}-3,4-dihydro-2 (1H)-quinolinone (table 1), is an atypical antipsychotic agent used in treatment of schizophrenia and mania associated with bipolar disorder. A thorough literature survey has revealed few methods for the estimation of aripirazole using spectrophotometrictechnique. Nandini and Sachdev [2] have developed two simple spectrophotometric methods for the estimation of aripirazole in tablet formulation. The methods were based on formation of chloroform extractable complex with rosanilin HCl and bromocresol purple. Sankar [3] et al used three different reagents for its determination which are 2, 6-dichloroquinone-4-chlorimide (DCQC), 1,2-naphthoquinone-4-sulphonic acid (NQS) and sodium nitroprusside (SNP) in presence of hydroxyl amine and alkali. Validation of spectrophotometric methods for its determination in UV region have been developed [4-7]. Chromatographic methods for its determination like HPLC [8] and LC-MS/MS [9] have been reported.

Sumatriptan succinate (II), 3-[2- (Dimethylamino) ethyl] –N-methyl-1H indole-5 - methane sulphonamide succinate (table 1), is antimigraine drug. It is official in United States Pharmacopoeia [10], which suggests chromatographic methods for its determination in bulk and tablet formulations.

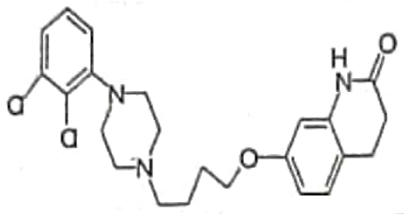
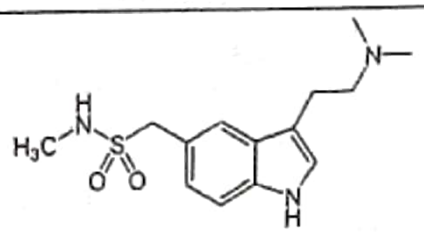
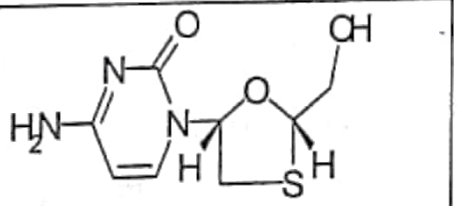
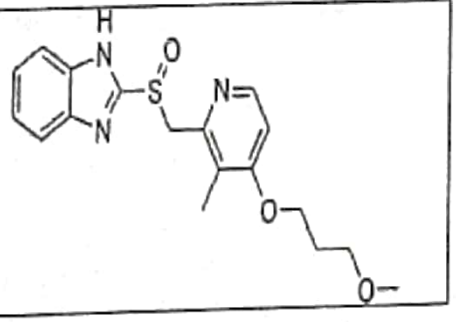
Literature survey reveals that LC-Tandem MS [11], HPLC-coloumetric [12], RP-HPLC-UV [13] and voltammetric [14] methods have been reported for its determination. Ramu and Raghubabu [15] use different spectrophotometric methods for its determination such as condensation reaction with aromatic aldehyds as vanillin or para- dimethylamino cinnamaldehyde. Nucleophilic substitution reaction using Folin reagent [16], ion pair formation with (tropaeolin OOO) [17] and formation of purple red colored product using sod-nitroprusside-acetaldehyde reagent [18]. Also, the drug was quantitated bromometrically [19].

Lamivuidine (III), 4-amino-1-{(2R, 5S)-2-(hydroxymetyl)-1,3-oxathiolan-5-yl}-1,2-dihydropyrimidin -2-one ,(table 1), is a potent nucleoside analog reverse transcriptase inhibitor. It is used for treatment of chronic hepatitis B. It is official in United States Pharmacopoeia [10], which suggests chromatographic methods for its determination. Different spectrophotometric methods have been developed for its determination either alone or in combination with other drugs.

Simultaneous estimation of lamivuidine with other drugs as stavudine and nevirapine [20], silymarin [21] or abacavir and zidovudine [22] is considered a common method for its determination in combined dosage forms. Hydrotropic solubilization [23] is a simple method for its determination which involves using of 5.0 M sodium benzoate to increase its aqueous

solubility and measuring at 315nm. Also, 0.1 N HCL and 0.1 N NaOH are used as solvent for its spectrophotometric determination in UV region [24].

Table 1: Chemical structures of the cited drugs

Drug	Chemical structure
Aripirazole	
Sumatriptan	
Lamivuidine	
Rabeprazole sodium	

Basavaiah and Somashekar developed methods for the determination of lamivudine using different oxidants as chloramine T [25], bromate-bromide mixture, [26] potassium iodate was used followed by determination of residual oxidant by fixed amount of either methyl orange or indigo carmine [27]. Using iron (III)–MBTH (3-methyl-2-benzothiazolinone hydrazone hydrochloride) [28], as an indirect method, and formation of schiff's base by using p-dimethyl amino benzaldehyde have been used as two colorimetric methods for its determination.

There is also a report on the development of the methods [29] using diazo coupling, redox (folin-ciocalteu reagent) and redox complexation (ferric chloride-orthophenanthroline) reactions for the estimation of lamivudine in pharmaceuticals. Formation of coloured condensation products with three aromatic aldehydes [30] is also used by Baig et al for the determination of lamivudine. Capillary electrophoresis [31] and chromatographic methods as RP-HPLC [32] and HPTLC [33] have been also reported for its determination.

Rabeprazole sodium (IV), 2-{{{4-(3-methoxypropoxy)-3-methyl-2-pyridinyl}methyl} sulfinyl}-1H-benzimidazole sodium salt (table 1), is a proton pump inhibitor which suppresses gastric acid secretion by inhibiting the gastric H^+/K^+ ATPase at the secretory surface of the gastric parietal cell. Several chromatographic techniques such as HPLC [34], HPTLC [35,36], LC [37] and RP-TLC densitometric method [38] have been used for its determination.

Many authors have described the simultaneous spectrophotometric methods for estimation of the drug either with itopride hydrochloride [39,40] or with another drug that combined with rabeprazole in pharmaceutical dosage form [41-44]. Visible spectrophotometric technique also used for its determination using different reagents. Ion pair complexes with orange G [45] and (bromothymol blue,bromocresol green, bromophenol blue and bromocresol purple) [46]and charge transfer complex with DDQ [47]. Oxidation with either potassium iodate [48] and extracting of the liberated iodine with cyclohexan or with iron (III) [49] and subsequent reaction with ferricyanide which yield Prussian blue product. Formation of metal chelate [50] with iron in ethanol media has been used to validate the structural ability of the drug to chelate certain metal ions which essentially present in biological fluids.

The present study deals with development and validation of visible spectrophotometric methods for the determination of the cited drugs in bulk form and pharmaceutical preparations; based on the formation of charge transfer complexes between the studied drugs as n-electron donors with three different reagents acting as electron acceptor either π-acceptor such as p-chloranilic acid (PCA) and 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) or σ-acceptor as iodine (Figures 1-3). The methods are sensitive, simple, cost effectiveness.

EXPERIMENTAL

Equipment

A shimadzu UV -and visible recording spectrophotometer (UV260) with matched 10 mm quartz cells was employed for all absorbance measurements.

Materials

All reagents and chemical used were of analytical grade. Solvents were of spectroscopic grade.

Pure Samples

Aripiprazole, Sumatriptan succinate and Rabeprazole sodium were kindly provided from SIGMA pharmaceutical industries. Their purities were found to be 99.9 %, 99.7 % and 100.39 %, respectively according to HPLC. Lamivuidine was obtained from EVA Pharm for pharmaceutical and medical appliance.

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Market Samples

Aripiprex® tablet (SIGMA pharmaceutical industries for AL Andalus medical company) containing 10 mg of aripiprazole /tablet. Sumigran® tablet (SIGMA pharmaceutical industries) containg 25 mg of sumatriptan succinate/tablet. Lamidine® capsule (EVA Pharm for pharmaceutical and medical appliance) containing 150 mg of lamivuidine/ caps. Bepra®tablet (Global Napi Pharmaceuticals) containing 20 mg of rabeprazole sodium/tablet.

Reagents and chemicals

PCA (Sigma Aldrich, USA) 0.16 %, 0.25 %, 0.1 %, and 0.1 % w/v in acetonitrile for (I), (II), (III) and (IV) respectively DDQ (Merck-Schuchardt-Germany) 0.3 %, 0.3 % and 0.2 % w/v in methanol for (I), (II) and (III) respectively. Iodine (BDH-Poole-UK) 0.13 %, 0.08 % and 0.04 % w/v in chloroform for (I), (II) and (IV), respectively.

Standard stock solution

Aripirazole 0.3 %, 0.1 % and 0.02 % w/v was prepared in chloroform for PCA, DDQ and iodine methods respectively. Sumatriptan 0. 144% was prepared in acetonitrile (for PCA), 0.07 % and 0.014 % w/v, in chloroform for (DDQ and iodine methods). Lamivuidine 0.04 % w/v in methanol for P. CA and DDQ. Rabeprazole 0.04% w/v in acetonitrile for PCA and 0.004%w/v in chloroform for iodine method

Preparation of sumatriptan base

The appropriate amount of the drug salt was weighed accurately, transferred into 125 ml separating funnel. The powder was dissolved in 25ml water, then 10ml saturated solution of sodium hydroxide was added and 2X10 ml chloroform was used for extraction. The chloroformic extract was filtered through anhydrous sodium sulphate into 25 ml volumetric flask and the volume was completed to the mark with chloroform. In case of PCA method chloroformic extract was evaporated at 70°C, then the residue was dissolved in acetonitrile.

Construction of calibration curves

Calibration curves were constructed according to the optimum conditions as given in table (2).

General procedures

To accurately measured aliquots of working solution of the cited drugs, the specified volume of the acceptor was added in a10 ml volumetric flask. The content of each flask was mixed and diluted to volume with suitable solvent, the absorbance was measured at the convenient λ max against blank, table (2).

Assay for the dosage forms

For Tablets of (I), (III) and (IV)

Weigh and finely powder 10 tablets, dissolve a quantity equivalent to known concentration of each drug in the corresponding organic solvent (as shown in standard stock solution), filtered and then proceed as in general procedures. *For Tablets (II)*

Sumigran tablets were weighed and finely powdered. An accurately weighed amount of the powder equivalent to 36, 17.5 and 3.5 mg of sumatriptan base for PCA, DDQ and Iodine respectively was dissolved in about 25ml distilled water, filtered then transfer into 125ml separating funnel.

The base was extracted and diluted as described above then the procedures for calibration of sumatriptan using PCA, DDQ and Iodine were followed as under general procedures.

Capsules: the content of 10 capsules were emptied, known weight of the powder equivalent to 10 mg of Lamivuidine was transferred into 25 ml volumetric flask .The procedure was completed for both PCA and DDQ as descried under the general procedures.

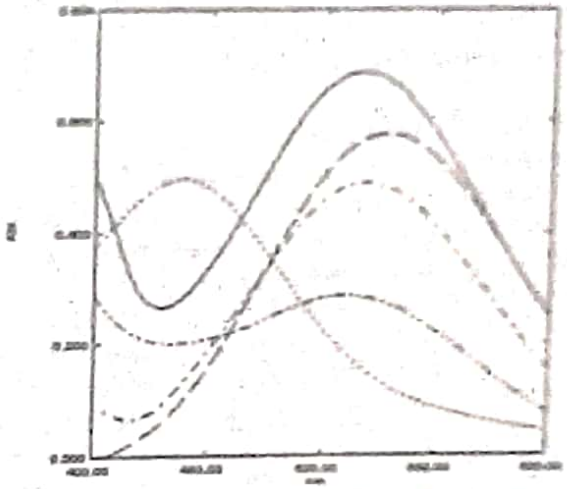

Fig. (1): Absorption spectra of reaction between PCA and 230µg/ml of Aripirazole (——), 251µg/ml of Sumatriptan (——), 140 µg/ml of Lamivuidine (– –) and 47 µg/ml of Rabeprazole sodium (——) against blank solution (.....).

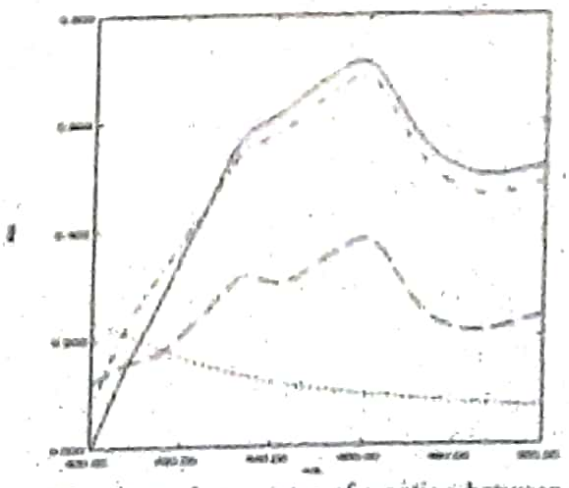

Fig. (2): Absorption spectra of reaction between DDQ and 85 µg /ml of Aripirazole (——), 24 µg/ml of Sumatriptan (——) and 32 µg/ml of amivuidine (– –) against blank solution (.....).

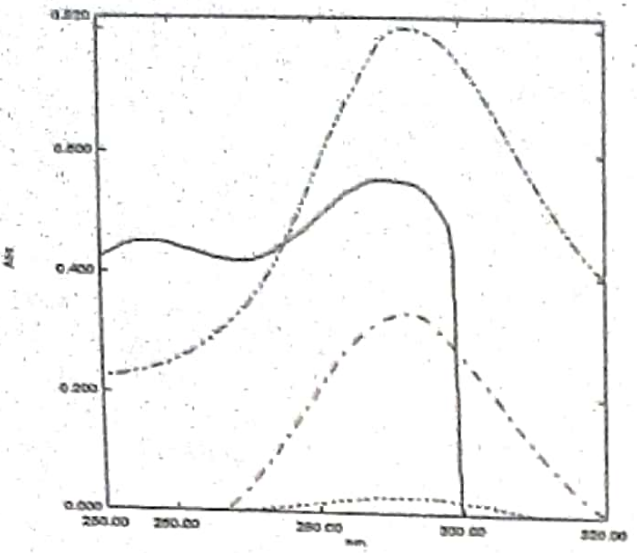

Fig. (3): Absorption spectra of reaction between iodine and 10 µg /ml of Aripirazole (——), 8.6 µg/ml of Sumatriptan (——) and 5.5 µg/ml of Rabeprazole sodium (— — ·) against blank solution (.....).

RESULTS AND DISCUSSION

The investigated drugs act as electron donor when they react with the selected acceptors (PCA, DDQ and iodine) they produce a new absorption band which is considered characteristic for each complex.

π-acceptors are known to yield charge transfer complexes with a variety of electron donors. In non polar solvent the molecular charge transfer complexes are formed, whereas in polar solvent, the radical anions are the predominant species [51]

$D+A \leftrightarrow (D\text{-}A) \leftrightarrow D^+ + A^-$ radical anion

D= drug, A=acceptor

When the drugs are mixed with PCA (acetonitrile-polar solvent), a radical anion is formed by proton transfer from PCA to basic centre (B) in the drug molecule as in the following equation:

$H_2A \leftrightarrow H^+ + HA^-$

$B + H \leftrightarrow BH^+$ colourless

BH^+ form an ion pair salt with HA^- giving purple color which is responsible for the quantitative measurement. DDQ is also π-acceptor which react with the cited drug to form charge transfer complex at 460nm. This band may be attributed to formation of DDQ radical anion which probably resulted from dissociation of complex in polar solvents (methanol and acetonitrile).

Iodine method

In chloroformic solution violet colour of iodine show absorption band at 520 nm. On the addition of the cited drugs the violet colour changed into yellowish purple with two different bands a high absorption band at 290nm and a lower band at 360nm. This is attributed to charge transfer complexation having an ionized structure $DI^+\text{-}I_3^-$ The formation of triode ion pair, measurable species, is due to transformation of an outer complex to an inner complex liberating I^- ions which react with free molecular I_2 [52]. The following scheme shows in a simple way the mechanism of reaction

$D + I_2 \rightleftharpoons D\text{-}I_2$ (outer complex)

$D\text{-}I_2 \leftrightarrow [D\text{-}I]^+ I^-$ (inner complex)

$[D\text{-}I_2]^+ I^- + I_2 \leftrightarrow [D\text{-}I]^+ I_3^-$ (triode ion pair)

Investigation of the assay parameters

Effect of acceptor concentration

The most suitable concentration and volumes for carrying out the assay in case of PCA, DDQ and iodine were illustrated in table (2) (figures 4-6).

Effect of solvent

For PCA, DDQ and iodine many solvents were tried such as acetonitrile, chloroform, methylene chloride, ethanol and benzene. Acetonitrile gave the best results with PCA and DDQ but in case of iodine chloroform was found to be convenient solvent as it gave high and stable results.

Effect of time

Maximum color was obtained after 5min in case of PCA reaction and the color was stable for at least 2 hrs, for DDQ maximum color intensity obtained at once for (II) and remain stable for 40min, 5 and 10min were sufficient for (III)and (I) respectively and the color was stable for 1hrs with (III) and 1/2hrs with (I). On the other hand, 5,10 and 15 min were sufficient for complete reaction between iodine and (II), (I) and (IV) respectively and the color was stable for 2 hrs.

Effect of temperature

Reaction of PCA, DDQ and iodine occur at room temperature. However, in case of DDQ higher temperature gave low results.

Method validation

Linearity

Under the described experimental conditions, standard calibration curves for the studied drugs were constructed by plotting absorbance versus concentration at the specific λ max for each drug in the range given in table (1), standard deviation, relative standard deviation and standard error for the cited drugs were presented in tables (3-5).

Application

The methods are successfully applied to the determination of the studied drugs in their pharmaceutical formulations.

Satisfactory results (tables 6-8) are obtained for the recoveries of the drugs and are in good agreement with the label claim.

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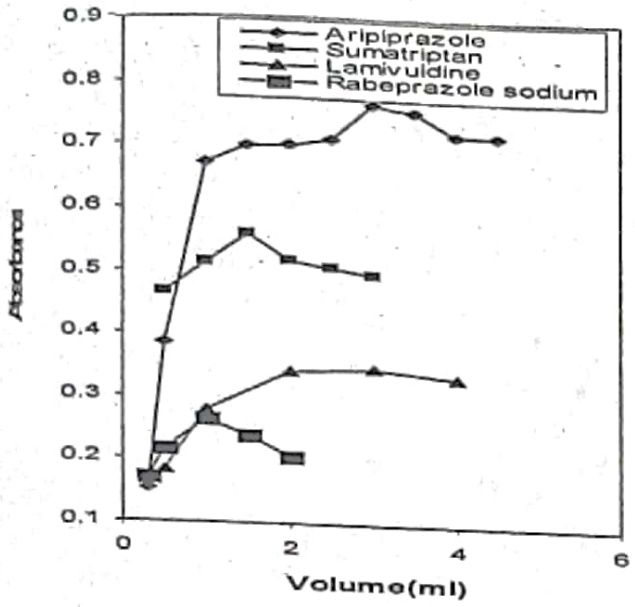

Fig. (4): Effect of volume of PCA on the absorbance of the reaction product between Aripirazole 240 µg/ml) and 0.16gm% P.CA, Sumatriptan (288 µg/ml) and 0.25gm % P.CA Lamivuidine (80 µg/ml) and 0.1 gm % P.CA and Rabeprazole sodium (40 µg/ml) and 0.1 gm% P.CA

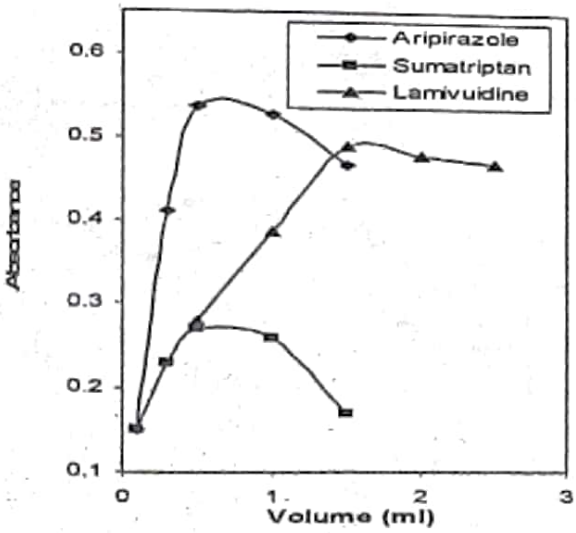

Fig. (5): Effect of volume of DDQ on the absorbance of the reaction product between Aripirazole (80 µg/ml) and ml 0.3 gm % DDQ, Sumatriptan (105 µg/ml) and 0.3 gm% DDQ and Lamivuidine (45µg/ml) and 0.2 gm% DDQ.

Accuracy and precision

The inter-and intra-day precision and accuracy are determined by preparing four different concentration of each drug and each concentration is analysed in six replicates. The relative standard deviation as precision and percentage relative error (Er %) as accuracy of the suggested methods are calculated. The analytical results for accuracy and precision, (shown in table 9) show that the proposed methods have good repeatability and reproducibility.

Under the described experimental conditions, standard calibration curves for the studied drugs were constructed by plotting absorbance versus concentration at the specific λ max for each drug in the range given in table (1), standard deviation,relative standard deviation and standard error for the cited drugs were presented in table (3-5).

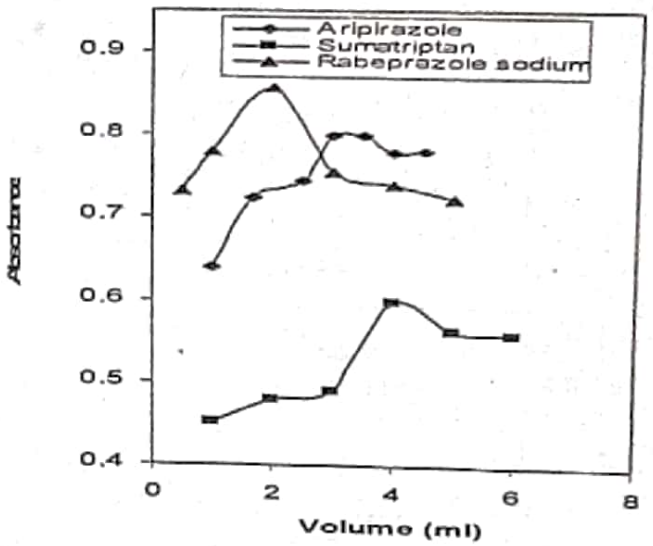

Fig. (6): Effect of volume of iodine on the absorbance of the reaction product between Aripirazole (16 µg/ml) and 0.13 gm% iodine, Sumatriptan (14 µg/ml) and 0.08 gm% iodine and Rabeprazole sodium (6 µg/ml) and 0.04 gm % iodine.

The percentage recoveries of the pure drugs using the proposed methods compared with that given by reference methods [4,19,24,47] are illustrated in table (10). The validity of the proposed method is evaluated by statistical analysis [55] between the there is no significant difference between the results obtained and that of reference methods. Regarding the calculated Student's t-test and F-test, there is no significant difference between the proposed and the reference methods regarding accuracy and precision.

Stoichiometric Relationship

The stoichiometry of the reaction was studied by Job's method of continuous variation [53]. In case of PCA the molar ratio was found to be 1:1 (donor:acceptor) for (I) and (III) and 2:1 for (II) and (IV) (fig 7). While in DDQ method the molar ratio was found to be (1:1) for (I), (III) and (3:2) for (II). (fig 8).

Stoichiometric Relationship

This was determined by Molar Ratio Method (Yoe and Jones method) [54]. It was found that molar ratio between the reactants (donor:acceptor) is 1:3 for (I), (II) and 1:2 for (IV) (Figure 9).

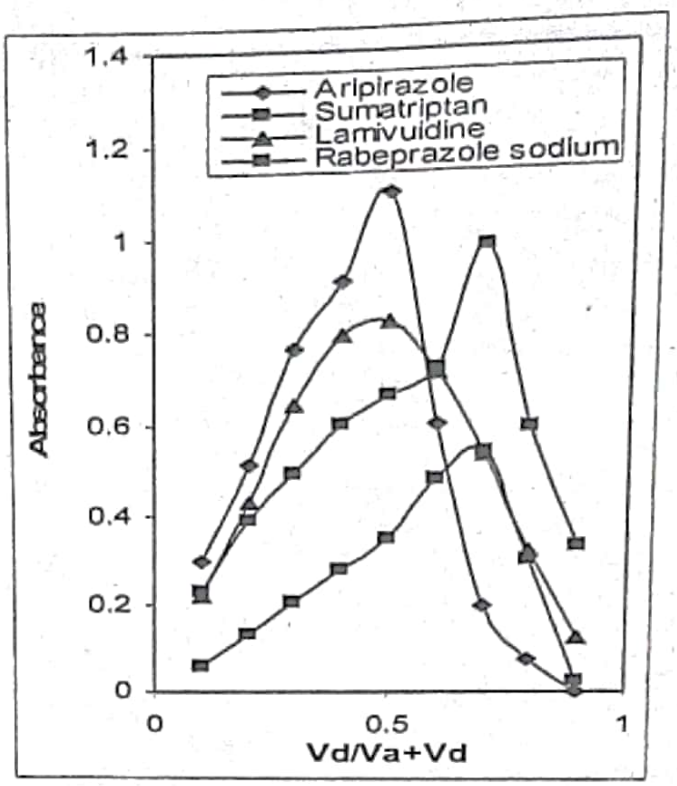

Fig. (7): Continuous variation plot for the reaction of the investigated drugs with P.CA using Aripirazole, sumatriptan and Lamivuidine ($2X10^{-3}$M) and P.CA($2X10^{-3}$M); Rabeprazole sodium ($1X10^{-3}$M) and P.CA ($1X10^{-3}$M).

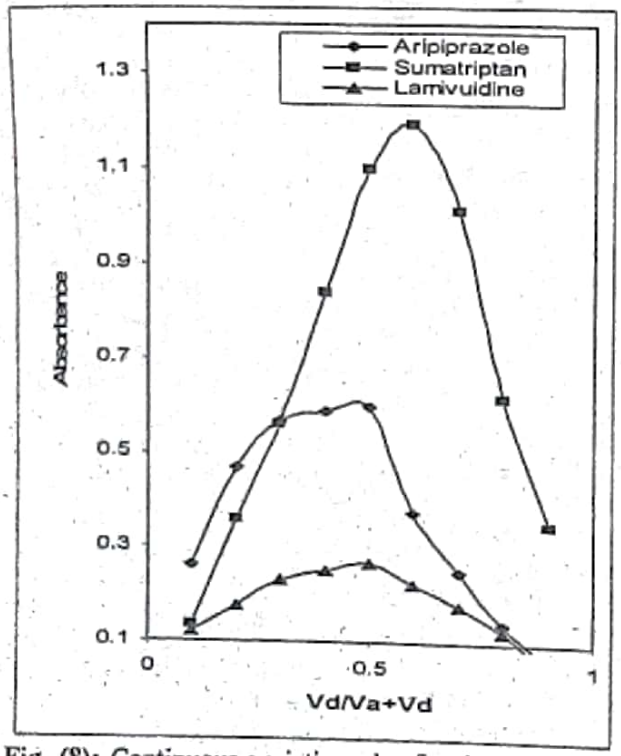

Fig. (8): Continuous variation plot for the reaction of the investigated drugs with DDQ using: sumatriptan and Lamivuidine ($2X10^{-3}$M) and DDQ ($2X10^{-3}$M); Aripirazole($1X10^{-3}$M) and DDQ ($1X10^{-3}$M).

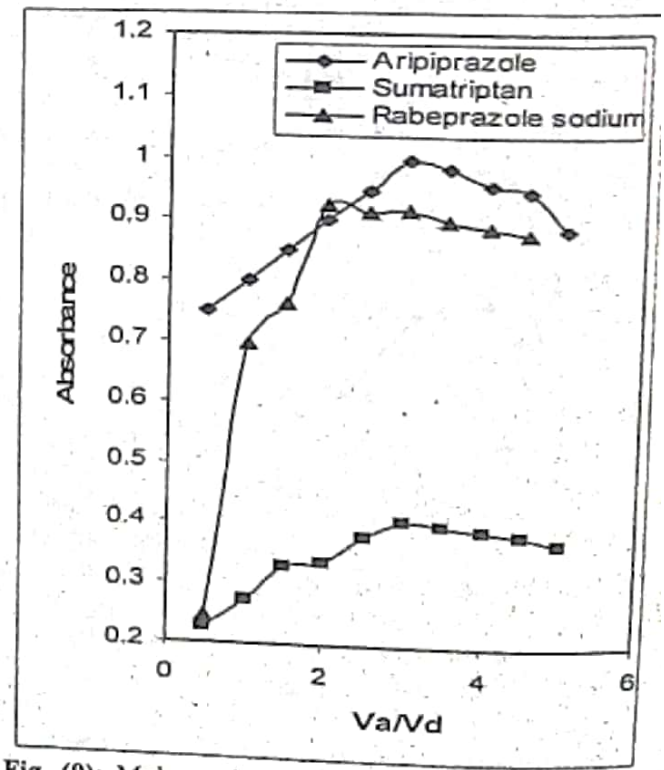

Fig. (9): Molar ratio curves of drug iodine reaction using:Aripiprazole ($4X10^{-4}$M) and iodine solution ($4X10^{-4}$M); sumatriptan ($5X10^{-4}$M) and iodine solution ($5X10^{-4}$M); Rabeprazole sodium ($2X10^{-4}$M) and iodine solution ($2X10^{-4}$M).

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Table (2): Analytical parameters for PCA, DDQ and iodine methods for determination of investigated drugs.

parameter / Acceptor	drug	Beer's law limits (µg/ml)	Conc of acceptor gm%w/v	solvent	Temp. (C^0)	Time for complete reaction (min)	λmax
PCA	Aripirazole	60-270	3ml of 0.16%	Acetonitrile	25^0C	5	515
	Sumatriptan	72-288	1.5ml of 0.25%	Acetonitrile	25^0C	5	517
	Lamivuidine	40-140	2ml of 0.1%	Acetonitrile	25^0C	5	528
	Rabeprazole sodium	20-100	1ml of 0.1%	Acetonitrile	25^0C	5	509
DDQ	Aripirazole	50-110	1/2ml of 0.3%	Acetonitrile	25^0C	10	458.5
	Sumatriptan	70-280	1/2ml of 0.3%	Acetonitrile	25^0C	Immediate	458.5
	Lamivuidine	20-80	1.5ml of 0.2%	Acetonitrile	25^0C	5	460
Iodine	Aripirazole	2-18	3ml of 0.13%	Chloroform	25^0C	10	289
	Sumatriptan	4.2-15.4	4ml of 0.08%	Chloroform	25^0C	5	293
	Rabeprazole sodium	1-7	2ml of 0.04%	Chloroform	25^0C	15	292

Table (3): Determination of the studied drugs using PCA method in pure form.

Aripirazole		Sumatriptan		Lamivuidine		Rabeprazole sodium	
Taken (µg/ml)	Recovery %	Taken (µg/ml)	Recovery %	Taken (µg/ml)	Recovery %	Taken (µg/ml)	Recovery %
60	98.89	72	100.00	40	98.75	20	100.00
120	100.00	108	100.00	60	100.83	40	98.75
180	100.93	144	99.31	80	101.25	50	99.67
210	100.00	180	100.83	100	101.00	70	100.00
240	99.86	216	100.00	120	101.04	80	99.38
270	99.75	288	100.00	140	99.82	90	99.07
						100	99.50
Mean*±S.D	99.90±0.6508	100.02±0.4845		100.45±0.9721		99.48±0.4627	
N	6	6		6		7	
V	0.424	0.235		0.945		0.214	
R.S.D.	0.6514	0.4843		0.9677		0.4651	
S.E.	0.266	0.198		0.397		0.175	
LOD	18.99	20.37		13.13		8.56	
LOQ	63.31	67.88		43.76		28.52	
1.34×10^3	Molar absorbitivity	5.64×10^2		8.97×10^2		2.29×10^3	
3.35×10^{-1}	Sandell's sensitivity (µg cm^{-2})	5.24×10^{-1}		2.56×10^{-1}		1.29×10^{-1}	

* mean of three different experiments

Table (4): Determination of the studied drugs using DDQ method in pure form.

Aripirazole		Sumatriptan		Rabeprazole sodium	
Taken (µg/ml)	Recovery %	Taken (µg/ml)	Recovery %	Taken (µg/ml)	Recovery
2	99.11	4.20	100.11	1	100.00
4	99.55	5.60	101.46	2	99.65
6	101.49	7.00	100.56	3	99.07
8	99.11	8.40	100.11	4	100.52
10	100.00	12.6	101.01	5	101.40
12	101.04	14.0	100.65	6	100.70
14	100.00	15.4	100.35	7	99.40
16	100.45				
18	99.80				
Mean*±S.D	100.06±0.8138	100.62±0.4926		100.11±0.8157	
N	9	7		7	
V	0.662	٠.٢٤٣		٠.٦٦٥	
R.S.D.	0.8134	0.4895		0.8149	
S.E.	0.271	0.174		0.308	
LOD	0.375	1.28		0.365	
LOQ	1.25	4.27		1.22	
Molar absorbitivity	2.48×10^{4}	1.19×10^{4}		5.52×10^{4}	
Sandell's sensitivity (µg cm^{-2})	1.81×10^{-2}	2.48×10^{-2}		5.35×10^{-3}	

* mean of three different experiments

Table (5): Determination of the studied drugs using iodine method in pure form.

Aripirazole		Sumatriptan		Lamivuidine	
Taken (µg/ml)	Recovery %	Taken (µg/ml)	Recovery %	Taken (µg/ml)	Recovery %
50	100.17	70	101.43	20	98.89
60	100.14	105	100.00	25	99.56
70	100.95	140	100.48	40	99.44
80	101.15	175	100.57	45	100.74
100	100.17	210	100.32	70	99.68
110	100.53	245	100.65	80	99.72
		280	100.71		
Mean*±S.D	100.52±0.4413	100.60±0.4401		99.67±0.6039	
N	6	7		6	
V	0.195	0.194		0.365	
R.S.D.	0.4390	0.4375		0.6059	
S.E.	0.18	0.156		0.246	
LOD	15.00	20.23		6.67	
LOQ	50.00	67.44		22.22	
Molar absorbitivity	3.61×10^{3}	9.12×10^{2}		2.6×10^{3}	
Sandell's sensitivity (µg cm^{-2})	1.24×10^{-1}	3.24×10^{-1}		8.83×10^{-2}	

* mean of three different experiments

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Aripirazole			Sumatriptan			Lamivuidine			Rabeprazole sodium		
Taken (µg/ml)	Added (µg/ml)	Recovery %	Taken (µg/ml)	Added (µg/ml)	Recovery %	Taken (µg/ml)	Added (µg/ml)	Recovery %	Taken (µg/ml)	Added (µg/ml)	Recovery %
60		98.89	108		98.15	40		98.75	20		100.00
	60	98.89		72	100.00		40	99.38		20	100.00
	90	98.15		108	99.07		50	101.50		40	99.17
	150	100.00		144	98.61		60	100.83		50	101.33
	180	100.19		180	100.28		80	100.94		60	99.44
	210	98.57					100	101.75		70	99.29
										80	99.79
Mean*±S.D		99.16±0.894	99.49±0.780			100.66±0.906			99.84±0.796		
S.E.		0.400	0.390			0.405			0.356		
V		0.800	0.609			0.821			0.635		

* mean of three different experiments

Table (6): Determination of the studied drugs using PCA method in their dosage forms.

Table (7): Determination of the studied drugs using DDQ method in their dosage forms.

Aripirazole			Sumatriptan			Lamivuidine		
Taken (µg/ml)	Added (µg/ml)	Recovery %	Taken (µg/ml)	Added (µg/ml)	Recovery %	Taken (µg/ml)	Added (µg/ml)	Recovery %
50		100.17	70		100.95	20		98.89
	50	100.17		70	100.48		20	98.89
	55	100.61		105	99.68		30	100.00
	60	100.69		140	98.10		35	99.05
	65	102.69		175	100.00		40	100.83
	70	100.95		210	100.16		50	100.00
	75	100.11						
Mean*±S.D		100.87±0.9485	99.68±0.9323			99.69±0.9051		
S.E.		0.387	0.416			0.404		
V		0.900	0.869			0.819		

* mean of three different experiments

Table (8): Determination of the studied drugs using iodine method in their dosage forms.

Aripirazole			Sumatriptan			Rabeprazole sodium		
Taken (µg/ml)	Added (µg/ml)	Recovery %	Taken (µg/ml)	Added (µg/ml)	Recovery %	Taken (µg/ml)	Added (µg/ml)	Recovery %
2		99.11	4.2		100.11	2		99.65
	2	99.11		4.20	99.57		1	100.00
	4	100.89		5.60	101.06		2	99.65
	8	99.55		7.00	100.65		3	101.40
	10	100.18		9.80	101.35		4	100.87
				11.2	101.06		5	100.00
Mean*±S.D		99.93±0.7762	100.73±0.6980			100.38±0.7251		
S.E		0.388	0.312			0.324		
V		0.603	0.487			0.526		

* mean of three different experiments

Table (9): The intra-day and inter-day precision and accuracy data for the studied drugs.

		Intra-day				Inter-day		
		Added (µg/ml)	found±S.E (µg/ml)	Precision RSD%	Accuracy R.M.E.%	found±S.E (µg/ml)	Precision RSD%	Accuracy R.M.E.%
PCA method	Aripirazole	120	119.33±0.422	1.039	-0.56	119.50±0.282	0.694	-0.42
		180	182.67±0.404	0.974	+01.48	180.50±0.576	1.406	+0.28
		240	239.11±0.594	1.461	-0.37	238.44±0.600	1.480	-0.65
		270	272.61±0.467	0.467	+0.97	270.83±0.576	1.406	+0.31
	Sumatriptan	72	72.50±0.408	0.993	+0.69	72.42±0.352	0.856	+0.58
		108	109.25±0.588	1.424	+1.16	109.33±0.247	0.598	+1.23
		144	144.67±0.587	1.431	+0.46	145.67±0.494	1.197	+1.16
		180	180.50±0.408	0.997	+0.28	179.33±0.628	1.544	-0.37
	Lamivuidine	40	40.46±0.362	0.876	+1.15	40.54±0.253	0.613	+1.35
		80	80.38±0.391	0.954	+0.47	81.54±0.253	0.609	+1.39
		100	100.83±0.631	1.534	+0.83	100.29±0.634	1.548	+0.29
		140	138.50±0.626	1.550	-1.07	138.54±0.557	1.378	-1.04
	Rabeprazole sodium	20	19.75±0.154	0.381	-1.25	19.97±0.256	0.628	-0.14
		40	39.92±0.231	0.566	-0.21	39.69±0.19	0.468	-0.76
		50	50.47±0.217	0.526	+0.94	50.64±0.19	0.459	+1.28
		70	70.44±0.268	0.651	+0.63	70.50±0.336	0.817	+0.71
DDQ method	Aripirazole	50	50.10±0.177	0.432	+0.19	49.83±0.18	0.442	-0.33
		70	69.90±0.227	0.557	-0.14	69.86±.298	0.731	-0.20
		80	79.25±0.241	0.595	-0.94	79.67±0.309	0.760	-0.42
		90	88.88±0.307	0.762	-1.25	88.71±0.274	0.680	-1.44
	Sumatriptan	70	70.67±0.211	0.512	+0.95	70.94±0.234	0.566	+1.35
		140	141.44±0.33	0.799	+1.03	141.94±0.434	1.048	+1.39
		210	211.78±0.444	1.080	+0.85	212.11±0.535	1.298	+1.01
		280	283.39±0.425	1.029	+1.21	283.94±0.434	1.048	+1.41
	Lamivuidine	20	20.06±0.140	0.140	+0.28	19.96±0.094	0.23	-0.19
		40	39.59±0.200	0.495	-1.02	39.78±0.242	0.595	-0.56
		45	45.30±0.121	0.293	+0.66	45.39±0.381	0.926	+0.86
		70	68.74±0.420	1.048	-1.80	68.74±0.483	1.205	-1.80
Iodine method	Aripirazole	8	7.96±0.018	0.045	-0.45	7.93±0.013	0.032	-0.89
		12	12.01±0.043	0.105	+0.07	11.96±0.048	0.119	-0.35
		16	15.89±0.046	0.113	-0.71	15.88±0.040	0.100	-0.78
		18	17.79±0.036	0.089	-1.17	17.77±0.041	0.101	-1.26
	Sumatriptan	5.6	5.66±0.033	0.081	+0.99	5.69±0.023	0.056	+1.60
		7	7.07±0.029	0.071	+0.97	7.10±0.023	0.056	+1.41
		12.6	12.70±0.044	0.106	+0.80	12.73±0.052	0.127	+1.01
		14	14.20±0.021	0.052	+1.43	14.11±0.022	0.055	+0.76
	Rabeprazole sodium	2	2.02±0.31	0.076	+1.11	2.00±0.014	0.034	-0.12
		3	3.03±0.024	0.059	+0.85	3.03±0.015	0.035	+1.13
		4	4.00±0.033	0.081	+0.06	3.96±0.024	0.060	-1.05
		5	5.05±0.026	0.063	+1.07	5.07±0.027	0.066	+1.4

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Table (10): Statistical data for the determination of the studied drugs using proposed method compared with reference method

Drug		Proposed procedures			Reference or reported method
		Reagents			
		p-CA	DDQ	Iodine	
Aripiprazole	Mean ± S.D.	99.9±0.6508	100.52±0.4413	100.06±0.8138	100.17±0.6258
	Variance	0.424	0.195	0.662	0.392
	Student-t-test	0.696 (2.262)*	1.09(2.262)*	0.26 (2.179)*	---
	F-test	1.082(5.19)*	2.01(5.19)*	1.69 (3.84)*	---
	n	6	6	9	5
Sumatriptan	Mean ± S.D.	100.02±0.4845	100.6±0.4401	100.62±0.4926	100.13±0.2536
	Variance	0.235	0.194	0.243	0.064
	Student-t-test	0.412(2.306)*	1.936 (2.262)*	1.82 (2.262)*	---
	F-test	3.67(5.41)*	3.03 (4.76)*	3.797 (4.76)*	---
	n	6	7	7	4
Rabeprazole sodium	Mean ± S.D.	99.48±0.4627	----	100.11±0.8157	99.87±0.6520
	Variance	0.214	----	0.665	0.425
	Student-t-test	1.31 (2.16)*	-----	0.633 (2.16)*	---
	F-test	1.99 (3.87)*	-----	1.56 (3.87)*	---
	n	7	-----	7	8
Lamivuidine	Mean ± S.D.	100.45±0.9721	99.67±0.6039	------	99.99±0.6236
	Variance	0.945	0.365	-----	0.389
	Student-t-test	0.831 (2.306)*	0.811(2.306)*	-----	---
	F-test	2.43 (5.41)*	1.07(5.41)*	-----	---
	n	6	6	-----	4

* The corresponding theoretical values for t and F tests at (p=0.05)

CONCLUSION

The proposed methods are simple, accurate and free from such experimental variables as heating or extraction hence they are suitable for routine analysis in quality control laboratories.

REFERENCES

1. **Martindale,** The Complete Drug Reference, 35th ed., Pharmaceutical Press, London, p 861 (a), 568 (b), 802 (c), 1590 (d) , (2007).
2. Nandini A., Sachdev Y., **Ind. Pharm.,** 8(88), 69, (2009).
3. Sankar D. G., Krish M. V., **Anal. chem., (Indian journal).,** 4, 4, (2007).
4. Kalaichelvi R., Thangabalan B., Rao D. S., Jayachandran E., **E J. Chem.,** 6(S1), S87, (2009).
5. Nagamallika J., Mahesh D. A., **Asian J. Pharm. Ana.,** 1(3), 46, (2011).
6. Patle H. S., Chandewar A. V., Kshirsagar M. D., **Inter. J. Current Pharm. Res.,** 3(3),45, (2011).
7. Dey S., Chauhan N., Malairajan D. P., Murugan R., Das R. C., Ahmad S., **Inter. J. Drug Development Res.,** 3(1), 205, (2011).
8. Shimokawa Y., Akiyama H., Kashiyama E., Koga T., Miyamoto G., **J. Chromatogr. B.,** 821, 8 (2005).

9. Kubo M., Mizooku Y., Hirao Y., Osumi T., **J. Chromatogr. B.,** 822, 294 (2005).
10. **The United States Pharmacopiea,** 30 ,National Formulary 25, US Pharmacoppieal Convention, Rockville MD.(2007).
11. Cheng K. N., Redrup M. J., Barrow A., Williams P. N., **J. Pharm.Biomed. Anal.,** 17, 399 (1998).
12. Franklin M., Odontiadis J., Clement E. M., **J. Chromatogr.,** 681(2), 416, (1996).
13. Ravi S., Darwish Y., Khan N., **Acta. Chromatogr.,** 213, 421, (2009).
14. Sagar K., Alvarez J. M. F., Hua C., Smyth M. R., Munden R., **J. Pharm. Biomed .Anal .,** 10(1), 17, (1992).
15. Ramu B. K., Raghubabu K., **IJABPT,** 2(1), (2011).
16. Ramu B. K., Raghubabu K., **Int . J. Pharm. Biomed. Sci.,** 1(3), 49, (2010).
17. Ramu B. K., Raghubabu K., **IJPPS.,** 3(3), (2011).
18. Ramu B. K., Raghubabu K., **Der. Pharma. Chemica.,** 3(1), 223, (2011).
19. Satyanarayane K. V. V., Rao P. N., **E J. chem.,** 8(1), 269, (2011).
20. Samee W., Srilamai P., Ongart S., Suwannaratana R., Somchaithawatwong C., Vorarat S., **TPHSJ.,** 2 (1), 39, (2007).
21. Dube D., Vyas S. P., **Int. J. Pharm. Pharm. Sci.,** 1(2), 107, (2009).
22. Nagulwar V. P., Bhusari K. P., **IJRAP.,** 2(2), 610, (2011).
23. Sharma M. C., Sharma S., **Int. J. Chem. Tech. Res.,** 3(2), 988, (2011).
24. Shalini S., Shanooja V. P., Abdul Jameel S., Basima,Harilal K. K., Rajak H., Ravichandran V., **Dig. J. Nanomater. Bios.,** 4, 357, (2009).
25. Basavaiah K., Somashekar B. C., **Indian J. Chem. Techn.,** 13, 7, (2006).
26. Basavaiah K., Somashekar B.C., **J. Sci. Ind. Res.,** 65, 349, (2006).
27. Basavaiah K., Somashekar B. C., Ramakrishna V., **J. Anal. Chem.,** 62(6), 542, (2007).
28. Chaithanya K., Padma A., Swapna A., Rani K. S., Ramalingam P., **Int. J. Chem. Tech. Res.,** 3(2) 733, (2011).
29. Appalaraju S., Karadi A. B., Kamalapurkar G. S., Sarasambia P. S., **Asian. J. Chem.,** 14, 475, (2002).
30. Baig M. V., Kapse G.S., Raju S. A., **Asian .J .Chem.,** 13, 185, (2001).
31. Fan B., Stewart J. T., **J. Liq. Chromatogr. Rel. Technol.,** 25, 241, (2002).
32. Pallad M. S., Rajesh P. M. N., Chatter M., Bhat A. R., **Indian. J. Pharm. Sci.,** 67, 110, (2005).
33. Wankede S. B., Gupta K. R., Wadodkar S. G., **Ind. J. Pharm. Sci.,** 67, 96, (2005).
34. Suhagia B. N., Patel J. R., Patel M. M., Patel B. H., **J. Liq. Chromatogr. Rel. Technol.,** 30(3), 439, (2007).
35. Patel J. R., Patel M. M., Suhagia B. N., Patel B. H., **J. Chromatogr. sci.,** 46(4), 304, (2008).
36. Suganthi A., John S., Ravi T.K., **Ind. J. Pharm. Sci.,** 70, 366, (2008).
37. Garcia C. V., Paim C. S., Steppe M., **J. AOAC Int.,** 87(4), 842, (2004).
38. Shirkhedkar A. A., Surana S. J., **EJAC,** 4(1) (2009).
39. Heralgi R. V., Simpi C. C., Kalyane N. V., Karajgi S R., **Asian. J. Pharm.,** 2, 148, (2008).
40. Pattanayak P., Sharma R., Chaturvedi S. C., **Anal. Lett.,** 40 (12), 2288, (2007).
41. Lohe R. W., Suruse P. B., Kale M. K., Barethiya P. R., Kasture A. V., Lohe S. W., **Asian J. Res. Chem.,** 1(1), 26, (2008).
42. Prasad R. K., Sharma R., **J. Chem. Pharm. Res.,** 2(2), 186, (2010).
43. Dobaria N. B., Vadia N. H., Rajput S. J., **Inter. J. Chem. Tech. Res.,** 1(4), 1162, (2009).
44. Patel A. H., Patel J. K., Patel K.N., Rajput G. C., Rajgor N. B., **Inter. J. Pharm. Biological . Res.,** 1(1), 1, (2010).
45. Pillai S., Singhvi I., **Ind. J. Pharm. Sci.,** 68, 682, (2006).
46. Patel P. M., Desai H. J., Patel N. M., **Ind. J. Pharm. Sci.,** 69, 318, (2007).
47. Khan N. A., Chaudhary A. B., Patro B., Rani A. D., **Science Asia.,** 35, 365, (2009).
48. Mohamed G. G., Nour el-Din F. A., Khalil S. M., El-Tantawy A. S. M., **Drug Test. Anal.,** 2(1), 28, (2010).
49. Syed A. A., Syeda A., **Ind. J. Pharm. Sci.,** 70, 507, (2008).
50. Madhuri D., Chandrasekhar K. B., Ramakotaiah M., Somasekhar G., Harinadhababa K., Kumar K. R., **Inter. J. Res. Pharm.Sci.,** 1(2), 209, (2010).
51. Moustafa A. A., Bebawy L. I., Refaat H. H., **J. Pharm. Biomed. Anal.,** 27(6), 889-899 (2002).
52. Moustafa A. A. M., **J. Pharm. Biomed. Anal.,** 22(1), 45, (2000).
53. Rose J., **Advanced physico chemical experiments,** Pittman, London, PP., 54, (1964).
54. Yoe J. H., Jones A. L., **Ind. Engng. Chem. Analyt.,** Edn, 16, 111, (1944) .
55. Caulcut R., Boddy R., **Statistics for Analytical Chemists;** Chapmann and Hall:London, (1983).

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التحليل الكمى لبعض المستحضرات الصيدلية باستخدام تفاعل نقل الشحنات

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فى هذا البحث تم استخدام ثلاث طرق سهلة و دقيقة لتعيين كلا من اريبريزول، سكسينات السماتربتان ، لاميفيودين و ريبيبرازول الصوديوم فى صورة نقية او في المستحضرات الصيدلية.
تعتمد الطريقة على استخدام نقل الشحنات خلال حامض الباراكلورانيليك و ثنائى كلوروثنائى سيانوبنزوكينون و اليود كطريقة طيفية لتحليل الادوية السابقة . وقد تم دراسة العوامل المؤثرة على التفاعل .
وقد قورنت النتائج التى تم التوصل اليها بالطرق المرجعية وثبت تميز الطرق المقترحة بالدقة و الاتقان و البساطة.