Review Article

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Development and validation of RP-HPLC method for the simultaneous estimation of Chordiazepoxide, Clidinium bromide, Dicyclomine hydrochloride and Rabeprazole sodium in bulk and pharmaceutical dosage forms

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ABSTRACT

A simple, specific and accurate RP-HPLC method was developed for the simultaneous determination of Chlordiazepoxide, Clidiniumbromide, Dicyclomine hydrochloride and Rabeprazole sodium in tablet dosage forms. A waters C_{18} column (50 mm × 4.6 mm, 5 µm) with mobile phase consisting of acetonitrile and phosphate buffer 30:70 (v/v) (pH 2.5 adjusted with triethylamine) were used. The flow rate was 1.0 ml/ min and effluents were monitored at 250 nm. The retention time of Chlordiazepoxide, Clidinium bromide, Dicyclomine hydrochloride and Rabeprazole sodium in tablet formulation were found to be 4.0 min, 7.3 min, 5.9 min, 6.8 min respectively. The method was validated according to the ICH guidelines for specificity, LOD, LOQ, precision, accuracy, linearity, ruggedness and robustness. The method showed good reproducibility and recovery with % RSD less than 2. So the proposed method was found to be simple, specific, precise, accurate and linear. Hence it can be applied for routine analysis of Chlordiazepoxide, Clidinium Bromide, Dicyclomine Hydrochloride and Rabeprazole sodium in pharmaceutical combined dosage forms.

Keywords: RP-HPLC, Chlordiazepoxide, Clidiniumbromide, Rabeprazolesodium, ICH guidelines.

INTRODUCTION

Now a days combined dosage forms are mostly preferred when compared to single dosage forms. Chlordiazepoxide, Clinidium bromide, Dicyclomine hydrochloride, Rabeprazole sodium is available in combined pharmaceutical dosage form. The brand name is [1] Coliwin –R tab containing 5mg of chlordiazepoxide,2.5 mg of clinidium bromide,10 mg of dicyclomine hydrochloride,10 mg of rabeprazole sodium [1] used in the treatment of anxiety and Alcohol withdrawal. Literature survey reveals that various analytical methods have been reported for single dosage forms. The present paper aims to report a simple, accurate, precise, RP-HPLC method for estimation of

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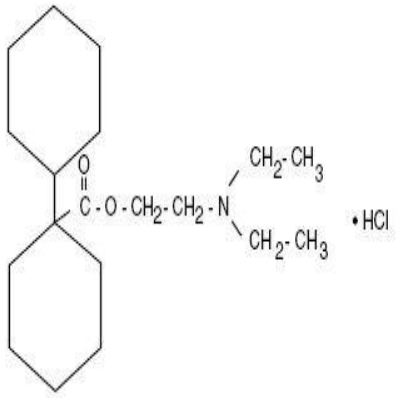
chlordiazepoxide, clinidium bromide, dicyclominehydrochloride, rabeprazole sodium in combined dosage forms.

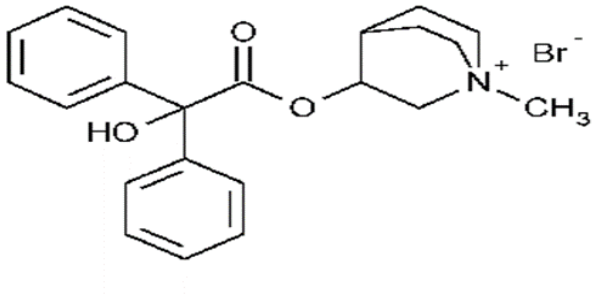
Drug profile of dicyclomine hydrochloride



Dicyclominehydrochloride [2, 9]

It is a 2-Diethylaminoethyl bicyclohexyl-1carboxylate hydrochloride .CAS number is 77-19-0, and it acts as a antispasmodic agent and it is white odourless crystalline powder .and it is soluble in water, alcohol, chloroform, and insoluble in ether.

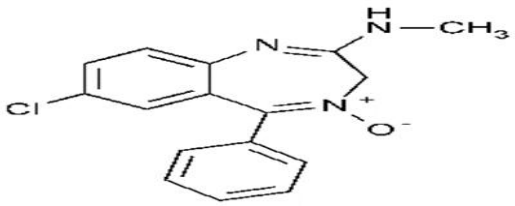
Drug profile of clidinium bromide



Clinidium bromide [3, 4, 9]

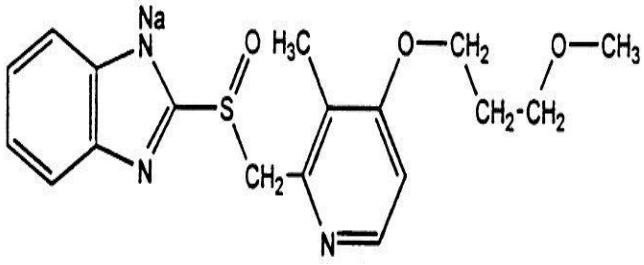
It is a 3-[(2-hydroxy-2,2-diphenylacetyl)oxy]-1-methyl-1 azabicyclo[2.2.2]octan-1-ium bromide,CAS number is 3485-62-9,and it acts as a Antimuscarinics and it is white crystalline substance and it is soluble in water and alcohol,and methanol.

Drug profile of chlordiazepoxide [5, 6, 9]



It is a 7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine-4-Oxide,CAS number is 58-25-3. It belongs to benzodiazepine category and it is a white crystalline substance and it is soluble in water.

Drug profile of rabeprazole sodium



It is a [7, 9] 2-[4-(3-Methoxypropoxy)-3-methyl-2-pyridyl]methyl]sulfinyl]-benzimidazole sodium, CAS number is 117976-90-6, it acts as a proton pump inhibitor and it is white crystalline solid and it is soluble in water and methanol ,freely soluble in ethanol ,chloroform, and ethyl acetate and insoluble in ether and n – hexane

MATERIALS AND METHODS

Optimised chromatographic conditions [8]

Suitable High Performance Liquid Chromatography equipped with UV-visible detector was used. HPLC (waters, 2695 separation module) SOFTWARE (Empower, version 2.0)

Column : Waters C18, 50 mm x 4.6 mm, 5µm.
Wavelength : 250 nm
Injection Volume : 10µL
Column Temperature : Ambient
Flow rate : 1.0 mL/min

Retention time of Chlordiazepoxide (4.0mins), Dicyclomine HCL (5.9mins), Rabeprazole (6.8mins), clidiniumbromide (7.3mins).

Chemicals and Reagents

Tri ethyl Amine (HPLC Grade), Octane-1-Shlphonic Acid (AR grade), Acetonitrile (HPLC grade), HPLC grade Water (Milli Q or equivalent) and Ortho Phosphoric Acid (HPLC Grade).

Drug samples

Dicyclomine hydrochloride, Chlordiazepoxide procured from lifeline laboratories and Clidinium bromide, Rabeprazole sodium were procured from icon laboratories, Vijayawada, Krishna district.

Preparation of diluent

HPLC grade water and HPLC grade methanol (20+80 v/v) was prepared.

Preparation of standard solution

Chlordiazepoxide

Accurately 5mg of Chlordiazepoxide working standard was transferred into a 100 mL volumetric flask. 70 mL of diluent was added, sonicated to dissolve and diluted to final volume with diluent.

Dicyclomine HCl

Accurately 10 mg Dicyclomine HCl working standard was transferred into a 100 mL volumetric flask. 70 mL of diluent was added, sonicated to dissolve and diluted to final volume with diluent.

Rabeprazole Sodium

Accurately 10 mg Rabeprazole Sodium working standard was transferred into a 100 mL volumetric flask. 70 mL of diluent was addded, sonicated to dissolve and diluted to volume with diluent.

Clidinum Bromide

Accurately 2.5 mg Clidinum Bromide of working standard was prepared and transferred into a 100 mL volumetric flask. 70 mL of diluent was

added, sonicated to dissolve and diluted to final volume with diluent. Further diluted each 5mL of Solution- A, B, C and D to 50 mL with the diluent.

Preparation of sample solution

Weighed 10 capsules or tablets and crushed into powder and then one tablet weight equivalent of sample is transferred into a 250 mL volumetric flask. 200 mL of diluents was added, sonicated to dissolve and diluted to volume with diluent. Further diluted 5 mL to 100 mL with the diluent. Filtered through 0.45µ Nylon syringe filter.

Procedure

10µL of standard preparation,sample preparation were injected five times into chromatographic column . Recorded the chromatograms and measured the peak responses for Chlordiazepoxide, DicyclomineHCl, Rabeprazole Sodium, Clidinum Bromide. The System suitability parameters were satisfied. From the peak responses, calculated the content of Chlordiazepoxide, DicyclomineHCl, Rabeprazole Sodium, Clidinum Bromide in the sample.

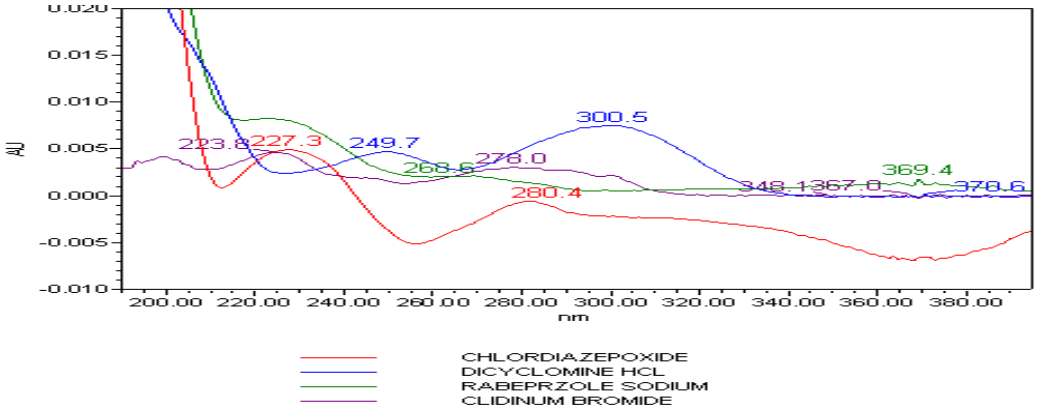
Assay calculations

DRUG	LABELED AMOUNT(mg)	AMOUNT PRESENT(mg)	% ASSAY
Dicyclomine hydrochloride	10	10.5	99.8
Chlordiazepoxide	5	5.1	100.2
Clidinium bromide	2.5	2.6	100.4
Rabeprazolesodium	10	10.1	100.8

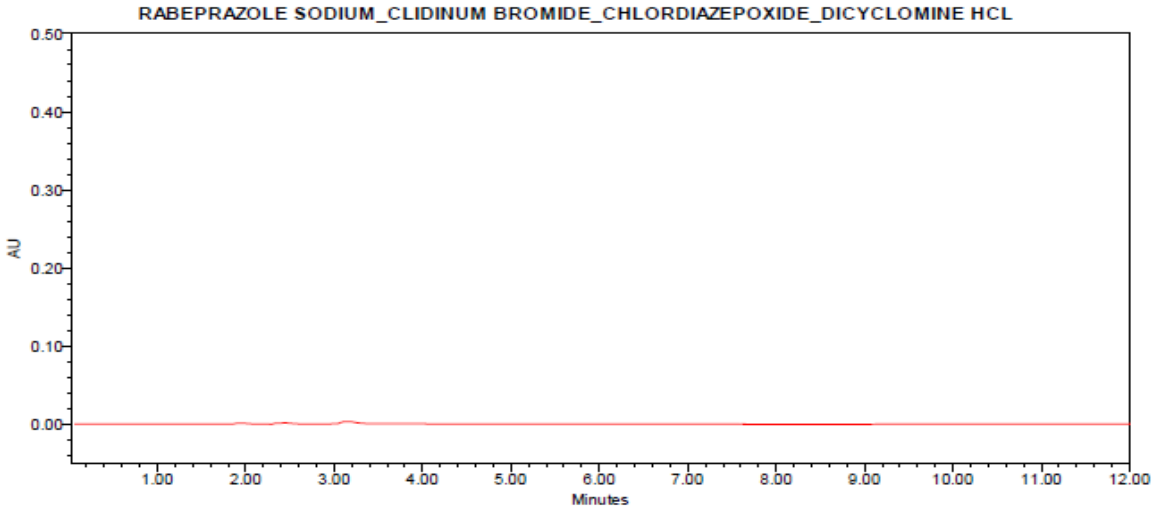
Validation parameters

Parameter	Acceptance Criteria	Chlordiazepoxide	Clidinium Bromide	Dicyclomine Hydrochloride	Rabeprazole Sodium
Linearity Range	Correlation coefficient $r^2 > 0.999$ r	$r^2 = 0.9985$	$r^2 = 0.9982$	$r^2 = 0.9985$	$r^2 = 0.999$
System Precision	RSD < 2%	%RSD = 0.43	%RSD =0.317	%RSD = 0.119	%RSD = 0.148
Intermediate Precision	RSD < 2%	%RSD = 0.627	%RSD =1.909	%RSD = 1.896	%RSD = 1.755
Method precision	RSD < 2%	%RSD = 0.130	%RSD =0.868	%RSD = 0.336	%RSD = 0.879
Accuracy	Recovery 98- 102% (individual)	% recovery=100.3	%recovery=100.5	% recovery=104.5	% recovery=100.5
Solution Stability	> 12 hour	Stable up to 24 hour	Stable up to 24 hour %RSD = 0.741	Stable up to 24 hour %RSD = 0.253	Stable up to 24 hour %RSD = 0.187
Robustness	RSD NMT 2% in modified	Complies	Complies	Complies	Complies
	condition	%RSD= 0.415	%RSD= 0.268	%RSD= 1.638	%RSD= 1.070
	Flow minus	%RSD= 0.669	%RSD= 1.077	%RSD= 0.749	%RSD= 0.861
	Flow plus	%RSD=0.338	%RSD=0.168	%RSD=0.865	%RSD=0.171
	Organic plus	%RSD=0.272	%RSD=0.085	%RSD=0.698	%RSD=1.530
	Organic minus	%RSD= 0.35	%RSD= 0.46	%RSD= 0.4	%RSD= 0.35
	Wavelength plus	%RSD= 0.099	%RSD= 0.236	%RSD= 0.489	%RSD= 0.239
	Wavelength minus				

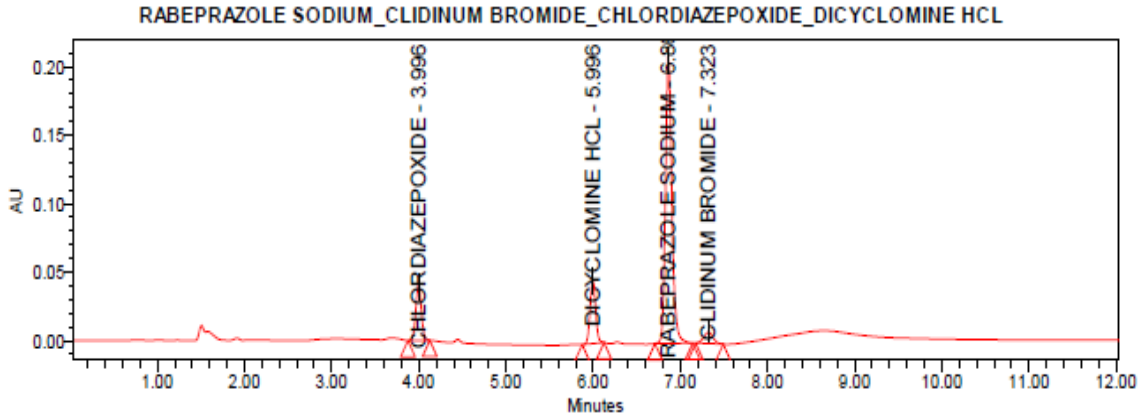
Tables/Figures



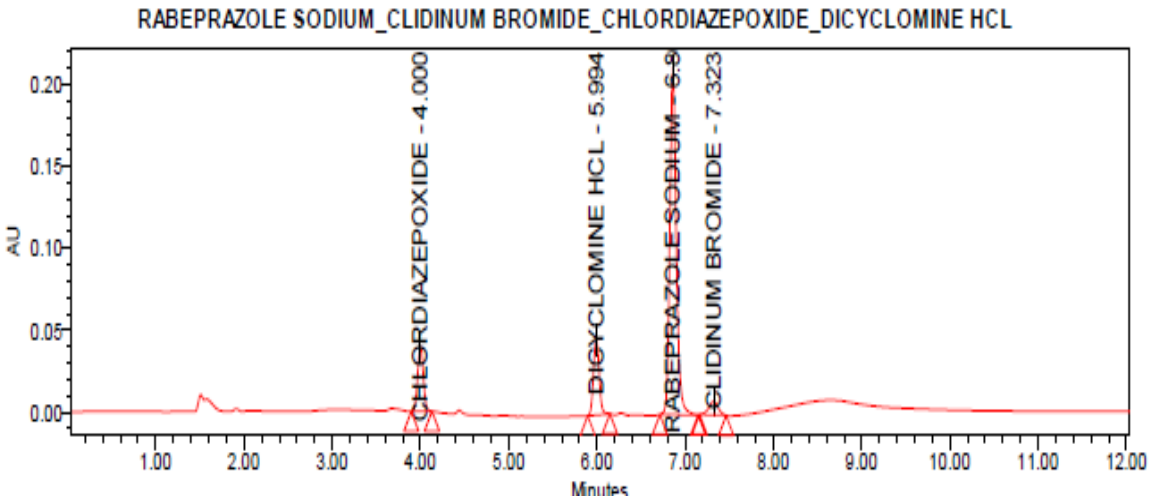
Overlay Spectrum of Chlordiazepoxide, Clidinium Bromide,Dicyclomine Hydrochloride, Rabeprazole Sodium, (250nm)



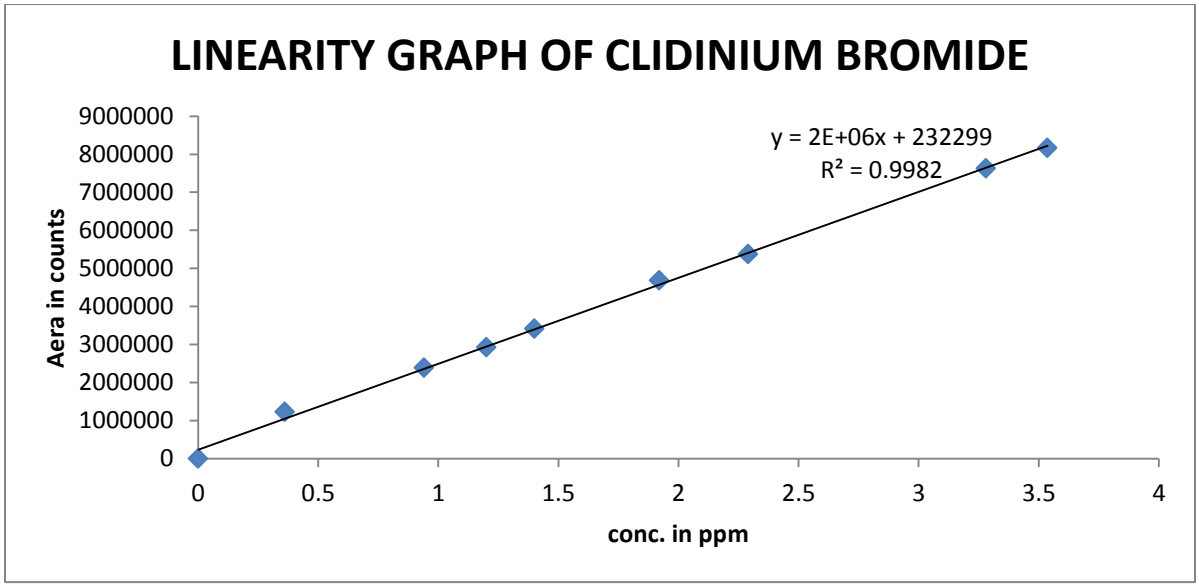
A Representative chromatogram of blank

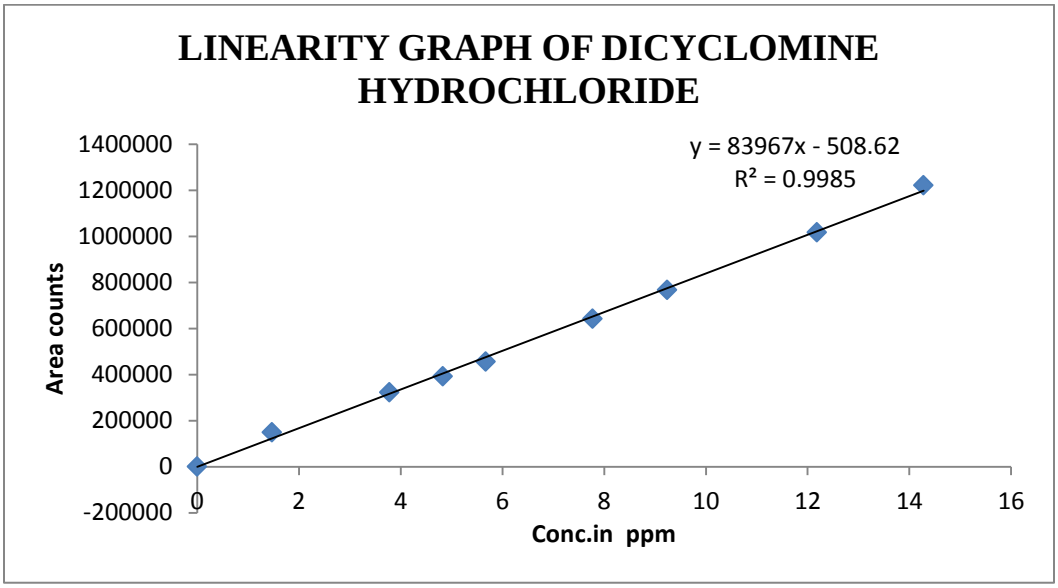


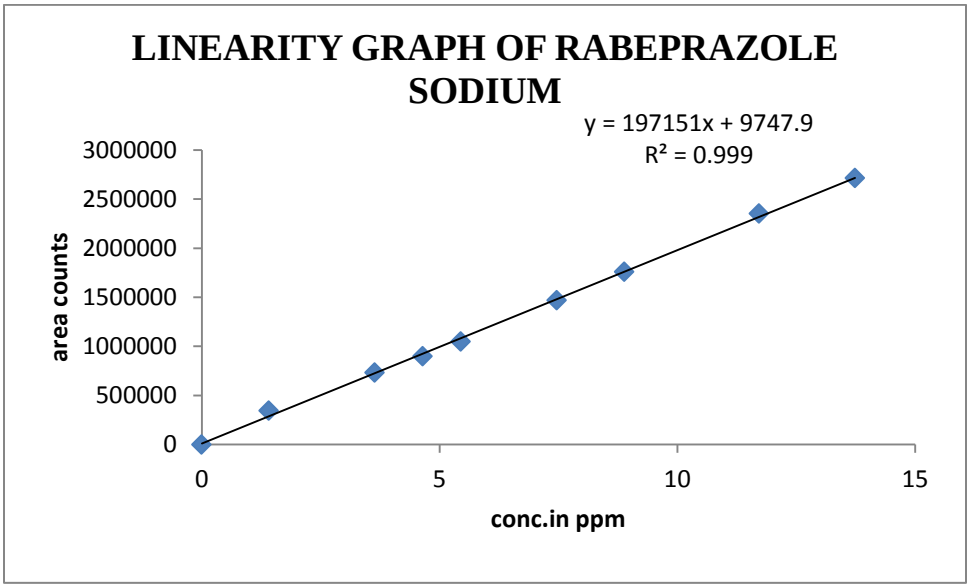
A Representative chromatogram of Standard

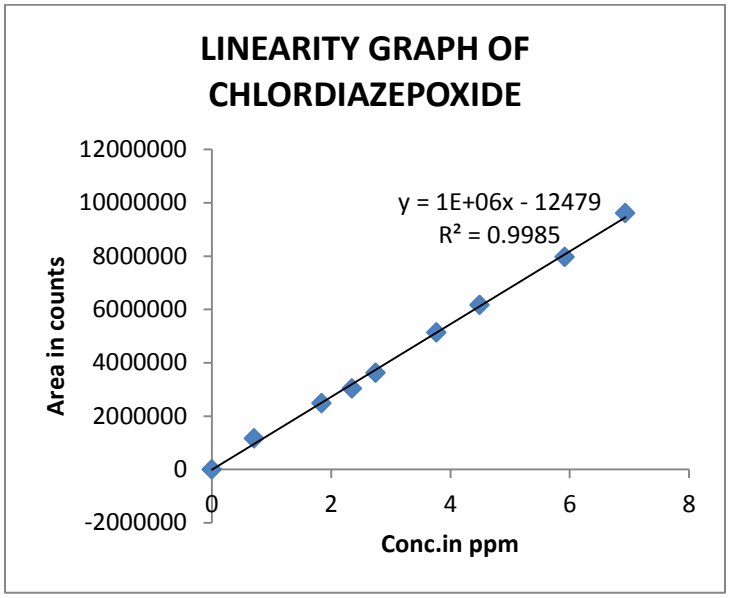


A Representative chromatogram of sample




LINEARITY GRAPH OF DICYCLOMINE HYDROCHLORIDE
y = 83967x - 508.62
R² = 0.9985
Area counts
1400000
1200000
1000000
800000
600000
400000
200000
0
-200000
0
2
4
6
8
10
12
14
16
Conc.in ppm


LINEARITY GRAPH OF RABEPRAZOLE SODIUM
y = 197151x + 9747.9
R² = 0.999
area counts
3000000
2500000
2000000
1500000
1000000
500000
0
0
5
10
15
conc.in ppm



DISCUSSION

In the present investigation new analytical method has been developed for the estimation of potent drugs Chlordiazepoxide, Clidinium bromide, DicyclomineHCl and Rabeprazole sodium in combined dosage form. Since there is no analytical method developed for this combined dosage form, the developed method provides a wide choice for the routine determination of Chlordiazepoxide, Clidinium bromide, DicyclomineHCl and Rabeprazole sodium in bulk and Pharmaceutical dosage forms according to ICH guidelines.

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