

ABSTRACT

Cephalosprins consist of a fused β -Lactam dihydrothiazine two ring system known as 7-aminocephalosporanic acid (ACA). The quantitative analysis of these compounds gives rise to many problems, due to the chemical instability of β -Lactam nucleus. Quantitative estimations of β -Lactam antibiotics have been based on measurements of colour reaction of their degradation products or formation of their derivatives, most of these quantitative estimations are not precise and they require expensive instruments, the objective of this study is to carry out these estimations with accurate conventional and locally available instrumental techniques.

Cephalosporins are organic acids, but with rather strong carboxylic group due to adjacent electronegative group, with pK 1.7-2.6; therefore, they can be quantitatively determined, titrimetrically, conductometrically and potentiometrically in aqueous solutions.

Two cephalosporins antibiotics in their pharmaceutical products, cephalexin and amoxicillin capsules were used in this study, Cephalexin samples are products of Amipharma, Changahi, Elie and Wafra pharmaceutical companies in addition to cephalexin monohydrate used as a standard. Amoxicillin samples are products of Amipharma, Changahi, G.M, Wafra pharmaceutical companies in addition to amoxicillin trihydrate used as a standard.

In this study, aqueous sample solutions were conventionally titrated (directly and indirectly) and, potentiometrically, with sodium hydroxide, but, conductometrically with both sodium and ammonium hydroxide. Spectrophotometric and HPLC methods were also applied.

Conductometric titration methods show one neutralization point for cephalexin and two neutralization points for amoxicillin. These two points indicate diprotic behavior of amoxicillin. due to the presence of phenolic ring in

its structure which reacts with excess added base. It also forms intermolecular hydrogen bonding, that facilitates deprotonating of the OH group of the phenolic ring to neutralize further the base to form the second point. For the same reason the potentiometric titration curves show two separate neutralization points for amoxicillin.

The statistical analyses of the results obtained were carried out excluding that of the back titration method which gave very poor results due to the degradation of the antibiotics in alkaline medium.

A significant difference at level ($P < 0.001$) was calculated for both cephalexin and amoxicillin results by direct titration, conductometric, potentiometric, spectrophotometric and HPLC methods.

A significant difference at level ($P < 0.001$) was calculated for cephalexin results by direct titration, conductometric and potentiometric methods.

No significant difference at level ($P > 0.05$) was calculated for results by direct titration, conductometric and potentiometric methods.

Statistically direct titration, conductometric, potentiometric, spectrophotometric and HPLC methods, show symmetrical mean results.

The mean results of direct titration, conductometric and potentiometric methods, show acceptable results as that of high performance liquid chromatography (HPLC) method.

الخلاصة

السفالسبورينات تحتوي على نظام حلقتين بيتا-لاكتام ديهيدروثيازين مضغوطة ، تعرف بحامض ٧-امينو سفالسبورين. التحليل الكمي لهذه المركبات يظهر عدة مشاكل بسبب عدم الأستقرار الكيميائي لنواة البيتا-لاكتام التقدير الكمي للمضادات الحيوية التي تحتوي على البيتا-لاكتام تعتمد على لون التفاعل الناتج من التكسير الكيميائي او المشتقات الناتجة.معظم هذه التقديرات الكمية غير دقيقة وتتطلب اجهزة آلية عالية الثمن ، لذلك كان البحث عن طرق تعطى نتائج جيدة وتتطلب اجهزة متوفرة ورخيصة الثمن كان هو هدف هذا البحث . السفالوسبورينات تعتبر احماض عضوية لها مجموعة كاربوكسيلية قوية نوعا ما و لها قيمة pK تتراوح بين ١.٧-٢.٦ لذلك يمكن ان تقدر كميا باطرق التسحيحية والموصلية والجهدية في المحاليل المائية. لذلك اختير اثنين من مضادات السفالسبورين الحيوية على هيئة نواتج صيدلانية (كبسولات السفالكسين وكبسولات الاموكسيسيلين) لهذه الدراسة.

عينات السفالكسين ناتج شركات اميفارما، شنغهاي، ايلي ووفره، بالاضافه الى سفالكسين مونوهيدريد. عينات الاموكسيسيلين ناتج شركات اميفارما، شنغهاي ، G.M, ووفره بالاضافة الى اموكسيسيلين ترايهيدريد. فى هذه الدراسة تم تحليل محاليل العينات المائية بالتسحيح التقليدى المباشر والرجعى، والمجهادى مع محلول هايدروكسيد الصوديوم، وبالموصلية مع كلا محلولى هايدروكسيد الصوديوم والامونيوم. بالاضافة إلى طرق المضوائية الطيفية والكروموتوغرافيا السائلة عالية الأداء.

أوضحت الطرق الموصلية نقطة تعادل واحدة بالنسبة للسفالكسين ونقطتى تعادل مع الاموكسيسيلين وهذا يوضح خاصية ثنائية البرتون للاموكسيسيلين وذلك لوجود حلقة الفينول فى بنيته ، حلقة الفينول تتفاعل مع القاعدة الزائدة وكذلك تحدث رابطة هيدروجينية جزئية تؤدي الى سرعة ازالة الهيدروجين من مجموعة الهيدروكسيد فى الفينول لى تتعادل مع القاعدة، لنفس السبب فان الطريقة المجهادية اظهرت نقطتى تعادل بالنسبة للاموكسيسيلين.

التحليل الإحصائى لنتائج تلك التجارب ماعداتجربة التسحيح الرجعى نسبة لان نتائجها كانت ضعيفة جدا وذلك نتيجة لتفكك تلك المضادات الحيوية فى الوسط القاعدى. أظهرت النتائج فروقا معنوية السفالكسين والاموكسيسيلين باستخدام طرق التسحيح المباشر و الموصلية و المجهادية و المضوائية الطيفية والكروموتوغرافيا السائلة عالية الأداء فى المستوى ($P < 0.001$)

اظهرت النتائج فروقا معنوية فى المستوى ($P < 0.001$) السفالكسين باستخدام طرق التسحيح المباشر و الموصلية و الجهدية.

لاتوجد فروق معنوية فى المستوى ($P > 0.05$) لنتائج الاموكسيسيلين باستخدام طرق التسحيح المباشر و الموصلية و المجهادية.
احصائيا فان الطرق الاتية التسحيح المباشرة و الموصلية و المجهادية و الكروموتغرافيا السائلة فائقة الأداء لها متوسطات متماثلة، وعموما فان الطرق الاتية التسحيح المباشر و الموصلية و المجهادية أعطت نتائج مقبولة مقارنة مع طريقة الكروموتغرافيا السائلة عالية الاداء.

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TABLE OF CONTENTS

Title	Page
DEDICATION	
ABSTRACT	i
ABSTRACT in Arabic	iii
ACKNOWLEDGMENT	V
TABLE OF CONTENTS	Vi
LIST OF TABLES	xvii
LIST OF FIGURES	xx
LIST OF CHROMATOGRAMS	xxiv
CHAPTER ONE INTRODUCTION	1
1.1 Cephalosporins	1
1.2 Potentiometry	4
1.2.1 Potentiometric titration	5
1.3 Conductometry	6
1.3.1 General consideration	6
1.3.2 The basic of conductometric titration	7
1.3.3 Apparatus and measurements	7
1.4 Chromatography	10
1.4.1 Types of chromatography	10
1.4.2 Quantitative analysis	11
1.4.3 Methods for quantitative analysis	11
1.4.4 Detectors	12
CHAPTER TWO LITERATURE REVIEW	13
2.1 Cephalixin	13

2.1.1	Structure	13
2.1.2	Action and use	13
2.1.3	Preparation	13
2.1.4	Defination	13
2.1.5	Characters	13
2.1.6	Methods for determination of cephalixin	14
2.1.6.1	The chromatographic method	14
2.1.6.2	Spectrophotometric methods	15
2.1.6.3	Other methods	17
2.2	Amoxcillin trihydrate	18
2.2.1	Structure	18
2..2.2	Action and use	18
2.2.3	Preparations	18
2.2.4	Definition	18
2.2.5	Characters	18
2.2.6	Methods for determination of amoxicillin	19
2.2.6.1	Chromatographic methods	19
2.2.6.2	Spectrophotometric methods	22
2.2.6.3	Other methods	23
CHAPTER THREE MATERIALS , METHOD AND RESULTS		25
3.1	Cephalexin	25
3.1.1	Direct titration of cephalixin	25
3.1.1.1	Cephlexin monohydrate	25
3.1.1.1.1	Reagents	25
3.1.1.2	Elie cephalixin capsule	25
3.1.1.2.1	Reagents	25

3.1.1.3	Changahi cephalixin capsule	25
3.1.1.3.1	Reagents	25
3.1.1.4	Amipharma cephalixin capsule	25
3.1.1.4.1	Reagents	25
3.1.1.5	Wafra cephalixin capsule	26
3.1.1.5.1	Reagents	26
3.1.1.6	General apparatus	26
3.1.1.7	General procedure	26
3.1.1.8	Results of direct titration methods with NaOH	26
3.1.1.8.1	Cephalixin monohydrate	26
3.1.1.8.2	Elie cephalixin capsule	27
3.1.1.8.3	Amipharma cephalixin capsules	27
3.1.1.8.4	Changahi cephalixin capsules	28
3.1.1.8.5	Wafra capsule cephalixin	29
3.1.2	Back titration methods with NaOH solution	29
3.1.2.1	Cephalixin monohydrate	29
3.1.2.1.1	Reagents	29
3.1.2.2	Elie Cephalixin capsule	29
3.1.2.2.1	Reagents	29
3.1.2.3	Changahi cephalixin capsules	30
3.1.2.3.1	Reagents	30
3.1.2.4	Amipharma cephalixin capsule	30
3.1.2.4.1	Reagents	30
3.1.2.5	Wafra capsules cephalixin	30
3.1.2.5.1	Reagents	30
3.1.2.5.2	General apparatus	30

3.1.2.5.3	General procedure	30
3.1.2.6	The blank titration for cephalixin monohaydreate	31
3.1.2.7	Blank titration for others cephalixin	31
3.1.2.8	Back titration methods results	31
3.1.2.8.1	Cephalexin monohydrate	31
3.1.2.8.2	Elie Cephalexin capsules	32
3.1.2.8.3	Amipharma Cephalxin capsules	33
3.1.2.8.4	Changahi Cephalexin capsules	34
3.1.2.8.5	Wafra Cephalexin capsules	35
3.1.3	Conductometric titration of cephalixin with NaOH solution	36
3.1.3.1	Cephalexin monohaydreate	36
3.1.3.1.1	Reagents	36
3.1.3.2	Elie Cephalexin capsule	36
3.1.3.2.1	Reagents	36
3.1.3.3	Changahi Cephalexin capsule	36
3.1.3.3.1	Reagents	36
3.1.3.4	Amipharma Cephalexin capsule	36
3.1.3.4.1	Reagents	36
3.1.3.5	Wafra Cephalexin capsule	37
3.1.3.5.1	Reagents	37
3.1.3.5.2	General apparatus	37
3.1.3.5.3	General procedure	37
3.1.3.6	Results of conductometric titration with NaOH	38
3.1.3.6.1	cephalexin monohydrate	38
3.1.3.6.2	Elie cephalixin capsules	41

3.1.3.6.3	Amipharma cephalixin capsules	44
3.1.3.6.4	Changahi cephalixin capsules	47
3.1.3.6.5	Wafra cephalixin capsules	50
3.1.4	Conductometric titration of cephalixin with NH ₄ OH solution	53
3.1.4.1	Cephalixin monohydrate	53
3.1.4.1.1	Reagents	53
3.1.4.2	Elie cephalixin capsules	53
3.1.4.2.1	Reagents	53
3.1.4.3	Changahi cephalixin capsules	53
3.1.4.3.1	Reagents	53
3.1.4.4	Amipharma cephalixin capsules	53
3.1.4.4.1	Reagents	53
3.1.4.5	Wafra cephalixin capsules	53
3.1.4.5.1	Reagents	53
3.1.4.5.2	General apparatus	53
3.1.4.5.3	General procedure	54
3.1.4.6	Results of conductometric titration of cephalixin with NH ₄ OH	55
3.1.4.6.1	Cephalixin monohydrate	55
3.1.4.6.2	Elie cephalixin capsules	58
3.1.4.6.3	Amipharma cephalixin capsules	61
3.1.4.6.4	Changahi cephalixin capsules	64
3.1.4.6.5	Wafra cephalixin capsules	67
3.1.5	Potentionmetric titration of cephalixin with NaOH solution	70
3.1.5.1	Cephalixin monohydrate	70

3.1.5.1.1	Reagents	70
3.1.5.2	Elie cephalixin capsules	70
3.1.5.2.1	Reagents	70
3.1.5.3	Changahi cephalixin capsules	70
3.1.5.3.1	Reagents	70
3.1.5.4	Amipharma cephalixin capsules	70
3.1.5.4.1	Reagents	70
3.1.5.5	Wafra cephalixin capsules	70
3.1.5.5.1	Reagents	70
3.1.5.5.2	General apparatus	70
3.1.5.5.3	General procedure	71
3.1.5.6	Results of potentionmetric titration of cephalixin with NaOH	72
3.1.5.6.1	Cephalixin monohydrate	72
3.1.5.6.2	Elie cephalixin capsules	76
3.1.5.6.3	Amipharma cephalixin capsules	80
3.1.5.6.4	Changahi cephalixin capsules	84
3.1.5.6.5	Wafra cephalixin capsules	88
3.1.6	Spectrophotometric determination of Cephalixin	92
3.1.6.1	Reagent	92
3.1.6.2	Apparatus	92
3.1.6.3	Procedure	92
3.1.6.4	Results of spectrophotometric method	93
3.1.7	Detemination of cephalixin using high performance liquid chromatography (HPLC)	95
3.1.7.1	Reagents	95

3.1.7.2	Apparatus	95
3.1.7.3	Procedure	95
3.1.7.4	Result of HPLC determination of Cephalexin	96
3.1.7.4.1	Amipharma cephalalexincapsules	96
3.1.7.4.2	Elie cephalalexin capsules	96
3.1.7.4.3	Wafra cephalalexin capsules	97
3.2	Amoxicillin	117
3.2.1	Amoxicillin trihydrate	117
3.2.1.1	Direct titration of Amoxicillin trihydrate	117
3.2.1.1.1	Reagents	117
3.2.1.2	Amipharma amoxicillin capsules	117
3.2.1.2.1	Reagents	117
3.2.1.3	Changahi amoxicillin capsules	117
3.2.1.3.1	Reagents	117
3.2.1.4	Wafra amoxicillin capsules	117
3.2.1.4.1	Reagents	117
3.2.1.5	G.M. amoxicillin capsules	117
3.2.1.5.1	Reagents	117
3.2.1.6	General apparatus	117
3.2.1.7	General procedure	118
3.2.1.8	Direct titration methods results	118
3.2.1.8.1	Amoxcillin trihydrate	118
3.2.1.8.2	Amipharma Amoxicillin capsules	119
3.2.1.8.3	Changahi Amoxicillin capsules	119
3.2.1.8.4	G .M Amoxicillin capsules	120
3.2.1.4.5	Wafra amoxicillin capsules	120

3.2.2	Back titration methods with sodium hydroxide solution	121
3.2.2.1	Amoxicillin trihydrate	121
3.2.2.1.1	Reagents	121
3.2.2.2	Amipharma amoxicillin capsule	121
3.2.2.2.1	Reagents	121
3.2.2.3	Changahi amoxicillin capsules	121
3.2.2.3.1	Reagents	121
3.2.2.4	Wafra amoxicillin capsules	121
3.2.2.4.1	Reagents	121
3.2.2.5	G.M amoxicillin capsules	122
3.2.2.5.1	Reagents	122
3.2.2.6	General apparatus	122
3.2.2.7	General procedure	122
3.2.2.7.1	Blank titration procedure for amoxicillin trihydrate	122
3.2.2.7.2	Blank titration procedure for others amoxicillin	123
3.2.2.8	Results of back titration methods	123
3.2.2.8.1	Amoxicillin trihydrate	123
3.2.2.8.2	Amipharma Amoxicillin capsules	124
3.2.2.8.3	Changah Amoxicillin capsules	125
3.2.2.8.4	G.M Amoxicillin capsule	126
3.2.2.8.5	Wafra Amoxicillin capsules	127
3.2.3	Conductometric titration of amoxicillin with NaOH solution	128
3.2.3.1	Amoxicillin tri hydrate	128
3.2.3.1.1	Reagents	128
3.2.3.2	Amipharma amoxicillin capsule	128

3.2.3.2.1	Reagents	128
3.2.3.3	Changahi amoxicillin capsule	128
3.2.3.3.1	Reagents	128
3.2.3.4	Wafra amoxicillin capsule	128
3.2.3.4.1	Reagents	128
3.2.3.5	G.M amoxicillin capsule	129
3.2.3.5.1	Reagents	129
3.2.3.6	General apparatus	129
3.2.3.7	General procedure	129
3.2.3.8	Results of conductometric titration methods with NaOH	130
3.2.3.8.1	Amoxicillin trihydrate	130
3.2.3.8.2	Amipharma Amoxicillin capsules	133
3.2.3.8.3	Changahi Amoxicillin capsules	136
3.2.3.8.4	G.M amoxicillin capsules	139
3.2.3.8.5	Wafra Amoxicillin capsules	142
3.2.4	Conductometric titration of amoxicillin with NH_4OH solution	145
3.2.4.1	Amoxicillin trihydrate	145
3.2.4.1.1	Reagents	145
3.2.4.2	Amipharma amoxicillin capsules	145
3.2.4.2.1	Reagents	145
3.2.4.3	Changahi amoxicillin capsules	145
3.2.4.3.1	Reagents	145
3.2.3.4	Wafra amoxicillin capsules	145
3.2.4.4.1	Reagents	145
3.2.4.5	G.M amoxicillin capsules	145

3.2.4.5.1	Reagents	145
3.2.4.6	General apparatus	145
3.2.4.7	General procedure	145
3.2.4.8	Result of conductometric titration method with NH_4OH	146
3.2.4.8.1	Amoxicillin trihydrate	146
3.2.4.8.2	Amipharma Amoxicillin capsules	150
3.2.4.8.3	Changahi Amoxicillin capsules	153
3.2.4.8.4	G.M Amoxicillin capsules	156
3.2.4.8.5	Wafra Amoxicillin capsules	159
3.2.5	Potentionmetric titration of amoxicillin with NaOH	162
3.2.5.1	Amoxicillin trihydrate	162
3.2.5.1.1	Reagents	162
3.2.5.2	Amipharma amoxicillin capsules	162
3.2.5.2.1	Reagents	162
3.2.5.3	Changahi amoxicillin capsules	162
3.2.5.3.1	Reagents	162
3.2.5.4	Wafra amoxicillin capsules	162
3.2.5.4.1	Reagents	162
3.2.5.5	G.M. amoxicillin capsules	162
3.2.5.5.1	Reagents	162
3.2.5.6	General apparatus	162
3.2.5.7	General procedure	162
3.2.5.8	Results of potentiometric titration method with NaOH	163
3.2.5.8.1	Amoxicillin trihydrate	163
3.2.5.8.2	Amipharma amoxicillin capsules	168
3.2.5.8.3	Changahi amoxicillin capsules	172

3.2.5.8.4	G.M amoxicillin capsules	176
3.2.5.8.5	Wafra amoxicillin capsules	180
3.2.6	Spectrophotometric determination of amoxicillin	184
3.2.6.1	Reagents	184
3.2.6.2	Apparatus	184
3.2.6.3	Procedure	184
3.2.6.4	Results of spectrophotometric determination of amoxicillin	186
3.2.7	Determination of amoxicillin using HPLC	188
3.2.7.1	Reagent	188
3.2.7.2	Apparatus	188
3.2.7.3	Procedure	188
3.2.7.4	Results of HPLC determination of amoxicillin	190
3.2.7.4.1	Amipharma amoxicillin capsules	190
3.2.7.4.2	G.M amoxicillin capsules	190
3.2.7.4.3	Changahi amoxicillin capsules	190
3.2.7.4.4	Wafra amoxicillin capsules	191
CHAPTER FOUR DISCUSSION AND CONCLUSIONS		214
4.1	Discussions	214
4.2	Conclusions	223
4.3	Suggestions for further studies	223
REFERANCES		224

LIST OF TABLES

Table	Title	page
3.1	Conductometric titration of 50ml cephalexin monohydrate with 0.025M NaOH	39
3.2	Conductometric titration of 50ml Elie Cephalexin capsule with 0.2814M NaOH	42
3.3	Conductometric titration of 50ml Amipharma cephalexin capsules with 0.2814M NaOH	45
3.4	Conductometric titration of 50ml Changahi cephalexin capsules with 0.2814M NaOH	48
3.5	Conductometric titration of 50ml Wafra cephalexin capsules 0.284M NaOH	51
3.6	Conductometric titration of 50ml cephalexin monohydrate with 0.0935M NH ₄ OH	56
3.7	Conductometric titration of 50ml Elie cephalexin capsule with 0.220M NH ₄ OH	59
3.8	Conductometric titration of 50ml Amipharma cephalexin capsule with 0.220M NH ₄ OH	62
3.9	Conductometric titration of 50ml Changahi cephalexin capsules with 0.220M NH ₄ OH	65
3.10	Conductometric titration of 50ml Wafra cephalexin capsules with 0.25M NH ₄ OH	68
3.11	Potentiometric titration of 50ml cephalexin monohydrate with 0.025M NaOH	73
3.12	Potentiometric titration of 50ml Elie cephalexin capsule with 0.2814M NaOH	77
3.13	Potentiometric titration of 50ml Amipharma cephalexin capsule	81

	with 0.2814M NaOH	
3.14	Potentiometric titration of 50ml Changahi cephalixin capsules with 0.2814M NaOH	85
3.15	potentiometric titration of 50ml wafra cephalixin capsules with 0.284M NaOH	89
3.16	Conductometric titration of 50ml amoxicillin tri hydrate with 0.09224M NaOH	131
3.17	Conductometric method of 50ml Amipharma amoxicillin capsule with 0.09211M NaOH	134
3.18	Conductometric method of 50ml amoxicillin Changahi capsule with 0.0917M NaOH	137
3.19	Conductometric method of 50ml G M amoxicillin capsules with 0.0917M NaOH	140
3.20	Conductometric method of Wafra amoxicillin capsules with 0.0745M NaOH	143
3.21	Conductometric titration of 50ml amoxicillin tri hydrate with 0.0794M NH ₄ OH	148
3.22	Conductometric method of 50ml Amipharma amoxicillin capsules amoxicillin with 0.07883M NH ₄ OH	151
3.23	Conductometric method of 50ml Changahi amoxicillin capsule with 0.0723M NH ₄ OH	154
3.24	Conductometric method of 50ml G.M amoxicillin capsule with 0.07886M NH ₄ OH	157
3.25	Conductometric method of Wafra amoxicillin capsules with 0.1202M NH ₄ OH	160
3.26	potentiometric titration of 50ml amoxicillin trihydrate with 0.09244M NaOH	165
3.27	potentiometric titration of 50ml Amipharma amoxicillin capsule	169

	with 0.09211M NaOH	
3.28	Potentiometric titration of 50ml Changahi amoxicillin capsule with 0.09211M NaOH	173
3.29	Potentiometric titration of GM amoxicillin capsules with 0.0917M NH ₄ OH	177
3.30	Potentiometric titration of wafra amoxicillin capsules with 0.0745M NaOH	181
4.1	Analysis of variance for effect of different methods of determination cephalixin contents	215
4.2	means separation of Cephalixin determination methods	215
4.3	Analysis of variance for effect of different methods of determination cephalixin contents	216
4.4	means separation of Cephalixin determination methods	216
4.5	Analysis of variance for effect of different methods of determination amoxicillin contents	217
4.6	means separation of Amoxicillin determination methods	217
4.7	Analysis of variance for effect of different methods of determination amoxicillin contents with HPLC method	218
4.8	means separation Amoxicillin determination methods	218

LIST OF FIGURES

Figure	Title	Page
1.1	Wheatstone bridge circuit measuring conductivity	9
1.2	Conductivity cells	9
3.1	Conductmetric titration of 50ml cephalexin monohydrate with 0.025M sodium hydroxide	40
3.2	Conductmetric titration of 50ml Elie cephalexin capsules with 0.2814M sodium hydroxide	43
3.3	Conductmetric titration of 50ml Amipharma cephalexin capsules with 0.2814M sodium hydroxide	46
3.4	Conductmetric titration of 50ml Shangahi cephalexin capsules with 0.2814M sodium hydroxide	49
3.5	Conductmetric titration of 50ml Wafra cephalexin capsules with 0.284M sodium hydroxide	52
3.6	Conductmetric titration of 50ml cephalexin monohydrate with 0.0935M ammonium hydroxide	57
3.7	Conductmetric titration of 50ml Elie cephalexin capsules with 0.220M ammonium hydroxide	60
3.8	Conductmetric titration of 50ml Amipharma cephalexin capsules with 0.220M ammonium hydroxide	63
3.9	Conductmetric titration of 50ml Shangahi cephalexin capsules with 0.220M ammonium hydroxide	66
3.10	Conductmetric titration of 50ml Wafra cephalexin capsules with 0.025M ammonium hydroxide	69
3.11	Potentiometric titration of 50ml cephalexin monohydrate with 0.025M sodium hydroxide -1	74
3.12	Potentiometric titration of 50ml cephalaxin monohydrate with	75

	0.025M sodium hydroxide -2	
3.13	Potentiometric titration of 50ml Elie cephalixin capsules with 0.2814M sodium hydroxide -1	78
3.14	Potentiometric titration of 50ml Elie cephalixin capsules with 0.2814M sodium hydroxid -2	79
3.15	Potentiometric titration of 50ml Amipharma cephalixin capsules with 0.2814M sodium hydroxide -1	82
3.16	Potentiometric titration of 50ml Amipharma cephalixin capsules with 0.2814M sodium hydroxide -2	83
3.17	Potentiometric titration of 50ml Shangahi cephalixin capsules with 0.2814M sodium hydroxide -1	86
3.18	Potentiometric titration of 50ml Shangahi cephalixin capsules with 0.2814M sodium hydroxide -2	87
3.19	Potentiometric titration of 50ml Wafra cephalixin capsules with 0.284M sodium hydroxide -1	90
3.20	Potentiometric titration of 50ml Wafra cephalixin capsules with 0.284M sodium hydroxide -2	91
3.21	Standard cephalixin mono hydrate calibration curve of spectrophotometric method	94
3.22	Standard cephalixin monohydrate calibration curve of chromatographic method	107
3.23	Conductometric titration of 50ml amoxicillin trihydrate with 0.09224M sodium hydroxide	132
3.24	Conductometric titration of 50ml Amipharma amoxicillin capsules with 0.09211M sodium hydroxide	135
3.25	Conductometric titration of 50ml Changahi amoxicillin capsules	138

	with 0.0917M sodium hydroxide	
3.26	Conductometric titration of 50ml G.M amoxicillin capsules with 0.0917M sodium hydroxide	141
3.27	Conductometric titration of 50ml Wafra amoxicillin capsules with 0.0745M sodium hydroxide	144
3.28	Conductometric titration of 50ml amoxicillin trihydrate with 0.0794M ammonium hydroxide	149
3.29	Conductometric titration of 50ml Amipharma amoxicillin capsules with 0.07883M ammonium hydroxide	152
3.30	Conductometric titration of 50ml Changahi amoxicillin capsules with 0.0723M ammonium hydroxide	155
3.31	Conductometric determination of 50ml G.M amoxicillin capsules with 0.07886M ammonium hydroxide	158
3.32	Conductometric titration of 50ml Wafra amoxicillin capsules with 0.1202M ammonium hydroxide	161
3.33	Potentiometric titration of 50ml amoxicillin trihydrate with 0.09244M sodium hydroxide -1	166
3.34	Potentiometric titration of 50ml amoxicillin trihydrate with 0.09244M sodium hydroxide 2	167
3.35	Potentiometric titration of 50ml amipharma amoxicillin capsules with 0.09211M sodium hydroxide -1	170
3.36	Potentiometric titration of 50ml amipharma amoxicillin capsules trihydrate with 0.09211M sodium hydroxide-2	171
3.37	Potentiometric titration of 50ml Changahi amoxicillin capsules with 0.0917M sodium hydroxide -1	174
3.38	Potentiometric titration of 50ml Changahi amoxicillin capsules with 0.0917M sodium hydroxide -2	175
3.39	Potentiometric titration of 50ml G.M amoxicillin with 0.0917M	178

	sodium hydroxide-1	
3.40	Potentiometric titration of 50ml G.M amoxicillin 0.0917M with sodiumhydroxide-2	179
3.41	Potentiometric titrationof 50ml Wafra amoxicillin capsules with 0.0745M sodium hydroxide -1	182
3.42	Potentiometric titration of 50ml Wafra amoxicillin capsules with 0.0745M sodium hydroxide -2	183
3.43	Standard amoxicillin tri hydrate calibration curve of spectrophotometric method	187
3.44	Chromatographic standard amoxicillin curve of chromatographic method	201
4.1	Reactivity and degradation of penicillins and cephalaxins in neutral and alkaline medium	221
4.2	Reaction of amino acid with acid and base	221
4.3	Ionic species of amoxicillin	222

LIST OF CHROMATOGRAMS

Chromotogram plot	Title	Page
3.1	(R1.1) standard cephalixin monohydrate	98
3.2	(R1.2) standard cephalixin monohydrate	99
3.3	(R1.3) standard cephalixin monohydrate	100
3.4	(R2.1) standard cephalixin monohydrate	101
3.5	(R2.2) standard cephalixin monohydrate	102
3.6	(R2.3) standard cephalixin monohydrate	103
3.7	(R3.1) standard cephalixin monohydrate	104
3.8	(R3.2) standard cephalixin monohydrate	105
3.9	(R3.3) standard cephalixin monohydrate	106
3.10	(R1) Amipharma cephalixin capsules	108
3.11	(R2) Amipharma cephalixin capsules	109
3.12	(R3) Amipharma cephalixin capsules	110
3.13	(R1) Elie cephalixin capsule	111
3.14	(R2) Elie cephalixin capsules	112
3.15	(R3) Elie cephalixin capsules	113
3.16	(R1)Wafra cephalixin capsules	114
3.17	(R2)Wafra cephalixin capsules	115
3.18	(R3)Wafra cephalixin capsules	116
3.19	(R1.1) Standard Amoxicillin Tri hydrate	192
3.20	(R1.2) Standard Amoxicillin Tri hydrate	193
3.21	(R1.3) Standard Amoxicillin Tri hydrate	194
3.22	(R2.1) Standard Amoxicillin Tri hydrate	195
3.23	(R2.2) Standard Amoxicillin Tri hydrate	196
3.24	(R2.3) Standard Amoxicillin Tri hydrate	197
3.25	(R3.1) Standard Amoxicillin Tri hydrate	198

3.26	(R3.2) Standard Amoxicillin Tri hydrate	199
3.27	(R3.3) Standard Amoxicillin Tri hydrate	200
3.28	(R1) Amiparma amoxicillin capsules	202
3.29	(R2) Amiparma amoxicillin capsules	203
3.30	(R3) Amiparma amoxicillin capsules	204
3.31	(R1) G.M amoxicillin capsules	205
3.32	(R2) G.M amoxicillin capsules	206
3.33	(R3) G.M amoxicillin capsules	207
3.34	(R1) Changahi amoxicillin capsules	208
3.35	(R2) Changahi amoxicillin capsules	209
3.36	(R3) Changahi amoxicillin capsules	210
3.37	(R1) Wafra amoxicillin capsules	211
3.38	(R2) Wafra amoxicillin capsules	212
3.39	(R3) Wafra amoxicillin capsules	213