

การหาปริมาณตัวยาที่เป็นกรดอ่อนด้วยวิธีของแกรนาคัวทะเลลายผสม



นางสาวจุฑามาศ สุขบรรเทิง

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาคามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต  
ภาควิชาเภสัชเคมี  
บัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย  
พ.ศ. 2531

ISBN 974-568-978-5

ลิขสิทธิ์ของบัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

014215

QUANTITATIVE DETERMINATION OF WEAK ACIDIC DRUGS  
BY USING GRAN'S METHOD IN MIXED SOLVENTS

Miss Juthamas Sukbuntherng

A Thesis Submitted in Partial Fulfillment of the Requirements  
for the Degree of Master of Science in Pharmacy

Department of Pharmaceutical Chemistry

Graduate School

Chulalongkorn University

1988

ISBN 974-568-978-5



จุฬามาศ สุขบรรเทิง : การหาปริมาณตัวยาที่เป็นกรดอ่อนด้วยวิธีของแกรนในตัวทำละลายผสม  
(QUANTITATIVE DETERMINATION OF WEAK ACIDIC DRUGS BY USING GRAN'S  
METHOD IN MIXED SOLVENTS) อ.ที่ปรึกษา : ดร.มิตร ปทีปวิษ . ๑๖๔ หน้า.

การตกตะกอนของยาที่เป็นกรดอ่อนบางตัว เมื่อทำการวิเคราะห์โดยการติเตตรกับต่างแกในตัว  
ทำละลายที่เป็นน้ำ สามารถแก้ไขได้โดยทำการติเตตรในตัวทำละลายผสมระหว่างน้ำและตัวทำละลายอินทรีย์  
(เอธิลแอลกอฮอล์ , เมธิลแอลกอฮอล์ และ โพรพิลีนไกลคอล)

การติเตตรระหว่างตัวยาที่เป็นกรดอ่อนและต่างแกในตัวทำละลายผสมดังกล่าวกระทำโดยอาศัย  
เทคนิคทางโพเทนทิโอเมตรี พบว่าสามารถใช้วิธีของแกรนในการตรวจหาจุดยุติเพื่อนำมาคำนวณหาปริมาณ  
ของตัวยาที่มีความถูกต้องและแม่นยำได้ เช่นเดียวกับวิธีการติเตตรในตัวทำละลายที่ไม่ใช่น้ำ ซึ่งมีปรากฏอยู่ใน  
ตำรายาแห่งชาติของสหรัฐอเมริกาฉบับที่ ๒๐

ภาควิชา ..... เกสัชเคมี .....  
สาขาวิชา ..... เกสัชเคมี .....  
ปีการศึกษา 2530 .....

ลายมือชื่อนิสิต ..... *จุฬามาศ สุขบรรเทิง* .....  
ลายมือชื่ออาจารย์ที่ปรึกษา ..... *มิตร ปทีปวิษ* .....



JUTHAMAS SUKBUNTHERNG : QUANTITATIVE DETERMINATION OF WEAK ACIDIC DRUGS BY USING GRAN'S METHOD IN MIXED SOLVENTS. THESIS ADVISOR : MITR PATHIPVANICH, Ph.D. 168 PP.

Mixed solvent systems between water and organic solvents (ethyl alcohol, methyl alcohol and propylene glycol) were employed to avoid the precipitation which had occurred when titrating some weak acid salt drugs with strong base in aqueous solvent.

Potentiometric titration of weak acidic drugs with strong base in those mixed solvents, Gran's method could yield end point volumes and calculated percentage purities of drugs with the same degree of accuracy and reproducibility as non-aqueous titration method which were described in USP XX.

ภาควิชา ..... เกสัชเคมี  
สาขาวิชา ..... เกสัชเคมี  
ปีการศึกษา ..... 2530

ลายมือชื่อนิสิต Juthamas Sukbuntherng

ลายมือชื่ออาจารย์ที่ปรึกษา Mitr Pathipvanich



## CONTENTS

	Page
THAI ABSTRACT.....	iv
ENGLISH ABSTRACT.....	v
ACKNOWLEDGEMENTS.....	vi
LIST OF TABLES.....	vii
LIST OF FIGURES.....	x
ABBREVIATION.....	xxvi
CHAPTER	
I INTRODUCTION.....	1
II PURPOSE OF INVESTIGATION.....	22
III EXPERIMENTAL.....	23
IV RESULTS AND DISCUSSION.....	33
V CONCLUSION.....	159
REFERENCES.....	161
APPENDIX.....	166
VITA.....	168



## ACKNOWLEDGEMENTS

I wish to express my deepest sincere gratitude and appreciation to Dr. Mitr Pathipvanish and Assistant Professor Somkiat Rujirawat of Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Science, Chulalongkorn University, for their guidance, assistance, kindness and encouragement during the entire course of this study.

The helpful cooperation of the staff members of the Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Chulalongkorn university is appreciated.

I would like to express my thank to Chew Brother Co.,Ltd. for their generous supply of weak acidic drugs for this study.

I also wish to express my thank to Prince of Songkla University and The Graduate School, Chulalongkorn University, for granting partial financial support to conduct this study.

Finally, I would like to express my gratitude to Lecturer Surapong Kengthorng and my friend, Mr.Chakri Thongplengsri for all of their help.



## LIST OF TABLES

Table No.	Page
1. Express of Variables in Gran's Plot.....	31
2. Selected pKa Values of Weak Acidic Drugs.	32
3. Average Percentage Purities by Gran's Method for Titration of Triprolidine Hydrochloride in Methanol-Water Solvent Systems with 0.08624 N NaOH.....	36
4. Average Percentage Purities by Gran's Method for Titration of Triprolidine Hydrochloride in Ethanol-Water Solvent Systems with 0.08624 N NaOH.....	44
5. Average Percentage Purities by Gran's Method for Titration of Triprolidine Hydrochloride in Propylene Glycol-Water Solvent Systems with 0.08328 N NaOH.....	53
6. Average Percentage Purities by Gran's Method for Titration of Quinine Sulfate in Methanol-Water Solvent Systems with 0.08234 N NaOH.....	61
7. Average Percentage Purities by Gran's Method for Titration of Quinine Sulfate in Ethanol-Water Solvent Systems with 0.08234 N NaOH.....	68
8. Average Percentage Purities by Gran's Method for Titration of Quinine Sulfate	

Table No.	Page
	in Propylene Glycol-Water Solvent
	Systems with 0.08340 N NaOH..... 74
9.	Average Percentage Purities by Gran's Method for Titration of Dextromethorphan Hydrobromide in Methanol-Water Solvent Systems with 0.08624 N NaOH..... 81
10.	Average Percentage Purities by Gran's Method for Titration of Dextromethorphan Hydrobromide in Ethanol-Water Solvent Systems with 0.08624 N NaOH..... 87
11.	Average Percentage Purities by Gran's Method for Titration of Dextromethorphan Hydrobromide in Propylene Glycol-Water Solvent Systems with 0.08340 N NaOH..... 93
12.	Average Percentage Purities by Gran's Method for Titration of Diphenhydramine Hydrochloride in Methanol-Water Solvent Systems with 0.08328 N NaOH..... 99
13.	Average Percentage Purities by Gran's Method for Titration of Diphenhydramine Hydrochloride in Ethanol-Water Solvent Systems with 0.08328 N NaOH..... 106
14.	Average Percentage Purities by Gran's Method for Titration of Diphenhydramine Hydrochloride in Propylene Glycol-Water Solvent Systems with 0.08340 N NaOH..... 113



Table No.	Page
15. Average Percentage Purities by Gran's Method for Titration of Chlorpheniramine Maleate in Methanol-Water Solvent Systems with 0.08184 N NaOH.....	120
16. Average Percentage Purities by Gran's Method for Titration of Chlorpheniramine Maleate in Ethanol-Water Solvent Systems with 0.08137 N NaOH.....	132
17. Average Percentage Purities by Gran's Method for Titration of Chlorpheniramine Maleate in Propylene Glycol-Water Solvent Systems with 0.08184 N NaOH.....	142



## LIST OF FIGURES

Figure No.	Page
1. Titration curves of triprolidine hydrochloride with sodium hydroxide in 30-90% v/v methanol/water.....	37
2. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 30% v/v methanol/water.....	38
3. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 40% v/v methanol/water.....	38
4. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 50% v/v methanol/water.....	39
5. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 60% v/v methanol/water.....	39
6. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 70% v/v methanol/water.....	40
7. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 80% v/v methanol/water.....	40
8. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 90% v/v methanol/water.....	41

Figure No.	Page
9. Titration curves of triprolidine hydrochloride with sodium hydroxide in 30-90% v/v ethanol/water.....	45
10. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 30% v/v ethanol/water.....	46
11. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 40% v/v ethanol/water.....	46
12. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 50% v/v ethanol/water.....	47
13. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 60% v/v ethanol/water.....	47
14. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 70% v/v ethanol/water.....	48
15. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 80% v/v ethanol/water.....	48
16. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 90% v/v ethanol/water.....	49
17. Titration curves of triprolidine hydrochloride with sodium hydroxide in 40-70% v/v propylene glycol/water...	54

Figure No.	Page
18. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 40% v/v propylene glycol/water.....	55
19. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 50% v/v propylene glycol/water.....	55
20. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 60% v/v propylene glycol/water.....	56
21. Gran's plot for the titration of triprolidine HCl with sodium hydroxide in 70% v/v propylene glycol/water.....	56
22. Relative purities of triprolidine hydrochloride in methanol-water solvents by using G plot, V plot and E plot.....	59
23. Relative purities of triprolidine hydrochloride in ethanol-water solvents by using G plot, V plot and E plot.....	59
24. Relative purities of triprolidine hydrochloride in propylene glycol-water solvents by using G plot, V plot and E plot.....	60
25. Titration curves of quinine sulfate with sodium hydroxide in 40-90% v/v methanol/water.....	62

Figure No.	Page
26. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 40% v/v methanol/water.....	63
27. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 50% v/v methanol/water.....	63
28. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 60% v/v methanol/water.....	64
29. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 70% v/v methanol/water.....	64
30. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 80% v/v methanol/water.....	65
31. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 90% v/v methanol/water.....	65
32. Titration curves of quinine sulfate with sodium hydroxide in 40-90% ethanol/water	69
33. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 40% v/v ethanol/water.....	70
34. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 50% v/v ethanol/water.....	70

Figure No.	Page
35. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 60% v/v ethanol/water.....	71
36. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 70% v/v ethanol/water.....	71
37. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 80% v/v ethanol/water.....	72
38. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 90% v/v ethanol/water.....	72
39. Titration curves of quinine sulfate with sodium hydroxide in 40-70% v/v propylene glycol/water.....	75
40. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 40% v/v propylene glycol/water.....	76
41. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 50% v/v propylene glycol/water.....	76
42. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 60% v/v propylene glycol/water.....	77
43. Gran's plot for the titration of quinine sulfate with sodium hydroxide in 70% v/v	

Figure No.	Page
propylene glycol/water.....	77
44. Relative purities of quinine sulfate in methanol-water solvents by using G plot, V plot and E plot.....	78
45. Relative purities of quinine sulfate in ethanol-water solvents by using G plot, V plot and E plot.....	78
46. Relative purities of quinine sulfate in propylene glycol-water solvents by using G plot, V plot and E plot.....	79
47. Titration curves of dextromethorphan Hydrobromide with sodium hydroxide in 50-90% v/v methanol/water.....	82
48. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 50% v/v methanol/water....	83
49. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 60% v/v methanol/water....	83
50. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 70% v/v methanol/water....	84
51. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 80% v/v methanol/water....	84

Figure No.	Page
52. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 90% v/v methanol/water....	85
53. Titration curves of dextromethorphan hydrobromide with sodium hydroxide in 40-90% v/v ethanol/water.....	88
54. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 40% v/v ethanol/water.....	89
55. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 50% v/v ethanol/water.....	89
56. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 60% v/v ethanol/water.....	90
57. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 70% v/v ethanol/water.....	90
58. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 80% v/v ethanol/water.....	91
59. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 90% v/v ethanol/water.....	91
60. Titration curves of dextromethorphan hydrobromide with sodium hydroxide	



Figure No.	Page
in 60-70% v/v propylene glycol/water...	94
61. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 60% v/v propylene glycol/water.....	95
62. Gran's plot for the titration of dextromethorphan HBr with sodium hydroxide in 70% v/v propylene glycol/water.....	95
63. Relative purities of dextromethorphan hydrobromide in methanol-water solvents by using G plot, V plot and E plot.....	96
64. Relative purities of dextromethorphan hydrobromide in ethanol-water solvents by using G plot, V plot and E plot.....	96
65. Relative purities of dextromethorphan hydrobromide in propylene glycol-water solvents by using G plot, V plot and E plot.....	97
66. Titration curves of diphenhydramine hydrochloride with sodium hydroxide in 30-90% v/v methanol/water.....	100
67. Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 30% v/v methanol/water.....	101
68. Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide	

Figure No.	Page
	in 40% v/v methanol/water..... 101
69.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 50% v/v methanol/water..... 102
70.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 60% v/v methanol/water..... 102
71.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 70% v/v methanol/water..... 103
72.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 80% v/v methanol/water..... 103
73.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 90% v/v methanol/water..... 104
74.	Titration curves of diphenhydramine hydrochloride with sodium hydroxide in 30-90% v/v ethanol/water..... 107
75.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 30% v/v ethanol/water..... 108
76.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 40% v/v ethanol/water..... 108
77.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide

Figure No.	Page
	in 50% v/v ethanol/water..... 109
78.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 60% v/v ethanol/water..... 109
79.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 70% v/v ethanol/water..... 110
80.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 80% v/v ethanol/water..... 110
81.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 90% v/v ethanol/water..... 111
82.	Titration curves of diphenhydramine hydrochloride with sodium hydroxide in 40-70% v/v propylene glycol/water..... 114
83.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 40% v/v propylene glycol/water..... 115
84.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 50% v/v propylene glycol/water..... 115
85.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide in 60% v/v propylene glycol/water..... 116
86.	Gran's plot for the titration of diphenhydramine HCl with sodium hydroxide

Figure No.	Page
in 70% v/v propylene glycol/water.....	116
87. Relative purities of diphenhydramine hydrochloride in methanol-water solvents by using G plot, V plot and E plot.....	117
88. Relative purities of diphenhydramine hydrochloride in ethanol-water solvents by using G plot, V plot and E plot.....	117
89. Relative purities of diphenhydramine hydrochloride in propylene glycol -water solvents by using G plot, V plot and E plot.....	118
90. Titration curve of chlorpheniramine maleate with sodium hydroxide in 30% v/v methanol/water.....	121
91. Titration curve of chlorpheniramine maleate with sodium hydroxide in 40% v/v methanol/water.....	121
92. Titration curve of chlorpheniramine maleate with sodium hydroxide in 50% v/v methanol/water.....	122
93. Titration curve of chlorpheniramine maleate with sodium hydroxide in 60% v/v methanol/water.....	122
94. Titration curve of chlorpheniramine maleate with sodium hydroxide in 70% v/v methanol/water.....	123

Figure No.	Page
95. Titration curve of chlorpheniramine maleate with sodium hydroxide in 80% v/v methanol/water.....	123
96. Titration curve of chlorpheniramine maleate with sodium hydroxide in 90% v/v methanol/water.....	124
97. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 30% v/v methanol/water....	125
98. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 40% v/v methanol/water....	125
99. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 50% v/v methanol/water....	126
100. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 60% v/v methanol/water....	126
101. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 70% v/v methanol/water....	127
102. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 80% v/v methanol/water....	127
103. Gran's plot for the titration of chlorpheniramine maleate with sodium	

Figure No.	Page
hydroxide in 90% v/v methanol/water....	128
104. Titration curve of chlorpheniramine maleate with sodium hydroxide in 30% v/v ethanol/water.....	133
105. Titration curve of chlorpheniramine maleate with sodium hydroxide in 40% v/v ethanol/water.....	133
106. Titration curve of chlorpheniramine maleate with sodium hydroxide in 50% v/v ethanol/water.....	134
107. Titration curve of chlorpheniramine maleate with sodium hydroxide in 60% v/v ethanol/water.....	134
108. Titration curve of chlorpheniramine maleate with sodium hydroxide in 70% v/v ethanol/water.....	135
109. Titration curve of chlorpheniramine maleate with sodium hydroxide in 80% v/v ethanol/water.....	135
110. Titration curve of chlorpheniramine maleate with sodium hydroxide in 90% v/v ethanol/water.....	136
111. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 30% v/v ethanol/water.....	137

Figure No.	Page
112. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 40% v/v ethanol/water.....	137
113. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 50% v/v ethanol/water.....	138
114. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 60% v/v ethanol/water.....	138
115. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 70% v/v ethanol/water.....	139
116. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 80% v/v ethanol/water.....	139
117. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 90% v/v ethanol/water.....	140
118. Titration curve of chlorpheniramine maleate with sodium hydroxide in 30% v/v propylene glycol/water.....	143
119. Titration curve of chlorpheniramine maleate with sodium hydroxide in 40% v/v propylene glycol/water.....	143
120. Titration curve of chlorpheniramine maleate with sodium hydroxide in 50% v/v	

Figure No.	Page
propylene glycol/water.....	144
121. Titration curve of chlorpheniramine maleate with sodium hydroxide in 60% v/v propylene glycol/water.....	144
122. Titration curve of chlorpheniramine maleate with sodium hydroxide in 70% v/v propylene glycol/water.....	145
123. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 30% v/v propylene glycol/ water.....	146
124. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 40% v/v propylene glycol/ water.....	146
125. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 50% v/v propylene glycol/ water.....	147
126. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 60% v/v propylene glycol/ water.....	147
127. Gran's plot for the titration of chlorpheniramine maleate with sodium hydroxide in 70% v/v propylene glycol/ water.....	148



Figure No.	Page
128. Relative purities of chlopheniramine maleate in methanol-water solvents by using G plot, V plot and E plot.....	149
129. Relative purities of chlopheniramine maleate in ethanol-water solvents by using G plot, V plot and E plot.....	149
130. Relative purities of chlorpheniramine maleate in propylene glycol-water solvents by using G plot, V plot and E plot.....	150

## ABBREVIATION

- V : Volume of titrant (ml)
- Ve : Volume of titrant at end point (ml)
- Ve<sub>1</sub> : Volume of titrant at first end point (ml)
- Ve<sub>2</sub> : Volume of titrant at second end point (ml)
- N : Normality of titrant
- K<sub>a</sub> : Dissociation constant of acid
- K<sub>w</sub> : Ionization constant of water
- C<sub>a</sub> : Initial concentration of weak acid, a (g/l)
- V<sub>o</sub> : Initial volume of weak acid solution (ml)
- [a] : Concentration of substance a
- ml : Milliliter
- meq : Milliequivalence
- g : Gram
- G plot : Gran's plot of titration data prior to equivalence point which accounted for autoprotolysis of water
- V plot : Gran's plot of titration data prior to equivalence point which did not accounted for autoprotolysis of water
- E plot : Gran's plot of titration data after equivalence point