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DESIGN AND *IN VITRO* EVALUATION OF ACYCLOVIR SUSTAINED RELEASE TABLET
USING HYDROPHILIC MATRIX SYSTEM



Miss Chitralada Vasarach

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จุดประสงค์ของการศึกษาในครั้งนี้เพื่อที่จะออกแบบยาเม็ดอะซัยโคลเวียร์แบบออกฤทธิ์นานชนิดรับประทาน โดยศึกษาเปรียบเทียบการใช้พอลิเมอร์แบบชอบน้ำ 4 ชนิด คือไฮดรอกซีโพรพิลเมทิลเซลลูโลส แชนแทนกัม โซเดียมอัลจิเนท และคาโบพอล 934พี เมทริกซ์ที่ประกอบด้วยไฮดรอกซีโพรพิลเมทิลเซลลูโลส, แชนแทนกัม และโซเดียมอัลจิเนท มีคุณสมบัติการปลดปล่อยฤทธิ์นาน แต่เมทริกซ์ที่ประกอบด้วยคาโบพอล 934พี ไม่มีคุณสมบัติการปลดปล่อยฤทธิ์นานของยาอะซัยโคลเวียร์ จากการศึกษาปัจจัยที่มีอิทธิพลต่อการปลดปล่อยยา คือ ปริมาณของพอลิเมอร์ ชนิดของสารเพิ่มปริมาณ ความเป็นกรด-เบส และความแรงออสโมติกของตัวกลางการละลาย พบว่าปริมาณพอลิเมอร์ที่เพิ่มขึ้นมีผลให้อัตราในการปลดปล่อยยาช้าลง แต่อย่างไรก็ตามค่าการละลายที่ต่ำของตัวยาและของสารเพิ่มปริมาณในตัวกลางการละลาย และความแข็งแรงของชั้นเจลรอบเม็ดยาอาจจะแสดงบทบาทที่สำคัญกว่าในการควบคุมการปลดปล่อยยาจากเมทริกซ์ ส่งผลให้เกิดการบดบังผลของปริมาณพอลิเมอร์ที่มีต่ออัตราการปลดปล่อยยา ผลของชนิดของสารเพิ่มปริมาณต่ออัตราการปลดปล่อยยาขึ้นอยู่กับปริมาณและค่าการละลายของสารเพิ่มปริมาณในตัวกลางการละลาย ความเป็นกรด-เบสของตัวกลางการละลายส่งผลกระทบต่ออัตราการปลดปล่อยยาจากเมทริกซ์ที่ประกอบด้วยไฮดรอกซีโพรพิลเมทิลเซลลูโลส และแชนแทนกัม ซึ่งสามารถอธิบายได้ด้วยความแตกต่างของความแข็งแรงของชั้นเจลรอบเม็ดยา และค่าการละลายของยาในตัวกลางการละลายที่มีความเป็นกรด-เบสแตกต่างกัน และเนื่องจากการละลายของโซเดียมอัลจิเนทขึ้นอยู่กับความเป็นกรด-เบสของตัวกลางการละลายจึงส่งผลให้เกิดความแตกต่างของรูปแบบและกลไกการปลดปล่อยยาจากเมทริกซ์ที่ประกอบด้วยโซเดียมอัลจิเนท ความแรงออสโมติกที่เพิ่มขึ้นทำให้ชั้นเจลรอบเม็ดยาแข็งแรงขึ้นและส่งผลให้อัตราในการปลดปล่อยยาช้าลง ลักษณะการปลดปล่อยยาที่แตกต่างกันสามารถอธิบายได้จากพฤติกรรมของตัวและการกร่อนของเม็ดยาที่แตกต่างกัน ส่วนประกอบของเมทริกซ์และภาวะของตัวกลางการละลายส่งผลกระทบต่อกลไกการปลดปล่อยยา การแพร่ของยาในตัวกลางการละลายและการกร่อนของเมทริกซ์ควบคุมการปลดปล่อยยา

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ปีการศึกษา 2546

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ลายมือชื่ออาจารย์ที่ปรึกษา.....
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....

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 CHITRALADA VASARACH: DESIGN AND *IN VITRO* EVALUATION OF
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The purpose of this study was to design an oral acyclovir sustained release tablet. The use of four hydrophilic polymers, hydroxypropyl methylcellulose, xanthan gum, sodium alginate and carbopol 934P, as matrix forming agents was evaluated. Sustained release of acyclovir was achieved from hydroxypropyl methylcellulose, xanthan gum and sodium alginate containing matrices, whereas carbopol 934P did not produce sustained release property. The following factors that might influence drug release were also investigated: amount of polymer, type of diluent, pH and ionic strength of dissolution medium. An increase in amount of polymer led to a decrease in drug release rate. Nevertheless, the stronger gel layer around the matrices and low solubilities of the drug and the diluent might play a more important role for controlling drug release from the matrices and thus obscured the effect of the amount of polymer on drug release rate. The effect of type of diluent on drug release rate depended on amount and solubility of the diluent in the dissolution medium. The strong influence of pH of dissolution medium on drug release rate of HPMC and xanthan gum containing matrices was observed. The differences in strength of the gel barrier and drug solubilities in media with different pH values could be attributed to this finding. In case of sodium alginate matrices, the difference in pH value of dissolution medium gave the different patterns of drug release profile and also drug release mechanisms due to the pH dependent solubility of the polymer. The ionic strength of dissolution medium also affected the drug release rate. The stronger gel layer around the matrices corresponded well with the increased ionic strength of dissolution medium, resulting in the slower drug release rate. The difference in drug release characteristics could be explained in terms of the differences in swelling and erosion behaviors of the matrices. The dependence of drug release mechanism on the compositions of the matrices and the conditions of dissolution medium could be noted. Both diffusion and matrix erosion controlled the drug release from the matrices.

Department Manufacturing Pharmacy Student's signature..... ฉัตรดา หารัตน์
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ศูนย์วิทยทรัพยากร
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CONTENTS

	Page
ABSTRACT (THAI).....	iv
ABSTRACT (ENGLISH).....	v
ACKNOWLEDGEMENT.....	vi
CONTENTS.....	vii
LIST OF TABLES.....	viii
LIST OF FIGURES.....	xviii
LIST OF ABBREVIATIONS.....	xxvii
CHAPTER	
I INTRODUCTION.....	1
II LITERATURE REVIEW.....	3
III EXPERIMENTAL.....	23
IV RESULTS AND DISCUSSION.....	41
V CONCLUSIONS.....	155
REFERENCES.....	157
APPENDICES.....	163
VITA.....	242

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

LIST OF TABLES

Table	Page
1 Diffusion exponent and solute release mechanism.....	15
2 Formulation of acyclovir matrix tablets.....	26
3 The amount and the type of polymer and diluent used in each formulation of acyclovir matrices	27
4 Formulation of placebo tablets.....	29
5 The amount and the type of polymer and diluent used in each formulation of placebo tablets.....	30
6 Physical properties of acyclovir matrices containing various amounts of hydroxypropyl methylcellulose, xanthan gum, sodium alginate or carbopol 934P (n=20).....	42
7 The percent drug content of acyclovir matrices (n=3).....	43
8 The solubilities of acyclovir in various media at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ (n=3).....	44
9 The drug release rate of sodium alginate matrices with different polymer content and diluents in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8) at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ (mean (SD); n=3).....	92
10 The pH and ionic strength of dissolution medium.....	96
11 Values of release exponent (n) and coefficient of determination (r^2) of hydroxypropyl methylcellulose (HPMC) matrices in various dissolution media (mean(SD),n=3).....	131
12 Values of release exponent (n) and coefficient of determination (r^2) of xanthan gum matrices in various dissolution media (mean (SD), n=3).....	134
13 Values of release exponent (n) and coefficient of determination (r^2) of sodium alginate matrices in various dissolution media (mean (SD), n=3)....	139
1A Absorbance of acyclovir in 0.1 N HCl solution at 255 nm.....	164
2A Absorbance of acyclovir in phosphate buffer pH 6.8 solution at 251 nm.....	165
3A Absorbance of acyclovir in phosphate buffer pH 6.8 solution adjusted ionic strength equivalent to 0.1 with sodium chloride solution at 251 nm.....	165
4A Absorbance of acyclovir in deionized water at 251 nm.....	166

LIST OF TABLES (cont.)

Table	Page
5A Absorbance of acyclovir in 0.05 M sodium chloride solution at 251 nm.....	166
6A Absorbance of acyclovir in 0.1 M sodium chloride solution at 251 nm.....	167
7A Absorbance of acyclovir in 0.2 M Sodium chloride solution at 251 nm.....	167
8A Percentage of analytical recovery of acyclovir assayed by the HPLC method	175
9A Data of within run precision assayed by HPLC method.....	177
10A Data of between run precision assayed by HPLC method.....	177
11A The tailing factors of acyclovir.....	179
12A The analytical method validation parameter of HPLC for acyclovir.....	179
1B The absorbance (with out dilution) from dissolution study of placebo tablets in 0.1 N HCl solution.....	180
2B The absorbance (with out dilution) from dissolution study of placebo tablets in phosphate buffer pH 6.8 solution.....	180
3B The absorbance (with out dilution) from dissolution study of placebo tablets in deionized water (DI water).....	181
4B The absorbance (with out dilution) from dissolution study of placebo tablets in 0.2 M sodium chloride solution (0.2 M NaCl).....	181
5B The absorbance (with out dilution) from dissolution study of placebo tablets in phosphate buffer pH 6.8 solution adjusted ionic strength equivalent to 0.1 with sodium chloride (PBS pH 6.8 + NaCl).....	182
1C The viscosities of HPMC solution in various media.....	183
2C The viscosities of xanthan gum solution in various media.....	184
3C The viscosities of sodium alginate solution in various media.....	184
4C The viscosities of carbopol 934 P solution in PBS pH 6.8.....	185
1D Percentage amounts of acyclovir release blank matrices containing lactose (Formulation blank A) or dibasic calcium phosphate (Formulation blank B) as diluent in 0.1 N HCl solution.....	186

LIST OF TABLES (cont.)

Table	Page
2D	Percentage amounts of acyclovir release blank matrices containing lactose (Formulation blank A) or dibasic calcium phosphate (Formulation blank B) as diluent phosphate buffer pH 6.8 solution.....187
3D	Percentage amounts of acyclovir release blank matrices containing lactose (Formulation blank A) or dibasic calcium phosphate (Formulation blank B) as diluent in deionized water188
4D	Percentage amounts of acyclovir release blank matrices containing lactose (Formulation blank A) or dibasic calcium phosphate (Formulation blank B) as diluent in 0.2 M Sodium chloride solution189
5D	Percentage amounts of acyclovir release from hydroxypropyl methylcellulose matrices containing 10% polymer and lactose (Formulation F1) or dibasic calcium phosphate (Formulation F13) as diluent in 0.1 N HCl solution190
6D	Percentage amounts of acyclovir release from hydroxypropyl methylcellulose matrices containing 15% polymer and lactose (Formulation F2) or dibasic calcium phosphate (Formulation F14) as diluent in 0.1 N HCl solution191
7D	Percentage amounts of acyclovir release from hydroxypropyl methylcellulose matrices containing 20% polymer and lactose (Formulation F3) or dibasic calcium phosphate (Formulation F15) as diluent in 0.1 N HCl solution192
8D	Percentage amounts of acyclovir release from xanthan gum matrices containing 10% polymer and lactose (Formulation F4) or dibasic calcium phosphate (Formulation F16)as diluent in 0.1 N HCl solution193
9D	Percentage amounts of acyclovir release from xanthan gum matrices containing 15% polymer and lactose (Formulation F5) or dibasic calcium phosphate (Formulation F17)as diluent in 0.1 N HCl solution194

LIST OF TABLES (cont.)

Table	Page
10D	Percentage amounts of acyclovir release from xanthan gum matrices containing 20% polymer and lactose (Formulation F6) or dibasic calcium phosphate (Formulation F18) as diluent in 0.1 N HCl solution.....195
11D	Percentage amounts of acyclovir release from sodium alginate matrices containing 10% polymer and lactose (Formulation F7) or dibasic calcium phosphate (Formulation F19) as diluent in 0.1 N HCl solution.....196
12D	Percentage amounts of acyclovir release from sodium alginate matrices containing 15% polymer and lactose (Formulation F8) or dibasic calcium phosphate (Formulation F20) as diluent in 0.1 N HCl solution.....197
13D	Percentage amounts of acyclovir release from sodium alginate matrices containing 20% polymer and lactose (Formulation F9) or dibasic calcium phosphate (Formulation F21) as diluent in 0.1 N HCl solution.....198
14D	Percentage amounts of acyclovir release from carbopol 934 P matrices containing 10% polymer and lactose (Formulation F10) or dibasic calcium phosphate (Formulation F22) as diluent in 0.1 N HCl solution.....199
15D	Percentage amounts of acyclovir release from carbopol 934 P matrices containing 15% polymer and lactose (Formulation F11) or dibasic calcium phosphate (Formulation F23) as diluent in 0.1 N HCl solution.....200
16D	Percentage amounts of acyclovir release from carbopol 934 P matrices containing 20% polymer and lactose (Formulation F12) or dibasic calcium phosphate (Formulation F24) as diluent in 0.1 N HCl solution.....201
17D	Percentage amounts of acyclovir release from HPMC matrices containing 10% polymer and lactose (Formulation F1) or dibasic calcium phosphate (Formulation F13) as diluent in phosphate buffer pH 6.8 solution.....202
18D	Percentage amounts of acyclovir release from HPMC matrices containing 15% polymer and lactose (Formulation F2) or dibasic calcium phosphate (Formulation F14) as diluent in phosphate buffer pH 6.8 solution.....203

LIST OF TABLES (cont.)

Table	Page
19D	Percentage amounts of acyclovir release from HPMC matrices containing 20% polymer and lactose (Formulation F3) or dibasic calcium phosphate (Formulation F15) as diluent in phosphate buffer pH 6.8 solution.....204
20D	Percentage amounts of acyclovir release from xanthan gum matrices containing 10% polymer and lactose (Formulation F4) or dibasic calcium phosphate (Formulation F16) as diluent in phosphate buffer pH 6.8 solution.....205
21D	Percentage amounts of acyclovir release from xanthan gum matrices containing 15% polymer and lactose (Formulation F5) or dibasic calcium phosphate (Formulation F17) as diluent in phosphate buffer pH 6.8 solution.....206
22D	Percentage amounts of acyclovir release from xanthan gum matrices containing 20% polymer and lactose (Formulation F6) or dibasic calcium phosphate (Formulation F18) as diluent in phosphate buffer pH 6.8 solution.....207
23D	Percentage amounts of acyclovir release from sodium alginate matrices containing 10% polymer and lactose (Formulation F7) or dibasic calcium phosphate (Formulation F19) as diluent in phosphate buffer pH 6.8 solution.....208
24D	Percentage amounts of acyclovir release from sodium alginate matrices containing 15% polymer and lactose (Formulation F8) or dibasic calcium phosphate (Formulation F20) as diluent in phosphate buffer pH 6.8 solution.....209
25D	Percentage amounts of acyclovir release from sodium alginate matrices containing 20% polymer and lactose (Formulation F9) or dibasic calcium phosphate (Formulation F21) as diluent in phosphate buffer pH 6.8 solution.....210

LIST OF TABLES (cont.)

Table	Page
26D	Percentage amounts of acyclovir release from carbopol 934 P matrices containing 10% polymer and lactose (Formulation F10) or dibasic calcium phosphate (Formulation F22) as diluent in phosphate buffer pH 6.8 solution.....211
27D	Percentage amounts of acyclovir release from carbopol 934 P matrices containing 15% polymer and lactose (Formulation F11) or dibasic calcium phosphate (Formulation F23) as diluent in phosphate buffer pH 6.8 solution.....212
28D	Percentage amounts of acyclovir release from carbopol 934 P matrices containing 20% polymer and lactose (Formulation F12) or dibasic calcium phosphate (Formulation F24) as diluent in phosphate buffer pH 6.8 solution.....213
29D	Percentage amounts of acyclovir release from HPMC matrices containing 15% polymer and lactose (Formulation F2) or dibasic calcium phosphate (Formulation F13) as diluent in phosphate buffer pH 6.8 solution adjusted ionic strength equivalent to 0.1 M with sodium chloride.....214
30D	Percentage amounts of acyclovir release from xanthan gum matrices containing 15% polymer and lactose (Formulation F5) or dibasic calcium phosphate (Formulation F17) as diluent in phosphate buffer pH 6.8 solution adjusted ionic strength equivalent to 0.1 M with sodium chloride.....215
31D	Percentage amounts of acyclovir release from sodium alginate matrices containing 15% polymer and lactose (Formulation F8) or dibasic calcium phosphate (Formulation F20) as diluent in phosphate buffer pH 6.8 solution adjusted ionic strength equivalent to 0.1 M with sodium chloride.....216
32D	Percentage amounts of acyclovir release from HPMC matrices containing 15% polymer and lactose (Formulation F2) or dibasic calcium phosphate (Formulation F14) as diluent in deionized water.....217

LIST OF TABLES (cont.)

Table	Page
33D Percentage amounts of acyclovir release from xanthan gum matrices containing 15% polymer and lactose (Formulation F5) or dibasic calcium phosphate (Formulation F17) as diluent in deionized water.....	218
34D Percentage amounts of acyclovir release from sodium alginate matrices containing 15% polymer and lactose (Formulation F8) or dibasic calcium phosphate (Formulation F20) as diluent in deionized water.....	219
35D Percentage amounts of acyclovir release from HPMC matrices containing 15% polymer and lactose (Formulation F2) or dibasic calcium phosphate (Formulation F14) as diluent in 0.05 M sodium chloride solution.....	220
36D Percentage amounts of acyclovir release from xanthan gum matrices containing 15% polymer and lactose (Formulation F5) or dibasic calcium phosphate (Formulation F17) as diluent in 0.05 M sodium chloride solution.....	221
37D Percentage amounts of acyclovir release from sodium alginate matrices containing 15% polymer and lactose (Formulation F8) or dibasic calcium phosphate (Formulation F20) as diluent in 0.05 M sodium chloride solution.....	222
38D Percentage amounts of acyclovir release from HPMC matrices containing 15% polymer and lactose (Formulation F2) or dibasic calcium phosphate (Formulation F14) as diluent in 0.1 M sodium chloride solution.....	223
39D Percentage amounts of acyclovir release from xanthan gum matrices containing 15% polymer and lactose (Formulation F5) or dibasic calcium phosphate (Formulation F17) as diluent in 0.1 M sodium chloride solution.....	224

LIST OF TABLES (cont.)

Table	Page
40D	Percentage amounts of acyclovir release from sodium alginate matrices containing 15% polymer and lactose (Formulation F8) or dibasic calcium phosphate (Formulation F20) as diluent in 0.1 M sodium chloride solution.....225
41D	Percentage amounts of acyclovir release from HPMC matrices containing 15% polymer and lactose (Formulation F2) or dibasic calcium phosphate (Formulation F14) as diluent in 0.2 M sodium chloride solution.....226
42D	Percentage amounts of acyclovir release from xanthan gum matrices containing 15% polymer and lactose (Formulation F5) or dibasic calcium phosphate (Formulation F17) as diluent in 0.2 M sodium chloride solution.....227
43D	Percentage amounts of acyclovir release from sodium alginate matrices containing 15% polymer and lactose (Formulation F8) or dibasic calcium phosphate (Formulation F20) as diluent in 0.2 M sodium chloride solution.....228
44D	Percentage amounts of acyclovir release from HPMC matrices containing 10% polymer and lactose in pH change medium.....229
1E	Percentage swelling of matrices containing 15% HPMC and lactose (Formulation F12) in various dissolution media.....230
2E	Percentage erosion of matrices containing 15% HPMC and lactose (Formulation F12) in various dissolution media.....231
3E	Percentage swelling of matrices containing 15% xanthan gum and lactose (Formulation F5) in various dissolution media.....232
4E	Percentage erosion of matrices containing 15% xanthan gum and lactose (Formulation F5) in various dissolution media.....233
5E	Percentage swelling of matrices containing 15% sodium alginate and lactose (Formulation F8) in various dissolution media.....234
6E	Percentage erosion of matrices containing 15% sodium alginate and lactose (formulation F8) in various dissolution media.....235

LIST OF TABLES (cont.)

Table	Page
1F	The relative dissolution times (RDT) of hydroxypropyl methylcellulose matrices containing 10% polymer and lactose (Formulation F1) or dibasic calcium phosphate (Formulation F13) as diluent in 0.1 N HCl solution and phosphate buffer pH 6.8 solution.....236
2F	The relative dissolution times (RDT) of xanthan gum matrices containing 10% polymer and lactose (Formulation F4) or dibasic calcium phosphate (Formulation F16) as diluent in 0.1 N HCl solution and phosphate buffer pH 6.8 solution.....236
3F	The relative dissolution times (RDT) of sodium alginate matrices containing 10% polymer and lactose (Formulation F7) or dibasic calcium phosphate (Formulation F19) as diluent in 0.1 N HCl solution and phosphate buffer pH 6.8 solution.....237
4F	The relative dissolution times (RDT) of hydroxypropyl methylcellulose matrices containing 15% polymer and lactose (Formulation F2) or dibasic calcium phosphate (Formulation F14) as diluent in various dissolution media.....237
5F	The relative dissolution times (RDT) of xanthan gum matrices containing 15% polymer and lactose (Formulation F5) or dibasic calcium phosphate (Formulation F17) as diluent in various dissolution media.....238
6F	The relative dissolution times (RDT) of sodium alginate matrices containing 15% polymer and lactose (Formulation F8) or dibasic calcium phosphate (Formulation F20) as diluent in various dissolution media.....238
7F	The relative dissolution times (RDT values) of hydroxypropyl methylcellulose matrices containing 20% polymer and lactose phosphate (Formulation F3) or dibasic calcium phosphate (formulation F15) as diluent in 0.1 N HCl solution and phosphate buffer pH 6.8 solution.....239
8F	The relative dissolution times (RDT values) of xanthan gum matrices containing 20% polymer and lactose phosphate (Formulation F6) or dibasic calcium phosphate (formulation F18) as diluent in 0.1 N HCl solution and phosphate buffer pH 6.8 solution.....239

LIST OF TABLES (cont.)

Table		Page
9F	The relative dissolution times (RDT values) of xanthan gum matrices containing 20% polymer and lactose phosphate (Formulation F9) or dibasic calcium phosphate (formulation F21) as diluent in 0.1 N HCl solution and phosphate buffer pH 6.8 solution.....	240
10F	Area under the curve (AUC) at each time interval of drug release profile of hydroxypropyl methylcellulose matrices containing 10% polymer and lactose as diluents (Formulation F1) in 0.1 N HCl solution.....	241



ศูนย์วิทยทรัพยากร
 จุฬาลงกรณ์มหาวิทยาลัย

LIST OF FIGURES

Figure	Page
1	Picture of the top of a swellable matrix tablet during drug release showing the three fronts..... 5
2	The chemical structure of acyclovir.....15
3	The chemical structure of hydroxypropyl methylcellulose..... 18
4	The chemical structure of xanthan gum.....19
5	Structural characteristics of (a) alginate monomers, (b) chain conformation, (c) block distribution.....20
6	Chemical structure of carbomer.....22
7	Diagrammatic of dissolution profile for explaining RDT calculation. ABC is area between upper line (M_{∞}) and the dissolution curve; M_{∞} is maximum drug release at infinite time and M_t is amount of drug release at any time t.....38
8	The viscosity of hydroxypropyl methylcellulose (HPMC), xanthan gum (XG), sodium alginate ^a (SA) and carbopol 934P ^b (CP) in media with different pH values: 0.1 N HCl solution (pH 1.2), phosphate buffer pH 6.8 solution (PBS pH6.8) and phosphate buffer pH 6.8 solution with ionic strength adjusted to 0.1 (PBS pH6.8 + NaCl).....46
9	The viscosity of polymer solutions in media with various ionic strengths....49
10	The release profiles of blank A matrices in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8).....52
11	The release profiles of blank B matrices in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8)..... 52
12	The release profiles of blank A matrices in deionized water (DI water) and 0.2 M sodium chloride solution (0.2 M NaCl).....54
13	The release profiles of blank B matrices in deionized water (DI water) and 0.2 M sodium chloride solution (0.2 M NaCl).....54
14	The release profiles of blank A and blank B matrices in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8)..... 55

LIST OF FIGURES (cont.)

Figure	Page
15	The release profiles of blank A and blank B matrices in deionized water (DI water) and 0.2 M sodium chloride solution (0.2 M NaCl).....55
16	The release profiles of matrices containing lactose and hydroxypropyl methylcellulose (HPMC) in various amounts in 0.1 N HCl solution.....57
17	The release profiles of matrices containing dibasic calcium phosphate and hydroxypropyl methylcellulose (HPMC) in various amounts in 0.1 N HCl solution.....57
18	The release profiles of matrices containing lactose and hydroxypropyl methylcellulose (HPMC) in various amounts in phosphate buffer pH 6.8 solution58
19	The relationship between the relative dissolution time (RDT value) and the percentage of hydroxypropyl methylcellulose contained in each formulation when using lactose or dibasic calcium phosphate (DCP) as diluent in 0.1 N HCl solution.....59
20	The relationship between the relative dissolution time (RDT value) and the percentage of hydroxypropyl methylcellulose contained in each formulation when using lactose or dibasic calcium phosphate (DCP) as diluent in phosphate buffer pH 6.8 solution..... 59
21	The release profiles of matrices containing dibasic calcium phosphate and hydroxypropyl methylcellulose (HPMC) in various amounts in phosphate buffer pH 6.8 solution61
22	The release profiles of matrices containing lactose and xanthan gum (XG) in various amounts in 0.1 N HCl solution62
23	The release profiles of matrices containing dibasic calcium phosphate and xanthan gum (XG) in various amounts in 0.1 N HCl solution62
24	The release profiles of matrices containing lactose and xanthan gum (XG) in various amounts in phosphate buffer pH 6.8 solution.....63
25	The release profiles of matrices containing dibasic calcium phosphate and xanthan gum (XG) in various amounts in phosphate buffer pH 6.8 solution63

LIST OF FIGURES (cont.)

Figure	Page
26	The relationship between the relative dissolution time (RDT value) and the percentage of xanthan gum contained in each formulation when using lactose or dibasic calcium phosphate (DCP) as diluent in 0.1 N HCl solution.....64
27	The relationship between the relative dissolution time (RDT value) and the percentage of xanthan gum contained in each formulation when using lactose or dibasic calcium phosphate (DCP) as diluent in phosphate buffer pH 6.8 solution.....64
28	The release profiles of matrices containing lactose and sodium alginate (SA) in various amounts in 0.1 N HCl solution67
29	The release profiles of matrices containing dibasic calcium phosphate and sodium alginate (SA) in various amounts in 0.1 N HCl solution68
30	The release profiles of matrices containing lactose and sodium alginate (SA) in various amounts in phosphate buffer pH 6.8 solution.....68
31	The release profiles of matrices containing dibasic calcium phosphate and sodium alginate (SA) in various amounts in phosphate buffer pH 6.8 solution69
32	The relationship between the relative dissolution time (RDT value) and the percentage of sodium alginate contained in each formulation when using lactose or dibasic calcium phosphate (DCP) as diluent in 0.1 N HCl solution.....69
33	The relationship between the relative dissolution time (RDT value) and the percentage of sodium alginate contained in each formulation when using lactose or dibasic calcium phosphate (DCP) as diluent in phosphate buffer pH 6.8 solution.....70
34	The release profiles of matrices containing lactose and carbopol 934P (CP) in various amounts in 0.1 N HCl solution.....71
35	The release profiles of matrices containing dibasic calcium phosphate and carbopol 934P (CP) in various amounts in 0.1 N HCl solution71
36	The release profiles of matrices containing lactose and carbopol 934P (CP) in various amounts in phosphate buffer pH 6.8 solution.....72

LIST OF FIGURES (cont.)

Figure	Page
37	The release profiles of matrices containing dibasic calcium phosphate and carbopol 934P (CP) in various amounts in phosphate buffer pH 6.8 solution72
38	The release profiles of matrices containing lactose or dibasic calcium phosphate (DCP) and hydroxypropyl methylcellulose (HPMC) in various amounts in 0.1 N HCl solution.....75
39	The release profiles of matrices containing lactose or dibasic calcium phosphate (DCP) and xanthan gum (XG) in various amounts in 0.1 N HCl solution.....77
40	The release profiles of matrices containing lactose or dibasic calcium phosphate (DCP) and sodium alginate (SA) in various amounts in 0.1 N HCl solution78
41	The release profiles of matrices containing lactose or dibasic calcium phosphate (DCP) and hydroxypropyl methylcellulose (HPMC) in various amounts in phosphate buffer pH 6.8 solution.....80
42	The release profiles of matrices containing lactose or dibasic calcium phosphate (DCP) and xanthan gum (XG) in various amounts in phosphate buffer pH 6.8 solution.....81
43	The release profiles of matrices containing lactose or dibasic calcium phosphate (DCP) and sodium alginate (SA) in various amounts in phosphate buffer pH 6.8 solution.....82
44	The release profiles of matrices containing lactose and hydroxypropyl methylcellulose (HPMC) in various amounts in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8).....85
45	The release profiles of matrices containing dibasic calcium phosphate and hydroxypropyl methylcellulose (HPMC) in various amounts in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8).....85
46	The relationship between the relative dissolution time (RDT value) and the percentage of hydroxypropyl methylcellulose contained in each formulation when using lactose or dibasic calcium phosphate (DCP) as diluent in different dissolution media.....86

LIST OF FIGURES (cont.)

Figure	Page
47	The release profiles of matrices containing lactose and xanthan gum (XG) in various amounts in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8).....87
48	The release profiles of matrices containing dibasic calcium phosphate and xanthan gum (XG) in various amounts in 0.1N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8).....87
49	The relationship between the relative dissolution time (RDT value) and the percentage of xanthan gum contained in each formulation when using lactose or dibasic calcium phosphate (DCP) as diluent in different pH dissolution media.....88
50	The release profiles of matrices containing lactose and sodium alginate (SA) in various amounts in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBSpH6.8).....91
51	The release profiles of matrices containing dibasic calcium phosphate and sodium alginate (SA) in various amounts in 0.1 N HCl solution and phosphate buffer solution pH 6.8.....91
52	The relationship between the relative dissolution time (RDT value) and the percentage of sodium alginate contained in each formulation when using lactose or dibasic calcium phosphate (DCP) as diluent in different pH dissolution media.....95
53	The release profiles of matrices containing lactose and 15% hydroxypropyl methylcellulose in 0.1 N HCl solution, phosphate buffer pH 6.8 solution (PBS pH 6.8) and phosphate buffer pH 6.8 solution with ionic strength adjusted to 0.1 with sodium chloride (PBS pH 6.8+NaCl).....97
54	The release profiles of matrices containing dibasic calcium phosphate and 15% hydroxypropyl methylcellulose in 0.1 N HCl solution, phosphate buffer pH 6.8 solution (PBS pH 6.8) and phosphate buffer pH 6.8 solution with ionic strength adjusted to 0.1 with sodium chloride (PBS pH 6.8+NaCl).....97

LIST OF FIGURES (cont.)

Figure	Page
55	The relative dissolution times (RDT values) of hydroxypropyl methylcellulose matrices containing lactose or dibasic calcium phosphate (DCP) as diluent in 0.1 N HCl solution, phosphate buffer pH 6.8 solution (PBS pH 6.8) and phosphate buffer pH 6.8 solution with ionic strength adjusted to 0.1 with sodium chloride (PBS pH 6.8+NaCl).....98
56	The release profiles of matrices containing lactose and 15% xanthan gum in 0.1 N HCl solution, phosphate buffer pH 6.8 solution (PBS pH 6.8) and phosphate buffer pH 6.8 solution with ionic strength adjusted to 0.1 with sodium chloride (PBS pH 6.8+NaCl).....99
57	The release profiles of matrices containing dibasic calcium phosphate and 15% xanthan gum in 0.1 N HCl solution, phosphate buffer pH 6.8 solution (PBS pH 6.8) and phosphate buffer pH 6.8 solution with ionic strength adjusted to 0.1 with sodium chloride (PBS pH 6.8+NaCl)..... 99
58	The relative dissolution times (RDT values) of xanthan gum matrices containing lactose or dibasic calcium phosphate (DCP) as diluent in 0.1 N HCl solution, phosphate buffer pH 6.8 solution (PBS pH 6.8) and phosphate buffer pH 6.8 solution with ionic strength adjusted to 0.1 with sodium chloride (PBS pH 6.8+NaCl).....100
59	The release profiles of matrices containing lactose and 15% sodium alginate in 0.1 N HCl solution, phosphate buffer pH 6.8 solution (PBS pH 6.8) and phosphate buffer pH 6.8 solution with ionic strength adjusted to 0.1 with sodium chloride (PBS pH 6.8+NaCl).....101
60	The release profiles of matrices containing dibasic calcium phosphate and 15% sodium alginate in 0.1 N HCl solution , phosphate buffer pH 6.8 solution (PBS pH 6.8) and phosphate buffer pH 6.8 solution with ionic strength adjusted to 0.1 with sodium chloride (PBS pH 6.8+NaCl)...101
61	The release profiles of matrices containing lactose and 15% hydroxypropyl methylcellulose in various ionic strengths of the dissolution medium.....103

LIST OF FIGURES (cont.)

Figure	Page
62	The release profiles of matrices containing dibasic calcium phosphate and 15% hydroxypropyl methylcellulose in various ionic strengths of the dissolution medium104
63	The relationship between the relative dissolution time (RDT value) of hydroxypropyl methylcellulose matrices containing lactose or dibasic calcium phosphate (DCP) and ionic strength of the dissolution medium....104
64	The release profiles of matrices containing lactose and 15% xanthan gum in various ionic strengths of the dissolution medium.....107
65	The release profiles of matrices containing dibasic calcium phosphate and 15%xanthan gum in various ionic strengths of the dissolution medium107
66	The relationship between the relative dissolution time (RDT value) of xanthan gum matrices containing lactose or dibasic calcium phosphate (DCP) as diluent and ionic strength of the dissolution medium108
67	The release profiles of matrices containing lactose and 15%sodium alginate in various ionic strengths of the dissolution medium.....111
68	The release profiles of matrices containing dibasic calcium phosphate and 15%sodium alginate in various ionic strengths of the dissolution medium..112
69	The relationship between the relative dissolution time (RDT value) of sodium alginate matrices containing lactose or dibasic calcium phosphate (DCP) as diluent and ionic strength of the dissolution medium.....112
70	The release profile of matrices containing 10% HPMC and using lactose as diluent (Formulation F1) in pH change medium115
71	The percent swelling (S) and percent erosion (E) of matrices containing 15% HPMC and lactose in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8).....118
72	The percent swelling (S) and percent erosion (E) of matrices containing 15% HPMC and lactose in deionized water (DI water) and 0.2 M sodium chloride solution (0.2 M NaCl).....120

LIST OF FIGURES (cont.)

Figure	Page
73	The percent swelling (S) and percent erosion (E) of matrices containing 15% xanthan gum and lactose in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8).....122
74	The percent swelling (S) and percent erosion (E) of matrices containing 15% xanthan gum and lactose in deionized water (DI water) and 0.2 M sodium chloride solution (0.2 M NaCl).....124
75	The percent swelling (S) and percent erosion (E) of matrices containing 15% sodium alginate and lactose in 0.1 N HCl solution and phosphate buffer pH 6.8 solution (PBS pH 6.8).....127
76	The percent swelling (S) and percent erosion (E) of matrices containing 15% sodium alginate and lactose in deionized water (DI water) and 0.2 M sodium chloride solution (0.2 M NaCl).....129
77	Surface morphology of HPMC (A), xanthan gum (B) and sodium alginate matrices(C) before dissolution test (X75).....144
78	Surface morphology of HPMC matrices containing lactose as diluent, hydrated in 0.1 N HCl solution (left column) and phosphate buffer pH 6.8 solution (right column) for 2hr (1A,2A), 6hr (1B,2B) and 12 hr (2C) (x75).....145
79	Surface morphology of HPMC matrices containing lactose as diluent hydrated in deionized water (left column) and 0.2 M sodium chloride solution (right column) for 2hr (1A,2A), 6hr (1B,2B) and 12hr (1C,2C) (x75).....146
80	Surface morphology of xanthan gum matrices containing lactose as diluent, hydrated in 0.1 N HCl solution (left column) and phosphate buffer pH 6.8 solution (right column) for 2hr (1A,2A), 6hr (1B,2B) and 12 hr (1C,2C) (x75).....148
81	Surface morphology of xanthan gum matrices containing lactose as diluent hydrated in deionized water for 2hr (1A) and 0.2 M sodium chloride solution for 2 hr (2A), 6hr (2B) and 12 hr (2C) (x75).....149

LIST OF FIGURES (cont.)

Figure	Page
82	Surface morphology of sodium alginate matrices containing lactose as diluent, hydrated in 0.1 N HCl solution (left column) and phosphate buffer pH 6.8 solution (right column) for 2hr (1A,2A), 4hr (1B,2B) and 6hr (1C,2C) (x75).....151
83	Surface morphology of sodium alginate matrices containing lactose as diluent, hydrated in deionized water (left column) and 0.2M sodium chloride solution (right column) for 2hr (1A,2A), 4hr (1B,2B) and 6hr (1C,2C) (x75).....152
1A	Calibration curve of acyclovir in 0.1 N HCl solution at 255 nm.....168
2A	Calibration curve of acyclovir in phosphate buffer pH 6.8 solution at 251 nm.....168
3A	Calibration curve of acyclovir in phosphate buffer pH 6.8 solution adjusted ionic strength equivalent to 0.1 with sodium chloride at 251 nm.....169
4A	Calibration curve of acyclovir in deionized water at 251 nm.....169
5A	Calibration curve of acyclovir in 0.05 M sodium chloride solution at 251 nm.....170
6A	Calibration curve of acyclovir in 0.1 M sodium chloride solution at 251 nm.....170
7A	Calibration curve of acyclovir in 0.2 M sodium chloride solution at 251 nm.....171
8A	Asymmetrical Chromatographic Peak.....173
9A	HPLC chromatograms of standard solutions of acyclovir.....174
10A	Calibration curve of acyclovir assayed by HPLC method.....178

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LIST OF ABBREVIATIONS

°C	degree Celsius (centigrade)
cps	centipoises (S)
CV	coefficient of variation
DI	deionized
e.g.	example and others
et al.	et alli and others
g	gram(s)
Fig.	Figure
HBMC	hydroxybuthyl methyl cellulose
HCl	hydrochloric acid or hydrochloride
HEMC	hydroxyethyl methylcellulose
HPMC	hydroxypropyl methylcellulose
hr	hour(s)
kp	kilopound(s)
M	molarity
µg	microgram(s)
mg	milligram(s)
ml	milliliter(s)
mm	millimeter(s)
N	normality
No.	number
nm	nanometer(s)
PBS	phosphate buffer solution
pH	the negative logarithm of the hydrogen ion concentration
pK _a	the negative logarithm of the dissociation constant
®	Registered
r ²	coefficient of determination
rpm	revolution per minute
SD	standard deviation
UV	ultraviolet

LIST OF ABBREVIATIONS (cont.)

UV-VIS	ultraviolet-visible
w/w	weight by weight
%	percentage
λ_{\max}	wavelength of maximum absorbance
>	more than
<	less than



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