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STABILITY OF FLUCONAZOLE SYRUP

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ฟลูโคนาโซลเป็นยาฆ่าเชื้อรากลุ่มอะโซลซึ่งใช้ในการรักษาการติดเชื้อราแคนดิดา ฟลูโคนาโซลความเข้มข้น 50 มิลลิกรัมต่อ 5 มิลลิลิตรเตรียมโดยวิธีใช้ตัวทำละลายร่วมเพื่อเพิ่มการละลาย ของยาในน้ำ ระบบตัวทำละลายร่วมที่ใช้ในการเตรียมยาน้ำเชื่อมฟลูโคนาโซล ประกอบด้วยคือ ระบบผสม ของโพลิเอทิลลีนไกลคอล 4000 ร้อยละ 4 โดยน้ำหนักต่อปริมาตร เอทานอล ร้อยละ 7 โดยปริมาตรต่อ ปริมาตร โพรพิลีนไกลคอล ร้อยละ 7 โดยปริมาตรต่อปริมาตร และน้ำร้อยละ 82 โดยปริมาตรต่อปริมาตร การศึกษาความคงตัวของตำรับยาน้ำเชื่อมฟลูโคนาโซลที่มีการเติมสารต้านออกซิเดชันชนิดและความเข้ม ข้นต่างๆ ลงในตำรับ ภายใต้สภาวะมีแลงเปรียบเทียบกับสภาวะไม่มีแลง โดยเก็บในตู้อบที่ควบคุม อุณหภูมิ 60 องศาเซลเซียส ตลอดช่วงการทดลอง 107 วัน พบว่ายาน้ำเชื่อมทุกตำรับมีสีเปลี่ยนเป็นน้ำ ตาลเข้มเนื่องจากการเปลี่ยนสีของน้ำเชื่อม ส่วนจลนศาสตร์การสลายตัวของฟลูโคนาโซลเป็นไปตาม ปฏิกิริยาอันดับศูนย์ ในการศึกษาครั้งนี้พบว่าสูตรตำรับที่คงตัวที่สุด คือตำรับยาน้ำเชื่อมฟลูโคนาโซลที่มี โพรพิลแกลเลทร้อยละ 0.001 โดยน้ำหนักต่อปริมาตรซึ่งเก็บในสภาวะที่ไม่ถูกแสง จากนั้นนำตำรับที่มี ความคงตัวที่สุดมาศึกษาเวลาที่ใช้ในการสลายตัวของยาร้อยละสิบใช้วิธีเร่งการเสื่อมสลายด้วยความร้อนที่ อุณหภูมิ 45, 55, 65, 70 องศาเซลเซียสรวมทั้งที่อุณหภูมิห้อง เมื่อเขียนกราฟระหว่างอัตราเร็วการเสื่อม สลายกับส่วนกลับของอุณหภูมิองศาเคลวิน จะได้เป็นเส้นตรง พบว่ามีค่าความร้อนแห่งการกระตุ้น 13.02 กิโลแคลอรีต่อโมล โดยเวลาที่ใช้ในการสลายตัวของยาร้อยละสืบมีค่าเท่ากับ 834 วัน

ภาควิชา	เกลัชกรรม	7
	เกล้ชกรรม	7
ปีการศึกษา		6

ลายมือชื่อนิสิต พัชาินทร์	ปลุยารกาจ
ลายมือชื่ออาจารย์ที่ปรึกษา	*/
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม	_

4076517933_{: MAJOR} PHARMACY

KEY WORD: FLUCONAZOLE / SYRUP / STABILITY / ANTIOXIDANT / LIGHT / SHELF LIFE
PATCHARIN PAKUNVARAKIT: STABILITY OF FLUCONAZOLE SYRUP. THESIS ADVISOR:
ASSOC. PROF. UBONTHIP NIMMANNIT, Ph. D. 203 pp. ISBN 974-331-956-5.

Fluconazole is an azole antifungal agent which is used for systemic candidiasis. Fluconazole syrups (50 mg/5 ml) were prepared by using cosolvent technique for increasing solubility of fluconazole in water. The mixed solvent used in this preparation was 4% w/v PEG 4000, 7% v/v ethanol, 7% v/v PG and 82% v/v water. The stability of fluconazole syrups, which contained various concentration of different kinds of antioxidants under the accelerated light, was studied and compared with light protecting condition at 60°C throughout 107 days. It was found that all formulations changed to dark brown color according to the color change of syrup. The kinetics proceeded according to a zero order reaction. In this study the most chemically stable formulation was the fuconazole containing 0.001% w/v of propyl gallate which was stored under light protecting condition. The shelf-life study was evaluated by accelerated testing technique at 45°C, 55°C, 65°C, 70°C and at ambient temperature. A linear regression line was obtained from Arrhenius plot of the reaction rate (k) against reciprocal of degree kelvin (1/T). The heat of activation was found to be 13.02 kcal/mol and the estimated shelf life was 834 days.

ภาควิชา	เภสัชกรรม	ć
สาขาวิชา	เกลัชกรรม	6
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ปีการศึกษา		2

ลายมือชื่อนิสิต ทั้ช์ในทร์ ปลุณภาทิจ ลายมือชื่ออาจารย์ที่ปรึกษา <u>Шามาในค W. mman uit</u> ลายมือชื่ออาจารย์ที่ปรึกษาร่วม



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CONTENTS

ABSTRACT [THAI]iv
ABSTRACT [ENGLISH]v
ACKNOWLE	DGMENTSvi
CONTENTS.	vii
LIST OF TAE	BLESviii
LIST OF FIG	URESxv
LIST OF ABE	BREVIATIONSxix
CHAPTER	
I	INTRODUCTION1
II	LITERATURE REVIEW4
Ш	MATERIALS AND METHODS43
IV	RESULTS AND DISCUSSION58
V	CONCLUSIONS118
REFERENCE	S121
APPENDIX I.	129
APPENDIX II	135
APPENDIX II	l143
APPENDIX I\	/146
APPENDIX V	187
APPENDIX V	l193
APPENDIX V	II197
VITA	203

LIST OF TABLES

TABLE	PAGE
4	Every place of permadicated every pa
1.	Examples of nonmedicated syrups8
2.	Preservatives commonly used in syrups11
3.	Oxygen content of water under air and pure oxygen at
	atmospheric pressure and various temperatures21
4.	Fluconazole syrup formulations designed for investigation
	of antioxidant effect53
5.	Percent analytical recovery of fluconazole in ethanol by
	UV spectrophotometry59
6.	Within run precision data by UV spectrophotometry61
7.	Between run precision data by UV spectrophotometry61
8.	Data for calibration curve of fluconazole in ethanol by
	UV spectrophotometry62
9.	Percent analytical recovery of fluconazole in solution by HPLC66
10.	Percent analytical recovery of fluconazole in syrup by HPLC67
11.	Within run precision data by HPLC69
12.	Between run precision data by HPLC69
13.	Data for calibration curve of fluconazole in ethanol by HPLC70
14.	Observed solubilities of fluconazole in pure and mixed solvents
	at 30°C79
15.	Observed solubilities of fluconazole in polyethylene glycol 4000
	-water at 30°C81

TABLE

5
3
7
0
92
93
6
7
)

27	. Stability of fluconazole in fluconazole syrup containing
	0.001% w/v propyl gallate at 45°C110
28.	Stability of fluconazole in fluconazole syrup containing
	0.001% w/v propyl gallate at 55°C111
29.	Stability of fluconazole in fluconazole syrup containing
	0.001% w/v propyl gallate at 65°C112
30.	Stability of fluconazole in fluconazole syrup containing
	0.001% w/v propyl gallate at 70°C113
31.	Arrhenius relation of fluconazole degradation of fluconazole
	syrup containing 0.001% w/v propyl gallate114
32.	Observed solubilities of fluconazole in pure solvents at 30 $^{\circ}$ C
	(24 hrs)136
33.	Observed solubilities of fluconazole in pure solvents at 30 $^{\circ}$ C
	(48 hrs)136
34.	Observed solubilities of fluconazole in cosolvent (ethanol-water)
	at 30 ° C (24 hrs)137
35.	Observed solubilities of fluconazole in cosolvent (ethanol-water)
	at 30 ° C (48 hrs)137
36.	Observed solubilities of fluconazole in cosolvent
	(propylene glycol-water) at 30 ° C (24 hrs)138
37.	Observed solubilities of fluconazole in cosolvent
	(propylene glycol-water) at 30 ° C (48 hrs),
38.	Observed solubilities of fluconazole in cosolvent
	(PEG 400-water) at 30 ° C (24 hrs)139

39. Observed solubilities of fluconazole in cosolvent
(PEG 400-water) at 30 ° C (48 hrs)139
40. Observed solubilities of fluconazole in cosolvent
(PEG 4000-water) at 30 ° C (24 hrs)140
41. Observed solubilities of fluconazole in cosolvent
(PEG 4000-water) at 30 ° C (48 hrs)140
42. Observed solubilities of fluconazole in cosolvent
(PEG 4000-ethanol-PG-water) at 30 $^{\circ}$ C (24 hrs)141
43. Observed solubilities of fluconazole in cosolvent
(PEG 4000-ethanol-PG-water) at 30 $^{\circ}$ C (48 hrs)142
44. The correlation coefficient (r) of fluconazole syrups stored in the
presence of light144
45. The correlation coefficient (r) of fluconazole syrups stored in the
absence of light145
46.Stability data of fluconazole syrup stored at 60 °C
(Absence of light, formulation 1; no antioxidant)147
47. Stability data of fluconazole syrup stored at 60 ° C
(Absence of light, formulation 2; propyl gallate 0.001 %w/v)149
48. Stability data of fluconazole syrup stored at 60 °C
(Absence of light, formulation 3; propyl gallate 0.005 %w/v)153
49. Stability data of fluconazole syrup stored at 60 °C
(Absence of light, formulation 4; propyl gallate 0.010 %w/v)153
50. Stability data of fluconazole syrup stored at 60 °C
(Absence of light, formulation 5; sodium bisulfite 0.050 %w/v)155

51.	Stability data of fluconazole syrup stored at 60 ° C
	(Absence of light, formulation 6; sodium bisulfite 0.075 %w/v)157
52.	Stability data of fluconazole syrup stored at 60 ° C
	(Absence of light, formulation 7; sodium bisulfite 0.100 %w/v)159
53.	Stability data of fluconazole syrup stored at 60 ° C
	(Absence of light, formulation 8; disodium edetate 0.005 %w/v)161
54.	Stability data of fluconazole syrup stored at 60 ° C
	(Absence of light, formulation 9; disodium edetate 0.010 %w/v)163
55.	Stability data of fluconazole syrup stored at 60 ° C
	(Absence of light, formulation 10; disodium edetate 0.050 %w/v)165
56.	Stability data of fluconazole syrup stored at 60 ° C
	(Presence of light, formulation 1; no antioxidant)167
57.	. Stability data of fluconazole syrup stored at 60 ° C
	(Presence of light, formulation 2; propyl gallate 0.001 %w/v)169
58.	. Stability data of fluconazole syrup stored at 60 ° C
	(Presence of light, formulation 3; propyl gallate 0.005 %w/v)171
59	. Stability data of fluconazole syrup stored at 60 ° C
	(Presence of light, formulation 4; propyl gallate 0.010 %w/v)173
60	. Stability data of fluconazole syrup stored at 60 °C
	(Presence of light, formulation 5; sodium bisulfite 0.05%w/v)175
61	. Stability data of fluconazole syrup stored at 60 °C
	(Presence of light, formulation 6; sodium bisulfite 0.075%w/v)177
62	. Stability data of fluconazole syrup stored at 60 °C
	(Presence of light, formulation 7; sodium bisulfite 0.100%w/v)179

63. Stability data of fluconazole syrup stored at 60 ° C	
(Presence of light, formulation 8; disodium edetate 0.005%w/v)	181
64. Stability data of fluconazole syrup stored at 60 ° C	
(Presence of light, formulation 9; disodium edetate 0.010%w/v)	183
65. Stability data of fluconazole syrup stored at 60 ° C	
(Presence of light, formulation 10; disodium edetate 0.050%w/v)	185
66.Stability data of fluconazole syrup containing propyl gallate	
0.001%w/v at room temperature	188
67. Stability data of fluconazole syrup containing propyl gallate	
0.001%w/v in hot air oven at 45 ° C	189
68. Stability data of fluconazole syrup containing propyl gallate	
0.001%w/v in hot air oven at 55 ° C	190
69. Stability data of fluconazole syrup containing propyl gallate	
0.001%w/v in hot air oven at 65 ° C	191
70. Stability data of fluconazole syrup containing propyl gallate	
0.001%w/v in hot air oven at 70 ° C	192
71. Example for calculation C $_{o}$, k, a, r	194
72. Tests of the effect of storage condition on the degradation rate	
of fluconazole syrup without antioxidant	198
73. Tests of the effect of propyl gallate on the degradation rate	
of fluconazole syrups stored at 60 °C, presence of light	199
74. Tests of the effect of propyl gallate on the degradation rate	
of fluconazole syrups stored at 60 °C, absence of light	199

75.	Tests of the effect of sodium bisulfite on the degradation rate	
	of fluconazole syrups stored at 60 °C, presence of light	200
76.	Tests of the effect of sodium bisulfite on the degradation rate	,
	of fluconazole syrups stored at 60 °C, absence of light	200
77.	Tests of the effect of disodium edetate on the degradation rate	
	of fluconazole syrups stored at 60 °C, presence of light	.201
78.	Tests of the effect of disodium edetate on the degradation rate	
	of fluconazole syrups stored at 60 °C, absence of light	201

LIST OF FIGURES

FIGURE
1. Chemical structure of propyl gallate31
2. Chemical structure of disodium edetate33
3. Chemical structure of sodium metabisulfite35
4. The calibration curve of fluconazole in ethanol by
UV spectrophotometry62
5. Spectra of fluconazole in ethanol from UV Spectrophotometer63
6. Spectra of various solvent from UV Spectrophotometer64
7. The calibration curve of fluconazole by HPLC70
8. Chromatograms of standard solutions of fluconazole71
9. Chromatograms of fluconazole in fluconazole syrup
and in solution72
10. Chromatograms of phosphate, syrup USP, sorbital, cosolvent,
disodium edetate, sodium bisulfite, pepermint in phosphate buffer.73
11. Chromatograms of sodium saccharin and paraben concentrate
in PBS74
12. Chromatograms of decomposition of mixed solvent of
ethanol-propylene glycol-polyethylene glycol-water,
disodium edetate, sodium bisulfite, propyl gallate, PBS, sorbitol,
peppermint, sodium saccharin, paraben concentrate in PBS76
13. Chromatograms of decomposed fluconazole syrup, fluconazole,
syrup USP77

FIGURE PAGE

14.	Comparison of solubilities of fluconazole in various mixed	
	solvents80	
15.	Linear plot of drug concentration remaining vs. time of fluconazole	
;	syrup in the presence of light at 60° C96	
16.	Linear plot of drug concentration remaining vs. time	
	of fluconazole syrup (no antioxidant) in the absence of light	
	at 60° C97	
17.	Plots of rate constant vs. concentration of propyl gallate100	
18.	Plots of rate constant vs. concentration of sodium bisulfite103	
19.	Plots of rate constant vs. concentration of disodium edetate106	
20.	Arrhenius plot of the natural logarithm of specific rate constant (k)	
	versus the reciprocal of degree kelvin (1/T) of fluconazole in	
	fluconazole syrup containing 0.001% w/v propyl gattate115)
21.	Linear plot of drug concentration remaining vs. time of	
	fluconazole syrup (without antioxidant) in the absence of light	
	at 60 ° C148	}
22.	Linear plot of drug concentration remaining vs. time of	
	fluconazole syrup (with propyl gallate 0.001 %w/v) in the absence	
	of light at 60 ° C15	0
23.	Linear plot of drug concentration remaining vs. time of	
	fluconazole syrup (with propyl gallate 0.005 %w/v) in the absence	
	of light at 60 ° C15	2
24.	Linear plot of drug concentration remaining vs. time of	
	fluconazole syrup (with propyl gallate 0.010 %w/v) in the absence	
	of light at 60 ° C15	4

FIGURE PAGE

25.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with sodium bisulfite 0.050 %w/v) in the absence
	of light at 60 ° C156
26.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with sodium bisulfite 0.075 %w/v) in the absence
	of light at 60 ° C158
27.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with sodium bisulfite 0.100 %w/v) in the absence
	of light at 60 ° C160
28.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with disodium edetate 0.005 %w/v) in the absence
	of light at 60 ° C162
29.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with disodium edetate 0.010 %w/v) in the absence
	of light at 60 ° C164
30.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with disodium edetate 0.050 %w/v) in the absence
	of light at 60 ° C166
31.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (without antioxidant) in the presence of light
	at 60 ° C168
32	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with propyl gallate 0.001 %w/v) in the presence
	of light at 60 ° C170

FIGURE PAGE

33.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with propyl gallate 0.005 %w/v) in the presence
	of light at 60 ° C172
34.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with propyl gallate 0.010 %w/v) in the presence
	of light at 60 ° C174
35.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with sodium bisulfite 0.050 %w/v) in the presence
	of light at 60 ° C176
36.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with sodium bisulfite 0.075 %w/v) in the presence
	of light at 60 ° C
37.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with sodium bisulfite 0.100 %w/v) in the presence
	of light at 60 ° C180
38.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with disodium edetate 0.005 %w/v) in the presence
	of light at 60 ° C182
39.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with disodium edetate 0.01 %w/v) in the presence
	of light at 60 ° C184
40.	Linear plot of drug concentration remaining vs. time of
	fluconazole syrup (with disodium edetate 0.050 %w/v) in the presence
	of light at 60 ° C186

LIST OF ABBREVIATIONS

ANCOVA = analysis of covariance

°C = degree Celcius

CV = coefficient of variation

EDTA = ethylenediamine tetraacetic acid

ETOH = ethanol

PBS = phosphate buffer solution

HPLC = high performance liquid chromatography

k = degradation rate constant

+L = presence of light

-L = absence of light

M = molar

 μ = micrometer

 $\mu g = microgram$

mg = milligram

ml = millilitre

PAR = peak area ratio

PEG = polyethylene glycol

PG = propylene glycol

r = correlation coefficient

r² = coefficient of determination

SD = standard deviation

SPSS = Statistical Package for the Social Sciences

v/v = volume by volume

W = watt

w/v = weight by volume