



THE INFLUENCE OF OLEIC ACID INTO DIFFUSION RATE OF PIROXICAM IN AQUPEC HV-505 GEL BASE

Boesro Soebagio¹, Dolih Gozali², Nadiyah³
¹Faculty of Pharmacy, Padjadjaran University, Bandung, Indonesia.

ABSTRACT

The purpose of this research was to find out the influence of oleic acid as enhancer in piroxicam gel. An in vitro research about the effect of oleic acid in diffusion of piroxicam gel in aqupec 505 HV base had been done. Piroxicam is an anti-inflammatory agent for treatment of arthritis rheumatoid. Piroxicam gels was made in aqupec 505 HV using oleic acid of 0, 1, 3, 5% in the formula F0, F1, F2, and F3 respectively. The results of stability test including organoleptic, pH, measuring of viscosity and piroxicam homogeneity showed that piroxicam gel fulfilled the requirements of a pharmaceutical dosage form. The optimum increased of diffusion rate was shown in F2, with addition of 3% oleic acid.

Keyword: diffusion rate, piroxicam, gel, aqupec HV 505

1. INTRODUCTION

Piroxicam is well absorbed following oral administration; however, its used has been limited by a number of side effect, including bleeding and ulceration. Transdermal administration of piroxicam can overcome this side effect, To improve the permeability of drug through the skin, penetration enhancers had been incorporated into a formulation that would reversibly reduce the barrier resistant of the skin (Doliwa, 2001; Cordero, 1997; Dallas, 1997). Significant improvement in permeation can be made by optimizing the thermodynamic activity of the drug in the formulation and with the judicious use of permeation enhancers.

Oleic acid commonly used as emulgators in topical preparation. It also can be used as enhancers in transdermal preparations. (Wade and Weller, 1994

2. EXPERIMENTALS

Materials and Equipment

Piroxicam (PT. Kimia Farma) *Aqupec HV-505* (Sumitomoseika), aquadest, potassium dihydrogen phosphate, potassium hidroksid, methyl paraben, propylenglycol, triethanolamin (TEA).

The following equipment used in this experiment: Franz's Diffusion cell apparatus, UV Spectrofotometer apparatus (Specord), pH meter (744 Methrohm), Viscotester Rion (VT-04 F).

Preparation of Gels

Aqupec HV-505 powder was dispersed in hot water while being stirred with a stirrer at 2500 rpm. Triethanol amine were added into the gels until clear gels were obtained. Piroxicam dissolved in Triethanol amine and water was added with stirring. Other ingredients were added with continuous stirring. Formulation of gels listed in Table 1.

Table 1. Formula of Piroxicam Gels with Various Concentration of Oleic Acid as Enhancers

INGREDIENTS	F0	F1	F2	F3
Piroxicam (%)				
<i>Aqupec HV-505</i> (%)	0,5	0,5	0,5	0,5
TEA (%)	1	1	1	1
Propylenglycol (%)	3	3	3	3
Ethanol (%)	15	15	15	15
Methyl Paraben (%)	0,1	0,1	0,1	0,1
Oleic acid (%)	0	1	3	5
Aquadest ad (%)	100	100	100	100

*) F₁ = Piroxicam gel with 1% Oleic acid, F₂ = Piroxicam gel with 3% Oleic acid, F₃ = Piroxicam gel with 5% Oleic acid, F₀ = piroxicam gels without Oleic acid as enhancers.

Physical stability investigation

It was including organoleptic, pH and viscosity and consistency.

Uniformity of Gel content

The investigation was conducted by measuring the uniformity of content in 10 gram of gels sample by UV Spectrofotometer. The measurement were in triplicate.

Safety Test

The safety Test was conducted into 10 volunteers using Patch Test Method.

Diffusion Study

The diffusion study was conducted through Whatman membrane which was soaked in Spangler solution. The membrane was mounted on the Franz's Diffusion Cell. One gram of gel was applied on the membrane. The receptor medium

was pH 7.4 phosphate buffered, which was maintained its constant temperature by a circulating water bath which their temperature was maintained at 37°C. The sample were withdrawn from the receptor compartment at 5,10,20,30,40,50,60,80,100, dan 120 minutes and replaced by an equal volume of fresh buffer solution. The sample solution were analyzed spectrophotometrically.

3. RESULT AND DISCUSSION

Physical stability investigation

Organoleptic investigation showed that all gels were pale yellow, clear, transparent and well spreadable. It didn't change during 56 days of storage. It means that Aqupec HV 505 had best physical stability as gel base.

pH stability evaluation was examined during 56 days of storage. The result showed in Table 2.

Table 2. pH of Piroxicam gels using Oleic Acid as Enhancers

Days	Formula			
	F0	F1	F2	F3
1	7,48	7,41	7,37	7,29
3	7,51	7,46	7,45	7,37
5	7,51	7,47	7,47	7,40
7	7,77	7,61	7,50	7,44
14	7,86	7,72	7,63	7,56
21	7,89	7,83	7,75	7,60
28	8,01	7,89	7,80	7,71
35	8,21	8,14	7,96	7,92
42	8,34	8,23	8,07	8,05
49	8,42	8,22	8,16	8,07
56	8,46	8,32	8,16	8,08

From the research it is known that the pH of gels were 7,41 to 8,46. Ideal pH for piroxicam gel was 6-8. Statistical analysis gave result that there was significant change in pH during 56 days of storage. Newman Keuls Test also showed that variation in concentration also gave significant change into pH.

Viscosity Evaluation

Addition of oleic acid into gels caused the increase in gels' viscosity. It may be caused by the increase of lipophylic phase which cause concentrate and viscous gels happened. Viscosity of Piroxicam gels using Oleic acid as enhancer during time of storage shown in Figure 1.

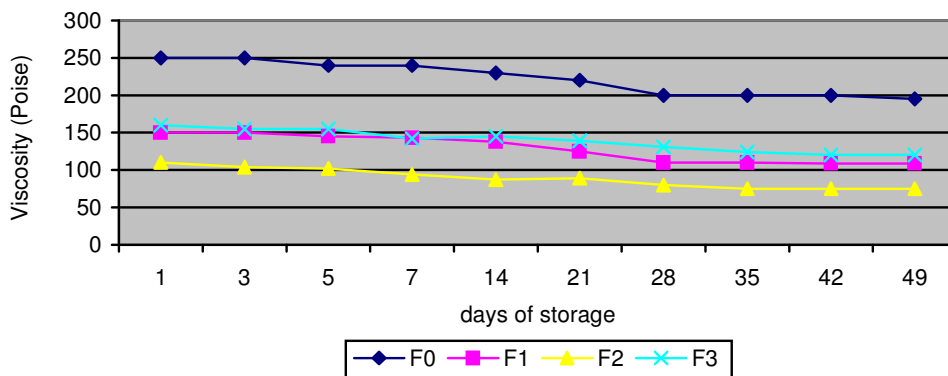


Figure 1. Viscosity of Piroxicam gels using Oleic acid as enhancer during time of storage

Uniformity of Gel content

The results of the measurement on Uniformity of Gel content shown in Table 3. From the research it can be concluded that gel content homogeneity was good (0,482 – 0,513%) and can be used for next study to which Diffusion Study.

Table 3. Uniformity of Piroxicam Gel content

Formula	Piroxicam content (%)		
	1	2	means
F0	0,48	0,49	0,487 ± 0,006
F1	0,49	0,46	0,482 ± 0,019
F2	0,495	0,51	0,513 ± 0,015
F3	0,50	0,53	0,51 ± 0,02

Safety Test

The safety test gave result that all gels were save to be used because it didn't give the allergic reaction to the volunteers.

Diffusion Study

The study was conducted to investigate the effect of various concentration of Oleic acid as enhancers on the permeation of piroxicam from gels using Aqupec HV 505 base. The percentage of Piroxicam diffused into the membrane shown in Table 4. Diffusion profile of Piroxicam from gels with Oleic acid as enhancer shown in Figure 2.

Table 4. The percentage of Piroxicam diffused into the membrane

Time (minutes)	Piroxicam diffused into membrane			
	F0	F1	F2	F3
5	0,532 ± 0,21	0,385 ± 0,21	1,56 ± 0,21	0,46 ± 0,31
10	0,696 ± 0,21	0,544 ± 0,21	2,28 ± 0,11	0,54 ± 0,43
20	0,700 ± 0,42	1,21 ± 0,11	2,96 ± 0,003	0,62 ± 0,33
30	0,922 ± 0,53	1,97 ± 0,11	3,65 ± 0,10	0,77 ± 0,32
40	1,223 ± 0,74	2,81 ± 0,42	5,73 ± 0,32	1,59 ± 0,009
50	1,231 ± 0,34	3,791 ± 0,74	7,79 ± 0,22	1,83 ± 0,11
60	1,309 ± 0,20	5,74 ± 0,29	9,70 ± 0,11	2,06 ± 0,002
80	1,46 ± 0,42	8,75 ± 0,09	12,49 ± 0,003	2,96 ± 0,002
100	1,61 ± 0,22	12,91 ± 0,21	16,48 ± 0,11	3,87 ± 0,21
120	1,84 ± 0,11	16,79 ± 0,11	20,52 ± 0,21	4,86 ± 0,11

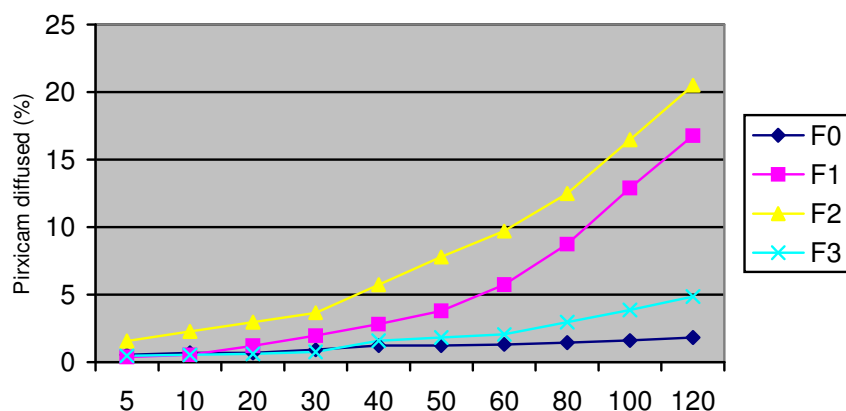


Figure 2. Diffusion profile of Piroxicam from gels with Oleic acid as enhancer

4. CONCLUSIONS

The results showed that Oleic Acid could increase the diffusion rate of Piroxicam in Aqupec HV 505 gels through membrane. It can be concluded that it also can increase penetration rate through human skin because the membrane in Spangler solution is a model of human skin lipoprotein.

The increase of diffusion rate in gels containing 3% Oleic acid was best one. Oleic acid increase diffusion of hydrophobic drug by lowering Lipid Transition Temperature (Tm) in order to increase conformation and flexibility of Endogenous lipid alkyl chain above its Tm.

1. Organoleptic investigation showed that all gels were pale yellow, clear, transparent and well spreadable. It didn't change during 56 days of storage.
2. From the research it is known that the pH of gels were 7,41 to 8,46. Statistical analysis gave result that there was significant change in pH during 56 days of storage. Newman Keuls Test also showed that variation in concentration also gave significant change into pH.
3. Addition of oleic acid into gels caused the increase in gels' viscosity.
4. gel content homogeneity was good (0,482 – 0,513%)
5. The safety test gave result that all gels were save to be used
6. The results showed that Oleic Acid could increase the diffusion rate of Piroxicam in Aqupec HV 505 gels through membrane

5. REFERENCES

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