

FORMULATION OF PROPANOLOL CREAM WITH VCO (VIRGIN COCONUT OIL) CONTAINED BASE

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Abstract

Background. Propranolol is a β -blocker agent with low oral bioavailability (15-23%) so that transdermal route can be used as alternative drug delivery.

Objective. This study was purposed to know the influence of VCO (Virgin coconut Oil) to the propranolol release rate in cream base preparation.

Methods. Cold cream base in various concentration of VCO, i.e 0%(F0), 14%(F1), 28%(F2), 42% (F3) contained 7% propranolol HCl were tested their dissolution using dissolution tester (paddle shaped stirrer). Acetat buffer solution 0,01 M pH 5 was used as medium, the temperature was set up at 36°C, stirring rate was controlled at 100 rpm. The parameter of this study was DE (dissolution efficiency) value.

Outcome measured. Dissolution Efficiency value (DE_{30})

Results. The result showed that DE_{30} value (in %) of F0, F1, F2, and F3 were $4,73 \times 10^{-3} \pm 0,53 \times 10^{-3}$; $6,41 \times 10^{-3} \pm 0,63 \times 10^{-3}$; $9,18 \times 10^{-3} \pm 1,78 \times 10^{-3}$; $12,65 \times 10^{-3} \pm 2,08 \times 10^{-3}$ respectively.

Conclusion. It can be concluded that VCO increase propranolol dissolution significantly ($p < 0,05$) and the optimum VCO concentration as cold cream base was 42% with DE_{30} propranolol value 267% compare with control formula.

Keywords : Propranolol , VCO (Virgin Coconut Oil), Dissolution, Cream, Cold Cream.

INTRODUCTION

Propranolol is an unselective β -antagonist with low oral bioavailability (15-23%) (Katzung, 2001), so that it is needed to develop an alternative delivery. Transdermal delivery can be choiced, because of its advantages, i.e. (1) it is convenient because of non invasive, (2) it can be used by patient as self delivery, (3) it can be design as one daily dose or less frequent, and (4) the plasma level can be maintained at constant value because of its zero order kinetic delivery (intra venous infusion like kinetics) (Nugroho, 2005).

There are many kinds of dosage form used transdermally. Cold cream is suitable dosage form to deliver propranolol transdermally because it is lipophyl, while propranolol is hidrophyl. This contradictive properties can enforce propranolol release from its base and difuse through the skin.

The dissolution is the first step of absorbtion, and it makes available the drug to be absorbed. This process is releasing the drug from the cream base on the interphase of the cream and thin film water on the skin. Since the drug on this interphase was releasing, the drug concentration on this interphase was below than in the bulk phase, and the diffusion from bulk phase to this interphase will be happened simultaneously (Martin et al, 1993).

In the cold cream dosage form, oil is needed as disperse medium. In this research, VCO (Virgin Coconut Oil) was used. VCO contains 92% saturated fatty acid, composed of 48% - 53% lauric acid, 1.5% - 2.5% oleic acid, and anothers, i.e. caprilic acid and capric acid (Syah, 2005). Oleic acid and lauric acid enhance the rate of permeation of estradiol, progesteron, acyclovir, 5-fluorouracyl, salicylic acid (Niazy, 1991), and piroxicam (Santoyo and Pygartua, 2000) through the skin. It is hoped that propranolol cold cream has a good dissolution and permeation properties. In this research, dissolution properties was observed.

MATERIAL AND METHOD

Material

Pharmaceutical grade of propranolol HCl was purchased from PT. Indofarma, Jakarta. VCO (*Virgin Coconut Oil*) is Vinuto[®] produced by Wira Husada Yogyakarta was purcahsed from Apotek Nurani, Godean, Yogyakarta. As base materials were used pharmaceutical grade of cera alba, cetacium, olive oil, and aquadest. The acetic buffer pH 5, 0,01 M (made from E Merk analytical grade glacial acetic acid and acetic sodium) was used as dissolution medium. The dissolution observation was performed using using paddle stirrer Dissolution Tester (Erweka DT600) as shown in figure 1. The cream was filled in the diffusion cell and covered by stretched cellophane membrane. The propranolol concentration was measured using Spectrophotometer UV-Vis (Shimadzu 1700).

Method

Propranolol Coldcream Formulation

The propranolol coldcream composition was listed in table I. Cera alba and cetacium were melted in water steamer, than olive oil and VCO were added and mixed in mortir porcelen. Propranolol HCl was dissolved in warm water

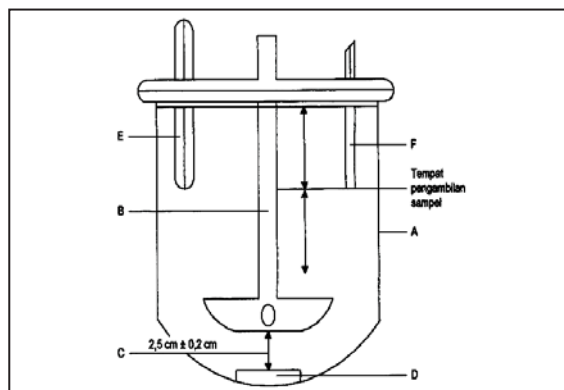


Figure 1. Erweka Dissolution Tester, A: chamber dissolution medium, B: Paddle, C: space between paddle and dissolution cell, D: Dissolution cell, E: Thermometer, F: sampling line.

and added to the oil phase. The strong blending will homogenize this coldcream.

100 µg/ml), was determined its absorbance at maximum wavelength to construct calibration curve.

Table I. The propranolol coldcream formulation

Material	Concentration in coldcream (%)			
	F0	F1	F2	F3
Propranolol HCl	7	7	7	7
VCO	-	14	28	42
Olive oil	56	42	28	14
Cera Alba	12	12	12	12
Cetaceum	12,5	12,5	12,5	12,5
Aquadest	14	14	14	14

Propranolol Coldcream Physical Characteristic Observation

Before dissolution observation, the physical characteristics of propranolol coldcream were determine, including spreadability, adhesiveness, water protection, and its pH.

Propranolol Coldcream Dissolution Observation

The propranolol coldcream was filled in cilindric diffusion cell (2 cm in diameter and 0,4 cm height). The cellophane was swollen by soaking in aquadest for 30 minutes, than put on the diffusion cell to cover the coldcream. This cell was put in Erweka Dissolution Tester, the paddle was moved down, and stirred 100 rpm. The temperature was maintained in 37°C ± 0,5°C. The dissolution was began by filling the dissolutin chamber with acetic buffer pH 5, 0,01 M. The aliquot 5,0 ml of dissolution samples were withdrawn in various minute: 0, 5, 10, 15, 20, 25, 30, 60, 90, and 120. The propranolol concentration in these samples were determined using spektrofotometer UV-Vis (Anggraeni *et al.*, 2012). The propranolol HCl solution (40 µg/ml) in 0,01 M acetic buffer pH 5 was scanned its absorbance at 200 – 300 nm to identify its maximum wavelength. The same solution, in various concentration of propranolol HCl (1 –

RESULT AND DISCUSION

Propranolol Spectrum

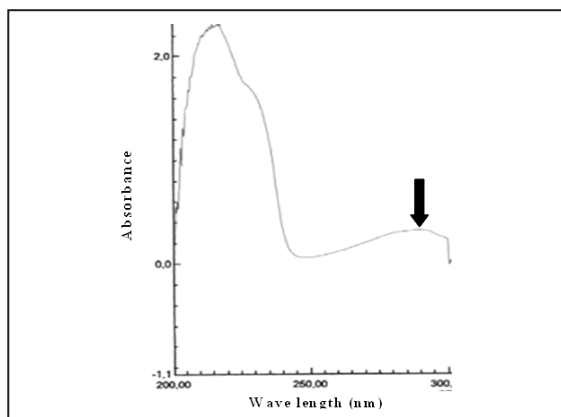


Figure 2. The spectrum of propranolol HCl 40 µg/ml in 0,01 M acetic buffer pH 5. It is shown (↓) that this solution has maximum wavelength at 288 nm.

Propranolol Calibration Curve

The calibration curve was needed to calculate the concentration of propranolol. The absorbance of propranolol HCl solution in various concentration was recorded in 288 nm based on the maximum wavelength shown in figure 2. The linear curve and its regresion-correlation between absorbance and concentration was shown in figure 3. This callibration curve has a high corellation since

$r_{\text{calculated}}$ (0,993) is higher than r_{table} for 12 degree of freedom (0,532) and can be used to calculated the propranolol concentration.

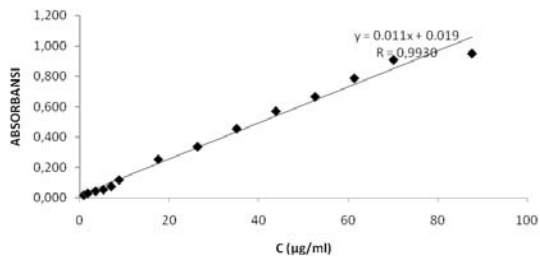


Figure 3. The calibration curve of propranolol has a linear regression $y = 0,011x + 0,019$.

Physical Characteristics of Propranolol Coldcream

Physical characteristic of cream support patient convenient and delivery of the drug to and through the skin. This coldcream characteristics were listed in table II. The VCO has less consistency than olive oil, so that the higher the VCO concentration the higher the spreadability, and the cream is more easy to use. The adhesiveness of these coldcream, insures the enough contact time between cream and skin to deliver propranolol. This coldcream is w/o emulsion base, so that it can resist the water diffusion. It is the advantage of coldcream, because of its capability to increase the skin hydration. The skin hydration enforce the skin fluidity and enhance the drug permeability.

Propranolol Coldcream Dissolution Observation

Propranolol coldcream dissolution make available the propranolol on molecular size in water layer of skin. Based on Fick's Law, concentration is the driving force of simple diffusion process. Enhancing the rate of dissolution make the higher concentration of propranolol available to be absorbed, so that the rate of absorption will be increase. In this research, the dissolution of coldcream tested using Paddle Dissolution Tester, and the datas were shown in figure 4.

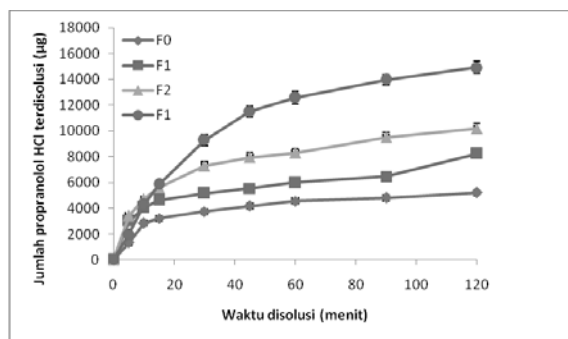


Figure 4. Dissolution profile of propranolol coldcream in average from 5 replication. The standard deviation (SD) was shown by \bar{E} symbol.

It is shown in figure 3 that the dissolution profile is affected by VCO concentration in the coldcream formula. The higher the concentration of VCO, the better the dissolution profile, and from the value of standard deviation, it can be predicted that their differences are significant. In formulas 1, 2, and 3, some olive

Table II. Physical characteristics of propranolol coldcream

Formula	Spreadability (cm ²)	Adhesiveness (minutes)	Protection (for 5 minutes)	pH
F0	3,1	>15	able to protect	about 5
F1	5,9	>15	able to protect	about 5
F2	6,8	>15	able to protect	about 5
F3	10,2	>15	able to protect	about 5

oil was replaced by some VCO increase respectively. VCO has saturated fatty acid (92%) (Syah, 2005) more than olive oil. Since the saturated fatty acid is more lipophilic than unsaturated fatty acid, the oil with higher

45 minutes dissolution test in a cm^2 area of dosage form-medium contact. The value of DE_{30} and $t_{45 \text{ minute}}$ of propranolol were shown in table III.

Table III. Dissolution expression of propranolol coldcream

No	Formula	Average DE_{30} (%) + SD (n=5)	Average $t_{45 \text{ minute}}$ (mg/cm^2) + SD (n=5)
1	F0	$4,73 \times 10^{-3} \pm 0,53 \times 10^{-3}$	$1,326433 \pm 0,17803$
2	F1	$6,41 \times 10^{-3} \pm 0,63 \times 10^{-3}$	$1,764129 \pm 0,279653$
3	F2	$9,18 \times 10^{-3} \pm 1,78 \times 10^{-3}$	$2,529994 \pm 0,59868$
4	F3	$12,65 \times 10^{-3} \pm 2,08 \times 10^{-3}$	$3,660567 \pm 0,729533$

containing of fatty acid will be more lipophilic, and the hidrofiliic drug, including propranolol HCl, will be released more rapidly. The other reason is the spreadability of coldcream. It is shown in table 2 that formulas with VCO have the higher value of spreadability. This physical characteristic is linear with coldcream fluidity, and the fluidity is linear with diffusion coefficient (D). From the Fick's equation (Martin et al, 1993), it can be evaluated that the diffusion will be easier in an unviscous matterial.

The disolution parameter can be calculated from its dissolution profile. There are many kind of dissolution parameters, including DE (dissolution efficiency), $t_{x\%}$ (time necessary to release x % of drug), and $t_{x\text{min}}$ (percent drug released in x minute) (Costa and Lobo, 2001). The DEx parameter is a ratio between area under curve of dissolution profile for x minute and area of rectangle shaped by times of x minute dissolution time and amount of drug in tested pharmaceutical dosage form (Khan, 1975). The parameter $t_{x\text{min}}$ is the simplest expression and frequently used by pharmacopies (i.e. $t_{45}=80\%$). But this expression is powerless if aplicate in semisolid dosage forms dissolution test using cell diffusion which are the mass of dosage forms introduced in medium can be varieted, because only some of the dosage form contact with dissolution medium in a constant area. In this research we introduced new definition of $t_{45 \text{ minute}}$ in semisolid dosage form as the drug dissolved in

Statistical analysis (Anova test followed by Tukey HSD) showed that there are no significant differences in DE_{30} and $t_{45 \text{ minute}}$ between formula 1 and control (formula 0), but the formula 2 and 3 showed the significant higher value in DE_{30} and $t_{45 \text{ minute}}$ compare with control (F1).

CONCLUSION

The VCO (Virgin Coconut Oil) can be used as base material for propranolol coldcream instead of olive oil. VCO containing propranolol coldcream has the better dissolution characteristics and spreadability compare with olive oil alone, but they have the same characteristic in adhesiveness, water protection, and pH.

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