International Research Journal of Pharmaceutical and Applied Sciences
Available online at www.irjpas.com
Int. Res J Pharm. App Sci., 2012; 2(4):31-34

Research Article

Effect of iontophoresis and propylene glycol on the in vitro diffusion of ethyl vitamin c cream

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(Received: 21 July, 2012; Accepted: 06 August, 2012; Published: 29 August, 2012)
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ABSTRACT
Chemical instability properties of L-ascorbid acid/vitamin C can be decreased by derivatization 3-O-ethyl-L-ascorbic acid/ethyl vitamin C. Ethyl vitamin C, as lightening skin, in cream formulation could not be absorbed by the skin optimally because of the low permeability of the skin. Propylene glycol as a penetration-enhancing substances and iontophoresis method can increase the number of permeated chemical compound. The purpose of this study is to determine the effect of propylene glycol as penetrance enhancers and application of iontophoresis method on diffusion of ethyl vitamin C cream preparation in vitro. The study was performed with flow through method for 6 hours using porcine ears skin as a diffusion membran. The results obtained that the F3 (PG 6% and iontophoresis), had the greatest % permeation (19,61±3,85%). The combination of propylene glycol and iontophoresis indicated synergistic effect in permeation rate. Iontophoresis application, F2 (without PG 6%), was stronger permeation rate than propylene glycol as penetrance enhancers, F1(PG 6%).
Key words: vitamin C, Propylene glycol, Iontophoresis, diffusion

INTRODUCTION

L-Ascorbic acid (vitamin C) is very unstable to air, moisture, light, heat, metal ions, oxygen, and base, and it easily decomposes into biologically inactive compounds such as 2,3-diketo-Lgulonic acid, oxalic acid, L-threonic acid, L-xylonic acid, and L-Lyxonic acid. Therefore, the applications of vitamin C in the fields of cosmetics, dermatologicals, and pharmaceuticals are limited despite of its useful functions. Thus to overcome chemical instability of vitamin C, is to derivatize the vitamin C as a salt such as ascorbyl palmitate or magnesium ascorbyl phosphate, or as ester 3-O-ethyl-L-ascorbic acid/ ethyl vitamin C [1].

Ethyl vitamin C can be formulated in topical preparation to achieves dermatological functions; it promotes collagen biosynthesis, provides photoprotection, causes melanin reduction, and scavenges free radical[2]. However, The stratum corneum behaves as a barrier for most of drugs percutaneous absorption into the body. The ability of drug to penetrate the stratum corneum can be improved by using physical and chemical methods[3].

Previous in vitro study showed that Ethyl vitamin C cream with 6% propylene glycol can improve 7% percutaneous permeation of Ethyl vitamin C [4].

Propylene glicol indicated synergistic effect with iontophoresis method in absorption of metopimazine[5]. The purpose of this study is to determine the effect of propylene glycol as penetrance enhancers and application of iontophoresis method on diffusion of ethyl vitamin C cream preparation in vitro.

MATERIALS AND METHOD

Materials

Silver (Ag) wire 99,99% (PT. Antam TBK), Platina (Pt) wire (PT. Antam TBK). Cera alba (Brataco), ethy vitamin C (CHEMLAND Co., Ltd.), KCl 0,1 M (Merck), KH_2PO_4 0,2 M (Brataco), sodium tetraborat (Brataco), parafin liquidum (CV Quadrant), propylene glicol (Bratachem), and NaOH 0,2 N (Brataco).

Preparation of Ethyl Vitamin C Cream

Water phase (Sodium tetraborat, ethyl vitamin C, and propylene glicor) and Oil phase (liquid paraffin oil and cera alba mixed at 70 ° C) were mixed carefully until got a creamy mass forms and homogeneous.

Table 1. Formulation of Ethyl Vitamin C Cream

FORMULA	F0	F1	F2	F3
Ethyl vitamin C (%)	1	1	1	1
Cera alba (%)	16	16	16	16
Parafin liquidum (%)	50	50	50	50
Sodium tetraborat (%)	0,8	0,8	0,8	0,8
Propilene glycol (%)	-	6	-	6
Aquadest ad	100	100	100	100

Preparation of Membrane

Porcine ears were obtained from a slaughterhouse. The skin was carefully removed leaving the fat tissue behind. Any skin, in which the barrier was disrupted, was removed. The skin was cut into 2 cm x 2 cm samples for permeation studies[6]. Thickness of skin tissue is 1200 µm (full thickness). Skin immediately stored at -20 º C until the experiments were carried out[7].

Preparation of Electrodes

Iontophoresis experiments were conducted using silver/silver chloride electrodes. The silver chloride electrodes were prepared as follows: silver wires (0.1 cm diameter; length 3.1 cm) were immersed in 0.1N HCl solution and connected to the anode of an amperostatic state (1 mA) and time of electrolysis 6 hours with 0.1 M KCl.

Preparation of Iontophoresis

The Iontophoresis tools were newly-designed in this study, collaboration with Biomedical Engineering Laboratory, School of Electrical Engineering and Informatics, Institut Teknologi Bandung. The series were set to produce a constant current density of 0.5 mA/m2. The amperemeter was used for calibrating constant current before the experiment were carried out.

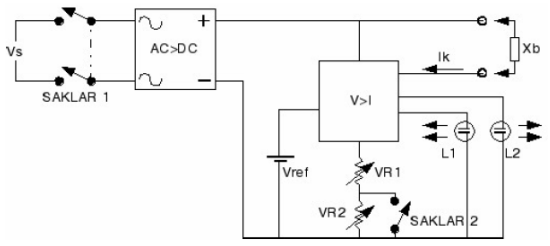

Figure 1 Diagram of Constant Current Iontophoresis Device

In vitro diffusion test

In vitro diffusion test was performed using the flow through method with Modified-Franz diffusion cell (Figure 2). All formulas was weighed as much as 1.0 g, flattened above the membrane with a surface area of 2 cm2. System's temperature 37 ± 0.5 ºC with the receptor phosphate buffer pH 7.4 (2.77 g Na2HPO4. 12H2O and 0.31g Na2HPO4. 12H2O in 200ml) about 50 mL. Each process were carried out for 6 hours without and with iontophoresis. Aliquot were taken from the receptor fluid as much as 5 ml and replaced with phosphate buffer pH 7.4 at the 30th, 60th, 120th, 180th, 240th, and at the 360th minutes[8], then were analyzed by Spectro UV-VIS method .

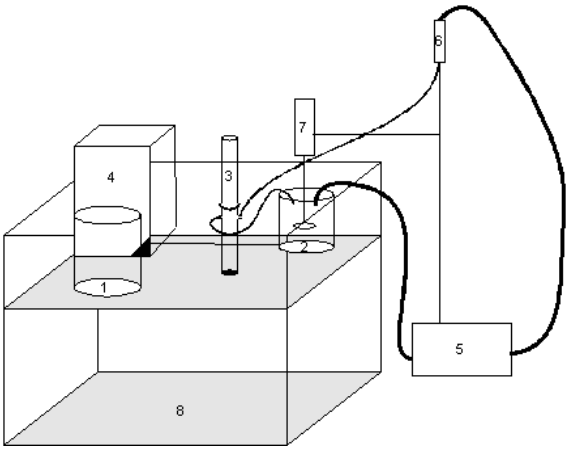

Figure 2 *Invitro* Diffusion Test[8]
1 = Receptor fluid replacement, 2 = receptor compartment , 3 = donor compartment ,4 = thermostat, 5 = peristaltic pump, 6 = busting bubbles, 7 = stirrer, 8 = water bath

RESULT AND DISCUSSION

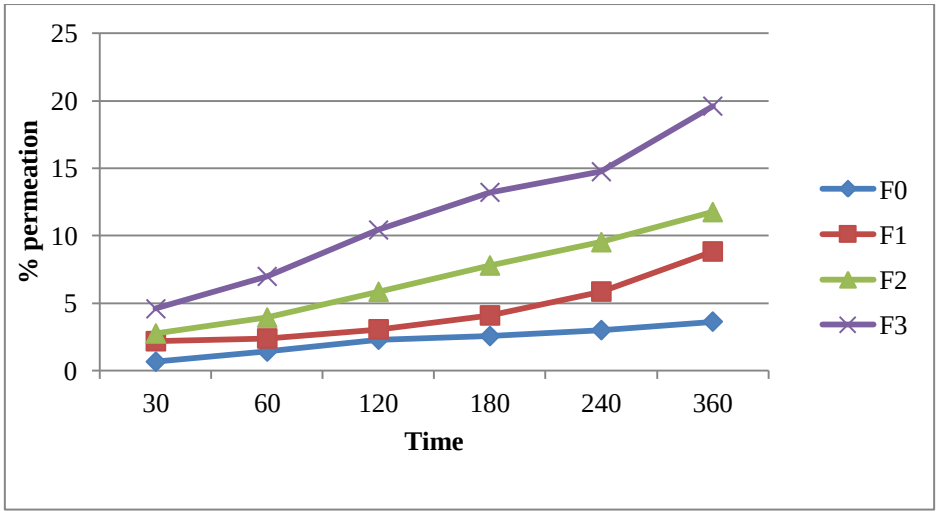

Figure 3. Permeation of ethyl vitamin C

Note: F0 : without propylene glycol, F1 : with 6% propylene glycol, F2 : without propylene glycol, with iontophoresis application, F3 : with propylene glycol and iontophoresis application, (n=2)

Ethyl vitamin C in the anionic form in pH 7.4, so that the flow of ions with iontophoresis application will occur from the cathode to the anode. Ag wire as the anode was placed in the receptor compartment, and the AgCl cathode in the donor compartment. In vitro diffusion test (figure 3) showed that permeation rate of ethyl vitamin C in formula F2 (11.76±1,17%) is greater than the formula F1 (8.84±0,96%). With iontophoresis application, ethyl vitamin C was more easily penetrated into the stratum corneum due to the electromigration process than the F1 formula. Propylene glicol have known to disrupt the horny layer intercalating into the structured lipids of the skin, which renders the structure more fluid and increase the coefficient of the permeant[9]. The ability of propylene glycol to disrupt the horny layer not good enough to defeat the electromigration process which is converted into molecular ions due to strong currents. Drainage of electrons is converted into ion flux through the electrode reaction. The process of ion transport through the skin is a process to maintain a neutral electrical charge (electronetrality)[10]. The F3 formula was a formulation with the greatest permeation rate of ethyl vitamin C (19,61±3,85%). In the F3 formula containing propylene glycol 6%. The use of a combination of propylene glycol and iontophoresis produce a synergistic effect that gives the diffusion of ethyl vitamin C higher than the penetration-enhancing substances or methods iontoforesis separately.

While in the F0, the smallest rate of permeastion (3.64±0,61%) compared with F1, F2, and . F3. This is due to the absence of addition of penetration enhancers propylene glycol on F0, so there is no agent that helps increase the permeation of ethyl vitamin C. Concentrations of ethyl vitamin C determined by spectrophotometer at a wavelength of 246 nm.

CONCLUSION

The study reveals the synergistic effect of combination between propylene glycol as penetrance enhancers and application of iontophoresis method on diffusion of ethyl vitamin C cream preparation in vitro. Iontophoresis application was stronger permeation rate than propylene glycol as penetrance enhancers.

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