# THE EFFECT OF PROPYLENE GLYCOL CONCENTRATION ON THE PHYSICAL CHARACTERISTIC AND RELEASE RATE OF CAFFEINE IN GEL

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## Abstract

*The aims of this research were to find if any the effects of the propylene glycol concentration on the physical characteristics of the gel which includes organoleptic, pH, viscosity, and of the caffeine releasing test within 360' that includes the value of dissolution-%, DE-%, lag time, and diffusion coefficient.*

*Caffeine gel formulation consisted of F I (with 10% of propylene glycol addition), F II (with 20% of propylene glycol addition), F III (with 30% of propylene glycol addition), IV (without of propylene glycol addition) and the F V used as a positive control, an anti cellulite gel preparation that was available in the market used. Based on physical characteristic test, it could be drawn that the increasing propylene glycol concentration increased clarity, pH, and gel viscosity. Increasing propylene glycol concentration also decreased dissolution-%, decreased DE-%, increased lag time and decreased diffusion coefficient. The physical characteristic test and the caffeine releasing test were analyzed by using the one-way ANOVA with 95% and probability (p=0,05) level SPSS.*

*Based on the results of the research, it could be concluded that the different propylene glycol concentration as humectant, affects significanthy to the physical characteristics, such as the pH and viscosity tests, and to the caffeine releasing in gel, such as the dissolution-%, DE-%, lag time, and diffusion coefficient.*

**Keywords :** *Caffeine, gel, propylene glycol, lag time, dissolution*

## INTRODUCTION

Cellulite is topographical skin alteration that happen in 85% post-adolescent women (Hexsel *et al.*, 2006). It is normally occured on the skin thighs, belly, and buttocks of whom that have an adrenergic receptor (Djajadisastra, 2008). Topical anticellulite is used to reducing cellulite. Caffeine is used as active ingredient that based on stimulation beta adrenergic receptor mechanism.

Hydrophyllic gel are suitable to be used as cosmetic base because of its cooling effect, good appearance, and not sticky. Carbomer have also be choosen as gel-base because it can form a thicked gel (Allen, 2002) and produce a stable product (Amnuakit, 200). Gel component are usually consisted of humectant, a substance that can control water evaporation change between the product and the air, in the container or in the

ISBN : 978-979-18458-5-4

skin (Rukminingsih, 2009). Propylene glycol is commonl used as humectant that has mechanism in repairing irregular epidermis appearance of the skin cellulite condition. Propylene glycol can increase a solubility of many subtances, one of which is caffeine (Rowe *et al.*, 2009) and it can influence a swelling and viscoelasticity of carbomer (Islam *et al.*, 2004). Propylene glycol is also known as a subtance that influence release rate of active subtances (Amnuakit *et al.*, 2005).

## METHODS

Object of this research was a physical characteristic and release rate of caffeine in gel as humectant in different concentration of 10%, 20%, and 30%. The parameter used to determine caffeine release rate was the value of lag time and cofficient difusion based on Higuchi's Equation.

Free variable in this research was propylene glycol concentration of 10%, 20%, and 30%. Bound variable in this research were physical characteristics and release rate of caffeine. Physical characteristic gel consisted of organoleptic, value of pH, and viscosity. The value of lag time and diffusion coefficient could perform the rate of its caffein's release.

The instruments used were mortar and stamper, glass tools, porcelain cup, *Hot Plate stirrer* model L-81 (Labinco), Tablet Dissolution Apparatus VDA-6DR USP *Standards* (VEEGO), pH 210 *Microprocessor* pH meter (HANNA), spektrofotometer UV mini 1240 UV-*Visible* (Shimadzu), viscosimeter Rion VT-04, and *paddle over disk*.

The materials used to form a caffeine gel, physical characteristic test and release rate were anhydrous caffeine, carbomer, propylene glycol, TEA, nipagin, $KH_2PO_4$, NaOH, cellophane membran, buffer pH 7 and buffer pH 4.

The method of this research was dissolving a caffeine into mixture of propylene glycol and water with magnetic stirrer until it dissolved well then added to carbomer gel base which was swelled and added enough water. Each formula consisted of a different propylene glycol concentration (table I).

Each formula has been tested its physical characteristic, of organoleptic, pH, and viscosity, and been done a release test of caffeine in gel using cellophane membrane and paddle over disk. The 2 grams of preparation gel were put into paddle over disk which cellophane membrane equipped, then put it into the dissolution vessel contained of 900 ml of phosphat buffer pH 7,4 at 37°C, and was stirred at 50 rpm speeds. The sample was taken a 10,0 ml of it, at 5', 10', 15', 30', 45', 60', 90', 120', 150', 180', 240', 300', and 360' minutes stirring time. The absorbance of caffeine was viewed at the maximum wavelenght of 273 nm on the 7,4 pH phosphate buffer blanko. The result datas were analyzed by using One way ANOVA for the normal distribution, and Kruskall Wallis for the abnormal distribution data.

## RESULTS AND DISCUSSION

Based on the result on this research, it could be concluded that the increased propylene

**Table I. The Calculation of component Caffeine Gel Preparation**

| Substances | Calculation | FI (g) | FII (g) | FIII (g) | FIV (g) |
|---|---|---|---|---|---|
| Caffeine | 3% x 150 g | 4,5 | 4,5 | 4,5 | 4,5 |
| Carbomer | 0,5% x 150 g | 0,75 | 0,75 | 0,75 | 0,75 |
| TEA | 0,5% x 150 g | 0,75 | 0,75 | 0,75 | 0,75 |
| Propylene- Glycol | 10% x 150 g | 15 | - | - | - |
| | 20% x 150 g | - | 30 | - | - |
| | 30% x 150 g | - | - | 45 | - |
| Nipagin | 0,2% x 150 g | 0,3 | 0,3 | 0,3 | 0,3 |
| Aqua destilata | Up to 150 g | Up to 150 | Up to 150 | Up to 150 | Up to 150 |

ISBN : 978-979-18458-5-4

glycol concentration can increas clarity, pH's value, viscosity caffeine gel. Propylene glycol can increase caffeine solubility in gel and tend to be more alkalized, than carbomer that makes the carbomer swelling more easily, so that the gel clarity and pH were also increased. Carbomer swelling proccess causes increasing in the polymer cross-linked so then the viscosity is also increased. The result of the organoleptic test were shown at table II.

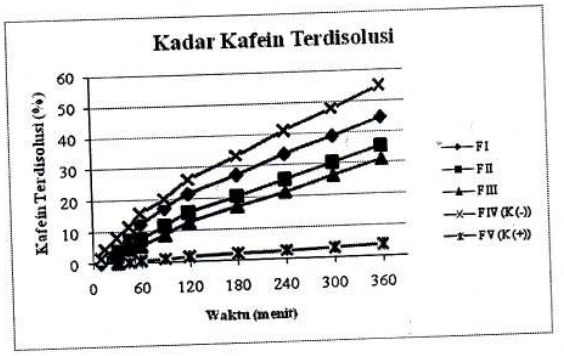
Table II. Result of Physical Characteristic and Caffeine Release Rate Test

| Determine | Formula | | | | |
|---|---|---|---|---|---|
| | F I | F II | F III | F IV | F V |
| Organoleptic:<br>• Form<br>• Colour<br>• Odour<br>Taste | Gel<br>Clear<br>-<br>Cool | Gel<br>Clear<br>-<br>Cool | Gel<br>Clear<br>(the most clear)<br>-<br>Cool | Gel<br>Turbid<br>-<br>Cool | Gel<br>Green and clear<br>Tea's aromatic<br>Cool |
| pH | 5,57 ± 0,03 | 5,75 ± 0,02 | 6,04 ± 0,02 | 5,20 ± 0,04 | 6,31 ± 0,02 |
| Viscosity (P) | 171,67 ± 2,58 | 182,50 ± 2,74 | 200 ± 0,00 | 158,33 ± 2,58 | 38,33 ± 5,16 |
| *Lag time* (menit) | 9,9987 ± 0,1092 | 16,8348 ± 0,5452 | 21,8593 ± 0,5473 | 7,2659 ± 0,2131 | 42,2219 ± 0,4138 |
| Diffusion coefficient ($10^{-7}$ x cm$^2$/minutes) | 9,6967 ± 0,1470 | 5,7465 ± 0,1831 | 4,3986 ± 0,1093 | 13,2191 ± 0,3799 | 2,2763 ± 0,,234 |
| % Dissolution | 44,4888 ± 2,1111 | 35,3835 ± 1,3010 | 31,2257 ± 2,2495 | 54,8373 ± 3,7105 | 3,7876 ± 0,2986 |
| % DE *(Dissolution Efficiency)* | 56,2986 ± 3,7196 | 54,2677 ± 1,8589 | 51,5982 ± 2,1647 | 58,1339 ± 3,1156 | 52,7523 ± 1,8602 |

Caffeine release test was used to know the total caffeine solubilized and caffeine release rate. Caffeine release test was used negative control, that was a preparation gel without adding propylene glycol and the positive control, that was anti cellulite preparation that available in the market. Based on the result data, the relation between solubilized caffeine with in certain time interval, and the total solubilized caffeine of each formula (picture 1).

Formula I showed a highest value of dissolution-% among other formulas, because amount of adding propylene glycol was just 10% and consisted more water than of formula II and formula III, so caffeine were more easily solubilized into the dissolution medium. The different water amount in each formula actually didn't give a significant effect on the caffeine gel preparation's release, if it was compared to the formula IV as negative control that showed the highest amount release becaused at the most of it preparation contained water, and without be added with propylene glycol. The negative control showed a highest release amount, because it did not contain a inhibitor of releasing factor such as propylene glycol. Formula V as positive control is showed a lowest result. It was becaused the preparation was formulated for slow release and consisted of other active anticellulite beside caffeine. Based on statistical test showed that increased propylene glycol concentration of 10% did not make any

ISBN : 978-979-18458-5-4




Picture 1. Caffeine dissolution content

significant difference reduction of dissolution-%.

Having in mind the levels of dissolution, then it was calculated the levels of Dissolution Efficiency (DE) that states the ratio between the area under the curve in the time t and the rectangular area that limits the 100% ordinate and absciss. Area under the curve or AUC describes the levels of drug content in time as a measure of size ant total of the bioavailability of drug. DE is ussually used to determine the ability or efficiency of the drug is dissolved in the media until a certain time. Increased concentrations of 10% propylenglycol in the formula however did not cause a decrease in DE-% value significantly. While 20% increased propylenglycol concentration in the formula caused a decrease in DE-% value significantly.

The release rate of caffeine in gel were counted by applying the Higuchi equation. Caffeine release rate could be seen from the value of lag time and the value of diffusion coefficient. Release rate of active substance in gel were influenced by physical gel characteristic that was gel viscosity. Increasing gel viscosity was caused by density of polymer crossed-linked forms. Increasing the crossed-linked polymer density caused a gel hidrophobisity and inhibiting release rate of active subtance (Sinko, 2006 : 519). A hidrophobisity also causes steric hydrance effect hydro so that inhibiting hydroxyl group interaction with its medium, that inhibits caffeine release rate.

Based on the result it concluded that, increasing propylene glycol leads to the increasing of lag time value and decrease the diffusion coefficient. The increased lag time value showed an inhibiting caffeine release rate from the gel basis up to thelimit between its base and membrane surface. Based on the statistical test of lag time and diffusion coefficient, each formula tested with various concentration of propylene glycol showed significant differences.

Caffeine gel preparation as anticellulite worked locally and didn't enter systemic circulation. Adding propylene glycol as humectant in gel preparation are expected to improve skin appearance in cellulite condition and to restrain caffeine release rate in order to keep it work locally and doesn't enter the systemic circulation.

## CONCLUSION

Based on the result of this research, can be concluded that :

1. Increased propylene glycol concentration gives significant effect to increase clarity, pH value, and viscosity value of caffeine gel preparation.
2. Increased 10% of propylene glycol concentration in the formula doesn't give significant effect of caffeine dissolution-% and DE-%.
3. Lag time value is increased and diffusion coefficient value is decreased, as result of increasing propylene glycol concentration.
4. The best formula is Formula III. It has the most clear physical characteristic, the longest release rate, and the less caffeine content, and best function as humectant.

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