PROCEEDING

The International Conference on Pharmacy and Advanced Pharmaceutical Sciences
Yogyakarta, Indonesia, 2009

Editors:

Pudjono
Hilda Ismail
Ronny Martien
Triana Hertiani
Ritmaleni
Preface from the Editor

The proceeding was produced based on papers and posters presented at the international Conference on Pharmacy and Advanced Pharmaceutical Sciences, held in Yogyakarta, Indonesia, 5 – 6 October 2009.

The proceeding clearly reflects broad interest; from there are participants coming from all around the world. Many contributions on Pharmaceutical Sciences there are quite a substantial number of papers on Pharmacist role in general. The papers presented file into a broad spectrum in Pharmaceutical sciences including Pharmacology, Toxicology, Analytical Chemistry and Drug Design, Drugs Synthesis, Formulation of Drugs, Pharmacy Social, Pharmacoepidemy, Traditional Medicine Natural Product Chemistry and Phytochemistry, etc.

In addition there are substantial numbers of paper deal with professional aspect of Pharmacist in general health care.

In this an opportunity, I would like to express my appreciation to the editorial team of the proceeding who have been working hard to review manuscripts, and making the first edition of this proceeding be possible.

I would like also to thanks to all invited speakers and presenters who participated in the International Conference on Pharmacy and Advanced Pharmaceutical Sciences and your contribution to this proceeding.

Finally, I hope this proceeding will give contribution to the advanced scientific research in the field of pharmaceutical sciences

Yogyakarta, July 2010

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Welcome Message
From the committee

Welcome to Yogyakarta

On behalf of the Scientific and Organizing Committees, it is a great pleasure for me to welcome all participants to Yogyakarta, to the International Conference on Pharmacy and Advanced Pharmaceutical Science 2009.

The international conference is organized by the faculty of Pharmacy UGM to celebrate its 63th anniversary and the Lustrum XII of Gadjah Mada University, as a collaboration work between the Faculty of Pharmacy UGM with the Nara Institute of Science and Technology (Japan) and the Universiti Sains Malaysia (Malaysia). In this conference 15 lectures within the field of Pharmaceutical Care and Advanced Pharmaceutical Science will be given by invited speakers. Besides, 55 posters and 75 paper will be presented in the parallels presentation sessions. Herewith, we express our gratitude to all speakers and presenter, who would like to share their advance knowledge in this scientific event.

The Organizing Committee gratefully acknowledges the Nara Institute of Science and Technology and the Universiti Sains Malyasia, for the nice collaboration in bringing forth this conference. A special acknowledgment is addressed to the Rector of Gadjah Mada University and the sponsors, for all supports that make this symposium possible. Furthermore, personally, I want to express my deep appreciation to the members of the Organizing Committee, for the good teamwork and their great effort given in the preparation for this symposium.

Finally, I wish all participants a scientifically rewarding and an enjoyable meeting in Yogyakarta.

Chairman

Dr. Hilda Ismail, M.Si., Apt.
Remark of the Dean Faculty

Assalamu’alaikum wr. wb.
Distinguished ladies & gentlemen.

First of all, on be half of the Faculty of Pharmacy Universitas Gadjah Mada, I would like come to all of you in Yogyakarta, thank you very much for your attention to come and to attend the international Symposium on Pharmacy and Advanced Pharmaceutical Sciences. I hope we are all in health condition.

Ladies and gentlemen,
The symposium is organized by the Faculty of Pharmacy UGM in collaboration with the Faculty of Pharmaceutical Sciences Universiti Sains Malaysia and the Nara Institute of Science and Technology Japan, and held as part to celebrate the 63th anniversary of the Faculty of Pharmacy UGM.
In the symposium, I hope we can communicate our recently information concerning social / clinical pharmacy and pharmaceutical sciences. I hope the symposium will be very fruitfull, very useful for all of us.
I addres special thanks to the plenary speakers both from domestic and aboard, the oral and poster presenters, as well as to those who come just to know the development of clinical or social pharmacy and pharmaceutical science. Your willingness to come, to communicate and to share your experiences is highly appreciated.

Special thanks also I address to my colleague the Dean of Faculty of Pharmacy USM who has been coordinating USM students to attend this symposium. The hope is not to set up networking between the pharmacy students of USM and UGM.

Therefore, during almost whole day discussing scientific matter related to human health and welfare, I hope we can make a wonderful opportunity to make a scientific closer relationship while we enjoy the cultural performances of Yogyakarta presented by our pharmacy student.

Finally, I hope that this meeting will give benefits to all of us, and we may see each other again in a similar event in the near future.

I look forward to thank you all for attending this event.

Wassalamu’alaikum wa rahmatullahi wa barakatuh,
Dean of Faculty of Pharmacy UGM

Prof. Dr. Marchaban, DESS., Apt.
Speech of the Senior Vice Rector  
For Education, Research and Community Services,  
Gadjah Mada University

Assalamu’alaikum wa rahmatulLahi wa barakatuh,

On behalf of the Rector, I would like to welcome all of you to our campus Gadjah Mada University and to our home town Yogyakarta. It is a great honor for me and Gadjah Mada University to host the Two-day International Conference on Pharmacy and Pharmaceutical Sciences that is conducted by the Faculty of Pharmacy, Gadjah Mada University. The increasing problems and new cases of some diseases in the world, both the infectious and the degenerative diseases, have demanded the development of medical and pharmaceutical sciences and technologies for supporting the developments of early detection methods of the diseases, the accurate diagnoses, as well as the appropriate and effective medications or therapy. Pharmaceutical Science and Technology have been developing very fast within recent years. The development trend shows using much more biotechnological approach in both diagnose establishment and medication administrations. For examples the usage of some serums, enzymes, hormones, vaccines, etc., and their recombinant products. The science and technology for finding prevention method against infectious diseases or degenerative diseases now have been developing so amazing, for example the usage of growth hormones, vaccines, and stem cells for it.

Gadjah Mada University has been committed to become World Class University; therefore international networking in education, research and publication is much needed. I really support to this international conference on Pharmaceutical Science and Technology which can keep us in touch with the state of the art of pharmaceutical science. I do believe that by conducting this kind of international meeting, we can get and exchange new information and best practices on pharmaceutical science and technology, and it is very important to inspire our young researchers and enhance our research networking internationally. In this occasion, I would like to express my great gratitude to all the guest speakers and speakers, who have contributed their advanced presentations in this international conference. I also would like to extend my gratitude to the Organizing Committee from the Faculty of Pharmacy, Gadjah Mada University, who has already successfully arranged this international conference. I would also thank to all institutions or companies who have sponsored and supported this conference.

Finally, have a fruitful conference and enjoy Yogyakarta. Thank you
Wassalamu’alaikum wa rahmatulLahi wa barakatuh,

Senior Vice Rector for Education, Research and Community Service  
Gadjah Mada University

Prof. Dr. Retno Sunarminingsih, M.Sc., Apt.
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**DISCUSSION**

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The Characteristics and Release of Diclofenac Sodium of Niosome System in Carbomer 940 Gel Base Preparation (Niosome System of Diclofenac Sodium - Span 60 - Cholesterol with Molar Ratio 1:5 :5)

Esti Hendradi*, Tutiek Purwanti, Bety Nurfia Puspitarini, Bianda Ida Kurnia

Department of Pharmaceutics of Faculty of Pharmacy, Airlangga University, Surabaya, Indonesia
Corresponding: esti_hendradi@yahoo.com

Abstract

The present study was designed to determine the characteristics and release of diclofenac sodium of niosome system in Carbomer 940 gel base preparation. The compositions of niosome was diclofenac sodium, Span 60 and cholesterol 1:5:5. Diclofenac sodium non niosome system was used as a control. The evaluation included organoleptic, pH and sodium diclofenac released test of each formula. The result of drug entrapment efficiency of this system was 73.32 ± 0.68%. The characteristics of gel preparation showed that niosomal system increases consistency, decreases pH of diclofenac sodium gel and also showed similarity of diclofenac sodium release compared with that control. The rate (flux) of diclofenac sodium release in control formula was 71.49 ± 3.96 µg/cm²/minute ½ and formula of the niosome system was 73.06 ± 2.01 µg/cm²/minute ½. It was analysed by statistic programmed SPSS 16.0 using independent-sample T-test with degree of believed 95% (α=0.05). The result showed that there was not a significant difference between each formula.

Key words: diclofenac sodium, niosome, Span 60, Cholesterol, flux released

Introduction

Diclofenac sodium is NSAID, the drug causes gastric irritation and undergoes hepatic first-pass metabolism (40-50%) (Ganiswara, 1995). Diclofenac sodium has log P 1.13 (Budavari et al, 2001), so it hydrophobic compound and has small solubility in water and distribution in the gel based not well. One of the methods used to increase distribution in the gel based by made vesicle, niosome (Choi and Maibach, 2005). Niosome is well documented for transdermal drug delivery. Niosome system is unilamellar or multilamellar vesicle where in an aqueous solution is enclosed in highly ordered bilayer made up of nonionic surfactant with or without cholesterol and dicetyl phosphate (Biju et al, 2006). The recent study, to improve the released of diclofenac, a niosome composed of Span 60, cholesterol was prepared. The factor that influence on characteristics include size of noisome vesicle, entrapment efficiency (Ep) and released was amount, type of surfactant (HLB) and it contain of cholesterol (Patel, 2005). The research of Shabwala and Misra (2002), niosome made from active compound of Nimesulid and used Span 20-cholesterol with molar ratio 1:3:3 has given Ep 39,00 ± 0,001%, and using molar ratio 1:6:6 the value of Ep was 91,21 ± 0,010 %.

In this study, the influence of niosome system was made from diclofenac sodium, Span 60 and cholesterol with molar ratio 1:5:5 on preparation characteristics and released of diclofenac sodium from Carbomer 940 gel base was evaluated.

Methodology

Materials

Diclofenac sodium was obtained as a gift sample from PT Deka Medika, Carbomer 940 (Noveon Asia Pacific Ltd, Hongkong), Span 60 (Sigma), Cholesterol (Sigma), KCl (E.Merck), NaCl p.a (E.Merck), NaH2PO4.12 H2O p.a (E.Merck), KH2PO4 p.a. (E.Merck). trietanolamin was purchased from PT. Tristar. Compound was used without mention the specification was a pharmaceutical grade.
Preparation and characterization of niosome

The composition of niosome system showed in Table 1 and the formulation of sodium diclofenac gel preparations showed in Table 2.

Table 1. The composition of noisome system.

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<td>Diclofenac Sodium</td>
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<td>0.2002 g</td>
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<tr>
<td>Span 60</td>
<td>5</td>
<td>1.3301 g</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>5</td>
<td>1.2201 g</td>
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<tr>
<td>Chloroform</td>
<td>-</td>
<td>10 mL</td>
</tr>
<tr>
<td>Aqua free of CO₂</td>
<td>-</td>
<td>9 mL</td>
</tr>
<tr>
<td>PBS pH 7.4</td>
<td>-</td>
<td>6 mL</td>
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</tbody>
</table>

Niosomes were prepared by using Reverse Phase Evaporation Technique (REV). The molar ratio of diclofenac sodium, Span 60 and cholesterol is 1:5:5. Drug, non ionic surfactant and Cholesterol were weighed as indicated in Table 1. Cholesterol and Span were dissolved in chloroform, diclofenac sodium in 9 mL aquaest than mixed and sonification at temperature 4-5°C for 16 minutes. The mixture was added 6 mL PBS pH 7.4 ± 0.05 and sonification again 12 minutes. Than the mixture was rotavaporated at 40°C, 200 mmHg until chloroform disappeared (+ 1.5 h) and the end evaporated using waterbath at 60°C until 15 minutes to make the concentrated suspension of niosome system. The diclofenac sodium of niosome system was analyzed for percent drug entrapment by spectrophotometric method.

The niosome system than adding the Carbomer gel with the composition as indicated in Table 2.

Table 2. The formulation of diclofenac sodium preparation.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Concentration</th>
<th>Control</th>
<th>Niosome System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac Sodium</td>
<td>0.2001 g</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Span 60</td>
<td>1.3602 g</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>1.2201 g</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PBS pH 7.4</td>
<td>6 mL</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chloroform</td>
<td>10 mL</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Aqua free of CO₂</td>
<td>9 mL</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total amount of control component</td>
<td>12.344 g *</td>
<td>-</td>
<td>12.852 g**</td>
</tr>
<tr>
<td>Niosom with EP 75%</td>
<td>-</td>
<td>12.852 g**</td>
<td></td>
</tr>
<tr>
<td>Carbomer 940</td>
<td>0.1000 g</td>
<td>0.1000 g</td>
<td></td>
</tr>
<tr>
<td>TEA</td>
<td>0.2 mL</td>
<td>0.2 mL</td>
<td></td>
</tr>
</tbody>
</table>

* Total amount of the control after concentrated
** Total amount of niosome system
The Characteristics and Release of Diclofenac..............

Determination of the entrapment efficiency of diclofenac sodium in the niosome system.

The entrapment of diclofenac in the niosome system was calculated using equation 1:

$$E_p(\%) = \left[ \frac{(C_t - C_f)}{C_t} \right] \times 100\% \ldots \ldots \ldots (1)$$

where,

$E_p$: diclofenac sodium entrapment in the niosome system
$C_f$: concentration of diclofenac free (un entrapped)
$C_t$: total concentration of diclofenac sodium in the formulation of niosome system.

Determination of pH on the formulation

The pH of preparation was done by mixed the preparation in the aqua free of CO$_2$ in ratio 1:9. Mix well and then the pH of preparation was measured using pHmeter.

Determination of diclofenac released from the preparation.

Permeation study was performed apparatus 5 paddle over disk completely with diffusion cell (Figure 1) at 37°C for 6 h. As a membrane was cellophane and as donor compartment was filled by preparation of niosome system in Carbomer 940 gel. As receptor solution was phosphate buffer saline pH 7.4. At the appropriate time sample was taken from receptor solution.

**Figure 1.** Apparatus 5-paddle Over Disk (The USP Convention, 2002)
Diclofenac concentration of sample solution was measured using Spectrophotometer. Released of diclofenac sodium was calculated using equation 2 (Higuchi, 1959).

\[
Q = \frac{q}{x} = \left[ D t (2A-Cs) Cs \right]^{1/2} 
\]

where,
\[
Q \quad : \text{flux of drug released} \\
D \quad : \text{coefficient diffusion of drug in} \\
\text{the based} \\
A \quad : \text{concentration of drug in the based} \\
Cs \quad : \text{solubility of drug in the based} \\
t \quad : \text{time}
\]

**Results and Discussions**

The morphology of niosome system showed at the figure 2 and 3.

![Figure 2](image1.png)  
**Figure 2.** Morphology of niosome system using light microscope (Olympus BX 41) with magnify 1000X.

![Figure 3](image2.png)  
**Figure 3.** Morphology of niosome system using Scanning Electron Microscope (Jeol tipe JSM T-100) with magnify 2000X.
The percent entrapment of diclofenac sodium in the niosome system was shown at Table 3.

Table 3. The entrapment efficient (Ep) of diclofenac sodium in niosome system

<table>
<thead>
<tr>
<th>Replication</th>
<th>% Ep</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>74.60</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>75.14</td>
<td>75.32 ± 0.68</td>
</tr>
<tr>
<td>III</td>
<td>76.23</td>
<td></td>
</tr>
</tbody>
</table>

The organoleptic of Carbomer gel of diclofenac preparation showed in Table 4.

Table 4. The organoleptic of diclofenac sodium in Carbomer gel preparations.

<table>
<thead>
<tr>
<th>Formula</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Consistency</td>
</tr>
<tr>
<td>Control</td>
<td>Fluidity</td>
</tr>
<tr>
<td>Niosome System</td>
<td>Smooth and Viscous</td>
</tr>
</tbody>
</table>

The pH value of diclofenac in Carbomer 940 preparations were shown at Figure 4.

Based on the statistical result of the pH using independent T-test that found the t calculated (2.980) > t tabel (2.776), it means there was significant different between control and niosome system preparation.

Flux is the most useful index to evaluate the released of drug. The cumulative amount of drug released was plotted as function of root time. From the result of linear regression of steady state condition I get flux at the slope.
Figure 5. The profile of diclofenac released from the Carbomer 940 gel preparations. Data was the mean of three replications ± SD. (●: Control; • Niosome System).

As shown in the Figure 5, the released profile shows the sufficient linearity with the coefficient $r$ was $\geq 0.98$.

Flux released of diclofenac sodium from Carbomer 940 gel base shown in Figure 6. In this Figure shown that the flux released of diclofenac from preparation of niosom system diclofenac sodium: Span 60: cholesterol with molar ratio 1:5:5 in Carbomer 940 gel base was insignificantly different compared with that of control. It caused the niosome system that used in the formulation was without separated the entrapment and not entrapment. So the profile was similar. Beside that maybe it caused the experiment was done only until 6 hours.

Figure 6. Flux released of diclofenac from Carbomer 940 gel base. Data was the mean of three replications ± SD.

From the results of the experiment we suggest that the experiment must done longer than 6 hours and the vesicle of niosome is separated from diclofenac sodium that is not entrapment in the vesicle.

As shown in the Figure 5, the released profile shows the sufficient linearity with the coefficient $r$ was $\geq 0.98$. 
Conclusion
The conclusions of the experiment were:
1. The drug entrapment efficiency (Ep) of the niosome system was 73.32 ± 0.68%.
2. The characteristics of gel preparation showed that niosomal system increased consistency, decreased pH of diclofenac sodium gel.
3. The flux of diclofenac sodium release in control formula was 71.49 ± 3.96 µg/cm²/minute\(^{1/2}\) and formula of the niosome system was 73.06 ± 2.01 µg/cm²/minute\(^{1/2}\). The statistic result of the flux of diclofenac released showed that there was not a significant difference between each formula.

References