Effects of Oil and Drug Concentrations on Droplets Size of Palm Oil Esters (POEs) Nanoemulsion

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Abstract: Aim of the present work is to study the effects of oil and drug concentrations on droplets size of a nanoemulsion. Newly introduced oil, palm oil esters (POEs) by Universiti Putra Malaysia researchers was selected for the oil phase of the nanoemulsion, because the oil was reported to be a good vehicle for pharmaceutical use. Nanoemulsions were prepared with different concentrations of oil and drug and their effects on droplets size were studied by laser scattering spectroscopy (Nanophox). The results of droplets size analysis shows the droplets size increase with increasing concentration of oil and drug concentrations. It can be concluded from this study, that oil and drug concentrations have an effect on the droplets size of POEs nanoemulsion system.

Key words: oil, drug, droplets size, nanoemulsion, palm oil esters

1 INTRODUCTION

Nanoemulsions are a class of emulsions with very small and uniform droplets size, typically in the range of 20~500 nm¹-². Due to their nano-size droplets nanoemulsions are transparent or translucent, resembling micro-emulsions¹. In contrast to micro-emulsions, nanoemulsions are not thermodynamically stable³, but they may have high kinetic stability because their small droplets size makes them stable against sedimentation and creaming³. The droplets size of a nanoemulsion is an important characteristic for evaluating a nanoemulsion¹,³. The droplets size of nanoemulsion could be affected by drug loading, oil and surfactant concentrations.

The oil selected to prepare the nanoemulsion in this study is palm oil esters (POEs), is modified oil from palm oil. Palm oil is derived from the fruit of the palm tree Elaeis guineensis and is rich in C₁₆ and C₁₈ fatty acids⁴. Palm oil consists of triglycerides, a combination of glycerol and different fatty acids. Alcoholysis of triglycerides from palm oil to produce palm oil esters using lipase as a catalyst is a relatively simple process⁵-⁷. The POEs is a new ingredient for pharmaceutical industry⁵-⁷.

Formulation and in vitro evaluation of POEs nanoemulsion for topical delivery have already been discussed in our previously published article⁸. In this paper we report the effects of oil and drug concentrations on droplets size in nanoemulsion formulated using POEs as oil phase.

2 MATERIALS

Ketoprofen was purchased from Eurochem Asia limited, China. Tween80® was chosen as the surfactant (Sigma pharmaceuticals, USA). Palm oil esters (POEs) was provided by co-researchers in Universiti Putra Malaysia. Water used in this study was distilled water.

3 EXPERIMENTAL PROCEDURES

3.1 Preparation of nanoemulsion

In this study nanoemulsions were prepared by spontaneous emulsification process (titration method) as reported by Sakeena et al. (2010)⁹. Palm oil esters and Tween 80®
are left for 30 mins under magnetic stirring 600 rpm at 25°C to mix thoroughly. Then weighed amount of ketoprofen was added into the solution and mixed thoroughly, until a clear dispersion was formed, which indicated that all the drug solubilization was completed. To the resulting mixture water was added drop by drop while mixing with the aid of magnetic stirrer at 600rpm and temperature of 25°C.

3.2 Nanoemulsion droplets size analysis

The droplets size distribution of the prepared samples were measured by laser scattering spectroscopy technique (Nanophox, SympaTec, Germany). The samples were placed in the temperature-controlled sample holder at least 5 min before starting the measurement. Light scattering was set at an angle of 90° and the temperature was maintained at 25°C. From each sample, three correlation functions were measured over periods of at least 450s. Second cumulant method of analysis was used to calculate the mean sample size according to the intensity of scattered light (Z-average diameter). The results are the mean and standard deviation (S.D.) of at least 3 measurements of the samples.

4 RESULTS AND DISCUSSION

Droplets size is the most important characteristic to classify an emulsion into a micro or a nanoemulsion. The define size of nanoemulsion are varies in literature. However a well accepted nano-metric droplet size, for nanoemulsion is in the range of 20~500 nm. In the present study the effect of oil content on droplets size were studied. The droplets size results obtained by Nanophox (SympaTec) are shown in Fig. 1. The droplets size of nanoemulsions prepared by mixing specified quantity of oil and water with different percentage of Tween 80® appeared to increase with the increase of oil content. This is clearly shown in Table 1; in the Table the change of diameter of the oil droplets of nanoemulsion with changing oil ratio is shown. The mean diameter of nanoemulsion droplets increased with the increasing concentration of oil in the formulations. The average droplets size of formulation containing 25% oil was 84.75 nm and was the lowest, while formulation containing 53% oil had an average droplet size of 131.37 nm was the highest. All of the nanoemulsion formulated had the droplet size in nano-range. Similar effects of oil with droplets size were observed by other researchers. All the blank formulations (without drug) had the droplets size in nano-range (Table 1 and Fig. 1). The droplets size results of these blank formulations are in agreement with the results obtained by other researchers on nanoemulsions produced by using POEs and non-ionic surfactants; Span 20® and Tween 60® without drug. The size of the nanoemulsion droplets produced was below 200 nm (ranging from 78~120 ± 2 nm and 105~180 ± 1 nm). The nanoemulsion delivery system is an effective formulation option, especially for poorly water soluble actives or drugs. The nano-sized droplets leading to an enormous increase in interfacial areas associated with nanoemulsion would influence the transport properties of the drug and has been shown to increase bioavailability and efficacy of a number of compounds. The result shown in Table 1 also shows that as the concentration of surfactant increases, the mean droplet diameter decreases. This could be due to...

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**Table 1** The mean droplet size of nanoemulsion produced based on formulae.

<table>
<thead>
<tr>
<th>Percentage of water, surfactant and POEs.</th>
<th>Mean droplets size diameter (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>37, 38, 25</td>
<td>84.75</td>
</tr>
<tr>
<td>30, 30, 40</td>
<td>113.74</td>
</tr>
<tr>
<td>23, 24, 53</td>
<td>131.37</td>
</tr>
</tbody>
</table>

**Fig. 1** Effect of oil percentage on droplets size. (A) 25% of oil, (B) 40% of Oil, (C) 53% of Oil
Effects of Oil and Drug Concentrations on Droplets Size of POEs Nanoemulsion

Table 2  Percentage of each components and ketoprofen in the nanoemulsion prepared and mean droplets size of the nanoemulsion.

<table>
<thead>
<tr>
<th>Percentage of Ketoprofen (w/w)</th>
<th>Percentage of Oil (w/w)</th>
<th>Percentage of Surfactant (w/w)</th>
<th>Percentage of water (w/w)</th>
<th>Mean droplet size of nanoemulsion (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>25</td>
<td>38</td>
<td>37</td>
<td>84.75</td>
</tr>
<tr>
<td>1.25</td>
<td>24.69</td>
<td>37.52</td>
<td>36.54</td>
<td>116.68</td>
</tr>
<tr>
<td>2.5</td>
<td>24.35</td>
<td>37.05</td>
<td>36.1</td>
<td>229.64</td>
</tr>
<tr>
<td>5</td>
<td>23.75</td>
<td>36.1</td>
<td>35.15</td>
<td>1049.62</td>
</tr>
</tbody>
</table>

higher concentration of surfactant enable it to cover and stabilise large total surface area resulted by the decrease in mean droplet size.

In the present study, different amount of ketoprofen (1.25, 2.5 and 5%) were added in nanoemulsion to study the drug effect. The formulation consisted of POEs and Tween 80® at the percentage of 25 and 38%, respectively. The percentages of all the components and mean droplets size of the nanoemulsion are shown in Table 2. The effects of ketoprofen on the average droplets size and distribution were studied by laser scattering spectroscopy (Nanophox). In the case of nanoemulsion prepared without ketoprofen, the mean droplet size was lowest and the size distribution was uniform (Fig. 2A). On the other hand with high drug concentration 5% ketoprofen, the droplets size was the biggest and the formulation was unstable (Fig. 2C). The results of this study clearly show that the average droplets size of these nanoemulsions increased when the concentration of ketoprofen increased (Table 2 and Fig. 2).

One hypothesis to explain the increased diameters of the oil droplets when concentration of ketoprofen in the nanoemulsion increased is that; ketoprofen may exhibit amphiphilic properties, a fraction of the drug molecules can incorporate itself as a spacer into the surfactant monolayer at the oil-water interface, leading to an increase in droplets size\(^1\). The other reason for the increase in nanoemulsion average droplets size when the drug content increased might be due to higher amount of drug present in the lipophilic core of surfactants. In addition to this, increase in size might be related to formation of the drug aggregates on the surface of oil droplets if the drug used was in excess and remained undissolved\(^2\).

5 CONCLUSION

This study proved that oil and drug concentrations have an effect on the droplet size of a nanoemulsion system. The results of droplets size analysis shows the droplets size increase with increasing concentration of oil, and increasing concentration of ketoprofen.

Fig. 2  Effect of drug concentration on droplets size. (A) Ketoprofen concentration 1.25%, (B) Ketoprofen concentration 2.5%, (C) Ketoprofen concentration 5%.

ACKNOWLEDGEMENT

The authors wish to thank Chong Kah Huong, Faculty of Science, University Putra Malaysia for her helpful comments and advice during the laser scattering spectroscopy analysis. NBD-Malaysia for the research grants allocation.
Universiti Putra Malaysia for preparing and supplying the POEs.

References