Aerosol-Ot Stabilized Micro and Nano-Scale Emulsions for Pharmaceutical Formulations

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Submission: December 15, 2017; Published: December 18, 2017

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Abstract

In this work we present the formation of micro- and nano-scale oil and water emulsion droplets stabilized by an anionic surfactant, Aerosol-OT. The stabilizing effects of AOT were tested with high and low molecular organic phase (oil), and in the presence and absence of ethanol acting as a co-solvent and emulsion enhancer. The key findings of this work are formation of -

a) Nano emulsions with lower molecular weight alkanes as the organic phase,

b) Micro emulsions in with higher molecular weight organic phase,

c) Stable emulsions over a period of 3 weeks in the absence of alcohol.

Keywords: Emulsions; Pharmaceuticals; Aerosol-OT; Octane; Hexadecane

Introduction

Emulsions of micro and nano sizes are used in topical applications for their increased bioavailability [1,2]. The smaller size of the droplets provides more surface area resulting in greater absorption of the pharmaceutical on the epidermal layer [3,4]. Aerosol-OT (AOT) is an anionic surfactant and is widely used as a stabilizer to form oil and water emulsions [5,6]. Due to its biocompatibility, AOT is also used in drug delivery and oral formulations and for the treatment of chronic constipation [7-12]. The objective of this work is to form stable micro and nano-scale emulsions which can potentially be used for drug delivery and pharmaceutical applications. We used octane (C8) and hexadecane (C16) as model organic phases to a) mimic the mineral oil which is also used as a laxative lubricant and b) demonstrate the ability of AOT to emulsify organics of different molecular weights [13]. Many emulsions based studies reported in the literature have used ethanol to stimulate the formation of the emulsion droplets by reducing the surface tension of water. Here, we report the formation of stable emulsions in the absence of ethanol, which is highly desirable in drug delivery and pharmaceutical applications. The resultant emulsions were prepared with equal ratios (by weight) of oil to deionized water. AOT constituted 60% by weight of the dispersant and was added to octane and hexadecane in the presence and absence of ethanol. Two different oil to water ratios-1:10 and 1:1 were tested. The formation of emulsions droplets, their size and stability were recorded by viewing them under an optical microscope for three weeks. The presence of emulsified phase in the vials were also visually inspected and reported through photographs in Figures 1 & 2. Table 1 summarizes the experimental test parameters such as oil/water ratio, type of oil (organic phase) used, and the resultant droplet size on Day 1 and Day 21 of the study.

Table 1: Experimental Matrix, Formulation Name and Size.

<table>
<thead>
<tr>
<th>Oil Used</th>
<th>Ratio of Oil to Water</th>
<th>Presence of Ethanol</th>
<th>Droplet Size (Day 1)</th>
<th>Droplet Size (Day 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Octane</td>
<td>1:1</td>
<td>Yes</td>
<td>48 nm</td>
<td>46 nm</td>
</tr>
<tr>
<td></td>
<td>1:1</td>
<td>No</td>
<td>158 nm</td>
<td>90 nm</td>
</tr>
<tr>
<td>Hexadecane</td>
<td>1:1</td>
<td>Yes</td>
<td>6.95μm</td>
<td>7μm</td>
</tr>
<tr>
<td></td>
<td>1:1</td>
<td>No</td>
<td>7.5μm</td>
<td>8.8μm</td>
</tr>
</tbody>
</table>
Conclusion

Aerosol-OT resulted in the formation of Oil-in-Water emulsion (O/W) in both octane and hexadecane organic phases. Such behavior is attributed to the HLB (hydrophilic lipophilic balance) value of the surfactant. The HLB value is a measure of balance between the hydrophilic and lipophilic groups on the surfactant. Values of HLB in the range of 8-18 favor the formation of O/W emulsions [14]. HLB of AOT is reported to be 10.5 at a critical micellar concentration of 0.64 mM [15]. Thus, it is inherent of AOT to form O/W emulsions. In the presence of ethanol and octane as the organic phase, nanoscale emulsions of droplet size between 46-48 nm were observed throughout the study which reflects on the stability of the droplets as observed in Figure 1 (a, b). Creaming of emulsions is observed with time as represented in Figure 1. Creaming occurs in oils which have lower density than water. The droplets concentrate due to their lower density tend to move upwards [15]. Creaming is not breaking of emulsion but separation of the emulsions into two, in which one emulsion has a richer dispersed phase than the other. The rate of creaming is can be estimated from Stokes’ law,

\[ v = 2r^2 \left( \rho - \rho_0 \right) g / 9 \eta \]

where, \( v \) is the rate of creaming, \( r \) is the radius of droplet, \( \left( \rho - \rho_0 \right) \) is the density difference between the droplet density and the density of the medium, \( \eta \) is the viscosity of dispersion and \( g \) is the acceleration due to gravity [16]. Thus, no significant change is observed in the stability and the volume of the emulsions and the droplets size remained unchanged during the experimental period indicating an absence of coalescence. The absence of ethanol and with octane as the organic phase (Figures 1c & 1d), the emulsions formed did not have any significant change in the volume of emulsions formed or in the droplets’ size of the emulsions.

The size of the droplets also remained in nanoscale (90nm on Day 21) which is suggestive of the fact that ethanol did not have a significant effect on the formation of the emulsion. With a higher molecular weight alkane (Hexadecane), micro emulsions of droplet size 5-8 µm are formed, and ethanol did not affect the formation of emulsions as shown in Figure 2. We attribute the difference in viscosity of both the oils as a factor for responsible for the formation of micro and nano scale droplet size. The viscosity of n-octane and hexadecane at 300 K is 0.51 mPa s and 2.89 mPa s respectively and that of the continuous phase (water).
is 0.85 mPa s. The higher ratio of νD/ηC (viscosity of dispersed phase by continuous phase) makes the droplets resistant to disruption by shear force. With higher viscosity of organic phase, droplets do not disrupt to smaller sizes and hence the size difference [17]. Our preliminary studies on using biocompatible and safe surfactants for the formation of stable micro and nano emulsions indicate that such systems can potentially be used for pharmaceutical applications. We demonstrated successful emulsions oil and water (1:1) formation with low and high molecular weight organic phases in the presence and absence of ethanol which is used as a co-solvent and emulsifier.

References


