

Study of surface activity of piroxicam at the interface of palm oil esters and various aqueous phases

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Abstract: The surface activity of some non-steroidal anti-inflammatory agents like ibuprofen was investigated extensively. This fact has attracted the researchers to extend this behavior to other agents like piroxicam. Piroxicam molecules are expected to orient at the interface of oil and aqueous phase. The aim of this study was, firstly, to assess the surface and interfacial tension behaviour of newly synthesised palm oil esters and various pH phosphate buffers. Furthermore, the surface and interfacial tension activity of piroxicam was studied. All the measurements of surface and interfacial tension were made using the tensiometer. The study revealed that piroxicam has no effect on surface tension values of all pH phosphate buffers and palm oil esters. Similarly, various concentrations of piroxicam did not affect the interfacial tensions between the oil phase and the buffer phases. Accordingly, the interfacial tension values of all mixtures of oil and phosphate buffers were considerably high which indicates the immiscibility. It could be concluded that piroxicam has no surface activity. Additionally, there is no surface pressure activity of piroxicam at the interface of palm oil esters and phosphate buffers in the presence of Tweens and Spans.

Keywords: Surface activity, palm oil esters, phosphate buffers, piroxicam.

INTRODUCTION

Generally, mixing of two immiscible liquids produces an interface having different characteristics from that of each liquid. This is due to the mutual effect of each liquid on the other. The imbalance between the inward and the outward attraction forces on the molecules at the surface results in an attractive forces pulling the surface molecules into the bulk (Hans Mollet and Payne, 2001). This imbalance usually refers to surface tension, which is the force per unit length required to counteract the inward bulky attraction forces.

On the other hand, similar imbalance of attractive forces also exists at the interface between two immiscible liquids, which is alternatively called the interfacial tension that is the force per unit length acting in a parallel to the interface of 2 immiscible liquids. In other words, interfacial tension reflects the mutual miscibility of each liquid in the other. Mathematically, interfacial tension is measured as: $\gamma_{12} = \gamma_1 + \gamma_2 - W_{ad}$. Whereas γ_1 and γ_2 are the surface tension of the first and second liquids, respectively W_{ad} is the work of adhesion (Sinko, 2006).

Work of adhesion is the energy needed to break the attraction between two liquids. On the other hand, work of cohesion is the energy required to break the attraction

of two sections in a liquid. The term spreading coefficient is basically employed to describe the difference between the magnitude of adhesion and cohesion work of two immiscible liquids. It represents the ability of immiscible liquids to spread on each other, in other words, the ability of oil to form a film on the aqueous phase rather than accumulating as globules or lens on the surface. Spreading coefficient is equal to $W_{adh} - W_{coh}$. Spreading coefficient is supposed to have an essential role in the spreading of creams and topical formulations on the skin. The surface activity of some non-steroidal anti-inflammatory drugs (NSAIDs) have been reported. Ibuprofen and bumefenac are weak acidic NSAIDs which may work as surface active agents under certain pH conditions at which these drugs are in the ionized form (Chakradhara *et al.*, 1992). It was found that Ibuprofen molecules could form micelles in water. The critical micelle concentration, cmc, of ibuprofen was detected to be 180 mM (Ridell *et al.*, 1999). Correspondingly, the surface activity of NSAIDs could be extended to their gastric irritation property. These agents may alter the lipophilic properties of the gastric phospholipids through their amphiphilic ability to incorporate and fluidize the lipid-lipid interactions of the phospholipid layer (Lenard *et al.*, 2006).

Nonetheless, piroxicam was found to have no surface activity at the aqueous surface. However, it was able to

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reduce the interfacial tension of the surface consisting of phospholipid and stearylamine. This reducing effect was supposed to be related to the surface pressure activity of piroxicam. In other words, piroxicam molecules are able to form certain molecular interactions with the interface ingredients which could press on the surface to reduce the potential of surface activity. These were mostly lipophilic interaction between the piroxicam and phospholipid and stearylamine chains (Klang *et al.*, 1996). This short article is discussing the surface pressure activity of piroxicam in the presence of different surfactants than the phospholipid and stearylamine.

The oil phase was the palm oil esters (POEs) which was synthesized by our colleagues group in UPM. POEs was synthesized by reacting of palm oil with oleyl alcohol and the reaction was catalysed by the use of lipase enzyme to produce POEs containing high molecular weight esters with an even number of carbon ranging from 12-32.

The aim of this study was to detect the interfacial tension values between palm oil esters, a newly synthesised oil, and different pH phosphate buffers and to calculate the spreading coefficient of the oil onto the aqueous phase. These measurement may indicate the degree of miscibility of the oil phase with various aqueous phases which is directly related to the occurrence of the Ostwald ripening (Cepak, 2004). Spreading coefficient of the oil also give an indication of the spreadability of the topical preparation on the skin (Sinko, 2006). Furthermore, most importantly, piroxicam surface activity was also studied by measuring its effect on the interfacial tension values between palm oil esters and the specified phosphate buffers.

MATERIALS AND METHODS

Materials

Potassium dihydrogen phosphate and sodium hydroxide were supplied by R&M Chemicals (UK). Orthophosphoric acid was supplied by BDH (UK). Palm oil ester was a gift from UPM. Tween 80 and Span 20 were purchased from Sigma-Aldrich (USA). Piroxicam was supplied by Novaltek Lifescience, Shanghai (China).

Methods

Tensiometer (white, Elec. Ins; Co., Ltd.) using the du nouy ring technique was used to measure the surface tension of all samples. Surface tension values of palm oil esters and phosphate buffers pH 4, 6 and 7.4, was determined individually. The surface tension of phosphate buffers pH 4, 6 and 7.4 containing piroxicam concentrations of 20, 10, 5, 2.5, 1.25 µg/mL, was also measured.

The interfacial tension between palm oil esters and phosphate buffers pH 4, 6 and 7.4 was also determined by tensiometer. Additionally, the interfacial tensions of the

same mixtures containing 1 w/w % surfactant mixture were also detected. The surfactant mixture used was Tween 80 and Span 20 at a ratio of 80:20. Phosphate buffers pH 4.0, 6.0 and 7.4 were prepared each containing different concentrations of piroxicam (20, 10, 5, 2.5 and 1.25 µg/mL) and 1 w/w % of surfactant mixture. The interfacial tension between these mixtures and palm oil esters was measured and all measurements were done in triplicate parallel trials.

In brief, the surface tension was measured by rotating the torsion knob attached to the torsion wire to adjust the instrument reading to zero. The liquids were poured into a clean glass container. The container was then placed on a movable table that can be moved upward and downward to adjust the attachment of the ring to the liquid surface. The ring was detached by rotating the knob and the calibrated dial reading was recorded.

Similarly, the interfacial tension was measured by the same procedure with the heavier liquid to be poured first into the glass container. The ring was adjusted to attach the surface of the liquid. The other liquid was applied slowly on the first liquid. The mixture was allowed to rest for 2 hours then the readings were recorded.

The spreading coefficient was measured using the following equation $\gamma_S - (\gamma_L + \gamma_{SL})$

Where: γ_S is the surface tension of the spreading liquid. While, γ_L is the surface tension of the sublayer liquid. γ_{SL} is the interfacial tension.

Graphpad software was used to determine the statistical differences between the performed measurements using t-test.

RESULTS

Table 1 shows surface tension measurements of palm oil esters and the phosphate buffers which were used as the external phases of the microemulsion systems prepared by our team (Abdulkarim *et al.*, 2010a). It could be seen that the oil showed lower surface tension value as compared to the buffers.

Table 1: Surface tension measurements of oil and phosphate buffers

Solvent	Surface tension (Nm/m)
Oil	34.5 ± 0.31
Buffer pH 4	50.6 ± 0.21
Buffer pH 6	52.5 ± 0.17
Buffer pH 7.4	55.0 ± 0.06

Mean ± SD, N=3.

Fig. 1 shows that various Piroxicam concentrations did not affect surface tension measurements at all pHs of the

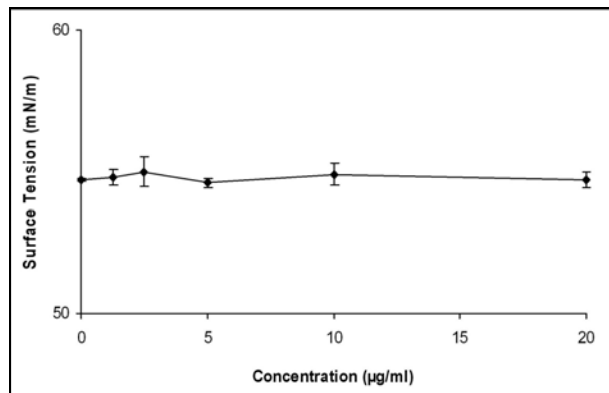


Fig. 1: Effect of piroxicam concentration on surface tension measurements of phosphate buffer pH 7.4. Mean \pm SD, N=3.

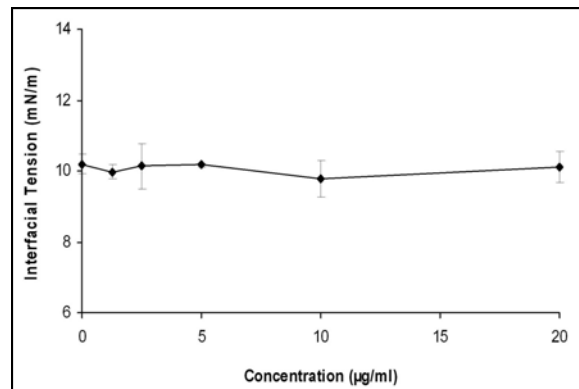


Fig. 2: Interfacial tension measurements of oil against phosphate buffer pH 7.4 containing 1% surfactant mixture and various piroxicam concentrations.

phosphate buffers and palm oil esters (fig. showing the surface tensions of pH 7.4 was only shown since data of pH6 and pH4 are similar to pH 7.4).

Interfacial tension measurements of oil against various pH phosphate buffers are shown in table 2. It can be seen that the interfacial tension values of all mixture of oil and phosphate buffers were similar and considerably high. These high values are the potential of the high immiscibility of the highly hydrophobic palm oil esters and phosphate buffers of pH 4, 6 and 7.4.

Table 2 shows that 1 w/w % surfactant mixture of Tween 80 and Span 20 (80:20) reduced the interfacial tension measurements of all mixtures of oil and buffers.

Additionally, piroxicam addition to the mixtures of palm oil esters and various buffers containing 1% surfactants mixture, were studied. Fig. 2 illustrates the interfacial tension values of the oil phase and pH 7.4 phosphate buffer (only pH 7.4 data was illustrated as these for pH 4.0 and pH 6.0 were similar to that of pH 7.4). The addition of piroxicam caused a very slightly reduction in the interfacial tension values.

Table 2: Interfacial tension measurements of oil against various phosphate buffers with and without 1% surfactants mixture of Tween 80 and Span 20 (80:20)

Solvent	Interfacial tension (Nm/m) without surfactant	Interfacial tension (Nm/m) with presence of 1% surfactant mixture	Spreading coefficient (Nm/m)
Oil- Buffer pH 4	48.7 \pm 0.30	10.2 \pm 0.23	-65.30 \pm 0.41
Oil- Buffer pH 6	49.65 \pm 0.12	10.2 \pm 0.26	-68.15 \pm 0.86
Oil- Buffer pH 7.4	51.0 \pm 0.36	10.1 \pm 0.42	-72.00 \pm 1.02

Mean \pm SD, N=3.

DISCUSSION

In general, the surface tensions of hydrophilic solvents are higher than that of the lipophilic solvents. This is due to the higher attractive forces resulting from H-bonds between hydrophilic solvent molecules as compared with the weaker van der Waals forces between lipophilic solvent molecules (Sinko, 2006). Table 1, fig. 1 exhibit that piroxicam does not possess any surface activity. Additionally, these measurements indicate that piroxicam interface behaviour is unlike some other NSAIDs such as ibuprofen which demonstrates a surface activity (Al-Saidan, 2004).

As shown in table 2, the high immiscibility between oil and water phases could be a reason to hinder Ostwald ripening phenomena which has the most destabilizing effect on microemulsion systems (Capek, 2004). This concept of Ostwald ripening can be further strengthened by the negative spreadability coefficient values obtained (table 2). These measurements can interpret the Ostwald ripening absence of the system containing palm oil esters as the internal phase and phosphate buffer as the external phase during the measurement of its stability (Abdulkarim et al., 2010b). Moreover, table 2 shows the effect of Tween 80 and Span 20 mixture on interfacial tension,

Surfactants mixture of Tween 80 and Span 20 with HLB value of 13.72 was found to be very efficient to reduce the interfacial tension in previous studies. The usage of mixture of Tween and Span to produce stable cream was established through many studies (Song *et al.*, 2000; Gullapalli and Sheth, 1999), since such mixtures of non-ionic surfactants can produce a closely tight layer around the dispersed droplets (Sinko, 2006).

Fig. 2 shows that piroxicam has insensible effect on interfacial tension measurement. The measurement of piroxicam solubility clarified that piroxicam is highly soluble at the interface of Tween 80 layer (Abdulkarim *et al.*, 2010). Piroxicam high solubility in Tween 80 seemed to be related to the interaction with polyoxyethylene chains of Tween 80. Furthermore, the amphiphilic nature of piroxicam makes it adsorbable at the interface of oil and aqueous phases (Sarathi *et al.*, 2009). Hence, piroxicam is supposed to get accumulated at the interface and therefore is expected to interact with the surfactant also presented at the interface (Yuan *et al.*, 2006). The tendency of piroxicam to increase the surface pressure at the interface was mentioned and it was used to explain the piroxicam on the interfacial tension of the system studied by Klang *et al.* (1996). Increasing the surface pressure at the interface of 2 immiscible liquids, reduces the interfacial tension between them (Rosoff, 1998).

However, piroxicam in this study had no reducing effect on the interfacial tension. It is supposed that the phenolic OH group of piroxicam has the ability to interact with the polyoxyethylene chains of the surfactant, while the hydrophobic part of the drug can orient itself into the hydrophobic part of the surfactants and the oil phase at the interface and to show a reduction in the interfacial tension measurement. However, in the present study, the addition of piroxicam to the system had no considerable effect on interfacial tension values. This can be due to the closed packed interface formed by the interaction of Tween 80 and Span 20 so that there was no more space for piroxicam hydrophobic part to be oriented at the interface to increase the surface pressure and thereby reducing the interfacial tension. On the other hand, it can be seen that the presence of the drug at the interface did not increase the interfacial tension measurements. Hence, it could be illustrated that the presence of piroxicam at the interface does not have destabilization activity on the system (Akoh, 1992).

CONCLUSION

This study shows that piroxicam molecules have no direct surface or interfacial activity. Moreover, it could be concluded that there is no molecular interaction between piroxicam and the surfactant mixtures of Tweens and Spans. The lack of interaction between the lipophilic chains of the ingredients of the drug and surfactants results in no surface pressure activity of piroxicam and no

reduction of interfacial tension. Additionally, the degree of miscibility between the newly synthesized palm oil esters and the phosphate buffers of various pH values were low indicating that the combination would yield a stable emulsion against Ostwald ripening.

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