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Short communication

Langmuir films study on lipid-containing artificial tears

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ABSTRACT

Lipid-containing artificial tears are a type of artificial tears that use lipid components in order to restore the lipid layer of the tear film. One of these components is lecithin which can be applied in spray solutions containing lecithin liposomes. In this work the behavior of three of these commercial tears based on lecithin, Innoxa, Opticalm and Optrex, are studied using the Langmuir technique. The obtained isotherms are presented, discussed and compared. This technique seems useful in order to see the film behavior of the lipid components of these tears and determine some important parameters such as fluidity and extension at the air-water interface, and allows us to discern differences between these commercial tears. Innoxa and Optrex tears are more similar to each other than to Opticalm tears. Opticalm presents more fluidity, probably due to the presence of more insaturations in the fatty acid chains of the phospholipids of the lecithin used in fabrication.

1. Introduction

The use of artificial tears is related with dry eye problems or ocular irritations [1–3]. Different types of artificial tears exist [4–6] and several studies have been reported on them [7–15]. One type of them is the lipid-containing artificial tears which help to repair or improve the lipid layer present in the outermost part of the tear film, and some studies have been reported in literature [7,16–18]. In these studies the artificial tears are used as eye drops. Several lipid-containing artificial tears are present on the market and commercialised by several companies. In the composition of some of these lipid-containing tears a phospholipid component (lecithin of soya), which is composed mainly of phospholipids such as phosphocholine (also named phosphatidylcholine or PC) occurs as a principal item. Lecithin of soya is obtained from soya grains by mechanical extraction or chemically using hexane. It has a high content of PC, especially refined lecithin, but also other lipids are present. The fatty acid chains present in these PCs are mainly palmitic or stearic, in C1, and oleic or linoleic, in C2. Refined lecithin is used mostly for pharmaceutical applications and research. In commercial lipid-containing artificial tears others components are also present.

The film formation at the water/air interface (Langmuir film technique) has been applied to study the behaviour of Meibomian lipids [19–23] and especially to study the interaction of them with lachrymal proteins [24–27]. The Langmuir technique has been applied previously by the author to study the behaviour of lipid and phospholipid films [28,29]. In this work Langmuir films have been obtained from lipid-containing artificial tears and the corresponding surface pressure-area isotherms registered. Three commercial lipid-containing artificial tears have been used, Innoxa, Opticalm and Optrex, the composition of which is shown in Table 1. These tears are supplied in little bottles for liposomal ocular spray applications. To the knowledge of the author, it is the first time that a Langmuir film study has been performed on lipid-containing artificial tears supplied as sprays.

2. Materials and methods

2.1. Materials

Commercial lipid-containing tears are those of Innoxa (Manufacturer: Optima Pharmazeutische GmbH, Distributor: Omega Pharma España), Opticalm (Manufacturer: Medena AG, Distributor: Omega Pharma) and Optrex (Manufacturer: Optima Medical Swiss AG, Distributor: Reckitt Benckiser Healthcare). Their composition is indicated below (Table 1). It is seen that a priori the composition of all the products is the same or similar. These products are supplied as ocular sprays. Water was ultrapure Milli-Q (18.2 MΩ cm), NaCl and chloroform were of analytical grade.

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Table 1
Composition of three commercial lipid-containing artificial tears.

Composition in 1 mL	Innoxa (Optimyst)	Opticalm (Lipomyst)	Optrex (Actimist)
Lecithin of soya	10 mg	10 mg	10 mg
Sodium chloride	8 mg	2.8 mg	8 mg
Ethanol	8 mg	8 mg	8 mg
Phenoxyethanol	5 mg	–	5 mg
Vitamin A-palmitate	0.25 mg	0.25 mg	0.25 mg
Vitamin E	0.02 mg	0.02 mg	0.02 mg
Purified water			

2.2. Techniques and equipment

The isotherm experiments have been done in a NIMA Teflon trough, model 1232D1D2 (area 1200 cm^2), with two movable barriers and using a Wilhelmy plate to measure the surface pressure. The linear velocity of the barriers was 2.5 cm/min, which mean 50 cm^2/min in the trough used. The Teflon trough and barriers were cleaned with chloroform and ultrapure water. The Brewster angle microscopy images were captured with a MicroBAM microscope from NIMA-Nanofilm, with lateral resolution of 8 μm.

As the volume sprayed from the commercial ocular sprays is not well controlled, and in addition the amount sprayed each time is so large, the experiments with control of the volume were done in the following way: several sprays were collected in a vial and the desired volume of the artificial tears was taken with a microsyringe and extended onto the subphase, as usual in Langmuir film formation. Experiments were conducted at room temperature of 23 °C.

3. Results and discussion

Fig. 1A shows the isotherms obtained spreading 15 μL of Innoxa (a), Optrex (b) and Opticalm (c) tears on water subphase. In order to discus the isotherms in more depth, the area in the *X*-axis has been transformed to area per molecule assuming the concentration indicated in the product and that the phospholipid present in the lipid tears is POPC. This is an arbitrary selection but is in accordance with the composition reported previously for lecithin of soya, and the selection of another PC does not significantly change the discussion since the molecular weight is not much different. In the tear composition other surface active compounds are also present (vitamin A and E) but in a much lower concentration, and for that reason they have not been considered in the calculation of the area per molecule. It is seen in Fig. 1A that for Innoxa and Optrex tears the initial surface pressure was 0. On the contrary, the Opticalm tear showed a non-zero initial surface pressure. The isotherm position for Optrex tear is between those of Innoxa and Opticalm, though closer to Innoxa. The characteristic values of the isotherms are shown in Table 2.

Fig. 1B presents the inverse of the compressibility modulus, Eq. (1), for the isotherms of Fig. 1A. This parameter is more suitable to compare the three tears because according to Eq. (1) the use of area or area per molecule does not affect the calculated values of C_s^{-1}. In respect to compressibility, Optrex is also closer to Innoxa than to Opticalm. All the tears show low values of C_s^{-1} which corresponds to a liquid expanded state [30], that is, the phospholipids are not organized enough in the film and conserve certain fluidity.

$$C_s^{-1} = -A\left(\frac{d\pi}{dA}\right)_T \quad (1)$$

The collapse is attained as a plateau at surface pressures around 44–49 mN/m. All cycle isotherms present hysteresis when the collapse is reached, but the hysteresis is small if the collapse is not reached or it is just at its beginning (see Fig. S1 in Supplementary material). Isotherms have also been obtained in a saline subphase (0.9% NaCl concentration, as occurs in natural tears) and no significant influence of this subphase has been observed. Opticalm has a NaCl concentration lower than that of Innoxa and Optrex, but according to the previous observation the difference observed in the isotherms cannot be due to NaCl. Observing Table 1, a significant difference in composition is that Innoxa and Optrex contain phenoxyethanol, while Opticalm doesn't. Phenoxyethanol is usually used as a preservative and has a certain surface activity, but as this compound is not present in Opticalm it cannot be responsible for the higher surface activity of Opticalm.

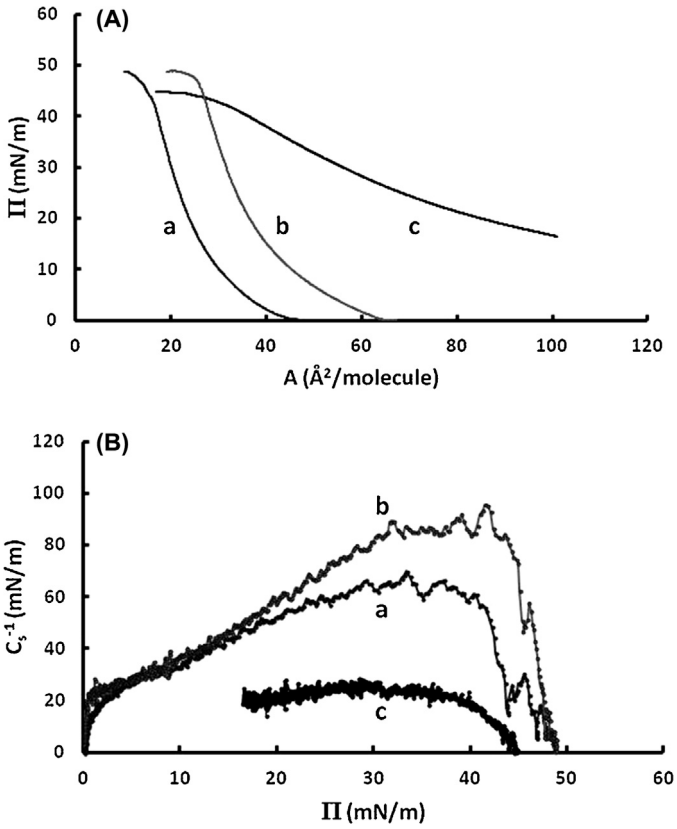

Fig. 1. (A) Surface pressure–area isotherms for the lipid-containing tears: (a) Innoxa, (b) Optrex, (c) Opticalm. (B) Inverse of the compressibility modulus for the isotherms of (A).

Table 2 shows the values of several isotherm parameters found in literature for several PCs in order to compare these values with those of the isotherms reported here for the lipid-containing tears. Before proceeding to the discussion, a consideration is needed. Even though vitamin A [35,36] and vitamin E [37,38] are surface active, their concentration is low in respect to lecithin (PC), in a ratio lower than 3%, and thus the major contribution is due to PC. In references [37,38] it can be seen that the influence of tocopherol (vitamin E) on POPC or *Escherichia Coli* lipid extracts is small even though tocopherol was present in a molar fraction of 0.25 or 0.20.

The collapse area observed in all the tear isotherms is less than that of POPC [30] and other PCs (see Table 2) which could indicate that part of the lipid is still in a bilayer state, that is the liposomes present in the product are not completely extended as a monolayer when deposited on the water surface. Thus, the values of Π at the collapse and C_s^{-1} can be discussed more confidently than the area values. Another fact that points to the presence of a partial bilayer is that when spreading lower volumes of tear, the lift-off area (expressed in area per molecule) in the isotherm increases or the isotherms shift to higher area per molecule values (see Fig. S2 in Supplementary material), which is due to a better extension of the