Effects of nonsteroidal anti-inflammatory drugs (NSAID) on the structure of a DPPC membrane: relevance to their toxic effects

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Objectives

Non Steroidal Anti-inflammatory Drugs NSAIDs are one of the worlds most prescribed group of drugs for acute and chronic inflammatory conditions, and their continuous use is associated with several gastric toxicity. The development of novel NSAIDs showing less serious side effects will depend on the understanding of the processes initiating and promoting gastric injury. Despite the complexity of the acid resistance properties of the gastric inner surface, the extracellular lining of surfactant-like phospholipids on the surface within the mucus gel layer represents an initial line of defence of the stomach. NSAIDs may chemically associate with phospholipids and destabilize them from the mucus gel layer. The aim of the present study was therefore to investigate the ability of NSAIDs to bind to or to penetrate into layers of surface-active phospholipids. The results may explain the compromising effects on the integrity of the gastric mucosal barrier.

Achievements

Two different NSAIDs (nimesulide and piroxicam) were studied. Using the liquid surface spectrometer at BW1, the structure of the condensed phase at the air/water interface has been analysed by Grazing Incidence X-Ray Diffraction (GIXD) at several film pressures (20, 30 and 40 mN/m) of the DPPC spread on a HEPES buffer (pH 7.4). Pure DPPC exhibits three diffraction peaks indicating an oblique lattice structure. The effect of the two drugs studied is very similar and at all the surface pressures, there are two Bragg peaks, one at zero Qz and the other at Qz>0 which are typical of alkyl chains organized in a distorted hexagonal (centered rectangular) lattice. As the film pressure increases, the second peak moves towards smaller Qz values: the distortion of the lattice and the tilt angle decrease. Consequently, NSAIDs are incorporated into DPPC lattice and induce a rearrangement of the chains to a more upright orientation with respect to the normal to the interface (Figure 1).

	π (mN/m)	Q_{xy} ($Å^{-1}$)	Q_z ($Å^{-1}$)	d (Å)
DPPC	20	1.46	0.00	4.30
		1.30	0.80	4.83
	30	1.35	0.75	4.66
		1.38	0.61	4.55
		1.47	0.14	4.28
	40	1.37	0.63	4.57
		1.41	0.49	4.47
		1.47	0.14	4.26
DPPC + PIROXICAM	20	1.46	0.00	4.29
		1.34	0.71	4.71
	30	1.47	0.00	4.28
		1.37	0.64	4.58
	40	1.41	0.59	4.47
		1.47	0.01	4.27
DPPC + NIMESULIDE	20	1.47	0.00	4.28
		1.36	0.75	4.64
	30	1.47	0.00	4.27
		1.38	0.65	4.55
	40	1.41	0.00	4.47
		1.48	0.59	4.25

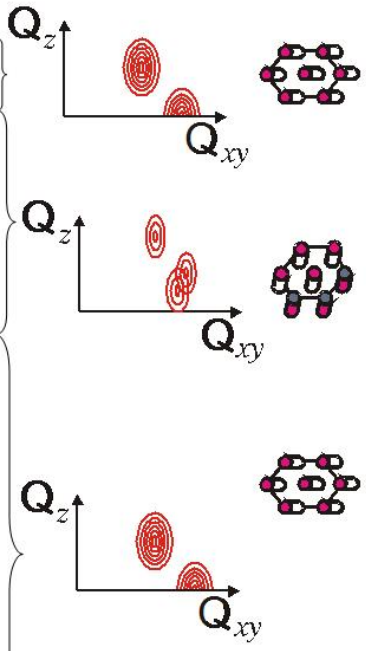

Figure 1: Diffraction peak positions of the monolayers of DPPC on aqueous buffered subphase or subphase containing the NSAIDs nimesulide and piroxicam at different surface pressures and at 20º C. The in-plane (Q_{xy}) and out-of-plane (Q_z) of the scattering vector Q are given by selected best-fit values .