P49

The influence of different media on the physical stability of bilosomes

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Objective. To assess the physical stability of bilosomes prepared with different concentrations of sodium deoxycholate (NaDC) in the presence of different media.

Methods. 5,6-Carboxyfluorescein (CF)-loaded bilosomes were prepared by the rotary film evaporation method. Phosphate buffered saline (PBS, 200 mmol, pH 7.4) containing 100 mM CF and different NaDC concentrations (0, 6.3, 12.5, 25 and 50 mM) was added to a lipid film composed of 150 µmol lipid mixture (glycerol monopalmitate : dicetyl phosphate : cholesterol, 4.5:4.5:1 molar ratio) and shaken. The resulting vesicles were extruded through a polycarbonate membrane (0.8 µm pore size). Vesicle stability was assessed over 4 h by determining the leakage of encapsulated CF in the following media: fasted state simulated intestinal fluid (FaSSIF); fed state simulated intestinal fluid (FeSSIF); simulated gastric fluid (SGF), simulated gastric fluid with pepsin (SGF_{pepsin}). PBS was used as control.

Results. Table 1. The percentage of CF retained (ret) in bilosomes made with different concentration of NaDC (mM) after incubation at 37°C in the presence of different media for 4 h, (mean ± S.D., n = 3).

Medium	NaDC concentration (mM) used to make bilosomes				
	0 mM	6.3 mM	12.5 mM	25 mM	50 mM
	CF ret (%)	CF ret (%)	CF ret (%)	CF ret (%)	CF ret (%)
FaSSIF	53.5 ± 8.9	68.2 ± 11.4	95.0 ± 1.5	95.2 ± 1.1	96.3 ± 1.3
FeSSIF	35.3 ± 1.2	33.0 ± 3.6	80.9 ± 3.8	75.7 ± 5.1	80.0 ± 4.1
SGF_{pepsin}	36.3 ± 7.9	50.0 ± 6.8	49.7 ± 0.3	45.9 ± 7.8	85.2 ± 2.8
SGF	98.4 ± 0.2	99.1 ± 0.3	99.7 ± 0.9	99.6 ± 0.9	99.6 ± 0.9

Discussion. The results suggest that bilosomes prepared with ≥ 12.5 mM NaDC which is above its critical micelle concentration (CMC) of 6 mM, are more stable in physiological media than bilosomes prepared with NaDC concentration of 6.3 mM which is close to its CMC and bile salt-free vesicles. Therefore, bilosomes may be suitable as oral drug delivery systems under fasted and fed conditions.

P50

Genetic variations at activator protein-1 among patients with steroid-insensitive asthma

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Objective. Corticosteroids, a group of potent anti-inflammatories, are the corner stone of current anti-asthma therapy. However, there are suggestions that some inflammatory pathways (e.g. activator protein-1 (AP-1)) are not efficiently suppressed by existing corticosteroid therapy. This study was designed to investigate the relationship of some common genetic variations in AP-1 with treatment responses to corticosteroids in asthma.

Methods. Asthma treatment outcomes following corticosteroids, categorised as steroid-insensitive asthma or steroid-sensitive asthma, were determined according to the American Thoracic Society guidelines (2000). Blood and induced sputum samples were collected from subjects for differential cell analysis, for the determination of the nature of airway inflammation. DNA was extracted from the blood samples and analysed for single nucleotide polymorphisms (SNP) at AP-1 related genes. Haplotype analysis was also performed on 16 SNP on c-Jun-N-terminal-kinase gene.

Results. Twenty subjects were recruited (7 steroid insensitive asthma sufferers and 13 steroid sensitive asthma sufferers). The differential white cell counts from sputum samples showed a greater percentage of eosinophils compared to non-asthmatic subjects, but no significant difference in differential cell analysis were observed between the two group of subjects. Five common haplotypes (frequency >5%) were identified among the subjects, with no significant difference in their presentation between the two groups ($p>0.10$).

Discussion. The common genetic variations at AP-1 and c-Jun-N-termial kinase gene were not found related to asthma treatment outcomes with corticosteroids. However, this finding is believed to be critically influenced by the nature of airway pathology, where no significant difference in airway inflammation between the two groups of subjects was identified (indicated by sputum eosinophil counts). The effect of other genetic variations (not measured in this study) should also be taken into consideration. In addition, the small sample size had significantly reduced the power of this study.