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## Toxicological profiles and surface properties at physiological pH of N-decanoyl amino acids

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**Purpose.** N-acyl amino acids based surfactants are an attractive class of anionic amphiphiles alternative to sulphate-based surfactants potentially employed as excipients in all pharmaceutical applications at which an anionic surfactant (eg. sodium dodecyl sulphate SDS) is needed [1, 2]. The aim of this work is to correlate surface properties of N-decanoyl amino acids at physiological pH and their toxicological profile in order to explore the potential use of these surfactants for pharmaceutical applications.

**Methods.** A series of N-decanoyl amino acids with different polar heads (leucine, methionine, serine and proline) was synthesized and characterized in isotonic phosphate buffer pH 7.3 in term of surface properties and cell toxicity in comparison to SDS, a common and widely employed surfactant in pharmaceutical formulations. Three different cell lines (Caco-2, A549, Calu-3) and erythrocytes were selected as model for oral, respiratory or parenteral administration in order to evaluate surfactant cellular toxicity (MTT, LDH, hemolytic assay).

**Results.** The different polar heads did not strongly affect surface properties of surfactants, differently to their cell toxicity profiles which were specifically influenced by the structure of the amino acid polar head. According to cell toxicity assays, all N-decanoyl surfactants resulted to be less toxic than SDS. In particular, cell viability (MTT assay) was found to be dependent on the hydrophobicity of the lateral group of the amino acid in all tested cell lines, while LDH and hemolytic assay highlighted the low effect of N-decanoyl amino acid on disrupting cell membranes.

**Conclusions.** Overall, such results suggested that hydrophilic interactions between amphiphiles and cell membranes play a key role in determining cellular toxicity.

[1]Pinazo A, Pons R, Pérez L, Infante MR. 2011. *Industrial & Engineering Chemistry Research* 50: 4805-17

[2]Moran MC, Pinazo A, Perez L, Clapes P, Angelet M, et al. 2004. *Green Chemistry* 6: 233-40