Metabolic Capacities of in vitro Alternatives for Chemical Testing in Skin: Insights from the COLIPA Skin Metabolism Project

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Human skin represents a large contact site for all kinds of potentially harmful substances. The relevance of testing chemicals for skin irritation, sensitization and genotoxicity in cosmetics is unquestioned, but using animals for that purpose will be prohibited in the EU from 2009 on by the 7th Amendment to the EU Cosmetics Directive. Skin models as alternative testing methods exist, but little is known about the differences in their xenobiotic metabolism capacities compared to human skin.

Therefore, the aim of this study is to characterize enzymatic activity of human skin compared to the following skin cell-derived *in vitro* models: keratinocyte-based cell lines, primary keratinocytes and a three-dimensional epidermal model. Skin was processed to yield cytosolic and microsomal extracts, while the epidermal model was examined in intact form as well as in cytosolic and microsomal preparations.

Phase I detoxification enzymes assayed in our project include Cytochrome P450 (CYP) and Cyclooxygenases, while phase II activity tests are carried out for GST, NAT and UGT. Obtained results of undetectable basal CYP activity were consistent in skin and all models. Production of PGE2 metabolites was measurable in cell lines and epidermal model and will be checked for skin extracts. Preliminary results of phase II detoxification enzymes indicate a good correlation of human skin and skin models in the detoxification of chemicals.

Our findings will help evaluating the potential of these *in vitro* models to serve as alternative toxicological screening methods for human skin.