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Correlation of the allergenicity and tolerogenicity of two cow’s milk protein products with their intestinal uptake – a study in Brown Norway (BN) rats

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Background: It remains largely unknown which features of food proteins that render them allergenic versus tolerogenic. However, it has been suggested that protein-chemical properties, in particular aggregation status, affect protein uptake in the intestine, and that uptake route may impact on the risk of sensitisation. The aim of this study was to investigate the interplay between protein-chemical features, the allergenic versus tolerogenic properties and the intestinal uptake of two whey products.

Method: The allergenic versus tolerogenic capacity of a heat-treated whey product, containing partly denatured and aggregated proteins, was compared to the same untreated product in BN rat models of: 1) i.p. and 2) oral sensitisation, 3) oral primary prevention and 4) oral desensitisation. Elicitation was measured by in vivo tests and antibody responses by ELISAs. The intestinal uptake was compared by quantifying BLG levels in small intestinal tissues at different time points after oral dosing of the two products in naïve BN rats. The findings were supported by in vitro uptake experiments in cell cultures.

Results: Unmodified and heat-treated whey had similar tolerance inducing and de-sensitising capacity, but the sensitising and eliciting capacity of the heat-treated product was significantly reduced compared to the untreated product, despite the immunogenicity of the two products were similar. Collectively the in vivo and in vitro uptake experiments suggested that uptake kinetics and the major intestinal uptake route differed between the two products.

Conclusion: Heat-treatment, which induced partly protein aggregation, changed the immunological properties of a whey protein product. This might in part be explained by the different intestinal uptake of the unmodified and heat-treated products. The heat-treated product had a reduced allergenicity combined with a high tolerogenicity, which highlights this product’s promising potential for induction of cow’s milk tolerance.