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Digested BLG can induce tolerance when co-administered with intact BLG in Brown Norway rats

Katrine L. Bøgh[1], Vibeke Barkholt[2], Charlotte B. Madsen[1]

[1]National Food Institute, Division of Toxicology and Risk Assessment, Technical University of Denmark, Søborg, Denmark.
[2]Department of Systems Biology, Enzyme and Protein Chemistry, Technical University of Denmark, Lyngby, Denmark.

Background: Milk is a major constituent of small children's diet. Milk allergy is also one of the most common allergies in small children. Prevention, treatment and general understanding of this allergy are therefore important.
Methods: Intact BLG was digested in an *in vitro* model simulating the human gastro-duodenal digestion process. Four different fractions of BLG-digest was made, based on sizes of peptides or aggregates hereof. Intact BLG and the four fractions of BLG-digesta were characterized by protein chemical analyses. Brown Norway (BN) rats were immunised i.p. three times without the use of adjuvant with either PBS (control), 200 µg of intact BLG, 30 µg of intact BLG, 200 µg of digested BLG (with 30 µg of intact BLG), 200 µg of digested BLG, 200 µg of a fraction of large complexes or 200 µg of a fraction of small complexes (all three without intact BLG). Sera from BN rats were analysed for specific IgG and IgE responses and avidity of specific antibodies was measured.
Results: Native BLG is relatively resistant to digestion. However, when first broken down to larger fragments these are rapidly digested to smaller peptides of sizes ≤ 4.5 kDa. The small peptides did aggregate to complexes of larger sizes. Specific antibody responses revealed that both the high (200 µg) and low (30 µg) amount of intact BLG had both immunogenic and allergenic sensitising capacity, while digested BLG had no sensitizing capacity. In contrast digested BLG and the fraction of large complexes retained their antibody binding capacity. Most importantly, while intact BLG showed a significant sensitising capacity when administered alone, the sensitising capacity of the intact BLG was significantly reduced when co-administered with digested BLG.
Conclusion: Co-administration of intact and digested BLG reduced sensitising capacity of intact BLG, indicating induction of tolerance or other protective mechanism by the digested BLG.