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The role of SCFAs to reduce endotoxin and asprosin induced inflammation in human lung epithelial and adipocyte cells

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Weight gain in obesity is known to exacerbate chronic inflammation, which in turn may worsen symptoms related to comorbidities including asthma. The source of this inflammation may arise internally, due to pro- inflammatory adipokines or gut permeability, which allows pro-inflammatory factors to cross into the bloodstream [(1)]. Endotoxin, found on the outer membrane of gram-negative bacteria, is known to induce inflammation in obesity [(2)]. A novel adipokine asprosin is also increased in obesity and may exacerbate other inflammatory diseases [(3–4)]. Current treatments for asthma only relieve symptoms rather than targeting inflammation at the source. Prebiotics may offer a dietary method to mitigate inflammation directly through the improvement of gut heath, reducing the severity of associated diseases. Prebiotics are non-digestible carbohydrates that increase the number of beneficial bacteria in the gut and produce anti-inflammatory metabolites called short chain fatty acids (SCFAs). This study aims to determine the role of SCFAs (acetate, butyrate, and propionate) on endotoxin and asprosin induced inflammation in lung and adipose tissue, in order to explore the mechanisms of prebiotics as a potential treatment for asthma. Human airway epithelial cells (BEAS2B-R1) and human adipocytes (Chub-S7) were treated over time (6, 12, 24hrs) with 100ng/mL endotoxin (lipopolysaccharide; LPS) or 10ng/mL asprosin to induce inflammation, and/or a mixture of SCFAs (2 mM acetate, 0.25 mM butyrate, 0.25 mM propionate). Protein and gene expression of inflammatory markers in the nuclear factor kappa-light-chain-enhancer of activated B cells (NFkB) pathway were measured by western blot (n = 6) and RT-qPCR (n = 6).In airway epithelial cells, SCFAs were able to reduce LPS-induced inflammation, through reduction of NFkB gene expression (↓74%, 12hrs, $p < 0.05$) and inhibitor of nuclear factor kappa-B kinase subunit beta (IKKb) protein expression (↓60%, 24hrs, $p < 0.001$). SCFAs also reduced asprosin-induced inflammation in airway epithelial cells, by reducing NFkB gene (↓54%, 24hrs, $p < 0.05$) and protein expression (↓55%, 12hrs, $p < 0.001$), IKKb protein expression (↓49%, 24hrs, $p < 0.01$), and gene expression of pro-inflammatory interleukin-8 (IL-8; ↓57%, 12hrs, $p < 0.01$). Furthermore, SCFAs reduced asprosin gene expression by 72% (12hrs, $p < 0.05$). In adipocytes, SCFAs were able to reduce NFkB protein expression at 24hrs in cells treated with LPS (↓61%, $p < 0.01$) and asprosin (↓56%, $p < 0.05$). Although LPS was able to increase the gene expression of NFkB (4.6-fold, $p < 0.0001$) and IL-8 (63-fold, $p < 0.0001$) within 6hrs, SCFAs were unable to mitigate this inflammation. SCFAs were however able to reduce NFkB gene expression compared to the control (↓26%, 12hrs, $p < 0.01$).These findings suggest that SCFAs have the capacity to mitigate endotoxin and asprosin induced inflammation in airway epithelial and adipocyte cells.

Taken together, these data suggest that increasing SCFA production through dietary prebiotic interventions may provide a novel management tool to relieve cellular inflammation in tissues and diseases exacerbated by systemic inflammation.

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References

1. Lad N, Murphy A, Parenti C, *et al.* (2021) *Clin Sci* **135**, 2729–2748.
2. Piya MK, Harte AL & McTernan PG (2013) *Curr Opin Lipidol* **24**, 78–85.
3. Romere C, Duerrschmid C, Bournat J, *et al.* (2016) *Cell* **165**, 566–79.
4. Ugur K & Aydin S (2019) *Int J Endocrinol*e 2019, 2521096.