

The Effect of Butyrate on TGF- β 1 Generation and Function. Potential Renal Benefit for Acacia(sen) SUPER GUM™ (Gum Arabic)?

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Summary

Anecdotal evidence suggests that high fibre supplementation of dietary intake may have health benefits in renal disease related to alterations in circulating levels of short chain fatty acids. The aim of this study was to examine the effect of dietary supplementation with a gum arabic sample of standardised molecular characteristics, *Acacia(sen) SUPER GUM™ EM2* (SUPERGUM™), on systemic levels of butyrate in normal human subjects, and to examine the potential role of butyrate in modifying the generation of the pro-fibrotic cytokine TGF- β 1 by renal epithelial cells *in vitro*. Following 8 weeks of dietary supplementation with 25g/day of SUPERGUM™ there was a 2 fold increase in serum butyrate (n=7, p=0.03). *In vitro* work demonstrated that exposure of renal epithelial cells to elevated concentrations of butyrate suppressed both basal and stimulated TGF- β 1 synthesis. The action of butyrate was mediated by suppression of the ERK MAP kinase signalling pathway. In addition, butyrate exposures reduced the response of renal epithelial cells to TGF- β 1 as assessed by luciferase activity of a TGF- β responsive reporter construct. Attenuation of TGF- β 1 signalling was associated with reduced phosphorylation of Smad 2/3 and decreased trafficking of TGF- β 1 receptors into signalling, non-lipid raft associated membrane fractions. The potential importance of these findings to renal disease is discussed.