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Improvement of bile acid-induced disorders by synbiotics

胆汁酸誘導性病態に及ぼすシンバイオティクスの改善作用

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Bile acid (BA) contributes to digestion and/or absorption of hydrophobic nutrients due to its amphipathic nature. Altered BA metabolism is observed in some metabolic disorders not only in dyslipidemia but also in other diseases such as arteriosclerosis and hyperglycaemia. A high-fat diet consumption increases BA secretion and aging raises the ratio of cholic acid (CA)/chenodeoxycholic acid in the primary BAs. Instrumental analysis revealed that BAs exist at the range of 10^{-3} to 10^{-6} M in the blood, intestinal contents and feces, which can be used as a biomarker to evaluate health conditions. In our previous observation, dietary supplementation with CA in rats can be a reasonable model of non-communicable disease (NCD) that reflects BA metabolism in aging and high-fat diet consumption. The aim of the study is to investigate whether a dietary intervention with a synbiotic material ameliorates the CA-induced NCD. Some aspects of the CA-induced NCD were also clarified.

Intestinal bacteria are responsible for the production of secondary BAs. Also, an increase in the production of secondary BAs modulates the intestinal microbiota due to the bactericidal effects and raises the risk of carcinogenesis in the liver and colon. The ingestion of *Bacillus coagulans* improves constipation via the activation of bowel movement to promote defecation in humans, which may alter the BA metabolism in the intestinal contents. We studied whether *B. coagulans* lilac-01 and soy pulp as a prebiotics influence both BA metabolism and health conditions in the CA-supplemented diet-fed rats. In the CA-fed rats, soy pulp significantly increased the production of secondary BAs, such as DCA and ω -muricholic acid although the ingestion of soy pulp alleviated problems the CA-induced disorders such as decrease in plasma adiponectin and disruption of gut permeability. When combined soy pulp with *B. coagulans*, the synbiotics ingestion successfully suppressed the increased production of secondary BA in the CA-fed rats compared to soy pulp itself, without impairing the beneficial effects of soy pulp. It is possible that a combination of prebiotics and probiotics can be used to avoid an unnecessary increase in the secondary BA production in the large intestine in maintaining beneficial functions of prebiotics. The consumption of the synbiotics also normalized the CA-induced lipid metabolism. The synbiotics in combination of *B. coagulans* and soy pulp reduced gut permeability regardless of the CA-supplementation

to the diet. These results indicate that the synbiotic material is applied to avoid development of fatty liver and disruption of gut permeability.

The CA supplementation increased the fecal DCA and portal taurocholic acid (TCA) concentration in the previous experiments. It is possible that TCA is involved in the increase of gut permeability although some reports show deterioration of gut permeability by DCA. We examined whether TCA attenuates gut permeability by using isolated intestinal tissues. As a result, an existence of TCA in the luminal side increased permeability only at distal part of ileum. There was no effect of luminal TCA on the permeability in the other parts of small intestine, indicating that BA incorporation into the epithelial cells is involved in the TCA-induced increase of ileal permeability.

In conclusion, synbiotics can be used as a supplement to alleviate the BA-induced disorders including fatty liver without increase in the secondary BA production that often observed by prebiotics consumption. The CA-induced NCD is considered to be a new experimental model to evaluate the effect of dietary intervention and food components on health maintenance.