#### GOS for improved gut heaths in cats & dogs By Dr Neville M Fish

In recent years, we have learnt that almost everything we and our pets eat has an effect on the microbes in the gastrointestinal tract, the gut microbiota, which in turn have an effect on health and wellbeing. Gut health and the importance of increasing the "good" microflora is a significant trend in the food industry which is also being applied to the pet food industry. Galacto-oligosaccharides (GOS) is a proven food ingredient that has a "prebiotic" effect both adapting and stimulating the gut microbiota to create good gut health in the way nature intended. GOS has an established function in human infant and adult nutrition, and it is being shown that this function applies also to companion animals and other species.

### Gut health

The relationships and bonds that are shared between companion animals and humans transcend the physical, emotional and psychological interactions as, for example, dog owners share more microbiota with their own dogs (Coelho *et al.*, 2018) than with other dogs, albeit with the effect being greatest on the skin microbiota (Song *et al.*, 2013).

Dogs and cats have evolved as carnivores, have a relatively simple gastrointestinal tract (GIT) compared to humans and do not rely on microbial fermentation for energy (although butyrate from fibre fermentation is an energy source for intestinal epithelial cells). balance, faecal microbial phylogeny and functional capacity of the canine and feline gut are similar to those of the human gut. In addition, dietary intake, including the intake of prebiotics, may modulate the composition, activity and stability of the microbiota as it does in humans (Deng *et al.*, 2015).

Whilst the "natural" diets of companion animals differ from those of humans, they can suffer from diseases for which microbiota associations have been demonstrated in humans. In addition to allergic responses and periodontal diseases these include: obesity, diabetes, cardiovascular diseases and digestive disorders such as diarrhoea and inflammatory bowel disease in dogs (Suchodolski *et al.*, 2012). The influence of diet and fibre on kittens and cats has been demonstrated in different studies (Deusch *et al.*, 2014; Deusch *et al.*, 2015; Hooda *et al.*, 2013; Barry *et al.*, 2012). In early studies (Hussein *et al.*, 1999) it was shown that the inclusion of prebiotics in pet foods helped combat the effect of colonic fermentation of protein to putrefactive components which leads to: strong faecal odours, increased numbers of pathogens (e.g. *Clostridium perfringens*) and possible colorectal cancer problems. Fermentation of prebiotics increased the numbers of bifidobacteria and lactobacilli, and the production of SCFAs, decreased gut pH, pathogen numbers and faecal odours. The efficacy of prebiotics, in combating pet oral malodour due to volatile sulphur compounds is less clear. However, as with the gastrointestinal microbiome (Barko *et al.*, 2018), progress is being made in the identification of , and ascribing function to the oral bacteria (Nakano *et al.*, 2018).

# What are galacto-oligosaccharides?

A prebiotic has been defined as "a substrate that is selectively utilized by host micro-organisms conferring a health benefit" (Gibson et al., 2017), and typically prebiotics are non-digestible oligosaccharides. Galacto-oligosaccharides (GOS) are non-digestible, soluble fibres which are manufactured from lactose by an enzyme catalysed process. In this respect they share some aspects with milk oligosaccharides from lactating mammal sources, e.g. they are based on a lactose core.



With a typical form of (gal)<sub>n</sub>-glc galactooligosaccharides may have up to 8 monosaccharide components. These variations in molecular length and intramolecular bonds result in a variety of structures that vary from simple galactosyllactoses, that are relatively easily fermented, to longer more complex structures that persist to the distal colon.

Galacto-oligosaccharide products contain galactosyllactoses (3'-, 4'- and 6'-galactosyllactose) as the most common galacto-oligosaccharides; these are present in the colostrum and milk from other

sources (Newburg *et al.*, 2016). Traditional usage for galacto-oligosaccharides has been in mother's milk alternatives as GOS due to the resemblance to oligosaccharides found naturally in breast milk from humans (HMOs) as well as pets (cats and dogs). In addition, the bifidogenic performance of galacto-oligosaccharides is similar to that of the oligosaccharides found in human breast milk (HMOs). For these reason, and because of their safety, stability, and resistance to digestion in the upper digestive tract, prebiotics such as galacto-oligosaccharides have been used widely in infant formula over the past two decades, having had their efficacy proven in a number of clinical trials.

Unlike some other oligosaccharide products, galacto-oligosaccharides are stable under a range of processing conditions including high temperatures and low pH. The stability under these conditions makes this product suitable for a range of applications including pet food production.

## Mode of action for GOS

GOS as an prebiotic ingredients feeds healthy bacteria's such as bifidobacteria and lactobacilli as well as supporting growth of Bacteroides and firmicutes leading to a diverse range of short chain fatty acids. GOS also has an direct effect by interacting with the epithelial cells in the gut wall leading to an increased integrity of the gut helping to resist inflammatory bowel diseases. GOS in conjunction with bifidobacteria has also been shown to suppress intestinal allergically inflammations.



### Modes of action and potential beneficial effects of GOS inclusion in the diet

Galacto-oligosaccharides are not digested but are metabolised by, and promote the growth of, *Bifidobacteria* (Bouhnik *et al.*, 1997) and *Lactobacilli* (Ito *et al.*, 1990). These health-promoting bacteria have long been regarded as important components of the intestinal microbiota supporting intestinal health (Macfarlane and Macfarlane, 2002) through a number of effects, illustrated in figure 1, including the production of acetic acid and lactic acid which intestinal bacteria such as *Bacteroides* spp., *Clostridium* spp. and other *Firmicutes* can also utilise and produce other short chain fatty acids (SCFAs) including butyric and propionic acid (Louis and Flint, 2009; Louis *et al.*, 2010; Bindels *et al.*, 2015; De Vuyst and Leroy, 2011). The associated benefits of these short chain fatty acids (SCFAs) are that they can:

- 1. serve as a source of energy (den Besten et al., 2013; Suzuki et al., 2008);
- 2. inhibit potential pathogens by anti-microbial action (Tan et al., 2014; Cherrington et al., 1991);
- 3. enhance the immune defences of the host (Pratt et al., 1996);
- 4. improve morphology of the gut mucosa by increasing mucin production (Burger-van Paassen *et al.*, 2009);
- 5. inhibit the growth of colonic cancer cells (Gamet et al., 1992)
- 6. enhance mineral absorption (e.g. calcium or magnesium) in the large intestine (Whisner *et al.*, 2013)

Galacto-oligosaccharides also have an direct effect by interacting with the epithelial cells in the gut wall leading to an increased integrity of the gut helping to resist inflammatory bowel diseases. GOS in conjunction with *Bifidobacterium breve* has also been shown to suppress suppress food allergy symptoms through mechanisms that give a reduction in intestinal allergic inflammation.

### Latest research from Saputo Dairy UK and IQI on the impact of galactooligosaccharides on cats and dogs

Saputo Dairy UK and IQI have recently conducted a series of trials in conjunction with Utrecht University to validate the hypothesis that galacto-oligosaccharides have a beneficial effect on the gut microbiota and decreases in protein fermentation and the associated metabolites.

In cats an increased amino acid fermentation and better fat digestion was found. In dogs the results of faecal analysis were consistent with less protein fermentation. An increase in lactic acid in faecal samples and a tendency towards more acetic acid and butyric acid in the test group were indicative of more carbohydrate fermentation and the changes in the microbiota - an unclassified *Lachnospiraceae* species, anaerobic and likely a butyrate producer, and *Bifidobacterium* spp., positively responded to galacto-oligosaccharides in both cats and dogs. These results are consistent with galacto-oligosaccharide feeding trials in other species.



Relative abundance of Lachnospiraceae spp. (Otu0036) and Bifidobacterium spp. (Otu0039)

### IQI's galacto-oligosaccharide product portfolio

IQI's GOS portfolio is branded under the Nutrabiotic®-PET brand name. The portfolio consists of a range of product with different polymer levels as well as syrup or powder format. All products are produced from natural food grade raw materials in a sustainable biological process

The recommended dosage rate for pet food is 2 %(w/w) Nutrabiotic® GOS syrup (equivalent to 1 %(w/w) galacto-oligosaccharides) in the pet food.

For more information related to Nutrabiotic®-PET please visit IQI website or contact the IQI team directly

# Bibliography

- Barko, P.C., McMichael, M.A., Swanson, K.S., Williams, D.A. (2018) "The Gastrointestinal Microbiome: A Review" Journal of Veterinary Internal Medicine 32(1) 9-25
- Barry, K.A., Middelbos, I.S., Vester Boler, B.M., Dowd, S.E., Suchodolski, J.S., Henrissat, B., Coutinho, P.M., White, B.A., Fahey, G.C., Swanson, K.S. (2012) "Effects of Dietary Fiber on the Feline Gastrointestinal Metagenome" Journal of Proteome Research 11(12) 5924-5933
- Besten, G. den, Eunen, K. van, Groen, A.K., Venema, K., Reijngoud, D.-J., Bakker, B.M. (2013) "The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism" Journal of Lipid Research 54(9) 2325-2340
- Bindels, L.B., Delzenne, N.M., Cani, P.D., Walter, J. (2015) "Towards a more comprehensive concept for prebiotics." Nature Reviews Gastroenterology and Hepatology 12(5) 303-310
- Bouhnik, Y., Flourié, B., D'Agay-Abensour, L., Pochart, P., Gramet, G., Durand, M., Rambaud, J.-C. (1997) "Administration of transgalacto-oligosaccharides increases fecal Bifidobacteria and modifies colonic fermentation metabolism in healthy humans." The Journal of Nutrition 127(3) 444-448
- Burger-van Paassen, N., Vincent, A., Puiman, P.J., van der Sluis, M., Bouma, J., Boehm, G., van Goudoever, J.B., van Seuningen, I., Renes, I.B. (2009) "The regulation of intestinal mucin MUC2 expression by short-chain fatty acids: implications for epithelial protection" Biochemical Journal 420(2) 211-219
- Cherrington, C.A., Hinton, M., Pearson, G.R., Chopra, I. (1991) "Short chain organic acids at pH 5.0 kill Escherichia coli and Salmonella spp. without causing membrane perturbation." Journal of Applied Bacteriology 70(2) 161-165
- Coelho, L.P., Kultima, J.R., Costea, P.I., Fournier, C., Pan, Y., Czarnecki-Maulden, G., Hayward, M.R., Forslund, S.K., Schmidt, T.S.B., Descombes, P., Jackson, J.R., Li, Q., Bork, P. (2018) "Similarity of the dog and human gut microbiomes in gene content and response to diet" Microbiome 6 72
- Deng, P. and Swanson, K.S. (2015" "Gut microbiota of humans, dogs and cats: current knowledge and future opportunities and challenges" British Journal of Nutrition 113(S1) S6-S17
- Deusch, O., O'Flynn, C., Colyer, A., Morris, P., Allaway, D., Jones, P.G., Swanson, K.S. (2014) "Deep Illumina-Based Shotgun Sequencing Reveals Dietary Effects on the Structure and Function of the Fecal Microbiome of Growing Kittens" PLoS ONE 9(7) e101021
- Deusch, O., O'Flynn, C., Colyer, A., Swanson, K.S., Allaway, D., Morris, P. (2015) "A Longitudinal Study of the Feline Faecal Microbiome Identifies Changes into Early Adulthood Irrespective of Sexual Development." PLoS ONE 10(12) e0144881
- De Vuyst, L., Leroy, F. (2011). "Cross feeding between bifidobacteria and butyrate-producing colon bacteria explains bifidobacterial competitiveness, butyrate production, and gas production". International Journal of Food Microbiology 149(1) 73-80
- Gamet, L., Daviaud, D., Denis-Pouxviel, C., Remesy, C., Murat, J.-C. (1992) "Effects of short-chain fatty acids on growth and differentiation of the human colon-cancer cell line HT29" International Journal of Cancer 52(2) 286-289
- Gibson, G.R., Hutkins, R., Sanders, M.E., Prescott, S.L., Reimer, R.A., Salminen, S.J., Scott, K., Stanton, C., Swanson, K.S., Cani, P.D., Verbeke, K., Reid, G. (2017) "Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics." Nature Reviews Gastroenterology and Hepatology 14(8) 491-502
- Hesta, M., Janssens, G., Debraekeleer, J., Millet, S., De Wilde, R. (2003) "Fecal odor components in dogs: nondigestible oligosaccharides and resistant starch do not decrease fecal H2S emission." The Journal of Applied Research in Veterinary Medicine 1(3) 225-232
- Hooda, S., Boler, B.M.V., Kerr, K.R., Dowd, S.E., Swanson, K.S. (2013) "The gut microbiome of kittens is affected by dietary protein:carbohydrate ratio and associated with blood metabolite and hormone concentrations." British Journal of Nutrition 109(9) 1637-1646
- Hussein, H.S., Flickinger, E.A., Fahey, G.C. (1999) "Petfood Applications of Inulin and Oligofructose" Journal of Nutrition 129(7) 1454S-1456S
- Ito, M., et al. (1990) "Effects of administration of galactooligosaccharides on the human faecal microflora, stool weight and abdominal sensation." Microbial Ecology in Health and Disease 3(6) 285-292

- Louis, P. and Flint, H.J. (2009) "Diversity, metabolism and microbial ecology of butyrateproducing bacteria from the human large intestine" FEMS Microbiology Letters 294(1) 1-8
- Louis, P., Young, P., Holtrop, G. and Flint, H.J. (2010) "Diversity of human colonic butyrate-producing bacteria revealed by analysis of the butyryl-CoA: acetate CoA-transferase gene."Environmental Microbiology 12(2) 304-314
- Louis, P. and Flint, H.J. (2017) "Formation of propionate and butyrate by the human colonic microbiota" Environmental Microbiology 19(1) 29-41
- Macfarlane, G.T. and Macfarlane, S. (2002) "Diet and metabolism of the intestinal flora." Bioscience and Microflora 21(4) 199-208
- Nakano, Y., Suzuki, N., Kuwata, F. (2018) "Predicting oral malodour based on the microbiota in saliva samples using a deep learning approach." BMC Oral Health 18 128
- Newburg, D.S., Ko, J.S., Leone, S., Nanthakumar, N.N. (2016) "Human Milk Oligosaccharides and Synthetic Galactosyloligosaccharides Contain 3'-, 4-, and 6'-Galactosyllactose and Attenuate Inflammation in Human T84, NCM-460, and H4 Cells and Intestinal Tissue *Ex Vivo*." The Journal of Nutrition 146(2) 358-367
- Pratt, V.C., Tappenden, K.A., McBurney, M.I., Field, C.J. (1996) "Short-Chain Fatty Acid-Supplemented Total Parenteral Nutrition Improves Nonspecific Immunity After Intestinal Resection in Rats." Journal of Parenteral and Enteral Nutrition 20(4) 264-271
- Song, S.J., Lauber, C., Costello, E.K., Lozupone, C.A., Humphrey, G., Berg-Lyons, D., Caporaso, J.G., Knights, D., Clemente, J.C., Nakielny, S., Gordon, J.I., Fierer, N., Knight, R. (2013) "Cohabiting family members share microbiota with one another and with their dogs." eLife 2, e00458
- Suchodolski, J.S., Markel, M.E., Garcia-Mazcorro, J.F., Unterer, S., Heilmann, R.M., Dowd, S.E., Kachroo, P., Ivanov, I., Minamoto, Y., Dillman, E.M., Steiner, J.M., Cook, A.K., Toresson, L. (2012) "The Fecal Microbiome in Dogs with Acute Diarrhea and Idiopathic Inflammatory Bowel Disease" PLoS ONE 7(12) e51907
- Suzuki, T., Yoshida, S., Hara, H. (2008) "Physiological concentrations of short-chain fatty acids immediately suppress colonic epithelial permeability." British Journal of Nutrition 100(2) 297-305
- Tan, J., McKenzie, C., Potamitis, M., Thorburn, A.N., Mackay, C.R., Macia, L. (2014) "The role of short-chain fatty acids in health and disease." Advances in Immunology 121 61-119
- Whisner, C.M., Martin, B.R., Schoterman, M.H.C., Nakatsu, C.H., McCabe, L.D., McCabe, G.P., Wastney, M.E., van den Heuvel, E.G.H.M., Weaver, C.M. (2013) "Galacto-oligosaccharides increase calcium absorption and gut Bifidobacteria in young girls: a double-blind cross-over trial." British Journal of Nutrition 110(7) 1292-1303