Native inulin as a prebiotic ingredient in food for infants and young children

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INTRODUCTION

Breastfeeding is acknowledged worldwide as the golden standard for infant feeding. WHO recommendations are that infants should be exclusively breastfed for the first 4 to 6 months of life. However, in those cases when a mother cannot or chooses not to breastfeed her child, the use of infant formula is an acknowledged alternative for breastfeeding. As the first months of a newborn infant are a very crucial life phase – the intestinal flora being built up immediately after birth – careful attention has to be paid to the composition and safety aspects of infant food formulae. Novel ingredients are continuously being evaluated for their efficacy to obtain optimal health and growth of infants. The composition and nutritional effects of breast milk are key for these developments for infant formulae.

Besides lactose (68 g/l), fat (37 g/l) and protein (10-12 g/l) human milk contains 10-20 g/l of oligosaccharides. These oligosaccharides have a complex molecular structure with galactose, glucose, fucose, N-acetylglucosamine and sialic acid as building blocks (1). This rich diversity is unique to human milk. They are not digested in the infants' gastrointestinal tract (2) and a variety of functions are attributed to them, including prebiotic activity and anti-infective action (3).

In cow's milk these oligosaccharides are absent, and infant formulae that are based on cow's milk, lack these properties. In order to improve the functionality of formulae attempts are made to improve

Table I – Overview of studies with inulin or oligofructose from chicory in infants

Ref.	Subjects		Inulin or oligofructose			Results*	
	N	Age	Inulin (g/d)	Oligo-fructose (g/d)	Added to	*Bifidobacterium*	Other bacteria
7	67	4 mo		1.7	formula	↑	
8	140	1-2 y (after antibiotic)	2.3**		formula	↑	
9	67	1-12 y (cancer patients)	0.8**		enteral formula	NS	*Lactobacillus* ↑
10	14	12 w	1.5		formula	↑	*Lactobacillus* ↑
11	56	Preterm 0-2 wk		4 g/l	formula	↑	*Bacteroides* ↑, *E. coli* and *Enterococci* ↓
12	72	2-6 wk		1.5 or 3 g/l	formula	↑ after 7d NS after 5 wk NS with 3g/d	NS
13	212	Healthy term		1.5 or 3 g/l	formula	NS	NS
14	454	7-8 y	5		milk	↑	↑
15	20	7-19 mo		2	powder	NS	*Clostridia* ↓ *Staphylococci* NS
16	36	5-12 mo	0.75-1.25		in food	↑ at 1.25 g/d	*Clostridia* ↓ at all dosages

* ↑: significant increase ($p<0.05$); ↓: significant decrease ($p<0.05$) NS: no significant changes
** 70/30 mixture of inulin/oligofructose

the nutritional properties by including prebiotic oligosaccharides (e.g. 4,5) or probiotic bacteria (e.g. 6).

For the prebiotics applied so far much attention has been paid to fructooligosaccharides derived from sucrose (17), or lactose based galacto-oligosaccharides, GOS (5), oligofructose from chicory (7,8) or mixtures thereof (e.g. 4,18). An overview of the studies with chicory derived prebiotics in studies with infants and young children is given in Table I. Most studies used oligofructose alone or mixed with inulin, but studies with native inulin are scarce. Data of the Sensus-supported studies with native inulin are described below, and the potential health benefits are discussed.

Not only for infant formulae, but also for follow-on formulae, and foods for older children prebiotics may be useful. Not surprisingly therefore also for this category of foods research is carried out to include these ingredients for their prebiotic activity with connected health benefits. And inulin-type fructans may be particularly useful for these developments since not only are their prebiotic effects well documented, but also many health effects.

PREBIOTIC EFFECTS OF NATIVE INULIN IN INFANTS OF DIFFERENT AGES

Formula-Fed Infants ± 12 weeks of age (10)

In a cross-over designed study a daily dosage of native inulin of 0.25 g/kg body weight/d was used; 3 weeks of inulin consumption were followed by 3 weeks without or *vice versa*. The study group consisted of 14 infants with an average age of 12.6 weeks (±6.4 weeks) and the inulin was mixed into the standard formula they received. The average intake of inulin was 1.5 (±0.3) g/d.

Growth of the subjects was not affected by the consumption of inulin: with inulin the weight increase in 3 weeks was 509 g (±372 g), and without inulin it was 411 g (±394 g; p=0.5051). No adverse effects were reported during the periods of inulin consumption (in total 42 weeks).

The consumption of inulin increased the content of *Bifidobacterium* and *Lactobacillus* in the faeces of formula-fed babies, whereas the number of *Bacteroides* or the total anaerobic count was not affected (Table II). As found with adults also in these formula-fed infants the increase in bifidobacteria was higher with the lowest number of bifidobacteria at the start of the treatment (Figure 1). Table II also shows that with inulin the amount of faeces increased significantly whereas stool consistency showed a tendency to become softer (p=0.058) and that the frequency of defecation was not affected by the consumption of inulin.

Table II – Microbial composition of faeces and some stool parameters in formula-fed infants

Bacteria	Inulin treatment	Control treatment
Total anaerobes	10.58 (0.224)	10.27 (0.344)
Bacteroides	9.51 (0.389)	9.40 (0.344)
Bifidobacterium	9.85 (0.523) *	9.22 (0.741)
Lactobacillus	9.09 (0.377) *	8.61 (0.741)
Stool Parameter		
pH	6.3 (0.34)	6.51 (0.49)
Consistency	1.8 (2.7)	2.4 (4.2)
Amount (g/d)	167 (80) **	75 (30)
Frequency	1.6 (2.4)	1.2 (1.6)

Microbiological data are expressed in log colony forming units per g of faecal matter as the average of 14 subjects with the standard deviation in parentheses.
Data with * in the same row are significantly different (*p* < 0.05)
All other data are given as the average of 14 measurements with the standard deviation in parentheses. Consistency was scored on a scale from 1-4 (watery to hard). Data with ** in the same row are significantly different (p < 0.01)

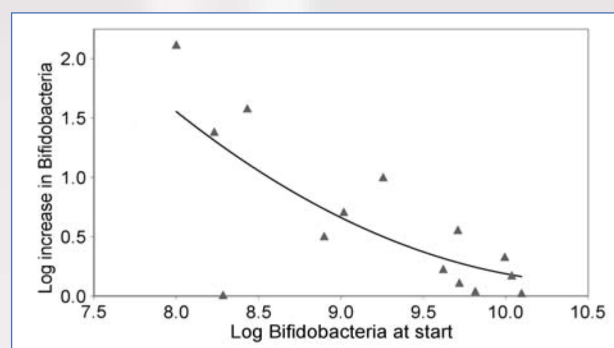

Figure 1 – Increase in Bifidobacterium *sp. in formula-fed babies as a function of the original number of* Bifidobacterium *sp. The faecal content of* Bifidobacterium *sp. was determined without and with inulin supplementation of the formula, and the logarithmic increase was calculated for each infant.*
Figure from Ref. 10 and published with permission from the publisher

Weaned Infants ± 8 months of age (16)

The effects of inulin on the microbial composition and faecal characteristics in 36 healthy, formula-fed infants (average age 7.7 months) given three different daily dosages of native inulin (0.75 g/day, 1.00 g/day, and 1.25 g/day) were studied. Three parallel groups of infants were treated with inulin in the dosages mentioned for 14 days after a run-in period of 7 days. The data as given in Table III were determined after 7 days of run-in or after 2 weeks of inulin treatment.

At all levels of inulin consumption a significant (p<0.05) reduction of potential pathogenic micro-organisms such as clostridia was found. An intake of 1.25 g/day of inulin caused a significant (p<0.05) increase of *Bifidobacterium* spp. as well as a significant (p<0.05) decline in Gram-positive cocci and coliform bacteria (not shown).

For stool parameters inulin consumption resulted in a significant (p <0.05) decrease in faecal pH value. Most likely this is due to the increased production of short chain fatty acids by the colonic microbiota (19). The changes in faecal weight, faecal texture, and defecation frequency did not reach statistical significance. As with the study from Kim *et al.* (10) no adverse effects of inulin consumption were reported in these older children.

Table III – Faecal characteristics of weaned infants with different daily dosages of native inulin
Data from Ref. 16

Parameter	Inulin dosage	Run in period	Inulin period
Composition of Faecal Microbiota			
Bifidobacteria	0. 75 g/d	9.16 ± 0.57	9.36± 0.58
	1.0 g/d	9.64 ± 0.28	9.77 ± 0.38
	1.25 g/d	9.23 ± 0.38	9.55 ± 0.17 *
Clostridia	0. 75 g/d	10.15 ± 0.15	9.28 ± 0.35 *
	1.0 g/d	9.98 ± 0.32	8.95 ± 0.20 *
	1.25 g/d	9.66 ± 0.32	8.78 ± 0.39 *
Faecal Parameters			
Faecal pH	0. 75 g/d	6.8 ± 0.5	6.7 ± 0.6
	1.0 g/d	6.8 ± 0.6	6.3 ± 0.5 *
	1.25 g/d	6.7 ± 0.7	5.9 ± 0.3 *
Faecal consistency	0. 75 g/d	2.9 ± 3.7	2.4 ± 3.9
	1.0 g/d	2.3 ± 2.6	2.0 ± 2.7
	1.25 g/d	2.6 ±4.2	2.1 ± 3.7
Defecation frequency (per day)	0. 75 g/d	1.07 ± 0.25	1.13 ± 0.25
	1.0 g/d	1.28 ± 0.13	1.22 ± 0.18
	1.25 g/d	1.56 ± 0.17	1.48 ± 0.15

All bacterial data are expressed as colony forming units per g of faeces, faecal consistency was scored on a scale from 1-4 from 1: watery to 4: hard pellets.
All data are given as average ± SD.
Data with * are significantly different from the data of the run in period (p < 0.05)

Older Children Aged 7-8 years (14)

In a study with Vietnamese children with an average age of 7.7 years Lien *et al.* (14) showed that 5 g/d of native inulin had a bifidogenic effect. The results as shown in Figure 2 are not easy to interpret as also with regular milk (without

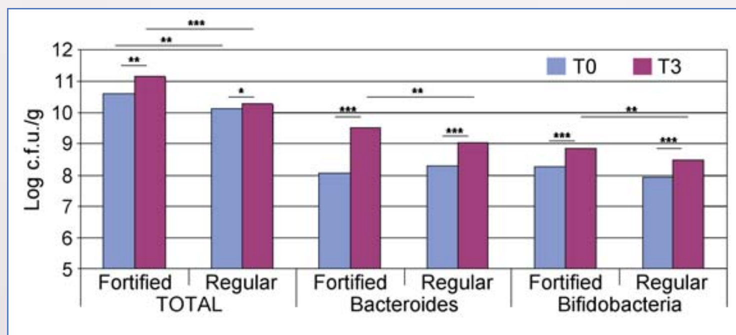

Figure 2 – Levels of faecal bacterial groups before and after 3 months of intervention with (inulin) fortified milk (n=32) and regular milk (n=39)

inulin) the numbers of (bifido)bacteria increase. This is most likely due to undigested lactose entering the colon.

However if one calculates the increase in bifidobacteria in real numbers and takes into account that higher starting levels of *Bifidobacterium* lead to less increase (see for instance Figure 2, and 20), the increase with fortified milk is bigger than with regular milk. This is even true with the higher starting numbers in the group receiving inulin-fortified milk. LIEN *et al*. (14) also showed improvement of general health in children with fortified milk consumption. It is not clear from the data whether this is due to the inulin as the fortified milk also contained vitamins and minerals. Not only is this the first report of a study with native inulin in older children, but it also shows a bifidogenic effect in older children for the first time.

Modulating the composition of the colonic microbiota is one thing, but does this also lead to health benefits. Although this was not investigated in the studies above, good indications were obtained for such effects. In the study by KIM *et al*. (10) an increase in the amount of faeces was found which in combination with the trend for softer faecal consistency might be helpful in constipated children. YAP *et al*. (16) did show similar changes in these stool parameters, but these did not reach statistical significance. The increase in magnesium and zinc absorption as reported earlier by these authors (19) shows the potential benefits of inulin consumption in these children. In adolescents it has been shown that inulin consumption leads to increased calcium absorption and improved bone mineral density (21).

Results from other studies further show the potential benefits for the immune system especially in children. According to SEIFERT and WATZL (22) the first results from human intervention studies suggest that the intake of inulin and oligofructose has beneficial effects on the gut-associated lymphoid tissue. Especially data from studies with infants suggest that supplementation with prebiotics positively affects postnatal immune development and increases faecal secretory IgA.

For instance, WALIGORA-DUPRIET *et al*. (15) showed that with 2 g/d of oligofructose fewer episodes with diarrhoea or fever occurred and ARSLANOGLU *et al*. (23) reported similar data with a GOS/inulin mixture. This prebiotic mixture caused a reduction of the number of infectious periods, especially of that of respiratory infections (24).

MORO *et al*. (25) showed a reduced incidence of atopic dermatitis in children given a prebiotic mixture consisting of GOS and inulin during the first 6 months of life. However, according to a Cochrane review (26) data are too limited to draw firm conclusions. Further trials are needed to determine whether the reduction in eczema that has been reported in high risk infants is reproducible and whether it would persist over a longer period of time.

The results of a vaccination study in 8-months old infants are also interesting. Infants who received 1 g per day of a 30/70 mixture of native inulin and oligofructose for 10 weeks showed higher IgG antibody titres after measles vaccination compared to the control group that did not receive the prebiotic (27), but DUGGAN *et al*. (28) could not find such an effect with *Haemophilus influenzae* vaccination and oligofructose consumption (0.7 g/d). To further elucidate the mechanism by which prebiotics change the immune response after vaccination, studies on cellular immune reaction and with different types of vaccines are needed (29). In a review on the efficacy of inulin and oligofructose in paediatric applications, VEEREMAN (30) concludes that the bifidogenic effect probably is not the only mechanism involved but it may be key to important immune mediated effects.

CONCLUSION

These studies show that native inulin has a prebiotic effect in infants at a dosage of about 1.25-1.5 g/d both in formula-fed and in weaned infants. The addition of native inulin to infant food offers therefore good opportunities to increase the functionality of these food products. The effects on bowel habit – an increased amount with possible softening of the stools – may be helpful in infants with constipation. Based on these data this type of inulin may be used as a prebiotic ingredient in infant foods as an alternative for currently applied prebiotics such as mixtures of galacto-oligosaccharides with different types of inulin or of inulin mixtures.

In this respect native inulin seems to behave similar at all ages, as it is also prebiotic in children aged 7-8 years (with 5 g/d) and in adults – at the same dosage of 5 g/d, (31). Thus it can also be used in foods for older children to increase the health features and the daily fibre intake in this target group. Fibre intake is less relevant for infants below about 1 year, but it is for children in higher age groups as these will not consume enough dietary fibres (32).

Indeed if one takes into account the data that native inulin has prebiotic effects in people up to 90 years of age (33,34) one can even conclude that this type of inulin is the prebiotic for people of any age, be it an infant or an older person. This clearly is the first time that a prebiotic has been shown to be effective in people of "all" ages.

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