Sn-2 palmitate

Scientific summary

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Summary

Human milk supplies vital nutrients to infants and is the gold standard to which all infant formulas are compared. While many infant formulas supply necessary nutrients comparable to human milk, the type of fat can differ significantly. Human milk fat primarily consists of triglycerides with a unique placement of palmitic acid in the sn-2 position. Although infant formulas, traditionally produced with blends of vegetable oils, contain palmitic acid, the placement of palmitic acid at the sn-2 position is much lower compared to human milk. Like in human milk fat, high sn-2 palmitic acid triglycerides serve as a functional ingredient when added to infant formulas. Studies show that when compared with infant formulas using traditional fat sources, high sn-2 infant formula (high sn-2 IF), much like human milk, leads to increased fatty acid absorption, increased calcium absorption, reduced formation of fecal calcium soaps, softer stools, and other associated benefits.

Introduction

For exclusively breastfed infants, human milk (HM) is the sole source of nutrients during the first several months of life. As human milk supplies all the nutrients required for growth, development, and immune support, it is often considered the best source of infant nutrition. However, for a variety of reasons, exclusive breastfeeding is not always possible, and commercial infant formula can serve as a suitable supplement or substitute.

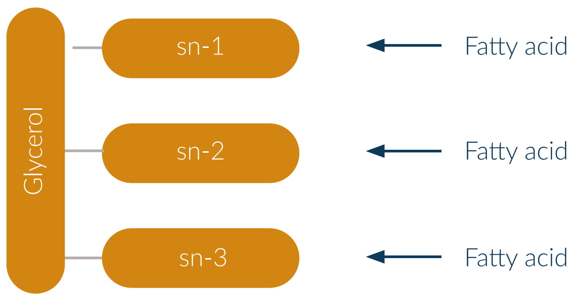
Over the years, infant formulas have become more sophisticated through the addition of nutrients which naturally occur in human milk, including prebiotic oligosaccharides, nucleotides, carotenoids, and probiotic bacteria. However, there is one key component found in human milk that has not been widely applied to infant formula: the distinctive fat structure.

The fat structure in human milk is unique and serves a functional purpose (1,2). Human milk consists of only about 3-4% fat; however, the fat makes up 50-60% percent of the energy intake for infants, and is involved in nutrient absorption (1). Thus, the fat in human milk plays an essential role in infant nutrition and digestion.

In nature, fat molecules exist as fork-shaped triglycerides, which can have different fatty acids bonded to the sn-1, sn-2, or sn-3 position on a glycerol backbone (Figure 1).

Key words:
infant formula, fat, human milk (HM), oleic-palmitic-oleic (OPO), sn-2 palmitate, palmitic acid, calcium absorption, gut health

Figure 1 Triglyceride structure with three fatty acids attached.



sn-1 and sn-3 are the outer fatty acid positions and sn-2 the mid-position fatty acid. (sn means stereospecific numbering)

A high sn-2 fat structure allows babies to absorb more palmitic acid and calcium

Fatty acids are classified into one of three types: saturated fatty acids (SAFA), monounsaturated fatty acids (MUFA), or polyunsaturated fatty acids (PUFA). Fatty acids can vary in carbon chain length from short (<C:6), medium (C:6-C:12), long (C:12-C:20), to very long (C:22) (Figure 2).

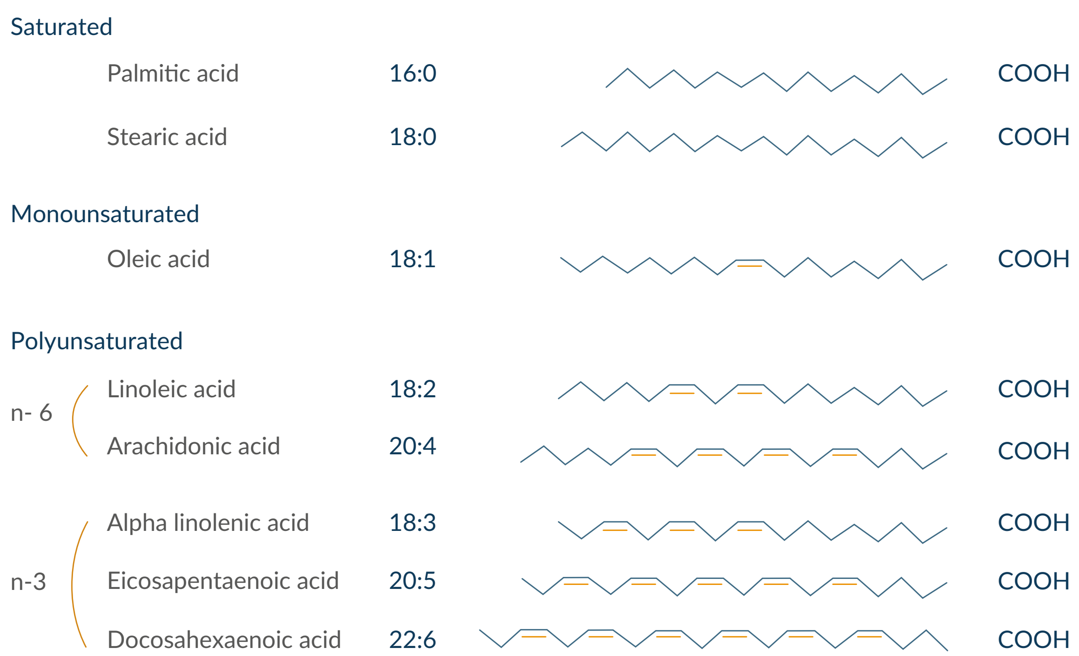
Palmitic acid (C16:0) is a 16-carbon chain length saturated fatty acid (SAFA). It makes up 20-25% of the total fatty acids in human milk (2). In human milk, palmitic acid largely exists (about 70%) in the sn-2 (or middle) position of the triglyceride backbone, while the sn-1 and sn-3 positions are commonly occupied by unsaturated fatty acids such as oleic (C18:1) and linoleic (C18:2) acid (3). A similar fatty acid profile to human milk can be achieved in infant formulas via the use of vegetable oils. However, the specific placement of palmitic acid in the triglyceride in human milk cannot be matched with vegetable oils. While palmitic acid exists primarily in the sn-2 position in human milk fat, in most vegetable oils and conventional infant formulas, palmitic acid exists primarily (about 80%) in either the sn-1 or sn-3 position (3). This difference in palmitic acid placement plays a crucial role in infant uptake, digestion, and metabolism of milk fat (4).

High sn-2 nutritional lipids derived from vegetable oils were introduced in the early 1990's by their inventor, Bunge Loders Croklaan, under the brand name Betapol®. This introduction allowed infant formulas to replicate the functional fat structure of human milk, and created a whole new category: high sn-2 infant formulas (high sn-2 IF). The original Betapol® contained oleic acid predominantly in positions sn-1 and sn-3, with palmitic acid in the sn-2 position, leading the ingredients in this category to be commonly known as OPO (oleic-palmitic-oleic).

High sn-2 nutritional lipids are manufactured through a position-specific enzymatic interesterification process using palm oil triglycerides and oleic acid. Unlike common triglycerides found in most infant formulas, the nutritional lipids in high sn-2 IF are more like human milk fat, and can have up to 60% of their palmitic acid attached to the sn-2 position, with sn-1 and sn-3 positions occupied by unsaturated fatty acids. Studies have shown that the addition of high sn-2 nutritional lipids as the fat source of an infant formula can play a beneficial role in lipid absorption, energy availability, calcium absorption, and stool softness in both preterm and term infants when compared with conventional formulas that contain low levels of sn-2 palmitic acid (4-9).

In addition, novel infant formulas which contain high sn-2 and other ingredients naturally found in human milk (such as oligosaccharides) have shown additional benefits like increased probiotic bifidobacteria (10-14), a sign of healthy gut microbiota. Table 1 summarizes research on the efficacy of high sn-2 IF.

Figure 2 Different types of dietary fatty acids.

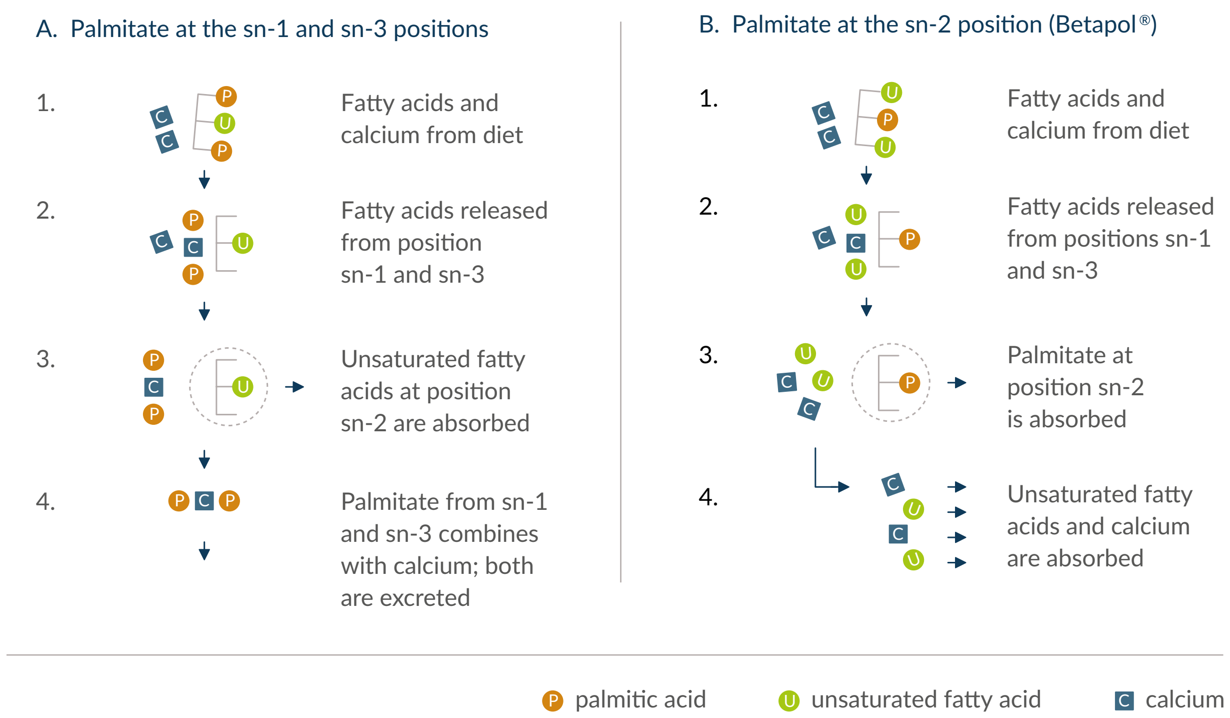


The link between lipid and calcium absorption

Lipid absorption is essential for the energy requirements of growing infants. In addition, some lipids found in human milk, such as DHA, EPA, and rumenic acid also serve roles in other key biological functions such as cognition and immune function (15-17). The rate of lipid absorption is influenced by both the type of fatty acid and the position of the fatty acid on the triglyceride backbone (3). When triglycerides are consumed, the fats bonded to the sn-1 and sn-3 positions are freed by digestive enzymes in the small intestine, leaving the fatty acid in the sn-2 position as a monoglyceride and free fatty acids to be absorbed.

Generally, short- or medium-chain fatty acids are more readily absorbed than long-chain fatty acids, and unsaturated fatty acids are better absorbed than saturated fatty acids (3,18). Palmitic acid is more favorably absorbed in the sn-2 position as a monoglyceride than as a free fatty acid from the sn-1 or sn-3 position (19-21). Free palmitic acid tends to complex with minerals such as calcium, and form insoluble soaps which cannot be absorbed in the small intestine and are thus excreted in the feces (1,22) as illustrated in Figure 3. That is why high sn-2 fats result in higher lipid and calcium absorption.

Figure 3 Lipid digestion and fatty acid absorption pathways.



When palmitic acids exist in the sn-1 and sn-3 position (A), they can bind with minerals after digestion and reduce absorption. When palmitic acid exists in the sn-2 position (B), it does not bind with minerals and is more readily absorbed.

Table 1 Summary of clinical studies performed on high sn-2 IF or high sn-2 IF with a combination of ingredients. (1/2)

Reference	No. infants	Duration	Intervention IF	Control	Outcomes
Carnielli 1995	24 (preterm) up to 38 days of age, 2 groups	1 week crossover	58% sn-2 palmitate (n=12)	9.8% sn-2 palmitate (n=12)	28% decrease in fecal calcium (p<0.05) Significant increase in intestinal absorption of myristic, palmitic and stearic acid (p<0.01) Significant decrease in fecal myristic, palmitic and stearic acid content (p<0.004)
Carnielli 1996	27 (term) male infants up to 5 weeks of age, 3 groups	5 weeks	66% (Beta) (n=9) and 39% (Intermediate) sn-2 palmitate (n=9)	13% (regular) sn-2 palmitate (n=9)	Significant decrease in fecal calcium and significant increase in intestinal calcium absorption with the Beta formula. Significant decrease in fat excretion with Beta formula (p<0.001) Significant decrease in fecal lauric, myristic, palmitic and stearic acid content (p<0.001) with the Beta formula Significant difference in stool consistency p=0.003)
Lucas 1997	24 (preterm) up to 10 days of age, 3 groups	3 weeks	74% (Betapol) sn-2 palmitate (n=8)	8.4% (Diet A) (n=9) and 28% (Diet B) (n=7) sn-2 palmitate	Significant increase in calcium absorption with high sn-2 IF (p<0.03) Significantly less fecal fatty acid soaps with high sn-2 IF (p<0.03) Significant increase in palmitic acid absorbed with high sn-2 IF (p<0.03)
Kennedy 1999	323 (term) up to 8 days of age, 3 groups	12 weeks	50% (Betapol) sn-2 palmitate (n=100)	12% (Control) sn-2 Palmitate (n=103) and breast fed (n=120)	Significant increase in BMC (p<0.02) and BMD with high sn-2 IF (p<0.009) Significantly lower soap fatty acids (p<0.001) and total fatty acids in feces (p<0.05) with high sn-2 IF Significantly fewer hard or formed stools at six weeks with high sn-2 IF (p<0.004)
Lopez-Lopez 2001	36 (term) from birth, 3 groups	8 weeks crossover	Group C (n=12) was fed with alpha formula (19% sn-2 palmitate) for 4 weeks, then with Beta formula (44% sn-2 palmitate) for another 4 weeks	Group A (n=12) was breast-fed Group B (n=12) was fed with alpha formula (19% sn-2 palmitate)	Significantly lower fecal palmitic acid in the Groups A and C between month 1 and month 2 Significantly decrease in fecal calcium in Groups A and C after 2 months
Bongers 2007	35 (term) constipated infants up to 29 weeks in age, 2 groups	3 weeks	41% sn-2 palmitate containing oligosaccharides and whey hydrolyzed protein (New formula) (n=20)	11.5% sn-2 palmitate, without oligosaccharides and hydrolyzed whey protein (standard formula) (n=15)	Significant improvement in stool consistency for New formula (p=0.04)

Table 1 Summary of clinical studies performed on high sn-2 IF or high sn-2 IF with a combination of ingredients. (2/2)

Reference	No. infants	Duration	Intervention IF	Control	Outcomes
Savino 2005	Total 168 (term) infants with regurgitation (n=79) and/or constipation problems (n=95), among them 6 having both symptoms; up to four months of age, 2 groups	14 days	High sn-2 IF, with GOS/FOS and partially hydrolyzed whey protein (n=55 with constipation; n=42 with regurgitation)	Listed as standard IF (n=40 with constipation; n=37 with regurgitation)	Increased stool frequency on day 7 and day 14 with high sn-2 IF; a reduction of the numbers of regurgitation episodes on day 7 and day 14 with high sn-2 IF.
Savino 2003	604 infants completed, among them 214 with colic, 201 with regurgitation problems, 232 with constipation, some infants with 2 or 3 of these problem; up to 90 days of age	14 days	High sn-2 IF, with FOS/GOS and partially hydrolyzed whey protein	None	169 (of 214) infants (79%) had a reduction in frequency of colic at the end of the study (p<0.005). 141 (of 201) infants (70%) had less regurgitation symptoms at the end of the study (p<0.005). 147 (of 232) infants (63%) demonstrated an increase in daily stool number (p<0.05).
Savino 2006	199 infants with infantile colic of up to four months of age, 2 groups	14 days	High sn-2 IF, prebiotic oligosaccharides and partially hydrolyzed whey protein (n=96)	Listed as Standard formula and simethicone (n=103)	Fewer colic episodes after 1 week (p<0.001) and crying episodes after 2 weeks (p<0.001)
Yao 2014	369 term infants completed (7-14 days old), 5 groups	8 weeks	36-37% sn-2 palmitate (Betapol) alone (n=72) sn-2+3 g/L oligofructose (n=75) sn-2+5 g/L oligofructose (n=75)	11.7% sn-2 palmitate (standard) (n=74) human milk (n=73)	Sn-2 vs. control with standard formula, decreased stool soap palmitate (46% less, p<0.001) and softer stools (20% more mushy soft stools, p=0.026; 50% fewer formed stools, p=0.003). Addition of OF resulted in even fewer formed stools vs control, with 5 g/L OF more closely resembling that of HM-fed infants. Both sn-2 (p<0.05) and sn-2 with OF groups (p<0.01) had significantly higher fecal bifidobacteria concentrations than control at week 8, not differing from HM-fed infants.
Schmelzle 2003	102 healthy full term infants aged younger than 2 weeks, 2 groups	12 weeks	High sn-2 IF with oligosaccharides and hydrolyzed whey protein (New Formula) (n=49)	Listed as standard formula without oligosaccharides and hydrolyzed whey protein (n=53)	At six weeks, new formula produced softer stool (p=0.005) and produced higher counts of probiotic Bifidobacteria (p<0.005) than the standard formula.
Wu 2021	174 term infants completed, 3 groups	24 weeks	46.3% sn-2 palmitate formula with Betapol (sn-2 group, n=58)	10.3% sn-2 palmitate formula (control group, n=59) human milk (HM group, n=57)	At week 16, the sn-2 group scored higher than the control group for fine motor skills, with lower risk of scoring close to or below the minimum threshold for typical development (p=0.036) and did not differ from the HM group (p=0.513). At weeks 16 and 24, the sn-2 group had higher relative abundance of fecal Bifidobacteria than the control group (p=0.001 and p=0.028) and did not differ from the HM group (p=0.674 and p=0.749).

Over 25 years of clinical research supports the functionality of high sn-2 nutritional lipids

The presence of fecal palmitic acid represents a needless loss of available dietary energy for an infant. Nutrient absorption is paramount in preterm term infants, as their digestive systems are not as developed as those of full-term infants. Consistent with the functional nature of high sn-2 nutritional lipids, high sn-2 IF has been shown to improve lipid absorption in preterm infants (2,23,24).

A five-day study compared the lipid absorption in 24 preterm infants fed high sn-2 IF (73% palmitic acid in the sn-2 position) vs. two other groups with only 28% or 8% of palmitic acids in the sn-2 position (4). The study found that 91% of the palmitic acid was absorbed from high sn-2 IF vs. 79% of the palmitic acid from the other groups (p<0.01).

A similar one-week crossover trial in 12 preterm infants (born after gestation of 20-32 weeks) compared intestinal absorption of saturated fatty acids from high sn-2 IF vs. control IF (with only 13% of palmitic acid in the sn-2 position). High sn-2 IF showed significantly greater intestinal absorption of palmitic (43.1%), myristic (12.5%), and stearic (6.7-fold increase) acids compared to control IF (p<0.01) (5).

The effects of high sn-2 IF on lipid absorption have also been shown in full-term infants. A five-week study in full-term infants compared high sn-2 IF (up to 60% palmitic acid in the sn-2 position) to a conventional infant formula (13% palmitic acid in the sn-2 position) and an intermediate infant formula (39% of palmitic acid in the sn-2 position) (6). The infant intestinal absorption of saturated fatty acids was significantly greater (p<0.001) after consumption of high sn-2 IF compared to standard formula: lauric (125.5%), myristic (760.9%), palmitic (123.6%), and stearic (120.8%). The amount of fatty acids recovered in feces was lower in the formula containing high sn-2 IF (0.15 g/kg/day) vs. the conventional (0.68 g/kg/day, p<0.05) and intermediate formulas (0.44 g/kg/day, NS).

Another study was performed on 36 full-term infants. Group A consumed human milk (66% sn-2 palmitic acid estimated) for two months. Group B consumed conventional infant formula (19% sn-2 palmitic acid) for two months. Group C was fed the formula from Group B for one month and then a high sn-2 IF (44.5% sn-2 palmitic acid) for the second month (9). After two months, the authors reported significantly less fecal palmitic acid in Groups A and C compared to Group B, indicative of increased palmitic acid absorption.

Beginning with initial studies performed in the mid 1990's through today, research has consistently shown that high sn-2 IF significantly increases fatty acid absorption and reduces the amount of excreted fatty acids in both preterm and term infants compared with IF with low sn-2 palmitic acid (see Table 1). It is worth noting that the only high sn-2 nutritional lipid commercially available until 2007 was Betapol®, so most landmark research on high sn-2 IF was performed using Betapol®.

High sn-2 IF tends to increase calcium absorption

Calcium absorption is important, as calcium is a vital mineral involved in bone building, and also serves as a cellular signal in several biological processes. When saturated fatty acids are bonded to the sn-1 and sn-3 positions of a triglyceride, they can be released to form free fatty acids during digestion. These free fatty acids can bind to minerals such as calcium to form soaps which are excreted in an infant's feces, thus decreasing the amount of calcium available for absorption.

Indeed, fecal calcium content is positively correlated with fecal saturated fatty acid content in infants, but is not correlated with mono- or polyunsaturated fatty acids (5). A study in preterm infants found that fecal calcium was significantly lower (58.8 mg/kg/day) in infants fed high sn-2 IF vs. control formula (82.0 mg/kg/day) ($p<0.05$) (5). Another study in preterm infants comparing high sn-2 IF (72% sn-2 palmitic acid) with formulas containing only 8% (formula A) and 28% (formula B) palmitic acid in the sn-2 position found a higher absorption of dietary calcium in the high sn-2 IF (57%) vs. the A and B formulas (44% and 40% respectively) ($p<0.03$) (4). A significantly lower amount of fecal calcium soaps were found in the high sn-2 IF group (3.3%) vs. the B formula group (7.2%) ($p<0.03$).

Similar effects on calcium absorption with high sn-2 IF have been observed in term infants. A study of full-term infants showed significantly lower amounts of fecal calcium (43.3 mg/kg/day) and significantly higher intestinal calcium absorption (53.1%) for high sn-2 IF vs. a conventional infant formula (68.4 mg/kg/day; 32.5% absorption) ($p<0.05$) (6).

Another study was performed on 36 term infants (12 infants per group), which compared the effects of human milk and two infant formulas with different sn-2 palmitic acid percentages for two months (9). Group A was fed human milk containing approximately 66% sn-2 palmitic acid. Group B was fed conventional infant formula containing 19% sn-2 palmitic acid. Group C was fed the formula from Group B for one month and then a higher palmitic acid sn-2 formula (44.5% sn-2 palmitic acid) for the second month. After two months, fecal calcium decreased in Group A (0.19 mg per 100 mg of feces) and Group C (0.24 mg per 100 mg of feces), but no change was observed in Group B. It is worth noting that Groups B and C did not differ in fecal calcium levels despite the significant decrease in C and no change in B. This is presumably due to the short treatment time (only one month of high sn-2 IF).

A study in 323 infants fed high sn-2 IF, a conventional IF, or HM found that there was a 5% increase in both bone mineral density (BMD) ($p<0.009$) and bone mineral content (BMC) ($p<0.02$) in high sn-2 IF-fed infants vs. those fed conventional IF (7). The BMD and BMC in the high sn-2 IF group were similar to the HM group. Calcium absorption in infants is especially important due to its critical role in bone formation and development. Increased calcium absorption in infants fed high sn-2 IF is likely to have led to the improved bone development measurements in this study.

High sn-2 IF, microbiota, and potential effects on developmental outcomes

Fine motor skills are broadly interpreted as small muscle movements requiring eye-hand coordination, which could be subcategorized into skills such as reaching, grasping, grabbing, holding, and manipulating (30). They are essential in early learning, and have long been recognized as an important foundation for development in other domains (31). Fine motor skills can be evaluated through the *Ages and Stages Questionnaires Edition 3* (ASQ-3), which is a vital monitoring tool in screening for developmental delays in children younger than 5.5 years old (32).

A study was performed on 199 healthy infants in China, which compared the effects of human milk (HM group) and two infant formulas for 24 weeks. The two infant formulas were comparable, except that one contained high (46.3%) sn-2 palmitate (sn-2 group) and the other had low (10.3%) sn-2 palmitate (control group). At week 16, after adjusting for maternal education level, infants in the sn-2 group scored significantly higher than the control group for fine motor skills, with significantly lower risk of scoring close to or below the minimum ASQ-3 threshold scores for typical fine motor skill development in similar-aged infants ($p=0.036$). The sn-2 group's fine motor skill scores did not differ significantly from the HM group ($p=0.513$) (29).

Interestingly, at weeks 16 and 24, the sn-2 group had a significantly higher relative abundance of fecal bifidobateria than the control group (week 16: $p=0.001$ and week 24: $p=0.028$) and did not differ from the HM group (week 16: $p=0.674$ and week 24: $p=0.749$) (29).

Bifidobacterium are non-pathogenic bacteria, and are major inhabitants of the intestine, which may aid in digestion and benefit the immune system (26). Multiple studies have shown higher abundance of bifidobacterial in high sn-2 IF-fed infants compared to infants fed conventional formula (14,27,28,33). Although more research is needed, it is worth highlighting this initial link between high sn-2 IF, infant microbiota, and improved neurodevelopmental outcomes.

Stool softness and related benefits for infants and parents

When saturated fatty acids in the sn-1 or sn-3 position are freed during digestion and bind with minerals, not only does this reduce the amount of available minerals such as calcium, but the resultant fatty acid-calcium soaps accumulate in the feces. This in turn results in harder stools, which may lead to constipation or obstruction. Breastfed infants typically have lower amounts of fecal calcium soaps and softer stools than formula-fed infants. Quinlan et al. (8) visually tested stools from 30 infants, and found breastfed infants to have softer stools than conventional IF-fed infants. Analytically, they found that conventional IF-fed infants had approximately nine times the amount of fatty acid calcium soaps in the feces compared to breastfed infants. This comparatively high level of calcium soaps accounted for nearly 30% of the dry weight of the stool vs. only 3% in the breastfed group. High sn-2 IF has been shown to be similar to human milk regarding its effects on infant stool softness.

A study using term infants found significantly softer stools when infants were fed high sn-2 IF (66% sn-2 palmitic acid) vs. a conventional IF with 13% sn-2 palmitic acids (6) ($p=0.003$). Consistency was evaluated based on photographs by a subjective scoring method using four levels. The degree of stool softness observed in this study was independent of water content, and directly proportional to the amount of fatty acid soaps in the stool. Another study showed stool softness and proportion of fecal fatty acid soaps of infants after six and twelve weeks of consuming high sn-2 IF to be similar to breastfed infants (7). At six weeks, the percentage of hard or formed stools was significantly lower ($p=0.004$) than those seen in infants fed conventional IF.

High sn-2 IF effects on stool softness are consistent with its effects on calcium palmitate soap formation, described in previous sections. Stool hardness can lead to pain, discomfort, and constipation, and might be related to disrupted sleep and more crying. The positive effects of high sn-2 nutritional lipids on stool softness might therefore underpin observations of reduced crying and better sleep for infants fed high sn-2 IF (13).

Efficacy of high sn-2 IF in combination with other ingredients

Infant formula manufacturers endeavor to discover and include more ingredients which are naturally found in human milk. This includes oligosaccharides, which are non-digestible carbohydrates that appear naturally in human milk. When added to infant formula, oligosaccharides have been shown to soften stool, increase numbers of probiotic bacteria, and potentially have some immune benefits as well (10-14,25). Thus, high sn-2 IF containing oligosaccharides is a closer match to human milk than conventional IF.

Studies have been performed on infants using a combination of high sn-2 IF, oligosaccharides, and other ingredients. An infant formula containing fructo- and galacto-oligosaccharides, partially hydrolyzed whey proteins, and low levels of lactose was used in a study to reduce constipation in 232 infants for fourteen days (10). After seven days, 147 infants (63%) demonstrated a significant increase in the daily number of stools (p<0.05).

In a similar study, 168 full-term infants with digestive problems such as constipation were fed high sn-2 IF containing prebiotic oligosaccharides and partially hydrolyzed whey protein (11). A conventional IF was used as a control. Stool consistency and frequency were measured on days one, seven, and fourteen of the study. Infants on the high sn-2/oligosaccharide/partially hydrolyzed whey formula had a higher number of evacuations, with an increase of 0.60 between day one and day seven (p=0.004), and 0.53 between day seven and day fourteen (p=0.015) relative to the conventional IF group.

A study used a combination of high sn-2 IF, prebiotic oligosaccharides, and partially hydrolyzed whey protein to evaluate its effects on term infants with constipation vs. conventional IF (12). The study consisted of 38 constipated infants aged three to twenty weeks randomized to the high sn-2/oligosaccharides formula or the conventional formula. After three weeks, a greater increase in defecation frequency was observed in the high sn-2 IF/oligosaccharides group, from 3.5 to 5.6 defecations per week post treatment vs. the conventional infant formula group, which increased from 3.6 to 4.9 defecations per week post treatment. Improvement from hard stools to soft stools was found more often in the high sn-2 IF/oligosaccharides group (90%) vs. the standard infant formula group (50%), but did not reach statistical significance. However, a significant improvement of stool consistency was noted for the high sn-2 IF/oligosaccharide group (p=0.04). In addition, a two-week study using this same formula to measure comfort in infants less than four months old found decreased colic (at one week, p<0.001) and crying episodes (after two weeks, p<0.001) in 199 infants with infantile colic compared to a conventional (low sn-2 palmitic acid) infant formula (13).

Another study found further benefits of the combination of high sn-2 IF with oligosaccharides. In a clinical trial on 102 healthy full-term infants for twelve weeks, stool softness and probiotic bifidobacteria growth was measured in an infant formula containing high sn-2, oligosaccharides, and hydrolyzed protein vs. control formula. At six weeks, the high sn-2 IF with oligosaccharides and hydrolyzed protein produced softer stool (p=0.005) and higher counts of probiotic bifidobacteria (p<0.005) than the control formula (14).

In another example, 300 healthy, full-term, formula-fed infants at seven to fourteen days old were fed either conventional formula (control), high sn-2 IF, high sn-2 IF with 3 g/L oligofructose (OF), or high sn-2 IF with 5g/L OF for eight weeks. HM-fed infants (n=75) were also studied in parallel. High sn-2 IF led to 46% less stool soap palmitate (p<0.001) than the control formula, as well as 20% more soft stools (p=0.026) and 50% fewer formed stools (p=0.003). High sn-2 IF also led to significantly higher fecal bifidobacteria concentrations vs. control formula after eight weeks (p<0.05). The addition of OF had an even greater effect on stool softness, with 65% fewer formed stools for high sn-2 with 3 g/L OF and 79% fewer for high sn-2 with 5 g/L OF vs. control formula. Stool samples from the high sn-2 with 5 g/L OF group closely resembled those of HM-fed infants. The high sn-2 IF with added OF also resulted in significantly higher fecal bifidobacteria concentrations vs. control formula after eight weeks (p<0.01), with levels comparable to those of HM-fed infants (27).

The objectives of each of these studies were not to determine the efficacy of individual ingredients. Nonetheless, these studies suggest that IF with added components which appear in human milk, such as high sn-2 nutritional lipids and oligosaccharides, can be more beneficial for infants than IF which does not contain them.

Conclusion

In conclusion, human milk supplies vital nutrients to infants and is the gold standard to which all infant formulas are compared. While many infant formulas supply necessary nutrients comparable to human milk, the type of fat can differ significantly, especially in the distribution of palmitic acid among triglyceride positions sn-1, sn-2, and sn-3. Specially designed infant formula fats containing high sn-2 nutritional lipids like Betapol® more closely resemble the fat structure found in human milk fat and serve as a functional ingredient. Studies show that high sn-2 IF, much like human milk, leads to increased fatty acid absorption, increased calcium absorption, increased bone mineralization, reduced formation of fecal calcium soaps, softer stools, and healthier microbiota when compared with IF produced with conventional vegetable oils. This overall positive effect on gut health seems to also lead to less crying, better sleep, and potentially better neurodevelopmental outcomes.

No infant formula is superior to human milk, but the nutritional similarities of high sn-2 IF to human milk fat and the proven functional benefits suggest the importance of including high sn-2 nutritional lipids in all infant formulas.

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