CODEX ALIMENTARIUS COMMISSION



Food and Agriculture Organization of the United Nations



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Agenda Item 5a
NFSDU/41 CRD 38

Original language only

JOINT FAO/WHO FOOD STANDARDS PROGRAMME CODEX COMMITTEE ON NUTRITION AND FOODS FOR SPECIAL DIETARY USES

Forty-first Session

Dusseldorf, Germany 24 - 29

ESSENTIAL FATTY ACID COMPOSITION IN RUTF

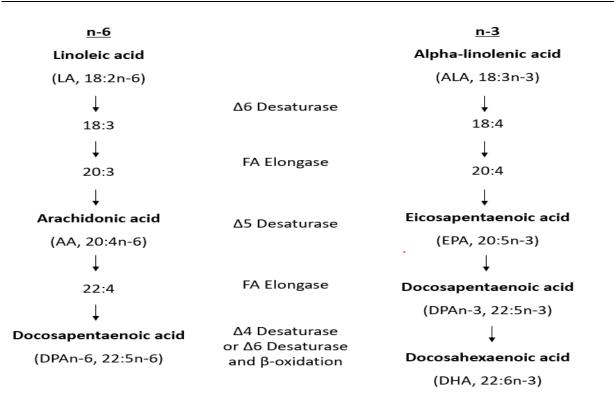
Comments by UNICEF

Summary

Ready to use therapeutic food (RUTF) are used for the medical and dietary management of infants and young children with severe acute malnutrition (SAM) and are provided to millions of infants and children each year using community-based management protocols. Current RUTF formulations contain 45 - 60% fat, with 3 - 10% omega6 and 0.3 - 2.5% omega-3 fatty acids. The fatty acid profile in RUTF was not designed to optimize long term long-chain polyunsaturated fatty acid (LCPUFA) status (Briend A et al 2015 *Food Nutr Bull*). Infants and young children need LCPUFA to support their rapidly growing brain and nervous system during the first 2 years of life. (EFSA Journal 2010). Since the publication of the 'The Joint Statement' ¹ (World Health Organization/World Food Programme/United Nations System Standing Committee on Nutrition, United Nations Children's Fund, 2007), new scientific data has been published indicating that an alternative fatty acid profile maintains and enables the child's own production of DHA, supporting brain and nervous system development.

Fat is an important source of energy for infants and young children. Children suffering from SAM have increased energy requirements for catch-up growth and need energy dense diets for recovery (Michaelsen KF et al 2011 *Mat Child Nutr*). Fat content is the most important factor influencing energy density in RUTF, as the energy density of fat (9kcal/g) is more than double that of protein and carbohydrate (4kcal/g). Essential fatty acids cannot be synthesized by the body and must be supplied in the diet. Linoleic acid (LA, 18:2 omega-6) and alpha-linolenic acid (ALA, 18:3 omega-3) are essential fatty acids required for human health and are included in the nutritional composition for the Codex Guideline for RUTF. Docosahexaenoic acid (DHA, 22:6 omega-3) and eicosapentaenoic acid (EPA, 20:5 omega-3) are LCPUFA of special importance during pregnancy, infancy and the first 2 years of life. DHA is particularly important for infants as it is highly concentrated in the developing brain and eye. Deficiency of ALA and DHA results in adverse clinical neurological symptoms. Metabolism of fatty acids occurs primarily in the liver, where synthesis and elongation of LCPUFA relies on several enzymes. While the omega-6 and omega-3 fatty acid families share desaturation and elongation enzymes, they do not inter-convert in humans. LA competes with ALA for enzymes within the metabolic pathways to produce LCPUFA.

¹ WHO, WFP, SCN and UNICEF, Community Based Management of Severe Acute Malnutrition Joint Statement, 2007



While consuming dietary sources of DHA such as fish, improves DHA status, the consumption of the intermediate metabolites for DHA including ALA, docosapentaenoic acid (DPA omega-3), or EPA does not result in higher DHA (Brenna JT et al 2009 *Prostaglandins Leukot Essent Fatty Acids*). Increasing ALA in the diet while holding LA levels constant can improve levels of DHA precursor EPA, but not DHA. Improving DHA status can be achieved in one of two ways – reducing high levels of dietary LA or consumption of preformed DHA. Diets high in LA suppress the body's own endogenous production of LCPUFA and inhibit incorporation of DHA and EPA into tissues. The balance of LA:ALA in the diet is critical to any discussion of fatty acids levels for formulation and manufacturing of RUTF (Brenna JT et al 2015 *BMC Med*, Hsieh JC et al 2015 *J Pediatr Gastroenterol Nutr*, Jones KD et al 2015 *BMC Med*). LCPUFA status and utilization can be improved by decreasing LA and omega-6 fatty acids in the diet.

A balanced ratio of LA:ALA enables endogenous LCPUFA production and the maintenance of healthy blood LCPUFA status. Current standard peanut based RUTF formulations are high in LA (> 7.9% total energy) with LA:ALA ratios approximately between 11.3:1 and 53:1 (Brenna JT et al 2015 *BMC Med*).

The scientific justification for lowering LA levels and providing a balanced ratio of LA:ALA to improve the lipid composition in RUTF is supported by three clinical studies in children with SAM (Babirekere-Iriso E et al 2016 *Br J Nutr*, Hsieh JC et al 2015 *J Pediatr Gastroenterol Nutr* and Jones KD et al 2015 *BMC Med*). These studies demonstrate improvement/maintenance of LCPUFA status with alternative formulations of RUTF using either low LA (7.2% total energy, LA:ALA ratio 1:1) or preformed dietary DHA and EPA (214 mg, LA:ALA ratio 2.3:1) compared to standard RUTF; DHA and LCPUFA status deteriorated with standard RUTF treatment.

An observational study in Uganda measured blood FA in children with SAM from hospital admission to 16 weeks after admission and showed lowered LCPUFA status with standard RUTF feeding (Babirekere-Iriso E et al 2016 *Br J Nutr*). DHA and EPA levels declined 22.8% and 38.9%, respectively, after beginning treatment with standard RUTF feeding and remained below admission levels at 16 week follow up. The high levels of dietary LA typically found in standard RUTF suppressed the endogenous production of LCPUFA (DHA and EPA) and suggest that the current lipid composition of therapeutic feeds and RUTF cannot replenish or correct LCPUFA deficiency in children recovering from SAM.

Another study in Malawi showed that children with SAM fed standard RUTF with high LA (13.3% total energy) and LA:ALA ratio 53:1 exhibit 25% significantly lower DHA status after four weeks of treatment, when compared to an intervention group fed an experimental RUTF with lower LA:ALA ratio containing high oleic (18:1 omega-9) peanuts (Hsieh JC et al 2015 *J Pediatr Gastroenterol Nutr*). The alternative RUTF formulation with lower LA (7.2% total energy) and LA:ALA ratio of 1:1, improved/maintained LCPUFA (DHA and EPA) status compared to standard RUTF. EPA significantly increased 64%, DPA omega-3 significantly increased 79%, and DHA increased 4% non-significantly. Importantly, these are the first results that demonstrate the ability of children with SAM to endogenously synthesize DHA, DPA omega-3 and EPA during nutritional rehabilitation with high oleic peanut based RUTF (low LA) and LA:ALA ratio of 1:1.

The study conducted in Kenya compared standard RUTF (LA:ALA ratio 11.3:1) containing high LA (7.9% total energy), ALA (0.7% total energy) to an alternative formulation RUTF with and without preformed dietary LCPUFA (Jones KD et al 2015 *BMC Med*). The alternative formulation RUTF (LA:ALA ratio 2.3:1) contained high LA (7.6% total energy), high ALA (3.3% total energy), and preformed LCPUFA, provided as fish oil (approximately 80mg DHA, 135mg EPA). Preformed dietary DHA and EPA improved the LCPUFA status in children with SAM, while children treated with standard RUTF or alternative formulation RUTF without preformed LCPUFA had 11-21% significantly decreased plasma DHA levels after receiving treatment. High dietary LA in standard RUTF suppressed endogenous production of DHA, and similarly, the high levels of both LA and ALA in the alternative formulation RUTF also inhibited DHA synthesis. Increasing the DHA precursor, ALA, increased EPA but did not increase levels of DHA. The fish oil (DHA and EPA) provided with alternative formulation RUTF was effective in improving DHA levels in children with SAM.

Lower levels of LA and a balanced ratio of LA:ALA enables endogenous DHA production in children with SAM. DHA is the key LCPUFA for neural development. During weaning and after cessation of breastfeeding, infants and young children are at a high risk for insufficient DHA because complementary foods in typical plant-based diets contain high LA and little or no DHA (Michaelsen KF et al 2011 *Matern Child Nutr*). Lipid composition of RUTF may be improved by decreasing LA levels to support maintenance of healthy blood LCPUFA status for neural development and promote long term recovery from SAM.

Table 1. Current RUTF fatty acid composition compared to new proposed composition

	Current RUTF fatty acid profile	Proposed RUTF fatty acid profile composition to support LCPUFA/DHA status in children with SAM			
Nutrient	% total energy	% total energy	kcal/100g	g/100g	g/100kcal
Energy			520 - 550		
Lipids		45 - 60%	234 - 330	26 - 36.34	4.7 - 6.9
Omega 6 fatty acids / LA	3-10% of total energy	2.5 – 7.2% of total energy	13.00–39.60	1.44 - 4.40	0.26 – 0.85
Omega-3 fatty acids /ALA	0.3-2.5% of total energy	• 0.5 – 2.5% of total energy	2.60 - 13.75	0.29 – 1.51	0.05 - 0.29

Proposal for RUTF Guideline:

The following changes to RUTF lipid composition are proposed, based on the currently available scientific evidence on omega-6 and omega-3 fatty acid metabolism of SAM children from clinical studies in Kenya, Malawi and Uganda:

- Ensure a ratio of LA:ALA between 1:1 and 5:1
- Decrease the minimum and maximum level of omega-6 fatty acids/AL to 2.5-7.2% (from 3-10%) of total energy
- Increase the minimum level of omega-3 fatty acids/ ALA to 0.5-2.5% (from 0.3-2.5%) of total energy
- Consideration of provision of preformed DHA and EPA as a permissible optional ingredient in the RUTF codex guideline.