Structured MLCTs

Scientific summary

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1 Introduction

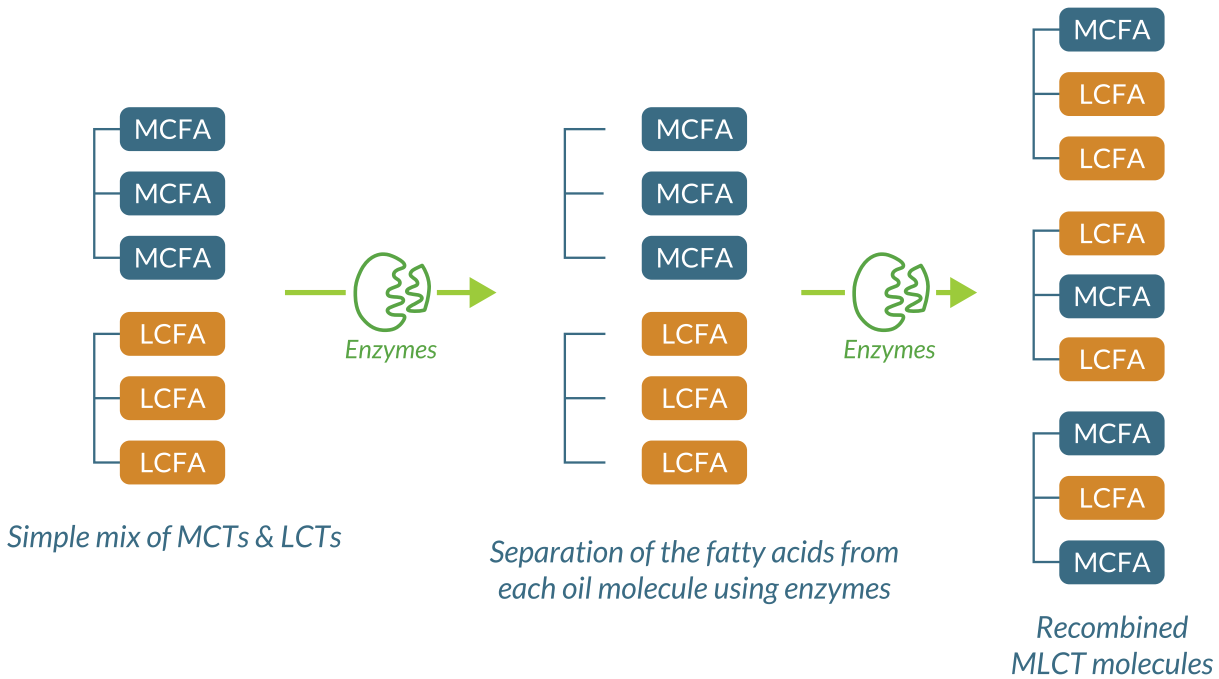
Structured lipids are lipid molecules that have been selected or developed to have a specific structure. In the case of tri-glycerides, such structure constitutes the specific arrangement of its three component fatty acids. Structured triglycerides, if they are abundant in a natural source, can be enriched using fractionation techniques. More often, however, the production of structured triglycerides aims to generate molecules which are scarce in nature or unavailable in plant-based sources of lipids. A typical example of this are oleic-palmitic-oleic (OPO) triglycerides. Although abundant in human milk and proven to be beneficial to infant nutrition [1], they are rare in plant-based oils [2]. Hence, OPO triglycerides are produced for infant formula by recombining plant oil raw materials using a technique called interesterification. This technique can combine fatty acids from multiple sources to create a specific structured triglyceride.

Interesterification can be achieved through either chemical or enzymatic means. Both methods produce similar end results. However, chemical interesterification results in higher level of contaminants in the end-products due to the temperatures employed. Hence, at Bunge, all structured lipids for infant, medical, and sports nutrition applications are produced enzymatically.

Structured medium- and long-chain triglycerides (structured MLCTs) are the product of interesterification whereby fatty acids of medium-chain triglycerides (MCTs) and long-chain triglycerides (LCTs) are randomly recombined to create new triglycerides (Figure 1). The newly formed lipid molecule contains both medium-chain fatty acids (MCFAs)–such as caprylic (C8:0) and capric (C10:0) acids—and long-chain fatty acids (LCFAs)—such as oleic (C18:1), linoleic (C18:2), and linolenic (C18:3) acids.

In this article, we review scientific literature supporting the use of structured MLCTs in adult nutrition applications, with a specific focus on muscle health. It is worth noting that structured MLCTs suited for infants differ from the structured MLCTs specifically designed for adult nutrition applications. To learn more or discuss the science behind MLCTs, reach out to nutrition@bunge.com.

Figure 1 Enzymatic interesterification to produce structured MLCTs



2 Structured MLCTs absorption and distribution

An important feature of structured MLCTs is their unique absorption mechanism. The length of a fatty acid's carbon chain affects its digestion and absorption. The longer the chain length, the lower the degree of uptake [3]. LCTs are subject to de-esterification in the intestine, resulting in the release of two free LCFAs and the formation of an sn-2 monoglyceride. These enter the cells that line the intestine (enterocytes), largely by diffusion. Once inside the enterocytes, LCFAs and monoglycerides are re-esterified into triglycerides, then packed into structures called chylomicrons along with phospholipids, esterified cholesterol, and apolipoproteins. These chylomicrons are released into the lymphatic system from which they drain into the subclavian vein via the thoracic duct [4, 5]. In this manner, LCTs reach the circulatory system to become available to peripheral tissues and become long-lasting sources of energy.

MCTs are processed in a completely different manner [4, 6]. In the intestine, they are hydrolyzed into free MCFAs and glycerol. MCFAs also diffuse into the enterocytes, but are generally not re-esterified. Instead, they continue moving by diffusion into the portal vein where they form complexes with albumin [6]. MCFAs bonded to albumin are then directly taken up by the liver [7]. In the liver, MCFAs are rapidly catabolized in the mitochondria through ß-oxidation without a significant amount of them reaching the peripheral circulation [4, 7].

Structured MLCTs combine the properties of both MCTs and LCTs [8-11]. They are de-esterified in the lumen of the intestine, and diffuse into enterocytes as monoglycerides and fatty acids. Inside the enterocytes, the MCFAs, LCFAs, and monoglycerides are mostly re-esterified and follow the chylomicron route to the lymphatic system. These chylomicrons enter the circulatory system, taking MCFAs to peripheral tissues where they can become fast sources of energy. Meanwhile, the LCFAs, also part of those chylomicrons, can support more long-lasting energetic needs (Table 1 & Figure 2).

In summary, MCTs and structured MLCTs are completely different due to their distinctive absorption mechanisms. MCTs are metabolized rapidly in the liver without significant levels of MCFAs reaching other parts of the body. In contrast, structured MLCTs deliver MCFAs to the peripheral circulation that irrigates and brings energy to muscles (Figure 3).

Table 1 Metabolic performance of structured MLCTs, compared to MCTs, LCTs, MCT/LCT mixes

	Structured MLCTs	MCTs	LCTs	MCT/LCT mixes
Absorption route	Hydrolysis into MCFAs, LCFAs and 2-monoglycerides. Reformed as MLCTs and packed into chylomicrons. Transported into the thoracic duct to reach peripheral circulation.	Hydrolysis into MCFAs that diffuse into the portal vein to reach the liver.	Hydrolysis into LCFAs and 2-monoglycerides. Reformed as LCTs and packed into chylomicrons. Transported into the thoracic duct to reach peripheral circulation.	MCFAs from MCTs follow the portal vein route. LCFAs from LCTs follow the thoracic duct route.
Absorption speed	Faster than LCTs, but slower than MCTs.	Fast.	Slow.	Fast for MCTs; slow for LCTs.
Energy supply	Balanced energy supply, containing MCFAs and LCFAs, for tissues.	Rapid (MCFAs) energy supply for the liver.	Slower (LCFAs) energy supply for tissues.	Rapid (MCFAs) energy for the liver; slower (LCFAs) energy for tissues.
Protein synthesis	Improved compared to MCTs, LCTs or MCT/LCT mixes.	No specific effect in healthy individuals.	No specific effect in healthy individuals.	No specific effect in healthy individuals.
Triglyceride clearance	Fast clearance.	Fast clearance.	Slower clearance.	Fast for MCTs; slower for LCTs.
Side effects	Improved tolerance compared to MCTs.	Potential for liver side-effects and metabolic acidosis at high doses.	Improved tolerance compared to MCTs.	Driven by MCT dosage.

Figure 2 Structured MLCTs absorption mechanism

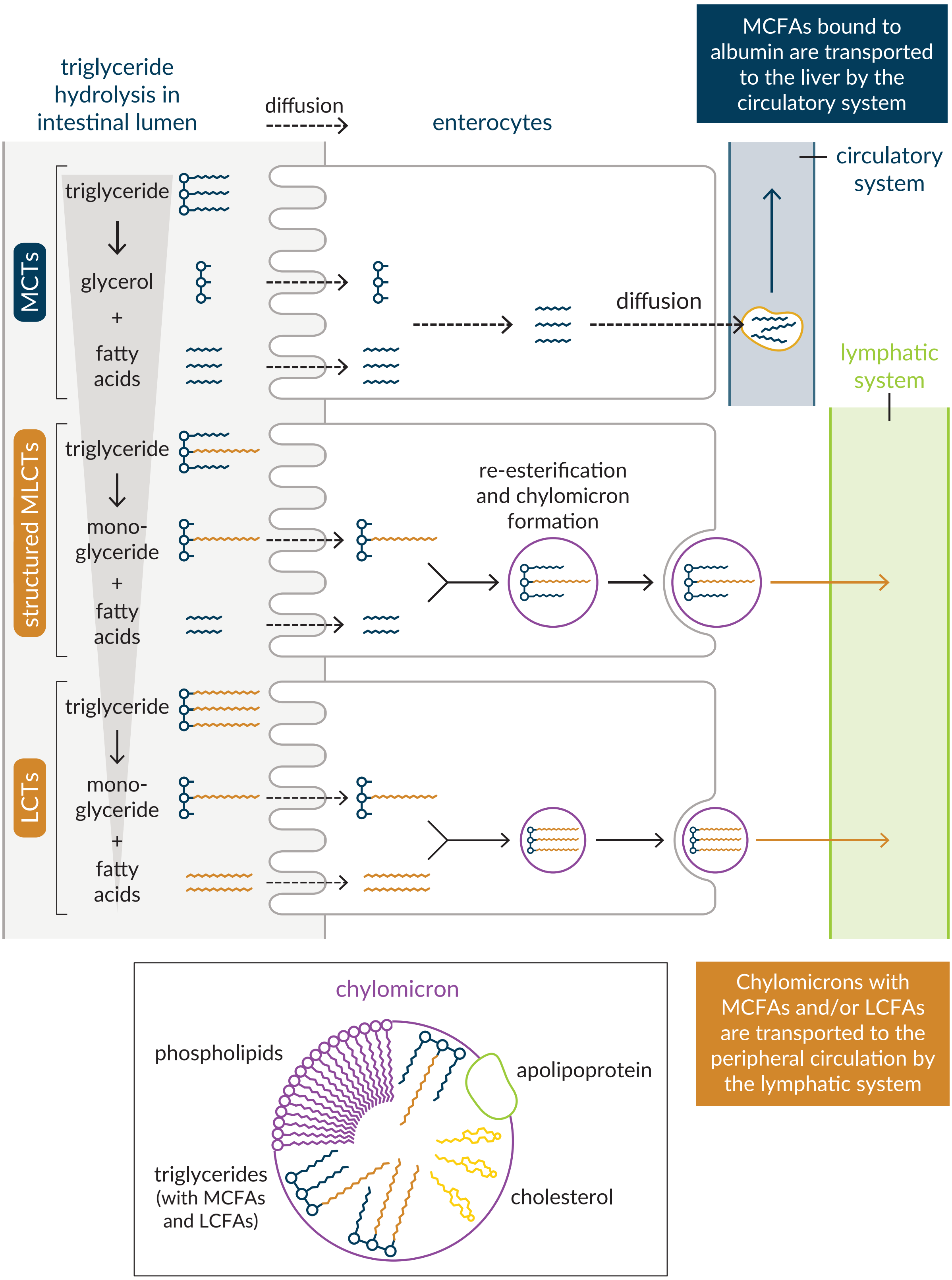
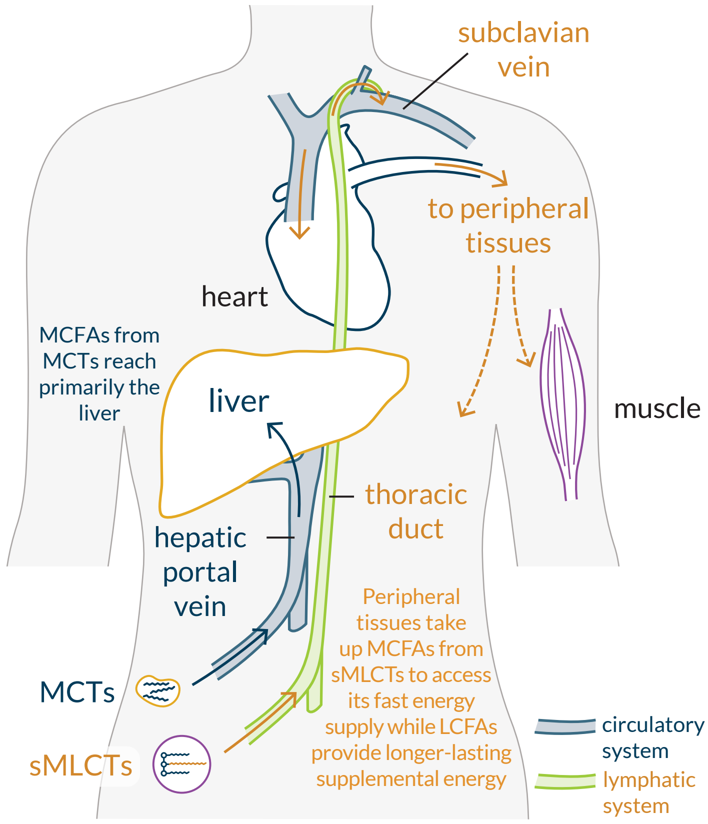


Figure 3 MCFAs from structured MLCTs reach muscles



3 Benefits of structured MLCTs as a functional ingredient in medical nutrition

MCTs with medical nutrition applications were first developed in the 1950s and 1960s to provide a source of energy for individuals diagnosed with various malabsorption, maldigestion, and related disorders [6, 12]. Since then, various preparations for oral, enteral, and parenteral use have become available. To add essential fatty acids to MCT preparations, and to address concerns when using MCTs alone in medical nutrition applications [13], mixtures of MCTs and LCTs were subsequently developed. Structured lipids containing both MCFAs and LCFAs followed. In addition to providing the benefits of mixtures of MCTs and LCTs, these structured MLCTs showed a series of other advantages resulting from their distinct absorption and distribution within the body [10, 14-16].

3.1 Structured MLCTs for dietary management of digestive disorders

MCTs are digested more easily than LCTs, mainly because MCFAs are absorbed faster [3, 6]. Hence, MCTs have been extensively used as source of nutrition in the management of disorders that affect nutrient absorption across all age groups [12, 17-23]. In these applications, ingestion of MCTs is well-tolerated, with limited side-effects. However, long-term usage of MCTs at high doses, due to their absorption and metabolism, might cause excessive burden on liver function (Table 1). Furthermore, MCTs do not provide essential fatty acids, so patients on high doses of MCTs must supplement their total fat intake with LCTs.

Structured MLCTs combine the characteristics of both MCTs and LCTs, supplying essential fatty acids, providing energy sources that are easy to absorb, and supporting energy delivery to peripheral tissues, including muscle. These combined properties make structured MLCTs ideal for Oral Nutritional Supplementation (ONS) and enteral (tube) feeding when nutritional status and physical health are part of the treatment's priorities. Indeed, structured MLCTs have been used in oral supplementation, early enteral feeding, and transition away from total parenteral nutrition in children of one to thirteen years of age with conditions like cystic fibrosis, malabsorption, maldigestion, inflammatory bowel disease, celiac disease, pancreatic insufficiency, and short bowel syndrome. Structured MLCTs have also been used in adults with gastroenteric dysfunction or feeding issues, including short bowel syndrome, bowel resection, malabsorption, pancreatic insufficiency, chronic diarrhea, Crohn's disease, bile salt deficiency, diverticulosis, celiac disease, and cystic fibrosis.

For example, structured MLCTs containing linoleic acid have been shown to support faster absorption of this essential fatty acid compared to higher amounts of the fatty acid supplied as LCTs in cystic fibrosis patients with pancreatic insufficiency [24, 25]. In these studies, the authors hypothesized that because structured MLCTs supply a patient's energetic needs—presumably through MCFAs—linoleic acid is left to play its cellular function rather than being consumed as an energy source. Another study on individuals with chronic malabsorption or maldigestion showed the benefits of a peptide-based ONS containing structured MLCTs with similar composition to Bunge's NuliGo™ lipids. Although the study emphasized the tolerability of the peptide-based formula—an essential advantage to ensure compliance in these types of patients—it also showed the suitability of these specific structured MLCTs as efficient energy sources leading to improved nutritional status [26].

3.2 Structured MLCTs for dietary management of obesity

Most of the literature describing the effects of structured MLCTs on obesity-related parameters (e.g., satiety, fat oxidation, body fat composition, plasma lipids) lacks control groups administered equivalent doses of MCFAs as MCTs. The control groups in all articles we reviewed were administered regular oils composed mostly of LCTs. Hence, it is our opinion that the structured MLCTs used in those studies present no advantage over conventional MCTs for the dietary management of obesity. This opinion is supported by the lack of differential effects on satiety and fat oxidation observed with structured MLCTs compared to a physical mix of MCTs and LCTs [27]. It is worth noting that Swift et al. [28] observed higher plasma lipids, which results in higher fat oxidation, in the MCT group compared to the structured MLCT group, but the effect was confounded by different MCFA dosages between the groups and could be explained by the effects of MCFAs from MCTs in the liver.

As further reading and for additional references, see the reviews by Lee et al. [29] and Wang et al. [30].

3.3 Structured MLCTs in critical care

Although not the primary focus of this article, it is important to review the data from structured MLCT applications in critical care for two reasons: (1) critical care settings are well controlled, leading to more reproducible measurements, and (2) there are multiple high-quality clinical trials comparing parenteral structured MLCT use with isocaloric physical mixes of MCTs and LCTs. Absorption studies have shown that structured MLCTs reach peripheral circulation after ingestion. Thus, parenteral infusion data provides insights into the physiological effects of structured MLCTs when taken orally, and are a good proxy for understanding the effects on muscle health.

Meta-analyses of clinical trial results show a strong positive effect of structured MLCTs on nitrogen balance [15, 16, 31]. Nitrogen is mainly introduced into the body by ingestion of foods or water containing nitrogen as proteins or salts, with protein being the main source. In critical care, parenteral nutrition provides a controlled amount of nitrogen through amino acids, typically at 1 g/kg of body weight per day. Nitrogen remains in the body when it is incorporated into proteins or is excreted, mainly through urine. Nitrogen balance is the difference between nitrogen intake and excretion. Nitrogen balance is positive when more nitrogen is entering than leaving the body. This is an indication that proteins are being synthesized faster than the rate at which they are being consumed or destroyed, a state called anabolic state. Nitrogen balance is negative when proteins are being consumed by the body, a state called catabolic state. In this state more nitrogen is leaving than entering the body. Nitrogen balance data in critical care shows that structured MLCTs push the body towards a more anabolic state in which proteins are being built. As 50-75% of the total protein in our bodies is in skeletal muscles [32], much of this protein synthesis occurs there.

It is worth iterating that all of these clinical studies compare structured MLCTs with physical mixes of MCTs and LCTs, indicating that a simple blend of MCT oil and another oil rich in LCTs cannot achieve the same effect. Wu et al. [15] suggested that the efficacy of structured MLCTs is due to parallel uptake of MCFAs and LCFAs by cells, leading to better use of each energy source via optimal oxidation and faster clearance of structured MLCT molecules from the bloodstream. This conclusion was supported by lower plasma triglyceride levels and improved nutritional status in patients administered structured MLCTs, as measured by albumin and pre-albumin levels [15, 16].

4 Structured MLCTs could support muscle health across all stages of life

A review of the absorption and distribution data (see Section 2), and the evidence supporting the benefits of structured MLCTs in medical nutrition (see Section 3) suggest that structured MLCTs deliver a balanced source of energy composed of MCFAs and LCFAs to peripheral tissues, including muscles. This seems to optimize usage of each energy source and lead to a state of increased protein synthesis.

Exercise, especially under conditions requiring endurance, leads to a decrease of muscle glycogen deposits, the main source of energy for the muscle. Reductions in glycogen levels trigger the activity of enzymes that oxidate specific amino acids to satisfy some of the energy requirements, transitioning the muscle into a catabolic state [33]. Access to supplemental sources of energy, such as circulating triglycerides, allows muscles to continue performing longer, improving endurance by slowing the rate of glycogen depletion [34]. Structured MLCTs reach the peripheral circulation carrying MCFAs which are rapidly converted into energy once they enter muscle, unlike traditional MCTs which are mainly metabolized in the liver. Structured MLCTs therefore have potential as an ideal supplemental source of circulating triglycerides for energy to support muscle performance during long-lasting effort, while sparing amino acids for protein synthesis. Indeed, this might explain the positive nitrogen balance effect observed with structured MLCTs in medical nutrition [15, 16, 31]. Furthermore, structured MLCTs have also been associated with reduced inflammation, as reflected by significantly lower C-reactive protein concentrations [16], which may lead to more efficient tissue repair and recovery after strenuous exercise.

What constitutes strenuous exercise and the limits of endurance vary with level of training and with age. Muscle condition plays an important role in maintaining health and quality of life during aging. However, muscle mass and strength reach their peaks at around age 30, then start to decline rapidly after age 40, and continue degrading until 35-40% of total muscle mass and 20-40% of strength is lost by around age 80 [35]. If not addressed, muscle mass and strength loss can threaten health and independence by resulting in impaired mobility, balance, and increased risk of falls and fractures [36]. Focusing on muscle health conditions during the aging process is therefore critical. Structured MLCTs could prove useful for muscle health support in the elderly by providing quick-to-metabolize MCFAs, with the additional benefits of reducing inflammation and sparing amino acids for protein synthesis. Nutritional supplementation leading to improved muscle health, together with a balanced diet and the right amount of exercise, is likely to support older adults in maintaining muscle mass and, concomitantly, the mobility required to lead a more active life.

In summary, the evidence reviewed in Sections 2 and 3 suggests that specific structured MLCT supplementation could be the ideal tool to satisfy an athlete's extreme muscle energy and endurance demands, to aid with muscle recovery and repair, and to support a longer active life.

5 Dosage and applications for structured MLCTs

Structured MLCTs comprise a diverse group of molecules. This section refers specifically to Bunge's NuliGo® lipids, and does not apply to other structured MLCTs.

From a safety perspective, the approval of structured MLCT for safe use in clinical nutrition, both enterally and parenterally, supports that they are safe for use in food. NuliGo® lipids are deemed Generally Recognized As Safe (GRAS) in the U.S. [37]. In Europe, structured MLCTs—including NuliGo® lipids—can be used in general foods, foods for special medical purposes, and infant formulas intended for specific therapeutic conditions [38]. In Australia and New Zealand, structured MLCTs are permitted to be used as dietary supplements and in supplemented food [39, 40]. In China, structured MLCTs have been approved as novel food in 2012 [41], but specific compositions are required.

The GRAS panel which reviewed NuliGo® lipids' data suggested a daily dose for adults of 73 g/day of NuliGo® lipids to end with a conservative exposure based on NHANES fat intake data [42]. Clinically-relevant dosages will vary with each application and target consumer population, but, in our opinion, are much lower than the 73 g/day maximum. For NuliGo® lipids' clinical research program in active adults and the elderly, we will test dosages of 4 to 9 g of NuliGo® oil per serving on a two-serving regime. For professional athletes and highly-trained individuals, NuliGo® lipids' clinical research and field testing programs are being conducted using 20 to 60 g/day as a supplement to the traditional carbohydrate intake, while keeping caloric intake constant.

Please reach out to nutrition@bunge.com to discuss the science behind structured MLCTs, learn more about the applications of different types of structured MLCTs, obtain regulatory support for specific countries, or develop the right dosage for your target consumer and application.

6 References

1 **Havlicekova, Z., Jesenak, M., Banovcin, P., & Kuchta, M. (2015).** Beta-palmitate — a natural component of human milk in supplemental milk formulas. *Nutrition Journal*, 15:28.

2 **Brockerhoff, H., & Yurkowski, M. (1966).** Stereospecific analyses of several vegetable fats. *J Lipid Res*, 7(1):62-64.

3 **McKimmie, R.L., Easter, L., & Weinberg, R.B. (2013).** Acyl chain length, saturation, and hydrophobicity modulate the efficiency of dietary fatty acid absorption in adult humans. *Am J Physiol Gastrointest Liver Physiol*, 305(9):G620–G627.

4 **Bloom, B., Chaikoff, I.L., & Reinhardt W.O. (1951).** Intestinal lymph as pathway for transport of absorbed fatty acids of different chain lengths. *Am J Physiol*, 166(2):451-455.

5 **Randolph, G.J., & Miller, N.E. (2014).** Lymphatic transport of high-density lipoproteins and chylomicrons. *J Clin Invest*, 124(3):929–935.

6 **Bach, A.C., & Babayan, V.K. (1982).** Medium-Chain Triglycerides: An Update. AJCN, 36(5):950-962.

7 **Schönfeld, P., & Wojtczak, L. (2016).** Short- and Medium-Chain Fatty Acids in Energy Metabolism: The Cellular Perspective. *J Lipid Res*, 57(6):943-954.

8 **Mu, H., & Høy, C.E. (2001).** Intestinal Absorption of Specific Structured Triacylglycerols. *J Lipid Res*, 42(5):792-798.

9 **Carvajal, O., Nakayama, M., Kishi, T., Sato, M., Ikeda, I., Sugano, M., & Imaizumi, K. (2000).** Effect of Medium-Chain Fatty Acid Positional Distribution in Dietary Triacylglycerol on Lymphatic Lipid Transport and Chylomicron Composition in Rats. *Lipids*, 35(12):1345-1352.

10 **Tso, P., Lee, T., & DeMichele, S.J. (1999).** Lymphatic Absorption of Structured Triglycerides vs. Physical Mix in a Rat Model of Fat Malabsorption. *Am J Physiol Gastrointest Liver Physiol*, 277(2):G333-G340.

11 **Jensen, G.L., McGarvev, N., Taraszewski, R., Wixson, S.K., Seidner, D.L., Pai, T., Yeh, Y.Y., Lee, T.W., & DeMichele S.J. (1994).** Lymphatic absorption of enterally fed structured triacylglycerol vs physical mix in a canine model. *Am J Clin Nutr*, 60:518-24.

12 **Holt, P.R. (1967).** Medium Chain Triglycerides: A Useful Adjunct in Nutritional Therapy. *Gastroenterology*, 53(6):961-966.

13 **Miles, J.M., Cattalini, M., Sharbrough, F.W., Wold, L.E., Wharen Jr., R.E., Gerich, J.E., & Haymond, M.W. (1991).** Metabolic and Neuorologic Effects of an Intravenous Medium-Chain Triglyceride Emulsion. *JPEN*, 15(1):37-41.

14 **Mok, K.T., Maiz, A., Yamazaki, K., Sobrado, J., Babayan, V.K., Moldawer, L.L., Bistrian, B.R., & Blackburn, G.L. (1984).** Structured Medium-Chain and Long-Chain Triglyceride Emulsions are Superior to Physical Mixtures in Sparing Body Protein in the Burned Rat. *Metabolism*, 33(10):910-915.

15 **Wu, G. H., Zaniolo, O., Schuster, H., Schlotzer, E., & Pradelli, L. (2017).** Structured Triglycerides versus Physical Mixtures of Medium- and Long-Chain Triglycerides for Parenteral Nutrition in Surgical or Critically Ill Adult Patients: Systematic Review and Meta-Analysis. *Clinical Nutrition*, 36(1):150-161.

16 **Li, C., Ni, Q., Pei, Y., Ren, Y., & Feng, Y. (2019).** Meta-Analysis of the Efficacy and Safety of Structured Triglyceride Lipid Emulsions in Parenteral Nutrition Therapy in China. *Clinical Nutrition*, 38(4):1524-1535.

17 **Schizas, A.A., Cremen, J.A., Larson, E., & O'Brien, R. (1967).** Medium-Chain Triglycerides: Use in Food Preparation. *J Am Diet Assoc*, 51(2):228-232.

18 **Harkins, R.W., & Sarett, H.P. (1968).** Medium-Chain Triglycerides. *JAMA*, 203(4):272-274.

19 **Leyland, F.C., Fosbrooke, A.S., Lloyd, J.K., Segall, M.M., Tamir, I., Tomkins, R., & Wolff, O.H. (1969).** Use of Medium-Chain Triglyceride Diets in Children with Malabsorption. *Arch Dis Child*, 44(234):170-179.

20 **Sakurai, T., Matsui, T., Yao, T., Takagi, Y., Hirai, F., Aoyagi, K., & Okada, M. (2002).** Short-Term Efficacy of Enteral Nutrition in the Treatment of Active Crohn's Disease: A Randomized, Controlled Trial Comparing Nutrient Formulas. *JPEN*, 26(2):98-103.

21 **Erskine, J.M., Lingard, C.D., Sontag, M.K., & Accurso, F.J. (1998).** Enteral Nutrition for Patients with Cystic Fibrosis: Comparison of a Semi-Elemental and Nonelemental Formula. *J Pediatr*, 132(2):265-269.

22 **Nucci, A. M., Barksdale Jr, E. M., Yaworski, J. A., Beserock, N., & Reyes, J. (2002).** Enteral Formula Use in Children After Small Bowel Transplant. *Nutrition in Clinical Practice*, 17(2):113-117.

23 **Roy, C. C., Ste-Marie, M., Chartrand, L., Weber, A., Bard, H., & Doray, B. (1975).** Correction of the Malabsorption of the Preterm Infant with a Medium- Chain Triglyceride Formula. *J Pediatr*, 86(3):446-450.

24 **McKenna, M.C., Hubbard, V.S., & Bieri, J.G. (1985).** Linoleic Acid Absorption from Lipid Supplements in Patients with Cystic Fibrosis with Pancreatic Insufficiency and in Control Subjects. *J Pediatr Gastroenterol Nutr*, 4(1):45-51.

25 **Hubbard, V.S., & McKenna, M.C. (1987).** Absorption of Safflower Oil and Structured Lipid Preparations in Patients with Cystic Fibrosis. *Lipids*, 22(6):424-428.

26 **Nelson, J.L. (2019).** A Pilot Intervention Study to Evaluate Compliance to a Peptide-Based Oral Nutritional Supplement in an Adult Population with Impaired Gastrointestinal Function. *Clin Nutr Exp*, 28:123-130.

27 **Bendixen, H., Flint, A., Raben, A., Høy, C.E., Mu, H., Xu, X., Bartels, E.M., & Astrup, A. (2002).** Effect of 3 Modified Fats and a Conventional Fat on Appetite, Energy Intake, Energy Expenditure, and Substrate Oxidation in Healthy Men. *AJCN*, 75(1):47-56.

28 **Swift, L.L., Hill, J.O., Peters, J.C., & Greene, H.L. (1992).** Plasma Lipids and Lipoproteins During 6 d of Maintenance Feeding with Long-Chain, Medium-Chain, and Mixed-Chain Triglycerides. *AJCN*, 56(5):881-886.

29 **Lee, Y.Y., Tang, T.K., & Lai, O.M. (2012).** Health Benefits, Enzymatic Production, and Application of Medium- and Long-Chain Triacylglycerol (MLCT) in Food Industries: A Review. *J Food Sci*, 77(8):R137-R144.

30 **Wang, Y., Zhang, T., Liu, R., Chang, M., Wei, W., Jin, Q., & Wang, X. (2022).** Reviews of Medium- and Long-Chain Triglyceride with Respect to Nutritional Benefits and Digestion and Absorption Behavior. *Food Res Int*, 155:111058.

31 **Zhu, M., & Li, X. (2013).** Meta-Analysis of Structured Triglyceride Versus Other Lipid Emulsions for Parenteral Nutrition. *Nutrition*, 29(6):833-840.

32 **Duda, K., Majerczak, J., Nieckarz, Z., Heymsfield, S.B., & Zoladz, J.A. (2019).** Chapter 1 - Human Body Composition and Muscle Mass. *Muscle and Exercise Physiology*, pp. 3-26.

33 **Wagenmakers, A.J., Beckers, E.J., Brouns, F., Kuipers, H., Soeters, P.B., van der Vusse, G.J., & Saris, W.H. (1991).** Carbohydrate Supplementation, Glycogen Depletion, and Amino Acid Metabolism During Exercise. *Am J Physiol Endocrinol Metab*, 260(6):E883-E890.

34 **Hickson, R.C., Rennie, M.J., Conlee, R.K., Winder, W.W., & Holloszy, J.O. (1977).** Effects of Increased Plasma Fatty Acids on Glycogen Utilization and Endurance. *J Appl Physiol Respir Environ Exer*, 43(5):829-833.

35 **Keller, K., & Engelhardt, M. (2013).** Strength and Muscle Mass Loss with Aging Process. Age and Strength Loss. *Muscles, Ligaments and Tendons J*, 3(4):346-350.

36 **Xue, Q.L., Walston, J.D., Fried, L.P., & Beamer, B.A. (2011).** Prediction of Risk of Falling, Physical Disability, and Frailty by Rate of Decline in Grip Strength: The Women's Health and Aging Study. *Arch Intern Med*, 171(12):1119-1120.

37 Based on 21 CFR 170.30 (a) and (b) eligibility for classification as generally recognized as safe (GRAS).

38 Not a novel food based on regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods.

39 Based on New Zealand's Dietary Supplements Regulations 1985 (SR 1985/208).

40 Based on the Food Standard: New Zealand Food (Supplemented Food) Standard 2016.

41 China Ministry of Health (2012). Announcement on Approving Medium and Long Chain Fatty Acid Edible Oil and Wheat Oligopeptide as New Resource Foods. Bulletin No. 16.

42 Centers for Disease Control and Prevention of the United States of America. National Health and Nutrition Examination Survey (NHANES).

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