

Medium-chain triglycerides (MCTs) for the symptomatic treatment of dementia-related diseases: A systematic review

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Supplementary Material

Supplementary Table S1. Search strategy including database, search string, and filters.

Data base	Search	Filter
Pubmed	(medium chain OR medium-chain OR Caproic* OR Capryl* OR Capric* OR Lauric*) AND (fatty acid OR Triglyc* OR triacyl* OR acyl*OR oil) OR Tricaprilin OR Tricaprylin OR Caprylidene OR Axona OR coconut OR Palm oil OR (ketogenic AND (formula OR supplement OR agent OR Drink) OR MCFA OR MCT) AND (Dementia OR Alzheimer OR Lewy body OR Frontotemporal OR Parkinson OR MCI OR cognitive OR memory) AND (Impair* OR decline OR defect) AND (Trial OR study OR RCT OR intervention OR case) NOT (Review[Filter] OR Review[Title] OR mice[title] OR rat[title])	English, German
CENTRAL	#1 (Medium chain OR medium-chain OR Capryl* OR Capric* OR Lauric*) NEXT (Triglyc* OR Triacyl* OR fatty OR acid* OR acyl* OR oil*) OR MCFA OR MCT #2 Tricaprilin OR Tricaprylin OR Caprylidene OR Axona #3 Coconut* OR Palm OR Coconut Oil #4 keto* NEXT (Formula* OR Supplement* OR Agent* OR Drink*) #5 Dement* OR Alzheimer* OR ((cognit* OR memory) NEXT (Impair* OR decli* OR disorder*)) OR MCI OR Lewy body OR Frontotemporal OR Parkinson #6 Dementia and cognitive Improvement*.crg (#1 OR #2 OR #3 OR #4) AND (#5 OR #6)	Trials
LIVIVO	TI=(Medium chain OR medium-chain OR Caprylidene OR Tricaprylin OR Tricaprilin OR Axona OR MCT OR MCFA OR coconut OR Palm Oil OR ketogenic Formula OR ketogenic Agent OR Ketogenic Drink OR ketogenic Supplement) AND TI=(Dement* OR Alzheimer* OR cognitive impair* OR Cognitive disorder* OR Memory Disorder* OR MCI OR Lewy Body OR Frontotemporal OR Parkinson) NOT TI=(Review OR Meta)	English, German
Web of Science	TS=(medium chain OR medium-chain OR Caproic* OR Capryl* OR Capric* OR Lauric*) AND (fatty acid OR Triglyc* OR triacyl* OR acyl) OR Tricaprilin OR Tricaprylin OR Caprylidene) AND TS=(Dement* OR Alzheimer* OR MCI OR Lewy body OR Frontotemporal OR Parkinson OR (cognit* OR memory) AND (Impair* OR decli* OR disorder*)) AND LA=(English OR German) NOT TI=(Review OR Meta*)	English, German

Supplementary Table S2. Characteristics of included uncontrolled studies; MCT = medium chain triglycerides; m/f = male/female; CO = coconut oil; d = days; w = weeks; OLE = open label extension; Ø = mean; C8 = caprylic acid; C10 = capric acid; AD = Alzheimer's disease.

Author/year country	Diagnosis MMSE (Ø)	Age (Ø) m/f (%)	APOE (+/-)	N (analysis)	Drop-out rate	Intervention product (C8%/C10%) Application form Intake	Intervention duration Initial phase	Dosage	g MCT/d (g C8/C10)
Case Reports									
Newport et al., 2015 -	AD 23	58 100/0	100% (100/0)	1 (1)	-	CO/MCT mixture (4:3)	2 years 35 mL CO → 165 ml MCT/CO	3-4x 165 mL	132 g (68/31) ³
Farah et al., 2014 USA	AD 23	70 100/0	100% (0/100)	1 (1)	-	MCT-powder (C8)	109 d 10 → 40 g in 7d	1x 40 g	20 g (20/0)
Maynard et al., 2013 USA	AD 20,3	81,3 75/25	12,5% (100/0)	8 (8)	12,5%	MCT oil (C8)	Ø 14,6 months ² -	1x 20 g	20 (20/0)
Cohort studies									
Maynard et al., 2013 USA	AD 20,6	79,7 56/44	12,7% (29/71)	55 (55)	14,5%	MCT oil (C8)	Ø 19,8 months ²	1x 20 g	20 g (20/0)
Ohnuma et al., 2016 Japan	AD 18,1	63,9 55/45	100% (32/68)	24 (22)	8,3%	MCT powder Axona (100/0) As a drink in 118-236 mL ¹ Postprandial ¹	90 d 10 → 40 g in 6d; every 2d +10 g	1x 40 g	20 g (20/0)
Gandotra et al., 2014 Netherlands	AD 10,4	81,9 32/68	/	32 (31)	3,1%	CO native Pure or mixed in Postprandial for breakfast	4 weeks	1x 20 mL	11,7 g (1,4/1) ³
Croteau et al. 2018 Canada	AD 22	73,5 40/60	/	15 (-)	26,7%	1. MCT supplement Abitec (95/0) 2. MCT supplement Abitec (55/35) Emulsified in 250 ml lactose-free milk To the meals (2-3)	1 month each 4 weeks wash out 1 week	2x 15 g	14,25 g (14,3/0) 13,5 g (8,3/5,3)
Ota et al. 2019 Japan	AD 20	73,4 55/45	/	19 (-)	15,3%	MCT supplement Ketonformula (21,8/7) As drink in hot water Preprandial	12 weeks	1x 50 g	19,4 g (10,9/3,5)

¹ Information from external data from the manufacturer [95]

² The minimum number of months of treatment is six months

³ Estimated value based on 63,% MCT content 7,5% C8/5,7% C10

Supplementary Table S3. Characteristics of included controlled studies; MCT = medium chain triglycerides; LCT = long chain triglycerides; m/f = male/female; CO = coconut oil; d = days; w = weeks; OLE = open label extension; Ø = mean; C8 = caprylic acid; C10 = capric acid; AD = Alzheimer`s disease; ITT= intention to treat; PP = per protocol; DC = dosage compliant.

Author/year country	Diagnosis MMSE (Ø)	Age (Ø) m/f (%)	APOE (+/-)	N (IG/KG) N Analysis (IG/KG)	Drop-out rate (IG/KG)	Intervention product (C8%/C10%) Application form Intake	Intervention duration Initial phase	Dosage	Control	g MCT/d (C8/C10)
Parallel Design										
Chan et al. 2017 Malaysia	AD 10-24	70-79 35/65	/	40 (20/20) 22 (8/14)	45% (60/30)	CO native Pure, mixed in food/drinks	24 weeks 2 weeks 2x 15 ml/d	2x 30 mL	Placebo Water, coconut essence	35,1 g (4,1/3,1) ³
De la Rubia Ortí et al. 2019 Spain	AD 0-26	79,8 25/52	/	44 (22/22) N/A	N/A	CO Pure With meals (morning, midday) Base: Mediterranean diet	3 weeks	2x 20 mL	Mediterranean diet (15 E% protein, 55 E% complex carbohydrates, 30 E% fat, 20-30 g fiber)	23,4 g (2,8/2,1) ³
Henderson et al. 2009 USA	AD 19,6	76,9 48/52	88,6% (56/44)	152 (86/66) ITT 144 (77/63) PP 91 (45/46) DC 96 (46/50)	34% (44/21)	MCT powder AC-1202 (95/5) (64% acacia gum, 2,6% syloid, 33% MCT) As drink in 230 mL liquids (milk, juice, 12 weeks water); Protocol change: Mixed with Abbott 1 week Ensure meal replacement With meals	12 weeks	2x 30 g	Placebo (10% safflower oil, 51% acacia gum, 37% dextrose, 2% syloid); isocaloric	19,8 g (18,8/1)
Henderson et al. 2020 USA	AD 20,7	76,6 41/59	100% (31/69)	413 (208/205) 275 (137/138)	19,6% (23/16)	MCT supplement AC-1204 (100/0) As drink in 120 mL water ¹	6 months 2 weeks, every 4 d +10 g	1x 40 g	Placebo Sunflower oil, maltodextrin	20 g (20/0)
Rebello et al. 2015 USA	MCI 25-28	58-78 50/50	100% (50/50)	6 (3/3) 4 (2/2)	33% (33/33)	MCT oil Nestle In Yoplait 99% low-fat yogurt	24 weeks	1x 56 g	Placebo Safflower oil	56 g (39/16,8) ³
Torosyan et al. 2018 USA	AD 21,1	79,9 20/70	87,5% (57/43)	16 (14/2) 16 (14/2)	/	MCT powder Caprylidene (100/0) As drink in 118-236 mL liquids ² Postprandial (morning, midday)	45 days	1x 40 g	Placebo /	20 g (20/0)
BENEFIC Trial										
Fortier et al. 2019 Canada	MCI 27,4	74,6 35/65	95% (38/62)	52 (27/25) 39 (19/20)	25% (30/20)	MCT supplement Captex 355 (60/40) As drink emulsified in 250 mL lactose-free skim milk With meals (morning, evening)	6 months 2 weeks 50 → 250 mL	2x 15 g	Placebo Sunflower oil	30 g (18/12)
Fortier et al. 2021 Canada	MCI /	72,2 26/74	96% (24/76)	122 (63/58) 82 (39/43)	32,8% (38/26)					
Roy et al. 2021 Canada	MCI 27,2	74,6 46/54	97% (38/62)	33 (17/16)	/					
Roy et al. 2022 Canada	MCI 27,2	75,1 44/66	97% (35/65)	32 (17/15)	/					

Cross-Over Design													
Ota et al. 2019 Japan RCT	AD 20	73,4 55/45	/	20 (20) /	-	MCT supplement <i>Ketonformula</i> (21,8/7) As drink in hot water Preprandial	Single dose on two separate days of visit	1x 50 g	Placebo isocaloric LCT-formula	19,4 g (10,9/3,5)			
Juby et al. 2022 Canada	AD 22,6	72,6 55/45	95% (53/47)	20 (219) /	5%	MCT oil <i>Bulletproof Brain Octane</i> (>99,3/0,6)	3 months each 1 month wash-out 4 weeks 15 -> 45 ml	3x 15 mL	Placebo Olive oil	42,8 (42/0,3)	g		
Reger et al. 2012 USA	AD, MCI 22	74,7 /	/	20 (20) /	-	MCToil <i>Neobee 895</i> (95/5) As drink emulsified in 152 mL cream Preprandial	Single dose on two separate days of visit	1x 40 mL	Placebo Cream	38 (36,1/1,9)	g		
Xu et al 2018 USA	AD 19,2	75,1 37/63	100% (6/94)	53 (46) /	7,5%	MCT Jelly (75/25) Pure Preprandial 30 minutes before meals (morning, midday, evening)	30 days each 30 days wash-out	3x 6 g	Placebo Safflower oil jelly	17,3 (13/4,3)			

¹From trial protocol NCT02833012
²Information from external data from the manufacturer [49]
³Estimated value based on 63,5% MCT content and MCFA distribution of 7,5% C8/5,7% C10