

Additional File 4

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Beer	Beer vs. Non-alcoholic control drink	330 mL	Acute, randomized, controlled, crossover	19 healthy volunteers (n=4 urine, n=3 plasma, n=1 serum)	U(H)PLC-MS/MS (Targeted)	Serum, plasma, urine	<ul style="list-style-type: none"> • L-Tartaric acid • Ethyl sulfate • Ethyl-beta-D-gulcuronide • Indoxyl sulfate • Cresol sulfate • Resveratrol • Estrone sulfate • Dihydroepiandrosterone sulfate • (Isoxanthohumol)* • (Isocohumulone)* • (3-nitrotyrosine)* • (Indole-3-lactic acid)* • (Cortisol)* • (Cortisol sulfate)* (* Detected but not validated)	(1)
Beer	Amstel beer (RIAA) vs. Hahn Premium Light beer (TIAA) vs. Coopers Clear beer (HIAA)	470-770 mL (Amstel), 850-1500 mL (Hahn), 500-850 mL (Coopers Clear)	Acute intervention	5 healthy volunteers	U(H)PLC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Iso-alpha-acids (isohumulones) • Rho-iso-alpha-acids (RIAA) • Tetrahydro-iso-alpha-acids (TIAA) • Hexahydro-iso-alpha-acids (HIAA) 	(2)
Beer	Beer	330 mL	Acute intervention	10 healthy volunteers	LC-ESI-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Isoxanthohumol • Xanthohumol • 8-prenylnaringenin 	(3)
Beer	Beer + 300 g allopurinol (anti-hyperuricemic agent) vs. Beer alone vs. Allopurinol alone	10 mL/kg body weight	Acute crossover	5 healthy volunteers	Not reported (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • Hypoxanthine • Xanthine • Uric acid 	(4)
Beer	Volt-Damm beer	330 mL (women); 660 mL (men)	Acute intervention	7 healthy volunteers	Melatonin ELISA and HPLC (Targeted)	Serum	<ul style="list-style-type: none"> • Melatonin 	(5)
Beer	Beer vs. Vodka and carbonated water	1 L (standardized to 48 g alcohol content)	Acute crossover	7 healthy volunteers	GC-MS/MS (Targeted)	Urine, serum	<ul style="list-style-type: none"> • Mevalonic acid 	(6)

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Beer	Little Creatures Pale Ale (high-hopped) vs. Erdinger Weissbier (low-hopped)	613 to 802 mL	Acute crossover	5 healthy men	U(H)PLC-MS/MS (Targeted)	Whole blood, urine	<ul style="list-style-type: none"> Iso-alpha-acids (isohumulones) 	(7)
Beer	1 Beer, 2 Beers, 3 Beers (male); 1 Beer, 1.5 Beers, 2 Beers (female)	330 mL, 660 mL, 990 mL (males); 330 mL, 495 mL, 660 mL (females)	Acute dose-response, randomized, crossover	41 healthy volunteers	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Isoxanthohumol 	(8)
	Beer vs. Gin vs. non-alcoholic beer	660 mL (beer); 92 mL (gin) (standardized to 30 g ethanol/day); 990 mL non-alcoholic beer (equivalent amount of polyphenols)	4-week randomized, open, controlled, crossover	33 males with high CV risk				
	Beer	No beer drinkers vs. intermittent/daily beer drinkers (22 to 825 mL/day) (from FFQ)	Parallel-group, multicenter, controlled, randomized 5-year clinical trial	46 volunteers from PREDIMED cohort				
Beer	Non-alcoholic beer	2.5 L	Acute intervention	4 healthy volunteers	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Ethyl glucuronide Ethyl sulfate 	(9)
Beer	Low-alcohol beer	4 L over 4 hours	Acute intervention	5 healthy men	HPLC-PDA (Targeted)	Urine	<ul style="list-style-type: none"> Ferulic acid (total, free and glucuronidated) 4-Dihydroxy-3-methoxy-cinnamic acid 	(10)
Beer	Beer	0.5 g/kg body weight (594 to 986 mL)	Acute intervention	6 healthy volunteers	LC-MS (Targeted)	Urine	<ul style="list-style-type: none"> Ethanol Ethyl glucuronide 	(11)
Beer	Light beer	330 mL	Acute intervention	8 healthy volunteers	Enzymatic method (Targeted)	Capillary blood	<ul style="list-style-type: none"> Ethanol 	(12)
	Beer on empty stomach	660 mL	Acute intervention	9 healthy men				

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	Beer with meal	660 mL	Acute intervention	9 healthy men				
Beer	Low-alcohol beer (0.5%) vs. low-alcohol beer (0.9%)	3 L	Acute, randomized, crossover	20 healthy men	Alcohol dehydrogenase method (Targeted)	Blood	<ul style="list-style-type: none"> Ethanol 	(13)
Beer	Beer vs. whisky vs. white wine vs. dry sherry	~614 mL (beer); 240 mL (beer); 157 mL (sherry); 66.6 mL (whisky); standardised to 0.3 g/kg body weight ethanol	Acute, randomized, crossover	11 healthy men	Breathalyser (Targeted)	Blood	<ul style="list-style-type: none"> Ethanol 	(14)
Beer	Non-drinkers vs. drinkers after a drinking party	0 (non-drinkers); not reported (drinking party)	Cross-sectional	40 healthy men (non-drinkers); 13 healthy men (drinking party)	GC-MS (Targeted)	Urine	<ul style="list-style-type: none"> 1-Methyl-1,2,3,4-tetrahydro-beta-carboline 1,2,3,4-Tetrahydro-beta-carboline Tryptamine (after administration of dideuterated L-tryptophan) 	(15)
	Beer vs. whisky	500 mL (beer); 68 mL (whisky)	Acute intervention	4 healthy men				
Beer	Beer	16 mL/kg body weight	Acute intervention	4 healthy men (3 flushers and 1 non-flusher)	HS-GC (Targeted)	Blood, urine	<ul style="list-style-type: none"> Ethanol Acetaldehyde Acetate 	(16)
Beer	Beer	16 mL/kg body weight (non-flushers); 8 mL/kg (flushers)	Acute intervention	4 healthy men	HS-GC-FID (Targeted)	Urine	<ul style="list-style-type: none"> Free and bound ethanol Free and bound acetaldehyde Free and bound acetate Free and bound acetone Free and bound methanol 	(17)
Beer	Beer vs. rum vs. carbonate mixed rum	275 mL (beer); 40 mL (rum); standardised to 12 g ethanol	Acute parallel	30 healthy volunteers	TDx Abbott analyzer (Targeted)	Plasma	<ul style="list-style-type: none"> Ethanol 	(18)
Beer	Tusker or Pilsner beer	8-15 beers (500 mL each) for me; 8-12 beers for women	Acute intervention	17 volunteers	GC (detector not specified) (Targeted)	Urine, blood	<ul style="list-style-type: none"> Alcohol 	(19)

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Beer	Beer	762 to 1000 mL	Acute intervention	4 healthy volunteers	HS-GC-EI-MS (ethanol), U(H)PLC-ESI-MS/MS (hordenine) (Targeted)	Plasma	<ul style="list-style-type: none"> Ethanol Hordenine (N,N-dimethyltyramine) and glucuronidated and sulfated conjugates 	(20)
Wine, beer	Consumption of 10 alcoholic beverages (light/medium/full strength beer; red/white/sparkling wine; wine cooler, spirits/liqueurs, spirit-based mixed drinks, sherry/port, and other)	Frequency of intake (never or <1/month, 1–3 times/month, once/week, 2–4 times/week, 5–6 times/week, once/day, 2–3 times/day, 4–5 times/day, >6 times/day) for 10 alcoholic beverages (from FFQ)	Cross-sectional	1785 healthy volunteers from the Childhood Determinants of Adult Health study	NMR (Targeted)	Serum	<ul style="list-style-type: none"> Weak positive associations for fatty acids: total fatty acids, saturated fatty acids, MUFA, PUFA, omega-6 PUFA, linoleic acid, omega-3 PUFA, DHA (total alcohol, wine beer) Weak positive associations for low-molecular weight metabolites: Alanine (total, wine, beer), glutamine (wine), tyrosine (total, wine, beer), glucose (total, wine, beer), pyruvate (beer), glycerol (beer), acetoacetate (beer), beta-hydroxybutyrate (beer), albumin (beer), acetate (beer) 	(21)
Wine, beer	Red wine vs. beer vs. Dutch gin vs. water	4 glasses; standardised to 40 g/day alcohol	3-week, randomized, controlled, crossover	12 healthy men	HPLC-FLD/UV (Targeted)	Plasma	<ul style="list-style-type: none"> Alpha-tocopherol Gamma-tocopherol Lutein Beta-cryptoxanthin Lycopene Alpha-carotene 	(22)
Wine, beer	Red wine vs. Lager beer vs. Stout (alcoholic) vs. Stout (non-alcoholic) vs. Water with alcohol	1 drink: 341 mL 3 drinks: 3 X 155 mL (wine); 3 X 341 mL (lager beer); 3 X 341 mL (stout), 3 X 341 mL (water)	Acute intervention	12 healthy volunteers (1 drink); 8 healthy volunteers (3 drinks)	Sigma Alcohol kit, ELISA reader (Targeted)	Plasma	<ul style="list-style-type: none"> Ethanol 	(23)
Wine, beer	Alcohol intake (wine, beer and spirits)	Quartiles of alcohol intake as % total energy intake: Q1:0, Q2: 0.6, Q3: 2.3, Q4: 5.8 (from FFQ)	Association study	1457 healthy volunteers from the IMMIDIET cohort	GC-FID (Targeted)	Plasma	<ul style="list-style-type: none"> EPA (women and men) DHA (women) 	(24)

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Wine, beer	Beer, white wine, vodka/tonic	All beverages give 0.5 g ethanol/kg body weight (5.1% v/v beer, 12.5% v/v chardonnay, 20% v/v vodka and tonic)	Acute crossover	15 healthy men	HS-GC (Targeted)	Whole blood	<ul style="list-style-type: none"> Ethanol 	(25)
Wine, beer	Pilsen-type beer, Cabernet Sauvignon red wine, Scotch whisky, cachaca	All beverages give 0.5 g ethanol/kg body weight	Acute crossover	20 healthy volunteers	COBAS INTEGRA Ethanol Kit (Targeted)	Plasma	<ul style="list-style-type: none"> Ethanol 	(26)
Wine, beer	Swedish vodka and tonic (Absolut), French wine (La Garonne), Swedish export beer (Pripps Export)	All beverages give 1.0 mL ethanol/kg body weight	Acute intervention	6 healthy men	Not reported	Blood	<ul style="list-style-type: none"> Ethanol 	(27)
Wine, beer	White wine or beer	0.1 or 0.2 L (white wine); 0.33 L or 0.66 L (beer)	Acute intervention	12 healthy volunteers	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Ethyl glucuronide Ethyl sulfate 	(28)
Wine, beer	Choice of white wine or export beer	50 g or 80 g ethanol	Acute intervention	20 healthy volunteers ('social drinkers')	HS-GC, GC-MS, HPLC (Targeted)	Urine	<ul style="list-style-type: none"> Ethanol Methanol 5-Hydroxytryptophol 5-Hydroxyindol-3-ylacetic acid 	(29)
Wine	Dealcoholized red wine	272 mL/day	4-week, randomized, controlled intervention	36 elderly men	U(H)PLC-MS/MS (Targeted 67 metabolites)	Urine	<ul style="list-style-type: none"> (Epi)catechin glucuronides (Epi)catechin sulfates DHPV glucuronides DHPV sulfates Ethylgallate glucuronides Ethylgallate sulfate Methyl(epi)catechin glucuronides Methyl(epi)catechin sulfates Methylgallic sulfate MHPV glucuronide MHPV sulfates Hydroxybenzoic acids (especially gallic acid) Hydroxyphenylacetic acids Hydroxycinnamic acids 	(30)

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							<ul style="list-style-type: none"> Hydroxyphenylpropanoic acids Glycinates (vanilloylglycine) Hydroxyphenylvalerolactones Enterolactone Pyrogallol 	
Wine	Sparkling wine	0.1 to 0.2 L (9 or 18 g ethanol); 1 volunteer drank 0.54 L (49 g ethanol)	Acute intervention	9 healthy volunteers	LC-ESI-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Ethyl sulfate Ethyl glucuronide 	(31)
Wine	Merlot red wine	250 mL	Acute intervention	11 healthy men	HPLC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Resveratrol (trans-resveratrol) and metabolites (trans-piceid, taxifolin, hexestrol, trans- and cis-resveratrol glucuronides and sulfates) 	(32)
Wine	Red wine vs. dealcoholized red wine	272 mL/day	28-day, randomized, controlled, crossover	73 volunteers with high cardiovascular risk	U(H)PLC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Resveratrol (trans- and cis-resveratrol) and metabolites (trans-piceid, piceid glucuronides and sulfates, trans- and cis-resveratrol glucuronides and sulfates, dihydroresveratrol and its glucuronides and sulfates) 	(33)
Wine	Red wine vs. dealcoholized red wine	272 mL/day	4-week, randomized, controlled, crossover	36 men with high cardiovascular risk	U(H)PLC-MS/MS (Targeted 70 phenolic metabolites)	Plasma, urine	<p>Plasma:</p> <ul style="list-style-type: none"> 3-Hydroxyphenylacetic acid DHPV and glucuronides Gallic acid Methyl(epi)catechin glucuronides Methylgallic acid Methylgallic sulfate p-Coumaric acid (Epi)catechin glucuronides 3-Hydroxyphenylacetic acid <p>Urine:</p> <ul style="list-style-type: none"> (Epi)catechin glucuronides (Epi)catechin sulfates 2,4-Dihydroxybenzoic acid 2,5-Dihydroxybenzoic acid 2,6-Dihydroxybenzoic acid 3-Hydroxyphenylacetic acid DHPV and glucuronides and sulfates Ethylgallate and glucuronides and sulfates Gallic acid Methyl(epi)catechin glucuronides Methyl(epi)catechin sulfates Methylgallic acid 	(34)

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							<ul style="list-style-type: none"> • Methylgallic sulfate • p-Coumaric acid • Pyrogallol • Resveratrol • Syringic acid • Vanilloylglycine • 3-(3-hydroxyphenyl) propionate • DHBA • 3-Hydroxybenzoic acid • 3-Hydroxyphenylacetic acid • 4-Hydroxybenzoic acid • Caffeic acid • Enterolactone • Ferulic acid • MHPV glucuronides 	
Wine	White wine vs. red wine	300 mL/day	15-day, randomized, controlled, parallel	20 healthy volunteers	HPLC electrochemical method (Targeted)	Plasma	<ul style="list-style-type: none"> • Resveratrol 	(35)
Wine	Wine vs. grape juice vs. grape tablets enriched with trans-resveratrol (also compared to separate study with olive oil)	250 mL/day (wine); 1L/day (grape juice); 1 mg resveratrol/day (tablets)	4-day, randomized, controlled, crossover	12 healthy volunteers	GC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Hydroxytyrosol and its metabolite, homovanillic alcohol 	(36)
Wine	Red wine vs. no wine	250 mL/day	4-week, randomized, controlled, parallel	41 healthy volunteers	U(H)PLC-ESI-MS/MS (Targeted microbial-derived phenolics)	Feces	<ul style="list-style-type: none"> • 3,5-Dihydroxybenzoic acid • 3-Hydroxyphenylacetic acid • 3-Phenylpropionate • 4-hydroxy-5-(3,4-dihydroxyphenyl) valeric acid • 4-Hydroxy-5-(phenyl) valeric acid • 4-O-methylgallic acid • DHPV • Protocatechuic acid • Syringic acid • Vanillic acid 	(37)
Wine	Wine, grapes, peanuts, and red wine intake (along with total	Continuous intake of resveratrol, resveratrol 3-O-glucoside,	Association study	475 volunteers from the EPIC cohort	U(H)PLC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Resveratrol 	(38)

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	resveratrol intakes)	resveratrol aglycone, wine, grapes, peanuts, and red wine (from 24-h recalls and dietary questionnaire)						
Wine	White wine (and crackers)	250 mL	Acute intervention	10 healthy volunteers	HPLC-ECD (Targeted)	Plasma	<ul style="list-style-type: none"> • Caffeic acid • Ferulic acid • P-coumaric acid 	(39)
Wine	White wine	Volume to achieve ~0.5 g/kg body weight ethanol	Acute intervention	13 healthy volunteers	LC-MS/MS (Targeted)	Serum, urine	<ul style="list-style-type: none"> • Ethyl glucuronide • Ethyl sulfate 	(40)
Wine	Extra virgin olive oil, red wine, extra virgin olive oil + red wine	25 mL (EVOO), 150 mL (wine)	Acute, randomized, crossover	12 healthy volunteers	HPLC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Resveratrol (cis, trans, dihydro) • Tyrosol (free, sulfate, and glucuronide) • Hydroxytyrosol (free, sulfate, and glucuronide) • Ethyl glucuronide (wine) 	(41)
Wine	Red wine vs. dealcoholized red wine	200 mL	Acute crossover	10 healthy volunteers	HPLC-Coulochem II detector (Targeted)	Plasma	<ul style="list-style-type: none"> • Caffeic acid 	(42)
Wine	Test meal (Milanese beef cutlet and chips) with red wine	300 mL	Acute intervention	10 healthy men	HPLC-UV and HPLC-PDA-MS (Targeted)	Serum	<ul style="list-style-type: none"> • Trans-resveratrol (and 3- and 4' glucuronides) 	(43)
	Red wine	600 mL	Acute intervention	5 healthy volunteers	HPLC-UV-DAD and LC-MS/MS (Targeted)		<ul style="list-style-type: none"> • Trans-resveratrol (and 3- and 4' glucuronides) 	
	'Fat meal' with red wine vs. 'lean meal' with red wine	600 mL	Acute parallel	10 healthy volunteers			<ul style="list-style-type: none"> • Trans-resveratrol (and 3- and 4' glucuronides) 	
Wine	Red wine vs. dealcoholized red wine	272 mL/day	20-day, randomized, controlled, crossover	8 healthy volunteers	U(H)PLC-ESI-MS/MS (Targeted for microbial phenolics)	Feces	<ul style="list-style-type: none"> • 3,5-Dihydroxybenzoic acid • 3-O-Methylgallic acid • 4-Hydroxy-5-(phenyl) valeric acid • p-Coumaric acid • Phenylpropionic acid • Protocatechuic acid • Syringic acid 	(44)

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							<ul style="list-style-type: none"> • Vanillic acid 	
Wine	Red wine vs. dealcoholized red wine	120 mL	Acute crossover	9 healthy volunteers	GC-MS (Targeted)	Urine	<ul style="list-style-type: none"> • Catechin (free) and metabolites (catechin sulfate, glucuronide, glucuronide-sulfate) • 3'-methylcatechin and glucuronides and sulfates 	(45)
Wine	Red wine vs. alcohol abstinent	150 mL/day (females); 300 mL/day (males)	3-month, randomized, parallel	44 healthy volunteers	LC-MS/MS (Targeted)	Whole blood	<ul style="list-style-type: none"> • Phosphatidylethanol • Carbohydrate-deficient transferrin 	(46)
Wine	Red wine, ethanol, water	155 mL (wine, first dose), ethanol equivalent to achieve BAC of 40 mg/mL 310 mL (wine, second dose)	Acute, 2-dose, randomized, single-blind, crossover	13 healthy volunteers	GC (detector not specified) (Targeted)	Plasma	<ul style="list-style-type: none"> • Resveratrol • Catechin 	(47)
Wine	Red wine (at 3 different doses)	100 mL, 200 mL, or 300 mL	Acute, randomized, crossover	21 healthy men	LC-ESI-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Tartaric acid 	(48)
Wine	Mediterranean diet vs. occidental diet, with or without red wine	240 mL/day	3-month, randomized, parallel (1-month wine intake during second month)	42 healthy men	HPLC-electrochemical detection (beta-carotene), spectrophotometry (L-ascorbic acid), Folin-Ciocalteu method (polyphenols) (Targeted)	Plasma, urine (polyphenols)	<ul style="list-style-type: none"> • Vitamin C • Beta-carotene • Polyphenols (gallic acid equivalents) 	(49)
Wine	Wine	Non-wine consumers, intermittent wine consumers, daily wine consumers (from FFQ)	Prospective cohort	1000 volunteers with high CV risk from the PREDIMED cohort	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Resveratrol metabolites (trans- and cis-resveratrol glucuronides and sulfates) 	(50)

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Wine	Mencia red wine	1 glass/serving per day (volume not specified)	3-day intervention	25 healthy volunteers who are occasional wine drinkers	HPLC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> Resveratrol (trans) 	(51)
Wine	Sparkling wine vs. gin	300 mL/day (wine); 100 mL (gin), standardized to 30 g ethanol/day	28-day, randomized, controlled, crossover	10 healthy men	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Total resveratrol metabolites (cis- and trans- resveratrol glucuronides) 	(52)
	White wine vs. red wine	200 mL/day, standardized to 20 g ethanol/day	28-day, randomized, controlled, crossover	10 healthy women				
	Wine consumed at 3 different levels	Daily consumption, intermittent consumption, no consumption (from FFQ)	Prospective cohort	52 volunteers from the PREDIMED cohort				
Wine	Red wine vs. dealcoholized red wine	120 mL	Acute, randomized, crossover	9 healthy volunteers	GC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> Catechin and 3'-O-methylcatechin (and glucuronide and sulfate conjugates) 	(53)
Wine	Dealcoholized red wine reconstituted with water vs dealcoholized red wine reconstituted with water and ethanol	120 mL	Acute, randomized, crossover	9 healthy volunteers	GC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> Total (+)-Catechin 	(54)
Wine	Alcohol consumption, wine consumption	3 categories for total alcohol consumption, wine consumption (from FFQ)	Prospective cohort	1045 volunteers with high CV risk from the PREDIMED cohort	GC-MS (hydroxytyrosol); enzyme immunochemical method (ethyl glucuronide) (Targeted)	Urine	<ul style="list-style-type: none"> Hydroxytyrosol Ethyl glucuronide 	(55)

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Wine	Red wine vs. grape juice vs. red wine extract tablets	250 mL (wine); 1 L (juice); 10 tablets; standardized to 14 ug/kg resveratrol	Acute, randomized, controlled, crossover	11 healthy men	GC-MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Resveratrol (trans, cis), dihydroresveratrol 	(56)
Wine	Red wine	200 mL	Acute intervention	5 healthy men	LC-ESI-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Tartaric acid Malic acid Succinic acid 	(57)
Wine	Alcohol consumption	Quartiles of alcohol consumption, continuous intake of wine (from FFQ)	Association study	1000 volunteers with high CV risk from the PREDIMED cohort	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Total resveratrol metabolites (trans- and cis-resveratrol glucuronides and sulfates) 	(58)
Wine	Merlot red wine	250 mL	Acute intervention	11 healthy men	LC-ESI-MS/MS (Targeted)	Plasma LDL	<ul style="list-style-type: none"> Trans-resveratrol and metabolites (3-O-glucuronide, cis-3-O-glucuronide, cis-3-O-glucoside) 	(59)
Wine	Diet without vegetable, fruit, and wine vs. diet with vegetable and fruit vs. diet with wine and no vegetable or fruit vs. diet with wine, vegetable, and fruit	Grouped intakes of fruit, vegetable, and wine intake (from 24-h recall)	Cross-sectional	180 healthy free-living volunteers	HPLC-FLD (Targeted)	Plasma	<ul style="list-style-type: none"> (+)-Catechin 	(60)
Wine	Red wine vs. no red wine	375 mL/day	2-week, randomized, controlled, parallel	20 healthy free-living volunteers	HPLC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> Total phenolics (+)-Catechin glucuronide (-)-Epicatechin glucuronide Methyl catechin glucuronide Methyl epicatechin glucuronide 	(61)
Wine	Red wine	100, 200, 300 mL	Acute, dose-response intervention	5 healthy men	HPLC-Coulochem II detector (Targeted)	Plasma	<ul style="list-style-type: none"> Caffeic acid 	(62)

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Wine	Table red wine vs. Port red wine	250 mL (table red wine); 150 mL (Port red wine)	Acute crossover	4 healthy men	HPLC-DAD, HPLC-MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Total plasma anthocyanins and metabolites Delphinidin-3-O-glucoside Petunindin-3-O-glucoside Peonidin-3-O-glucoside Delphinidin-glucuronide Peonidin-glucuronide Malvidin-3-O-beta-glucuronide Malvidin-3-O-beta-glucoside 	(63)
Wine	Oak-aged red wine vs. strawberries vs. red raspberries vs. walnuts (all containing ellagitannins)	300 mL (wine); 250 g (strawberries); 225 g (raspberries); 35 g (walnuts)	Acute crossover	40 healthy volunteers	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Urolithin B derivatives (glucuronide more than aglycone) 	(64)
Wine	Wine vs. vodka (diluted in lemon-flavored water) vs. dealcoholised wine vs. placebo (lemon-flavored water)	147 mL	Acute, randomized, controlled, crossover	28 healthy men	Method not reported (Targeted)	Urine	<ul style="list-style-type: none"> Hydroxytyrosol 3'-Dihydroxyphenylacetic acid Homovanillic acid 4-Hydroxyphenylacetic acid 	(65)
Wine	Wine (alcohol consumption) vs. no wine (alcohol abstinent)	1 glass/day for women (16 g ethanol); 2 glasses/day for men (32 g ethanol)	3-month, randomized, controlled, parallel	44 healthy volunteers	LC-MS/MS (Targeted)	Hair	<ul style="list-style-type: none"> Ethyl glucuronide 	(66)
Wine	Red wine vs. red grape juice	400 mL	Acute crossover	9 healthy volunteers	HPLC-UV-VIS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Total anthocyanins Cyanidin-3-glucuronide Delphinidin-3-glucuronide Malvidin-3-glucuronide Peonidin-3-glucuronide Petunindin-3-glucuronide 	(67)
Wine	Red wine vs. dealcoholised red wine vs. red grape juice	500 mL	Acute, randomized, crossover	6 healthy men	HPLC-PDA (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Malvidin-3-glucoside 	(68)
Wine	Wine vs. mature whisky vs. new whisky	100 mL	Acute, randomized, crossover	9 healthy volunteers	Folin Ciocalteu method (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Total phenols (gallic acid equivalents) 	(69)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Wine	Red wine vs. Red grape juice	400 mL	Acute, randomized, crossover	9 healthy volunteers	HPLC-UV-VIS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Total anthocyanins Cyanidin-3-glucuronide Delphinidin-3-glucuronide Malvidin-3-glucuronide Peonidin-3-glucuronide Petunidin-3-glucuronide 	(70)
Wine	Wine	250 mL	Acute intervention	7 healthy volunteers	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Ethyl glucuronide 	(71)
Wine	Listerine mouth rinse vs. non-alcoholic wine vs. vodka	4.2 to 7.5 dL (wine); 3.75 mL (vodka)	Acute parallel	12 healthy volunteers	HPLC-MS/MS, HPLC-UV (Targeted)	Oral fluid, whole blood, urine	<ul style="list-style-type: none"> Ethyl glucuronide Ethyl sulfate 	(72)
Wine	Pinot noir red wine vs. Cabernet sauvignon red wine vs. dry semillon white wine vs. sauvignon blanc white wine vs. absolute alcohol in water	0.3 g/kg body weight ethanol	Acute, randomized, crossover	108 volunteers with previous illness	GLC (Targeted)	Blood	<ul style="list-style-type: none"> Ethanol 	(73)
Rice wine	Japanese rice wine (sake) vs. water	0.4 g/kg body weight ethanol	Acute intervention	63 healthy men	GC-FID (Targeted)	Breath, blood	<ul style="list-style-type: none"> Alcohol Acetaldehyde 	(74)
Rice wine	Sake vs. rice wine	100 mL (sake); 50 mL (rice wine)	Acute intervention	2 healthy volunteers	¹ H NMR (Targeted)	Urine	<ul style="list-style-type: none"> Ethyl glucoside 	(75)
Yoghurt	Yoghurt vs. milk	800 g	Acute, randomized, double-blind, crossover	14 healthy men	GC-MS (Targeted)	Serum	<ul style="list-style-type: none"> Lactose Galactose 	(76)
Yoghurt	Probiotic yoghurt with <i>Bifidobacterium animalis</i> subsp. <i>lactis</i> LKM512 or placebo yoghurt	100 g/day	4-week, double-blind, placebo-controlled, crossover	10 adults with moderate atopic dermatitis	HPLC-Scanning FLD (fecal polyamines); HPLC-Differential Refractometer (fecal	Feces	<ul style="list-style-type: none"> Butyrate vs baseline (no increases for other SCFAs measured, acetate, propionate, isobutyrate, valerate, and isovaleate) Spermidine (also some with increased putrescine, but spermine levels not detected) 	(77)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
					SCFAs) (Targeted)			
Yoghurt	Yoghurt consumers vs. non-consumers	>200 g/day (consumers), 0 g/day (non-consumers) (from 24-h food records)	Free-living cohort	30 (consumers) ad 21 (non-consumers) from the SU.VI.MAX cohort	GC (detector not specified) (SCFAs); GLC (for bile acids) (Targeted)	Feces	<ul style="list-style-type: none"> No significant differences in fecal SCFA (total, acetate, propionate, butyrate, iso-acids, valerate + caproate) No significant differences in neutral bile acids (cholesterol, coprostanol, cholestanol, coprostanone, beta-sitosterol, copro-beta-sitosterol) Increase in 7-keto-lithocholic (no significant differences in other acidic bile acids cholic, deoxycholic, ursocholic, 7-keto-deoxycholic, chenodeoxycholic, lithocholic, ursodeoxycholic, 7-keto-lithocholic, sum) 	(78)
Yoghurt	Probiotic yoghurt with <i>Bifidobacterium animalis</i> subsp. <i>lactis</i> LKM512 vs. placebo yoghurt	100 g/day	2-week, placebo-controlled, crossover	7 healthy adults	HPLC-Scanning FLD (fecal polyamines); HPLC-Differential Refractometer (fecal SCFAs) (Targeted)	Feces	<ul style="list-style-type: none"> Spermidine (putrescine not increased, spermine levels not detected) No significant changes in lactate or acetate 	(79)
Yoghurt	Fresh yoghurt (>10 ⁷ CFU) vs. heated yoghurt (<10 ² CFU)	500 g/day	15-day, randomized	12 healthy men with lactose malabsorption and 12 healthy men without lactose malabsorption	HS-GC-FID (SCFAs) (Targeted)	Plasma	<ul style="list-style-type: none"> Butyrate (in volunteers without lactose malabsorption for fresh yoghurt vs. heated) Propionate (in volunteers with lactose malabsorption for fresh yoghurt vs. baseline) No change in acetate 	(80)
Yoghurt	Whole milk, commercial unflavored yoghurt, heated yoghurt	400 mL (milk); 450 g (yoghurts)	Acute, randomized, crossover	8 healthy volunteers with lactose malabsorption	Enzymatic assay (Targeted)	Ileal fluid	<ul style="list-style-type: none"> Lactose (higher after heated yoghurt than yoghurt) Galactose (not significant) Glucose (not significant) Hexoses (higher after heated yoghurt than yoghurt) 	(81)
Cheese, yoghurt (general dairy)	Total dairy intake	Quintiles of total dairy intake: Q1: 0-2.07, Q2: 2.1-4.1, Q3: 4.13-6.65, Q4:	Association study	659 volunteers without diabetes from the	GC-FID (Targeted)	Serum	<ul style="list-style-type: none"> Pentadecanoic acid (15:0) Trans-palmitoleic acid (trans 16:1n-7) was not considered to be a specific marker for total dairy intake 	(82)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
		6.69-9.73, Q5: 9.8-31.08 (from FFQ)		IRAS cohort				
Cheese, yoghurt (general dairy)	Dairy fat intake	Continuous levels of dairy fat intake (from 1 week weighted diet records and FFQ)	Association study	81 healthy women	GC with (Targeted)	Subcutaneous adipose tissue	<ul style="list-style-type: none"> • Pentadecanoic acid (15:0) • Heptadecanoic acid (17:0) 	(83)
Cheese, yoghurt (general dairy)	Natural yoghurt, cheddar cheese, semi-skimmed milk, water (dairy as snack)	410 mL	Acute, randomized, crossover	40 overweight men	GC-FID (Targeted)	Plasma	<ul style="list-style-type: none"> • Amino acids (alpha-amino butyric acid, Ala, Asn, cysteine, Gly, Glu, His, Ile, Leu, Lys, Met, Orn, phe, Pro, Ser, Thr, Trp, Try, Val) 	(84)
Cheese, yoghurt (general dairy)	Dairy: Milk (1% fat), yoghurt (1.5% fat), cheese (34% fat) Control: fruit and vegetable juice, cashews and a cookie	3 servings/day (375 mL milk/day, 175 yoghurt/day, 30 g cheese/day)	4 week, randomized, free-living, multi-center, crossover	124 healthy volunteers	GC-FID (Targeted)	Plasma	<ul style="list-style-type: none"> • Pentadecanoic acid (15:0) • Heptadecanoic acid (17:0) • Trend towards higher cis-9, trans-11-18:2n-6, p=0.06) • Total SFA • 18:3n-6 • 22:1n-9 • SFA:MUFA and SFA:PUFA 	(85)
Cheese, yoghurt (general dairy)	Total dairy, high-fat dairy, low-fat dairy, milk, cream, yoghurt, cheese, butter	Continuous levels of total dairy, high-fat dairy, low-fat dairy, milk, cream, yoghurt, cheese, butter (from FFQ)	Association study	334 control and 1054 intervention volunteers from Food4Me	GC-FID (Targeted)	Dried blood spots	<ul style="list-style-type: none"> • Pentadecanoic acid (15:0) • Heptadecanoic acid (17:0) 	(86)
Cheese, yoghurt (general dairy)	Meat, dairy food, egg, and fish	Quartiles/levels of milk and dairy products, milk, cheese, total meat, red meat, processed meat, white meat, fish and shellfish, and	Association study	271 participants of the Second Bavarian Food Consumption Survey	LC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Trimethylamine-N-oxide with milk and dairy products, milk (not for other food groups) • No associations for betaine or choline 	(87)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
		eggs and egg products (from 24-h recalls)						
Cheese, yoghurt	Dairy (total dairy, milk, cheese, yoghurt, cream/butter) intake	Frequency of dairy consumption from never/ <1 time/month to ≥6 times/day (from FFQ)	Association study	2205 volunteers from the Framingham Health Study Offspring cohort and 866 volunteers from the Gen3 cohort	HILIC- and lipid-LC-MS and MS/MS (Targeted and Untargeted)	Plasma	<ul style="list-style-type: none"> Cheese: C46:0 triacylglycerol, C54:4 triacylglycerol, C54:5 triacylglycerol, C54:6 triacylglycerol Yoghurt: C20:5 cholesterol ester 	(88)
Cheese, yoghurt, fermented milk (general dairy)	Total milk products, cream, cheese, fermented milk, total milk, ice cream	Quartiles of total milk products, cream, cheese, fermented milk, total milk, ice cream, and 15:0 and 17:0 (from FFQ)	Prospective case-control nested within larger cohort NSHDS	444 cases of myocardial infarction and 556 controls	GLC (Targeted)	Plasma	<ul style="list-style-type: none"> Pentadecanoic acid (15:0) Heptadecanoic acid (17:0) 	(89)
Cheese, soy sauce	Soy sauce with a meal (not further specified) or Appenzeller cheese	9 mL soy sauce; 10 g cheese	Acute intervention	4 volunteers (cheese); 3 volunteers (soy sauce)	HPLC-IS-MS (Targeted)	Urine	<ul style="list-style-type: none"> 4-methylspinacemine (4-methyl-4,5,6,7-tetrahydro-1H-imidazo-[4,5-c]pyridine) 1,4-dimethylspinacemine 	(90)
Cheese	Probiotic cheese with <i>L. plantarum</i> TENSIA vs. control cheese	50 g/day	3-week, randomized, double-blind, placebo-controlled, parallel	25 hospitalized patients	GC-FID (Targeted)	Urine	<ul style="list-style-type: none"> Putrescine and acetylated putrescine in control group decreased vs baseline (no significant differences in other polyamines, tyramine or acetylated spermidine) Extent of change is significantly higher for probiotic cheese vs control for putrescine and acetylated putrescine 	(91)
Cheese	Cheese (from cows with linseed oil added to their diet) vs. control cheese	3 X 50 g/week	4-week, randomized, double-blind, crossover	30 healthy, free-living volunteers	GC-FID (Targeted)	Serum	<ul style="list-style-type: none"> C18:0 in test cheese group vs baseline No other significant differences in serum fatty acids compared to baseline for either group (12:0, 14:0, 16:0, 18:0, 16:1, 18:1, 18:2, 20:4) 	(92)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Soy	Untreated soymilk vs. beta-glucosidase soymilk vs. fermented soymilk	100 mL	7-day crossover	12 healthy volunteers	LC-MS (Targeted)	Serum, urine	<ul style="list-style-type: none"> Isoflavones (daidzein, genistein, glycitein) 	(93)
Soy	Breakfast casseroles containing tofu, tempeh, cooked soybeans, or texturized vegetable protein	30 g (texturized vegetable protein); 100 g (tempeh); 100 g (cooked soybeans); 300 g tofu	Acute, randomized, crossover	10 healthy women	HPLC with variable wavelength detector (Targeted)	Plasma, urine, feces	<ul style="list-style-type: none"> Isoflavones (daidzein, genistein) 	(94)
Soy	Breakfast with natto and spinach vs. detergent-solubilized K1 vs. low-vitamin K diet	200 g (natto) and 400 g (spinach)	Acute crossover	6 healthy men	HPLC-FLD (Targeted)	Serum	<ul style="list-style-type: none"> Vitamin K2 (menaquinones); higher than vitamin K1 (phyllloquinones in spinach) 	(95)
Soy	Fermented soy vs. non-fermented soy	112 g (tempeh); 125 g (soybeans)	9-day, randomized, crossover	22 healthy men	GC-MS (Targeted)	Urine	<ul style="list-style-type: none"> Isoflavoids (equol, O-desmethylangolensin, daidzein, genistein), daidzein and genistein recover greater with tempeh diet Lignans (enterolactone, enterodiol) decreased with soy intake 	(96)
Soy	Fermented soymilk containing <i>Bifodibacterium animalis</i> Bb-12 vs. non-fermented soymilk	200 mL/day, containing 20, 40, or 80 mg isoflavone/200 mL	14-day, randomized, double-blind, crossover	16 healthy postmenopausal women	HPLC-UV-VIS (Targeted)	Urine	<ul style="list-style-type: none"> Isoflavones (genistein, daidzein, glycitein) aglycones, and beta-glucoside isomers 	(97)
							<ul style="list-style-type: none"> Equol (tendency to increase in the fermented group over time but did not reach significance) 	(98)
Soy	Isogen capsules vs. soymilk vs. fermented soybeans	84.8 mg (isogen); 43.8 g (fermented soybeans); 600 mL (soymilk); standardised to 64.8 mg isoflavones	Acute, randomized, controlled, parallel	26 healthy women	HPLC (detector not specified) (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Isoflavones (genistein, daidzein) higher urinary recovery in fermented group, longer plasma half-life in fermented and isogen groups 	(99)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Soy	Tofu, natto (fermented soybean), soy milk, soy isoflavone supplement	180 g (tofu), 100 g (natto), 300 g (soymilk), 1 supplement, all standardized to 75 mg isoflavones	1-day intervention	20 healthy women (9 equol producers and 11 non-producers)	HPLC-UV (Targeted)	Urine	<ul style="list-style-type: none"> Isoflavones (genistein, daidzein) 	(100)
Soy	Fermented soy powder (aglycone-rich) with <i>Aspergillus oryzae</i> vs. non-fermented soy powder (glycoside-rich)	23 g (standardized to 95 umol isoflavones)	Acute, randomized, double-blind, crossover	11 healthy postmenopausal women	LC-MS/MS (Targeted)	Serum, urine	<ul style="list-style-type: none"> Isoflavones (total) increased bioavailability and urinary excretion; trend towards increased in daidzein, genistein, and glycitein as well, no significant difference in equol 	(101)
Soy	Stinky tofu	146 g	Acute intervention	36 healthy volunteers (18 equol producers, 18 non-producers)	HPLC-UV (Targeted)	Urine	<ul style="list-style-type: none"> S-equol, similar rates of excretion in producers and non-producers Daidzein and dihydrodaidzein Total daidzein (daidzein, dihydrodaidzein, S-equol, O-desmethylangolensin) 	(102)
Soy	Fermented soymilk with <i>Lactobacillus casei</i> Shirota (containing aglycones) vs. placebo soymilk (no aglycones)	100 mL	Acute, randomized, double-blind, placebo-controlled, crossover	7 healthy postmenopausal women	LC-MS/MS (Targeted)	Serum	<ul style="list-style-type: none"> Isoflavones (genistein, daidzein, glycitein, dihydrodaidzein, O-desmethylangolensin, equol) 	(103)
Soy	Natto (fermented with <i>Bacillus natto</i>)	Natto consumption frequency (questionnaire); 80 g in acute intervention	Cross-sectional, and acute intervention	Group 1: 49 postmenopausal women from Tokyo (8 also participated in acute intervention) Group 2: 25 postmenopausal	HPLC-FLD (Targeted)	Serum	<ul style="list-style-type: none"> Vitamin K2 (menaquinone-7) Phylloquinone (slightly higher in Japanese than British women) Menaquinone-4 (below limit of detection in most women) 	(104)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
				women from Hiroshima Group 3: 31 postmenopausal British women				
Soy	Soya milk vs. miso soup	250 mL (soymilk); 31 g Hacco miso; standardized to 48 mg isoflavones	1-day or 2 non-consecutive days, randomized, crossover	21 healthy women	LC-MS (Targeted)	Urine	<ul style="list-style-type: none"> Isoflavones (daidzein, genistein, equol) 	(105)
Soy	Fermented soy (tempeh) vs. non-fermented soy (soybean)	112 g (tempeh); 125 g (soybean)	9-day, randomized, controlled, crossover	17 healthy men	GC-MS (Targeted)	Urine	<ul style="list-style-type: none"> Isoflavones (daidzein, genistein) higher excretion for fermented group (although fermentation decreased isoflavone content of the soy product) 	(106)
Soy	Soy flour vs. fermented soybean paste	12.2 g (soy flour); 52 g (soybean paste); standardized to 20 mg isoflavones	Acute, randomized, controlled, crossover	10 healthy volunteers	LC-ESI-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> 20 isoflavone metabolites detected, consisting of daidzein and genistein glucuronides and sulfoglucuronides, daidzein sulfate, equol glucuronide, and ODMA glucuronides Isoflavones (especially glucuronides of daidzein, genistein) higher in fermented group 	(107)
Soy	Natto fermented with <i>Bacillus subtilis</i> , double-boiled natto with short interval, vitamin K syrup	50 g/day	3-day intervention with untreated natto; acute, crossover with natto, boiled natto, and vitamin K syrup	32 healthy volunteers	HPLC (detector not specified) (Targeted)	Plasma	<ul style="list-style-type: none"> Menaquinone-7 (increased following natto consumption; negligible levels of phylloquinone and menaquinone-4) Lower levels of menaquinone-7 following boiled natto consumption compared to regular natto and syrup 	(108)
Soy	Fermented soybean soup with <i>Aspergillus oryzae</i> vs. placebo soup	20 g powder with water; standardized to 24 mg isoflavones/day	4-week, randomized, double-blind, placebo-controlled, parallel	65 healthy postmenopausal women	HPLC-UV (Targeted)	Urine	<ul style="list-style-type: none"> Isoflavones (daidzein, genistein, glycitein), total isoflavones, especially daidzein and glycitein, were higher in fermented group 	(109)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Soy	Soybean milk, fried bean curd puff, fresh bean curd, soybeans, fermented bean curd, and other bean foods	Quartiles of soy product consumption, including soybean milk, fried bean curd puff, fresh bean curd, soybeans, fermented bean curd, and other bean foods (from FFQ)	Case-control nested within a large randomized trial of breast self-examination among textile workers in Shanghai	1823 women (1590 women without breast cancer, and 233 women with breast cancer)	LC-couarray and LC-MS (Targeted)	Serum	<ul style="list-style-type: none"> Isoflavones (daidzein, genistein) 	(110)
Soy	Regular natto vs. reinforced natto 1 vs. reinforced natto 2	50 g (775 ug/100g MK7; 1298 ug/100g MK7; 1765 ug/100g MK7)	7-day crossover	8 healthy men	HPLC (detector not specified) (Targeted)	Serum	<ul style="list-style-type: none"> Vitamin K2 (menaquinone-7) 	(111)
	Rare intake of natto vs. occasional intake vs. frequent intake	~0 (rare); a few times a month (occasional), a few times a week (frequent) (from food record)	Cross-sectional	134 healthy volunteers				
Soy	Biscuits with fermented soybean meal vs. biscuits with soybean meal	75 g; dose equivalent to 0.44 mg/kg body weight of isoflavones	Acute, randomized, double-blind, crossover	18 healthy volunteers	HPLC-DAD-FLD (Targeted)	Urine	<ul style="list-style-type: none"> Glycitein Daidzein Genistein Dihydrodaidzein O-demethylangolensin Dihydrogenistein 6-hydroxy-O-demethylangolensin Equol Total aglycones Total colonic metabolites 	(112)
Soy	Testmeals with fermented soybean vs. non-fermented soybean	33 g of soybean	Acute (2-dose), randomized, controlled, crossover	12 healthy volunteers	UPLC-DAD-QTOF-MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Soy isoflavones: genistein 5-O-glucoside, daidzein 7-O-glucoside (daidzin), glycitein 7-O-glucoside (glycitin), genistein 7-O-glucoside (genistin), daidzein 4'-O-(6"-O-malonyl)glucoside, genistein 5-O-(6"-O-malonyl)glucoside, daidzein 7-O-(4"-O-malonyl)glucoside, glycitein 7-O-(4"-O-malonyl)glucoside, daidzein 7-O-(6"-O-malonyl)glucoside, glycitein 7-O-(6"-O-malonyl)glucoside, daidzein 7-O-(6"-O-succinoyl)glucoside, daidzein 7-O-(6"-O-acetyl)glucoside, genistein 4'-O-(6"-O-malonyl)glucoside, genistein 7-O-(4"-O-malonyl)glucoside, glycitein 7-O-(6"-O-acetyl)glucoside, genistein 7-O-(6"-O-malonyl)glucoside, genistein 4'-O-(6"-O- 	(113)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
							acetyl)glucoside, daidzein, genistein 7-O-(6"-O-succinoyl)glucoside glycitein, genistein 7-O-(6"-O-acetyl)glucoside genistein, Sum of glucoside forms, simple glucoside, acetyl glucoside, succinyl glucoside, malonyl glucoside)	
Soy	Fermented soybean paste (Cheonggukjan g)	50 g/kg body weight	Acute intervention	48 healthy men	UPLC-QTOF-MS (Targeted)	Plasma	<ul style="list-style-type: none"> Isoflavone metabolites: Daidzein, Genistein, Glycitein, 3-hydroxydaidzein, 2-hydroxygenistein, Daidzein 4'-glucuronide, Daidzein 7-glucuronide, Daidzein diglucuronide, Daidzein 4'-sulfate, Daidzein 7-sulfate 4'-glucuronide, Genistein 7-glucuronide, Genistein diglucuronide, Genistein-7-glucuronide-4'-sulfate, Genistein 4'-sulfate, Genistein-7-sulfate, Dihydrogenistein, Dihydrodaidzein sulfate, Equol-7-glucuronide, Equol-4-sulfate, 5-hydroxy equol, O-Desmethylangolensin) 	(114)
Bread	Whole-grain and fibre-rich rye bread vs. refined wheat bread	174 g/day (wholegrain products); 188 g/day (refined white breads)	12-week, randomized, parallel	51 volunteers with metabolic syndrome	GC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> Alkylrecorsinols (AR homologs C17:0-25:0) 	(115)
Bread	Wholegrain wheat and rye	Continuous intake of various wholegrains (from FFQ)	Association study	360 postmenopausal women from the Danish Diet, Cancer and Health Study	GC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> Alkylrecorsinols (AR homologs C17:0-25:0) 	(116)
Bread	High-fiber rye bread	198 g (containing 45 mg ARs) and 21 g butter	Acute intervention	15 healthy volunteers	HPLC-CEAD (Targeted)	Plasma	<ul style="list-style-type: none"> Alkylrecorsinol metabolites DHBA and DHPPA 	(117)
Bread	Whole grain breads	Total daily whole grain intake (whole grain soft bread + dark crisp bread) (from FFQ)	Association	20 free-living women from the Swedish Mammography Cohort	GC-MS (Targeted)	Plasma, subcutaneous adipose tissue	<ul style="list-style-type: none"> Alkylrecorsinols (AR homologs C17:0-25:0) 	(118)
Bread	Wholegrain rye porridge vs. refined wheat bread	2 wholegrain rye porridges (40/55 g), 3 rye porridges with different inulin	Acute, randomized, crossover	21 healthy volunteers	NMR (36 plasma metabolites); GC-MS (short chain	Plasma	<ul style="list-style-type: none"> Valine, leucine, isoleucine, lysine, phenylalanine, 2-oxoisocaproate Acetate, butyrate, propionate, acetoacetate, 3-hydroxybutyrate 	(119)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
		(55 g); refined wheat bread (55 g)			fatty acids) (Targeted)			
Bread	Rye bran bread products vs. control wheat bread products	250 g	6-week, randomized, crossover	18 healthy postmenopausal women	HPLC-DAD (Targeted)	Urine	<ul style="list-style-type: none"> Ferulic acid 	(120)
Bread	Wheat bread vs. fresh pasta (both enriched with wheat bran)	132 g (bread); 119 g (pasta)	Acute, randomized, crossover	9 healthy men	GC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> L-Isoleucine, L-leucine, lactic acid, fructose, xylose, arabinose, 2,4-dihydroxybutanoic acid, L-phenylalanine, L-proline (treatment X time effect) 1,2-diglyceride, 1-methylhistidine, urea, sitosterol, glyceric acid, phosphate, fumaric acid (treatment effect) C14:0, C17:0, glycerol, beta-alanine, L-valine, L-tryptophan, L-tyrosine, inositol, succinic acid, citric acid, L-ornithine, mannose, 2-hydroxypiperidine, iminodiacetic acid, ribulose/xylulose (treatment and time effect) 	(121)
Bread	Wholegrain bread vs. bread enriched with aleurone fraction	94 g (wholegrain bread had 87 mg of ferulic acid, while aleurone bread had 43 mg)	Acute, single-blind, randomized, crossover	15 healthy volunteers	U(H)PLC-MS and MS/MS (Targeted)	Urine, plasma	<ul style="list-style-type: none"> Ferulic acid metabolites (especially ferulic acid-4'-O-sulfate, dihydroferulic acid-4'-O-sulfate, dihydroferulic acid-O-glucuronide) 	(122)
Bread	Wholegrain wheat crisp bread vs. wholegrain rye crisp bread	100 g/day	1-week, randomized, crossover	15 healthy volunteers	GC-MS (ARs), automatic fluorometric assay (enterolactone) (Targeted)	Plasma, erythrocytes, lipoproteins (ARs), serum (enterolactone)	<ul style="list-style-type: none"> Alkylresorcinols (AR homologs C17:0-21:0) Enterolactone 	(123)
Bread	Wholegrain rye and wheat bread vs. no wholegrain rye and wheat products (in habitual diet)	<p>1. Habitual diet of wholegrain rye bread (3-5 pieces/day) and wholegrain wheat bread (2 pieces/day)</p> <p>2. Habitual diet and wholegrain rye bread (2 pieces/day) and wholegrain</p>	<p>1. 1 week avoidance, 1 week habitual diet</p> <p>2. 2 weeks of habitual diet</p> <p>3. 2 weeks of gluten-free diet</p>	<p>1. 4 healthy volunteers</p> <p>2. 4 healthy volunteers</p> <p>3. 1 volunteer</p>	GC-MS (Targeted)	Plasma, erythrocytes	<ul style="list-style-type: none"> Alkylresorcinols (AR homologs C17:0-25:0) 	(124)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
		wheat bread (2 pieces/day) 3. Gluten-free diet with no wheat, rye, or barley products						
Bread	High-fiber rye bread	198 g (containing 100 mg ARs) and 21 g butter	Acute intervention	15 healthy volunteers	HPLC-CEAD (Targeted)	Urine	<ul style="list-style-type: none"> Alkylrecorsinol metabolites DHBA and DHPPA 	(125)
Bread	Bread, rye bread, refined wheat bread, bran-seed bread	Continuous intake of bread, rye bread, refined wheat bread, bran-seed bread (from 3-day food records)	Association study	31 free-living men with prostate cancer and 91 non-cancer control men	HPLC-CEAD (Targeted)	Plasma (DHPPA), urine (DHBA and DHPPA)	<ul style="list-style-type: none"> Alkylrecorsinol metabolites DHBA and DHPPA 	(126)
Bread	Wholegrain products	Continuous intake of wholegrain products, including rye bread, wholegrain bread, rolled oats and muesli, and crispbread (from FFQ)	Association study	43 893 volunteers from the Danish Diet, Cancer, and Health cohort (ARs were measured in subset of 516 volunteers)	GC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> Alkylrecorsinols (AR homologs C17:0-25:0) 	(127)
Bread	Wholegrain wheat vs. refined wheat	70 g/day biscuits (wholegrain); 33 g/day crackers and 27 g/day toasted bread (refined grain)	8-week, randomized, placebo-controlled, parallel	80 healthy obese/over weight volunteers	HPLC-MS/MS (Targeted)	Serum, urine, feces	<ul style="list-style-type: none"> Phenolic acids (dihydroferulic acid in serum, ferulic acid in feces following wholegrain wheat) 	(128)
Bread	Refined-grain wheat bread vs. wholegrain wheat bread	196 g (refined grain); 208 g (wholegrain), both with 21 g butter	Acute, crossover	12 healthy volunteers	LC-MS (Targeted)	Urine	<ul style="list-style-type: none"> Alkylrecorsinol metabolites (3,5-DHBA glycine, 3,5-DHPPTA, 3,5-DHBA, 3,5-DHPPA) 	(129)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Bread	Wholegrain rye bread vs. low-fiber wheat bread	214 g (rye); 178 (wheat)	8-week, randomized, crossover	39 healthy postmenopausal women	GC-MS (ARs); fluorimmunoassay (enterolactone) (Targeted)	Plasma	<ul style="list-style-type: none"> Alkylrecorsinols Enterolactone 	(130)
Bread	White wheat flour soft bread and white wheat flour crispbread vs. rye bran-enriched soft bread and whole grain rye crisp bread	142.8 g/day and 92.4 g/day; 180.6 g/day and 91.0 g/day	2-week, randomized, crossover	10 volunteers with previous proctocolectomy for ulcerative colitis	GC-MS (Targeted)	Ileal effluent	<ul style="list-style-type: none"> Alkylrecorsinols (AR homologs C17:0-25:0) 	(131)
Bread	Sourdough fermented bread vs. traditional sourdough bread vs. baker's yeast bread	215 mL (mimicking chewing and homogenisation of the bread portion + 160 mL water)	Acute, randomized, double-blind, crossover	36 healthy volunteers	Biochrom 30 series Amino Acid Analyzer (Targeted)	Plasma	<ul style="list-style-type: none"> Total free amino acids 	(132)
Bread	Rye-based bread vs. white wheat bread	75 g	3-day, randomized, controlled, crossover	38 healthy volunteers	GC (detector not specified) (Targeted)	Plasma	<ul style="list-style-type: none"> Acetate Butyrate Total SCFAs 	(133)
Cocoa	Sugar-free, flavanol-rich cocoa alone vs. low-dose sugar + cocoa vs. high-dose sugar + cocoa	0.125 g/kg body weight (cocoa); 8.75 kJ/kg (low-dose sugar); 17.5 kJ/kg (high-dose sugar)	Acute crossover	6 healthy volunteers	HPLC-coulometric multiple-array detection (Targeted)	Plasma	<ul style="list-style-type: none"> Total flavonols (epicatechin + catechin) 	(134)
	Sugar-free, flavanol-rich cocoa alone vs. bread+ cocoa vs. steak + cocoa vs. butter + cocoa (macronutrient-rich foods)	0.125 g/kg body weight (cocoa); 17.5 kJ/kg (foods)					<ul style="list-style-type: none"> Total flavonols (epicatechin + catechin) 	

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
	Sugar-free, flavanol-rich cocoa alone vs. bread + cocoa vs. milk + cocoa vs. grapefruit juice + cocoa	0.125 g/kg body weight (cocoa); 17.5 kJ/kg (foods)					<ul style="list-style-type: none"> Total flavonols (epicatechin + catechin) 	
	Water + cocoa vs. water + cocoa + Famotidine	0.125 g/kg body weight (cocoa); 20 mg (Famotidine)					<ul style="list-style-type: none"> No difference in flavonols 	
Cocoa	Semi-sweet chocolate (M&Ms chocolate mink baking bits) vs. vanilla milk chips	80 g	Acute, parallel	13 healthy volunteers	HPLC-Coulochem II detector (Targeted)	Plasma	<ul style="list-style-type: none"> Catechin Epicatechin 	(135)
Cocoa	Nestle Noir 70% dark chocolate	100 g	Acute intervention	5 healthy volunteers	LC-MS/MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> (-)-Epicatechin-3'-beta-D-glucuronide (-)-Epicatechin-3'-sulfate 3'-O-methyl epicatechin sulfates 	(136)
Cocoa	Cocoa powder + skimmed milk vs. skimmed milk	20 g/day with 250 mL skimmed milk; 500 mL/day skim milk	4-week, randomized, controlled, crossover	42 healthy volunteers	LC-MS/MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> (-)-Epicatechin (-)-Epicatechin glucuronides and sulfates O-methyl-epicatechin glucuronides and sulfates DHPV glucuronides and sulfates MHPV glucuronides and sulfates Vanillic acid 3,4-Dihydroxyphenylacetic acid 3-Hydroxyphenylacetic acid 	(137)
Cocoa	Cocoa powder + water vs. cocoa powder + whole milk vs. whole milk	40 g (cocoa powder) in 250 mL (milk or water)	Acute, randomized, crossover	21 healthy volunteers	HPLC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> (-)-Epicatechin glucuronide (-)-Epicatechin sulfates 	(138)
Cocoa	Dark chocolate vs. high sucrose chocolate vs. high milk protein chocolate vs. sucrose milk protein	40 g or 250 mL (for drinks)	Acute, randomized, crossover	6 healthy volunteers	HPLC-EAD (Targeted)	Serum	<ul style="list-style-type: none"> Epicatechin, catechin, and glucuronide and sulfate conjugates 	(139)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
	chocolate drink vs. non-nutritive sweetener milk protein chocolate drink							
Cocoa	Flavonoid-rich dark chocolate (72%) vs. flavonoid-free placebo (dyed) white chocolate	50 g	Acute, randomized, controlled, parallel	65 healthy men	HPLC-EAD (Targeted)	Plasma	<ul style="list-style-type: none"> • Epicatechin 	(140)
Cocoa	High-flavanol chocolate with mannitol vs. high-flavanol chocolate with sucrose vs. low-flavanol chocolate with sucrose	25 g; standardized to macro and micronutrients, theobromine, and caffeine	Acute, randomized, double-blind, crossover	15 healthy volunteers	HPLC-FLD/UV (Targeted)	Plasma	<ul style="list-style-type: none"> • Total cocoa flavanols (epicatechin, catechin, procyanidin oligomers) • 3' and 4'-O-methylated epicatechins 	(141)
Cocoa	Cocoa beverage vs. milk	40 g cocoa powder in 250 mL milk; 250 mL milk	Acute, randomized, controlled, crossover	36 healthy volunteers	Folin-Ciocalteu Assay (modified) (Targeted)	Urine	<ul style="list-style-type: none"> • Total polyphenols (+-categub equivalents) 	(142)
Cocoa	Cocoa with water	40 g cocoa powder in 250 mL water	Acute intervention	21 healthy volunteers	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Caffeic acid • Ferulic acid • 3-hydroxyphenylacetic acid • Vanillic acid • 3-hydroxybenzoic acid • 4-hydroxyhippuric acid • Hippuric acid • (-)-Epicatechin • Procyanidin B2 	(143)
Cocoa	Dark chocolate (70%) vs. white chocolate	45 g	2-week, controlled, parallel	20 healthy volunteers	HPLC-DAD (Targeted)	Plasma	<ul style="list-style-type: none"> • (-)-Epicatechin 	(144)
Cocoa	Cocoa beverage with milk vs. cocoa beverage with water	10 g cocoa powder in 250 mL milk or water	Acute crossover	9 healthy volunteers	HPLC-PDA, HPLC-MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • (Epi)catechin-O-sulfate • (-)-Epicatechin-O-glucuronide • (Epi)catechin-O-sulfate • O-Methyl-(epi)catechin-O-sulfate 	(145)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Cocoa	Hershey's milk chocolate	113 g	Acute intervention	6 nursing mothers	HPLC (detector not specified) (Targeted)	Plasma, saliva, breast milk	<ul style="list-style-type: none"> Theobromine 	(146)
Cocoa	Dark chocolate vs. white chocolate	6.3 g/day	18-week, randomized, controlled, parallel	44 healthy volunteers	LC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> Epicatechin Catechin Procyanidin B2 Procyanidin B2 galate 	(147)
Cocoa	Cocoa powder with no added methylxanthine vs. cocoa powder enriched with methylxanthine	15 g dissolved in 200 mL (milk)	Acute, randomized, controlled, crossover	13 healthy volunteers	HPLC-DAD, LC-QTOF, LC-DAD (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Theobromine Caffeine Paraxanthine Theophylline Methylxanthines (1-, 3-, 7, 1,7-, 3,7-, 1,3-, 1,3,7-) Methyluric acid (1-, 1,3-, 1,7-, 3,7-, 1,3,7-) 	(148)
Cocoa	Cocoa in skimmed milk vs. skimmed milk	40 g/day (cocoa powder) in 500 mL (milk)	4-week, randomized, crossover	42 volunteers with high CV risk	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> (-)-Epicatechin glucuronides and sulfates O-Methyl-epicatechin glucuronides and sulfates 5-(3-Methoxy-4-hydroxyphenyl)-gamma-valerolactone glucuronides and sulfates 5-(3,4-Methoxy-4-hydroxyphenyl)-gamma-valerolactone 3-Hydroxyphenylacetic acid 3,4-Dihydroxyphenylacetic acid Vanillic acid 	(149)
Cocoa	Dark chocolate (85%) vs. milk chocolate (<35%)	40 g	Acute, single-blind, crossover	20 healthy volunteers and 20 smokers	HPLC-UV (Targeted)	Serum	<ul style="list-style-type: none"> Epicatechin 	(150)
Cocoa	Cocoa beverage	0.375 g cocoa/kg body weight in 300 mL water	Acute intervention	5 healthy volunteers	HPLC-CEAD, LC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> Procyanidin dimer B2 [epicatechin-4beta-8)-epicatechin] Catechin Epicatechin 	(151)
Cocoa	Flavanoid-enriched chocolate bars vs. placebo	27 g/day with 90 mg catechin/day	1-year, randomized, controlled, parallel	93 postmenopausal women with type 2 diabetes	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Epicatechin monoglucuronide Methylepicatechin monoglucuronide Epicatechin monosulfate Methylepicatechin sulfate Epicatechin monosulfate monoglucuronide 	(152)
Cocoa	Cocoa in whole milk vs. cocoa in water vs. milk	40 g (cocoa powder) in 250 mL (milk or water)	Acute, randomized, crossover	21 healthy volunteers	LC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> (-)-Epicatechin glucuronide 	(153)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Cocoa	Cocoa beverage	Powder in 500 mL water; 10.7 mg cocoa flavanols/kg body weight	Acute intervention (X2)	7 healthy young volunteers	HPLC-FLD/UV/EC D (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • (-)-Epicatechin-3'-beta-D-glucuronide • (-)-Epicatechin-3'-sulfate • 3'-O-Methyl(-)-epicatechin-5-sulfate • 3'-O-Methyl(-)-epicatechin-7-sulfate 	(154)
	Cocoa beverage vs. acetaminophen in beverage	Powder in 500 mL water; 5.3 and 10.7 mg cocoa flavanols/kg body weight; 2X 500 mg acetaminophen in water	Acute, randomized, crossover	20 young healthy men and 20 elderly healthy men			<ul style="list-style-type: none"> • (-)-Epicatechin-3'-beta-D-glucuronide • (-)-Epicatechin-3'-sulfate • 3'-O-Methyl(-)-epicatechin-5-sulfate • 3'-O-Methyl(-)-epicatechin-7-sulfate 	
Cocoa	High-flavanol cocoa drink vs. low-flavanol cocoa drink	Powder in 300 mL water; 917 mg or 37 mg cocoa flavanols	Acute, randomized, double-blind, crossover	10 healthy men	HPLC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> • (-)-Epicatechin • Catechin • 4'-Methyl-epicatechin • Epicatechin-O-beta-D-glucuronide • 4'-O-Methyl-epicatechin-O-beta-D-glucuronide (highest) 	(155)
Cocoa	Dark chocolate	100 g	Acute intervention	Healthy volunteers (number not reported)	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • 3'-O-methyl(-)-epicatechin-5/7-O-sulfate • 4'-O-methyl(-)-epicatechin-5/7-O-sulfate 	(156)
Cocoa	High-flavanol chocolate vs. low-flavanol chocolate	40 g (first visit single dose); 20 g/day thereafter	Acute and 12-week, randomized, parallel	44 healthy pregnant women	HPLC-FLD (Targeted)	Plasma	<ul style="list-style-type: none"> • Epicatechin • Catechin • Caffeine • Theobromine • Theophylline 	(157)
Cocoa	Cocoa in milk vs. whole milk	40 g (cocoa powder) in 250 mL (milk)	Acute, randomized, crossover	5 healthy volunteers	LC-MS/MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • (-)-Epicatechin • (-)-Epicatechin glucuronide • (-)-Epicatechin sulfate 	(158)
Cocoa	Alkalized cocoa powder in water	20.3 g (cocoa powder) in 400 mL water	Acute intervention	8 healthy volunteers	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • N-[4'-hydroxy-(E)-cinnamoyl]-L-aspartic acid • N-[4'-hydroxy-(E)-cinnamoyl]-L-glutamic acid • N-[4'-hydroxy-3'-methoxy-(E)-cinnamoyl]-L-tyrosine 	(159)
Cocoa	Chocolate	80 g	Acute intervention	11 healthy volunteers	GC-MS, HPLC-ESI-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • M-Hydroxyphenylpropionic acid • Ferulic acid • 3,4-dihydroxyphenylacetic acid • M-hydroxyphenylacetic acid • Vanillic acid • M-Hydroxybenzoic acid 	(160)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Cocoa	Cocoa in whole milk vs. cocoa in water	40 g (cocoa powder) in 250 mL (milk or water)	Acute, randomized, crossover	21 healthy volunteers	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • 3,4-dihydroxyphenylacetic acid • Phenylacetic acid • Protocatechuic acid • 4-hydroxybenzoic acid • 4-hydroxyhippuric acid • Hippuric acid • Vanillic acid • Caffeic acid • Ferulic acid 	(161)
Cocoa	Cocoa beverage vs. whole milk	40 g (cocoa powder) in 250 mL water; 250 mL (milk)	Acute, randomized, crossover	21 healthy volunteers	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • (-)-Epicatechin glucuronide • (-)-Epicatechin sulfates 	(162)
Cocoa	Chocolate (M&Ms semi-sweet chocolate mink baking bits) at 4 doses	0, 27, 53, 80 g	Acute, randomized, crossover	20 healthy volunteers	LC-Coulochem II coulometric detector (Targeted)	Plasma	<ul style="list-style-type: none"> • (-)-Epicatechin 	(163)
Cocoa	Chocolate vs. cocoa	35 g cocoa powder in each	Acute crossover	5 healthy men	HPLC-MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • (-)-Epicatechin and metabolites (glucuronides, sulfates, sulfoglucuronides, non-methylated, methylated) 	(164)
Cocoa	Cocoa drink with low flavanols, medium flavanols, vs. high flavanols	18 g cocoa beverage mix in 250 mL water	Acute, randomized, double-blind, controlled, crossover	10 diabetic patients	HPLC-FLD (Targeted)	Plasma	<ul style="list-style-type: none"> • Total flavanols (epicatechin, catechin, and methylated, glucuronidated) 	(165)
	Cocoa drink with high flavanols vs. low flavanols		30-day, randomized, double-blind, controlled, parallel	40 diabetic patients				
Cocoa	High-flavanol dark chocolate vs. low-flavanol dark chocolate	46 g	2-week, randomized, double-blind, placebo-controlled, parallel	21 healthy volunteers	HPLC-ECD (Targeted)	Plasma	<ul style="list-style-type: none"> • Epicatechin 	(166)
Cocoa	Dark chocolate (85%) vs. milk chocolate (≤35%)	40 g	Acute, randomized, single-blind, crossover	20 patients with peripheral	HPLC-UV (Targeted)	Serum	<ul style="list-style-type: none"> • Epicatechin • Epicatechin-3-O-methylether • Epigallocatechin-3-gallate 	(167)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
				artery disease				
Cocoa	Chocolate vs. cola vs. caffeine capsules vs. theobromine capsules	82 g (chocolate); 800 mL (cola); 72 mg (caffeine capsules); 370 mg (theobromine capsule)	Acute crossover	7 healthy volunteers	HPLC-DAD (Targeted)	Plasma	<ul style="list-style-type: none"> • Methylxanthine • Caffeine • Paraxanthine • Theophylline • Theobromine 	(168)
Cocoa	Cocoa drink vs. sugar	36 g cocoa powder	2-week, randomized, controlled, parallel	15 healthy men	HPLC-amperometric ECD (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • Epicatechin 	(169)
Cocoa	Nestle Noir dark chocolate low-dose vs. high-dose	40 g; 80 g	Acute crossover	8 healthy men	HPLC-DAD/FLD (Targeted)	Plasma	<ul style="list-style-type: none"> • Theobromine • Epicatechin 	(170)
Cocoa	Dark chocolate vs. milk chocolate	200 g	3-day, randomized, controlled, parallel	58 healthy volunteers	Enzymatic method (oxalate)	Urine	<ul style="list-style-type: none"> • Oxalate 	(171)
Cocoa	Dark chocolate (70%) vs. white chocolate (4% cocoa)	1 g/kg body weight	Acute crossover	10 healthy volunteers	Not reported	Plasma	<ul style="list-style-type: none"> • Catechin • Epicatechin and metabolites 	(172)
Cocoa	Dark chocolate vs. theobromine sodium acetate oral solution	6 mg/kg body weight of theobromine (chocolate); 10 mg/kg body weight theobromine (oral solution)	7-day intervention (chocolate); acute intervention (oral solution)	12 healthy volunteers	HPLC-solvent scintillator flow cell detector (Targeted)	Urine, serum	<ul style="list-style-type: none"> • Theobromine 	(173)
Cocoa	Milk chocolate vs. chocolate powder vs. dark chocolate	40 g/day	7-day crossover	20 healthy volunteers	HPLC-PDA (Targeted)	Urine	<ul style="list-style-type: none"> • Theobromine 	(174)
Cocoa	Non-alkalized cocoa beverage vs. alkalized cocoa beverage	0.6 g/kg body weight (alkalized powder); 0.8 g/kg body	Acute, randomized, double-blind, crossover	12 healthy volunteers	HPLC-CEAD (Targeted)	Plasma	<ul style="list-style-type: none"> • Epicatechin 	(175)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
		weight (non-alkalized powder) in 6 mL/kg body weight skimmed milk						
Cocoa	Conventional cocoa beverage vs. flavanol-rich cocoa beverage	15 g (conventional); 25 g (flavanol rich) in 200 mL semi-skimmed milk	Acute, randomized, blind, crossover	13 healthy volunteers	HPLC-ESI-QTOF-MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • Epicatechin metabolites (Epicatechin-3-glucuronide, 3-methoxy-glucuronide, 3-sulfate, methoxy-sulfate) • Phenyl-gamma-valerolactone derivatives (DHPV lactones, 5-(3-Hydroxyphenyl)-γ-valerolactone-4-glucuronide, 5-(4-Hydroxyphenyl)-γ-valerolactone-3-glucuronide, 5-(Hydroxyphenyl)-γ-valerolactone-sulfate, 5-Phenyl-γ-valerolactone-methoxy-glucuronide, 5-Phenyl-γ-valerolactone-methoxy-sulfate, 5-(3-Hydroxyphenyl)-γ-valerolactone, 5-Phenyl-γ-valerolactone-3-glucuronide, 5-Phenyl-γ-valerolactone-3-sulfate) • Phenylvaleric acid derivatives (4-Hydroxy-5-(3,4-dihydroxyphenyl)valeric acid, 4-Hydroxy-5-(hydroxyphenyl)valeric acid-glucuronide, 4-Hydroxy-5-(hydroxyphenyl)valeric acid-sulfate) • Other microbial metabolites (3,4-Dihydroxyphenylpropionic acid, 3-Methoxy-4-hydroxyphenylpropionic acid 3-Hydroxyphenylpropionic acid 3,4-Dihydroxyphenylacetic acid, 3-Methoxy-4-hydroxyphenylacetic acid 3-Hydroxyphenylacetic acid, Ferulic acid Isoferulic acid, 3,4-Dihydroxybenzoic acid, 4-Hydroxyhippuric acid, 3-Hydroxyhippuric acid, Hydroxybenzoic acid) 	(176)
Cocoa	Milk chocolate vs. hazelnut and cocoa spread	60 g	Acute, randomized, single-blind, crossover	20 healthy smokers	Folin-Ciocalteu method (polyphenols); GC-MS (vitamin E) (Targeted)	Plasma (polyphenols); serum (vitamin E)	<ul style="list-style-type: none"> • Total polyphenols • Vitamin E 	(177)
Cocoa	Dark chocolate (90%)	50 g	Acute intervention	18 healthy men	U(H)PLC-ESI-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Epicatechin and metabolites (glucuronides, glucuronide-sulfate, sulfates, methyl-epicatechin sulfates) • Phenyl-gamma-valerolactones (5-(3-Hydroxyphenyl)-g-valerolactone-4-glucuronide, 5-Phenyl-g-valerolactone-glucuronide-sulfate, 5-(4-Hydroxyphenyl)-g-valerolactone-3-glucuronide, 5-Phenyl-g-valerolactone-3-glucuronide, 5-(Hydroxyphenyl)-g-valerolactone-sulfate isomers, 5-Phenyl-g-valerolactone-sulfate-methoxy, 5-Phenyl-g-valerolactone-3-sulfate) 	(178)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Cocoa	Cocoa-enriched dark chocolate (70%) vs. cocoa-depleted control chocolate	561 kcal	Acute, single-blind, randomized, crossover	16 healthy male cyclists	RP-HPLC-UV (Targeted)	Plasma	<ul style="list-style-type: none"> • Epicatechin • Theobromine 	(179)
Coffee	Coffee consumption	0, 1, 2-4, 5-8, >8 cups of coffee/day (from questionnaire)	Association study	3503 patients undergoing elective coronary angiography from the WECAC cohort	LC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Trigonelline • Nicotinamide • N-methylnicotinamide 	(180)
Coffee	Instant coffee (Nescafe Gold Blend)	3.4 g powder in 200 mL water	Acute intervention	5 volunteers with an ileostomy	HPLC-PDA-MS/MS (Targeted)	Ileal effluent, urine	<ul style="list-style-type: none"> • Total chlorogenic acid and metabolites • 3-, 4-, and 5-O-caffeoylquinic acids • 3-, 4-, and 5-O-caffeoylquinic acid sulfates • 3- and 4--O-caffeoylquinic acid glucuronides • 3-, 4-, and 5-O-feruloylquinic acids • 3-, 4-, and 5-O-feruloylquinic acid sulfate • 3- and 4-O-feruloylquinic acid glucuronides • 3- and 4-O-caffeoylquinic acid lactones • 3- and 4-O-caffeoylquinic glucuronides and sulfates • 4- and 5-O-p-coumaroylquinic acid • 3,4-, 3,5-, and 4,5-O-di-caffeoylquinic acid • Caffeic acid • Caffeic acid 4- and 3-O-sulfates • Ferulic acid • Ferulic acid-4-O-sulfate • Feruloylglycine • Dihydroferulic acid-4-O-sulfate • Isoferulic acid 3-O-sulfate and glucuronide • Dihydrocaffeic acid-3-O-sulfate 	(181)
Coffee	Instant coffee	200 mL	Acute intervention	11 healthy volunteers	HPLC-PDA-MS/MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • Dihydrocaffeic acid 3'-sulfate • Dihydrocaffeic acid-3'-O-glucuronide • Caffeic acid 4'-sulfate • Dihydroferulic acid 4'-sulfate • Caffeic acid 3'-sulfate • Dihydroferulic acid 4'-O-glucuronide • Ferulic acid 4'-sulfate • Isoferulic acid 3'-sulfate • Dihydroisoferulic acid 3'-O-glucuronide 	(182)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
							<ul style="list-style-type: none"> Isoferulic acid 3'-O-glucuronide 	
Coffee	Coffee vs. tea vs. Cola soft drink	At least 1 cup of coffee or tea, 500 mL soft drink	Acute intervention	146 healthy volunteers	HPLC-UV (Targeted)	Urine	<ul style="list-style-type: none"> 5-acetylamino-6-formylamino-3-methyluracil 1-methylxanthine 	(183)
Coffee	Low-polyphenol coffee vs. high-polyphenol coffee vs. caffeine in hot water	3.6 g ground coffee to 50 mL water; 110 mg caffeine	Acute, randomized, controlled, crossover	15 healthy men	U(H)PLC-ESI-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> Total chlorogenic acid metabolites 3-caffeoylquinic acid 4-caffeoylquinic acid Caffeic-4-O-sulfate 3-feroylquinic acid 4-feroylquinic acid 5-feroylquinic acid Ferulic acid Isoferulic acid Methylferulic acid Ferulic-4-O-glucuronide Isoferulic-3-O-glucuronide Ferulic-4-O-sulfate Isoferulic-3-O-sulfate 	(184)
Coffee	Caffeinated coffee vs. decaffeinated coffee vs. combination	2 cups (caffeinated); 2 cups (decaffeinated); 1 cup (caffeinated) + 1 cup (decaffeinated)	Acute, randomized, crossover	17 men with coronary artery disease performing a treadmill test	HPLC (detector not specified) (Targeted)	Serum	<ul style="list-style-type: none"> Caffeine 	(185)
Coffee	Coffee (mostly instant coffee) and tea	Number of cups of coffee and tea consumption (FFQ for usual consumers; 24h recall for current consumers)	Association study	111 free-living volunteers (usual consumers); 344 healthy volunteers (current consumers)	GC-MS (Targeted)	Urine	<ul style="list-style-type: none"> Isoferulic acid 	(186)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Coffee	Filtered coffee	0 (refrain from consumption), 4 cups/day, 8 cups/day (150 mL/cup)	1-month, crossover	47 habitual coffee drinkers	HPLC-MS, GC-MS (Targeted)	Serum, plasma	<ul style="list-style-type: none"> • Caffeine • Paraxanthine • Theobromine • Theophylline • Caffeic acid • Dihydrocaffeic acid • Ferulic acid • Isoferulic acid • Dihydroferulic acid • Dihydroisoferulic acid • 3-(3-Hydroxyphenyl)propanoic acid • 3-(3,4-Dimethoxyphenyl)propanoic acid • 3,4-Dimethylcaffeic acid • 3-Coumaric acid 	(187)
Coffee	Coffee	Cups of coffee consumption (1-2, 3-7, >8) (from survey)	Association study	284 healthy men	LC-ESI-MS/MS (Targeted 363 metabolites)	Serum	<ul style="list-style-type: none"> • Sphingomyelin SM(OH,COOH) • Sphingomyelin SM(OH) • Long- and medium-chain acylcarnitines 	(188)
Coffee	Coffee	Non-coffee consumers (0 mL/day), low-coffee consumers (≤100 mL/day), high-coffee consumers (>100 mL/day) (from 24h recalls and FFQ)	Association study	169 healthy volunteers	FIA-MS/MS, HPLC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • 3-, 4-, 5-Caffeoylquinic acid • 5-Feruloylquinic acid • 4-Ethylguaiaicol • 4-Vinylguaiaicol • Catechol • Pyrogallol • LysoPC C16:0/16:1 • LysoPC C18:0/18:1 	(189)
Coffee	Coffee and tea	Coffee and tea consumption (from FFQ and 3-day food record)	Association study	57 healthy women	HPLC-MS/MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • Caffeic acid • Chlorogenic acid 	(190)
Coffee	Coffee	Preparation: 48 g coffee powder in 900 mL water; 350 mL consumed	Acute intervention	13 healthy volunteers	HILIC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Trigonelline • N-methylpyridinium 	(191)
Coffee	Coffee vs. tea vs. water	Dose not specified	Acute intervention	13 healthy volunteers	CE-ESI-TOF-MS, HPLC-	Urine	<ul style="list-style-type: none"> • Chlorogenic acid • Caffeic acid • Coumaric acid 	(192)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
					MS/MS (Targeted)			
Coffee	Coffee	Preparation: 40 g coffee powder in 250 mL water' 190 mL consumed	Acute intervention	6 healthy volunteers	HPLC-UV, LC-MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • 3-, 4-, and 5-Caffeoylquinic acid (plasma) • 3,4-, 3,5-, and 4,5-Dicaffeoylquinic acid (plasma) • Feryloylquinic acid (plasma, only 1 volunteer) • Dihydrocaffeic acid (urine) • Gallic acid (urine) • Isoferulic acid (urine) • Ferulic acid (urine) • Vanillic acid (urine) • Caffeic acid (urine) • 5-caffeoylquinic acid (urine) • Sinapic acid (urine) • P-hydroxybenzoic acid (urine) • P-coumaric acid (urine) 	(193)
Coffee	Instant coffee with low chlorogenic acids vs. medium chlorogenic acids vs. high chlorogenic acids	3.4g coffee powder in 200 mL water	Acute, randomized, double-blind, controlled, crossover	11 healthy volunteers	HPLC-PDA-MS/MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • 3-Caffeoylquinic acid-O-sulfate • Dihydrocaffeic acid-3-O-sulfate • Dihydrocaffeic acid-3-O-glucuronide • 4-caffeoylquinic acid-O-sulfate • Caffeic acid-4-O-sulfate • Dihydroferulic acid-4-O-sulfate • Caffeic acid-3-O-sulfate • Dihydrocaffeic acid • Dihydroferulic acid-4-O-glucuronide • Ferulic acid-4-O-sulfate • 5-caffeoylquinic acid • 3-feruloylquinic acid • Isoferulic acid-3-O-sulfate • Dihydroisoferulic acid-3-O-glucuronide • Isoferulic acid-3-O-glucuronide • Feruloylglycine • 3-Caffeoylquinic acid lactone-O-sulfate • 4-Caffeoylquinic acid lactone-O-sulfate • 4-Feruloylquinic acid • Dihydroferulic acid • 5-Feruloylquinic acid 	(194)
Coffee	Coffee at 3 doses	2, 4, and 8 g coffee powder in 400 mL water	Acute, randomized, crossover	10 healthy volunteers	LC-ESI-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • 3-Feruloylquinic acid • 4-Feruloylquinic acid • 5-Feruloylquinic acid • 3-Caffeoylquinic acid • 4-Caffeoylquinic acid • 5-Caffeoylquinic acid 	(195)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
							<ul style="list-style-type: none"> • Ferulic acid • Caffeic acid • Isoferulic acid • Dihydroferulic acid • Dihydrocaffeic acid 	
Coffee	Coffee vs. no coffee	1 cup (acute); daily consumption of coffee	Acute intervention	Healthy volunteers (number not specified)	HPLC-UV (Targeted)	Urine	<ul style="list-style-type: none"> • N-methyl-2-pyridone-5-carboxamide • N-methyl-4-pyridone-5-carboxamide 	(196)
Coffee	Hot coffee consumed slowly vs. cold coffee consumed slowly vs. cold coffee consumed fast vs. sugar-free energy drink consumed fast vs. sugar-free energy drink consumed slowly	4.1 g coffee powder in 450 mL water; 450 mL energy drink	Acute, randomized, crossover	24 healthy volunteers	LC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Caffeine 	(197)
Coffee	Coffee vs. soy beverage vs. coffee + soy beverage	4 g coffee powder and/or 20 g soymilk powder in 200 mL water	Acute, randomized, crossover	6 healthy volunteers	HPLC-DAD, LC-MS (Targeted)	Urine	<ul style="list-style-type: none"> • 3-Caffeoylquinic acid • 4-Caffeoylquinic acid • 5-Caffeoylquinic acid • 3,4-Dicaffeoylquinic acid • 3,5-Dicaffeoylquinic acid • 4,5-Dicaffeoylquinic acid • Ferulic acid • Caffeic acid • Isoferulic acid • Dihydrocaffeic acid • Gallic acid • Vanillic acid • Benzoic acid • P-Hydroxybenzoic acid • Siringic acid • Sinapic acid • 3,4-Dihydroxyphenylacetic acid • Hippuric acid • Trans-3-hydroxycinnamic acid 	(198)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
							<ul style="list-style-type: none"> • 3-(4-Hydroxyphenyl) propanoic acid • 2,4-Dihydroxybenzoic acid 	
Coffee	Instant coffee	1 cup containing 4 mg caffeine/kg body weight	Acute intervention	6 healthy volunteers	HPLC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • AAMU/AFMU • 1-Methyluric acid • 1-Methylxanthine • 1,3-Dimethyluric acid • 1,7-Dimethyluric acid • 1,3,7-Trimethyluric acid • 3,7-Dimethylxanthine • Paraxanthine • 1,3-Dimethylxanthine • 1,3,7-Trimethylxanthine 	(199)
Coffee	Instant coffee	400 mL	Acute intervention	8 healthy volunteers	HPLC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • 3,4-Dimethoxycinnamic acid 	(200)
Coffee	Instant coffee	4 g in 400 mL water	Acute intervention	Healthy volunteers (number not specified)	LC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Caffeic acid • Dihydrocaffeic acid • Ferulic acid • Dihydroferulic acid • Isoferulic acid 	(201)
Coffee	Instant coffee	3.4 g in 200 mL	Acute intervention	11 healthy volunteers	HPLC-PDA-MS/MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • 3-O-Caffeoylquinic acid-O-sulfate • Dihydrocaffeic acid-3-O-sulfate • Dihydrocaffeic acid-3-O-glucuronide • 4-O-Caffeoylquinic acid-O-sulfate • Caffeic acid-4-O-sulfate • Dihydroferulic acid-4-O-sulfate • Caffeic acid-3-O-sulfate • Dihydrocaffeic acid • Dihydroferulic acid-4-O-glucuronide • Ferulic acid-4-O-sulfate • 5-O-Caffeoylquinic acid • 3-O-Feruloylquinic acid • Isoferulic acid-3-O-sulfate • Dihydro(iso)ferulic acid-3-O-glucuronide • Isoferulic acid-3-O-glucuronide • Feruloylglycine • 3-O-Caffeoylquinic acid lactone-O-sulfate • 4-O-Caffeoylquinic acid lactone-O-sulfate • 4-O-Feruloylquinic acid • Dihydroferulic acid • 5-O-Feruloylquinic acid 	(202)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Coffee	Instant coffee in water vs. instant coffee in milk vs. water	4 g in 200 mL water or milk	Acute, randomized, crossover	5 healthy volunteers	HPLC-DAD, LC-MS (Targeted)	Urine	<ul style="list-style-type: none"> • Hippuric acid • 3,4-Dihydroxyphenylacetic acid • Dihydrocaffeic acid • Vanillic acid • Gallic acid • Isoferulic acid • 4-Hydroxybenzoic acid • 2,4-Hydroxybenzoic acid • Trans-3-hydroxycinnamic acid • P-Coumaric acid • Syringic acid • Sinapinic acid 	(203)
Coffee	Freshly brewed coffee	30 g in 500 mL water	Acute intervention	10 healthy volunteers	HPLC-ESI-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Nicotinic acid • Nicotinamide • N-methylnicotinamide • N-methyl-2-pyridone-5-carboxamide • Nicotinuric acid 	(204)
Coffee	Green-roasted coffee	3.5 g in 250 mL water	Acute intervention	12 healthy volunteers	HPLC-DAD, LC-MS-QTOF (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • Caffeine • Paraxanthine • Theobromine • Theophylline • 1-Methylxanthine • 3-Methylxanthine • 7-Methylxanthine • 1-Methyluric acid • 1,3-Methyluric acid • 1,7-Methyluric acid • 1,3,7-Methyluric acid 	(205)
Coffee	Instant coffee	8 g in 400 mL water	Acute intervention	10 healthy volunteers	LC-ESI-MS/MS (Targeted 56 phenolic compounds)	Plasma	<ul style="list-style-type: none"> • Total phenolic acids, methyls, glucuronides, sulfates, and lactones (ferulic acid, caffeic acid, and all metabolites thereof) 	(206)
Coffee	Instant coffee	4 g in 400 mL water	Acute intervention	9 healthy volunteers	ESI-LC-ESI-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Ferulic acid • Caffeic acid • Isoferulic acid • Dihydrocaffeic acid • Dihydroferulic acid 	(207)
Coffee	Instant coffee vs. green tea	4 g in 400 mL water; 1.25% tea infusion	Acute crossover	9 healthy volunteers	ESI-LC-ESI-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Ferulic acid • Caffeic acid • Isoferulic acid • Dihydrocaffeic acid • Dihydroferulic acid 	(208)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Coffee	Instant coffee vs. instant coffee in whole milk vs. instant coffee with sugar and non-dairy creamer vs. no coffee	4 g in 400 mL water or 360 mL water + 40 mL whole milk or 30.5 g premixed instant coffee with sugar	Acute, randomized, crossover	9 healthy volunteers	ESI-LC-ESI-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Ferulic acid • Caffeic acid • Isoferulic acid 	(209)
Coffee	Coffee	0, 1, 2, or 3 cups/day	Cross-sectional	15 healthy men	LC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Hippuric acid 	(210)
Coffee	Nescafe Green Blend coffee	3.5 g in 240 mL water	Acute intervention	12 healthy volunteers	LC-MS-QTOF (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • Caffeic acid and metabolites • Ferulic acid and metabolites • Coumaric acid and metabolites • Dimethoxycinnamic acid and metabolites • Lactone derivatives • Phenolic acids 	(211)
Coffee	Coffee	Caffeinated coffee, other caffeinated drinks, decaffeinated coffee consumption (never, 1-4X/month, 1-4X/week, 5X/week, ≥1X/day) (from FFQ)	Association study	598 volunteers from the SKIPOGH cohort	HPLC-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Caffeine • Paraxanthine • Theophylline 	(212)
Coffee	Instant coffee	3.4 g in 200 mL water	Acute intervention	11 healthy volunteers	HPLC-PDA-MS (Targeted)	Urine	<ul style="list-style-type: none"> • Caffeic acid-3-O-sulfate • Caffeic acid-3-O-sulfate • Ferulic acid-4-O-sulfate • Isoferulic acid-3-O-glucuronide • Isoferulic acid-3-O-sulfate • Dihydrocaffeic acid-3-O-glucuronide • Dihydrocaffeic acid-3-O-sulfate • Dihydroferulic acid • Dihydroferulic acid-4-O-glucuronide • Dihydroferulic acid-4-O-sulfate 	(213)
Coffee	Coffee enema vs. ready-to-drink coffee beverage	500 mL (coffee enema); 180 mL (RTD coffee)	Acute crossover	11 healthy men	HPLC-UV (Targeted)	Plasma	<ul style="list-style-type: none"> • Caffeine 	(214)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Coffee	Decaffeinated coffee with high chlorogenic acids vs. medium vs. low	Coffee dose not reported; 4525, 2219, and 1052 umol chlorogenic acids in high, medium, and low doses, respectively	Acute, randomized, double-blind, crossover	5 healthy womn	HPLC-DAD-ESI-MS, ESI-MS/MS (Targeted)	Plasma, ileal effluent, urine	<ul style="list-style-type: none"> Chlorogenic acid metabolites (caffeoylquinic acids, feruloylquinic acids, caffeic acids, dihydrocaffeic acids, ferulic acids, isoferulic acids, dihydroferulic acids) 	(215)
Coffee	Instant coffee	400 mL (1% w/v)	Acute intervention	10 healthy volunteers	LC-MS (Targeted)	Plasma	<ul style="list-style-type: none"> Caffeic acid Dihydrocaffeic acid Ferulic acid Isoferulic acid Dihydroferulic acid Dimethoxycinnamic acid Dimethoxydihydrocinnamic acid 	(216)
Coffee	Coffee	2 cups	Acute intervention	14 healthy volunteers	2D-HR-GC-MS (Targeted)	Urine	<ul style="list-style-type: none"> 4-Ethylguaiaicol 4-Vinylguaiaicol (E)-Beta-damascenone Dimethyl trisulfide Furfuryl alcohol Guaiaicol Indole Methional Oct-1-en-3-one Skatole Vanillin 	(217)
Coffee	Mocha coffee vs. caffeinated soft drink vs. low-dose caffeine in aqueous solution vs. high-dose caffeine in aqueous solution	190 mL (soft drink), 50 mL (mocha), 70 mL (aqueous solution)	Acute, randomized, crossover	4 healthy men	HPLC (detector not specified) (Targeted)	Plasma	<ul style="list-style-type: none"> Caffeine Theophylline Paraxanthine Theobromine 1,3-Dimethylxanthine 1,7-Dimethylxanthine 3,7-Dimethylxanthine 	(218)
Coffee	Coffee (brewed or canned)	150 mL (brewed coffee) or 187 mL (canned coffee)	Acute intervention	10 healthy volunteers	FOX-I method (Targeted)	Urine	<ul style="list-style-type: none"> Hydrogen peroxide 	(219)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Coffee	Instant coffee	2.5 g instant coffee in 200 mL water	Acute intervention	10 healthy volunteers	FOX assay (Targeted)	Urine	<ul style="list-style-type: none"> Hydrogen peroxide 	(220)
Coffee	Instant coffee	2 cups, each with 4 g instant coffee powder in 250 mL water	Acute intervention	5 healthy men	HPLC-UV (Targeted)	Urine	<ul style="list-style-type: none"> Caffeic acid Ferulic acid Isoferulic acid Dihydroferulic acid 3-4-Hydroxy-3-methoxyphenyl-propanoic acid Vanillic acid Hippuric acid 3-Hydroxyhippuric acid 	(221)
Coffee	High roasted coffee vs. low roasted coffee vs. unroasted coffee vs. in vitro hydrolyzed unroasted coffee	3.4 to 4.5 g of instant coffee in 200 mL water	Acute, randomized, double-blind, crossover	12 healthy volunteers	LC-ESI-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> Dihydroferulic acid Caffeic acid-3-O-sulfate Isoferulic-3-O-glucuronide 5-4-Dihydro-m-coumaric acid 	(222)
Coffee	Decaffeinated coffee vs. regular coffee vs. stronger coffee vs. hot water vs. no intervention	17.5 to 25 g of coffee in 300 mL water	Acute, randomized, single-blind, crossover	8 healthy volunteers	HPLC (detector not specified) (Targeted)	Plasma	<ul style="list-style-type: none"> Caffeine 	(223)
Coffee	Coffee	4X7.5 g coffee pads and 500 mL water	Acute intervention	10 healthy volunteers	HPLC-ESI-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> Pyrazine-2-carboxylic acid 5-Hydroxypyrazine-2-carboxylic acid 5-Methylpyrazine-2-carboxylic acid 6-Methylpyrazine-2-carboxylic acid 	(224)
Coffee	Coffee drinkers vs. non-coffee drinkers	350 mL coffee or water	Acute, parallel	6 healthy volunteers	UPLC-HDMS (Untargeted)	Urine	<ul style="list-style-type: none"> Trigonelline N-methylpyridinium Dimethylxanthines Monomethylxanthines 1,3-Dimethyluric acid 1,7-Dimethyluric acid Ferulic acid conjugates 	(225)
	Caffeinated coffee	48 g coffee powder in 900 mL water	Acute intervention	13 healthy volunteers	UPLC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> 5-O-Caffeoyl quinic acid Ferulic acid Iso-ferulic acid Feruloylsulfate Iso-feruloylsulfate 	

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
							<ul style="list-style-type: none"> • Feruloylglucuronide • Feruloylglycine • Dihydroferulic acid • Dihydroferuloylsulfate • Dihydroferuloylglucuronide • Dihydrocaffeoylsulfate (sum of isomers) • Catecholsulfate • Catecholglucuronide • Guaiacolsulfate • Guaiacolglucuronide • Trigonelline • N-methylpyridinium • N-methylnicotinamide • N-methyl-4-pyridone-5-carboxamide • N-methyl-2-pyridone-5-carboxamide • Caffeine • Theophylline • Paraxanthine • Theobromine • 3-Methylxanthine • 7-Methylxanthine • 1,7-Dimethyluric acid 	
Coffee, cocoa	Green tea vs. grape-skin extract vs. cocoa beverage vs. instant coffee vs. grape fruit juice vs. orange juice vs. hot water	4 g (instant coffee), 10 g (cocoa powder) in 200 mL water	Acute, randomized, crossover	9 healthy volunteers	HPLC-ESI-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Chlorogenic acid • Caffeic acid • M-coumaric acid • 4-O-methylgallic acid • Epicatechin • Naringenin • Enterodiol • Enterolactone 	(226)
Coffee, wine	Coffee, chocolate, wine, dark bread, and other conventional foods	Continuous intake of various foods (from 2-day dietary record)	Association study	53 volunteers from the SU.VI.MAX cohort	HPLC-ESI-MS/MS (Targeted)	Urine	<ul style="list-style-type: none"> • Chlorogenic acid • Caffeic acid • Gallic acid • 4-O-methylgallic acid • Enterolactone • Enterodiol 	(227)
Coffee, wine (polyphenol-rich foods)	Citrus fruits, apple and pear, olives, coffee tea, all wine, red wine	Continuous intake of citrus fruits, apple and pear, olives, coffee tea, all	Association study	475 volunteers from the EPIC cohort	U(H)PLC-ESI-MS/MS (Targeted 34 polyphenols)	Urine	<ul style="list-style-type: none"> • Protocatechuic acid, 3,4-dihydroxyphenylpropionic acid, ferulic acid, and caffeic acid highly associated with coffee intake (also: gallic acid, apigenin, quercetin, homovanillic acid, protocatechuic acid, m-coumaric acid, hydroxytyrosol, and daidzein, based on ranked method) 	(228)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
		wine, red wine (from 24-h recalls and dietary questionnaire)					<ul style="list-style-type: none"> Hydroxytyrosol, tyrosol, resveratrol, gallic acid, and gallic acid ethyl ester highly associated with wine/red wine intake (also: homovanillic acid, 3-hydroxybenzoic acid, naringenin, 3,4-dihydroxyphenylpropanoic acid, 3,4-dihydroxyphenylacetic acid, p-coumaric acid, enterolactone, and catechin, based on ranked method) 	
Coffee, wine, cocoa (polyphenol-rich foods)	Coffee, tea, red wine, citrus fruit, apples and pears, and chocolate products	Continuous intake of coffee, tea, red wine, citrus fruit, apples and pears, and chocolate products (from 24-h recall and FFQ)	Association study	481 volunteers from the EPIC cohort	U(H)PLC-QTOF-MS (Targeted)	Urine	<ul style="list-style-type: none"> Dihydroferulic acid sulfate, guaiacol glucuronide, feruloylquinic acid, ferulic acid sulfate, feruloylquinic acid glucuronide, 3-O-caffeoylquinic acid, p-coumaric acid sulfate, caffeic acid sulfate, ferulic acid glucuronide, hydroxyhippuric acid, dihydrocaffeic acid sulfate, m-coumaric acid sulfate, dihydroferulic acid glucuronide, p-hydroxyphenyllactic acid, guaiacol sulfate, ethylcatechol glucuronide associated with coffee intake M-coumaric acid, gallic acid ethyl ester sulfate, hydroxytyrosol sulfate, dihydroresveratrol glucuronide, syringic acid sulfate, methylgallic acid sulfate, 4-O-methylgallic acid associated with red wine intake Methyl(epi)catechin sulfate, 4-hydroxy-(3'4'-dihydroxyphenyl)valeric acid sulfate, dihydroxyphenyl-gamma-valerolactone glucuronide, vanillic acid sulfate associated with chocolate intake 	(229)
Coffee, bread, cheese (general diet)	Wholegrain bread, non-wholegrain bread, lowfat cheese, highfat cheese, regular coffee, decaffeinated coffee, and other (non-fermented) food groups	Continuous intake of 45 different food groups (from FFQ)	Association study	2380 volunteers from the EPIC-Potsdam cohort	FIA-MS/MS (Targeted 127 metabolites, including acylcarnitines, amino acids, diacylphosphatidylcholines, acyl-alkylphosphatidylcholines, lyso-phosphatidylcholines, sphingomyelins, and hexoses)	Serum	<ul style="list-style-type: none"> Amino acids associated with all dairy Hexoses with non-wholegrain bread Acyl-alkyl-phosphatidylcholines and lyso-phosphatidylcholines with high-fat dairy Sphingomyelins with coffee 	(230)
Coffee, wine	Coffee, tea, wine, cereal, fruit, vegetable,	Continuous intake of coffee, tea, wine, cereal, fruit, vegetable, other	Association study	61 volunteers, most with CV risk; 2672	HPLC-UV (Targeted)	Plasma	<ul style="list-style-type: none"> Zeaxanthin Beta-carotene Alpha-carotene 	(231)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
	other food intake	foods (from 7-day weighted diet records); from FFQ		volunteers from the NORKOST 2 cohort				
Coffee, cocoa	Espresso coffee vs. espresso coffee + cocoa-based products containing coffee	3 cups espresso vs. 1 cup espresso + 2 cups cocoa-based products containing coffee	1-month, randomized, crossover	21 healthy volunteers	UHPLC-ESI-MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • Trigonelline (coffee) • N-methylpyridinium (coffee) • N-methylnicotinamide (coffee) • N-methyl-4-pyridone-5-carboxamide (coffee) 	(232)
Vinegar	Vinegar capsules vs. vinegar drink vs. non-carbonated mineral water	9 capsules (750 mg acetic acid); 100 mL vinegar (750 mg acetic acid); 150 mL water	Acute, randomized, controlled, crossover	30 healthy volunteers	GC-2010 (Targeted)	Serum	<ul style="list-style-type: none"> • Acetate 	(233)
Vinegar	Red wine vinegar vs. apple cider vinegar tablet	4 tablespoons/day (3.6 g acetic acid/day); 2 tablets/day (0.045 g acetic acid/day)	8-week, randomized, controlled, parallel	45 healthy volunteers with high waist circumference and at increased risk for metabolic complications	GC-MS, LC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> • Amino valerate • Indole-3-acetic acid • dTMP 	(234)
Sauerkraut	Sauerkraut	5-6 g/kg body weight	Acute intervention	4 volunteers	LC-MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> • D-phenyllactic acid 	(235)
Cider	Thatchers Redstreak apple cider	500 mL	Acute intervention	9 healthy and 5 ileostomy volunteers	HPLC-PDA-MS (Targeted)	Plasma, urine, ileal fluid	<ul style="list-style-type: none"> • Phloretin-2'-glucuronide • Phloretin-O-glucuronide-O-sulfate • Phoretin-O-sulfate 	(236)
Fermented orange juice	Fermented orange juice (fermented using yeast: <i>Pichia kluyveri</i> var. <i>kluyveri</i>) vs. unfermented orange juice	500 mL	Acute, randomized, controlled, crossover	7 healthy volunteers	HPLC-DAD (Targeted)	Plasma	<ul style="list-style-type: none"> • Beta-cryptoxanthin • Lutein 	(237)

Summary of Targeted Studies Presenting Candidate FIBs for Fermented Foods								
Fermented Food	All interventions	Dose	Study Design	n	Analytical Method	Biosample	Candidate FIBs ^a	Reference
Fermented ginseng	Fermented vs. non-fermented ginseng	3 g	Open-label, randomized, single-dose, crossover	24 healthy volunteers	LC-MS/MS (Targeted)	Plasma	<ul style="list-style-type: none"> Ginsenoside metabolite IH-901 (20-O-beta-D-glucopyranosyl-20(S)-protopanaxadiol) 	(238)
Fermented Red Beet Juice	Fermented red beet juice	200 mL/60 kg body weight	6-week, uncontrolled, intervention	24 healthy volunteers	Micro-HPLC-MS/MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Betalain and derivatives (isobetanin, isobetanidin, 17-decarboxy-betanin, 17-decarboxy-isobetanin, 17-decarboxy-neobetanin, neobetanin, 2,17-bidecarboxyneobetanin, 2,15,17-tiidecarboxyneobetanin, 2,17-bidecarboxyneobetanin, 2,15,17-tiidecarboxybetanin, 6'-O-feruloyl-betanin/isobetanin, , 2,15,17-tiidecarboxy-2,3-dehydro-neobetanin) 	(239)
Salgam, boza, kimiz, kefir	Salgam, boza, kimiz, kefir	300 mL	Acute, crossover	12 healthy volunteers	HS-GC-FID (blood ethanol); LC-MS/MS (urine ethyl glucuronide and sulfate) (Targeted)	Whole blood, urine	<ul style="list-style-type: none"> No change in blood alcohol levels or ethanol metabolites in urine 	(240)
Fermented red cabbage	Fermented red cabbage vs. fresh red cabbage	240 g	Acute, randomized, controlled, crossover	13 healthy volunteers	HPLC-MS/MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> Cyanidin derivatives 	(241)
Fermented rooibos tea	Fermented vs. unfermented rooibos tea	500 mL	Acute, randomized, controlled, crossover	10 healthy volunteers	HPLC-MS (Targeted)	Plasma, urine	<ul style="list-style-type: none"> C-linked dihydrochalcone and flavanone glucosides (O-methyl, sulfate, glucuronide metabolites of aspalathin and eriodictyol-O-sulfate) 	(242)
Pu-erh tea	Pu-erh tea	200 mL (containing 10 g of tea powder)	Acute and 2-week, randomized, controlled	20 healthy volunteers	U(H)PLC-QTOF-MS (Targeted)	Urine	<ul style="list-style-type: none"> Inositol Myristic acid 5-Hydroxytryptophan 4-Methoxyphenylacetic acid Pyroglutamic acid 	(243)

Abbreviations: AR, alkenylresorcinol; CE, capillary electrophoresis; CEAD, coulometric electrode array detector; CVD, cardiovascular disease; DHA, docosahexaenoic acid; DAD, diode array detector; DHBA, 3,5-dihydroxybenzoic acid; DHPPA, 3-(3,5-dihydroxyphenyl)-1-propanoic acid; DHPPTA, 5-(3,5-dihydroxyphenyl) pentanoic acid; DHPV, 5-(3,4-dihydroxyphenyl)- γ -valerolactone; EAD, enzyme activity/affinity detector; ECD, electrochemical detector; ELISA, enzyme-linked immunosorbent assay; EPA, eicosapentaenoic acid; ESI, electrospray ionization; FFQ, food frequency questionnaire; FIA, flow injection analysis; FIB, food intake biomarker; FID, flame ionization detector; FLD, fluorescence/fluorometric detector; FOX, ferrous ion oxidation xylenol orange; GC, gas chromatography; GLC, gas-liquid chromatography; HDMS, high definition mass spectrometry; HILIC, hydrophilic interaction liquid chromatography; HPLC, high-performance liquid chromatography; HR, high resolution; HS, headspace; LC, liquid chromatography; LDL, low-density lipoprotein; MHPV, 3'-methoxy-4'-hydroxyphenylvalerolactone; MS, mass spectrometry; MS/MS, tandem mass spectrometry; MUFA, monounsaturated fatty acid; NMR, nuclear magnetic resonance; PC, phosphatidylcholine; PDA, photometric diode array; PUFA, polyunsaturated fatty acid; QTOF, quadrupole time-of-flight; RP, reverse phase; SCFA, short chain fatty acid; SFA, saturated fatty acid; TOF, time-of-flight; U(H)PLC, ultra-high performance liquid chromatography; UV, ultraviolet; VIS, visible.

^a Candidate FIBs that are significantly increased compared to control or baseline in each study are reported.

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