

Supplemental table

Table S1. Dietary polyphenols activate/inhibit liver and intestinal FXR and TGR5

Source of polyphenols	Dose	Model	time	With receptor action form	Metabolic or Functional Effects	Refs
Apple Polyphenol Extract	0.5% of the diet	Male Sprague-Dawley strain rats fed AIN-93G diets containing 0.5% cholesterol	30 days	FXR agonism	CYP8B1, HNF-3 β , HNF-6 \uparrow ; CYP7A1 \downarrow	105
Aspirin eugenolester	27 mg/kg	Male Syrian golden hamsters fed a high-fat diet	12 weeks	FXR inhibition	CYP7A1, CYP8B1, ApoCA, G-BA \uparrow ; IsoLCA, T-BA, LysoPC \downarrow	106
	150 mg/kg	Male C57BL/6 mice fed a high-fat diet	12 weeks	Intestinal FXR inhibition	CYP7A1, PGC-1 α , PPAR α \uparrow ; FGF 15 \downarrow	107
Chlorogenic Acid	20/50/100 mg/kg	Male Wistar rats underwent bile duct ligation (BDL)	3/7 days	FXR inhibition	Bsep, Mrp 2/3/4 \uparrow ; Ntcp, Oatp 1a4, Oatp 1b2, ALT, AST, TBIL, and TBA \downarrow	108
Curcumin	50/100 mg/kg	Male C57BL/6 mice fed a high-fat and high-fructose diet	12 weeks	FXR agonism	SREBP-1c, FAS, LXR α \downarrow ; Nrf2, FXR, SHP, CYP3A, CYP7A1 \uparrow	109
Corn silk extract	100 mg/kg	Male C57BL/6 mice fed a high-fat diet	8 weeks	FXR inhibition	adipocytokines \uparrow ; HMG-CoA, ACAT \downarrow	110

Carob pod (<i>Ceratonia siliqua</i> L.) rich in polyphenols	3% of the diet	Male New Zealand rabbits fed dyslipidemic diet supplemented with 0.5% cholesterol + 14% coconut oil	8 weeks	FXR inhibition	HMG-CoA reductase, CYP7A1, LDL, SIRT1, PGC-1 α \uparrow ; hepatic lipase, glycerol phosphate acyltransferase, SREBP1c \downarrow	111
<i>Canarium album</i> L. ethanol Extract	760 mg/kg	Male Sprague-Dawley adult rats fed a high-fat diet, T2D is induced with STZ	8 weeks	FXR agonism	GLUT2, GK \uparrow ; PEPCK, G6Pase, SREBP-2, HMG-CoAR, SR-B1, CYP7A1, BSEP, MRP3, MRP4, NTCP, LDLR, ABCG8, FXR, SHP, TC, TNF- α \downarrow	112
Diosgenin	150/300 mg/kg	Male Sprague-Dawley rats fed a high-fat diet	12 weeks	FXR agonism	SRB1, CES-1, CYP7A1 \uparrow	113
Ecklonia cava	300 mg/kg	Male C57BL/6 mice fed a high-fat diet	10 weeks	FXR inhibition	CYP7A1, SIRT1 \uparrow ; TNF- α , IL-1 β , MCP-1, SREBP-1c, FAS, FXR, SHP \downarrow	114
Enzymatically modified isoquercitrin	0.1% of the diet	Male C57BL/6 mice fed a high-fat diet	2 weeks	FXR agonism	(PPAR) γ , SREBP1, (C/EBP) α , C/EBP β , sterol regulatory element-binding protein 1 \downarrow ; uncoupling protein (UCP) 2, carnitine palmitoyltransferase-1, sirtuin 1 \uparrow	115

Grape seed flour	10% of the diet	Male C57BL/6J mice fed a high-fat diet	9 weeks	Intestinal FXR inhibition	<i>Lbp, Kcnj8, Wfdc21, Serpine1, Trem2, Trim30a, Nlrp3, VEGFR/MAPK, Mmp19, Angptl4</i> ↓; <i>Adrb3, Sfrp5, Cers3</i> ↑	116
Grape seed procyanidin extract	250 mg/kg	Male C57BL/6 mice	14 hours	FXR agonism	<i>Ppara</i> , phosphorylated protein, <i>Fgf21</i> ↑; HDAC2 and 3 ↓	117
Grape Seed proanthocyanidin	250 mg/kg	Male Wistar rats	5 hours	FXR agonism	SHP, CYP7A1 ↑; TG, FFA, apoB48, apoAII, apoCI, apoCIII ↓	118
Procyanidins	250 mg/kg	FXR-deficient C57BL6 mice	/	FXR agonism	SREBP1 ↓; ApoA5, SHP ↑	119
<i>Inonotus obliquus</i>	100 mg/kg	C57BL/6J mice fed with the MCD diet, containing 0% methionine and 0% choline	7 days	FXR agonism	FXR, SHP ↑; REBP-1c, ACC1, FASN ↓	120
Mirtoselect, an anthocyanin-rich bilberry extract	0.1% of the diet	Female E3L mice were fed a Western-type diet (15% cocoa butter, 1% corn oil, 40.5% sucrose, 20% acid casein, 10% corn starch, and 6.2% cellulose; diet-T; AB-Diets, Woerden, The Netherlands), supplemented with 1% (w/w) cholesterol	20 weeks	FXR agonism	<i>Tnf, Emr1, Ccl2, Mpo, Cxcl1, Cxcl2, NF-κB</i> ↓	121
Olive Leaf Extract	3% of the diet	Male Wistar rats fed a high-carbohydrate, high-fat diet	16 weeks	TGR5 agonism	LDH, AST ↓	122

Olive Leaf Extract	0.1% of the diet	Male C57BL/6J mice fed a high-fat diet	10 weeks	TGR5 agonism	PGC-1 α , Sirt1, brain-derived neurotrophic factor (BDNF), CS activity in the hippocampus \uparrow ; LPO \downarrow	123
Oligonol (from Lychee Fruit)	1000 mg/kg	Wistar rats	3 days	FXR inhibition	CYP7A1 \uparrow	124
Oligomer Procyanidins from Lotus Seedpod	0.05/0.1/0.15g/kg	Sprague Dawley (SD) rats fed a high-fat diet	28 days	FXR agonism	SREBP-1c, FAS, ACC1, PPAR γ , CD36, ApoB, TG \downarrow ; SHP, AMPK \uparrow	125
Peanut skin-derived polyphenols	300 mg/kg	Male Wistar rats fed high-fat and high-cholesterol Western-style diet	10 weeks	FXR agonism	FAS, (SREBP)-1c, ACC1, PPAR γ \downarrow ; PPAR α \uparrow	126
Procyanidins extracted from the litchi pericarp	100 mg/kg	apolipoprotein E knockout mice fed a high-fat diet	24 weeks	FXR agonism	ABCA1, SHP, PPAR- α , LXR- α \uparrow ; HMG-CoA, SREBP-2 \downarrow	127
Resveratrol	0.04/0.08 % of the diet	<i>M. amblycephala</i> juveniles fed a high-carbohydrate diet	12 weeks	<i>Fxrα</i> inhibition in the hindgut, <i>tgr5</i> agonism in the hindgut	T-SOD, CAT, GPX, Cu/Zn-sod, ldlr, Cyp7a1 \uparrow ; hmgcr, acat2, mrp2, oatp1, oatp4 \downarrow	128
<i>Rhizoma Coptidis</i> alkaloids	140 mg/kg	Male B6 mice fed a high-fat high cholesterol diet	35 days	FXR and TGR5 agonism	SREBP2, LDLR, UCP2, CYP7A1 \uparrow ; HMGCR, TXNIP, TLR4, JNK \downarrow	129

Total Flavonoids from <i>Rosa laevigata</i> Michx Fruit	50/100/200 mg/kg	Male C57BL/6 mice fed LPS	7 days	FXR agonism	Nrf2, HO-1, NQO1, GCLC, GCLM, FOXO3a, CPT1 ↑; Keap1, NF-κB, IL(IL)-1β, IL-6, HMGB-1, COX-2, SREBP-1c, ACc1, FASN, SCD1 ↓	130
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