
Pharmacotherapy for dyslipidaemia--current therapies and future agents.

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Current lipid-altering agents that lower low density lipoprotein cholesterol (LDL-C) primarily through increased hepatic LDL receptor activity include statins, bile acid sequestrants/resins and cholesterol absorption inhibitors such as ezetimibe, plant stanols/sterols, polyphenols, as well as nutraceuticals such as oat bran, psyllium and soy proteins; those currently in development include newer statins, phytostanol analogues, squalene synthase inhibitors, bile acid transport inhibitors and SREBP cleavage-activating protein (SCAP) activating ligands. Other current agents that affect lipid metabolism include nicotinic acid (niacin), acipimox, high-dose fish oils, antioxidants and policosanol, whilst those in development include microsomal triglyceride transfer protein (MTP) inhibitors, acylcoenzyme A: cholesterol acyltransferase (ACAT) inhibitors, gemcabene, lifibrol, pantothenic acid analogues, nicotinic acid-receptor agonists, anti-inflammatory agents (such as Lp-PLA(2) antagonists and AGI1067) and functional oils. Current agents that affect nuclear receptors include PPAR-alpha and -gamma agonists, while in development are newer PPAR-alpha, -gamma and -delta agonists, as well as dual PPAR-alpha/gamma and 'pan' PPAR-alpha/gamma/delta agonists. Liver X receptor (LXR), farnesoid X receptor (FXR) and sterol-regulatory element binding protein (SREBP) are also nuclear receptor targets of investigational agents. Agents in development also may affect high density lipoprotein cholesterol (HDL-C) blood levels or flux and include cholesteryl ester transfer protein (CETP) inhibitors (such as torcetrapib), CETP vaccines, various HDL 'therapies' and upregulators of ATP-binding cassette transporter (ABC) A1, lecithin cholesterol acyltransferase (LCAT) and scavenger receptor class B Type 1 (SRB1), as well as synthetic apolipoprotein (Apo)E-related peptides. Fixed-dose combination lipid-altering drugs are currently available such as extended-release niacin/lovastatin, whilst atorvastatin/amiodipine, ezetimibe/simvastatin, atorvastatin/CETP inhibitor, statin/PPAR agonist, extended-release niacin/simvastatin and pravastatin/ aspirin are under development. Finally, current and future lipid-altering drugs may include anti-obesity agents which could favourably affect lipid levels.

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