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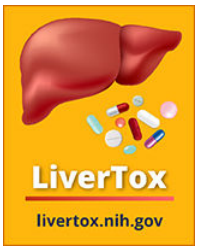


Fibrates

Updated: January 24, 2017.

OVERVIEW

Fibrates are fibric acid derivative agents and are used to lower plasma lipids and particularly triglyceride levels. Chronic therapy with fibrates has been associated with transient mild elevations in serum aminotransferase levels and with rare instances of acute liver injury, which can be severe and evolve into chronic hepatitis, with progressive fibrosis and cirrhosis.

Fibrates are derivatives of fibric acid. Therapy with fibrates in humans leads to a lowering of serum very low density lipoprotein (VLDL) levels leading to decreases in triglyceride and cholesterol levels. Several fibrates have also been found to decrease low density lipoprotein (LDL) and increase high density lipoprotein (HDL) levels, but their effects are, in general, less than what can be achieved with the statins. The fibrates are currently used largely in patients with hypertriglyceridemia and are used in combination with statins to treat hypercholesterolemia.

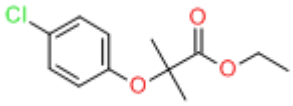
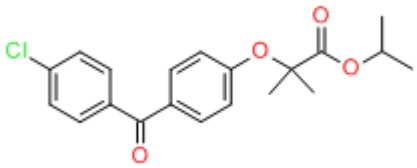
The mechanism by which the fibrates lower lipid levels is unknown, but they may act through interactions with the hepatic peroxisome proliferator activated receptors (PPARs) which regulate gene transcription of enzymes involved in lipid synthesis and secretion. The fibrates bind specifically to a PPAR alpha isozyme, which is found largely in the liver and which regulates fatty acid oxidation, increasing lipoprotein lipase levels which, in turn, enhances clearance of triglyceride rich lipoproteins.

Three fibrates have been used in the United States: Gemfibrozil (Lopid: 1981), Fenofibrate (Lofibra, Tricor, Antara, Lipofen, Triglide: 1993), and Clofibrate (Abitrate, Atromid-S). Clofibrate has been withdrawn from use, largely because of concerns regarding increased risk of cancer and studies showing that, despite its cholesterol lowering activity, clofibrate therapy is not associated with a decrease in cardiovascular mortality. All three of the fibrates are associated with mild-to-moderate serum aminotransferase elevations during therapy that are typically transient, asymptomatic and may resolve even without discontinuation. All three agents have also been linked to cases of clinically apparent acute liver injury, fenofibrate most frequently and convincingly. The frequency and pattern of hepatic injury varies with the different fibrates and they do not appear to share a common pathway or class effect in causing liver injury. For these reasons each fibrate is discussed separately. The acute liver injury from the fibrates can be severe and prolonged and, unlike most forms of drug induced liver injury, can lead to chronic liver disease and cirrhosis.

Drug Class: Antilipemic Agents

Drugs in the Subclass, Fibrates: Clofibrate, Fenofibrate, Gemfibrozil

CHEMICAL FORMULAS AND STRUCTURES

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Clofibrate	637-07-0	C12-H15-Cl-O3	
Fenofibrate	49562-28-9	C20-H21-Cl-O4	
Gemfibrozil	25812-30-0	C15-H22-O3