

Fibrate

In [pharmacology](#), the **fibrates** are a class of [amphipathic carboxylic acids](#). They are used for a range of [metabolic disorders](#), mainly [hypercholesterolemia](#) (high [cholesterol](#)), and are therefore [hypolipidemic agents](#).

Contents

Medical uses

Side effects

Pharmacology

Members

See also

References

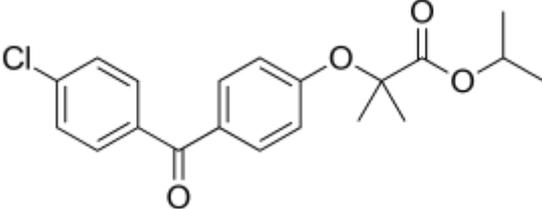
Medical uses

Fibrates are used in accessory therapy in many forms of [hypercholesterolemia](#), usually in combination with [statins](#).^[1]

These stimulate peroxisome proliferator activated receptor (PPAR) alpha, which controls the expression of gene products that mediate the metabolism of TG and HDL. As a result, synthesis of fatty acids, TG and VLDL is reduced, whilst that of lipoprotein lipase, which catabolises TG, is enhanced. In addition, production of Apo A1 and ATP binding cassette A1 is up-regulated, leading to increased reverse cholesterol transport via HDL. Consequently, fibrates reduce TG by up to 50% and increase HDL-C by up to 20%, but LDL-C changes are variable. Fewer large-scale trials have been conducted with fibrates than with statins and the results are less conclusive, but reduced rates of cardiovascular disease have been reported with fibrate therapy in the subgroup of patients with low HDL-C levels and elevated TG (e.g. TG > 2.3 mmol/L (200 mg/dL)). Fibrates are usually well tolerated but share a similar side-effect profile to statins. In addition, they may increase the risk of cholelithiasis and prolong the action of anticoagulants. Accumulating evidence suggests that they may also have a protective effect against diabetic microvascular complications.

Clinical trials do support their use as monotherapy agents. Fibrates reduce the number of non-fatal heart attacks, but do not improve all-cause mortality and are therefore indicated only in those not tolerant to statins.^{[2][3][4]}

Although less effective in lowering [LDL](#) levels, the ability of fibrates to increase HDL and lower triglyceride levels seems to reduce [insulin resistance](#) when the [dyslipidemia](#) is associated with other features of the [metabolic syndrome](#) ([hypertension](#) and [diabetes mellitus type 2](#)).^[5] They are therefore used in many [hyperlipidemias](#). Due to a rare paradoxical decrease in HDL-C seen in some patients on fenofibrate, as per US FDA label change, it is recommended that the HDL-C levels be checked within the first few months

Fibrates	
	<i>Drug class</i>
	
Fenofibrate, one of the most popular fibrates	
Class identifiers	
Use	hypertriglyceridemia and hypercholesterolaemia
ATC code	C10AB
Biological target	PPAR
Clinical data	
WebMD	MedicineNet
External links	
MeSH	D058607
In Wikidata	

after initiation of fibrate therapy. If a severely depressed HDL-C level is detected, fibrate therapy should be withdrawn, and the HDL-C level monitored until it has returned to baseline. [Medwatch \(https://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm342600.htm\)](https://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm342600.htm)

Side effects

Most fibrates can cause mild stomach upset and myopathy (muscle pain with CPK elevations). Fibrates decrease the synthesis of bile acid by down-regulation of cholesterol 7 α -hydroxylase and sterol 27-hydroxylase expression, therefore making it easier for cholesterol to precipitate and increasing the risk for gallstones.

In combination with statin drugs, fibrates cause an increased risk of rhabdomyolysis, idiosyncratic destruction of muscle tissue, leading to kidney failure. The less lipophilic statins are less prone to cause this reaction, and are probably safer when combined with fibrates.

Drug toxicity includes acute kidney injury.^[6]

Pharmacology

Although used clinically since the 1930s,^[7] if not earlier, the mechanism of action of fibrates remained unelucidated until, in the 1990s, it was discovered that fibrates activate PPAR (peroxisome proliferator-activated receptors), especially PPAR α ^[8]. The PPARs are a class of intracellular receptors that modulate carbohydrate and fat metabolism and adipose tissue differentiation.

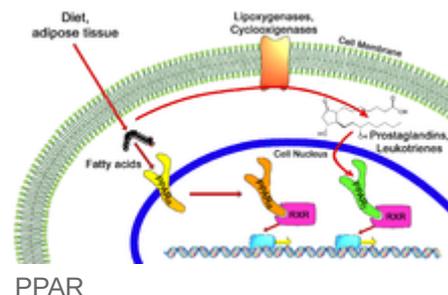
Activating PPARs induces the transcription of a number of genes that facilitate lipid metabolism.

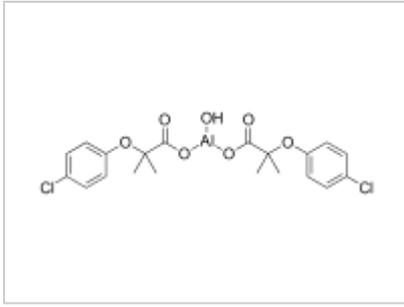
Fibrates are structurally and pharmacologically related to the thiazolidinediones, a novel class of anti-diabetic drugs that also act on PPARs (more specifically PPAR γ)

Fibrates are a substrate of (metabolized by) CYP3A4.^[8]

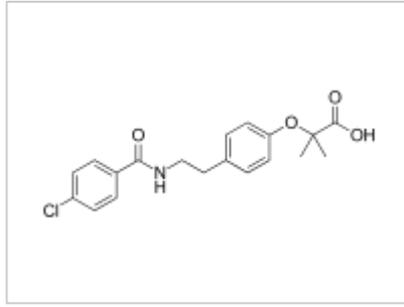
Fibrates have been shown to extend lifespan in the roundworm *C. elegans*.^[9]

Members

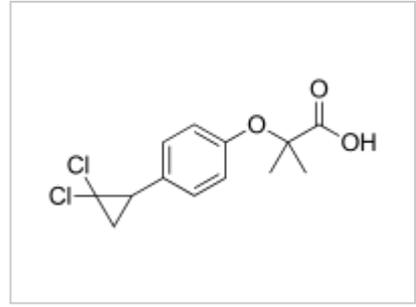




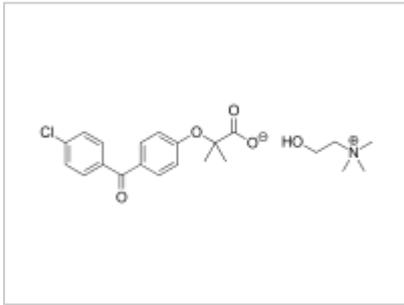
Aluminium clofibrate



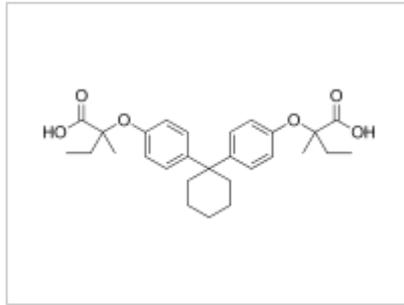
Bezafibrate



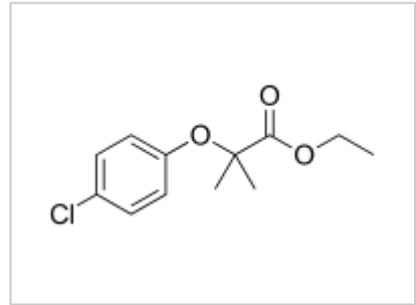
Ciprofibrate



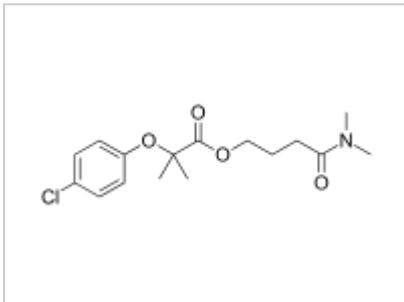
Choline fenofibrate



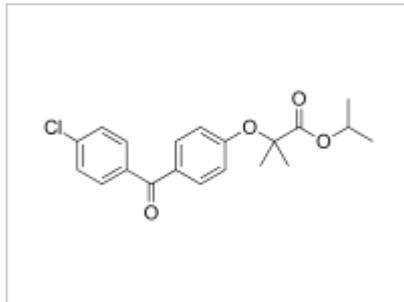
Clinofibrate



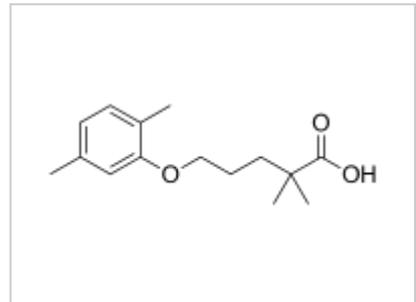
Clofibrate



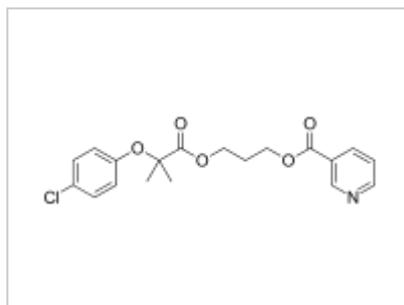
Clofibride



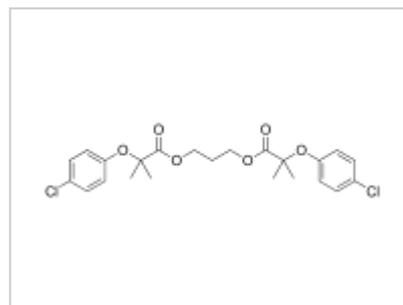
Fenofibrate



Gemfibrozil



Ronifibrate



Simfibrate

See also

- Statin
- Hypertriglyceridemia

References

1. Steiner G (December 2007). "Atherosclerosis in type 2 diabetes: a role for fibrate therapy?". *Diabetes & Vascular Disease Research*. **4** (4): 368–74. doi:10.3132/dvdr.2007.067 (https://doi.org/10.3132%2Fdvdr.2007.067). PMID 18158710 (https://pubmed.ncbi.nlm.nih.gov/18158710).
2. Abourbih S, Filion KB, Joseph L, Schiffrin EL, Rinfret S, Poirier P, et al. (October 2009). "Effect of fibrates on lipid profiles and cardiovascular outcomes: a systematic review". *The American Journal of Medicine*. **122** (10): 962.e1–8. doi:10.1016/j.amjmed.2009.03.030 (https://doi.org/10.1016%2Fj.amjmed.2009.03.030). PMID 19698935 (https://pubmed.ncbi.nlm.nih.gov/19698935).
3. Jun M, Foote C, Lv J, et al. (2010). "Effects of fibrates on cardiovascular outcomes: a systematic review and meta-analysis". *Lancet*. **375** (9729): 1875–1884. doi:10.1016/S0140-6736(10)60656-3 (https://doi.org/10.1016%2FS0140-6736%2810%2960656-3). PMID 20462635 (https://pubmed.ncbi.nlm.nih.gov/20462635).
4. Jakob T, Nordmann AJ, Schandelmaier S, Ferreira-González I, Briel M (November 2016). Cochrane Heart Group (ed.). "Fibrates for primary prevention of cardiovascular disease events" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6464497). *The Cochrane Database of Systematic Reviews*. **11**: CD009753. doi:10.1002/14651858.CD009753.pub2 (https://doi.org/10.1002%2F14651858.CD009753.pub2). PMC 6464497 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6464497). PMID 27849333 (https://pubmed.ncbi.nlm.nih.gov/27849333).
5. Wysocki J, Belowski D, Kalina M, Kochanski L, Okopien B, Kalina Z (April 2004). "Effects of micronized fenofibrate on insulin resistance in patients with metabolic syndrome". *International Journal of Clinical Pharmacology and Therapeutics*. **42** (4): 212–7. doi:10.5414/cpp42212 (https://doi.org/10.5414%2Fcpp42212). PMID 15124979 (https://pubmed.ncbi.nlm.nih.gov/15124979).
6. Zhao YY, Weir MA, Manno M, Cordy P, Gomes T, Hackam DG, et al. (April 2012). "New fibrate use and acute renal outcomes in elderly adults: a population-based study" (https://www.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&tool=sumsearch.org/cite&retmode=ref&cmd=prlinks&id=22508733). *Annals of Internal Medicine*. **156** (8): 560–9. doi:10.7326/0003-4819-156-8-201204170-00003 (https://doi.org/10.7326%2F0003-4819-156-8-201204170-00003). PMID 22508733 (https://pubmed.ncbi.nlm.nih.gov/22508733).
7. "Pharmaceutical composition and method for treatment of digestive disorders - Patent 4976970" (http://www.freepatentsonline.com/4976970.html). Retrieved 2008-12-20.
8. http://www.stacommunications.com/journals/cardiology/2004/June/Pdf/034.pdf
9. "Aging" (http://www.impactaging.com/papers/v5/n4/full/100548.html). *www.impactaging.com*. Retrieved 13 April 2018.

Retrieved from "<https://en.wikipedia.org/w/index.php?title=Fibrate&oldid=935210669>"

This page was last edited on 11 January 2020, at 05:47 (UTC).

Text is available under the [Creative Commons Attribution-ShareAlike License](#); additional terms may apply. By using this site, you agree to the [Terms of Use](#) and [Privacy Policy](#). Wikipedia® is a registered trademark of the [Wikimedia Foundation, Inc.](#), a non-profit organization.