Ursodeoxycholic acid

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Ursodeoxycholic acid (INN, BAN and AAN), also known as **ursodiol** (USAN) and the abbreviation**UDCA**, from the root-word for bear urso, as bear bile contains the substance, is one of the secondary bile acids, which are metabolic byproducts of intestinal bacteria.

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Endogenous effects [edit]

Primary bile acids are produced by the liver and stored in the gall bladder. When secreted into the intestine, primary bile acids can be metabolized into secondary bile acids by intestinal bacteria. Primary and secondary bile acids help the body digest fats. Ursodeoxycholic acid helps regulate cholesterol by reducing the rate at which the intestine absorbs cholesterol molecules while breaking up micelles containing cholesterol. Because of this property, ursodeoxycholic acid is used to treat (cholesterol) gallstones non-surgically. It is also used to relieve itching in pregnancy for some women who suffer obstetric cholestasis.

While some bile acids are known to be colon tumor promoters (e.g. deoxycholic acid), others such as ursodeoxycholic acid are thought to be chemopreventive, perhaps by inducing cellular differentiation and/or cellular senescence in colon epithelial cells.[1]

It is believed to inhibit apoptosis.[2]

Ursodeoxycholic acid has also been shown experimentally to suppress immune response such as immune cell phagocytosis. Prolonged exposure and/or increased quantities of systemic (throughout the body, not just in the digestive system) ursodeoxycholic acid can be toxic.[3]

Medical uses [edit]

An incomplete list of the current uses is as follows:

- Reduction in gallstone formation, either in patients with gallstones unfit for cholecystectomy, or obese patients undergoing rapid weight loss to prevent gallstone formation.[4]
- For the treatment of primary biliary cholangitis(PBC).[5]
- To aim to improve bile flow in patients with cystic fibrosis (controversial[6])
- In newborn infants with impaired bile flow[7]
- After bariatric surgery, to prevent cholelithiasis due to the rapid weight loss with biliary cholesterol oversaturation and also biliary diskinesia secondary to abnormalities in cholecystokinin and biliary enervation. [8]

Meta-analyses have borne out conflicting results on the mortality benefit of UDCA in PBC, however analyses that exclude trials of short duration (i.e. < 2 years) have demonstrated a survival benefit and are generally considered more clinically relevant.[9][*needs update*][10][11]Ursodiol was the only FDA approved drug to treat PBC until 2016.[12]

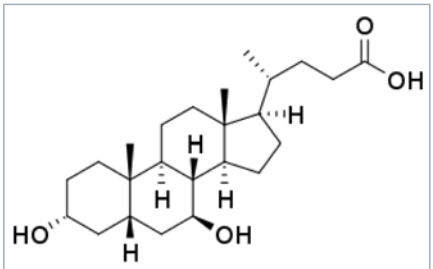
Ursodiol may be used for biliary stasis, [also known as intrahepatic cholestasis of pregnancy, to relieve the symptoms of itching, and to decrease infant mortality rate, which is generally believed to be 10% when Urso is not administered in this fairly rare, and largely undiagnosed pregnancy related disorder. Maternal mortality from hemorrhage is another outcome of the disease, but Urso is not believed to be the preventive cure for this outcome], and to decrease bile absorption.[13]

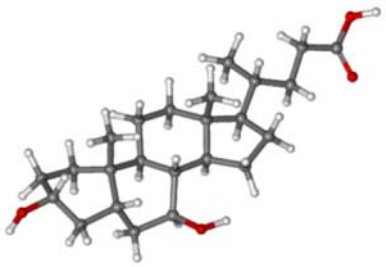
In children, ursodeoxycholic acid use is not licensed, as its safety and effectiveness have not been established. Evidence is accumulating that ursodeoxycholic acid is ineffective and unsafe in neonatal hepatitis and neonatal cholestasis.[14][15][16]

There is insufficient evidence to justify routine use of ursodeoxycholic acid in cystic fibrosis, especially that available data for analysis of long-term outcomes such as death or need for liver transplantation is lacking.[17]

In double the recommended daily dose ursodeoxycholic acid reduces elevated liver enzyme levels in those with primary sclerosing cholangitis, but its use was associated with an increased risk of serious adverse events (the development of cirrhosis, varices, death or liver transplantation) in patients who received ursodeoxycholic acid compared with those who received placebo. Serious adverse events, were more common in the ursodeoxycholic acid group than the placebo group. The risk was 2.1 times greater for death, transplantation, or minimal listing criteria in patients on ursodeoxycholic acid than for those on placebo.[18]

Ursodeoxycholic acid





Clinical data

Trade names	Actigall, Udcasid, others
AHFS/Drugs.com	Monograph
MedlinePlus	a699047
License data	US DailyMed: 19396 US FDA: Ursodiol
Pregnancy category	AU: B3 US: B (No risk in non-human studies)
Routes of administration	oral
ATC code	A05AA02 (WHO)

Legal status

Legal status	AU: S4 (Prescription only) CA: ℞-only UK: POM (Prescription only) US: ℞-only

Identifiers

IUPAC name	[show]
Synonyms	ursodeoxycholic acid, Actigall, Ursosan, Urso, Urso Forte
CAS Number	128-13-2 ✓
PubChem CID	31401
IUPHAR/BPS	7104
DrugBank	DB01586 ✓
ChemSpider	29131 ✓
UNII	724L30Y2QR
KEGG	D00734 ✓
ChEBI	CHEBI:9907 ✓
ChEMBL	CHEMBL1551 ✓
PDB ligand	IU5 (PDBe , RCSB PDB)
ECHA InfoCard	100.004.437

Chemical and physical data

Formula	$C_{24}H_{40}O_4$
Molar mass	392.56 g/mol
3D model (Jmol)	Interactive image
Melting point	203 °C (397 °F)
SMILES	[show]
InChI	[show]

(verify)

It is concluded that ursodeoxycholic acid use is associated with improved serum liver tests that do not always correlate with improved liver disease status. WHO Drug Information advises against its use in primary sclerosing cholangitis in unapproved doses beyond 13–15 mg/kg/day.[19]

Mechanism of action [edit]

The drug reduces cholesterol absorption and is used to dissolve (cholesterol) gallstones in patients who want an alternative to surgery. If the patient stops taking the drug the gallstones tend to recur if the condition that gave rise to their formation does not change.[20][21] For these reasons, it has not supplanted surgical treatment by cholecystectomy.

Also used to relieve itching in intrahepatic cholestasis of pregnancy (naltrexone may also be used).

Trade names [edit]

Ursodeoxycholic acid can be chemically synthesized and is marketed under multiple trade names, including Actigall, Biliver, Coric, Deursil, Egyurso, Udcasid, Udiliv, Udoxyl, Urso, Urso Forte, Ursocol, Ursofalk, Ursosan, Ursoserinox, Udimarin, Ursonova, and Stenerh.

See also [edit]

- Chenodeoxycholic acid—an enantiomer
- Hyodeoxycholic acid—an isomer

References [edit]

1. ^ Akare S, Jean-Louis S, Chen W, Wood DJ, Powell AA, Martinez JD (December 2006). "Ursodeoxycholic acid modulates histone acetylation and induces differentiation and senescence". *International Journal of Cancer. Journal International Du Cancer*. **119** (12): 2958–69. PMID 17019713 . doi:10.1002/ijc.22231 .
2. ^ Amaral JD, Viana RJ, Ramalho RM, Steer CJ, Rodrigues CM (September 2009). "Bile acids: regulation of apoptosis by ursodeoxycholic acid" . *Journal of Lipid Research*. **50** (9): 1721–34. PMC 2724780. PMID 19417220 . doi:10.1194/jlr.R900011-JLR200 .
3. ^ Material Safety Data Sheet on Ursodiol MSDS. https://fscimage.fishersci.com/msds/70916.htm
4. ^ https://www.uptodate.com/contents/ursodeoxycholic-acid-ursodiol-drug-information?source=preview&search=ursodeoxycholic%20acid&anchor=F232620#F232620
5. ^ https://www.uptodate.com/contents/ursodeoxycholic-acid-ursodiol-drug-information?source=preview&search=ursodeoxycholic%20acid&anchor=F232620#F232620
6. ^ https://www.uptodate.com/contents/cystic-fibrosis-hepatobiliary-disease?source=search_result&search=cystic%20fibrosis&selectedTitle=2~150#H106943356
7. ^ https://www.uptodate.com/contents/treatment-of-unconjugated-hyperbilirubinemia-in-term-and-late-preterm-infants?source=see_link#H30
8. ^https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0025733/
9. ^ Gong Y, Huang ZB, Christensen E, Gluud C (2008). Gong Y, ed. "Ursodeoxycholic acid for primary biliary cirrhosis". *Cochrane Database of Systematic Reviews*(3): CD000551. PMID 18677775 . doi:10.1002/14651858.CD000551.pub2 .
10. ^ Shi, Jian; Wu, Cheng; Lin, Yong; Chen, Yue-Xiang; Zhu, Liang; Xie, Wei-fen (2006-07-01). "Long-term effects of mid-dose ursodeoxycholic acid in primary biliary cirrhosis: a meta-analysis of randomized controlled trials" . *The American Journal of Gastroenterology*. **101** (7): 1529–38. ISSN 0002-9270 . PMID 16863557 . doi:10.1111/j.1572-0241.2006.00634.x .
11. ^ "Trials of ursodeoxycholic acid for the treatment of primary biliary cholangitis (primary biliary cirrhosis)" . *www.uptodate.com*. Retrieved 2016-12-27.
12. ^ Jackson H, Solaymani-Dodaran M, Card TR, Aithal GP, Logan R, West J (October 2007). "Influence of ursodeoxycholic acid on the mortality and malignancy associated with primary biliary cirrhosis: a population-based cohort study". *Hepatology*. **46** (4): 1131–37. PMID 17685473 . doi:10.1002/hep.21795 .
13. ^ Mayo Clinic Staff. "Cholestasis of pregnancy: Treatment and Drugs" . Mayo Clinic.
14. ^ Kotb MA (July 2008). "Review of historical cohort: ursodeoxycholic acid in extrahepatic biliary atresia". *Journal of Pediatric Surgery*. **43** (7): 1321–27. PMID 18639689 . doi:10.1016/j.jpedsurg.2007.11.043 .
15. ^ Paediatric Formulary Committee (2008). *British National Formulary for Children 2008*. London: Pharmaceutical Press. p. 91. ISBN 0-85369-780-9.
16. ^ Urso package insert. Birmingham, AL: Axcan Pharma U.S.; 2000 Jan.http://www.axcan.com/pdf/urso_patient_brochure.pdf
17. ^ Cheng K, Ashby D, Smyth RL (Dec 2014). "Ursodeoxycholic acid for cystic fibrosis-related liver disease". *Cochrane Database Syst Rev*. **12**: CD000222. PMID 25501301 . doi:10.1002/14651858.CD000222.pub3 .
18. ^ Lindor KD, Kowdley KV, Luketic VA, et al. (September 2009). "High-dose ursodeoxycholic acid for the treatment of primary sclerosing cholangitis" . *Hepatology*. **50** (3): 808–14. PMC 2758780. PMID 19585548 . doi:10.1002/hep.23082 .
19. ^http://www.who.int/medicines/publications/druginformation/issues/26-1.pdf
20. ^ Public Assessment Report for paediatric studies submitted in accordance with Article 45 of Regulation (EC) No1901/2006, as amended http://www.google.com.eg/search?q=public+MAH+UDCA&hl=en-EG&gbv=2&oq=&gs_l=
21. ^ PUBLIC ASSESSMENT REPORT of the Medicines Evaluation Board in the Netherlands http://mri.medagencies.org/download/NL_H_2516_001_PAR.pdf

External links [edit]

- Ursodeoxycholic acid information at MedlinePlus
- Ursodeoxycholic acid in the British National Formulary

VTE	Bile and liver therapy (A05)
Bile therapy	*bile acid* (Chenodeoxycholic acidCholic acidUrsodeoxycholic acid)Obeticholic acidNicotinyl methylamidePiproz
Liver therapy	Arginine glutamateSilymarinCitioloneEpomediolOrnithine oxoglutarateTidiacic arginineGlycyrrhizin

Categories: Bile acids