

PRODUCT DATA SHEET

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Ambroxol powered by Lipodisq™ Sterile Solution

Nano-formulated aqueous solution: Ready-to-use

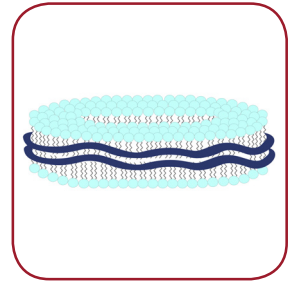
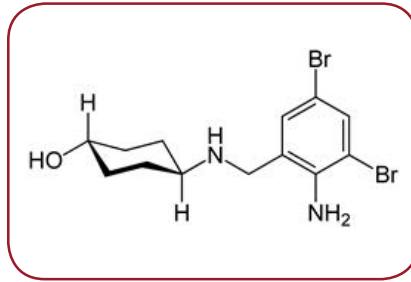
Cat. No.: IAX-700-108

Lot. No.:

Synonyms	Trans-4-[[[(2-amino-3,5-dibromophenyl)methyl]amino]cyclohexan-1-ol hydrochloride] in a detergent-free nano-formulation made of styrene-maleic acid lipid particles (SMALP)
Empirical Formula	C ₁₃ H ₁₈ Br ₂ N ₂ O.HCl
Concentration	1mg/ml (0.1% w/vol)
Size	1ml
MW	414.56 . 36.5
CAS	23828-92-4
Purity	≥ 95% (HPLC)
Solution pH	7.00 - 7.50
Solubility	Soluble in water, PBS, Tris and other physiological solutions as formulated in a proprietary, thermostable, aqueous lipid nanoparticulate formulation (Lipodisq™, Malvern Cosmeceutics Ltd., Malvern UK). Avoid the use of buffers with divalent ions such as Ca or Mg or pH <6.5 or >8.0, which can cause particle instability. Unformulated Ambroxol is soluble in DMF, DMSO or ethanol.
Formulation	Lipodisq™ are nanosized lipid-based discoidal particles that can be manufactured to incorporate hydrophobic, poorly water-soluble compounds, such as lipids, lipoproteins and glycolipids.
Appearance	Colourless clear aqueous solution
Handling	Keep sterile. Avoid skin and eye contact.
Activity	Cell culture tested (human macrophage cell line) (MTT). Recommended starting dilution: 1:200 or higher. Optimal working concentrations depend on the applications and need to be determined. Published procedures using Lipodisq™ formulations (Curcumin and IAXO TLR4 antagonists) <i>in vivo</i> rodent models at 3-10mg/kg. Recommended route of administration is subcutaneous (s.c.) with oral or nasal application as a possible alternative, which needs to be optimised. Carrier only control: Lipodisq™ Control Sterile Solution (Cat. No.: IAX-700-100).
Shipping	Ambient
Storage	2-8°C
Stability	12 months after receipt (unopened and as supplied)
MSDS	Available on request

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General Information

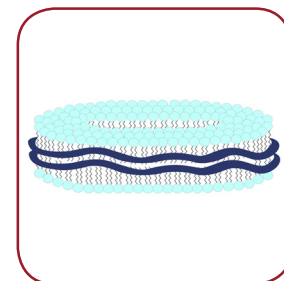
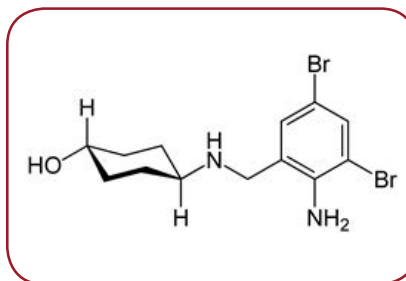
- Ambroxol is a mucolytic agent used in the treatment of respiratory diseases. Ambroxol is a basic (pKa = 9.01) cationic drug with lipophilic properties (logP = 2.9), enabling it to act as a lysosomotropic agent. In addition, ambroxol exhibits a novel mechanism by accumulating in lamellar bodies and acting as a lysosomal secretagogue.
- A wide range of pharmacological effects of ambroxol have been confirmed, including mucus regulation, anti-inflammatory, reduction of arachidonic acid metabolites and pro-inflammatory cytokines, and antioxidant properties. In addition, ambroxol aids in the enhancement of local defence molecules involved in respiratory viral replication.
- Ambroxol is a sodium channel blocker and mucolytic agent with antioxidant, anti-viral and anti-inflammatory properties. Inhibits tetrodotoxin (TTX)-resistant channels more potently than TTX-sensitive subtypes. Inhibits release of histamine, leukotrienes and cytokines from human leukocytes and mast cells. Inhibits viral replication and improves survival rate of mice infected with influenza (H3N2) virus. It is a candidate for use as an anti-COVID19 therapeutic.

Ambroxol References

- [1] *Ambroxol in the 21st century: pharmacological and clinical update.* Malerba M, Ragnoli B. *Expert Opin. Drug. Metab. Toxicol.* (2008); 4:1119 Review
- [2] *Ambroxol as a novel disease-modifying treatment for Parkinson's disease dementia: protocol for a single-centre, randomized, double-blind, placebo-controlled trial.* Silveira, CRA, et al. *BMC Neurol.* (2019); 19:20
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- [4] *Inhibition of acid sphingomyelinase by ambroxol prevents SARS-CoV-2 entry into epithelial cells.* Carpinteiro A, et al. *J. Biol. Chem.* (2021); 296: 100701
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Lipodisq™ Technology

- A nanoparticle (11-40nm) drug delivery system comprising a discoidal phospholipid bilayer membrane stabilised by a chaperone molecule annulus.
- Internal properties of the phospholipid membrane support the disposition and stabilisation of drug molecule candidates and preserve the native conformation of membrane molecules.
- The resulting encapsulated actives are rendered water-soluble and specialised for intra-cellular penetration/delivery via endosomal uptake mechanisms.
- Lipodisq™ solutions show a good safety profile and are suitable for *in vitro* and *in vivo* investigations.
- For a customizable biodegradable Lipodisq™ version with a higher concentration of actives or an alternative lipid option, contact Innaxon.

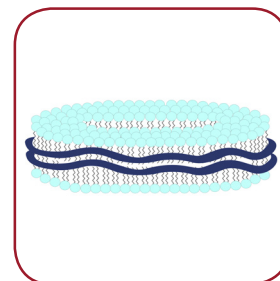
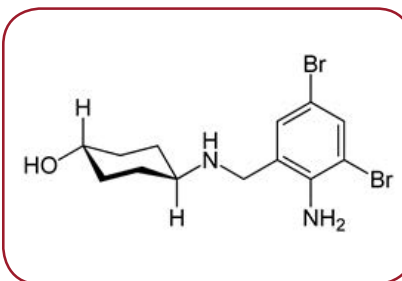
Component	Concentration	CAS #	EC #
Water (sterile)	QS	7732-18-5	231-791-2
Poly(styrene maleic acid)	25mg/ml	26762-29-8	607-996-1
Lecithin	9mg/ml	92128-87-5	295-786-7
Ambroxol hydrochloride	1 mg/ml	23828-92-4	245-899-2

Lipodisq™ References

- [1] *Mechanisms of Formation, Structure, and Dynamics of Lipoprotein Discs Stabilized by Amphiphilic Copolymers: A Comprehensive Review.* Orekhov PS, et al. *Nanomaterials* (2022); 12:361
- [2] *Applications of Synthetic Polymer Discoidal Lipid Nanoparticles to Biomedical Research.* Tanaka M. *Chem. Pharm. Bull.* (2022); 70:507
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- [6] *From polymer chemistry to structural biology: The development of SMA and related amphipathic polymers for membrane protein extraction and solubilization.* Bada Juarez JF, et al. *Chem. Phys. Lipids.* (2019); 221:167
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Lipodisq™ References

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- [11] Advances in the use of nanoscale bilayers to study membrane protein structure and function. Malhotra K and Alder NN. Biotechnol. Genet. Eng. Rev. (2014); 30:79
- [12] DEER EPR measurements for membrane protein structures via bifunctional spin labels and lipodisq nanoparticles. Sahu ID, et al. Biochemistry (2013); 52:6627
- [13] Detergent-free formation and physicochemical characterization of nanosized lipidpolymer complexes: lipodisq. Orwick MC, et al. Angew. Chem. (2012); 51:4653
- [14] Detergent-free incorporation of a seven-transmembrane receptor protein into nanosized bilayer lipodisq particles for functional and biophysical studies. Orwick-Rydmark M, et al. Nano Lett. (2012); 12:4687
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