

PRODUCT DATA SHEET

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Metformin powered by Lipodisq™ Sterile Solution

Nano-formulated aqueous solution: Ready-to-use

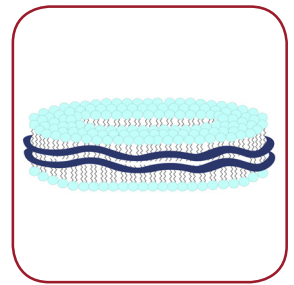
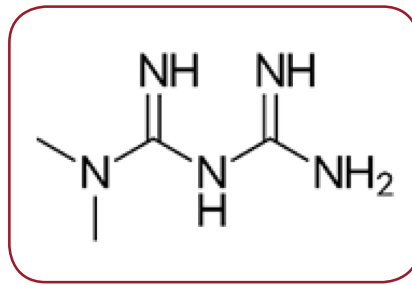
Cat. No.: IAX-700-103

Lot. No.:

Synonyms	Dimethylbiguanide in a detergent-free nano-formulation made of styrene-maleic acid lipid particles (SMALP)
Empirical Formula	C ₄ H ₁₁ N ₅ · HCl
Concentration	1 mg/ml (0.1% w/vol)
Size	1 ml
MW	129.2 · 36.5
CAS	1115-70-4
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 metformin is soluble in water or DMSO.
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

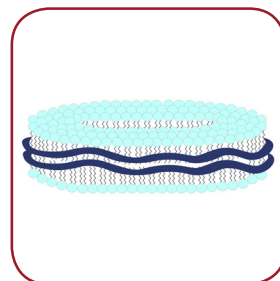
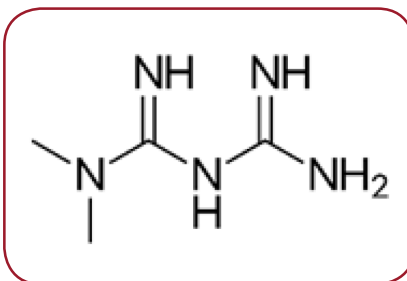
- Metformin is an antihyperglycemic agent of the biguanide class, used for the management of type II diabetes and is currently prescribed to at least 120 million people worldwide.
- AMPK activator
- Mitochondrial electron transport chain complex I inhibitor, reducing mitochondrial reactive oxygen species (ROS).
- Antidiabetic and anti-hyperglycemic agent that reduces blood glucose levels, improves insulin sensitivity, and decreases insulin resistance.
- Insulin sensitizer in non-alcoholic fatty liver disease (NAFLD).
- Increases plasma concentrations of the glucose-lowering gut incretin hormone glucagon-like peptide-1 (GLP-1), which may contribute to metformin's glucose-lowering effect.
- Anticancer agent with antiproliferative and proapoptotic activity in cancer cell lines.
- Autophagy activator
- Targets brown adipose tissue (BAT) in vivo and reduces oxygen consumption.
- Anti-inflammatory agent by inhibition of nuclear factor κB (NF-κB) via AMPK-dependent and independent pathways. Also described to inhibit NLRP3 inflammasome activation, subsequent caspase-1 cleavage and interleukin-1β secretion.
- Since the emergence of SARS-CoV-2, Metformin has been investigated as a prophylactic agent for the prevention of COVID-19.

Metformin References

- [1] *Cellular and molecular mechanisms of metformin: an overview.* Viollet B, et al. Clin. Sci. (2012); 122:253-70
- [2] *Metformin Use Is Associated With Reduced Mortality in a Diverse Population With COVID-19 and Diabetes.* Crouse AB, et al. Front. Endocrinol. (2021); 11:600439
- [3] *Metformin in 2019.* Flory J, Lipska K. JAMA (2019); 321:1926
- [4] *Metformin inhibition of mitochondrial ATP and DNA synthesis abrogates NLRP3 inflammasome activation and pulmonary inflammation.* Flory J, and Lipska K. Immunity (2021); 54:1463
- [5] *Metformin and Covid-19: Focused Review of Mechanisms and Current Literature Suggesting Benefit.* Ibrahim S, et al. JAMA (2019); 321:1926
- [6] *Metformin in Patients With COVID-19: A Systematic Review and Meta-Analysis.* Front. Med. (2021); 8:704666
- [7] *Outpatient metformin use is associated with reduced severity of COVID-19 disease in adults with overweight or obesity.* CT, et al. J. Med. Virol. (2021); 93:4273
- [8] *Metformin inhibition of mitochondrial ATP and DNA synthesis abrogates NLRP3 inflammasome activation and pulmonary inflammation.* Xian H, et al. Immunity (2021); 54:1463
- [9] *Metformin and Covid-19: Focused Review of Mechanisms and Current Literature Suggesting Benefit.* Ibrahim S, et al. Front. Endocrinol. (2021); 12:587801

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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.

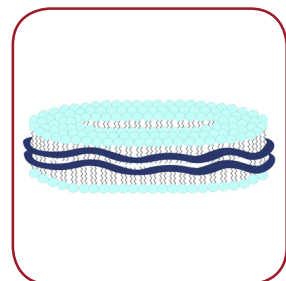
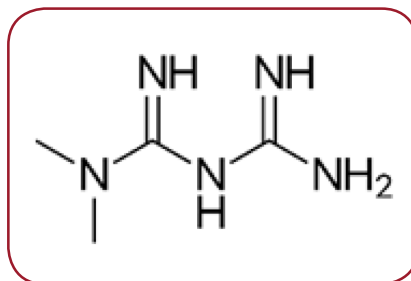
Component	Concentration	CAS #	EC #
Water (sterile)	QS	7732-18-5	231-791-2
Poly(styrene maleic acid)	25mg/ml	26762-29-8	607-996-1
Lecithin	9mg/ml	92128-87-5	295-786-7
Metformin hydrochloride	1 mg/ml	1115-70-4	214-230-6

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
- [3] *Understanding the Structural Pathways for Lipid Nanodisc Formation: How Styrene Maleic Acid Copolymers Induce Membrane Fracture and Disc Formation.* Bjørnstad VA, et al. *Langmuir* (2021); 37:6178
- [4] *Physicochemical Characterization, Toxicity and In Vivo Biodistribution Studies of a Discoidal, Lipid-Based Drug Delivery Vehicle: Lipodisq Nanoparticles Containing Doxorubicin.* Torgersen ML, et al. *J. Biomed. Nanotechnol.* (2020); 16:41
- [5] *Effects of charged lipids on the physicochemical and biological properties of lipid–styrene maleic acid copolymer discoidal particles.* Tanaka M, et al. *Biochim. Biophys. Acta. Biomembr.* (2020); 1862:183209
- [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
- [7] *The styrene–maleic acid copolymer: a versatile tool in membrane research.* Dörr JM, et al. *Eur. Biophys. J.* (2016); 45:3
- [8] *Reconstitution of membrane proteins: a GPCR as an example.* Goddard AD, et al. *Methods Enzymol.* (2015); 556:405

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- [9] Nano-size uni-lamellar lipodisq improved in situ auto-phosphorylation analysis of *E. coli* tyrosine kinase using (19)F nuclear magnetic resonance. Li D, et al. *Protein Cell* (2015); 6:229
- [10] Characterizing the structure of lipodisq nanoparticles for membrane protein spectroscopic studies. Zhang R, et al. *Biochim. Biophys. Acta.* (2015); 1848:329
- [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
- [15] In vitro and in vivo evaluation of tumor targeting styrene-maleic acid copolymer-pirarubicin micelles: survival improvement and inhibition of liver metastases. Daruwalla, J, et al. *Cancer Sci.* (2010); 101:1866
- [16] Poly(styrene-*alt*-maleic anhydride) derivatives as potent anti-HIV microbicide candidates. Fang W, et al. *Bioorg. Med. Chem. Lett.* (2009); 19:1903
- [17] SMA–doxorubicin, a new polymeric micellar drug for effective targeting to solid tumours. Greish K, et al. *J. Control. Release* (2004); 97:219
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