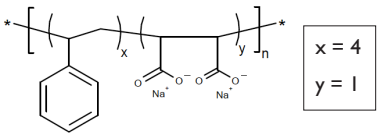
Innaxon
United Kingdom
Email: info@innaxon.com
Website: www.innaxon.co.uk

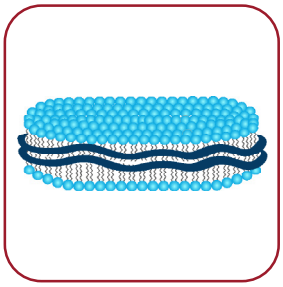
PRODUCT DATA SHEET

Lipodisq™ Styrene:Maleic Acid Copolymer 4:1 [SMA-400]

Cat. No.: IAX-700-204 **Lot. No.:**

Synonyms	Lipodisq™ Styrene:Maleic Anhydride Copolymer 4:1 (pre-hydrolyzed), [SMA-100], P(SMA) 4:1
Empirical Formula	 Poly(Styrene-maleic acid)
Molecular Formula	$C_{36}H_{34}O_4Na_2$
Size	100mg
MW	Polymer MW (average): M_W: 10,500 M_w: MW based on weight M_N: 4,500 M_N: MW based on number
CAS	26762-29-8
Purity	>98%
Solution pH	9.25 +/- 0.25 in 5% ddWater
Solubility	Soluble in water, and buffer solutions (pH 8.50-10.50) to allow the formulation a proprietary, thermostable, aqueous lipid nanoparticle (Lipodisq™, Malvern Cosmeceutics Ltd., Malvern UK). Avoid the use of buffers with divalent ions such as Ca^{++} or Mg^{++} (>2mM) or pH <8.5 or >10.5, which can cause P(SMA precipitation or interfere with SMA-Lipid Particle formulation or stability.
Formulation	Lipodisq™ are nanosized lipid-based discoidal particles that can be manufactured with P(SMA) and lipids such as DMPC (1,2-Dimyristoyl-sn-glycero-3-phosphocholine) (14:0 PC) (DMPC: IAX-700-400) to incorporate hydrophobic, poorly water-soluble active compounds, such as peptides, lipids, lipoproteins, transmembrane proteins and glycolipids. Applications of Lipodisq™ include functional and structural characterisation of the cargo and drug delivery with improved bioavailability, and biological half-life *in vivo* (PD/PK) or delivery of antigens preserved in their native conformation for immunization purposes.
Appearance	White powder
Handling	Keep dry. Avoid skin and eye contact.
Shipping	Ambient
Storage	2-8°C or 15-25°C
Stability	Upon receipt, store product at ambient temperature. Freezing is not recommended. In its unopened original vial, the product is stable for at least 36 months when stored at ambient temperature. Once the glass vial is opened, or solubilized in sterile, endotoxin-free ddWater (IAX-900-902) or for example in pH adjusted, diluted TRIS buffer (IAX-900-011) and aliquoted into sterile vials under sterile conditions, the SMA polymer solution (e.g. at 5%) remains stable for an additional one month when stored at 2-8°C and kept sterile.
MSDS	Available on request

Innaxon
United Kingdom
Email: info@innaxon.com
Website: www.innaxon.co.uk



PRODUCT DATA SHEET

Lipodisq™ Styrene:Maleic Acid Copolymer 4:1 [SMA-400]

Cat. No.: IAX-700-204 **Lot. No.:**

- A nanoparticle (11-40nm) drug delivery system comprising a discoidal phospholipid bilayer membrane stabilised by a chaperone molecular annulus.
- Lipodisq™ polymers are available as 4 defined structures (1:1, 2:1, 3:1 and 4:1 Styrene to Maleic Acid (SMA) rations) each individually operational within a selected pH range for optimal working conditions.
- Components are batch-tested for Lipodisq™ formation using buffer systems available, which are tested for nano-formulated drug analysis by Dynamic Light Scattering (DLS). These buffer solutions are endotoxin-tested and sterile.
- Lipodisq™ formation is highly efficient and nanodiscs show a good safety profile and are suitable for *in vitro* and *in vivo* (in experimental animals) investigations.

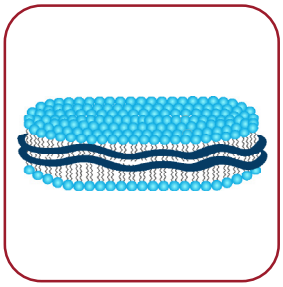
Lipodisq™ Styrene:Maleic Acid Copolymer / P(SMA) System: Introduction

Answering the call for Membrance Protein (MP) and MP reconstituting membrane simulants which do not necessitate the use of mediating detergent, is a copolyer of styrene and maleic anhydride subsequently hydrolysed into amphipathic polystyrene-co-maleic acid (SMA).
Nanodiscs resulting from SMA are also referred to as styrene maleic acid lipid particles (SMALP). SMA-lipid particles areformed by directly extracting membrane proteins either from native cellular membranes (giving native nanodiscs) or from an intermediary MP-reconstituted synthetic membrane system to ultimately form self-assembled nanodisc structures of a general 10–12 nm diameter.
The demonstration of SMA-lipid particles as a monodisperse MP reconstitution system was reported in 2009, although the interaction of SMA with phospholipids to generate disc shaped structures (now known as empty lipid nanodiscs), was previously established and investigated for use as a drug delivery system years preceding this discovery.
At a physiological pH of 7–8, SMA monomer ratios of 2:1 and 3 :1 are most commonly used due to their optimal efficiency for nanodisc extraction from phospholipid bilayers. Abilities of SMA to create monodisperse nanodiscs with size flexibility facilitates the reconstitution of a range of oligomeric MPs and MP complexes for analysis by various studies including fluorescence microscopy, NMR and single-particle cryo-EM. Whereas in a statistical version of SMA, like the commercial Malvern polymer Lipodisq™, monomers are evenly distributed throughout the polymer chain sequence in proportion to their ratio as well as exhibiting greater dispersity in chain length.

Lipodisq™ Procedure Overview

- Published procedures using a ratio of 2:1 (w/w) for P(SMA)/SMA polymer and phospholipid, such as 100mg P(SMA)/SMA polymer and 50mg DMPC. Selected hydrophobic drug candidate or peptides or transmembrane proteins (MP) are mixed with the aqueous phospholipid emulsion making up 2.5%. This is stirred at temperatures above the phase transition temperature of the lipid (>24°C for DMPC), before aqueous P(SMA)/SMA polymer at 5% is added drop-wise and with pauses until a approximate volume ratio of 1:1 is reached and the lipid emulsion clears.
- Alternatively, P(SMA)/SMA polymer solutions are mixed with native (cell or bacterial) membranes to form native nanodiscs.
- Stirring time, pH, selected buffer type and strength (e.g. HEPES, NaCl, TRIS or PBS w/o Ca^{++} and Mg^{++}) and temperature of the phospholipid emulsion containing the MP or active ingredient, need to be optimized.
- Further purification of formed Lipodisq™ can be achieved by ultracentrifugation at >100,000 x g to remove residual lipid, surplus P(SMA)polymer with the Lipodisq™ nanodiscs remaining in the supernatant. Alternatively, size exclusion (SEC) methods can also be applied.

Innaxon
United Kingdom
Email: info@innaxon.com
Website: www.innaxon.co.uk



PRODUCT DATA SHEET

Lipodisq™ Styrene:Maleic Acid Copolymer 4:1 [SMA-400]

Cat. No.: IAX-700-204 **Lot. No.:**

Catalogue	SMA Polymer Type	pH after dissolved in ddWater (5%)	Functional pH Range with Buffer	Moleculr Weight (M_W/M_N)
IAX-700-201	Lipodisq™ Styrene:Maleic Acid Copolymer 1:1 [SMA-100]	4.25 +/- 0.25	3.50 - 5.50	5,500 / 2,100
IAX-700-202	Lipodisq™ Styrene:Maleic Acid Copolymer 2:1 [SMA-200]	7.00 +/- 0.25	5.50 - 8.00	7,500 / 2,700
IAX-700-203	Lipodisq™ Styrene:Maleic Acid Copolymer 3:1 [SMA-300]	7.50 +/- 0.25	6.00 - 9.00	9,500 / 3,050
IAX-700-204	Lipodisq™ Styrene:Maleic Acid Copolymer 4:1 [SMA-400]	9.25 +/- 0.25	8.00 - 10.50	10,500 / 4,500

Lipodisq™ SMA Polymer 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.* Bjørnestad 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

[9] *Mechanistic considerations on styrene – maleic anhydride copolymerization reactions.* Klumperman B, Polym. Chem. (2010); 1:558

[10] *Polymer Nanodiscs and Their Bioanalytical Potential.* Farrelly DM, Martin LL, and Thang SH. Chem. Eur. J. (2021), 27:12922

[11] *Solubilization of lipids and lipid phases by the styrene-maleic acid copolymer.* Hall SCL, et al. Biomacromolecules (2018); 19:761

[12] *Solubilization of lipids and lipid phases by the styrene-maleic acid copolymer.* Pardo JJD, et al. Eur. Biophys. J. (2017); 46:91

[13] *Nanoparticle self-assembly in mixtures of phospholipids with styrene/maleic acid copolymers or fluorinated surfactants.* Vargas C, et al. Nanoscale (2015); 7:20685

[14] *Membrane proteins solubilized intact in lipid containing nanoparticles bounded by styrene maleic acid copolymer.* Knowles TJ, et al. J. Am. Chem. Soc. (2009); 131:7484

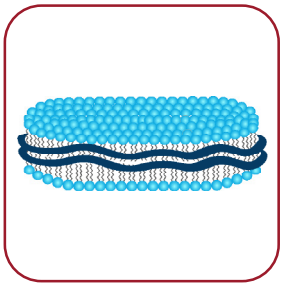
[15] *Responsive hydrophobically associating polymers: a review of structure and properties.* Tonge SR, Tighe BJ, Adv. Drug Delivery Rev. (2001); 53:109

[16] *The effectiveness of styrene-maleic acid (SMA) copolymers for solubilisation of integral membrane proteins from SMA-accessible and SMA-resistant membranes.* Swainsbury DJK, et al. Biochim. Biophys. Acta Biomembr. (2017); 1859:2133

[17] *Detergent-free purification of ABC (ATP-binding-cassette) transporters* Gulati S, et al. Biochem J. (2014); 461:269

[18] *Single-particle cryo-EM studies of transmembrane proteins in SMA copolymer nanodiscs.* Sun C, Gennis RB, Chem. Phys. Lipids (2019); 221:114

Innaxon
United Kingdom
Email: info@innaxon.com
Website: www.innaxon.co.uk



PRODUCT DATA SHEET

Lipodisq™ Styrene:Maleic Acid Copolymer 4:1 [SMA-400]

Cat. No.: IAX-700-204 **Lot. No.:**

Related Powered by Lipodisq™ Products for Nano-formulated Drug Delivery

IAX-700-100	Lipodisq™ Control Sterile Solution
IAX-700-101	Curcumin Lipodisq™ Sterile Solution
IAX-700-102	Melatonin Lipodisq™ Sterile Solution
IAX-700-103	Metformin Lipodisq™ Sterile Solution
IAX-700-104	Oxyresveratrol Lipodisq™ Sterile Solution
IAX-700-105	Resveratrol Lipodisq™ Sterile Solution
IAX-700-106	Umifenovir Lipodisq™ Sterile Solution
IAX-700-107	Dexamethasone Lipodisq™ Sterile Solution
IAX-700-108	Ambroxol Lipodisq™ Sterile Solution
IAX-700-109	Retinoic Acid Lipodisq™ Sterile Solution
IAX-700-201	Lipodisq™ Styrene:Maleic Acid Copolymer 1:1 [SMA-100]
IAX-700-202	Lipodisq™ Styrene:Maleic Acid Copolymer 2:1 [SMA-200]
IAX-700-203	Lipodisq™ Styrene:Maleic Acid Copolymer 3:1 [SMA-300]
IAX-700-204	Lipodisq™ Styrene:Maleic Acid Copolymer 4:1 [SMA-400]
IAX-700-400	DMPC (1,2-Dimyristoyl-sn-glycero-3-phosphocholine) (14:0 PC)

Endotoxin-free and Sterile Buffers and Related Products

IAX-900-001	PBS Endotoxin-free (sterile)
IAX-900-001DC	PBS Endotoxin-free (sterile) [For Nano-formulated Drug Analysis]
IAX-900-002	ddWater Endotoxin-free (sterile)
IAX-900-002DC	ddWater Endotoxin-free (sterile) [For Nano-formulated Drug Analysis]
IAX-900-003	Physiological Saline [Sodium Chloride 0.9% Endotoxin-free] (sterile)
IAX-900-003DC	Physiological Saline [Sodium Chloride 0.9% Endotoxin-free] (sterile) [For Nano-formulated Drug Analysis]
IAX-900-004	PBS with EDTA Endotoxin-free (sterile)
IAX-900-005	TRIS with EDTA [TE Buffer] (100x) Endotoxin-free (sterile)
IAX-900-006	EDTA (400mM) Endotoxin-free (sterile)
IAX-900-007	HEPES Buffer (500mM) Endotoxin-free (sterile)
IAX-900-008	DNA Loading Buffer with TRIS and EDTA (6x) (Blue)
IAX-900-009	HEPES Buffer (50mM) with NaCl [Sodium Chloride] (150mM) Endotoxin-free (sterile)
IAX-900-010	NaCl [Sodium Chloride] (1.5M) Endotoxin-free (sterile)
IAX-900-011	TRIS Buffer (1.5M) Endotoxin-free (sterile)
IAX-900-012	TRIS Buffer (30mM) with NaCl [Sodium Chloride] (150mM) Endotoxin-free (sterile)
IAX-900-013	PBS with Magnesium and Calcium Endotoxin-free (sterile)
IAX-900-014	ddWater with 0.9% Benzyl Alcohol [Bacteriostatic Water] Endotoxin-free (sterile)