IOI OLEOCHEMICAL

PHARMA

LIPIDS FOR SOLID DOSAGE FORMS

IOI Oleo GmbH

YOUR FORMULATION CHALLENGES – OUR SOLUTIONS

According to the Biopharmaceutical Classification System (BCS), more than 70% of the APIs used in pharmaceutical preparations are difficult to formulate due to poor solubility and/or permeabilities, and the majority of drug candidates have similar characteristics. Formulating these APIs into stable forms and achieving satisfactory active delivery and dissolution profiles is a key challenge for galenic scientists.

IOI Oleo PHARMA offers a variety of vegetable-derived mono-, di- and triglycerides for a wide range of dosage forms such as tablets, capsules, granules or powders.

The lipid nature of our products gives them an inherent compatibility towards these problematic API categories and can help to solve the galenic formulation hurdles. Most of our excipients are multifunctional and suitable for various drug delivery systems. Excipient dosing allows to accentuate specific functionalities of the excipient in the finished form.

Technologies and techniques such as SEDDS, SMEDDS, SNEDDS, SLN, Hot Melt Coating (taste masking), Hot Melt Extrusion or Hot Melt Granulation can be applied to enable delivery or enhance the dissolution profile of poorly soluble drugs.

PRODUCT	CHEMICAL DESCRIPTION	MONO-GRAPH	MELTING POINT °C	APPLICATIONS
DYNASAN® 114	Trimyristin	–	55 - 60	Lubricants for tablets & capsules Lipophilic matrices for fat-soluble actives Taste masking[1) 2) 3) 4) 5) 6) 7)] Release profile modification in oral solid dosage matrices and implants Body imparting & structure forming in semi-solids Crystallization accelerators and seeding agents in sticks, ovules & suppositories Matrix component for SLN[1), 2) 4), 5)]
DYNASAN® 116	Tripalmitin	–	63 - 68	
DYNASAN® 118	Glyceryl Tristearate	USP-NF	69 – 73	
IMWITOR® 900 (F) P, IMWITOR® 900 K	Glycerol Monostearate 40–55% Type I & II	Ph. Eur. USP-NF	54 - 64	Solid partial glycerides with surface-active properties Lipophilic matrices for oral solid dosage forms Granulation, Hot Melt Techniques Tablet lubricant Matrix component for SLN[6)] Emulsion stabilizer Dispersing agent for pigments
WITEPSOL® E 85	Hard Fat	Ph. Eur. USP-NF	42 - 44	Lipophilic matrix for use in bio-degradable subcutaneous implants[8)]
SOFTISAN® 154	Hydrogenated Palm Oil	–	53 - 58	Lipophilic matrix for SLN for controlled drug release[9)]

[1)] Lubricating properties of triacylglycerols related to the release of medicaments: M. Vitkova; M. Chalabala; J. Rak, Faculty of Pharmacy, 832-32, Bratislava, Czecho-Slovakia.

[2)] Taste masked lipid pellets with enhanced release of hydrophobic active ingredient: Vaassen, Jonathan; Bartscher, Kathrin; Breitkreutz, Joerg, International Journal of Pharmaceutics (Amsterdam, Netherlands) (2012), 429(1-2), 99-103.

[3)] Paclitaxels-containing nanometer liposome for injection and the preparation method thereof: Li, Shubin; Liu, Dan; Song, Jian; Bao, Jie; Ning, Hong; Li, Minghui; Guo, Zhifu; Wang, Hong; Yu, Na; Li, Lei, Faming Zhuanli Shenqing Gongkai Shuomingshu (2009), CN 101366697 A 20090218.

[4)] Active ingredient matrix dosage forms: Francas, Gernot; Przyklenk, Karl-Heinz, Ger. Offen. (2012), DE 102011051304 A1 20121227.

[5)] Optimization of 5-Fluorouracil solid lipid nano-particles: a preliminary study to treat colon cancer: Yassin, Alaa Eldeen B.; Khalid Anwer, Md.; Mowafy, Hammam A.; El-Ba- gory, Ibrahim M.; Bayomi, Mohsen A.; Alsarra, Ibrahim A., International Journal of Medical Sciences (2010), 7(6), 398-408.

[6)] New approaches in nanoparticulate drug delivery system - a review: Rakesh Bagul; Vjay Mahajan; Avinash Dhake, International Journal of Current Pharmaceutical Research, Vol 4, Issue 3 (2012).

[7)] Development of biodegradable implants for extended delivery of proteins, Inaugural Dissertation, Luisa Fernanda Duque Zapata, Freie Universität Berlin

[8)] Extruded depot form for sustained release of active ingredient, patent DE102017106216A1, 2017, Alexandra Partenhauser, AMW GmbH

[9)] Process, Optimization, and Characterization of Budesonide Loaded Nanostructured Lipid Carriers for the Treatment of Inflammatory Bowel Disease, Gurpreet Kaur Sinhmar et al., 2005

Application Survey of Solid Dosage Forms

PRODUCT	Lubricant	Taste Masking	Hot Melt Coating	Hot Melt Extrusion	Hot Melt Granulation	SLN	Implants
DYNASAN® 114	✓			✓		✓	✓
DYNASAN® 116	✓	✓	✓			✓	
DYNASAN® 118	✓	✓	✓	✓	✓	✓	
IMWITOR® 900 (F) P IMWITOR® 900 K	✓					✓	
WITEPSOL® E 85		✓	✓		✓	✓	✓
SOFTISAN® 154		✓	✓	✓	✓	✓	

Identified uses in commercial products and literature

Approved Ingredients:

- Vitamin preparations
- Expectorants (e.g. ACC/ NAC)
- Antiacidics (e.g. Hydrotalcite)
- Antihelmintics (e.g. Moxidectin)
- Non-steroidal anti-inflammatory drugs (e.g. ASA)
- Non-opioid Analgesics (e.g. Paracetamol)

DYNASAN® - VERSATILE EXCIPIENTS FOR SOLID DOSAGE FORMS

The DYNASAN® product range is a family of high-purity monoacid triglycerides.
Their chemical nature, raw materials, manufacturing and purification result in products with advantageous properties and impurity profile.

PRODUCT	CHEMICAL DESCRIPTION	MELTING POINT °C	HYDROXYL VALUE mg KOH/g
DYNASAN® 114	Trimyristin	55 - 60	Max. 10
DYNASAN® 116	Tripalmitin	63 - 68	Max. 10
DYNASAN® 118	Glyceryl Tristearate	69 – 73	Max. 5

* Additional DYNASAN® Triglycerides from mixed or pure fatty acids are technically feasible; please get in touch with us.

The optimized degree of esterification leads to almost no free OH functionality on the backbone of the excipients and removes formulation and stability challenges in tablets, typically encountered with lubricants based on metallic salts of fatty acids[10]:

- Metal salt impurities interacting with APIs
- API interaction with lubricants due to their ionic characteristics
- Microenvironmental pH shift into alkaline milieu, creating a risk of drug hydrolysis
- Initiation of redox cascades degrading APIs
- Metal ion-mediated degradation of APIs
- Ionic excipients and salt counter-ions show reactivity towards amines, which are common functional groups in APIs with metal soaps

Incompatibilities with metallic salts of fatty acids have been reported, e.g. for the following active ingredients: Acetylsalicylic Acid, Captopril, Cephalexin, Clopidogrel Besylate, Erythromycin, Glibenclamide, Glimepiride, Ibuprofen, Indomethacin, Ketoprofen, Norfloxacin, Oxacillin, Penicillin G, Temazepam

IOI Oleo GmbH

Hamburg, Germany | +49 40 28 00 31-0
pharma@ioioleo.de | www.ioioleo.de

DYNASAN® 118

Glyceryl Tristearate / USP-NF

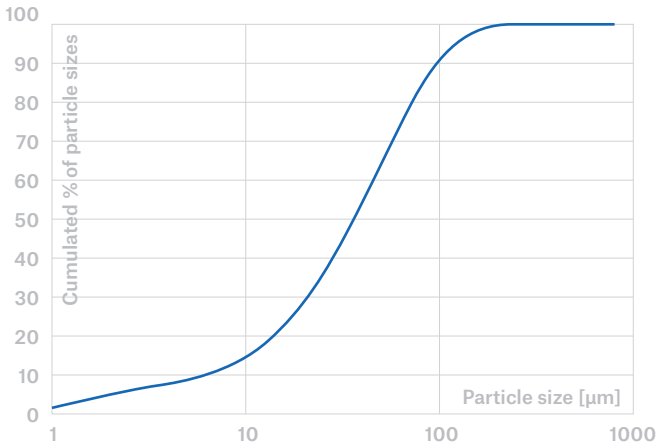
Characteristics

DYNASAN® 118 is a monoacid triglyceride based on C18 fatty acid with a high melting point. It is available as a microfine powder or in flaked form particularly suitable for oral solid dosage forms.

Uses

- Matrix for lipophilic actives
- Coated formulations for protection of sensitive drug molecules (or APIs) or for taste masking
- Solid Lipid Nanoparticles, Self-Emulsifying Drug Delivery Systems
- Processing by hot melt techniques like granulation and extrusion

Particle Size Distribution of DYNASAN® 118 (microfine powder)



Benefits for Tableting[11] [12]

- Effective lubricant for tablet production in low concentrations (~ 0.5%) without the risks of fatty acid soaps
- No influence on drug release up to a concentration of 1%, model drug Acetylsalicylic Acid
- Higher concentrations from 2 to 5% increase the hydrophobic characteristics of tablet matrix and introduce retardation effects into oral dosage forms for sustained release characteristics
- Enhances the tablet fracture stability due to an increased lubricity factor resulting from particle morphology and particle surface

[10] Lubricants in Pharmaceutical Solid Dosage Forms, Jinjiang Li and Yongmei Wu, Lubricants 2014, 2, 21-43

[11] Lubricating properties of triacylgycerols related to the release of medicaments: M. Vitkova; M. Chalabala; J. Rak, Faculty of Pharmacy, 832-32, Bratislava, Czecho-Slovakia

[12] A. Stamm, Sci. Techn. Pharm. 9 (1), 471 – 478 (1980)

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