

White Paper: Refined Sesame Oil IV-1



SIO Presentation

ADM-SIO, is a global manufacturer of injectable-grade pharmaceutical oils - used as API's or excipients for oil-soluble drugs. We offer an extensive range of highly purified oils, derived from vegetable origins that meet all relevant pharmaceutical regulations and are manufactured according to cGMP standards.

The company's injection-grade purified pharmaceutical oils, including refined soybean and olive oils, are currently primarily used as large volume emulsions for parenteral nutrition. ADM-SIO also brings a full portfolio of U.S. Pharmacopoeia (USP) and European Pharmacopoeia (EP) vegetable oils, including sunflower and rapeseed oil, which can be used as excipients in soft gels and capsules, as well as injection-grade purified sesame oil that responds to different formulation needs, such as controlled release. In addition, ADM-SIO offers contract manufacturing capabilities with cGMP production capacity and labs audited by the FDA.

Introduction to Sesame oil (4,5)

Sesame seeds (*Sesamum indicum* L.) have been grown in tropical regions throughout the world since prehistoric times. It has been one of the first crops processed for oil production.

Sesame oil has been used for healing wounds for thousands of years and is mentioned in the Vedas in India as is mentioned in the Vedas in India as ideally suited for the human species.

Nowadays it is used in food, nutraceutical, cosmetic and pharmaceutical industries.

The presence of endogenous antioxidant compounds named lignans comprising sesamin and sesamol contribute to the unique properties of sesame oil, including its noteworthy stability to oxidation.

provide a high quality product. The process enables production of oils with low level of impurities and trans fatty acids, while maintaining the excellent stability of the end product.

Use of Sesame Oil as an excipient in drug formulation

With an increasing number of lipophilic drugs under development, the use of vegetable oils as excipients can be a good mean to address the drug solubilization hurdle.

Sesame oil is commonly used as a solvent, oleaginous vehicle for subcutaneous drugs and intramuscular injections.

Soft gels and capsules formulations:

The development of a solubilized oral formulation in a capsule is normally driven by the desire to either increase or make reproducible the oral bioavailability of a poorly, water-soluble molecule compared to a solid oral dosage format.

For example Dronabinol (9-tetrahydrocannabinol), a natural component of the cannabis plant, used in the treatment of nausea or vomiting associated with cancer chemotherapy, is solubilized by sesame oil in soft gelatin capsules. If solubility and/or oral bioavailability is still not sufficient, the next level of complexity is to add a surfactant (1).

Injectable Formulations (Oil-Based Depot and other Long-Acting Intramuscular (2)):

Vegetable oils can solubilize very lipophilic drugs and are administered by intramuscular injection providing a depot for sustained drug delivery over 2–4 weeks as the oil diffuses within the intramuscular tissues. Sesame oil is commonly used for this kind of applications (1).

Haloperidol decanoate is the long acting, water-insoluble decanoate ester prodrug form of haloperidol, a drug to treat psychotic disorders, which is solubilized in sesame oil and administered intramuscularly. The peak plasma concentrations occur about 6 days after injection and thereafter decline with a half-life of about 3 weeks, thus requiring monthly individualized maintenance doses (1).

Testosterone enanthate, a prodrug of testosterone and used to treat hormone deficiency, is solubilized in sesame oil and is administered intramuscularly approximately every 2 weeks (1).

SIO technology for Sesame Oil IV-1 purification

The refining process used is an advanced purification process, designed to purify and to provide a high quality product. The process enables production of oils with low level of impurities and trans fatty acids, while maintaining the excellent stability of the end product. Production by batches (5600kg) is performed according to GMP requirements.

The last step of process is a fine filtration step on 0.45µm. Drum filling of the end product is performed in a classified ISO 8 cleanroom, fully qualified under conditions preventing oxidation (use of inert gas Nitrogen).

Due to its high purity and quality in addition to its compliance with the GMP requirements, Sesame Oil IV-1 can be used in all parenteral applications.

Sesame Oil IV-1 characteristics

Our refined Sesame Oil IV-1 is a highly refined oil, complying with the European Pharmacopoeia <0433> and USP/NF monograph specifications.

In addition to the monograph specifications, other parameters e.g. contaminants levels are guaranteed, such as:

- Residual solvents: compliance with ICH Q3C and EP 5.4 requirements
- Residues of metal catalysts or metal reagents: compliance with guideline EMEA/CHMP/4446/2000 and EP 5.20 requirements
- Absence of TSE/BSE risk
- Absence of mycotoxins and genotoxic impurities
- Due to our advanced refining process, color of the product is slightly yellow and very clear
- Heavy metals : NMT 10ppm
- Bacterial endotoxins: NMT 1.25 EU/ml

A shelf life of 36 months has been established from stability study data, implemented according to ICH conditions, and can be guaranteed by controlling the oxidation state throughout the process to the final packaging under nitrogen.

SIO GMP Standards :

SIO Refined Sesame Oil IV-1 is manufactured according to the Joint IPEC-PQG Good Manufacturing Practices Guide for pharmaceutical excipients (3).

Good Manufacturing Practices (GMP) are the practices required in order to conform to the guidelines recommended by agencies that control authorization and licensing for manufacture

and sale of excipients, API (Active Pharmaceutical Ingredients) and pharmaceutical products. These guidelines provide minimum requirements that a pharmaceutical manufacturer must meet to assure that the products are of high quality and do not pose any risk to the consumer or public.

The quality of excipients is critical to assure the safety, quality and efficacy of medicines. Excipients have a wide range of applications and are essential components of the drug product formulation. Characteristics that excipients impart to formulated drug products include cosmetic appearance, stability and delivery of the active ingredient. Therefore, applying appropriate GMP principles to excipients is essential.

IPEC-PQG Guide makes an essential contribution to the wider understanding and attainment of GMP's appropriate for the excipient supply industry. Industrials of the Pharmaceutical sector can be assured that excipients manufactured according to this Guide will meet internationally accepted GMP principles.

The manufacture of certain excipients for specialist applications presents additional challenges that are outside of the scope of this Guide. Examples include excipients for parenteral use. To meet those challenges SIO has implemented specific procedures to guarantee that products are pyrogen free and the absence of mycotoxins and genotoxic impurities.

We also truly believe that merging GMP principles for pharmaceutical excipient manufacturing into the ISO 9001 quality management system enhances not only quality management but also an organization's operational procedures.

References:

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