We Provide Healthy Life by
NANOMEDICINE

■ Overview:

Exir Nano Sina Company (ENSC) founded by Prof. Mahmoud R. Jaafari from School of Pharmacy, Mashhad University of Medical Sciences with the support of Iranian Nanotechnology Initiative Council in 2009. ENSC is a knowledge-based nanopharmaceutical company focused on the research, development and commercialization of innovative nanopharmaceutical products based on its proprietary drug delivery technologies. Our strengths lie in lipid-based formulation and scale-up for parenteral, oral and topical drugs using liposomes, micelles and nanoparticles to optimize the pharmacokinetics of drugs for better efficacy and lower toxicity, and thus prolong the product lifecycle of branded drugs.

■ Vision and mission:

ENSC is dedicated to maximizing the benefits of medications for patients and improving their quality of life through constantly advancing our technology & know-how. ENSC strives to become a local and global leading nanopharmaceutical company, to contribute more towards making a difference in the healthcare industry and make Iranian nanotechnology industry visible in the global arena.

■ Research and development:

ENSC is a research-oriented company aiming at the development of high quality pharmaceutical products in the field of innovative finished formulations. ENSC R&D DPT. is also actively involved in a number of research projects in collaboration with Universities and Research Centers across the Iran in order to investigate advanced and pioneering pharmaceutical technologies as well as their application on an industrial scale.

■ Our products mainly include:

- **SinaDoxosome®**
  (Doxorubicin HCl Liposome Injection 2 mg/ml)
- **SinaCurcumin®**
  (Curcumin 40,80 mg Nanomicelle Soft gel)
- **SinaAmphoLeish®**
  (Amphotericin B 0.4% Nanoliposomal Topical Gel)

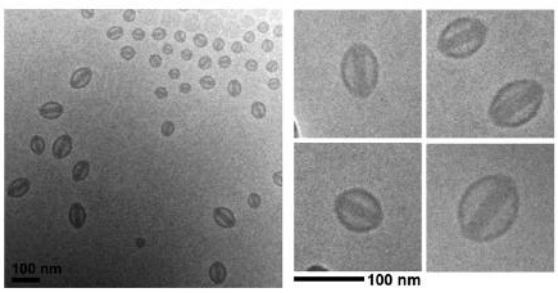
SinaDoxosome®

(Doxorubicin HCl Liposome Injection 2 mg/ml)

Doxorubicin HCl is a drug used in cancer chemotherapy. Doxorubicin is commonly used in the treatment of a wide range of cancers including hematological malignancies, many types of carcinoma, and soft tissue sarcomas. Doxorubicin's most serious adverse effect is life-threatening heart damage, which limits its application. Therefore, various efforts have been made to reduce its side effects, including encapsulating it in nanoparticle systems such as nanoliposomes. The nano-liposomal form of doxorubicin HCl (Caelyx® / Doxil®) which has been produced exclusively by some companies has entered the global market during the past few years by the approval of FDA.

Similar product has been manufactured in Iran under the trademark of SinaDoxosome®. The formulation and physicochemical properties of SinaDoxosome® is exactly equivalent to the foreign-made product.

SinaDoxosome® has been developed in the knowledge-based company of Exir Nano Sina with the support of Iran Nanotechnology Initiative Council. The product is produced in the site of Sobhan Oncology Pharmaceutical Co, Rasht, Iran. SinaDoxosome® has succeeded in obtaining production license from the Iranian Ministry of Health after passing laboratorial and operational phases.



Cryo-TEM of SinaDoxosome

■ Advantages:

- Slow Relese: reduced peak levels of free drug and prolonged tumor exposure
- Change in biodistribution : avoiding drug deposition in certain tissues will reduce tissue-specific toxicities
- Tumor targeting: passive accumulation by enhanced permeability andretention(EPR)effect
- Effectively reduce the side effects of drugs

Unique features of Siandoxosome are as follow :

- The polyethylene glycol coating (stealth polymer) reduces the uptake of liposomes by RES cells , there for increasing the life span of liposome in the blood (half life about 53hr.).
- The particle diameter of approximately 100 nm enables the nano particles to target the tumor tissues by enhanced permeation and retention mechanism.
- The lipid matrix with high phase transition temprature and low permeability provides stable encapsulation of the doxorubicin in nanoliposomes and internal aqueous buffer phase provides high loading efficiency for doxorubicin.

■ Indication:

This nanomedicine is used in the treatment of :

- Ovarian cancer
- Breast cancer
- Multiple myeloma
- Kaposi sarcoma associated with AIDS

SinaCurcumin®

(Curcumin 40,80 mg Nanomicelle Soft gel)

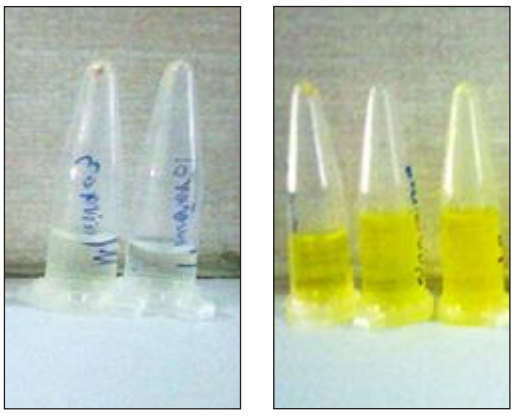
Curcumin, the yellow pigment in curry spice, turmeric, is the principal curcuminoid in the rhizome of Curcuma longa linn.

The size of curcumin nanomicelles is around 10 nm and improve the oral bioavailability of curcumin to more than 100 fold.

More than 98% of curcumin encapsulated in nanomicelles.

Increasing its absorption through the walls of gut and improving its take-up by our body, promising bioavailable herbal drugs and higher blood concentration.

After oral consumption, the soft gels of Sina Curcumin are completely dissolved in the acidic condition of stomach and then nanomicelles are released which are stable up to 6 hours in the acidic conditions of stomach. The nanomicelles are then delivered to intestine and absorbed from there.



(a) (b)

Mice Plasma following oral administration of SinaCurcumin (a) and Curcumin powder (b). It shows using Nano-micellar SinaCurcumin is absorbed completely and cause changing the color of plasma to yellow.

■ Indication:

Main effects included: Anti-inflammatory, antioxidant, Anticancer and immune regulative.

Due to its pleotropic character curcumin is useful in treatment of different disease and disorder:

- **Anti-inflammatory effects including:**

- Bone and Joint inflammation (Rheumatoid Arthritis, Osteoarthritis)
- Gastro-intestinal inflammation (Crohn's disease, Gastritis, Colitis, Irritated Bowel Syndrome)
- Dermatological conditions (Psoriasis, Eczema, Wound healing)
-Buccal Cavity inflammation(Gingivitis, plague)

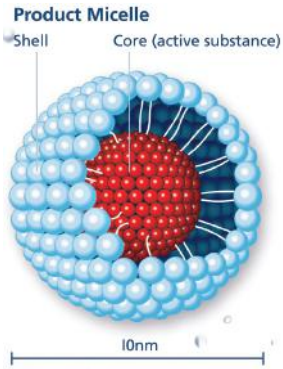
- **Effective supplement in prevention:**

- Different kind of cancers and reducing the adverse effect of chemotherapy and radiation
- Cardiovascular problems such as atherosclerosis
- Neuropathy and Retinopathy in diabetic patient as well as reduction in blood sugar
- Treatment of fatty liver and improvement of liver function
- Amelioration effect on some physiological condition such as premenstrual syndrome

- **Antioxidant effect:**

- Curcumin component exhibit strong antioxidant Activity, comparable to vitamins C and E.

-Indirectly increase glutathione levels there by aiding in hepatic detoxification of mutagens and carcinogens, and inhibiting nitrosamine formation. Its significant effect on reduction of aging is proved by numerous researches.



SinaAmpholeish®

(Amphotericin B 0.4% Nanoliposomal Topical Gel)

Amphotericin B is the most effective drug for the treatment of fungal and protozoan infections such as leishmaniasis.
Amphotericin B acts by binding to the sterol component of a cell membrane, forms pores or channels in sterol-containing membranes, which changes permeability of cell membrane and causes leakage of protons, monovalent cations and other cell constituents leading to cell death. The affinity of Amphotericin B for ergosterol (the primary sterol of fungal and leishmanial membrane) is almost 10-fold higher than cholesterol (the primary sterol of mammalian membrane). Therefore, in the therapeutic doses that Amphotericin B kills fungal and leishmanial microorganism has minimal effects on mammalian cells.
In cutaneous leishmaniasis the leishmania parasites lives and multiply within the phagolysosome of the infected macrophages in the dermal layer of skin. The formidable barrier nature of stratum corneum (SC) of skin does not allow the penetration of drugs like Amphotericin B (a big, amphipathic, water insoluble molecule) in conventional dosage form like ointment and cream. SinaAmpholeish is a very flexible nanoliposomal (100 nm diameter) formulation of Amphotericin B. After topical application some of the nanoliposomal vesicles pass through SC of intact skin and reach epidermis and dermis. In the dermis the infected macrophages phagocyte liposomes, and then encapsulated drug is released in the phagolysosome of the macrophage by acidic lysosomal enzymes where Leishmania parasite lives and multiply. Then Amphotericin B would be in contact of leishmania parasites and kill them very effectively.

■ Indication:

- Treatment of cutaneous leishmaniasis caused by different species of leishmania parasites
- Treatment of recurrent and chronic topical fungal infections including dermatophytes