

**PHYSICAL FORM:****TECHNOLOGY TYPE:****1. What are oily solutions?**

Oily solutions contain poorly water soluble drugs just dissolved in oil. They come under the definition of a Lipid Based Drug Delivery System (LBDDS). Oily solutions are the simplest type of lipid based system. From the number of commercialized products, they are the most common commercial lipid based delivery system.

Using the Pouton lipid formulation classification system, oily solutions fit into Type I formulations.

**2. Which administration route is our Oily Solution technology suitable for?**

These formulations are for oral administration.

**3. Which types of compounds are suited to oily solutions?**

Solubilization in oily solutions is suitable for poorly soluble greasy or lipophilic compounds which have high intrinsic solubility in oils and easily transfer from the oil phase to the GI tract epithelium. It is generally unsuitable for poorly soluble crystalline compounds which require a very high dose.

**4. How do oily solutions increase bioavailability?**

After oral administration, when the oily solution reaches the duodenum, the oil is emulsified by the bile salt/lecithin micelles in the intestinal fluid. No dissolution of the poorly soluble compound is required before absorption because the drug is dissolved in the oil. The solubility of the poorly soluble drug in the oily solution is increased compared to water alone. However, the oil formulations do NOT self-emulsify as such and in most cases drug-release requires prior digestion of the oily solution by enzymes.

**5. Which Phares services use the Oily Solution technology?**

Oily solutions can potentially be used at different stages of development. Although pre-clinically the formulation is easy to prepare, this approach is generally not suitable for *in vitro* evaluations. During Survey, we will assess the suitability of compounds in oily solutions which can facilitate early *in vivo* testing. However, considering the limited and low solubility of most poorly soluble drugs in oils and dependency on the individual dispersing and digesting capabilities of animals, bioavailability results may be variable and unpredictable. Oily solutions are only suitable for use in our Speed tox service and Icebreaker formulation development service if the intrinsic oil solubility of the poorly soluble

compound is sufficiently high. Oily solutions are only suitable for use in our Icebreaker service if the poorly soluble drug is oil soluble and requires only a low dose.

## **6. The advantages and disadvantages of oily solutions**

### **Advantages**

- Relatively easy to manufacture
- Encapsulating oily solutions into hard gelatin capsules (HGCs) or soft gelatin capsules (SGCs) is usually easier than micro or macroemulsion pre-concentrates because compatibility is superior

### **Disadvantages**

- The payload of the insoluble compound in these formulations is mostly limited (below 10 mg/unit dose) because of low solubility of most poorly soluble compounds in the oils
- Degree and reproducibility of oral absorption frequently depends on the dispersion and digestion activity of the gastro intestinal tract
- In common with all solubilized systems, the chemical stability of the poorly soluble drug may be limited compared to formulations where the insoluble drug is in a crystalline state

## **7. Scale-up of an oily solution**

Production of an oily solution is straight forward. Encapsulation in hard or soft gelatin capsules (HGCs or SGCs) requires specific filling equipment.

## **8. Phares oily solution expertise**

We have developed smart *in vitro* systems to identify possible leads rapidly and establish if this type of lipid based delivery system is the most suitable approach to deliver a poorly soluble compound. Optimization is supported by *in vitro* characterization, behaviour in biorelevant intestinal media and precipitation studies in simulated intestinal fluids.

The Phares team has developed and out-licensed a dissolution process for commercial production of high concentrations of a lipophilic compound in an oily solution using flash heating technology.

## **9. Oily solution products**

An example of an oily solution is Calcitrol in fractionated coconut oil triglyceride (Rocaltrol®, Roche) which contains 0.25 and 0.5 micrograms in soft gelatin capsules for the treatment of secondary hyperparathyroidism.

Another oily solution is the antiemetic dronabinol in sesame oil (Marinol®, Solvay Pharmaceuticals) which contains 2.5, 5 and 10 mg in soft gelatine capsules.

**KEY SERVICES:**

