Lipids
Lipids occur in all living matter as one of the main groups of biomolecules together with amino acids, carbohydrates and nucleic acids. They serve several purposes including as energy reserves (fat in adipose tissues) and as structural building blocks (biological membranes).

Lipids have been produced on an industrial scale for a long time from vegetable and animal sources, for example soybeans and milk, primarily for food. The processing chain results in several types and qualities of lipid materials from the food chain. These have always attracted interest from pharmacists as suitable compounds to use in drug and cosmetic formulations.

Lipids in medicine
In the second half of the 20th century specific lipids and lipid fractions started to be used for lipid-based drug delivery. Emulsions of triglycerides stabilized by phospholipids were established as injectable vehicles together with liposomes, spherical bilayer particles of membrane lipids.

Following on from such experiences, the principal area of research for improvement in lipid drug delivery has been lipid-water interactions. Various cream emulsions and liposomal formulations were, and are, being developed for topical drug delivery with the intention of finding lipid particles suitable as carriers for drugs.

As a result of this development, many lipids and lipid fractions have been tested and qualified for use in pharmaceutical products. Today, the toolbox of available lipids is extensive, versatile and well documented.

General structures and properties of lipids
The fundamental properties of lipids are related to their amphiphilic character, which is due to their chemical structures with hydrophobic hydrocarbon chains (fatty acids) combined with hydrophilic ester, hydroxyl or phosphate groups (polar head groups) within the same molecule.

They aggregate in water and accumulate and orient at interfaces to various degrees depending on their individual chemical structures – the lipids are said to be more or less polar. Thus, the degree of aggregation and interaction with water is a measure of lipid polarity.

The lipid orientation at interfaces is determined by the properties of the two phases that form the interface in question. For example, in the interface between water and air, lipids tend to form layers with the fatty chains in the gas phase and the polar head group in the aqueous phase.

Skin lipids
The outer layer of the skin, stratum corneum, consists of corneocytes (dead cells, continuously formed in epidermis) in a lipid matrix (Figure 1). The matrix lipids (mainly ceramides, fatty acids and cholesterol) may also contain lipids produced by the sebaceous glands, such as triglycerides.

The lipids in the matrix turn their polar head groups toward the hydrophilic corneocytes thereby forming a hydrophobic insulation around them in a brick and mortar system (Figure 2). This system forms the barrier to water loss from the body and also limits the penetration of water and foreign substances from the environment into the body.

Treatment of the skin with detergents (such as washing) or solvents may remove lipids from the stratum corneum. On the other hand, applying lipids onto the skin may add lipids to the existing matrix. In both cases the properties of the barrier will change. This is fundamental both to enabling topical drug delivery as well as an understanding of most uses in general skin care products.
**Lipid drug delivery**

The two most often used dosage forms which contain lipids or lipid-like components are ointments and creams. Ointments are semisolids of various compositions. Hydrocarbons, waxes and vegetable oils are common ingredients in the ointment bases. When applied onto the skin a greasy, occlusive layer is formed which gradually interacts with the skin surface. Ointments are generally poor solvents for most drugs.

Creams are generally oil-in-water emulsion systems. They differ compositionally from most ointments and often contain stearic acid, long-chain alcohols or esters combined with triglyceride oils or waxes. Creams form non-occlusive layers on the skin, initially consisting of the particles resulting from the lipid-water interaction in the original emulsion. Drugs can be incorporated in either the water compartment or in the oil compartment of the emulsion and need to be released for delivery.

In ointments and creams the lipid components are stabilized in a hydrophobic base (ointments) or as lipid-water aggregates or particles (creams), which in both cases complicate interaction with the skin surface. In both cases the initial thick layer needs to be rubbed into the skin before the lipids start to become released from the original ointment/cream system.

AKVANO® formulations consist of lipid components which are dissolved in a volatile, water-free solvent mixture. When this formulation is applied onto the skin, the solvent evaporates and a non-occlusive lipid layer is formed in an immediate interaction with the skin surface. This direct deposition of lipids makes the AKVANO principle fundamentally different from other dosage forms.

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**Ointments** = form an occlusive layer on the skin from which the active substance slowly diffuses into the stratum corneum

**Creams** = consist of small droplets from which the active substance has to pass two phase boundaries in order to reach the stratum corneum

**AKVANO®** = instantly forms a thin lipid layer in which the active substance is evenly distributed enabling quicker, direct penetration into the stratum corneum