

Annex A - Discussion paper on novel formulations of supplement compounds designed to increase oral bioavailability

Glossary

In this guide

[In this guide](#)

1. [Contents - Annex A](#)
2. [Background - Annex A](#)
3. [Novel formulations of supplement compounds - Annex A](#)
4. [Lipid-based delivery systems - Annex A](#)
5. [Other systems to increase bioavailability - Annex A](#)
6. [Uncertainties surrounding novel supplement formulations - Annex A](#)
7. [Market data and projected trends - Annex A](#)
8. [Case studies of supplement formulations with increased bioavailability - Annex A](#)
9. [Case study 1: Liposomal vitamin C - Annex A](#)
10. [Case study 2: Curcuminoids - Annex A](#)
11. [Case study 3: Cannabidiol - Annex A](#)
12. [Toxicology studies with novel supplement formulations - Annex A](#)
13. [Summary and discussion - Annex A](#)
14. [Questions for the Committee - Annex A](#)
15. [Abbreviations - Annex A](#)
16. [Glossary - Annex A](#)
17. [References - Annex A](#)
18. [Appendix A: Literature search for specific toxicology studies with novel supplement formulations](#)

Amphipathic – Refers to the property of a molecule containing both polar and nonpolar portions in its structure. The property of amphipathicity allows molecules, such as surfactants, to self-organise to create surfaces and structures that interface (or form a ‘surface’) between aqueous and polar solvents.

Bioaccessibility – the fraction of the total amount of a substance that is potentially available for absorption.

Biotransformation – The transformation of compounds by the body, often catalysed by enzymes. Biotransformation processes tend to produce compounds of higher water solubility, thereby increasing excretion. Biotransformation processes may produce compounds of lower or higher biological activity (detoxification vs. bioactivation, respectively).

Cargo molecules – These are the bioactive molecules formulated in novel ways and that are often encapsulated within nanostructures (e.g., micellar, liposomal, etc). The cargo are the molecules with the desired and/or advertised effect, the active ingredient.

Colloid – A substance containing one phase dispersed as droplets or other structures (e.g., spheres, planes, or cylinders) within another. Colloids are stable and do not settle, and examples include milk, gels, and sols. Emulsions are a specific type of colloid of two immiscible fluids with one fluid dispersed in the other, for instance, oil in water.

Comminution - The reduction of solid materials from one average particle size to a smaller average particle size by physical forces including crushing and grinding. In combination with deagglomeration, which separates clumped/agglomerated particles, comminution contributes to particles size reduction in micronisation techniques.

Intestinal milieu – the physiological conditions prevailing in the GIT including chemical composition, temperature, pH, ionic strength etc. Important modifiers to the milieu include fed state and presence/absence of exogenous lipids which stimulates the release of bile salts and lipases.

Liposomes – Vesicular structures composed of phospholipid bilayers with a similar structure to the cell membrane. Liposomes may contain one (unilamellar) or more (multilamellar) bilayers and may contain intravesicular vesicles.

Log P – The partition coefficient of distribution coefficient of a solute between water and octanol. Log P is calculated as the logarithm of the ratio of the concentrations of a given compound in the two immiscible phases. Molecules with a Log P of zero are equally partitioned between the aqueous and polar phase, those with a positive Log P are preferentially dissolved in the polar phase, and those with a negative Log P are preferentially dissolved in the aqueous phase. Because the value is logarithmic, a Log P of 1 means there is a 10:1 partitioning in the polar compared the aqueous phase.

Micelles – structures formed when an amphipathic substance (e.g., phospholipids) are added to an aqueous solution above a critical concentration known as the ‘critical micelle concentration’. Micelles spontaneously form as spherical structures in which the hydrophilic heads face inward to form the core, and the hydrophobic tails face outward to form the corona of the micelle. In lipid solution reverse micelles can form, in which the tail and head directions are reversed. When lipophilic molecules are added to the solution (e.g., supplement compounds), they associate with the hydrophobic portion of the micelle, to form what are sometimes referred to as ‘swollen micelles.’

Micro/nanoemulsion – a thermodynamically stable (microemulsion) or unstable (nanoemulsion) colloidal mixture of one phase (e.g., oil) dispersed in another (e.g., water), stabilised by an interfacial film of surface-active molecules.

Nanostructured lipid carriers – These are nanosized lipid droplets (20-200 nm) with a lipid core composed of two lipids, one liquid and one solid/crystalline. They may have complex internal structures, including the presence of nano-compartments of liquid lipid. NLCs exhibit reduced phase-transition in the lipid/oil compartment than SLNs and have larger intermolecular spaces. They are designed to increase loading capacity and stability of cargo molecules.

‘Novel’ formulations – formulations of supplements that have been designed specifically to increase the oral bioavailability of the active compound. Such formulations include emulsions, micelles, lipid nanoparticles, and other solubility enhancing systems.

Self-emulsifying (micro/nano) drug delivery system (S(M/N)EDDS) - Mixtures of oils, surfactants, solvents, and drug substance that spontaneously form oil-in-water (micro/nano) emulsions when introduced into aqueous phases under gentle agitation.

Solid lipid nanoparticles – These are nanosized (20-200 nm) lipid droplets dispersed in aqueous media and stabilised by an interfacial film of surface-active molecules. The core of these droplets is composed of partially or fully crystalline lipid, rather than liquid lipids as in emulsion systems.

Unilamellar- Refers to the membrane properties of liposomes. Unilamellar vesicles are bounded by a single bilayer of amphiphilic molecules (e.g., phospholipids, block copolymers). Multilamellar vesicles have several bilayers arranged on concentric rings within the largest vesicle.