Liposovit®-C

Liposomal vitamin C in powder form

HIGH STABILITY & BIOAVAILABILITY
NON-ALLERGENICITY
BROADER SPECTRUM OF APPLICATION

IMMUNITY • REGENERATION AFTER EXERCISE • VITALITY & MENTAL WELLBEING • SKIN HEALTH • PREVENTION OF CVD

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What is **Liposovit®-C**

Liposovit®-C is liposomal vitamin C available in the form of fine, free-flowing, **homogeneous powder**, intended for multi-factorial support of the body in states of increased demand for L-ascorbic acid. Works of the Research & Development Department of BART allowed us to achieve liposomes entrapping L-ascorbic acid (vitamin C) molecules in the aqueous phase. These liposomes have been subjected to drying process, which largely determines the special properties of the product.

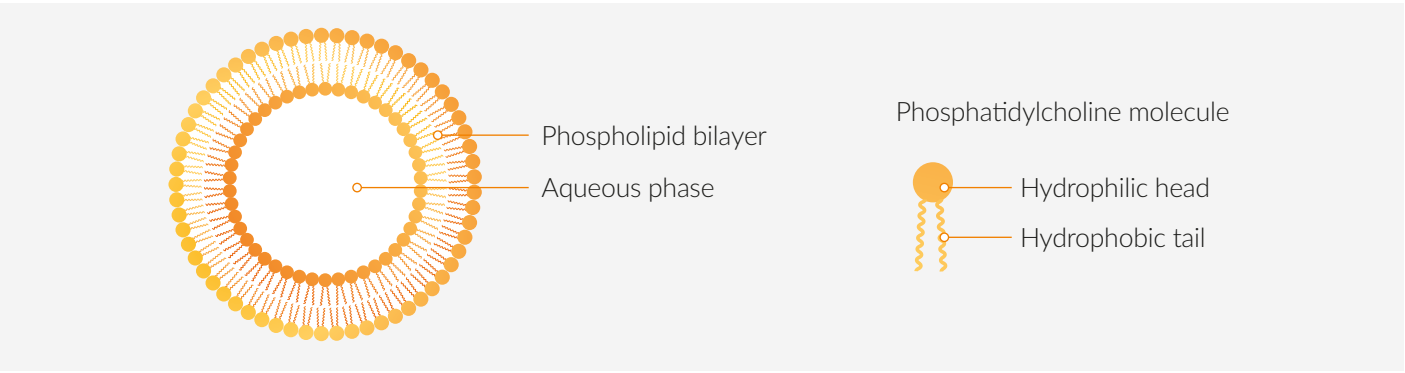

Figure 1. Schematic picture of a liposomal vesicle.

Uniqueness of the **Liposovit®-C** technology

The innovative technological solution applied, entailing i.a. dehydration of acquired liposomes:

- ✓ increases storage stability of **Liposovit®-C**, eliminating the need to ensure cooling conditions during transport and storage
- ✓ eliminates the need to add preservatives, making the product safe for people suffering from widely understood food hypersensitivity
- ✓ allows for complete elimination of alcohol and other organic solvents from both the production process and the final product
- ✓ ensures that the product can be easily encapsulated and applied directly in powder mixtures.

As proven in own research, **the drying process does not impact the quality and size of liposomes (< 300 nm).**

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Properties of **Liposovit®-C**

Liposovit®-C developed by us:

- ✓ protects vitamin C from chemical and enzymatic degradation during storage and during transit through the digestive tract
- ✓ protects gastrointestinal epithelium of the consumer from irritation resulting from taking increased doses of vitamin C
- ✓ as confirmed by the **clinical trial**, in comparison with vitamin C in its conventional form, enables to:
  - obtain a much better absorption of vitamin C into the bloodstream, which is equivalent to its higher bioavailability
  - prolong the presence of increased vitamin C concentration in the blood and, as a result, ensure its longer action
- ✓ enables slow and sustained release of vitamin C from the liposomal vesicle
- ✓ is fully safe, biodegradable and biocompatible.

Why liposomal Vitamin C?

Hydrophilic by nature, vitamin C has poor ability to diffuse through the lipid bilayer of intestinal epithelial cells (1), which limits its bioavailability. Ascorbic acid is unstable, sensitive to temperature, light (2,3) and elevated pH (2), extremely susceptible to oxidation (2,3).

Available literature data indicate that an effective way to increase the stability and bioavailability of vitamin C is nanoencapsulation, especially in lipid carriers. These types of carriers - most commonly used in the pharmaceutical, food and agricultural industries - include liposomes (3).

Liposomes are highly effective in entrapping active substances. They stabilise them (4,5,6) provide protection against degradation caused by i.a. the presence of oxygen, other food ingredients (4), incorrect pH, light or digestive enzymes (6). Liposomes also prevent the active substances from being metabolized prior to reaching target tissues (5). At the same time, encapsulation of nutrients in liposomal vesicles minimizes their side effects (7), such as epithelial irritation, also in the gut. Intake of liposomal vitamin C in supra-optimal daily doses of more than 1-2 g may also significantly reduce the risk of gastrointestinal disorders in sensitive individuals (c.f.: 8,9), including osmotic diarrhoea (10).

Structural similarity of liposomal vesicles to biological membranes facilitates intestinal absorption of active substances, thus increasing their bioavailability and, consequently, their effectiveness. In the case of liposomes, delivery of active substances to the cells takes place in a controlled manner, either by fusion or endocytosis (7). The results of numerous experimental studies, also involving animals and humans, indicate an advantage of liposomal forms of vitamin C over its conventional form (4,11,12). This was also confirmed by own research conducted in BART Ltd. on **Liposovit®-C**. The results thereof are presented below.

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Liposovit®-C own research

In order to confirm an increased bioavailability of **Liposovit®-C**, a randomized, double-blind, crossover, single-dose **clinical trial** was performed (n = 10[1], Bioethics Committee approval number: KB/121/2021). Healthy subjects took 1 g of **Liposovit®-C** (powder in a capsule), and – after a 2-week wash-out period – 1 g of conventional vitamin C (powder in a capsule). The ascorbic acid level (UPLC) was determined in blood samples collected from each subject immediately before the administration of the investigated supplement, and 30 minutes, 1h, 2h, 3h, 4h, 6h, 8h, 10h and 24h after its administration. Pharmacokinetic profiles and parameters obtained for both forms of vitamin C are presented, respectively, in Figure 2 and in Table 1.

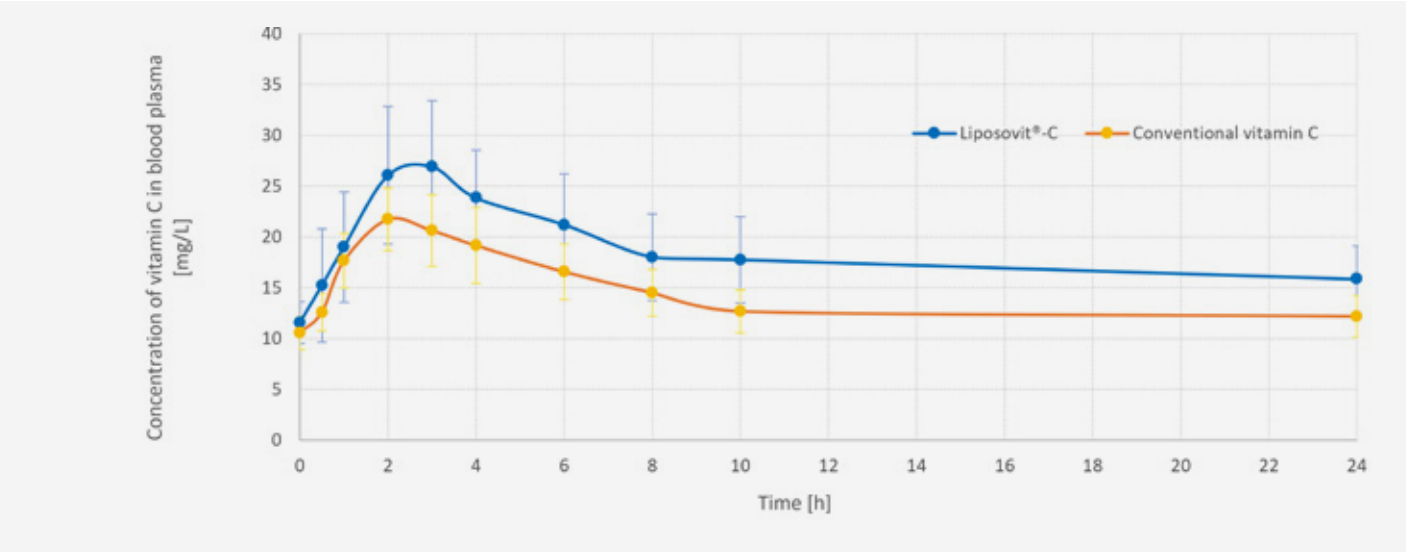

Figure 2. Pharmacokinetic profiles of Liposovit®-C and its non-liposomal equivalent.

Table 1. Pharmacokinetic parameters obtained for a dose of 1 g of investigated vitamin C forms

Specific parameter results represent the mean from the study on 9 participants ± SD.

	Conventional vitamin C	Liposovit®-C
AUC* [mg x h/L]	342.12 ± 45.22	444.95 ± 97.24
T_{max} [h]	2.33 ± 0.71	2.56 ± 0.53
c_{max} [mg/L]	22.52 ± 3.39	27.95 ± 6.46
C_{10h}** [mg/L]	12.68 ± 2.11	17.76 ± 4.24
C_{24h}* [mg/L]	12.18 ± 2.07	15.85 ± 3.26

* p<0.05, **p<0.01; n=9

[1] The results of one subject were rejected because the dietary interview revealed the consumption of vitamin C supplements.

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The results of the clinical trial have shown that in comparison with vitamin C in its conventional form, **Liposovit®-C enables to:**

- obtain a much better absorption of vitamin C into the bloodstream, which is equivalent to its higher bioavailability (AUC increase by 30%, $p<0.05$)
- prolong the presence of increased vitamin C concentration in the blood (C_{24h} higher by 30%, $p<0.05$) and, as a result, its longer action.

As a result, it may translate into achieving an equivalent therapeutic effect at lower doses of the active substance.

Figure 3 presents microscopic images of **Liposovit®-C** powder compared with images of competitive products.

The photos were taken with Leica DM2500LED optical microscope, magnification: 10x and 50x. When compared with competitive products, **Liposovit®-C** powder stands out through its uniform colour and molecule size. Additionally, unlike the solutions offered by competitors, **Liposovit®-C** is free of pure vitamin C crystals.

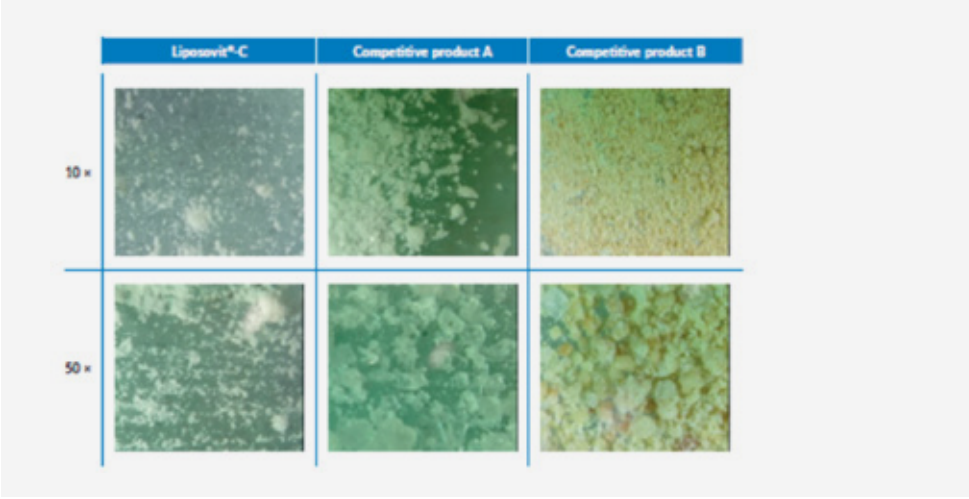

Figure 3. Microscopic photos of Liposovit®-C powder and competitive products.

The surface of **Liposovit®-C** powder was analysed with scanning electron microscopy (SEM).

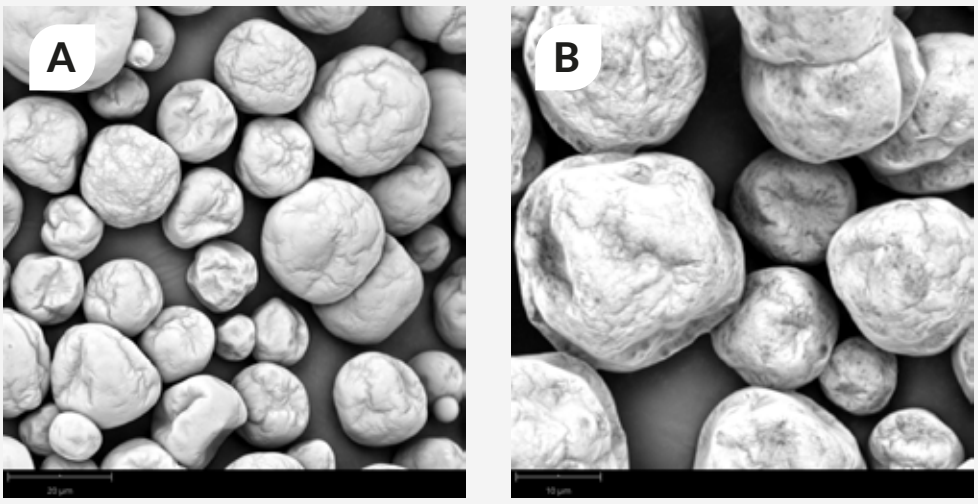

Fig. 4. Liposovit®-C powder particles in images obtained under the scanning electron microscope (Phenom XL, Phenom World BV). A. Magnification of 3000 x, B. Magnification of 4900 x.

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Figure 4 shows that the surface of microcapsules made of a carbohydrate vesicle which encloses liposomal particles remained intact after the drying process. This confirmed the effectiveness of lipid carriers microencapsulation process and the existence of an additional barrier to protect liposome-enclosed L-ascorbic acid against adverse external factors.

Visualizing the particles morphology is an important element in the assessment of liposome physical and chemical properties (13). Cryogenic electron microscopy (cryo-TEM) is the most useful tool to assess their shape and internal structure, including their lamellarity. With this technique you can examine the previously hydrated sample in a state most closest to its native condition (14).

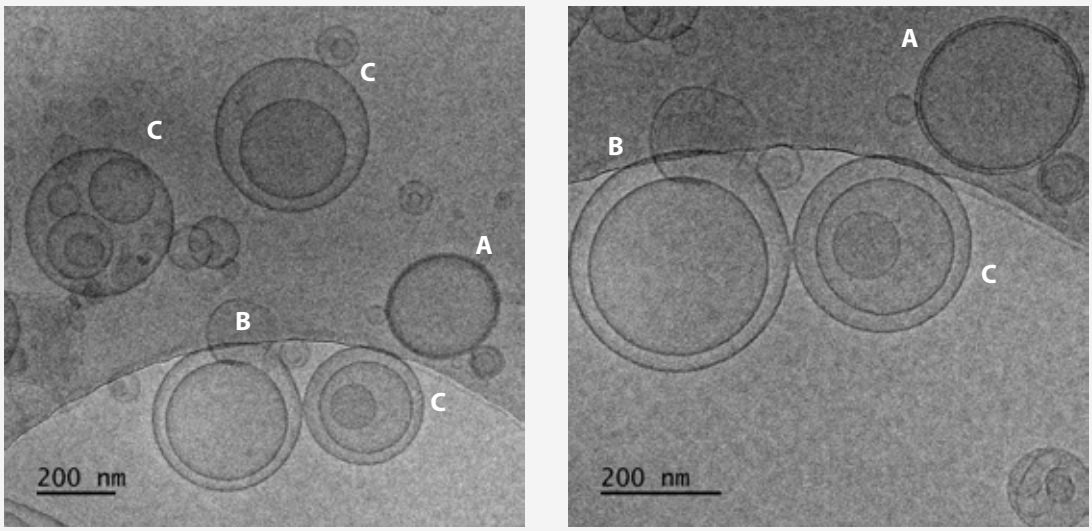

Fig. 5. Morphology of liposomes in Liposovit®-C, in images from the cryogenic electron microscope (Tecnai F20 X TWIN, FEI Company) A) large unilamellar vesicle (LUV), B) oligolamellar vesicle (OLV), C) multivesicular vesicle (MVV).

Figure 5 shows liposomes contained in **Liposovit®-C** powder. This has confirmed the presence of smooth-surfaced spherical vesicles with intact continuous phospholipid bilayer.

Our drying process, intended to transform liposomal vesicles from liquid to powder, has no adverse effect on the quality and size of formed carrier particles. This has been confirmed by a study of liposomes with the LUMiSizer® analyzer. Both the liquid form (obtained during the production process) and the final powder form of **Liposovit®-C** were analyzed. Measurement results are included in Table 2.
For both forms, the size of liposomes did not exceed 300 nm, and was, respectively:

- 267 +/-10 nm for the liquid variant of vitamin C,
- 261 +/-10 nm for the final, powder variant (**Liposovit®-C**).

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Table 2. Results of particle size measurements in the liquid and powder form of Liposovit®-C.

Quantiles	
Liposovit®-C liquid form	**Liposovit®-C powdered form**
10% of distribution ≤ 183.3 nm	10% of distribution ≤ 196.3 nm
16% of distribution ≤ 216.8 nm	16% of distribution ≤ 209.2 nm
50% of distribution (D50) ≤ 266.9 nm	50% of distribution (D50) ≤ 260.6 nm
84% of distribution ≤ 317.9 nm	84% of distribution ≤ 324.6 nm
90% of distribution ≤ 327.5 nm	90% of distribution ≤ 345.9 nm

Our unique technology combined with extremely beneficial properties of **Liposovit®-C** – including enhanced bioavailability and longer action compared to conventional vitamin C, shown in the clinical trial – confirm that it is meaningful to use innovative liposomal technologies in the production of dietary supplements. Undoubtedly, liposomes represent the future of this product segment.

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