

SEPISMART™ SR

Time to release your creativity



SEPPIC

WHAT WILL YOU
DISCOVER
IN THE FOLLOWING PAGES?

-
- Sustained release **opportunities in the food supplements market**
 - A concrete example of application: **vitamin C**
 - What **SEPISMART™ SR** is and the evidence of its **effectiveness**
 - Why you should **start using SEPISMART™ SR**
-



SUSTAINED RELEASE

a way to innovate in a dynamic market

Nutraceutical market

USD 138,9Bn in 2020
and expected to reach
USD 231,9Bn by 2027,
with a CAGR of 7,6%¹

Over the past few years, the importance of **taking care of our health**, and above all of, acting on it in a more preventive way, has been brought to the forefront. This has **positively impacted and boosted the global nutraceutical market**, which will probably continue to grow rapidly in the coming years.

Drivers of the market:



Aging population



Rising awareness



New lifestyles



COVID-19 pandemic

Within this market, despite a trend towards the diversification of galenic formats, **capsules and tablets remain references**². Sustained release solutions helping to reach an optimal performance of these formats are therefore a **way to innovate** in this promising market.

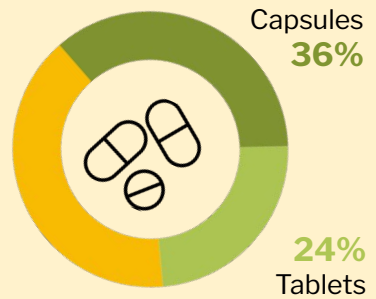


Figure 1. Market shares of the different galenic formats (study across North America and Europe on Vitamins and Dietary Supplements launches between Jan 2019 and Dec 2021)

Focus on vitamin C market

Expected to reach
USD 15,7Bn by 2030,
with a CAGR of 6-7%
(2022-2030)³

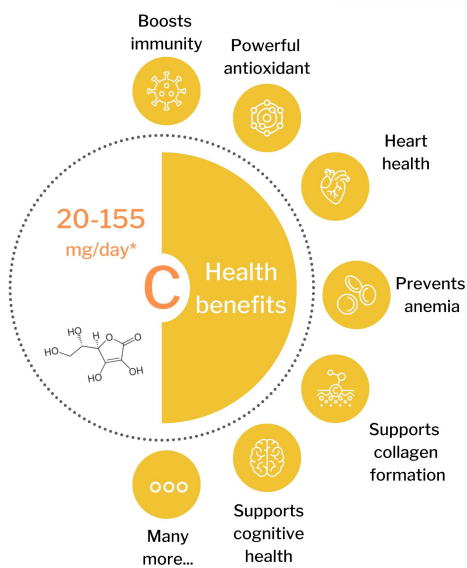


Vitamin C, a key active ingredient that offers a wide range of benefits, has seen **strong growth since the pandemic**.

With its **complex metabolic pathways**, it is a perfect example of active ingredient requiring sustained release solutions to ensure optimal absorption by consumers.

VITAMIN C

a star ingredient



*Population Reference Intake in Europe (from 1 to 18yo and more, pregnancy and lactation included)

Figure 2. Nutritional needs and health benefits of vitamin C
Seppic property

A popular and beneficial vitamin

Vitamins are essential nutrients and participate in maintaining the balance and development of our body. In humans, **vitamin C** also known as **ascorbic acid**, is an essential micronutrient required for an array of biological functions. Although present in some day-to-day foods, vitamin C is now widespread in the growing food supplement market because of its multiple health benefits⁴. As it cannot be accumulated in the organism, and that an average adult dose of **100mg/day** is required, supplements represent a solution to face deficiencies⁵.

The physico-chemical properties of vitamin C

Chemically, ascorbic acid is found in **2 forms**, L-ascorbic acid and D-ascorbic acid but only **L-ascorbic acid**, the natural form, is **biologically active**.

With chemical formula **C₆H₈O₆**, it is a crystallized compound which is found in the form of an **acid-tasting, odorless white powder**.

Vitamin C is a **highly water-soluble compound** which favors its circulation and excretion by the body. It is also a **sensitive** molecule (water, heat, air and light), so it can be easily altered by a multitude of factors and by the natural digestive process.

It is therefore important to take into consideration these different properties when formulating food supplements to ensure **optimal bioavailability** of ascorbic acid⁶.

Table 1. Vitamin C physico-chemical properties

PROPERTIES	
Aspect	White solid
Molecular weight	176,124 g/mol
Water solubility	333 g/L at 20°C

HOW VITAMIN C

interacts with our body?

A multi-stage path

The journey of vitamin C begins as soon as it is ingested. After going through the stomach, vitamin C continues its way to the **small intestine**, where it will be mainly absorbed due to its **high permeability**. This step allows the **entry** and **diffusion** of the molecule into the **bloodstream**, which will then supply the different targeted organs of the body. Vitamin C is then excreted by the kidneys or **reabsorbed** through enterohepatic circulation⁷.

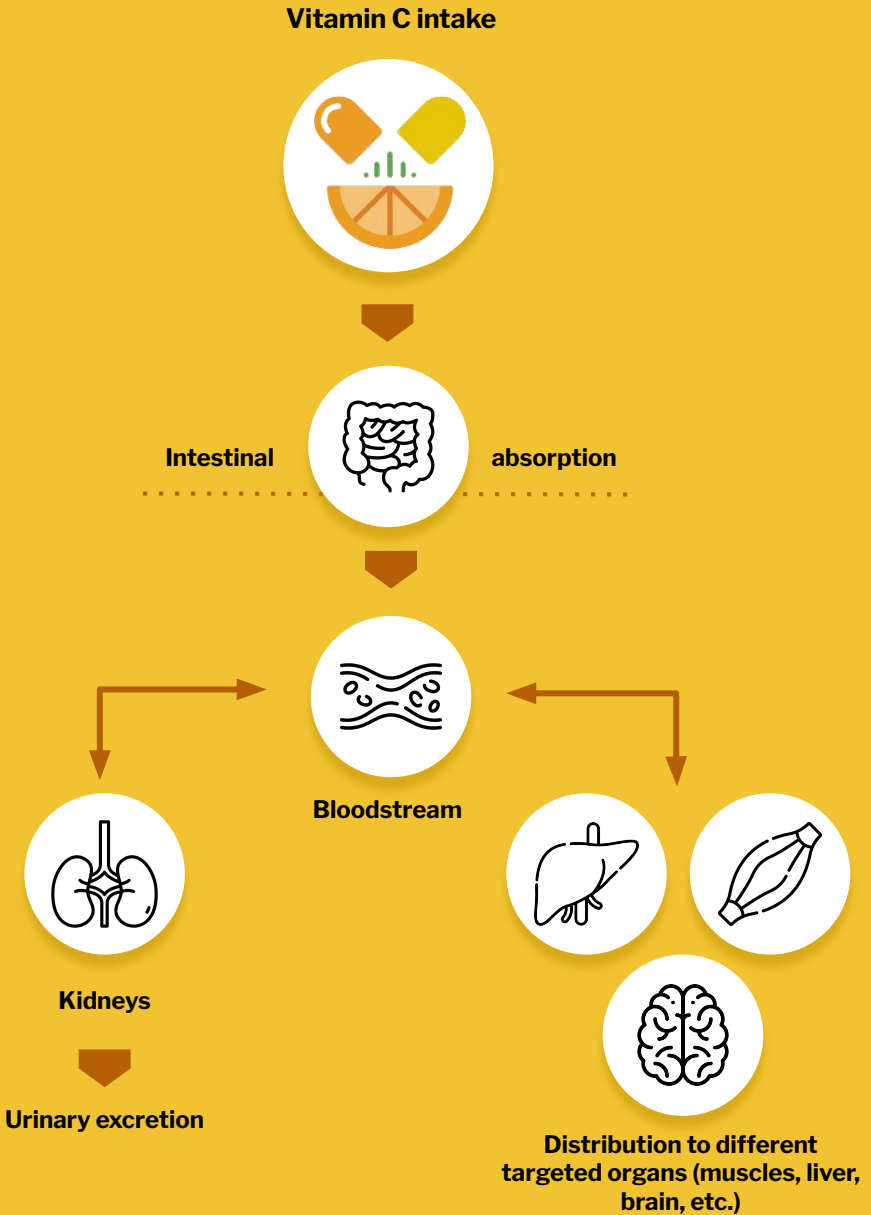


Figure 3. The pathway of vitamin C through the body
Seppic property

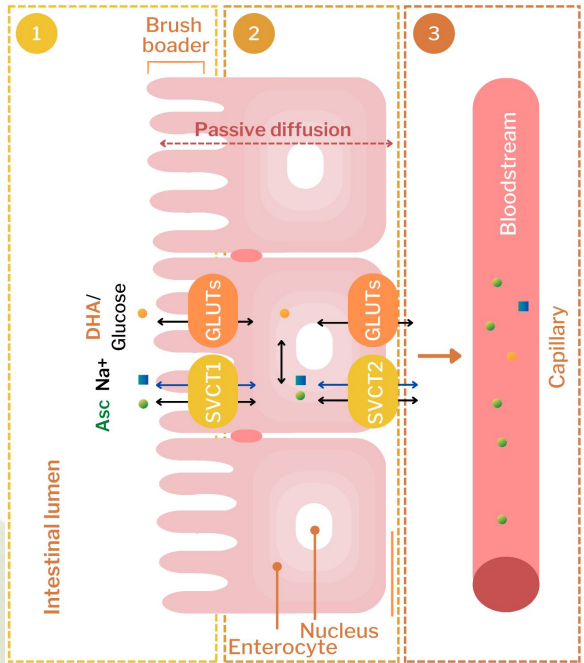
INTESTINAL ABSORPTION

a critical step

3 main stages⁷

1

At physiological pH, vitamin C is mainly found in its ionized form, named **ascorbate** (Asc) and to a lesser extent in its oxidized form, called **dehydroascorbic acid** (DHA). Once arrived in the **lumen of the small intestine**, both chemical forms have to cross the biological membranes of the **enterocytes** through the brush border. This first step depends mostly on the interaction with **2 different types of transporters**.



2

Figure 4. Stages of vitamin C intestinal absorption
Seppic property

There is a predominant mechanism provided by the **Sodium-dependent Vitamin C Transporters** (SVCTs) that are dedicated to the **transport of Asc only**.

These transporters are quite similar to each other but are differentially distributed within the body. In the small intestine, **SVCT1** is expressed at the apical side of the epithelial cell membrane. It enables the active transport of Asc against a concentration gradient, allowing cumulation in enterocytes.

DHA is transported by **facilitated diffusion** through **Glucose Transporters** (GLUTs), due to their structural similarities. Once inside the cell, DHA can be **easily and rapidly converted** in Asc thanks to chemical and enzymatic reduction reactions. At the intracellular level, **Asc is therefore dominant**.

3

Finally, Asc and DHA can migrate from the enterocytes towards the **capillaries**. This time, Asc is transported via **SVCT2** transporters located at the basolateral membrane. It also allows the reabsorption of Asc from the plasma to the intestinal epithelium. DHA, present in small quantities, is again transported in the blood by **GLUTs**. DHA transport is competitively inhibited by glucose. Indeed, an excess of glucose in the plasma or in the intestine can block the receptor binding site and thus decrease DHA transport. Within the capillaries, the bloodstream composed mainly of Asc (majority form found at more than **95%**) will then supply the various organs of the body.

A second minor mechanism also exists. Indeed, both Asc and DHA can, to a lesser extent, cross the membrane by passive diffusion without transporters according to a concentration gradient.

FINAL STEPS AND CHALLENGES

encountered with vitamin C

Excretion of vitamin C

Every day, blood is **filtered** by the **kidneys**. Indeed, **blood** containing among other things Asc and DHA passes through capillaries of the **renal corpuscle** and is excreted via the **glomerular filtration**.

Within the **proximal tubule**, a reabsorption phenomenon can occur to maintain body homeostasis. Asc is mainly reabsorbed by active transport by **SVCT1** transporters at the apical membrane. However, a passive diffusion phenomenon also exists.

The reabsorption of DHA seems **negligible** due to its very low concentration in plasma⁷.

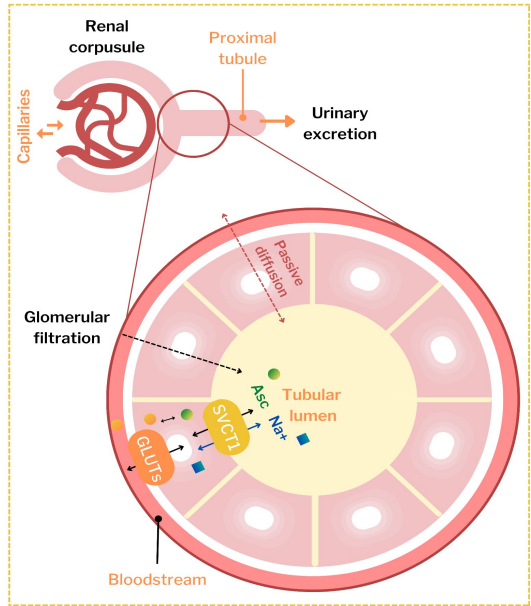


Figure 5. Excretion and reabsorption of vitamin C through kidneys
Seppic property

Bioavailability

Food supplements represent an interesting solution to overcome deficiencies and provide the recommended amounts of vitamin C for the proper functioning of the body (100mg/day for adults)⁵. However, the main issue encountered is the bioavailability of this molecule. For a normal dietary intake, about **70-90%** of vitamin C is absorbed. With higher intakes, usually more than 1g/day, as in the case of dietary supplements, this rate drops to **50% or less**⁷. This is due to the fact that **the body naturally tends to regulate the quantity of vitamin C in order to maintain its homeostasis**. The regulatory system of vitamin C mainly consists of the **saturation of the transporters** at the intestinal level and the **increase of the excretion** through the urinary tract when too much vitamin C is absorbed.

Limits of immediate release and interest of sustained release

In the food supplements market, different **release profiles** are possible depending on the active ingredient choice. **Immediate release** offers a quick release of vitamin C but raises issues such as the **saturation mechanism**, the elimination and **excretion** but also the associated **side effects** such as gastrointestinal disorders.

Sustained release provides solutions to these different problems and allows:

An **optimal absorption/action** over time and a reduction of daily intakes.

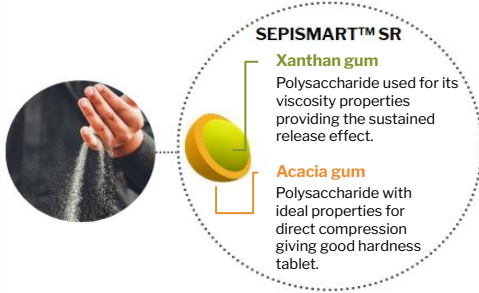
To **avoid plasma concentration peaks** associated with possible side effects.

To reduce **quantity per dose** (less waste and excretion).

SEPISMART™ SR

sustained release technology

SEPISMART™ SR is a ready-to-use synergistic co-granulation of Xanthan and Acacia gums from natural origin.



Formulated with active ingredients (AI) in food supplements, it gives a **sustained release effect** which allows the release of an effective amount of AI over time and at a continuous rate.

Figure 6. SEPISMART™ SR composition

How it works

The sustained release effect of SEPISMART™ SR is based on the mechanism similar to a **hydrophilic matrix** that is obtained thanks to a specific ratio of xanthan and acacia gums. Once ingested, the SEPISMART™ SR starts its hydration and **forms a gel** around the core for tablets or around the capsule shell for hard capsules. Depending on the AI characteristics, the dissolution will be mainly by **diffusion** for soluble AI or by **erosion** in case of insoluble AI.

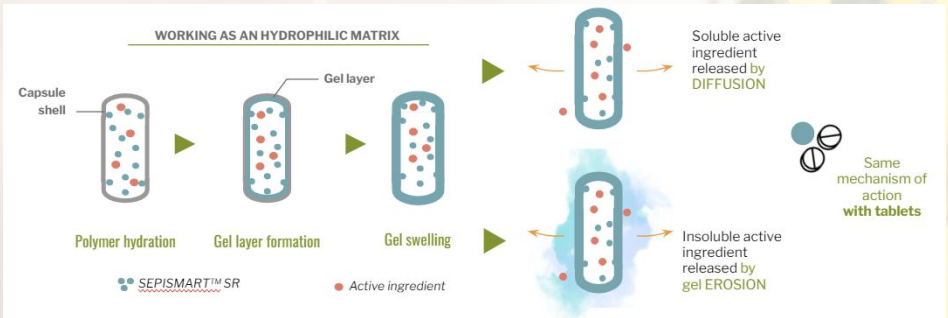


Figure 7. SEPISMART™ SR mechanism

Thanks to its mechanism of action, SEPISMART™ SR is as **compatible with tablets** as with **hard capsules** formulations.

Benefits of sustained release actives

Enhancing **absorption** and avoiding **potential side effects**.

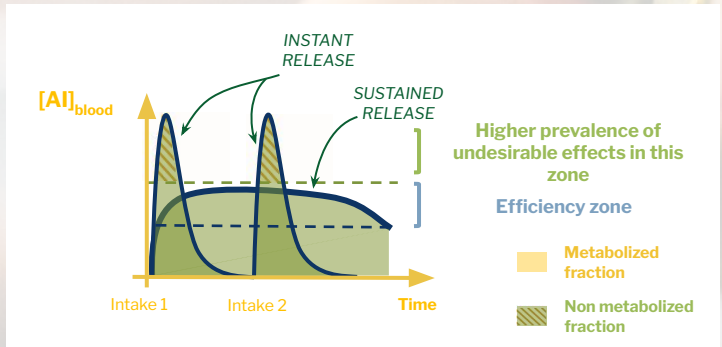


Figure 8. Blood AI concentration curve over time with/without sustained release mechanism

A PROVEN EFFICIENCY

on sustained release vitamin C food supplements

Methodology

Following USP guideline, the sustained release effect of SEPISMART™ SR has been evaluated in vitamin C food supplement:

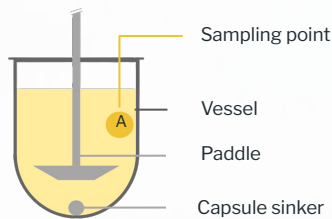


Figure 9. In vitro test with paddle apparatus II

Conditions and parameters used:

Dissolution media:

mimic of the gastric environment (0 to 2 hours at pH 1.2; 2 to 6 hours at pH 6.8)

Stirring speed:

60 rpm

Dissolution tests

performed three times

Media
Temperature: 37°
C ± 0.5

Volume:
1000mL of
dissolution medium

Samples are taken (5mL)
at different time intervals:
5, 10, 15, 30, 45, 60, 90,
120, 180, 360 min

Quantification of vitamin C (HPLC)

Determination of the vitamin C released in the dissolution media is performed using **chromatographic HPLC method** with following parameters :

- Chromatographic column: **Zorbax SB-C18 4.6 x 250mm 5 micron**
- Eluent: **water + 0.1% TFAA Isocratic elution**
- Injected volume: **20µL**

- Temperature: **30°C**
- Flux : **1 ml/min**
- Detector: **VWD lambda 254 nm**
- Analysis time: **6 minutes**

Test on Vitamin C chemical stability in the gastric fluid

Considering the **high solubility** of the ascorbic acid (1.9 g/ml at 37°C at pH 1.2, Class 1 BCS), a stability study has been carried out. 125mg of ascorbic acid has been dissolved in 500mL of gastric fluid reproducing the maximum theoretical concentration.

The results confirmed that the method used led to a very low loss of vitamin C.

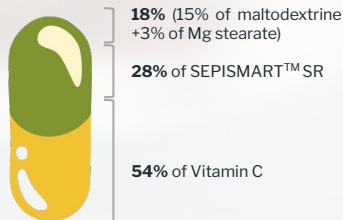


Figure 10. Vitamin C food supplement formula

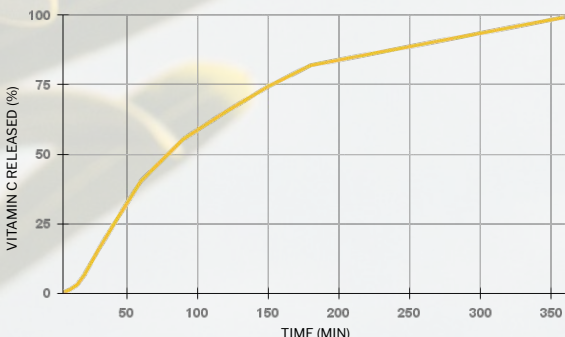


Figure 11. Dissolution profile of Vitamin C with 28% of SEPISMART™ SR

The graph obtained confirms the sustained release effect of SEPISMART™ SR. Indeed, **after one hour of dissolution, only 40% of the vitamin C has been released into the environment.**

This release kinetic can be accelerated by lowering the % of SEPISMART™ SR.

A UNIQUE SUSTAINED RELEASE EXCIPIENT

for an infinity of applications



Caffeine

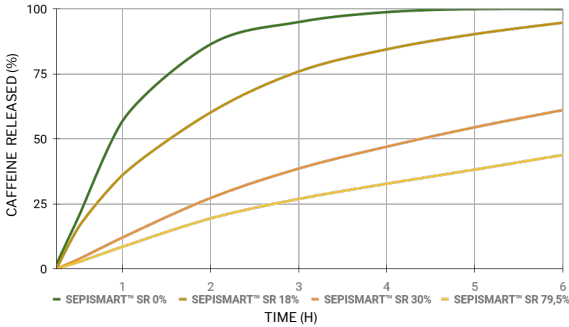


Figure 12. Evaluation of caffeine release in a capsule with different percentages of SEPISMART™SR

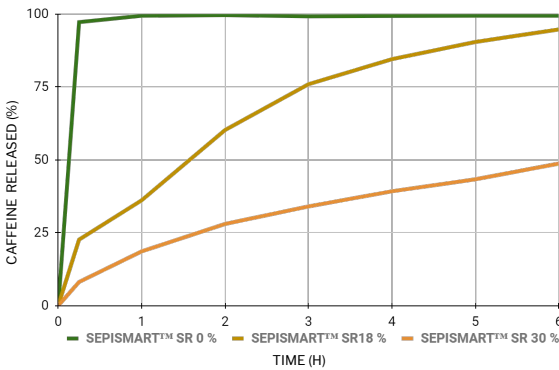


Figure 13. Evaluation of caffeine release in a tablets with different percentages of SEPISMART™SR



Melatonin

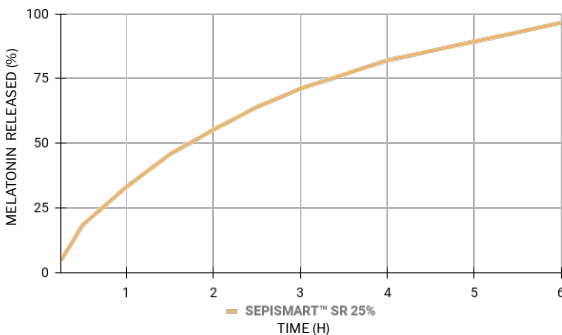


Figure 14. Evaluation of melatonin release in a capsules with different 25% SEPISMART™SR

Nota : all the information on pages 7 to 9 comes from studies conducted by Seppic

KEY FACTS

- Excellent **aptitude to compression** which makes it an effective excipient **for tablets**.
- Excellent **flowability** which makes it suitable for **hard capsules**.

IN A GLANCE

% of SEPISMART™ SR

↓	Tablets	Hard capsules
	0	99.4
18	36.1	36.1
30	18.6	12.0

% of caffeine released after 1 hour

For **both galenics**, SEPISMART™ SR shows a good sustained release effect.

Adjusting the percentage of SEPISMART™ SR allows to **fine-tune the release kinetic** of caffeine.

SEPISMART™ SR has also been tested for the well-known **concept of SLEEP** thanks to its association **with melatonin!**

Hormone which prepare the body for rest and sleep

With 25% of SEPISMART™ SR, **melatonin is continuously released from 15 min to 6 hours**. This type of sustained release kinetic of melatonin is adapted **for people who are subject to night awakenings**.

SEPISMART™ SR

made from nature

100% from natural source



Reasoned and sustainable harvest

Xanthan gum

Fermentation of **carbohydrates from natural sources** (maize, sugar beet, sugar cane).



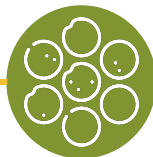
Acacia gum

Secure sourcing in the **acacia gum belt** (Africa).

Gum processed in Europe



Gum processed in France

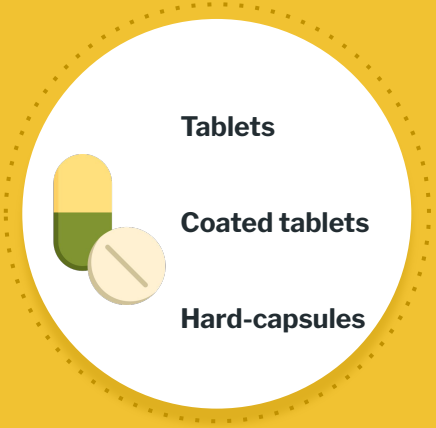


Eco-friendly co-granulation process using **no solvents**.

SEPISMART™ SR

in a nutshell

Suitable with various galenic options ...



Tablets

Coated tablets

Hard-capsules

From natural origin

Non-GMO



No additives/
preservatives



Halal
certified



Kosher
certified



Eco-friendly



Approves in
EU and US

... with an unrivalled
safety and quality.

CUSTOMER DEDICATION

If you want to provide concrete and efficient solutions for your actives with specific needs, then

SEPISMART™ SR is made for you.

Developed with strong science and with its natural composition, you can only stand out and offer the most innovative solutions.

REFERENCES

1. Brandessence Market Research And Consulting Private Limited. (2021, 18 octobre). At 7.6 % CAGR, Dietary Supplements Market Size Expected to Reach 231.9 Billion by 2027, says Brandessence Market Research. PR Newswire.
<https://www.prnewswire.com/news-releases/at-7-6-cagr-dietary-supplements-market-size-expected-to-reach-231-9-billion-by-2027--says-brandessence-market-research-301402190.html>
2. A report from Mintel Consulting for Seppic. (2022, february). *Trends in nutricosmetics*.
3. Precedence Research. (2022, 5 july). *Vitamin C Market Size to Worth Around USD 15.7 Billion by 2030*. GlobeNewswire.
<https://www.globenewswire.com/en/news-release/2022/07/05/2473878/0/en/Vitamin-C-Market-Size-to-Worth-Around-USD-15-7-Billion-by-2030.html>
4. Institute of Medicine. (2000). *Vitamin C - Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. National Center for Biotechnology Information.
<https://www.ncbi.nlm.nih.gov/books/NBK225480/>
5. European Food Safety Authority. (2017, 4 december). *Dietary Reference Values for nutrients Summary report*. EFSA
https://www.efsa.europa.eu/sites/default/files/2017_09_DRVs_summary_report.pdf
6. PubChem. (2011, 26 december). *Ascorbic acid*. National Center for Biotechnology Information.
<https://pubchem.ncbi.nlm.nih.gov/compound/Ascorbic-Acid>
7. Lindblad, M. Tveden-Nyborg, P. Lykkesfeldt, J. (2013). *Regulation of Vitamin C Homeostasis during Deficiency*. MDPI.
<https://www.mdpi.com/2072-6643/5/8/2860>
8. Office of Dietary Supplements. (s. d.). *Vitamin C*. National Institutes of Health.
<https://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/>

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