SONANOS™
Deliver Your Potential

AsahiKASEI

Hyaluronic acid nanogel Sonanos™

Novel pharmaceutical excipient primarily for injection formulation

Functions

Sustained release
Solubility enhancement

Business overview

Our rationale for Sonanos™

To respond to unmet medical needs, the pharmaceutical industry has recently attempted to develop drugs using various molecular modalities that can access targets that have previously been difficult to reach. Among such molecular modalities, there are many APIs that have problems such as poor water solubility, limited options to modulate release profiles, and toxicity, and they are difficult to develop into pharmaceuticals with current technology.

As a materials manufacturer, we strive to contribute to the development of new pharmaceuticals with high technical hurdles. We seek to achieve this through the new excipient, hyaluronic acid nanogel (Sonanos™), which has high biocompatibility and excellent functionality. Sonanos™ supports a wide range of modalities as a DDS material, and has functions such as sustained release and solubility enhancement. We aim to contribute to the improvement of patients' quality of life by developing pharmaceutical formulations that cannot be made with existing formulation technology.

As a solutions partner that expands the possibilities of DDS formulation and thus enabling our customers to truly "deliver your potential," we will continue to meet their needs and contribute to the health and daily lives of people around the world.

About Asahi Kasei

Asahi Kasei is a diversified Japanese chemical company with over a century of history.

We operate in the three business sectors of Material, Homes, and Health Care.

Material | **Homes** | **Health Care**

Creating for Tomorrow

The commitment of the Asahi Kasei Group:

To do all that we can in every era to help the people of the world make the most of life and attain fulfillment in living.

Since our founding, we have always been deeply committed to contributing to the development of society, boldly anticipating the emergence of new needs.

This is what we mean by "Creating for Tomorrow."

Versatile Facilitation

Expand the potential of DDS formulation.

Fully realizing your potential is a universal goal. To this end, the principle of Versatile Facilitation guides Sonanos™, Asahi Kasei's hyaluronic acid nanogel. Sonanos™ is an excipient that provides a variety of functions (Versatility) to better enable the formulation (Facilitation) of specifically targeted DDS. In short, it is a Multifunctional DDS Facilitator.

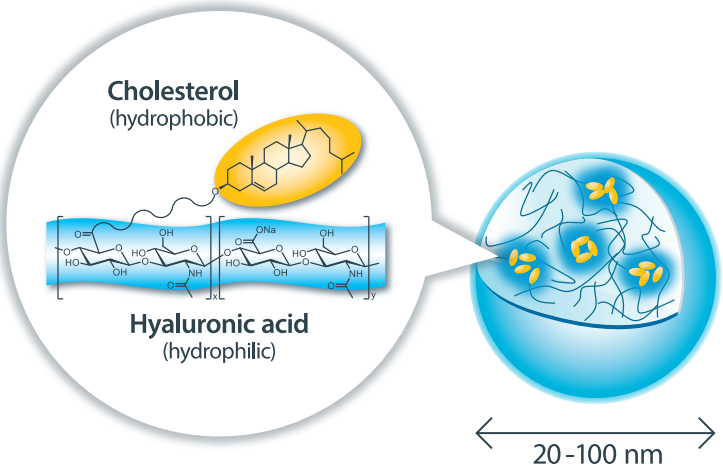
SONANOS™

Deliver Your Potential

Features

Structure

- Sonanos™ is composed of **Ch**olesterol-Modified **H**yaluronic **A**cid (**CHHA**). In water, the cholesterol portions self-associate due to hydrophobic interaction, forming nanometer-scale hydrogels.
- Sonanos™ can load APIs such as proteins, peptides, and small molecules. Multiple grades are available.



Functions

- Sustained release
- Solubility enhancement

Benefits to customers (pharmaceutical companies)

Multifunctional	Tunable solubility enhancement and sustained release profiles through grade selection.
API versatility	Capable of loading a wide range of small molecules, peptides and proteins with various molecular attributes.
Convenience	Formulation can be done simply and easily just by adding Sonanos™.
Safety	Sonanos™ is derived from naturally occurring substances that have high biocompatibility.

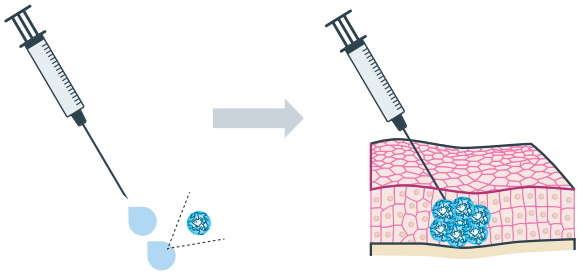
Benefits to end-users (patients)

Reduced patient burden	Fewer injections are needed, reducing the burden on patients.
Reduced side effects	Sonanos™ is made of materials with low toxicity, which reduces concerns about side effects derived from excipients.
Improvement in anticipated effects	Solving formulation issues, such as poor water solubility, can increase expectations for the anticipated effects of new pharmaceutical development.
Improvement in quality of life	Reducing the burden, anxiety and side effects for patients, and raising expectations for the development of new pharmaceuticals, will contribute to the overall improvement of patients' quality of life.

Grade lineup

- The Sustained Release Grade has exceptional ability to make protein or peptide complexes in high volumes. Furthermore, since in situ depot formation occurs under an *in vivo* environment, it is especially suitable for subcutaneous sustained release.
- The Solubility Enhancement Grade is markedly able to make complexes of poor water-soluble APIs in high volumes. In addition, since the dispersed state is maintained even under an *in vivo* environment, it is notably suitable as a solubilizer that can be administered intravenously.

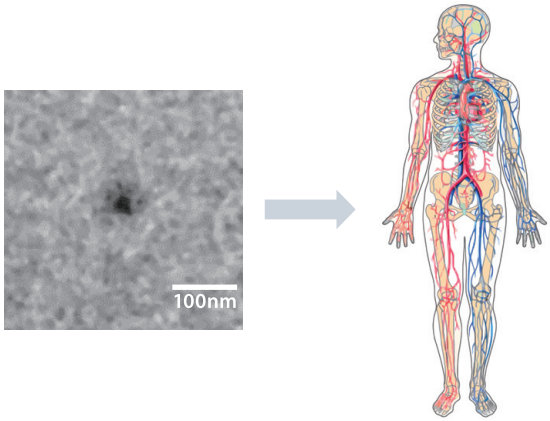
Sustained Release Grade



SC injection

In-situ depot formation in the subcutis

Solubility Enhancement Grade



SC/IV injection

Circulation in the body

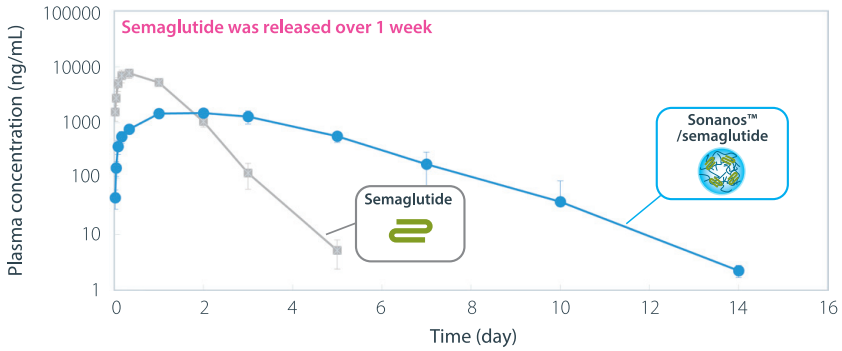
Grade lineup

Grade	**Sustained Release Grade**	**Solubility Enhancement Grade**
	Sonanos™ PG	Sonanos™ DS
Main target	**Sustained release of APIs after SC administration**	**Solubility enhancement of poorly water-soluble APIs**
Expected function	**In situ depot sustained release**	**Improvement of solubility**
Competitive features	• No chemical conjugation necessary (vs. PEGylation) • Applicable to protein (vs. PLGA-MS) • Simple formulation process (vs. PLGA-MS) • Aseptic filtration available	• Higher solubility enhancement ability (vs. polysorbate 80, CyD) • Applicable for large molecules (vs. CyD) • Improved safety (vs. existing solubilizers)

Sustained release

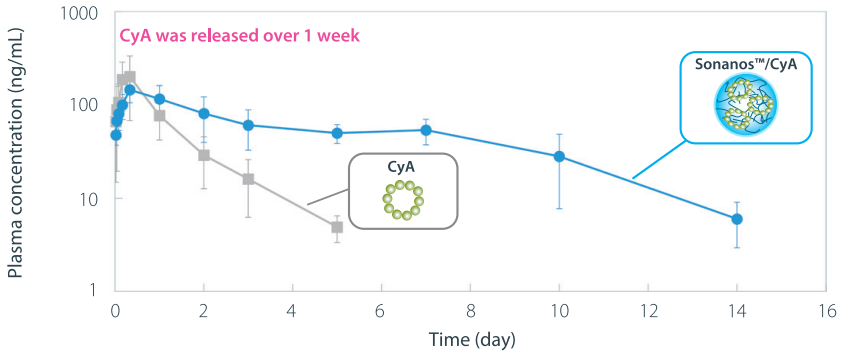
- Sonanos™ can sustain API release as *in situ* depot injection.
- It is applicable for the self-injectable subcutaneous sustained release formulation of proteins and medium/small-sized molecules without time-consuming formulation processes.

Sustained release of semaglutide



Plasma PK of semaglutide after SC in rats

Sustained release of cyclosporin A (CyA)



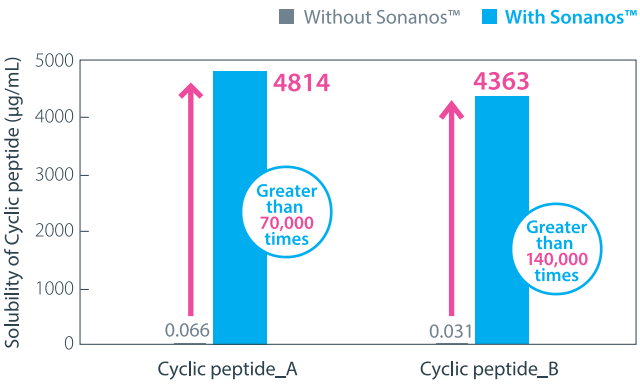
Plasma PK of cyclosporin A (CyA) after SC in rats

*PK: pharmacokinetics SC: subcutaneous injection

Solubility enhancement

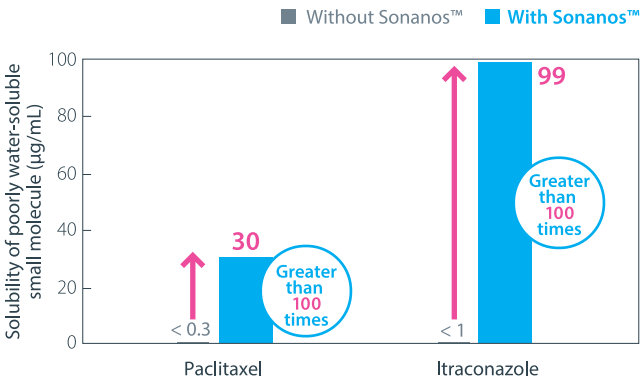
Sonanos™ can greatly improve the solubility of poorly water-soluble APIs with low toxicity compared with existing solubilizers. In particular, it can dramatically improve the solubility of medium-sized molecules (e.g., natural peptides, non-natural macrocyclic peptides, and nature's macrocycles).

Solubility enhancement of poorly water-soluble peptides



Cyclic peptide solubility was dramatically improved with 2.4% concentration of Sonanos™

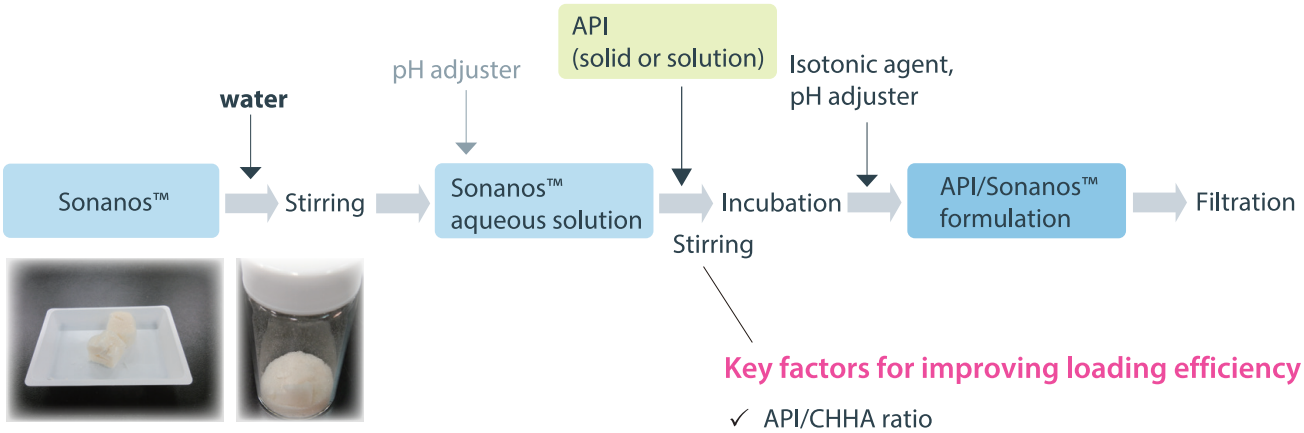
Solubility enhancement of poorly water-soluble small molecules



Small molecule solubility was improved with only 0.1% concentration of Sonanos™

Typical formulation process

Sonanos™ can encapsulate APIs basically through simple mixing.



Key factors for improving loading efficiency

- ✓ API/CHHA ratio
- ✓ optimization of pH
- ✓ incubation temperature
- ✓ incubation time
- ✓ ionic strength (lower is better)

*CHHA: **Ch**olesterol-Modified **H**yaluronic **A**cid

Requirements for formulation production facility

No need for special facilities

Encapsulation of API into Sonanos™ can be achieved by a simple mixing process and aseptic filtration.

*Optimization of formulation process parameters may be required to improve the loading efficiency.

Recommendations for CMO (if used)

Sonanos™ does not restrict the choice of CMO, unless the Sonanos™ concentration is too high to conduct sterile filtration.

Sonanos™ business model

Our business model is simple; we will sell Sonanos™ as a pharmaceutical excipient.

SONANOS™ Deliver Your Potential

AsahiKASEI ⟷ Pharmaceutical companies

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Intend to:

- Allow customers to do formulation research for pharmaceuticals utilizing Sonanos™.
- Allow customers to acquire patents on formulations limited to customer's proprietary APIs.

Note: If you wish to use Sonanos™ for cancer vaccines, please contact us first.

Collaboration steps

Feasibility study

- Sample supply for your testing (non-GMP/GMP)
- Technical support for formulation
- Only MTA is required
  - ✓ Future supply not ensured at this stage
  - ✓ Formulation research use only

Development

- According to your project stage, we will follow and support your development in a timely and flexible manner

We look forward to assisting you with development of your API formulations using Sonanos™.

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