CAVAMAX® AND CAVASOL®
CYCLODEXTRINS –
THE INNOVATOR’S MOLECULE
DISCOVER A NEW ALLROUND TALENT
AND A SOURCE OF INSPIRATION
Cyclodextrins were first documented in 1891 by Villiers, but it wasn’t until nearly 100 years later that commercial production of these molecules started. In 1990 following many years of research, WACKER started producing them biotechnically. Since then, many interesting applications have surfaced. Yet there is still a huge potential to be exploited commercially. This makes cyclodextrins truly an innovator’s molecule.

Cyclodextrins Offer Unique Opportunities in Many Industries:

- Personal care
- Agrochemistry
- Household
- Remediation
- Biocides
- Foods
- Nutraceuticals
- Pharmaceuticals
- Textiles
- Packaging
- Chemical synthesis
- Flavor & fragrances
- Industrial

Excellent Chances for First Movers

In many industries, product life cycles are getting shorter. This continually makes innovations and product improvements necessary. In many cases the use of cyclodextrins leads to a surprising and efficient way to realize innovations.

Talk to the Experts!

In the chemical world, WACKER is one of the most research intensive companies with a long history of developing new approaches for and with customers. Regarding cyclodextrins, WACKER is the only company in the world able to produce all three types of natural or parent cyclodextrins, has the broadest range of chemically modified derivatives, and has application development laboratories on two continents. With this background WACKER BIOSOLUTIONS is the perfect partner to help you realize ideas in your industry. Just talk to us, we are open to your ideas!
Chemically speaking, cyclodextrins are sugars. To innovative minds they are the key to a world of opportunities.

Natural Source
Cyclodextrins (CDs) are a naturally occurring group of cyclic oligosaccharides, consisting of 6 or more 1-4 linked α-anhydroglucose moieties. Produced biotechnically from starch by an enzymatic reaction, there are three commercially interesting natural or parent cyclodextrins. According to the number of glucose units, they are described as α-cyclodextrin (6 units), β-cyclodextrin (7 units) and γ-cyclodextrin (8 units).

WACKER is the only company worldwide offering all three parent cyclodextrins, which are marketed under the trademark CAVAMAX®. WACKER also manufactures and offers the chemically modified cyclodextrin derivatives, which are marketed under the trademark CAVASOL®.

A Unique Structure
It is the three dimensional structure of cyclodextrins that makes them so interesting. They resemble a hollow truncated cone or bucket. The secondary hydroxyl groups on the C2 and C3 of glucose are directed towards the wider top opening, whereas the primary hydroxyl groups on C6 are located around the narrower bottom opening, making the outside hydrophilic. The associated C-H groups and the ring of glycosidic oxygen bonds are directed inside the cavity causing its hydrophobic character.

Host-Guest Chemistry
The hydrophobic cavity in cyclodextrins is able to incorporate other “guest” molecules. This process of molecular encapsulation produces a cyclodextrin inclusion complex. Other commonly used expressions include, adduct, clathrate or complex. The modification of the guest with this molecular cage leads to the various applications of cyclodextrins. Through this, cyclodextrins can be used, e.g. to mask odors or tastes, to stabilize oils, protect UV sensitive molecules and much more.
Cyclodextrin Inclusion Complex Formation

Molecular Encapsulation
During the association no covalent or ionic bonds are formed. In solution the complex formation and dissociation are a dynamic equilibrium. One important aspect of the cyclodextrin inclusion complex formation is the geometry of the guest molecule. The size of a guest molecule must be compatible with the diameter of the cavity, which depends on the number of glucose units in the ring. This is the reason WACKER offers the three sizes of cyclodextrin cavities. So you can always find the right cyclodextrin for your molecule. For larger molecules, it has to be taken into consideration that only side groups penetrate into the cyclodextrin cavity. A second aspect is the requirement for hydrophobicity; the guest molecule must have some hydrophobic character. The final requirement is for the presence of water. The driving forces for complex formation are van der Waals forces, hydrophobic interactions, changes in solvation energy for both components and, to a lesser extent, hydrogen bonding. Therefore the stability of the complex corresponds to the hydrophobic character of the guest molecule; very polar or ionic molecules form only weak complexes. Considering this, a large variety of complexes for different uses are imaginable. Some of these have already been realised by WACKER. We can offer you ready made complexes for cosmetic, food, nutraceutical and other applications. Yet this is only the beginning of the cyclodextrin potential.

Cyclodextrins and the Advantages of Molecular Encapsulation
In water, the release of the guest is controlled by chemical equilibria. Complexes with CAVAMAX® cyclodextrins are stable against heat, oxidation, or UV light; they are compressible and the particle size can be adjusted by grinding. They are water dispersible and easily formulated.
HOW TO CAPTURE BUSINESS ADVANTAGES:

CONTROLLED RELEASE –
e.g. controlled release of an essential oil in water at 40 °C

SOLUBILITY –
e.g. improved water solubility of hydrocortisone
STABILIZATION –
e.g. prevention of melting of salicylic acid

ODOR & TASTE MODIFICATION –
e.g. reduction in odor intensity of garlic
e.g. reduction in the bitter taste effect of plant extracts
Unpleasant odors, e.g. garlic or onion, can be masked efficiently.

**Solubility**
Inclusion complex formation of a poorly soluble, apolar hydrophobic guest with a cyclodextrin in water results in a modification of the properties of the guest by those of the cyclodextrin. This generally leads to an apparent increase in the water solubility of the guest. This effect is strongest when the cyclodextrin used is a highly water-soluble derivative i.e. CAVASOL® W7 M. As can be seen in figure 1, the concentration of the guest increases linearly with the concentration of the cyclodextrin derivative.

Increased solubility of guests can lead to numerous applications, e.g. in addition to the advantages of having a higher concentration of guest in solution, we can consider non-detergent cleaning, phase transfer catalysis, separation and improved extraction processes.

**Odor & Taste Control**
Inclusion complex formation of organo-leptic or volatile compounds results in a modification of the sensory properties of the guest. If the guest has a strong odor or taste, then this will be reduced, or even removed. It is even possible to make inclusion complexes of gases. As illustrated by figure 2, a randomized panel was asked to evaluate the reduction in odor intensity of a test compound with different cyclodextrins. The odor intensity of the guest is reduced with both CAVAMAX® W6 and CAVAMAX® W7. The same effects can be seen with the taste of plant extracts. As shown by figure 3, a significant reduction in the bitter taste of some plant extracts was demonstrated with CAVAMAX® W8.
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SOLUBILITY –
e.g. improved water solubility of hydrocortisone
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ODOR & TASTE
MODIFICATION –
e.g. reduction in odor intensity of garlic
e.g. reduction in the bitter taste effect of plant extracts

Cyclodextrin-Menthol Complex
(CAVAMAX® W7/L-Menthol-Complex)
Stabilization
Inclusion complex formation of a poorly stable guest with cyclodextrins results in an improved stability of the guest due to protection by the rigid cyclodextrin molecule. Many examples of stabilization are known, for example reduced oxygen uptake of essential oils, vitamins or omega 3 or 6 oils; improved light or UV stability of vitamins and other compounds. Figure 4 demonstrates that cyclodextrin complexes protect the unsaturated bonds of the compounds in tea tree oil against damage by UV radiation in simulated sunlight (UV-A & UV-B) at elevated temperatures. The cyclodextrin complex of tea tree oil (brown line) shows no loss of content of the tea tree oil after 2 hours irradiation at 45°C. A physical mixture of tea tree oil and cyclodextrin (yellow line) loses 50% of the tea tree oil content after 30 minutes, and reaches 70% degraded after 1 hour.

Controlled Release
Inclusion complex formation of guest molecules with cyclodextrins in water is an equilibrium controlled process. This equilibrium process can be manipulated to provide controlled release of the guest from the cyclodextrin, over a significant period of time. At 40°C in water, 75% of the guest has evaporated in 2 hours. Under the same conditions, the inclusion complex with CAVASOL® cyclodextrins takes 6 hours to evaporate. However, with CAVAMAX® cyclodextrins 80% of the guest is still present after 16 hours (see figure 5).

In food and personal care, product performance can be improved by protecting ingredients such as vitamins.

Figure 4: Stability of Tea Tree Oil at 45 °C (Sunlight Test)

Figure 5: Controlled Release of Rosemary Oil in Water at 40 °C
Chemically, the main derivatives can be classified as either ethers or esters. They can be produced by either chemical or enzymatic modification of a parent cyclodextrin. This derivatization affects only the outer hydroxyl groups, and consequently does not usually affect the inner hydrophobic cavity.

The main benefit of derivatization is a significant increase in the water solubility of the cyclodextrin. This increase in water solubility enables cyclodextrins to solubilize low-soluble or hydrophobic guest molecules without the use of solvents or surfactants.

**Figure 6: Table of Water Solubility of CDs and Derivatives**

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<thead>
<tr>
<th>Solubility [g/100 ml]</th>
<th>CAVAMAX® W6, W7, W8 (parent)</th>
<th>CAVASOL® W6 HP, W7 HP, W8 HP</th>
<th>CAVASOL® W7 M</th>
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WACKER markets its cyclodextrin derivatives under the CAVASOL® trademark.
Introducing a new technology is sometimes a tough call. Not so with CAVAMAX®, CAVASOL® and WACKER. Here you have innovative yet natural and uncomplicated products. And a partner who is both strong in expertise and production capacity.

A Partner to Trust
As the world’s most important cyclodextrin producer, WACKER BIOSOLUTIONS offers unique expertise in this field. You profit from over 10 years of product know-how and a strong and experienced R&D team, which has held numerous presentations at conferences over the years.

With application development laboratories located in Adrian (Michigan, USA) and Burghausen (Germany), our application chemists are ideally positioned to help you develop innovative solutions for your industry’s problems and serve your key markets.

WACKER has several application patents for cyclodextrins.

“Green” and Safe Production
Cyclodextrins are natural, starch derived oligosaccharides. Since production starts with a renewable raw material source, the process has a low impact on the environment and is therefore truly “green”. Obviously, as a key global chemical player, WACKER can produce for its customers on an industrial scale.

A Reliable and Secure Source

WACKER has been working in biotechnology since the mid 1980s, and the first commercial products from our research activities are cyclodextrins.

Today, WACKER is the only company in the world able to produce commercially all three types of parent cyclodextrin, and their chemically modified variants or derivatives.

WACKER developed and owns intellectual property for the enzymes and the production process. A manufacturing plant using WACKER’s enzyme technology has been built in Eddyville (Iowa, USA), and has been producing cyclodextrins since March 1999. The reasons why this site was chosen include a plentiful supply of the raw material cornstarch and the fact that there is an economic outlet for the residual starch left over from the process.

Research and development is not the whole story. As a responsible manufacturer of chemical products, WACKER has generated and published significant data on the toxicology and environmental impact of cyclodextrins, and registered its products in the major markets around the world. So, our customers can feel safe and secure in using CAVAMAX® and CAVASOL® cyclodextrins in their own products and processes.

The natural cyclodextrins and their chemically modified variants are safe to use.

<table>
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<tr>
<th>Cyclodextrins: Regulatory and Registration Status</th>
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<td><strong>Product</strong></td>
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<tr>
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WACKER is one of the world’s leading and most research-intensive chemical companies, with total sales of €4.91 billion. Products range from silicones, binders and polymer additives for diverse industrial sectors to bio-engineered pharmaceutical actives and hyperpure silicon for semiconductor and solar applications. As a technology leader focusing on sustainability, WACKER promotes products and ideas that offer a high value-added potential to ensure that current and future generations enjoy a better quality of life based on energy efficiency and protection of the climate and environment. Spanning the globe with five business divisions, operating 25 production sites, WACKER is currently active in over 100 countries. The Group maintains subsidiaries and sales offices in 29 countries across Europe, the Americas and Asia – including a solidly established presence in China. With a workforce of 17,200, WACKER sees itself as a reliable innovation partner that develops trailblazing solutions for, and in collaboration with, its customers. WACKER also helps them boost their own success. Our technical centers employ local specialists who assist customers worldwide in the development of products tailored to regional demands, supporting them during every stage of their complex production processes, if required. WACKER e-solutions are online services provided via our customer portal and as integrated process solutions. Our customers and business partners thus benefit from comprehensive information and reliable service to enable projects and orders to be handled fast, reliably and highly efficiently. Visit us anywhere, anytime around the world at: www.wacker.com

All figures are based on fiscal 2011.
The data presented in this brochure are in accordance with the present state of our knowledge but do not absolve the user from carefully checking all supplies immediately on receipt. We reserve the right to alter product constants within the scope of technical progress or new developments. The recommendations made in this brochure should be checked by preliminary trials because of conditions during processing over which we have no control, especially where other companies’ raw materials are also being used. The information provided by us does not absolve the user from the obligation of investigating the possibility of infringement of third parties’ rights and, if necessary, clarifying the position. Recommendations for use do not constitute a warranty, either express or implied, of the fitness or suitability of the product for a particular purpose.