kosmetikos*

By Steve Herman

Amber Waves of Grain

"Iowa: We Do Amazing Things With Corn."[1]

Amazing things are indeed done with corn in Eddyville, Iowa. With a population of 1,100, Eddyville is situated on land once part of the colonial empire of Spain. Included in the Louisiana Purchase, it was sold by France to the United States. Iowa is the greatest grain producer in the US. Corn has lured Wacker Biochem out of the Alpine charm of southern Bavaria to establish its new cyclodextrin plant in Iowa.

Manufacturing is most economical when it is done in close proximity to the raw materials being used. On its website[2], Wacker Biochem describes the new plant as "adjacent to the corn milling complex of Cargil in Monroe County." Cyclodextrin is derived from starch, and starch from corn is abundant and inexpensive in Iowa. Bavaria is not famous for corn, and Wacker's production there is based on potatoes. Starch is a carbohydrate. Photosynthesis 101 decrees:

Sunlight + CO_2 + H_2O + chlorophyll = (+)-glucose

The (+)-glucose can be combined in different ways to form structural material (cellulose) or for energy storage (starch). A carbohydrate that cannot be hydrolyzed into a simpler substance is called a monosaccharide, otherwise it is a polysaccharide. These structures have conformational properties that affect the rotation of light, and the rotary prefix dextro contributes to the name "cycloDEXTRin."

The new plant is claimed to be creating 15 new production jobs, but the real worker is shown in Figure 1, an enzyme lovingly named "CGTase" (cyclodextrin glucosyl transferase). Why is there an enzyme that converts starch to cyclodextrin? The CGTase creates a carbohydrate in a form small enough to be ingested by a microscopic animal. The bacterium that produce CGTases also have a CDase (cyclodextrinase) bound in their membranes to degrade cyclodextrins for importation into the cell.[3]

Figure 1 CGTase

Cyclodextrin glucosyl transferase converts starch to cyclodextrin.
Photo by Tjaard Pijning and Joost Uitdehaag, University of Groningen, the Netherlands.

The first observations on cyclodextrin were made by Villiers in 1891, while he was digesting starch with *Bacillus amylobacter*. The fundamental principles of cyclodextrins were established by waves of research led first by Schardinger (ending in 1911), and for the next 24 years by Pringsheim. Unfortunately, much of the early work was unreliable.

The most damaging flawed information hit the literature in 1957, when French[4] reported on unpublished research where rats fed a cyclodextrin diet had died. The likelihood was that the cyclodextrin used in the rat study had a high toxic organic solvent level. Subsequent studies have shown pure cyclodextrin to be nontoxic, but many researchers avoided cyclodextrins for a quarter of a century because of the erroneous data.

By the 1970s, valid research began to accumulate. More than 13,000 publications have now appeared, and hundreds of patents have been issued. The 1980s and 1990s have been a Golden Age of cyclodextrin studies and applications.

Back to the corn and our enzyme. A small

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*Greek kosmEtikos, skilled in adornment or decorating.

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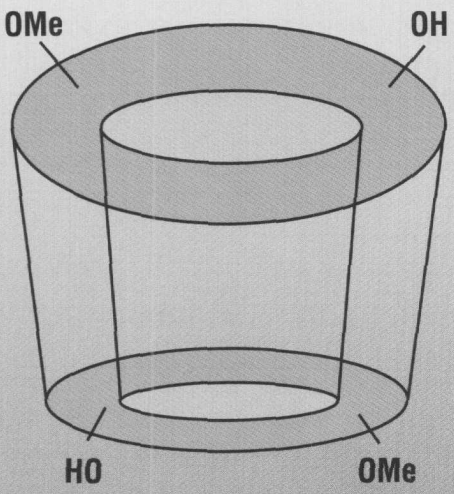
structure is created from glucose units by the action of CGTase on glucose. The assemblages created are thus polysaccharides. Cyclodextrins composed of 6, 7, or 8 units are designated α, β, or γ respectively. The macrostructure is shaped like a torus or a truncated cone (Figure 2), with some functional groups sticking out. Inner diameters are 0.57 nm for α-CD, 0.78 nm for β-CD and 0.95 nm for γ-CD. Different enzymes are used to generate the variations:

Figure 2 Structure of Cyclodextrin



Cyclodextrin has been used in a variety of ways from stabilizing catalysts for polymers to enhancing fungicide formulations.

α-CGTase, β-CGTase, and γ-CGTase.

One might assume that including more glucose units would create even larger cavities, but that is not the case. Larger structures lose their rigidity and collapse, so γ-CD has the greatest possible internal capacity. Smaller rings don't form because of conformational strain.

The distribution of hydrophilic and lipophilic groups in CD creates its most significant characteristics. CD can dissolve in water while solubilizing lipophilic species by inclusion complexation within the cavity. The guest molecules are generally non-polar organic molecules. The non-polar end of larger organic molecules can also be complexed, with some of the guest molecule outside the CD cone.

Since the α, β, and γ can correspond to different sizes of guest molecules, an exact match between CD and the complexed material is possible. For a mixture such as a perfume compound, a blend of the three forms of CD can be devised to maximize inclusion. It should be noted that Wacker has a patent on the enzyme which produces the γ-CD, giving them maximum flexibility.

Cyclodextrin has applications in many fields. It has been used to enhance the formulation of fungicides, reduce cholesterol in eggs, solubilize dyes for ink-jet printers, stabilize catalysts for polymers, and improve the rheology of paints. Shiseido has used CD to stabilize mercaptans, and Procter & Gamble for perfume stabilization.

The literature on cyclodextrin is vast. The reader interested in pursuing the topic further would do well to start with the excellent review by Szejtli.[5] Those interested in using CDs in new technical applications should certainly check the patent situation first, since the household, personal care and pharmaceutical possibilities have extensive coverage. Since the field is global and complex, an Internet search on a basic patent site may require augmentation from a more thorough service.[6]

However, the considerable work already conducted on CD should not discourage new investigators. A material with such unique qualities will surely yield further benefits to the creative researcher. Patents should be viewed not as roadblocks, but as platforms to even more imaginative applications.

Thanks to Mark Harrison of Wacker Biochem for providing valuable source material and insight. ■

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