



Present Status of Industrial Application of Cyclodextrins in Japan

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Abstract

The application of CDs in the food, cosmetic and textile industrial fields as solubilizing agents, stabilizers, emulsifiers etc., is reviewed briefly. Many CD-containing commodities that have been put to practical use are introduced. Technical developments of CDs and their commercialization have had a multilateral impact on economic activities in our country. The expansive effects of CD production on other industrial fields and the economic impact are discussed.

Application fields of CDs

Amounts of CD consumption in Japan

CDs were introduced in Japan during the early 80s as industrial products. As the amount of CDs in use has slightly increased year by year, the annual (2000) consumption of CDs in Japan is estimated to be about 1800 tons (24 million \$US in terms of sales). This made Japan the largest consumer in the world.

How we use CDs?

Most of the use is food-related.

Figure 1 shows the usage of CDs.

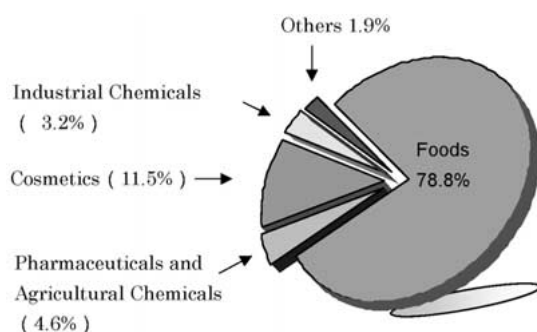


Figure 1. Segments of the CD-market.

About 78.8% and 11.5% of all CDs are consumed by the food and cosmetics industries, respectively. Nearly 3.2% of CDs produced are used to produce industrial chemicals. Around 4.6% are dedicated to the pharmaceutical industry and agricultural chemicals.

CD-related patent applications

Figure 2 shows CD-related patent applications during 1987 to 2000.

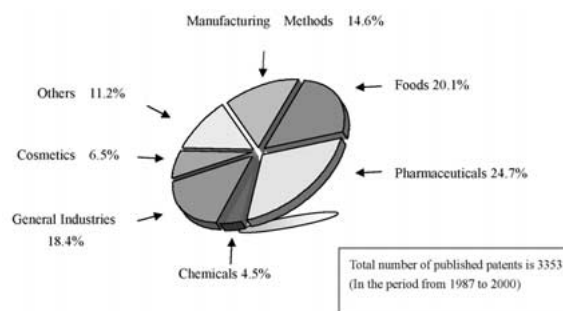


Figure 2. CD-related patent applications.

The total number of patent applications was 3,353.

Patent applications in the food field accounts for 20.1%, those in the pharmaceuticals field 24.7%, those in the cosmetics 6.5%, those in general industries 18.4%, while those in chemicals, manufacturing methods and others account for 4.5%, 14.6% and 11.2%, respectively.

As you can see food related patent applications occupied minor portions.

I think this indicates that CDs have great potential of wider applications in other products than food related.

Actual uses (practical example)

In food

CDs are used in the food industry to protect active ingredients against oxygen, light, heat and volatility, to reduce unpleasant tastes and odors; and to accelerate and stabilize the emulsion process. CDs are useful in mixing and dispersing, as well as in food preservation.

- Powdered flavors (apple, citrus fruits), spices (garlic, ginger, horseradish, mustard) and herbs (peppermint, basil) complexed with CDs have been on the market. The aromatic ingredients of these spices can be stabilized

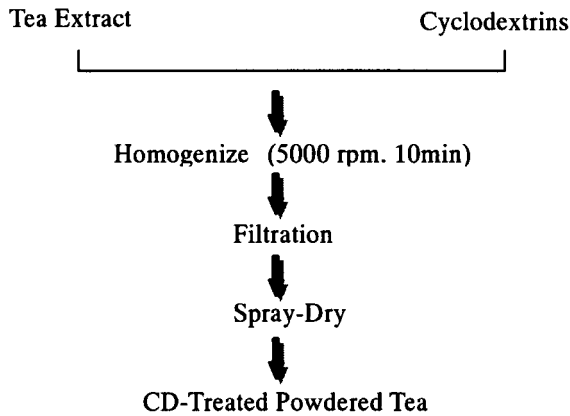


Figure 3. Process for producing powdered tea.

by CDs. These are highly valued for their high stability against heat during food processing (Picture 1).

- Bubbling coffee: this is a new product of Nestle. Granular sugar is coated with maple and vanilla flavor included with CD. (Picture 2).
- Powdered green tea: CDs are used to maintain flavor and color. This makes it possible to enjoy green tea flavor and color in ice cream, mousse and other Japanese confectioneries (Picture 3). The process for production of powdered tea is schematized in Figure 3.
- Supplements: many health care products containing amino acids and vitamins are available on the market. The amino acids and vitamins can be stabilized and protected by CDs (Picture 4).

In cosmetic and toiletry

CDs are used in the cosmetics field to solubilize fragrances, to suppress fragrances' volatility, and to allow products containing perfumes to be sprayed in micro-powder form. CDs are also used as stabilizers, emulsifiers and deodorants.

- Long-lasting perfumes and creams: these contain fragrance-CD complexes with CD used to enable slow release of fragrance (Picture 5).
- Ceramide-containing cosmetics (foundation): stable ceramide powder can be made using CDs. This ceramide powder is dispersible and suitable for cosmetics. Ceramide is a complex lipid which can be found in cytoplasm and plasma membrane. Ceramide has moisture-holding ability, which makes the skin moisture-rich and improves skin elasticity (Picture 6).

In textile

Recently, textile products having specific functions have been developed. CDs were essential ingredients to produce these new materials in the textile field. CDs are mainly used for

- Keeping moisture in squalane fibers.
- Reducing odors in fibers added plant extracts.
- Anti-Germ in fibers added antibacterial agent.

Using these functions for example, underwear suitable for dry skin, underwear suitable for people who have allergies, and socks which will reduce unpleasant bad smells were produced.

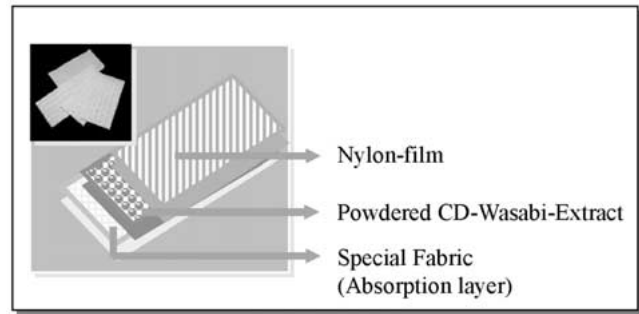


Figure 4. Structure of antibacterial sheet.

- Underwear containing the CD-squalane inclusion complex as an active ingredient is already on the market in Japan. CDs are used to bring squalane into powder form. Powdered squalane is combined with fibers using a special binder (Picture 7). Squalane is extracted from the liver oil of deep-sea sharks. It can prevent skin from drying and maintain skin moisture.
- Underwear for suppression of atopic dermatitis: this underwear can effectively prevent itching. CDs are used to bring gamma-linolenic acid into powder form. Powdered gamma-linolenic acid is fixed on each fiber of underwear. Gamma-linolenic acid can be absorbed directly from the skin. This substance is claimed to effectively prevent reduction of water retention ability. It is then processed to ensure that it remains effective after repeated washing (Picture 8).

In wrapping materials

Some unique applications have been explored by packaging specialists. The container and wrapping materials for foods are produced using foodstuffs which have preservatives and antibacterial properties. For instance: Wasabi is a plant with a hot-tasting spicy root. It is a traditional Japanese spice and widely used in the food field. Allyl isothiocyanate (A.I.T.C.) is the main component of Wasabi and is known to have antibacterial properties. However, it is volatile and rapidly decomposed by oxidation. CDs are used to stabilize it. Picture 9 shows the Wasabi plant and its structure.

- Anti-bacterial cooking sheets and trays: antibacterial sheets and trays that are included with the CDs-Wasabi inclusion complex have been on the Japanese market. The outer layer of the sheet is Nylon-film coated with vinylidene chloride, the middle layer is Wasabi-CD inclusion complex, and the inner layer is a special fabric (Figure 4). When moisture or dripping from food contacts this sheet, A.I.T.C. is gasified, packed foods will be surrounded by A.I.T.C. gas and breeding of bacteria or mold will be suppressed. CDs enable good release control and stabilize active ingredients. These products are used for packing meat and raw fish such as Sashimi to keep it fresh (Picture 10).



Picture 1. Spices.



Picture 2. Bubbling coffee.



Picture 3. Powdered green tea.



Picture 4. Health care.



Picture 5. Last-lasting perfumes and creams.




Picture 6. Foundation.



Picture 7. Squalane-underwear.



Picture 8. Underwear for suppression of atopic dermatitis.



$CH_2=CH-CH_2-N=C=S$

Allylisothiocyanate (A.I.T.C.)

Picture 9. WASABI (Japanese horseradish).



Picture 10. Anti-bacterial cooking sheet and tray.

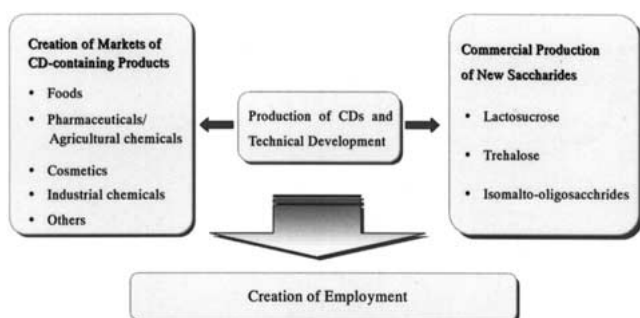


Figure 5. Expansive impacts of CD production on other industrial areas.

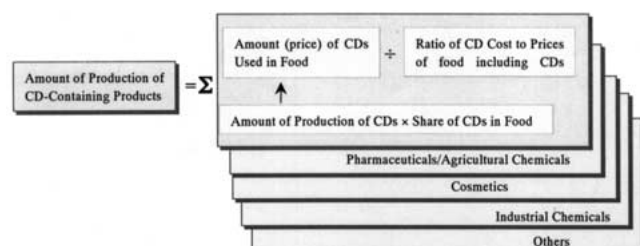


Figure 6. The impacts of creation of markets for CD-containing products.

Economic impact of cyclodextrin production on other industrial fields

Technical development of CDs and their commercialization have had a multilateral impacts on the economic activities in our country. Thus, it may be difficult to provide a complete picture of such impacts. The following is one aspect of the impact of CDs on economic activities.

Primary impact: Creation of markets for CD-containing products

The primary, direct impact of CD production is the utilization of the ability of CDs to form inclusion complexes. New markets for CD-containing products were created.

Since many of these CD-containing products are considered innovative new products, The Society for the Techno-Innovation of Agriculture, Forestry and Fisheries [1] in Japan performed a simulation of the economic impact of CDs as shown in Figure 5.

The amount of production (price) of CD-containing products is calculated as follows (Figure 6):

- The amount of production of CD-containing products is classified by CD utilization areas of such products (foods, pharmaceuticals, agricultural chemicals, cosmetics, industrial chemicals and others).
- The ratio of CD cost to an individual CD-containing product is estimated for every CD-utilization area.
- Dividing (a) by (b) for every CDs-utilization area will provide the production amount for every CDs-utilization area. For example, when the CDs cost in a certain CDs-utilization area is 1.5%, a final product in this area would be 67 times higher than the CDs cost.
- The prices of the CD-containing products can be added in all CDs utilization areas to obtain the total amount of products.

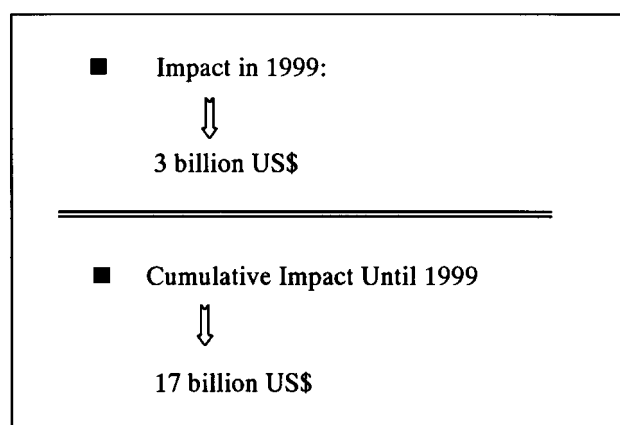


Figure 7. Economic impact for 1999.

The above formula has made it possible to calculate the economic impact for each year, with the following results (Figure 7). The impact in 1999 was 3 billion US\$, and the cumulative effect until 1999 was just over 17 billion US\$.

Secondary impact: Creation of new functional oligo-saccharides

In order to establish industrial production of CDs, various technical breakthroughs were made in processes such as enzyme reaction, decolorization and purification, concentration, separation, fractionation, powdering and others. Sophisticated technology is required, particularly in the process in which glucanotransferase is used for enzymatic reactions for CD production. Various technologies used in the reaction process for CD production have been applied to production of new oligo-saccharides on an industrial scale, resulting in the creation of many new products, mainly oligo-saccharides, which are claimed to be “good-for-health” in Japan. Some of these oligo-saccharides have bioregulatory functions such as selective proliferation of bifidobacteria and others, as additions to physicochemical functions.

Tertiary impact

Employment opportunities have been created thanks to the production of CDs and their related products as well as distribution of these products.

Prospects for the future

Although the current market size in Japan and abroad is far from large, I think that potential markets for CDs in the future will be substantially larger in view of application research efforts at development of end uses now in progress in various countries. For example, the prevention of air pollution using CD inclusion complexes has been researched. Methane is one cause of increased global warming. It is estimated that the world's population of ruminants produces about 15% of total atmospheric methane emission. Recent research has found that Wasabi-CD complexes were able to decrease methane production by decreasing methanogenes

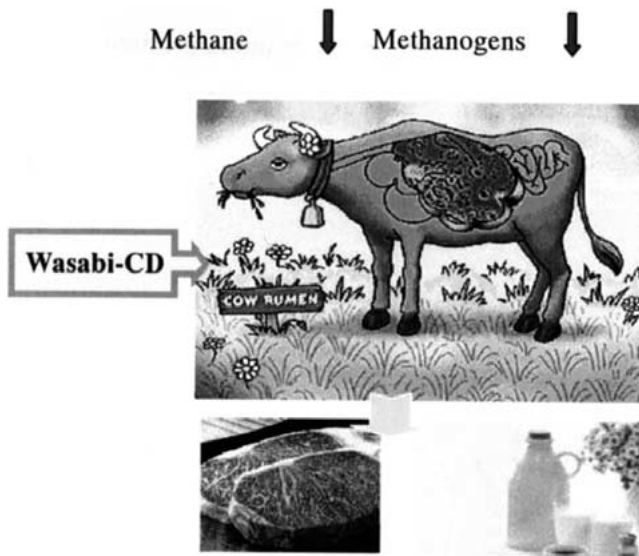


Figure 8. Effects of CD complex on ruminal methane formation.

without detrimental effects on rumen fermentation. We are studying the development of additives using CDs in the feed of ruminants for anti-methanogenic purpose (Figure 8). Research on this is still ongoing in our Lab.

We believe that CDs have many such potential abilities that we already know and those we may not know yet.

I believe that consolidating our research efforts to further advance CD application frontier, we can make significant contribution to overcome some important issues which we face today.

References

1. Annual Report (2000) of The Society for Techno-Innovation of Agriculture, Forestry and Fisheries (Japan).