Cyclodextrins (CDs) are water-soluble, cyclic, non-reducing oligosaccharides consisting of α-(1,4) linked D(+)glucopyranose units linked by α-(1,4) bonds (Figure 1A) (1,2). They are also known as cycloamyloses, cyclomaltoses and Schardinger dextrins and originate from the degradation of starch by means of α-glucosidase and α-amylase enzymes. β-CD is the most accessible, the lowest-priced and generally the most useful. The only drawback of this CD, sometimes the main advantage, is the poor water solubility (Table 1) and for this reason, starting from natural CDs, many derivatives have been obtained, featuring different characteristics, especially in terms of water solubility and toxicity (3), and paving the way for new and unexpected applications.

As for the shape, CDs are toroid molecules (Figure 1). They possess an internal hydrophobic cavity in which different organic compounds can be included, giving rise to the so-called “inclusion host-guest complex”. Conversely, the outer surface is hydrophilic making the host–guest inclusion complex mostly water soluble. No covalent bonds are formed or broken during complex formation and, in aqueous solution, the complexes are readily dissociated and free guest molecules are in equilibrium with the molecules bound within the CD cavity. This is a dynamic process whereby the guest molecule continuously associated and dissociated from the host CD. When the inclusion complex is included in a pharmaceutical or cosmetic product, upon administration or topical application, the guest molecule appears to be rapidly and quantitatively released from CD inclusion complexes. Dissociation due to dilution appears to be the major release mechanism although other factors appear to be involved (4). Most guest agents form 1:1 complexes with CDs (Figure 1B) (5). On the basis of the structure and properties of the

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Table 1. Some characteristics of natural CDs.

<table>
<thead>
<tr>
<th>Type of CD</th>
<th>Cavity diameter ((\AA))</th>
<th>Molecular weight</th>
<th>Solubility ((g/100\ mL))</th>
<th>Number of glucose units</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-CD</td>
<td>4.7-5.3</td>
<td>972</td>
<td>14.5</td>
<td>6</td>
</tr>
<tr>
<td>β-CD</td>
<td>6.0-6.5</td>
<td>1133</td>
<td>1.85</td>
<td>7</td>
</tr>
<tr>
<td>γ-CD</td>
<td>7.5-8.3</td>
<td>1297</td>
<td>23.2</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 2. Cosmetics containing CDs already present in the market.

<table>
<thead>
<tr>
<th>Personal care products</th>
<th>Ornaments, cosmetic powders, deodorants, bath preparations, self-tanning creams, perfumes, detergents, antiwrinkle creams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hair care products</td>
<td>Permanent wave, shampoos, lotions, conditioning products</td>
</tr>
<tr>
<td>Nails products</td>
<td>Lacquer removers</td>
</tr>
</tbody>
</table>

The cosmetic industry has begun transforming knowledge about CDs into products (7) and many different cosmetics formulated with CDs are already on the market, also because these oligosaccharides are characterized by a high degree of safety when used topically (8).

APPLICATION OF CDs IN THE COSMETIC INDUSTRY

CDs as solubilizing agents

A large number of cosmetic ingredients, such as vegetable oils, vitamins, antiplastic, preservatives, are nearly insoluble in water and are able to form inclusion complexes with CDs, becoming more soluble compared to pure compounds (6). Some examples of cosmetic active ingredients insoluble in water that have been successfully complexed with CDs are:

- salicylic acid, used as antibacterial and keratolytic agent;
- triclosan, that act as topical antiseptic and disinfectant in silica-based toothpastes;
- menthol, which acts as cooling agent;
- retinol, an antiwrinkle which also presents a problem of instability to light and atmospheric oxygen.

CDs are also used to increase the solubility of substances secreted by the skin, and thanks to the formation of an inclusion complex they are able to dissolve skin fat which can be easily removed. So they can be included in personal care products such as detergents.

CDs in the reduction of unpleasant odors

CDs may be useful in covering the unfavorable organoleptic characteristics of some cosmetic products due to the presence of a particular active. For example, dihydroxyacetone, used as tanning agent, is characterized by an unpleasant odor, which is difficult to cover with perfumes. When the inclusion complex of dihydroxyacetone with CDs is used, this odor completely vanishes. In addition, the complex with the CD releases this agent in a gradual manner, ensuring a uniform tanning of the skin.

Also glutathione, used as depigmenting and whitening agent, gives an unpleasant smell to the cosmetic product. It has been successfully complexed with different CDs (9). CDs are also used to cover the odor of mercaptans used in permanent wave products, avoid using perfumes, which may be responsible for allergic reactions.

Moreover, some authors (10) demonstrated that CDs, and in particular β-CD, are capable to interact and to form complexes with different components present in sweat and body secretion, responsible to cause body malodor, like tiols, steroid and acids. For this reason, β-CD could be an active component in deodorants as well as in other personal care formulations.

Other authors, instead, have focused their attention on some unsaturated aldehydes such as hexenal, octenal and nonenal which are responsible for the so called “aging odor”, because their levels markedly increase in the middle-aged and elderly (11). They demonstrated that Meβ-CD was the most effective CD in the deodorization of “aging odor”.

CDs in the conversion of liquid or oily materials to powder forms

Some active ingredients in cosmetic preparations, such as α-tocopherol and vitamin E, occur in oily form and thus are difficult to handle but especially to be included in the finished product. This problem can be easily overcome preparing a CD inclusion complex in the solid state. The inclusion complexes, in fact, may be obtained, using different methods of preparation, both in solution and in the solid state (12), depending on the characteristics of the guest molecule and the needs of the
formulator (final dose form desired and characteristics of other formulation ingredients).

**CDs in complexation and controlled release of fragrances**

CDs can be used to complex different fragrances, included in personal care products as shampoos, deodorants, detergents and absorbent powders such as bath- and baby-powder products (13). For example, the complexation with CDs of some scents, like rose and lemon oil, greatly reduces eyes irritation of shampoos while in most absorbent powders CDs are not only able to substitute starch, without risk of bacterial contamination, but they can also promote a long-lasting fragrance effect (more than 6 weeks after opening). In addition, when they are included in detergents for complexing fragrances, CDs also act as antifoam agents, considerably reducing the water consumption for rinsing.

**CDs as protecting agents against light and oxidation**

Hydroquinone, tea tree oil, kojic acid, retinol, natural tocopherol (α-tocopherol) are some examples of cosmetic active ingredients characterized by a certain instability when exposed to light and atmospheric oxygen. Hydroquinone, a skin whitening used in the past and now withdrawn in many countries, presents a limited-pH range of stability and for this reason it needs the presence of stabilizers during its formulation. Conversely, its CD inclusion complexes have a greater stability and show more depigmenting power than the hydroquinone itself. Tea tree oil, extracted from Melaleuca Alternifolia, is used for its antimicrobial activity but unfortunately, because of its high content of terpenes, it gives rise to p-cymene, a skin irritant, when exposed to light and oxygen. As a CD complex, tea tree oil is stable and the formation of undesired compounds is prevented without any modification of antimicrobial and anti-inflammatory properties (14). Even Kojic acid is used in cosmetic creams as whitening agent but its use is quite limited because it decomposes giving rise to a yellowish brown compound. This problem was overcome by complexing it with CD, and obtaining also an enhancement of bleaching activity (15). α-tocopherol, a very active antiradical agent, is an easily oxidized compound. Complexed with CD, its activity is greater than free α-tocopherol and is maintained for a much longer time (16).

**CDs in preventing skin irritation**

The β-CD is able to complex the polyunsaturated fatty acids present in sebum, preventing their oxidation and inhibiting free-radical formation, so it represents a great tool in anti-acne treatments (17).

**CDs as penetration enhancers**

CDs constitute a class of penetration enhancers that have advantages over other conventional penetration enhancers, such as fatty acids and surfactants (18). On the other hand, CDs have also been used to reduce permeability of compounds into skin (19). For example, it has been indicated that complexation of sunscreen enhances its photoprotective effects by preventing permeation of the sunlight into the skin.

**CDs in the stabilization of emulsions and suspensions**

Small CDs, in particular α or β seem preferable to γ-CD, are able to stabilize simple and multiple emulsions because they can form in situ surface active agents by including a fatty acid chain of the glycerides of the oily phase (20). So it is possible to formulate emulsions in the absence of classical surface agents, that are responsible of several side effects.

**CONCLUSIONS**

CDs have been known by more than 100 years but only recently, with the advent of biotechnological advancements, it was possible to produce them in greater quantities, with a high degree of purity and a significant reduction of their price. This has made their application possible in different fields. Thus, more than one century after their discovery, CDs have been finally and rapidly accepted not only as pharmaceutical excipients but also as food, textile additives and cosmetic ingredients. When the inclusion complex is included in a cosmetic product, upon application the guest molecule appear to be rapidly and quantitatively released from cyclodextrin inclusion complexes. Hence, CDs certainly represent a valid formulative support, solving different formulation problems and improving the performance of the cosmetic product.

**REFERENCES AND NOTES**