Characteristics and applications of cyclodextrin complexes

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Cyclodextrins are cyclic oligosaccharides linked by α-1,4-glycosidic bonds. Among the natural cyclodextrins, there are α-, β- and γ-cyclodextrins. By introducing various functional groups into the cyclodextrin ring, derivatives can be formed in order to improve their physicochemical properties. Due to the hydrophilic outer surface, the CDs are well soluble in water, while the inner space is hydrophobic, and may contain another hydrophobic substance.
Thanks to their various properties, they are used in various industries. Cyclodextrins are widely used in the pharmaceutical, cosmetic and food industries. The physicochemical properties of the free drug as well as the free cyclodextrin differ from the properties of the prepared inclusion complex. They increase the stability and solubility of poorly soluble substances in water. They reduce the unpleasant, bitter taste of substances such as diltiazem or ranitidine. Moreover, they may increase the thermal stability of drugs. In complexes with antibiotics, they can increase their antibacterial activity. In cosmetics, cyclodextrins are often used to eliminate odor, minimize skin irritation, and improve the solubility and stability of the active ingredient. Cyclodextrins also have the ability to form complexes with cholesterol or pesticides, which allows the production of products with a reduced cholesterol content and a positive impact on the environment.
This article presents several typical methods of complexation with cyclodextrins, their potential influence on the change of physicochemical properties of compounds, and some techniques used in terms of examination of their structure, interaction, stability, or solubility. Nowadays, it has been observed that research groups focused on analyzing the structure, interaction, stability in various environmental conditions (including photostability), and solubility of combinations of active substances with cyclodextrins. The work also concentrates on various analytical techniques that are used in the research of complexes of cyclodextrins with ingredients of medicinal products, food, and cosmetics.

Keywords: cyclodextrins, application, physicochemical properties.

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Introduction

The history begins in 1891 when Villiers discovered cyclodextrins (CDs) by breaking down starch with bacteria. He called them 'cellulose' at the time. Several years later, in 1903, microbiologist Franz Schardinger identified similar compounds α-dextrin and β-dextrin. In 1935, Freudenberg discovered γ-cyclodextrin and suggested that larger CDs may also exist. In the 1980s, the first pharmaceutical product with cyclodextrin was introduced to the Japanese market. It contained Prostaglandin E2 and β-CD. In the following years, similar products were introduced both in the US and Europe. Brexin tablets containing piroxicam and β-CD were the first products containing CDs in Europe, while in the USA the first was Sporanox, containing itraconazole and 2-hydroxypropyl-β-CD (HP-β-CD) [1].

Cyclodextrins are cyclic oligosaccharides, formed most frequently from 6 (α-CD) 7 (β-CD), or 8 (γ-CD) glucose molecules that are linked by α-1,4-glycosidic bonds (figure 1). CDs are obtained by degrading starch received from various sources, such as potatoes, corn, wheat, or rice, by the enzyme cyclodextrin glucosyltransferase. Until recently it was not possible to form CD from less than 6 glucose molecules until, Ikuta et al. presented methods of synthesis of the smallest CD-molecules consisting of 3 and 4 glucopyranose units [1]. Larger cyclodextrins consisting of more than 8 glucose molecules have also been isolated and described. Unfortunately, their use in the industry is limited due to high costs, low efficiency, and problems with purification. Furthermore, larger CDs have a reduced complexing ability due to the smaller cavity. Cyclodextrins are cone-shaped. There are hydrophilic groups outside, which make the molecule hydrophilic, while the cavity is hydrophobic and can complex another hydrophobic substance. Among natural CDs, γ-CD is best soluble in water, while β-CD is the least, but β-CD has the most suitable cavity size for the formation of inclusion complexes with various substances. It is also the cheapest and the most available.

Cyclodextrin derivatives have been developed to improve physicochemical properties such as solubility and complexation (table 1). Increased solubility is possible due to the formation of methoxy derivatives, resulting in the

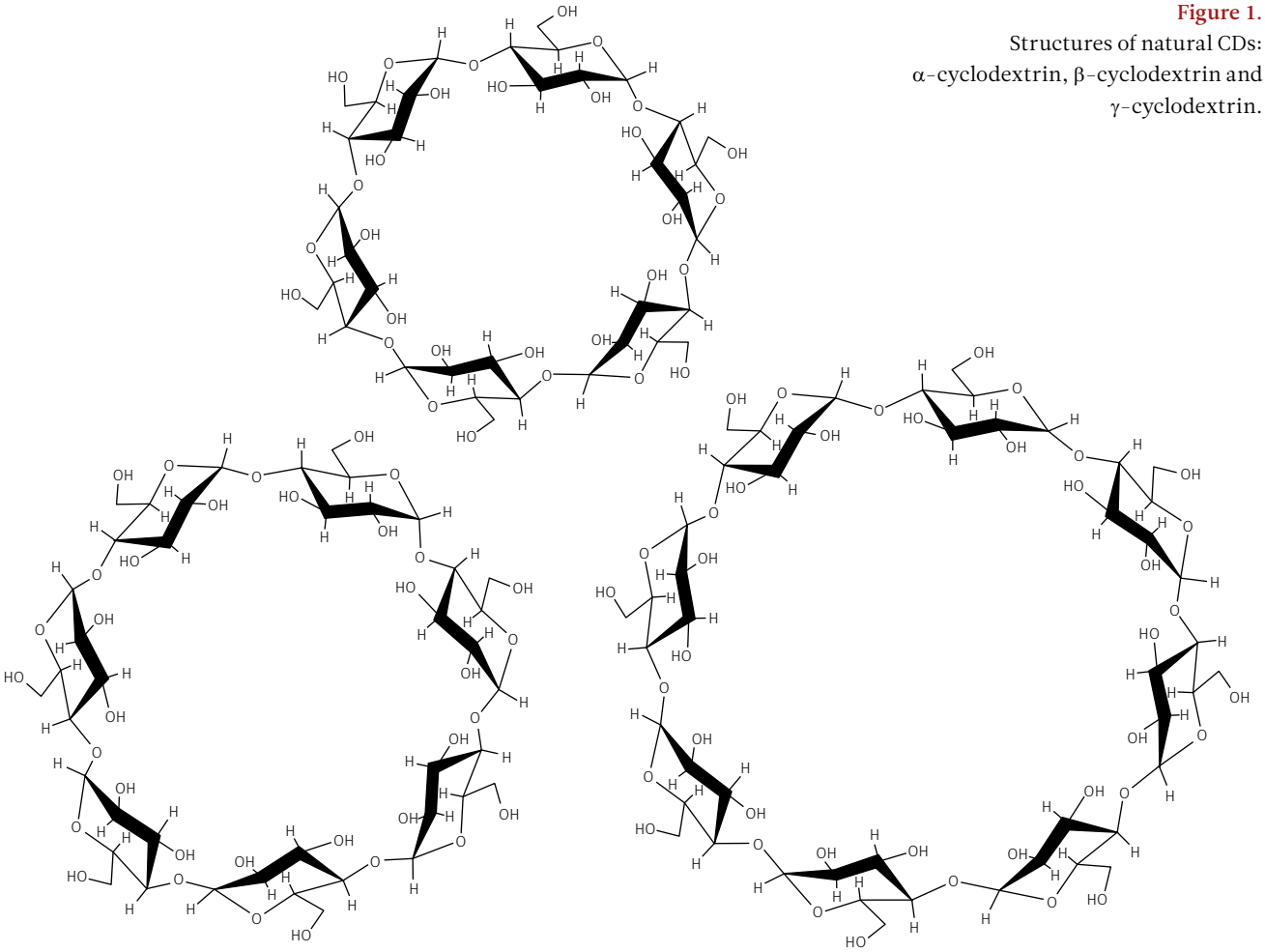

Figure 1.
Structures of natural CDs: α-cyclodextrin, β-cyclodextrin and γ-cyclodextrin.

Table 1. Structural and physicochemical properties of some cyclodextrins [1, 2].

CD	α-CD	β-CD	γ-CD	2-HPβCD	RMβCD	SBEβCD
Substituent	H	H	H	$CH_2CHOHCH_3$	CH_3	$(CH_2)_4SO_3Na$
Molecular weight (Da)	972	1135	1297	1400	1312	2163
Solubility (mg/mL, 25°C)	145	18.5	232	>1200	>500	>1200

2-HPβCD – hydroxypropyl-β-CD; RMβCD – randomly methyl-β-CD; SBEβCD – sulphobutylether-β-CD

transformation of the crystalline form into amorphous. Furthermore, substituents can lengthen the CD cavity, which improves the complexing capacity. Orally administered CDs have low bioavailability and are metabolized in the gastrointestinal tract. However, after parenteral administration, they have a low volume of distribution and are easily excreted in the urine [2].

The use of CDs in the food industry is based on animal toxicity studies. First, it is based on the observed effects, and the Acceptable Daily Intake (ADI) is calculated. For β-CD the ADI level was set at 5 mg/kg in a food product per day, while for both α-CD and γ-CD, ADI values have not been determined [3]. In 1998, β-CD was included in the list of Generally Recognized As Safe (GRAS) products as a safe agent, it can be used in food products in an amount of up to 2%. Depending on the route of administration, different toxicity of CDs is distinguished [4]. Orally administered cyclodextrins are non-toxic at low to moderate doses due to lack of absorption from the gastrointestinal tract. Due to nephrotoxicity and lower solubility β-CD cannot be administered parenterally. The approval status of o-methylated CDs varies according to the structure of the molecule, for example, heptakis-2,3,6-tris-o-methyl β-CD has hemolitic properties, and is nephrotoxic, and therefore is dangerous for humans while heptakis-2,6-di-o--methyl β-CD is hemolytic. However, derivatives such as HP-β-CD and sulphobutylether-β-CD are safe and can be administered parenterally.

Formation of inclusion complexes

The physicochemical properties of the free drug as well as the free cyclodextrin differ from the properties of the prepared inclusion complex. In aqueous solutions, the cyclodextrin cavity is occupied by water molecules, while during the formation of an inclusion complex, the hydrophobic active substances displace these water molecules. The formed complex easily dissociates causing the release of the drug molecule. Bonds, van der Waals and hydrophobic, are responsible for the formation of a stable inclusion complex. They also assure protection for the guest molecule against the attack of other reactive molecules and diminish the speed of processes such as oxidation, hydrolysis, racemization, and enzymatic degradation. The vast majority of complexes are in a stoichiometric ratio of 1 : 1, but the formation of higher-order complexes is also possible. Depending on the size of the cavity, CDs can form inclusion complexes with various molecules; α-CD can complex small molecules, while γ-CD forms complexes with the largest molecules, e.g. steroids [5]. Pharmaceutical preparations should contain as few CDs as possible, as they may affect the toxicology, weight, and price of the drug. It has been proven that complexation can be improved by selective functionalization or the addition of excipients. L-arginine added to the complex of cefuroxime axetil with β-CD significantly improved the physicochemical properties of the antibiotic. Thanks to this combination, it is possible to use less CD. Depending on the properties of the "guest" and CD, there are several ways to receive complexes.

Kneading method

This method is intended for substances poorly soluble in water, which slowly dissolve during the formation of the complex. The active substances are added to CD, knead in a mortar, and then dry. This method has good complexing efficiency but is not suitable for industrial complexing. This way was effective in the complexation of cefuroxime axetil, cefpodoxime proxetil, etoricoxib, or nimesulide [6].

Co-precipitation method

The substance is dissolved in organic solvents, e.g. benzene or chloroform. Then the suitable amount of CD is dissolved in water and added to the previously prepared solution. Then the mixture is cooled and crystals appear, which are washed with an organic solvent, and then dried at 50°C. This technique is useful for substances poorly soluble in water [6]. Due to its low efficiency, it is rarely used on an industrial scale. This method is used to form complexes with substances such as carvacrol, eugenol, catechin, meloxicam, and ketoconazole [7, 8].

Co-precipitation method based on phase solubility

The CD and the guest molecule are dissolved in water, and then slowly cooled. The resulting precipitate is separated by filtration and then dried. This is a time-consuming method and requires a large amount of water, therefore it is not used on an industrial scale [6].

Heating in a sealed container

The mixture of active substances and CD is sealed in a hermetic container, and heated in a temperature range of 43 to 142°C. In this way, a crystalline inclusion compound is formed. This technique is suitable for thermostable volatile substances, such as benzoic acid and paoenol [6].

Lyophilization

The specified proportion of active substance and CD are dissolved in water. Then the solvent is removed by ice sublimation under reduced pressure. The reaction is characterized by high efficiency, so it is possible to use this method in the industry [6]. Additionally, thanks to freeze-drying it is possible to use it for thermolabile compounds. Unfortunately, this method is expensive, and improperly stored products may get wet, which may result in e.g. microbiological contamination. The method has already been used to create complexes with drugs, such as valsartan, and trimethoprim [9, 10].

Spray drying

The "guest" and "host" molecules are dissolved in water and then dried in spray driers. This makes it possible to obtain a dry powder from a liquid. This technology may be used only for thermostable substances, due to the use of temperatures from 50 to 70°C. It is a quick and cheap method, so it can be used in large-scale production [6].

Antibacterial activity

Nowadays, antibiotic resistance is one of the biggest medical problems in the world. It is favored by their abuse and unjustified use. Thanks to the use of cyclodextrins, we can reduce the resistance of antibiotics by forming complexes, clogging the pores of pathogens by CDs, or reducing communication between cells.

Antimicrobial peptides are characterized by a broad spectrum of activity because they act on the bacterial membrane. Their positive hydrophilic groups react with the negatively charged cell membrane of bacteria, while the nonpolar groups react with fats of acidic residues. These reactions break the membrane of the bacteria. Using the microwave-assisted Huisgen reaction, CD derivatives were obtained, and their activity depended on the introduced substituents. The cyclic structure of the substituent showed greater antimicrobial activity than the linear chain on bacteria such as *S. aureus* and *E. coli*. Moreover, CDs with substituents of excessive hydrophobicity did not damage the bacterial membrane, unlike CD derivatives with lower hydrophobicity. The effect of CDs on antimicrobial activity was also studied in complexes with chlorhexidine (Cx) at various molar ratios (Cx to β-CD: 1:1, 1:2, 1:3, 1:4). The best antibacterial activity was shown by the inclusion of complexes in the ratio of 1:3 and 1:4. β-CD was ineffective in the MIC (minimum inhibitory concentration) test. The best results of obtained complexes may result both from the highest interaction of the complexes with the bacterial membrane, and the synergistic action of both compounds [11]. Calcagnile et al. conducted studies assessing the effect of cyclodextrins on the production of spiramycin by *Streptomyces ambofaciens*. They confirmed that methylo-β-CD stimulated the production of the antibiotic, while α-CD and β-CD did not cause significant changes [12].

The low water solubility of antibiotics results in low bioavailability after oral administration, which is associated with a reduced effect. The combination of cefdinir with β-CD and (2-HP)-β-CD improved the drug solubility and increased its antibacterial activity [13]. Other studies show that CDs also increase the solubility of e.g. enrofloxacin, cefpodoxime proxetil [14].

Linalool is an acyclic tertiary monoterpene alcohol that is found in many essential oils. It has antibacterial, analgesic, anti-inflammatory, and even local anesthetic properties. However, due to its volatility and poor water solubility, its use is limited. As an answer to these problems Aytac et al. proposed electrospinning technique using CD-linalool complexes. Three CDs were used in the research: HP-β-CD, methylated-β-CD, and HP-γ-CD. As a result, the thermal stability of linalool increased, which then released from CDs to a large extent inhibited the growth of *E.coli* and *S. aureus* [15].

Some food preservatives can be dangerous to health, e.g. sodium benzoate, a popular beverage preservative, can react with ascorbic acids to produce the carcinogenic benzene. Studies performed by Piper et al. on zebrafish larvae confirmed its neurotoxic and teratogenic effects [16]. Hexahydro-β-acids are natural substances obtained from *Humulus lupulus*, and can be used as safe food additives due to their antibacterial, antioxidant, and anti-inflammatory properties.

However, their use is limited because of their poor solubility in water. To overcome this problem, Zhao et al. prepared a hexahydro-β-acids/methyl-β-cyclodextrin inclusion complex (HBA/M-β-CD) inclusion complex. The study proved a favorable increase in solubility. In addition, the antimicrobial effect of the formed complex was confirmed by the disc diffusion method against most food-borne bacteria, e.g. *S. aureus*, *B. cereus*, *E. coli* [17].

Applicability of cyclodextrins

Cyclodextrins inclusion complexes with active substances can be analyzed by various methods. Each of them examines a specific property of the complex, so usually, several methods are needed to get a complete picture of the structure under study.

Spectroscopic techniques are based on the measurement of parameters such as absorbance, fluorescence, and NMR shift. Among the spectroscopic methods, we distinguish, among others: UV-VIS spectroscopy, circular dichroism spectroscopy, fluorescence spectroscopy, nuclear magnetic resonance (NMR) spectroscopy, and electron spin resonance. UV-VIS spectroscopy is usually used to detect inclusion complexes because slight shifts occur in the UV spectra of the complexed substances during complex formation, while NMR spectroscopy explains mainly the geometric adaptation of the visitor to the host cavity. Using spectroscopy, it is necessary to prepare a large number of samples, because the tests are carried out with a constant concentration of the "guest", and variable concentration of the host. The electroanalytical techniques include polarography and voltammetry, which are sensitive methods and do not require a large amount of sample for testing, as well as potentiometry and conductometry [18].

Separation techniques such as high-performance liquid chromatography (HPLC) or capillary electrophoresis (CE) are applied in the study of molecular interactions between the "guest" and cyclodextrin. Separation in CE is based on the different mobility of ionic compounds in the electric field. It is a highly efficient method and does not require a large amount of sample for analysis. Isothermal titration calorimetry (ICT) found application in determining the association constants and thermodynamic constants by measuring the heat released or absorbed during the binding process. Studies using ICT are time and sample-saving [19].

Cyclodextrine are mainly used in pharmacy, but also in the cosmetic and food industry. In the pharmaceutical industry, they are most often used as carriers of hydrophobic active substances, which solves the problem of absorption of orally insoluble drugs. It is known that increasing the solubility of active substances increases their bioavailability. Some medicinal substances have an unpleasant, bitter taste. This is very troublesome when they are intended to be used in the oral cavity, especially by pediatric patients. The use of complexes with CDs is a useful technique for masking unpleasant tastes. Jagdale et al. tried to remove the bitter taste of diltiazem hydrochloride used to treat high blood pressure and angina. The complexes of the drug with β-CD at a ratio of 1:1 were prepared using various techniques: freeze-drying, physical mixture, co-grounding, co-evaporation, and kneading method. To evaluate the taste, a scale of 1 to 5 was prepared, with 1 being no bitter taste and 5 with a very strong bitter taste. Free diltiazem hydrochloride was the control and showed a very strong bitter taste. Each of the 5 volunteers was administered free drug and next inclusion complexes. The study confirmed the ability of CDs to mask unpleasant taste, and the complex formed by freeze-drying had the least bitter taste [20]. Another study evaluated the impact of (2-HP)-β-CD on the taste of ranitidine hydrochloride using Insent TS-5000Z electronic tongue. The degree of taste masking is judged from the Euclidean distance between the inclusion complexes and the free drug. This is a more objective and safer method than human panels. The obtained results show that this distance increases with the increase of the molarity of the CD in the complex [21].

The use of curcumin may be limited due to its poor solubility in water and slightly acidic environment. The formation of an inclusion complex with CD reduces this problem leading to a significant increase in the water solubility of the drug product. Poor solubility also limits the use of chrysin, which is a bioflavonoid with anti-inflammatory and anti-cancer properties and occurs naturally in honey and plants. The formation of the complex of chrysin with CDs significantly improved the dissolving capacity of the bioflavonoid, and the permeability through the Caco-2 cell line. The experiment studied chrysin complexes with (2-HP)-β-CD, randomly-methyl-β-CD, β-CD, and sulphobutylated β-CD. Randomly-methyl- β-CD turned out to be the most effective [3].

CDs can also be used to increase the solubility and permeability of drugs administered in ophthalmology. They can also modify the rate of release, and diminish the irritant properties of these drugs. Eye drops containing α-CD and β-CD in an amount greater than 4% may cause

superficial epithelial toxicity, and the use of γ-CD and HP-β-CD is safer. HP-β-CD is used in eye drops containing substances such as flurbiprofen, nepafenac, amlodipine, or dexamethasone acetate [22]. Abdelkader et al. investigated the effects of various CDs on diclofenac administered after eye surgery to reduce pain and inflammation. The research was conducted using a drug and its complexes with α-CD, β-CD, γ-CD, and HP-β-CD. The evaluation was carried out using *in vitro* models and *in vivo* in rabbits. They confirmed that the addition of γ-CD and HP-β-CD resulted in faster healing without scarring compared to free diclofenac [23].

Photolability is an unfavorable feature of some medicinal substances. Effects of light on these substances may reduce their pharmacological effects or lead to serious adverse effects through the formation of toxic degradation products. In order to limit the degradation processes, several methods have been developed, such as the use of stabilizers, coating agents, selection of appropriate pH and solvent as well as the formation of inclusion complexes with cyclodextrins.

Tretinoin is a substance widely used in anti-acne products as well as in the treatment of psoriasis. Unfortunately, its disadvantage is thermal instability, which can significantly limit the effectiveness of therapy. Caddeo et al. investigated the effect of β-CD on the photostability and solubility of tretinoin. For this purpose, they prepared tretinoin-β-CD inclusion complexes using a freeze-drying procedure in the stoichiometric ratio of 1:1 and 1:3. The results showed the effectiveness of complexing in protection against UV radiation, and the 1:3 combination proved to be the most effective. In addition, the complexes were characterized by better solubility compared to free tretinoin [24]. Other popular drugs that show photolability are antihypertensive drugs with a dihydropyridine structure such as amlodipine, felodipine, isradipine, nifedipine, or nicardipine. The complexation of these drugs with β-CD also significantly improves their stability [25].

CDs can also improve the therapeutic effect of some drugs, which is associated with reduced frequency of intake and increased patient comfort. De Azevedo et al. demonstrated in rats that the oral dose of the drug could be reduced by combining captopril and α-CD [26].

Moreover, other studies show that CDs can also reduce the toxicity of the compound. For example, combining β-CD with nonsteroidal anti-inflammatory drugs such as etodolac, naproxen, and phenylbutazone, reduces gastric injury in rats [27].

Niemann-Pick disease type C is a rare genetic disorder caused by mutations in the NPC1 and NPC2 genes. It is characterized by the deposition of esterified cholesterol in cells, mainly the liver and central nervous system which leads to damage to these organs and ultimately to death. Most patients die between 10 and 25 years old. The study on mice showed that administration of allopregnanolone in a complex with HP-β-CD delayed the onset of neurological symptoms, and resulted in a reduction in cholesterol accumulation. Hastings et al. presented the efficacy, tolerability, and safety of the use of the complex in patients with Niemann-Pick disease. The drug proved to be well tolerated, easy to administer, and improved quality of life. However, further research into the safety assessment and the route of administration is required [28]. Another study shows the possible use of 6-o-α-maltosyl-β-CD in this disease. The studies were conducted on Chinese hamster ovary cells deficient in NPC1 and mice deficient in NPC1. Weekly subcutaneous injections improved cholesterol metabolism, increased serum transaminases, and hepatocytomegaly. In addition, this derivate is characterized by beneficial physicochemical properties such as low viscosity and low surface activity of the solution, therefore 6-O-α-maltosyl-β-cyclodextrin (G2-β-CD) may be a future drug candidate in the treatment of Niemann-Pick disease [29]. Some examples of the use of CDs in the pharmaceutical industry were presented in **table 2**.

Cyclodextrins are mainly used in cosmetic preparations to: improve the solubility of the active substance, increase the physical and chemical stability of the active substance, ensure controlled release, stabilize the emulsion or suspension, minimize skin irritation, and eliminate unwanted odors.

A large amount of active substances used in the cosmetic industry is very poorly soluble in water. Obtaining inclusion complexes solves this problem and improves biological activity. 7,3',4'-trihydroxyisoflavone is a compound very slightly soluble in water, which can be used in skin care products due to its antioxidant properties, protection against photodamage, and anti-cancer properties. The use of this compound in a complex with 2-HP-β-CD resulted in an increase in solubility and improved penetration through the skin [45]. Thanks to the possibility of complexing unpleasant odors, CDs are readily used in perfumes, antiperspirants, room fresheners, and also in diapers.

In the food industry CDs can protect the active ingredients from reactions caused by light or temperature. Citral, which is a component of essential oil, for example, lemons and oranges, under

Table 2. Examples of the use of cyclodextrins in the pharmaceutical industry.

Active substance	Cyclodextrin	Purpose of complexation	Ref.
Amylodipine besylate	β-CD	improving the bioavailability and stability	[30]
	β-CD, 2-HP-β-CD	increasing the photostability	[31]
Candesartan	β-CD	improving the bioavailability	[32]
Cefaclor	β-CD	increasing the stability	[33]
Donepezil	2-HP-β-CD	masking the bitter taste	[34]
Ezetimibe	2-HP-β-CD	increasing the solubility	[35]
Fenbendazole	HP-β-CD	increasing the solubility	[36]
Ketoconazole	β-CD	increasing the solubility	[8]
Meclizine	2-HP-β-CD	increasing the solubility	[37]
Nefopam	β-CD, Me-β-CD, HP-β-CD, HE-β-CD SBE-β-CD	increasing the solubility	[38]
Nimodipine	SBE-β-CD, HP-β-CD	increasing the solubility	[39]
Piroxicam	β-CD	improving the bioavailability	[40]
Ranitidine hydrochloride	2-HP-β-CD	masking the bitter taste	[21]
Rutin	β-CD	improving the stability and solubility	[41]
Sumatriptan	2-HP-β-CD	increasing the solubility and permeability through the biological membranes	[42]
Sulfanilamide	HP-β-CD	increasing the photostability and solubility	[43]
Tretinoin	β-CD	improving the photostability and solubility	[24]
Valsartan	β-CD	improving the solubility and dissolution rate	[44]

MeβCD – methylβ-CD; HeβCD – hydroxyethyl-β-CD; SBEβCD – sulphobutylether-β-CD

the influence of light cyclizes to photocytral. This reaction also produces p-cymene and other cyclic monoterpenes that can change the taste of citrus juices. However, when the citral was trapped in the β-CD molecule, no decomposition products were found after 6 hours of UV exposure. The effectiveness of thermal protection of CDs was also confirmed in a study using eugenol, a thermolabile essential oil with antimicrobial properties. The samples with β-CD and the complex were heated at 80°C for 2 hours. It was found that thanks to the use of the CD-eugenol complex it is possible to use this component at elevated temperatures while maintaining its antibacterial properties [46].

A popular use of CDs in the food industry is the removal of cholesterol from animal products. Adding CDs to the butter as a solid or solution allows the formation of a CD-cholesterol complex that is subsequently removed from the product. Alonso et al. confirmed the ability of β-CD to remove cholesterol from milk, natural egg, powdered egg, and duck liver pate [47]. They observed that a 5% concentration of β-CD is most suitable for removing about 80% of the cholesterol from these products. This technique allows obtaining products with a lower cholesterol content, which is especially important e.g. in the treatment of hypercholesterolemia.

CDs can also help to keep healthy body weight. It has been proved that α-CD reacts with dietary fat to form a stable complex that reduces the absorption of fats. Comerford et al. conducted a study assessing the effect of α-CD on the body weight of overweight people. The study participants were randomly divided into two groups: the control that was given tablets with cellulose, and the research group that was given tablets with α-CD. Participants were to take them with every meal containing fat, and not change their current lifestyle. Significant weight loss was found in the test group. There were also no side effects from α-CD, which however requires further confirmation [48].

CDs can also have an impact on the environment, by increasing the action, chemical, and thermal stability or reducing the volatility of plant protection products, which are currently very abused in agriculture. Oxadiargil is a pesticide used in rice cultivation, characterized by poor water solubility, therefore it easily accumulates in water reservoirs and soil, which causes rapid environmental poisoning. As an answer may be to increase its solubility by forming a complex with HP-β-CD. Thanks to the formation of inclusion complexes with CDs, the properties of carvacrol and linalool were also improved. These natural compounds are insecticidal and repellent, but

their use may be limited due to their low solubility and high photosensitivity [49]. The other study showed that methylo-β-CD improves the solubility of pesticides such as dimethoate, thiram, simazine, and linuron. This suggests that CDs can be used in combination with pesticides to increase their bioavailability and biodegradability [50].

For many years, the use of CDs in the analytical field has been quite common, due to the possibility of their use as chemical reagents in analyzes such as phosphorescence, fluorescence, UV visible light spectrophotometry, as well as in nuclear magnetic resonance methods. CDs are also used in the analysis of enantiomers by separation techniques such as capillary electrophoresis, high-performance liquid chromatography, thin layer chromatography, and gas chromatography. There are many examples in the literature of analyzes of different types of isomers (e.g. diastereoisomers, epimers), regarding drugs from various therapeutic groups and the use of different CDs, for example, amylodipine cetirizine, ibuprofen, tramadol, venlafaxine, cefuroxime axetil, and cefaclor [51–53].

Conclusion

Cyclodextrins are well-studied cyclic oligosaccharides. They are characterized by very good solvent properties and low toxicity, therefore they are most often used in the pharmaceutical industry as carriers of insoluble active substances. From the point of view of searching for new therapeutic strategies, cyclodextrins can modify the action of drugs, e.g. antibiotics, by changing their activity. They can also mask the unpleasant taste of orally active ingredients, reduce the toxicity of certain drugs, and increase the thermal stability of thermolabile substances. They have also gained popularity in analytical techniques, mainly due to the possibility of using them as chiral selectors. Due to their diverse properties, they are used in various disciplines (industry, laboratories), therefore, further studies are required in the search for new, more effective derivatives, resulting in broadening the spectrum of their application.

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