Abstract

Cyclodextrins (CDs) are cyclic oligosaccharides produced by enzymatic degradation of starch. The most common CDs are the main natural ones, α, β and γ, which are constituted of 6, 7 and 8 glucopyranose units, respectively. The CD structure forms a torus or doughnut ring and the molecule actually exists as a truncated cone. The outer side of the toroid is hydrophilic in nature due to the hydroxyl groups of the glucopyranose units while the internal cavity is relatively apolar. Thus, CDs have a high potential to entrap entirely or partially a wide variety of compounds in a process known as complexation. This gives them new physico-chemical properties and characteristics. The main applications of CDs in drug formulation rely on CD complexation and include the protection of easily oxidizable molecules or the improvement of aqueous solubility. The use of CDs in analytical chemistry is based on his host-guest recognition property, known as supramolecular complex formation. Currently, CDs are successfully used in molecular recognition-based methods like chromatographic separations, spectroscopic and electroanalyses. Quiral analytical separations are a CD area of special relevance. In this work, attention is paid to more recent references, especially to selected reviews.

Keywords: cyclodextrins, applications, encapsulation, controlled release, nano, food, cosmetic

1. Introduction

Cyclodextrins (CDs) at times referred as Schardinger sugars or cycloamylose dextrins, were fortuitously discovered [1, 2] by Vielliers in 1891, who named these compounds as “cellulosing.” Later on Schardinger, who is considered the founder of CD chemistry, gave a detailed description about preparation and separation of CD and, more recently, Kurkov and Loftsson [3] also made significant contributions to CD science.
Franz Schardinger, studying microorganisms which play a role in the deterioration of foods and by action of cyclodextrinase-Bacillus macerans amylase on the starch, obtained two distinct crystalline substances with similar properties to the already known partial degradation products of starch, the dextrins, so he named them α- and β-dextrin. The separation of the cycloalkyls may be carried out by selective precipitation by means of organic compounds or by high temperature chromatography on a cellulose column. French et al. demonstrated that CDs are cyclic oligosaccharides composed of several D-(+)-glucopyranose units in the form of a saddle [4]. In the second half of the 1930s, Freudenberg and his co-workers elucidated the cyclic structure of α-, and β-dextrin [5]. They consist of (α-1,4)-linked glucose units. A Greek letter preceding the abbreviation CD—for cyclodextrin—indicates the number of glucose units (α for 6, β for 7, and γ for 8) entering the composition of the cycloamylose. CDs constituted of less than 6 glucopyranose units cannot be formed due to steric hindrances [6]. Approximately, 1500 CD derivatives have been reported [7] in the literature.

CDs have a truncated cone appearance [7–12], and a doughnut, toroidal- or cylinder-like shape, due to the spatial arrangement characteristic of the various functional groups of the glucose units. As a consequence of this conformation, all the secondary hydroxyl groups (corresponding to the C2 and C3 carbon atoms of the glucose units) are at one of the edges of the cavity, whereas the primary hydroxyls are in the other end of the cavity. Rotation of these –OH groups reduces the effective size of the cavity, making it have a more open conical truncated aspect [13] toward the side of the secondary hydroxyls (Figures 1 and 2).

This spatial arrangement gives an apolar character to the interior of the cavity, whereas the presence of the –OH groups at the edges of the cone trunk makes them very water soluble. For instance, hydrophobic hosts will be housed inside the cavity because of the hydrophobic van der Waals type interactions, whereas simultaneously polar interactions

![Figure 1. Molecular structure of (a) α, (b) β, and (c) γ-CDs.](image-url)
can be established by the formation of hydrogen bridges between polar hosts and –OH of the primary hydroxyls. An endless number of physical and chemical processes [10, 14] are usually facilitated, that is, volatile substances may be stabilized by transforming in crystalline substances; oxygen-sensitive materials could find protection against oxidation; solubility and bioavailability of drugs could be improved [15–20] by participating in controlled delivery processes.

CDs have been the subject of a large number of studies dealing with complexation and molecular catalysis [21–25], as well as studies about hydrophobic effects and fine-tune models of biological processes. In 1953, the first patent on CDs and complexes was registered, but until 1970, only small amounts of relatively pure CDs were produced for industrial use due to their high production cost. Although in the beginning it was erroneously thought that CDs were toxic, currently, it is difficult to imagine a world without CDs [3] due to their potential use [26]. The number of possible applications seems to be unlimited, i.e., computer-aided drug design, pharmaceutical, medical, biomedical and biotechnological, drug and gene delivery, foods, foods additives and ingredients, food processing, cosmetic, textiles, industrial and analytical. Currently, patents on CDs are counted by thousands.

2. Inclusion complexes

An inherent interest surrounds these compounds due to their physical and chemicals properties [26–38]. The common feature of CDs is their ability to form inclusion complexes with a variety of molecules and ions, both in the solid state (crystalline substances) and in solution. As results of the structure of CDs, they can establish apolar-apolar interactions encapsulating other apolar molecules which may undergo structural changes [33–38], acting as molecular capsules [27–32]. However, the idea that one molecule could envelop another one to form a
new compound (adduct, inclusion complex) was not accepted until X-ray diffraction showed the formation of an inclusion complex between α-CD and iodine [37]. They constitute a significant example of relatively simple organic compounds showing complex formation with other organic molecules. They are excellent models of enzymes that lead to their use as catalysts [21, 24, 39], both in enzymatic and non-enzymatic reactions. Additionally, they are natural products and readily available to most researchers.

It is accepted [18, 38, 40–43] that the binding forces involved in complex formation are, in general:

i. van der Waals type interactions (or hydrophobic interactions) between the hydrophobic unit of the guest molecules and the CD cavity.

ii. Hydrogen bond between the polar functional groups of the guest molecules and the hydroxyl groups of the CD.

iii. Release of high energy water molecules from the cavity in the complex formation process.

iv. Release of strain energy into the ring structure system of the CD.

The role of the hydrogen bond is not universal since stable complexes are formed with hosts such as benzene, which do not form hydrogen bonds.

2.1. Factors affecting stability

Regardless of which type of stabilizing force is involved, the most important factors in determining the stability of the inclusion complex are [36, 40–45]:

- the geometric capability
- polarity of the guest molecules
- the medium
- temperature

Geometric, rather than chemical factors, are critical in determining the type of “guest” molecules that can penetrate into the cavity. If the guest is too small, it passes easily through the cavity and the bond will be weak or will not occur. The formation of complexes with molecules significantly larger than the cavity is also possible, but only some limited groups or side chains penetrate into the CD cavity.

The stability of an inclusion complex also depends on the polarity of the “guest” molecule. Only substrates that are less polar than water may form inclusion complexes with the CDs. The stability of a complex is proportional to the hydrophobic character of the “guest” molecule. Highly hydrophilic molecules form complex CDs very weakly or do not complex at all.

On the other hand, stability depends heavily on the nature of the medium used for complexation. In principle, the inclusion complexes may be formed either in solution [46–49] (generally carried out in the presence of water) or in the crystalline [40, 50–52] state. Although the formation of inclusion complexes also takes place [53] in an organic solvent, the guest molecules...
are weakly complexed. Additionally, although a 1:1 stoichiometry between the substrate and the CD molecule is typical [46, 54–56], with certain systems (Figure 3), 1:2 and 2:1 complex formations are possible. Experimentally determined formation constant can be the function (Figure 4) of the formation constants of the isomeric complexes [46]. In addition, substitution of one or more hydroxyls results in most cases in better water-soluble derivatives. For example, CDs can be polymerized [32, 36, 40, 42, 44, 45, 57] by suitable bio- or polyfunctional agents to oligomers, long-chain polymers or crosslinked or immobilized networks in various supports. Low molecular weight oligomeric CDs are readily soluble in water. Polymers (molecular mass over 10,000) are swollen gels which can be prepared in bead forms. The rigid structure of CDs “host” translates into well-defined and differentiated inclusion complex depending on the nature of the “guest” molecule.

Figure 3. Complexes of α-CDs and 1,4-disubstituted benzene [13].

Figure 4. Isomeric complexes from substrate and free ligand [55].
Finally, the stability of the inclusion complex, in general, decreases when temperature increases [46]. Enthalpy and entropy changes can be obtained from the temperature dependence of the equilibrium constant. An important issue, often overlooked in the CD field, is that the magnitudes of the standard free energy and entropy changes are dependent on the standard state chosen by the experimentalist.

### 3. Analytical and physicochemical applications

In the last years, CDs and their derivatives have been used in a variety of fields of analytical chemistry, especially in analytical separations [45, 58–63]. Spectral properties of CD and guest molecules can be altered due to the changes of the electrons distribution in the CD hole. CDs are used as reagent in different analyses such as UV-visible spectrophotometry, fluorescence [64, 65], phosphorescence [66, 67], and nuclear magnetic resonance methods [45, 68, 69].

The complexation of the analyte and/or the colored reagent can effectively change its properties. Among the most notable uses of this effect are: (i) enhancing the solubility of polar or non-polar analyte; (ii) enhancing the stability in polar or non-polar solution of reagents and colored complexes; (iii) increasing UV-visible absorption which improves the sensitivity of the colored reactions; and (iv) enhancing colored reactions selectivity. Luminescence techniques, in terms of fluorimetry and phosphorimetry, have reached a rapid development in routine analysis. However, many compounds luminesce very weakly in aqueous solution and the addition of CDs protects the excited (singlet or triplet) states of the possible dampers present in the solution since the rotation of the molecules is impeded due to the formation of the complex of inclusion with the result of a decrease in vibrational relaxation processes. The formation of inclusion complexes also increases the quantum fluorescence yield and hence the fluorescence intensities of numerous compounds. Sensitivity to certain characteristic reactions also increases.

CDs also increase the emission intensity of the chemiluminescent reactions. This improvement can be attributed to a number of factors, including an increase in the reaction rate and a greater efficiency in the process of excitation and protection of species that emit quenching phenomena. One of the most relevant applications of CDs is to allow the observation of phosphorescence at room temperature [67]. This is because they protect the excited triplet state of the molecules of the shock absorbers present in the solution, and in the case of molecular quenching phosphorescence. They are used as chiral reagents in NMR. In many cases, the formation of inclusion compounds modifies the general characteristics and chemical shifts of two enantiomers. Differences in the chemical shifts of two diastereoisomers can be used for the determination of the isomeric purity of the samples. The formation of inclusion complexes can very significantly modify the redox characteristics [13, 70, 71] of the included molecules. Voltammetric sensors capable of responding to anionic compounds have been developed. The changes produced after the complexation (selective interaction) allow the voltammetry to be used in the study of the complexation between CDs and organic molecules.
CDs increase the selectivity of chromatographic separations [72–74], because the separation process is more selective than that between the eluent and the stationary phase alone. In HPLC, the application of the CDs has achieved a spectacular success. Their incorporation into the mobile phase allows improving the separations, since they are soluble in water and provide reversible and selective complexation. In addition, they are stable and show no absorption in the UV-visible region of the electromagnetic spectrum. These characteristics mean that CDs are generally used in reverse phase separation processes, achieving the separation of isomers, diastereoisomers, and enantiomers [75–78]. The high resolution obtained is due to the differences in the stability constants of the complexes in the mobile phase and the different adsorption of these complexes in the stationary phase. CDs may also be incorporated as support for the stationary phases. Capillary electrophoresis has also found use in chiral analytical separations [79–82].

4. A primer on pharmaceutical, food and cosmetic cyclodextrin studies

4.1. Bioavailability

CDs have mainly been used as complexing agents to improve the aqueous solubility of molecules. This allows the use of CDs to reduce or prevent gastrointestinal or ocular irritation by lowering the local concentration of the free drug below the irritancy threshold. Also, unpleasant odor or taste of drugs can be hidden by complexation of the functional groups that produce them with CDs, occulting them from the sensory receptors [83–85], furthermore, reducing their hydrophobicity using CDs. Finally, CDs can increase percutaneous or rectal absorption of drugs and their derivatives can increase the guest molecule bioavailability [84]. Recently, CDs and their derivatives have been used in dispersed vehicle systems such as emulsions, microcapsules, microspheres, nanospheres, nanocapsules, liposomes, and beads [86]. Additionally, the host-guest property allows CDs to be used as building blocks in supramolecular chemistry [7]. Suvarna et al. [87] explain an insight in the use of CDs to increase the bioavailability to resolve the problem of solubility and stability of phytochemicals. The authors describe that some chemicals as quercetin, curcumin, artemisinin, resveratrol or naringenin increased their bioavailability due to the inclusion complexes with CDs. Authors concluded that CDs need to be more explored to cover some molecules that have potential biological activity but have not been approached.

4.2. Encapsulation

The encapsulation with CDs is gaining interest in different industries; this is reflected in the large number of publication and products related with it, such as drug delivery systems [7, 35]. This capacity of encapsulating compounds is used for a wide variety of things, among them is to protect the compounds, or to transport them to a target. This ability is due to the toroidal shape of CDs which makes possible to encapsulate hydrophobic molecules fully or
partially in their cavity [14, 35]. This characteristic let the CDs being used for oral, sublingual, ocular, nasal, rectal, pulmonary, dermal, and other drug delivery systems, especially in systems of type 1/1 (one molecule per CD). The encapsulation with CDs enhanced the bioavailability of lipophilic drugs, as they are 17β-estradiol, androstenediol, clomipramine, and others. A limitation of CD in sublingual route is that the quantity used for a proper formulation is too large to be considered. This increase in the bioavailability is also observed in the oral route for drugs such as diltiazem, flufenamic acid, molsidomine, salbutamol, having all of them a sustained release [88].

4.3. Controlled release

In order to optimize pharmacotherapy, drug release should be controlled in accordance with the therapeutic purpose and the pharmacological properties of the active substances. In recent years, the interest regarding the control of rate or time of delivery has significantly increased [88]. The multifunctional characteristics of CDs allow them to be used in most drug delivery systems [84]. The design process of drug delivery systems is currently more focused on the oral route, in which the release of the drug can be controlled by dissolution, diffusion, osmosis, density or pH. Challa et al. [89] give several examples of different uses in oral delivery. The use of β-CD increased the bioavailability of ketoprofen, terfenadine, and griseofulvin; but, the same CD, also demonstrated higher intensity or longer duration of therapeutic activity in tolbutamide or terfenadine. Although there are different effects depending on the modified CD used, for example, the solubility and dissolution rate can be increased using HP-β-CD, for drugs as albendazole, ketoprofen, phenytoin, and gliclazide; or an improvement of hydrolysis stability γ-CD, for drugs as digoxin, camptothesin and paclitaxel. For oral administration, all CDs can be used because they are not toxic.

4.4. Nano

The improvement of the efficacy and bioavailability of poorly soluble drugs can be achieved by nanoparticles, which are stable systems that are used to create drug delivery systems [83]. Nanoparticles are 100–10,000 times smaller than human cells and their uses revolutionize diagnosis, treatment, therapeutic efficacy, and patient compliance [83, 90]. However, nanoparticles are limited by their low drug loading and entrapment ability, which compromises their safety and efficacy [84]. The use of CDs as a polymer increases the loading capacity of nanoparticle systems [89]. Furthermore, the optimal drug bioavailability and biodistribution can be achieved with a proper manipulation of physico-chemical and biological mechanisms, which can be provided by the hybrid functionalities of CD nanosystems [91]. A new class of colloidal polymer is nanosponges, which consist of solid nanoparticles with colloidal shape and nanocavities. Examples of nanosponges are those based on CDs. It should be noted that the type, number, and position of the substituent on the CD affect the complexation ability of nanosponges. Thus, it is crucial to know which CD derivative to use. Tejashri et al. [92] expose the use of CD to make nanosponge, and the use of it to load drugs and use as carriers. The crosslinking of CDs with compounds, as carbonyl or dicarboxylate, creates the different types of nanosponge, polyamide, carbonate, etc. Authors concluded that this novel class of
CD-based nanosponge let drugs to be released in a controlled form at the target place, and its spherical shape let nanosponge to be administered as parental, aerosol, topical, tablets, and capsules forms.

4.5. Food

In last years the application of CDs in the food-industry have increased mainly due to the use of them as a protective agent against oxygen, to protect flavor of volatile compounds, to enriched food with vitamins and color components (such as anthocyanins) or to stabilize them [93, 94]. Another advantage for the food industry is that CD are tasteless, odorless, and non-caloric saccharides, and that they have an antidiabetic effect due to their low glycemic index and their capability to decrease the glycemic index of the food, and also to improve the cholesterol index. Human gastrointestinal enzymes cannot digest them, so it can be used as a dietary fiber, which is fermented by microflora, what makes them a prebiotic compound. All these properties make them nutraceuticals and bioactive food supplements [95, 96]. López-Nicolás et al. [97] analyzed the positive effects of CDs in the encapsulation of antioxidant, and the repercussion on important factors as Kf or pH values. They also reviewed the antioxidant capacity of CDs, but they concluded that there is a necessity of more studies in this aspect.

4.6. Cosmetic

The cosmetic industry is looking for products with a good biological activity and adequate delivery on the skin [98]. The applications of CDs in cosmetics are similar to the pharmaceutical ones, e.g., stabilizing substances or increasing their solubility [99–101]. Centini et al. [98] associated ferulic acid, which is a photoprotector agent and an antioxidant compound, and CD. However, ferulic acid is not too much used due to the instability of it in the presence of air, UV-light, and heat; so, the aim of the work was to enhance the physico-chemical stability. The authors concluded that the complex ferulic acid/CD have a better photostability and do not generate degradation products. Buschmann and Schollmeyer [99] explained the use of CD against the vaporization of slow release of the volatile compounds in perfumes; or the opposite, they also explained the use of CD to eliminate undesired odors, such as mercapto derivate used in waving lotion. More applications will become possible when CDs price decreases. CDs can also be used in the textile industry as depots of cosmetic molecules providing new cosmetic formulations.

4.7. Miscellaneous applications of cyclodextrins: tabular form

A more detailed picture of most recent selected applications in various areas, ranging from general reviews to inclusion complexes, metal and organometallic complexes, food, pharmaceutical, pharmacological, medical and biomedical, environmental chemistry, personal care and toiletry, industrial, nanotechnological, industrial and analytical applications to enzyme, biomimetic, bioactive assembles and recognition, as well as miscellaneous applications is compiled in Table 1, which gives an idea of the importance and relevance of the CDs field. Figure 5 shows the number of publications cited per year, whereas in Figure 6,
## General reviews

| Content                                                                 | Authors                        | Refs. |
|-------------------------------------------------------------------------|--------------------------------|-------|
| Overview about the work carried out on CDs concerning with: the general characteristics of CDs and derivatives, the preparation and evaluation of inclusion complexes, the use of CDs in the preparation of drug delivery systems, and their use for the preparation of biomaterials and nanoparticles. | Duchêne and Bochot (2016)      | [14]  |
| Comprehensive overview on the methods used for analysis of CDs and CD-derivatives. The paper intends to act as a guide in looking around the classical and modern instrumental analytical methods suitable for identification, characterization and determination of CDs themselves, CDs in finished products or even in biological samples. | Szente et al. (2016)           | [2]   |
| Current review on various aspects of CDs with regard to their chemical characteristics, properties, approaches used for complexation, characterization techniques, uses along with and future potential. | Khan and Durakshan (2013)       | [7]   |
| Pharmaceutical applications of CDs with an emphasis on their solubilizing properties, their tendency to self-assemble to form aggregates, CD ternary complexes, and their metabolism and pharmacokinetics. | Kurkov and Loftsson (2013)     | [3]   |
| Overview about several aspects related to the physico-chemical properties of CDs and their potential applications illustrated by recent examples. | Venturini et al. (2008)        | [102] |
| Inclusion complexation and CDs: physicochemical parameters of the guest molecule and improvements in the molecule’s solubility, stability, taste, safety, bioavailability, etc. | Mosher and Thompson (2007)     | [103] |
| CDs and their use in industrial products, technologies and analytical methods. | Martin del Valle (2004)        | [93]  |
| Overview about past, present, and future of CD research. Potential uses of CDs in pharmaceuticals, foods, cosmetics, and chemical products and technologies. | Szejtli (2004)                 | [26]  |
| CDs: structure, complex formation, drug solubility and non-conventional CD complexes. | Loftsson (2002)                | [9]   |
| Scientific and technological aspects of CDs: from computational chemistry to industrial uses of CDs. | D’souza and Lipkowitz (1998)   | [104] |
| History (the three stages in the development of CD chemistry), fundamentals of CD chemistry and future trends. | Szejtli (1998)                 | [105] |
| The properties and potential uses of CD derivatives: dimethyl- and dimethyl-βCD (DIMEB and TRIMEB). | Szejtli (1992)                 | [106] |
| Catalyses by CDs leading to practical usages: covalent, non-covalent and asymmetric catalyses by CDs. | Bender and Komiyama (1978)     | [107] |

## Inclusion complexes

| Content                                                                 | Authors                        | Refs. |
|-------------------------------------------------------------------------|--------------------------------|-------|
| The inclusion complex of oxyzresveratrol in modified CDs: a thermodynamic, structural, physicochemical, fluorescent and computational study. | Matencio et al. (2017)        | [108] |
| Content                                                                 | Authors                        | Refs  |
|------------------------------------------------------------------------|-------------------------------|-------|
| Summary of method for inclusion complex formation of CD with its guests and its applications. | Cheirsilp and Rakmai (2016)  | [42]  |
| Literature review to characterize the formation of inclusion complexes by different techniques in the solid and in the solution state complexation. | Maazaoui and Abderrahim (2015) | [44]  |
| Use of CDs as complexing agents to enhance the solubility of poorly soluble drugs and hence to resolve the many issues associated with developing and commercializing poorly water-soluble drugs. | Chaudhary and Patel (2013)   | [16]  |
| Survey of crystal structures of pure CD hosts and CD inclusion compounds carried out during the last six years. The entries range from simple alkylated derivatives to elegant multi-substituted target CD molecules, with and without included guests. | Caira (2011)                  | [40]  |
| CD inclusion of four phenylurea herbicides: determination of complex stoichiometries and stability constants using solution ¹H NMR spectroscopy. | Smith et al. (2010)            | [69]  |
| Comparison of the inclusion complexation between host and guest in CD chemistry with the coordination interaction between central ion (M⁺) and ligands in coordination chemistry. | Song et al. (2009)              | [36]  |
| Threading CDs molecules onto polymer chains to form crystalline inclusion complexes organized by non-covalent interactions. | Martinez and Gomez (2007)    | [109] |
| Practical considerations in development of solid dosage forms that contain CD. | Miller et al. (2007)          | [110] |
| CD inclusion complexes with a solvatochromic fluorescent probe: an undergraduate physical chemistry lab experiment to establish the solvatochromic nature of PRODAN and then use the changes in the emission spectra upon inclusion in β- or γ-CD to determine stoichiometry and formation constants for the complexes. | Baker et al. (2002)          | [111] |
| Some applications of CD/substrate inclusion complexes. | Crini et al. (2001)            | [8]   |
| Determination of thermodynamic parameters of the CD inclusion processes: an undergraduate physical chemistry lab experiment. | Valero et al. (1999)          | [112] |
| Complexation thermodynamics of CDs. | Rekharsky and Inoue (1998) | [113] |
| Applications of CDs to pharmaceutical industry and chemical catalysis. Analytical applications are also considered, since CDs inclusion improves the sensitivity and selectivity of most analytical methods. | Muñoz-Botella et al. (1995) | [37] |
| β-CD inclusion complexes with iodine: an advanced and inexpensive undergraduate chemistry experiment. | Diaz et al. (1994)          | [114] |
| Critical overview about past, present and future of CDs: properties, studies on CD inclusion compounds and its applications. | Davies et al. (1983)          | [115] |
| **Metal and organometallic complexes** | Prochowic et al. (2016)        | [116] |
| Synthesis, reactivity and structural diversity of well-defined metal complexes derived essentially from native CDs. Structural motifs for metal complexes based on CDs: from monomeric species, dinuclear systems, homo- and heterometallic sandwich-type complexes to cylindrical, extended structures. | Prochowic et al. (2016)        | [116] |
Overview of recent advances of CD catalyzed reactions, which is organized in the order of the following reaction types: the modified CD catalyzed organic reaction, CD catalyzed organic reaction of metal ion present, CD catalyzed organic reaction without metal ion, and CD catalyzed organic reactions in application of asymmetric synthesis and photochemical reactions.

Research and application of CDs and their derivatives in asymmetric and stereospecific syntheses, with their division into three main groups: (1) CDs promoting asymmetric and stereospecific catalysis in water; (2) CDs’ complexes with transition metals as asymmetric and stereospecific catalysts; and (3) CDs’ non-metallic derivatives as asymmetric and stereospecific catalysts.

Preparation and analysis of CD-based metal–organic frameworks: laboratory experiments adaptable for high school students.

Selectively functionalized CDs and their metal complexes: recent applications as chiral receptors and catalytic center in the mimicking of metalloenzymes.

Metal complexing properties of native CDs (including deprotonation in alkaline medium) and a report on some recent results on composition and stability of metal–CD complexes.

CDs as supramolecular hosts for organometallic complexes.

| Content | Authors | Refs. |
|---------|---------|-------|
| Overview of recent advances of CD catalyzed reactions, which is organized in the order of the following reaction types: the modified CD catalyzed organic reaction, CD catalyzed organic reaction of metal ion present, CD catalyzed organic reaction without metal ion, and CD catalyzed organic reactions in application of asymmetric synthesis and photochemical reactions. | Hong et al. (2015) | [117] |
| Research and application of CDs and their derivatives in asymmetric and stereospecific syntheses, with their division into three main groups: (1) CDs promoting asymmetric and stereospecific catalysis in water; (2) CDs’ complexes with transition metals as asymmetric and stereospecific catalysts; and (3) CDs’ non-metallic derivatives as asymmetric and stereospecific catalysts. | Macaev and Boldescu (2015) | [118] |
| Preparation and analysis of CD-based metal–organic frameworks: laboratory experiments adaptable for high school students. | Smith et al. (2015) | [49] |
| Selectively functionalized CDs and their metal complexes: recent applications as chiral receptors and catalytic center in the mimicking of metalloenzymes. | Bellia et al. (2009) | [119] |
| Metal complexing properties of native CDs (including deprotonation in alkaline medium) and a report on some recent results on composition and stability of metal–CD complexes. | Norkus (2009) | [120] |
| CDs as supramolecular hosts for organometallic complexes. | Hapiot et al. (2006) | [121] |

**Food applications**

Complexation of poorly water-soluble phytochemicals (flavonoids, phenolic derivatives, coumestans to triterpenes) with CDs to improve their aqueous solubility, stability, rate of dissolution and bioavailability.

CDs in food technology and human nutrition: benefits and limitations. The recent applications of CDs for reducing unwanted components, such as trans-fats, allergens, mycotoxins, acrylamides, bitter compounds, as well as in smart active packaging of foods are also overviewed.

History, chemistry, methods of complexation and application of CDs into different areas, particularly in the pharmaceutical and food industry.

Properties, enzymatic production, and food applications of α-CD, as well as its differences with β- and γ-CDs.

Studies on the complexes formed between several important types of antioxidant compounds and CDs.

Applications of CDs as food additives and in food processing: transport of previously nontransportable foods and prevention of the spread of microbial infections.

CDs as novel solutions for the food industry concerning with their role as dietary fiber, in food and drink with health-promoting additives, protect sensitive ingredients, improve taste and odor, or their positively influence to the texture and consistency of food.

Factors controlling flavors binding constants to CDs and their applications in foods.

| Content | Authors | Refs. |
|---------|---------|-------|
| Food applications | Suvarna et al. (2017) | [87] |
| Complexation of poorly water-soluble phytochemicals (flavonoids, phenolic derivatives, coumestans to triterpenes) with CDs to improve their aqueous solubility, stability, rate of dissolution and bioavailability. | Suvarna et al. (2017) | [87] |
| CDs in food technology and human nutrition: benefits and limitations. The recent applications of CDs for reducing unwanted components, such as trans-fats, allergens, mycotoxins, acrylamides, bitter compounds, as well as in smart active packaging of foods are also overviewed. | Fenyvesi et al. (2016) | [95] |
| History, chemistry, methods of complexation and application of CDs into different areas, particularly in the pharmaceutical and food industry. | Maazaoui and Abderrahim (2015) | [44] |
| Properties, enzymatic production, and food applications of α-CD, as well as its differences with β- and γ-CDs. | Li et al. (2014) | [122] |
| Studies on the complexes formed between several important types of antioxidant compounds and CDs. | López-Nicolás et al. (2014) | [97] |
| Applications of CDs as food additives and in food processing: transport of previously nontransportable foods and prevention of the spread of microbial infections. | Martina et al. (2013) | [123] |
| CDs as novel solutions for the food industry concerning with their role as dietary fiber, in food and drink with health-promoting additives, protect sensitive ingredients, improve taste and odor, or their positively influence to the texture and consistency of food. | Zipp (2012) | [96] |
| Factors controlling flavors binding constants to CDs and their applications in foods. | Astray et al. (2010) | [124] |
| Content                                                                 | Authors                     | Refs. |
|------------------------------------------------------------------------|-----------------------------|-------|
| CD encapsulation of essential oils and volatiles: methods for the      | Cabral Marques (2010)       | [33]  |
| preparation of inclusion complexes, analytical techniques and          |                             |       |
| applications.                                                          |                             |       |
| Practical aspects of the utilization of CDs and CD inclusion           | Moreira da Silva (2009)     | [125] |
| compounds to food manufacture, focusing on the technical advantages    |                             |       |
| of their use in food processing and as food additives.                 |                             |       |
| Use of CDs in the food industry: properties from a technological        | Astray et al. (2009)        | [94]  |
| point of view, such as solubility and their capability to form inclusion|                             |       |
| complexes are described.                                               |                             |       |
| Isolation and identification of native and branched-type (glucosylated| Szente et al. (2006)        | [35]  |
| and maltosylated) CDs in different enzyme- and heat-processed starch-|                             |       |
| containing food products.                                              |                             |       |
| Practical aspects of the utilization of CDs and CD complexes in the    | Szente and Szejtli (2004)   | [126] |
| food industry: molecular encapsulation of lipophilic food ingredients,|                             |       |
| long-term storage stability and technological advantages and food     |                             |       |
| processing technologies.                                               |                             |       |
| CDs: application to food processing.                                   | Yoshii (2004)               | [127] |

**Pharmaceutical applications**

**Reviews**

- CDs: history, chemical structure, synthesis, physicochemical properties, uses, complexation phenomenon, approaches for making inclusion complexes, and its characterisation, advantages of inclusion complexes, mechanism of drug release, regulatory status and its applications. Kanaka Durga Devi et al. (2010) [83]

- Basic science information and data on the development of drugs in CD-containing formulations. Loftsson and Brewster (2010) [128]

- Critical review about experimental methods for determination of the binding constant between CD and a guest molecule. Funasaki et al. (2008) [10]

- Historical development of CDs with emphasis on their use in pharmaceutical formulations. Loftsson and Duchêne (2007) [129]

- CD-based pharmaceutics: past, present and future applications. Davis and Brewster (2004) [130]

- CDs: structure, complex formation and drug solubility and non-conventional CD complexes. Loftsson (2002) [9]

- Main impetus for the research into CD-drug combinations. Frömming and Szejtli (1994) [131]

**Delivery release**

- Application of CD nanosystems for oral drug delivery: strategies for the synthesis of these nanosystems, and their potential for the intelligent navigation of the gastrointestinal tract for optimal bioavailability and biodistribution. Adeoye et al. (2017) [91]

- CD-mediated hierarchical self-assembly and its potential in drug delivery applications. Antoniuk and Amiel (2016) [132]

- Supramolecular nanostructures based on CD and poly(ethylene oxide): syntheses, structural characterizations and applications for drug delivery. Zheng and Wyman (2016) [133]
| Content                                                                                                                                                                                                 | Authors                          | Refs.  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|--------|
| Recent advances in drug delivery techniques utilizing CDs, and cyclic oligosaccharides consisting of α-1,4-linked α-D-glucopyranose units. Especially, drug delivery system consisting of combination systems of CDs and functional materials such as dendrimer, liposome and PEG are introduced. | Arima et al. (2015)             | [134]  |
| Relationship between CDs structure and physicochemical characteristics: self assembly and drug delivery. Importance of the nanoparticle technology preparation for the stability and application of this nanodevice.          | Bonnet et al. (2015)             | [135]  |
| CD-based carriers for delivery of chemotherapeutic cytotoxic anticancer drugs.                                                                                                                                              | Gidwani and Vyas (2015)          | [90]   |
| CD-based delivery systems for arthritic diseases: from development to experimental therapeutics.                                                                                                                                                   | Nascimento et al. (2015)        | [136]  |
| A vision for CD nanoparticles in drug delivery systems and pharmaceutical applications.                                                                                                                                               | Lakkakula and Krause (2014)     | [137]  |
| CD containing biodegradable particles: from preparation to drug delivery applications.                                                                                                                                               | Zafar et al. (2014)             | [138]  |
| State of the art and recent advances in the construction of CD-based assemblies and their applications for controlled drug delivery.                                                                                                                                               | Zhang and Ma (2013)              | [139]  |
| CD in drug delivery: complexing agents, bioavailability and industrial applications.                                                                                                                                                        | Chordiya Mayur and Senthilkumaran (2012) | [86]  |
| Recent developments of CDs in drug delivery using various routes of administration.                                                                                                                                                          | Laza-Knoerr et al. (2010)       | [140]  |
| Advantages of CD inclusion complexation, effects on important drug properties in formulation and applications in delivery systems (oral drug, rectal drug, nasal drug, transdermal drug, ocular drug, controlled and targeted drug, peptide and protein delivery, gene and oligonucleotide delivery, dermal and transdermal delivery, brain drug delivery or brain targeting). | Tiwari et al. (2010)            | [84]   |
| CD-based supramolecular architectures: syntheses, structures, and applications for drug and gene delivery.                                                                                                                                 | Li and Loh (2008)               | [141]  |
| Applications of CDs and their derivatives in different areas of drug delivery: parenteral, oral, ophthalmic and nasal drug delivery. Other routes including dermal, rectal, sublingual and pulmonary delivery are also briefly addressed. | Rasheed et al. (2008)           | [88]   |
| Applications and comparative benefits of use of CDs and their derivatives in the design of novel delivery systems like liposomes, microspheres, microcapsules, nanoparticles, CD grafted cellulosic fabric, hydrogels, nano- sponges, beads, nanogels/nanoassemblies and CD-containing polymers. | Vyas et al. (2008)              | [142]  |
| The utility of CDs for enhancing oral bioavailability.                                                                                                                                                                              | Carrier et al. (2007)           | [143]  |
| CDs as cosmetic delivery systems: study of ferulic acid/ CD association complexes at the light of its possible use as sunscreen.                                                                                                                                               | Centini et al. (2007)           | [98]   |
| Effects of hydrophilic CDs on drug permeation through membranes and possible mechanism of action based on the current knowledge of the structural characteristics of water and the unstirred water layer juxtaposed to the membrane of interest. | Loftsson et al. (2007)          | [144]  |
Interesting findings and applications of CDs and their derivatives in different areas of drug delivery, particularly in protein and peptide drug delivery and gene delivery. Applications in the design of various novel delivery systems like liposomes, microspheres, microcapsules, and nanoparticles.

CDs in drug delivery. Pharmaceutical products worldwide containing drug/CD complexes on the market.

Recent findings and applications of both unmodified and modified CDs for in vivo drug delivery. Use of CDs for parenteral, oral, ophthalmic, and nasal drug delivery. Other routes including dermal, rectal, and pulmonary delivery are also briefly addressed.

**Carrier**

Potential therapeutic application of dendrimer/CD conjugates with targeting ligands as advanced carriers for gene and oligonucleotide drugs.

Drug carrier systems based on CD supramolecular assemblies and polymers: present and perspectives.

CD-based polymeric nanoparticles as efficient carriers for anticancer drugs.

Potential use of chemically modified CDs as high-performance drug carriers in drug delivery systems with emphasis on the more recent developments.

CD drug carrier systems: characteristics, improvements of drug properties by CD complexation and CD-based drug delivery systems.

**Solubilization and permeation**

CDs in pharmaceutical formulations: solubilization, binding constant, and complexation efficiency.

Use of CDs as complexing agents to enhance the solubility of poorly soluble drugs and issues associated with developing and commercializing poorly water soluble drugs.

Pharmaceutical applications of CDs: effects on drug permeation through biological membranes.

General background to the use of CD as solubilizers as well as highlight kinetic and thermodynamic tools and parameters useful in the study of drug solubilization by CDs.

CDs as solubilizers as well as highlight kinetic and thermodynamic tools and parameters useful in the study of drug solubilization.

**Protein**

Use of CDs and their derivatives as antiaggregant agents in a number of proteins and some multimeric enzymes.

CD-based multivalent glycodisplays: covalent and supramolecular conjugates to assess carbohydrate–protein interactions.

CD interactions with protein-like structures in order to describe their possible applications in the formulation of pharmaceutical proteins.

| Content                                                                 | Authors                        | Refs. |
|------------------------------------------------------------------------|--------------------------------|-------|
| Interesting findings and applications of CDs and their derivatives in  | Challa et al. (2005)           | [89]  |
| different areas of drug delivery, particularly in protein and peptide  |                                 |       |
| drug delivery and gene delivery. Applications in the design of various  |                                 |       |
| novel delivery systems like liposomes, microspheres, microcapsules,    |                                 |       |
| and nanoparticles.                                                    |                                 |       |
| CDs in drug delivery. Pharmaceutical products worldwide containing     | Loftsson et al. (2005)          | [145] |
| drug/CD complexes on the market.                                       |                                 |       |
| Recent findings and applications of both unmodified and modified CDs  | Rajewski and Stella (1996)      | [54]  |
| for in vivo drug delivery. Use of CDs for parenteral, oral, ophthalmic,|                                 |       |
| and nasal drug delivery. Other routes including dermal, rectal, and    |                                 |       |
| pulmonary delivery are also briefly addressed.                        |                                 |       |
| Potential therapeutic application of dendrimer/CD conjugates with     | Arima et al. (2017)             | [146] |
| targeting ligands as advanced carriers for gene and oligonucleotide   |                                 |       |
| drugs.                                                                |                                 |       |
| Drug carrier systems based on CD supramolecular assemblies and         | González-Gaitano et al. (2017)  | [147] |
| polymers: present and perspectives.                                   |                                 |       |
| CD-based polymeric nanoparticles as efficient carriers for anticancer  | Duchène et al. (2016)           | [148] |
| drugs.                                                                |                                 |       |
| Potential use of chemically modified CDs as high-performance drug      | Rasheed et al. (2008)           | [88]  |
| carriers in drug delivery systems with emphasis on the more recent    |                                 |       |
| developments.                                                         |                                 |       |
| CD drug carrier systems: characteristics, improvements of drug         | Uekama et al. (1998)            | [149] |
| properties by CD complexation and CD-based drug delivery systems.     |                                 |       |
| CDs in pharmaceutical formulations: solubilization, binding constant, | Jambhekar and Breen (2016)      | [18]  |
| and complexation efficiency.                                           |                                 |       |
| Use of CDs as complexing agents to enhance the solubility of poorly    | Chaudhary and Patel (2014)      | [16]  |
| soluble drugs and issues associated with developing and commercializing|                                 |       |
| poorly water soluble drugs.                                            |                                 |       |
| Pharmaceutical applications of CDs: effects on drug permeation         | Loftsson and Brewster (2011)    | [150] |
| through biological membranes.                                          |                                 |       |
| General background to the use of CD as solubilizers as well as        | Brewster and Loftsson (2007)    | [15]  |
| highlight kinetic and thermodynamic tools and parameters useful in    |                                 |       |
| the study of drug solubilization by CDs.                              |                                 |       |
| CDs as solubilizers as well as highlight kinetic and thermodynamic    | Loftsson and Brewster (1996)    | [19]  |
| tools and parameters useful in the study of drug solubilization       |                                 |       |
| Use of CDs and their derivatives as antiaggregant agents in a number  | Oliveri and Vecchio (2016)      | [151] |
| of proteins and some multimeric enzymes.                              |                                 |       |
| CD-based multivalent glycodisplays: covalent and supramolecular       | Martínez et al. (2013)          | [152] |
| conjugates to assess carbohydrate–protein interactions.              |                                 |       |
| CD interactions with protein-like structures in order to describe     | Varca et al. (2010)             | [153] |
| their possible applications in the formulation of pharmaceutical proteins. |                                 |       |
| Content                                      | Authors                                   | Refs.   |
|---------------------------------------------|------------------------------------------|---------|
| **Encapsulation**                           |                                          |         |
| Encapsulation of CD/drug inclusion complex into conventional, deformable and double loaded liposomes: characteristics of these systems and advantages and disadvantages of each one. | Gharib et al. (2015)                      | [154]   |
| Encapsulation of biocides by CDs: toward synergistic effects against pathogens. | Nardello-Rataj and Leclercq (2014)       | [34]    |
| Use of CDs as encapsulating agents for bioactive plant molecules in the pharmaceutical field. | Pinho et al. (2014)                      | [35]    |
| **Excipients**                              |                                          |         |
| Background review for CDs used as excipients. | EMA/CHMP/333892/ (2013)                 | [155]   |
| CDs as functional excipients: methods to enhance complexation efficiency. | Loftsson and Brewster (2012)             | [156]   |
| **Formulations**                            |                                          |         |
| CDs in pharmaceutical formulations: structure and physicochemical properties, formation of complexes, and types of complex. | Jambhekar and Breen (2016)               | [17]    |
| Evaluation of CDs drug complexes in pharmaceutical formulation: preparation of sodium valproate phenytoin sodium/β-CD inclusion complex in a trial to stabilize the drug against moisture absorption and forming non-hygroscopic powders and preparation of phenytoin sodium/β-CD inclusion complex in a trial to stabilize the drug against moisture absorption and mask its bitter taste. | Akasha et al. (2014)                      | [157]   |
| CDs in topical drug formulations: drug delivery from aqueous CD solutions by diffusion and membrane controlled. | Loftsson and Masson, (2001)              | [158]   |
| **Miscellaneous**                           |                                          |         |
| Types of fluorophores which have been used for CD tagging: synthetic strategies used for the conjugation and pharmaceutical applications of these ‘visualized’ macrocycles including their use in photodynamic therapy. | Benkovics et al. (2017)                 | [159]   |
| CDs’ legacy as complexing agents and future prospects of this class of chemical entities in pharmaceutics as new active pharmaceutical ingredients. | di Cagno and Pio (2017)                  | [160]   |
| Use of CD in the different routes of drug administration. | Shimpi et al. (2005)                     | [161]   |
| Recent findings on the safety profiles of three natural CDs and several chemically modified CDs: stability against non-enzymatic and enzymatic degradations in various body fluids and tissue homogenates and their pharmacokinetics via parental, oral, transmucosal, and dermal routes of administration. | Irie and Hekama (1997)                   | [162]   |
| **Pharmacology**                            |                                          |         |
| Production, physiochemical properties, pharmacokinetics, toxicity and applications of γ-CD and its derivatives. | Saokham et al. (2017)                    | [15]    |
| Interactions between CDs and cellular components: medical applications. | Leclercq (2016)                          | [163]   |
| Inclusion of terpenes in CDs: preparation, characterization and pharmacological approaches. | Lima et al. (2016)                       | [164]   |
| Content                                                                 | Authors                                         | Refs.   |
|------------------------------------------------------------------------|-------------------------------------------------|---------|
| Self-assembly of CDs and their complexes in aqueous solutions.          | Ryzhakov et al. (2016)                          | [48]    |
| Diagnostic utility of flow cytometry and improvement of rocuronium-    | Takazawa et al. (2016)                          | [165]   |
| induced anaphylaxis with the use of sugammadex.                        |                                                 |         |
| Sugammadex for reversal of rocuronium-induced neuromuscular blockade   | Won et al. (2016)                               | [166]   |
| in pediatric patients: a systematic review and meta-analysis.          |                                                 |         |
| Improving the therapeutic response of analgesic drugs by CDs.          | De Oliveira et al. (2015)                       | [167]   |
| Types of CDs, and their efficacy, physicochemical properties and       | Lakkakula and Krause (2014)                     | [137]   |
| transformation into nanoparticles with interesting in vitro and in vivo |                                                 |         |
| applications.                                                          |                                                 |         |
| Potential therapeutic use of CDs and CD nanoparticles in neurodegenerative diseases, stroke, neuroinfections and brain tumors. | Vecseryès et al. (2014)                         | [168]   |
| Basic and clinical pharmacology of sulfobutylether-β-CD.               | Loftsson and Brewster (2010)                    | [128]   |
| Basic and clinical pharmacology of sulfobutylether-β-CD.               | Luke et al. (2010)                              | [169]   |
| CD introduction to anesthesia practice: form, function, and application. | Welliver (2007)                                 | [170]   |
| Findings on the safety profiles of three natural CDs and several        | Irie and Uekama (1997)                          | [162]   |
| chemically modified.                                                   |                                                 |         |
| Medical and biomedical                                                 |                                                 |         |
| Key features of the CDs therapeutic discovery. Application of         | Abdolmaleki et al. (2017)                       | [171]   |
| computational chemistry approaches such as QSAR/QSPR, molecular       |                                                 |         |
| docking, and molecular/quantum mechanics for modeling of CD-drug       |                                                 |         |
| system.                                                               |                                                 |         |
| Recent development of copolymeric delivery system for anticancer       | Feng et al. (2016)                              | [172]   |
| agents based on CD derivatives.                                        |                                                 |         |
| General features and applications of CDs and their interactions with   | Leclercq (2016)                                 | [163]   |
| isolated biomolecules leading to the formation of inclusion or         |                                                 |         |
| exclusion complexes: potential medical applications.                   |                                                 |         |
| Data on the general properties and complexing ability of CDs and       | Radu et al. (2016)                              | [173]   |
| assessment methods (phase solubility, DSC tests and X-ray diffraction, |                                                 |         |
| FTIR spectra).                                                        |                                                 |         |
| CD interactions with protein-like structures: possible applications in  | Vecseryès et al. (2014)                         | [168]   |
| the formulation of pharmaceutical proteins.                            |                                                 |         |
| Amphiphilic CDs and their applications: preparation of nanoparticles    | Parrot-Lopez et al. (2010)                      | [174]   |
| based on amphiphilic CDs for biomedical applications.                  |                                                 |         |
| A supramolecular approach to medicinal chemistry: essential roles      | Smith (2005)                                   | [175]   |
| played by intermolecular forces in mediating the interactions between   |                                                 |         |
| chemical molecules and biological systems.                             |                                                 |         |
| Medicinal applications of CDs: improvement of drug properties, use of  | Szejtli (1994)                                  | [176]   |
| drug/CD complexes, CDs in tabletting and direct treatment with CDs.    |                                                 |         |
| Environmental Chemistry and Applications                               |                                                 |         |
| Nanosponge CD polyurethanes and their modification with nanomaterials  | Leudjo Taka et al. (2017)                       | [177]   |
| for the removal of pollutants from waste water.                        |                                                 |         |
| Content                                                                 | Authors                        | Refs. |
|------------------------------------------------------------------------|-------------------------------|-------|
| Progress in the immobilization of β-CD and their application in adsorption of environmental pollutants. | Han et al. (2016)             | [178] |
| Interactions of CDs and their derivatives with toxic organophosphorus compounds. | Letort et al. (2016)          | [179] |
| CD inclusion of four phenylurea herbicides: determination of complex stoichiometries and stability constants using solution H NMR spectroscopy. | Smith et al. (2010)           | [69]  |
| Fluorescence spectroscopy as a tool to study the properties of CD host-guest complexes. Overview of recent studies concerned with exploiting the properties of CDs and their inclusion complexes to study energy transfer through the use of photochemical antennas and the development of chemical and environmental sensors. | Fakayode et al. (2007)        | [27]  |
| Synthesis and applications of adsorbents containing CDs in the field of chromatographic separations and in waste water treatment. | Crini and Morcellet (2002)    | [180] |
| **Personal care and toiletry**                                           |                               |       |
| CDs as cosmetic delivery system: study of ferulic acid/CD association complexes. | Centini et al. (2007)         | [98]  |
| Inclusion complex formation of CD with its guest and their applications in foods and flavors, personal care and toiletry, environment protection, pharmaceuticals among others. | Cheirsilp and Rakmai (2016)   | [42]  |
| Possible applications of CDs in cosmetic products and some examples of their present uses. | Buschmann and Schollmeyer (2002) | [99]  |
| **Industrial applications**                                             |                               |       |
| Enabling technologies and green processes in CD chemistry: microwaves, ultrasound and ball mills have become irreplaceable tools in the synthesis of CD derivatives. Examples of sonochemical selective modification of native α-, β- and γ-CDs including heterogeneous phase Pd- and Cu-catalysed hydrogenations and couplings. | Cravotto et al. (2016)        | [181] |
| Major fields of enzyme application and overview on previous protein engineering studies wherein natural enzymes were modified to meet the operational conditions required for industrial application. | Jemli et al. (2016)           | [24]  |
| Applications of CDs in medical textiles: general data properties and complexing ability of CDs and assessment methods (phase solubility, DSC tests and X-ray diffraction, FTIR spectra, analytical method). | Radu et al. (2016)            | [173] |
| Applications of CDs in various industrial products, technologies, analytical and chemical processes and recent industrial advancements. | Sharma and Baldi (2016)       | [182] |
| General features of β-CD and their applications in the textile industry: attachment technique of β-CD to the textile’s surface. | Bhaskara-Amrit et al. (2011)  | [183] |
| CDs in pharmaceutics, cosmetics, and biomedicine: current and future industrial applications. | Bilensoy (2011)               | [184] |
| Role of CDs in the textile chemical technology: remove the surfactants from the material or to inactivate them in liquid phase, to intensify the enzyme processes or as balancers in dyeing with reactive pigments. | Grigoriu and Popescu (2011)   | [185] |
| Amphiphilic CDs and their applications. Preparation of nanoparticles based on amphiphilic CDs for biomedical applications. | Parrot-Lopez et al. (2010)    | [174] |
| Content                                                                 | Authors                                      | Refs. |
|------------------------------------------------------------------------|----------------------------------------------|-------|
| Applications of CDs in pharmaceuticals with a major emphasis on drug delivery systems. Utility in a variety of foods, flavors cosmetics, packaging and textiles. | Singh et al. (2002)                           | [186] |
| Applications of CDs in pharmaceuticals, foods and flavours, cosmetics, chemical industry, agricultural industry and adhesives, coatings and other polymers. | Arenskötter et al. (2001)                     | [187] |
| Industrial applications of CDs. Production and analysis of complexes. | Hedges (1998)                                | [188] |
| Utilization of CDs in industrial products and processes: (i) textiles, fibers and papers; (ii) foods and cosmetics; (iii) plastics and rubber; (iv) photographic and recording materials; (v) biotechnology and (vi) environmental protection. | Szejtli (1997)                               | [189] |
| Overview about industrial uses of CDs and their derivatives.          | Duchêne and Wouessidjewe (1992)              | [190] |
| CD inclusion compounds in research and industry: production of pharmaceuticals, pesticides, foodstuffs, and toilet articles among others. | Saenger (1980)                               | [191] |
| **Nano**                                                               |                                              |       |
| General overview of CDs and pharmaceutical nanotechnology in oral delivery systems. Strategies for the synthesis of these nanosystems, and their potential for the intelligent navigation of the gastrointestinal tract for optimal bioavailability and biodistribution. | Adeoye and Cabral-Marques (2017)              | [91]  |
| Nanosponge CD polyurethanes and their modification with nanomaterials for the removal of pollutants from waste water. | Leudjo et al. (2017)                         | [177] |
| CD-based supramolecular host–guest interactions for engineering supramolecular nanoparticles: biomedical applications. | Mejia-Ariza et al. (2017)                    | [192] |
| CD-based polymeric nanoparticles as efficient carriers for anticancer drugs. | Duchene et al. (2016)                        | [148] |
| CD-based nanosponges: a versatile platform for cancer nanotherapeutics development. | Swanimathan et al. (2016)                    | [193] |
| Supramolecular nanostructures based on CD and poly(ethylene oxide): syntheses, structural characterizations and applications for drug delivery. | Zheng and Wyman (2016)                      | [133] |
| Nano-sized CD-based molecularly imprinted polymer adsorbents for perfluorinated compounds. | Karoyo and Wilson (2015)                     | [194] |
| Overall view of the diversity of designs of CD-based supramolecular nanosystems with a special focus on the advances materialized in the last five years, including clinical trials. | Simoes et al. (2015)                         | [195] |
| Recent advances in the construction of nanoassemblies driven by CD-based inclusion complexation and their application in biomedical and biomimetic fields. | Kang et al. (2014)                           | [196] |
| A vision for CD nanoparticles in drug delivery systems and pharmaceutical applications. | Lakkakula and Krause (2014)                  | [137] |
| Approaches tested to synthesize nano- to macro-size covalently cross-linked CD networks: (i) direct cross-linking through condensation with di- or multifunctional reagents, (ii) copolymerization of CD derivatives with acrylic/vinyl monomers, and (iii) grafting of CDs to preformed medical devices. | Concheiro and Alvarez-Lorenzo (2013)          | [197] |
Development of nanosponges as drug delivery systems, with special reference to CD based nanosponges.

Tejashri et al. (2013) [92]

Preparation, characterization and advantages for pharmaceutical and biomedical applications of CD-based nanogels.

Moya-Ortega et al. (2012) [198]

Formation and applications of CD nanoaggregates induced by guest molecules, the concerned thermodynamics behind the process and the effect of concentration of the guest molecules on the morphology of the aggregates.

Purkayastha et al. (2012) [199]

Approaches employed in delivering drugs to the central nervous system. Changes in blood-brain barrier function in several neurological disorders.

Martin-Banderas et al. (2011) [200]

Fabrication technologies of supramolecular systems including nanoplatforms and hydrogels as well as their applications in nanomedicine and pharmaceutical sciences.

Zhang and Ma (2013) [139]

Classification, physicochemical properties, efficacy and safety of nanoparticles prepared from different amphiphilic CDs are discussed in light of the current literature work with in vitro and in vivo findings.

Bilensoy and Hincal (2009) [201]

Analytical and physicochemical applications

Reviews

Classical and modern instrumental analytical methods suitable for identification, characterization and determination of CDs themselves, CDs in finished products or even in biological samples.

Szente et al. (2016) [2]

CDs in in sample preparation, sensitivity and selectivity improvement, enantio-separation, creating single-molecule sensors, and automatizing DNA sequencing.

Szente and Szeman (2013) [28]

CDs: from molecular recognition to CDs as enzyme models. Reactivity and chemistry, chromatography, X-ray, NMR plus other physicochemical methods, as well as model calculations, rotaxane and catenane structures, and applications in the pharmaceutical industry are overviewed.

Dodziuk (2006) [202]

Use of CDs in major areas of analytical chemistry such as chromatography, electrophoresis, spectroscopy, electrochemistry and as analytical sensors.

Mosinger et al. (2001) [203]

Role of CDs in three of the major areas of modern instrumental analysis: separations, spectroscopy and electrochemical analysis.

Armstrong (1998) [204]

Chirality

CD-functionalized monolithic capillary columns: preparation and chiral applications.

Adly et al. (2016) [205]

Recent developments in CD functionalized monolithic columns for the enantioseparation of chiral drugs.

Guo et al. (2016) [206]

Advances on the use of CDs in the chiral analysis of drugs by capillary electrophoresis.

Saz and Marina (2016) [80]
| Content                                                                                                                                                                                                 | Authors                  | Refs. |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|-------|
| Recent contributions to the understanding of the binding mechanism between chiral selectors and selectands in analytical enantioseparations including polysaccharide derivatives, CDs, cyclofructans, macrocyclic glycopeptides, proteins, brush-type selectors, ion-exchangers, polymers, crown ethers, ligand-exchangers, molecular micelles, ionic liquids, metal-organic frameworks and nucleotide-derived selectors. | Scriba (2016)            | [77]  |
| Development of cationic CDs for chiral separation. Update of the research endeavors of synthetic and analytical chemists in evaluating enantioselectivity of cationic CDs using different analytical methods and the study of the chiral recognition mechanism. | Zhou and Scriba (2016)   | [75]  |
| Advances in enantiomeric resolution on monolithic chiral stationary phases in liquid chromatography and electrochromatography.                                                                            | Al-Othman et al. (2014)  | [207] |
| Recent examples of mechanistic aspects of capillary enantioseparations with regard to mathematical modeling of enantioseparations, investigations of the analyte-complex structures as well as new chiral selectors and applications of chiral analyses by CE and CEC. | Jac and Scriba (2013)    | [208] |
| Review of the latest advances in developing modified CDs as chiral selectors for various chromatographic and electromigration techniques.                                                                        | Tang et al. (2013)       | [76]  |
| Chiral analysis of amphetamines, methadone and metabolites in biological samples by electrodriven methods.                                                                                             | Mandrioli et al. (2011)  | [209] |
| The growth and applications of CDs as chiral discriminator.                                                                                                                                              | Pathak and Pathak (2008) | [210] |
| CDs in capillary electrophoresis enantioseparations: recent developments and applications.                                                                                                                 | Scriba (2008)            | [90]  |
| Separation of enantiomeric barbiturates by capillary electrophoresis using a CD containing run buffer: a laboratory experiments for degree students.                                                        | Contradi et al. (1997)   | [82]  |

**Complexes characterization**

| Content                                                                                                                                                                                                 | Authors                  | Refs. |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|-------|
| Physicochemical characterization of CD-drug interactions in the solid state and the effect of water on these interactions.                                                                         | Ogawa and Takahashi (2015)| [52]  |
| Analytical techniques for characterization of CD complexes in the solid state.                                                                                                                      | Mura (2015)              | [51]  |
| Analytical tools which can be employed for the characterization of drug-CD inclusion complexes in solution, with emphasis on their respective potential merits, disadvantages and limits.                        | Mura (2014)              | [47]  |
| Surfactant-CD host-guest association: fundamentals, drawbacks and advantages of techniques commonly used to obtain insights on the structural and bulk solutions changes resulting from host-guest association mechanism, and corresponding methods for binding quantification. | Valente and Söderman (2014)| [30]  |
| CD inclusion complexes probed by NMR techniques.                                                                                                                                                    | Pessine et al. (2012)    | [45]  |
| A literature review of CD inclusion complexes characterization: X-ray diffraction, infrared spectroscopy and nuclear magnetic resonance.                                                          | Takahashi et al. (2012)  | [211] |
A literature review of CD inclusion complexes characterization: differential scanning calorimetry and thermogravimetry.  
**Takahashi et al. (2012)**  
[68]

A bilogarithmic method for the spectrophotometric evaluation of stability constants of 1:1 weak complexes from mole ratio data.  
**Boccio et al. (2006)**  
[212]

NMR studies of CDs and CD complexes. Comprehensive overview about the most important approaches to structural problems with CDs, mainly in solution.  
**Schneider et al. (1998)**  
[213]

The stability of CD complexes in solution: binding equilibria and kinetics, strengths and structures of CD complexes, the sources of CD complex stability and prediction of CD complex stability.  
**Connors (1997)**  
[46]

**Separation Methods**

State-of-the-art applications of CDs as functional monomers in molecular imprinting techniques.  
**Lay et al. (2016)**  
[214]

CDs in capillary electrophoresis: recent contributions, practical uses (e.g. solute-CD binding constant estimation and further potentials), developments and applications (mainly chiral and achiral analysis).  
**Escuder-Gilabert et al. (2014)**  
[79]

Recent developments and new trends.

- Separation processes in the presence of CDs using molecular imprinting technology and ionic liquid cooperating approach.  
  **Zhang et al. (2011)**  
  [59]

- Role of CDs in chromatography. Influence of The formation the physicochemical parameters of the guest molecule (adsorption capacity, polarity, hydrophobicity, etc.).  
  **Cserhat and Forgaes (2003)**  
  [71]

- Summary of the information concerning the synthesis of materials containing CDs and general overview of the different possible applications of CDs as sorbents in the field of separation techniques.  
  **Crini and Morcellet (2002)**  
  [180]

- CDs as a versatile tool in separation science. The techniques examined include gel electrophoresis, isotachophoresis, isoelectric focusing, preparative scale electrophoretic techniques, thin-layer chromatography, electrochemically modulated liquid chromatography, use of monolithic media in liquid chromatography, microdialysis, separation on hollow fibers, foam flotation enrichment, solid- and liquid-phase extractions, countercurrent chromatography, separation through liquid and composite membranes, and CD applications in molecularly imprinted polymers.  
  **Schneiderman and Stalcup (2000)**  
  [61]

- Utilization of CDs and their derivatives in gas-liquid and gas-solid-, gel-, inclusion-, thin-layer-, affinity-, and high performance liquid chromatography.  
  **Szejtli (1987)**  
  [215]

- Applications of CDs in chromatographic separations and purification methods.  
  **Hinze (1981)**  
  [73]

**Spectrofluorometric Methods**

- Spectrofluorometric analytical applications of CDs based on host-inclusion complex.  
  **Elbashir et al. (2014)**  
  [64]

- Room temperature phosphorescence in CDs: analytical applications.  
  **Muñoz de la Peña et al. (2000)**  
  [66]
### Electrochemical Methods

Advantages and detecting mechanism of electrochemical sensors based on CDs functionalized materials, and recent advances for CDs-based materials (including CDs/carbon nanotubes, CDs/graphene, CDs/conducting polymers and other CDs-based nanomaterials) in electrochemical sensing.

Zhu et al. (2016) [70]

Substrate/analyte solubilization and stabilization to the development of CD based sensors and detectors.

Szente and Szejtli (1998) [216]

State of the art of the electrochemistry of α-, β-, and γ-CDs and CD inclusion complexes and their polarographic and voltammetric assay.

Bersier et al. (1991) [71]

### Enzyme—Biomimetic-Bioactive assemblies recognition

General overview of three different categories of CD-based artificial enzymes including metal free CD-based artificial enzymes, CD-based artificial metalloenzymes and CD-based artificial enzymes with computational design, focusing on their rate acceleration factor.

Aghahosseini and Ramazani (2016) [21]

Major fields of enzyme application and overview on previous protein engineering studies wherein natural enzymes were modified to meet the operational conditions required for industrial application.

Jemli et al. (2016) [24]

Macromolecules based on recognition between CD and guest molecules: synthesis, properties and functions.

Liu et al. (2015) [217]

Representative contributions in the construction and the structural characteristics of CD-based supramolecular assemblies and their interactions with biologically important substrates.

Chen and Liu (2010) [218]

New chemistry based on the principles used by Nature: biomimetic chemistry.

Breslow (2009) [23]

Literature overview on reactions in which CDs bind substrates and then either catalyze their reactions or mimic a step in an enzymatic catalytic sequence.

Breslow and Dong (1998) [22]

Adjusting the lock and adjusting the key in CD chemistry. An introduction in biomimetic chemistry.

Breslow (1980) [219]

### Miscellaneous

Functioning via host–guest interactions: achievement of selective molecular adhesion, self-healing, toughness, and actuation properties. These functions have been achieved by reversible bond formation with CDs.

Takahama and Harada (2017) [29]

Qualitative and quantitative analysis of research outputs on molecular modeling in CDs.

Zhao et al. (2017) [220]

Supramolecular polymer assembly in aqueous solution arising from CD host-guest complexation. Effects of such complexation on properties at the molecular and macroscopic levels.

Wang et al. (2016) [32]

Superstructures with CDs: chemistry and applications.

Wenz and Monflier (2016) [221]
the number of papers cited by journal for the most cited journal (number of references ≥2) appears. Emphasis is stressed on reviews and taking into account the high number of references available, the authors apologize for those they may have overlooked or inadvertently omitted.

| Content                                                                 | Authors                        | Refs. |
|------------------------------------------------------------------------|-------------------------------|-------|
| Synthesis of CD half-channels derived by per-functionalization of the CD primary positions and their activity as channels assessed by the bilayer clamp technique. | Chui and Fyles (2014)         | [222] |
| Construction of supramolecular structures of CDs with some polymers (polyrotaxanes) and formation of supramolecular oligomers and polymers formed by CD derivatives. | Harada et al. (2009)          | [223] |
| Systematic analysis of methods that are available for modification of CDs. The focus is on methods for transformation where the number and the exact positions of modifications are ascertained and pure compounds with unambiguous structures are obtained. | Khan et al. (1998)            | [224] |
| Applications of computational chemistry to the study of CDs: molecular modeling, structural features of CDs, dynamical aspects of CD structure and computational studies of host–guest complexation. | Lipkowitz (1998)              | [225] |
| CD-based catenanes and rotaxanes.                                     | Nepogodiev et al. (1998)     | [226, 227] |
| Organic reactions mediated by CDs: effect in solid CD complexes.       | Takahashi (1998)              | [228] |

Table 1. Selected papers on food, pharmaceutical, pharmacology, cosmetic, industrial, and analytical applications of cyclodextrins (CDs).

![Figure 5. Number of publications cited per year.](image-url)
5. Conclusion

Currently, there are a large number of drugs with poor solubility, bioavailability, permeability issues, undesirable properties as taste and odor, and irritation potential, and CDs can become an useful tool for optimizing drugs problematic [84]. Additionally, new uses of cyclodextrins are being explored, in different fields as nanoparticles, liposome and microsphere. The ability of making inclusion complexes with drugs makes CDs have a great future, as reflected by the rising number of publications and patents having been filed. Some researchers also believe that there will be more a still wider use for CDs as the knowledge about their properties increase [7]. The studies of CD-based nanosystems have recently increased, as they become platforms providing pharmacokinetic and formulation design efficiency without posing security problems [91]. CDs are also generating interest for gene therapy and exploration of non-viral methods,
probably for the difficulties in viral gene delivery [7]. A new area which is going to increase, is the study of the effects of the environment in the reactivity between CD-guest molecules [115]. The creation of new types of CD is going to enhance due to the wide range of possibilities in the treatments of atherosclerosis, cancer, and degenerative brain disease that are considered lethal disease [160]. CDs will surprise us in the future with not predictable uses [184].

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**References**

[1] Crini G. Review: A history of cyclodextrins. Chemical Reviews. 2014;114(21):10940-10975

[2] Szente L, Szeman J, Sohajda T. Analytical characterization of cyclodextrins: History, official methods and recommended new techniques. Journal of Pharmaceutical and Biomedical Analysis. 2016;130:347-365

[3] Kurkov SV, Loftsson T. Cyclodextrins. International Journal of Pharmaceutics. 2013;453(1):167-180

[4] Berthelot M. Ciclodextrinas. In: Khymos FF, editor. Química y Medida. Madrid, Spain: Alhambra; 1969. pp. 312-438

[5] Cramer F, Hettler H. Inclusion compounds of cyclodextrins. Die Naturwissenschaften. 1967;54:625-632

[6] Gattuso G, Nepogodiev SA, Stoddart JF. Synthetic cyclic oligosaccharides. Chemical Reviews. 1998;98(5):1919-1958

[7] Khan NA, Durakshan M. Cyclodextrin: An overview. International Journal of Bioassays. 2013;2:858-865

[8] Crini G, Morcellet M, Morin N. Quelques applications des complexes d’inclusion cyclodextrine/substrat. L’Actualité Chimique. 2001;1:18-25

[9] Loftsson T. Cyclodextrins. Journal of Inclusion Phenomena and Macrocyclic Chemistry. 2002;44:213-218

[10] Funasaki N, Ishikawa S, Neya S. Advances in physical chemistry and pharmaceutical applications of cyclodextrins. Pure and Applied Chemistry. 2008;80(7):1511-1524
[11] Saenger W, Jacob J, Gessler K, Steiner T, Hoffmann D, Sanbe H, Koizumi K, Smith SM, Takaha T. Structures of the common cyclodextrins and their larger analogues beyond the doughnut. Chemical Reviews. 1998;98(5):1787-1802

[12] Saokham P, Loftsson T. γ-Cyclodextrin. International Journal of Pharmaceutics. 2017;516(1-2):278-292

[13] Maistrenko VN, Gusakov VN, Sangalov EY. Voltammetry of host-guest complexes. Journal of Analytical Chemistry (Engl. Trasl.). 1995;50:528-533

[14] Duchêne D, Bochot A. Thirty years with cyclodextrins. International Journal of Pharmaceutics. 2016;514(1):58-72

[15] Brewster ME, Loftsson T. Cyclodextrins as pharmaceutical solubilizers. Advanced Drug Delivery Reviews. 2007;59(7):645-666

[16] Chaudhary VB, Patel JK. Cyclodextrin inclusion complex to enhance solubility of poorly water soluble drugs: A review. International Journal of Pharmaceutical Sciences and Research. 2013;4(1):68-76

[17] Jambhekar SS, Breen P. Cyclodextrins in pharmaceutical formulations I: Structure and physicochemical properties, formation of complexes, and types of complex. Drug Discovery Today. 2016;21(2):356-362

[18] Jambhekar SS, Breen P. Cyclodextrins in pharmaceutical formulations II: Solubilization, binding constant, and complexation efficiency. Drug Discovery Today. 2016;21(2):363-368

[19] Loftsson T, Brewster ME. Pharmaceutical applications of cyclodextrins. 1. Drug solubilization and stabilization. Journal of Pharmaceutical Sciences. 1996;85(10):1017-1025

[20] Shieh WJ, Hedges AR. Properties and applications of cyclodextrins. Journal of Macromolecular Science Part A. 2006;33(5):673-683

[21] Aghahosseini H, Ramazani A. General overview on cyclodextrin-based artificial enzymes’ activity. Current Organic Chemistry. 2016;20(26):2817-2836

[22] Breslow R, Dong SD. Biomimetic reactions catalyzed by cyclodextrins and their derivatives. Chemical Reviews. 1998;98(5):1997-2012

[23] Breslow R. Biomimetic chemistry. The Journal of Biological Chemistry. 2009;284:1337-1342

[24] Jemli S, Ayadi-Zouari D, Hlima HB, Bejar S. Biocatalysts: Application and engineering for industrial purposes. Critical Reviews in Biotechnology. 2016;36(2):246-258

[25] Jabbari A, Sadeghian H. Amphiphilic cyclodextrins, synthesis, utilities and application of molecular modeling in their design. In: Demir Sezer A, editor. Recent Advances in Novel Drug Carrier Systems. Chapter 12. Rijeka: InTech; 2012. pp. 331-354. ISBN: 978-953-51-0810-8

[26] Szejtli J. Past, present, and future of cyclodextrin research. Pure and Applied Chemistry. 2004;76(10):1825-1845

[27] Fakayode SO, Lowry M, Fletcher KA, Huang X, Powe AM, Warner IM. Cyclodextrins host-guest chemistry in analytical and environmental chemistry. Current Analytical Chemistry. 2007;3(3):171-181
[28] Szente L, Szemán J. Cyclodextrins in analytical chemistry: Host-guest type molecular recognition. Analytical Chemistry. 2013;85:8024-8030

[29] Takashima Y, Harada A. Functioning via host-guest interactions. Journal of Inclusion Phenomena and Macrocyclic Chemistry. 2017;87(3-4):313-330

[30] Valente AJM, Söderman O. The formation of host-guest complexes between surfactants and cyclodextrins. Advances in Colloid and Interface Science. 2014;205:156-176

[31] Loftsson T, Másson M, Brewster ME. Self-association of cyclodextrins and cyclodextrin complexes. Journal of Pharmaceutical Sciences. 2004;93(5):1091-1099

[32] Wang J, Qiu ZQ, Wang YM, Li L, Guo XH, Pham DT, Lincoln SF, Prud’homme RK. Supramolecular polymer assembly in aqueous solution arising from cyclodextrin host-guest complexation. Beilstein The Journal of Organic Chemistry 2016;12:50-72

[33] Cabral Marques HM. A review on cyclodextrin encapsulation of essential oils and volatiles. Flavour Fragrance Journal. 2010;25(5):313-326

[34] Nardello-Rataj V, Leclerq L. Encapsulation of biocides by cyclodextrins: Toward synergistic effects against pathogens. Beilstein. The Journal of Organic Chemistry. 2014;10:2603-2622

[35] Pinho E, Grootveld M, Soares G, Henriques M. Cyclodextrins as encapsulation agents for plant bioactive compounds. Carbohydrate Polymers. 2014;101(1):121-135

[36] Song LX, Bai L, XM X, He J, Pan SZ. Inclusion complexation, encapsulation interaction and inclusion number in cyclodextrin chemistry. Coordination Chemistry Reviews. 2009;253(9-10):1276-1284

[37] Munoz-Botellas S, Del Castillo B, Martin MA. Cyclodextrins: Properties and applications of inclusion complex formation. Ars Pharmaceutica. 1995;36(2):187-198

[38] Li S, Purdy WC. Cyclodextrins and their applications in analytical chemistry. Chemical Reviews. 1992;92:1457-1470

[39] Szente L, Harangi J, Greiner M, Mandel F. Cyclodextrins found in enzyme- and heat-processed starch-containing foods. Chemistry & Biodiversity. 2006;3(9):1004-1014

[40] Caira MR. Structural aspects of crystalline derivatized cyclodextrins and their inclusion complexes. Current Organic Chemistry. 2011;15(6):815-830

[41] Iacovino R, Caso JV, Di Donato C, Malgieri G, Palmieri M, Russo L, Isernia C. Cyclodextrins as complexing agents: Preparation and applications. Current Organic Chemistry. 2017;21(2):162-176

[42] Cheirsilp B, Rakmai J. Inclusion complex formation of cyclodextrin with its guest and their applications. Biology, Engineering and Medicine. 2016;2(1):1-6

[43] Liu Y, Wang K. Thermodynamics of resulting complexes between cyclodextrins and bile salts. In: Morales-Rodriguez R, editor. Thermodynamics – Fundamentals and Its Application in Science. Chapter 12. Rijeka: InTech; 2012. pp. 305-318. ISBN: 978-953-51-0779-8
[44] Maazaoui R, Abderrahim R. Applications of cyclodextrins: Formation of inclusion complexes and their characterization. International Journal of Advanced Research. 2015;3(2):1030-1030

[45] Pessine FBT, Calderini A, Alexandrino GL. Review: Cyclodextrin inclusion complexes probed by NMR techniques. In: Kim D, editor. Magnetic Resonance Spectroscopy. Chapter 12. Rijeka: InTech; 2012. pp. 237-264. ISBN: 978-953-51-0065-2

[46] Connors KA. The stability of cyclodextrin complexes in solution. Chemical Reviews. 1997;97:1325-1357

[47] Mura P. Analytical techniques for characterization of cyclodextrin complexes in aqueous solution: A review. Journal of Pharmaceutical and Biomedical Analysis. 2014;101:238-250

[48] Ryzhakov A, Do Thi T, Stappaerts J, Bertoletti L, Kimpe K, Sá Couto AR, Saokham P, Van den Mooter G, Augustijns P, Somsen GW, Kurkov S, Inghelbrecht S, Arien A, Jimidar MI, Schrijnemakers K, Loftsson T. Self-assembly of cyclodextrins and their complexes in aqueous solutions. Journal of Pharmaceutical Sciences. 2016;105(9):2556-2569

[49] Smith MK, Angle SR, Northrop BH. Preparation and analysis of cyclodextrin-based metal-organic frameworks: Laboratory experiments adaptable for high school through advanced undergraduate students. Journal of Chemical Education. 2015;92(2):368-372

[50] Harata K. Structural aspects of stereodifferentiation in the solid state. Chemical Reviews. 1998;98(5):1803-1828

[51] Mura P. Analytical techniques for characterization of cyclodextrin complexes in the solid state: A review. Journal of Pharmaceutical and Biomedical Analysis. 2015;113:226-238

[52] Ogawa N, Takahashi C, Yamamoto H. Physicochemical characterization of cyclodextrin-drug interactions in the solid state and the effect of water on these interactions. Journal of Pharmaceutical Sciences. 2015;104(3):942-954

[53] Gelb RI, Schwartz LM, Radeos M, Edmonds RB, Laufer AA. Cyclohexaamylose complexation with organic solvent molecules. Journal of the American Chemical Society. 1982;104:6283-6288

[54] Rajewski RA, Stella VJ. Pharmaceutical applications of cyclodextrins. 2. In vivo drug delivery. Journal of Pharmaceutical Sciences. 1996;85(11):1142-1169

[55] Pendergast DD. Stability constants of α-cyclodextrin complexes of disubstituted benzenes: Interpretation of structural effects in terms of a binding. [PhD thesis]. University of Wisconsin-Madison; 1983

[56] Innocenti A. Stoichiometry and Research – The Importance of Quantity in Biomedicine. Rijeka: InTech; 2012. pp. 388. ISBN: 978-953-51-0198-7

[57] Martina K, Cravotto, G. Cyclodextrin as a food additive in food processing. In: Cirillo G, Spizzirri UG, lemma F, editors. Functional Polymers in Food Science: From Technology to Biology. Hoboken, NJ, USA: John Wiley & Sons, Inc., 2015
[58] Szejtli B, Zsadon T, Cserhati T. Cyclodextrin use in separations. In: Hinze WL, Armstrong DW, editors. Ordered Media in Chemical Separations. Washington, DC: ACS; 1987. pp. 200-217

[59] Zhang J, Shen X, Chen Q. Separation processes in the presence of cyclodextrins using molecular imprinting technology and ionic liquid cooperating approach. Current Organic Chemistry. 2011;1:74-85

[60] Khalafi L, Rafiee M. Cyclodextrin based spectral changes. In: Rádis Baptista G, editor. An Integrated View of the Molecular Recognition and Toxinology – From Analytical Procedures to Biomedical Applications. Chapter 19. Rijeka: InTech; 2013. pp. 471-493. ISBN: 978-953-51-1151-1

[61] Schneiderman E, Stalcup AM. Cyclodextrins: A versatile tool in separation science. Journal of Chromatography. B, Biomedical Sciences and Applications. 2000;745(1):83-102

[62] Singh V, He YP, Wang CF, JH X, Xu XN, Li HY, Singh P, York P, Sun LX, Zhang JW. A comparison report of three advanced methods for drug-cyclodextrin interaction measurements. Journal of Pharmaceutical and Biomedical Analysis. 2017;134:252-258

[63] Tablet C, Matei I, Hillebrand M. The determination of the stoichiometry of cyclodextrin inclusion complexes by spectral methods: Possibilities and limitations. In: Innocenti A, editor. Stoichiometry and Research – The Importance of Quantity in Biomedicine. Chapter 3. Rijeka: InTech; 2012. pp. 47-76. ISBN: 978-953-51-0198-7

[64] Elbashir AA. Supramolecular Analytical Applications of Cyclodextrins and their Derivatives Using Fluorescence Spectroscopy. New York: Nova Science Publishers; 2017. pp. 209-232

[65] Elbashir AA, Dsugi NFA, Mohmed TOM, Aboul-Enein HY. Spectrofluorometric analytical applications of cyclodextrins. Luminescence. 2014;29(1):1-7

[66] Muñoz de la Peña A, Mahedero MC, Bautista Sánchez A. Room temperature phosphorescence in cyclodextrins. Analytical applications. Analusis. 2000;28(8):670-678

[67] Gunshefski M, Santana JJ, Stephenson J, Stephenson J, Winefordnet JD. Solid-phase room-temperature phosphorescence. Applied Spectroscopy Reviews. 1992;27(2):143-192

[68] Takahashi AI, Veiga FJB, Ferraz HG. A literature review of cyclodextrin inclusion complexes characterization – Part III: Differential scanning calorimetry and thermogravimetry. International Journal of Pharmaceutical Sciences Review and Research. 2012;12(1):16-20

[69] Smith VJ, Bogdan D, Caira MR, Bogdan M, Bourne SA, Fărcaș SI. Cyclodextrin inclusion of four phenylurea herbicides: Determination of complex stoichiometries and stability constants using solution 1H NMR spectroscopy. Supramolecular Chemistry. 2010;22(3):172-177

[70] Zhu G, Yi Y, Chen J. Recent advances for cyclodextrin-based materials in electrochemical sensing. Trends in Analytical Chemistry. 2016;80:232-241
[71] Bersier PM, Bersier J, Klingert B. Electrochemistry of cyclodextrins and cyclodextrin inclusion complexes. Electroanalysis. 1991;3(6):443-455

[72] Cserhati T, Forgacs E. Cyclodextrins in chromatography. In: Smith RM, editor. RSC Chromatography Monographs. United Kingdom: Series; 2003. p. 170. DOI: 10.1039/1757-7063

[73] Hinze WL. Applications of cyclodextrins in chromatographic separations and purification methods. Separation and Purification Methods. 1981;10:159-237

[74] Zhu Q, Scriba GKE. Advances in the use of cyclodextrins as chiral selectors in capillary electrokinetic chromatography: Fundamentals and applications. Chromatographia. 2016;79(21-22):1403-1435

[75] Zhou J, Tang J, Tang W. Recent development of cationic cyclodextrins for chiral separation. Trends in Analytical Chemistry. 2015;65:22-29

[76] Tang W, Ng S, Sun D. In: Tang W, editor. Modified Cyclodextrins for Chiral Separation. Berlin Heidelberg: Springer-Verlag; 2013. pp. 258. ISBN: 978-3-642-37647-4

[77] Scriba GKE. Chiral recognition in separation science – An update. Journal of Chromatography. A. 2016;1467:56-78

[78] Guttman A, Aumateli A, Brunet S, Cooke N. Cyclodextrin array chiral analysis. American Laboratory. 1995;27(18):18-22

[79] Escuder-Gilabert L, Martín-Biosca Y, Medina-Hernández MJ, Sagrado S. Cyclodextrins in capillary electrophoresis: Recent developments and new trends. Journal of Chromatography. A. 2014;1357:2-23

[80] Saz JM, Marina ML. Recent advances on the use of cyclodextrins in the chiral analysis of drugs by capillary electrophoresis. Journal of Chromatography. A. 2016;1467:79-94

[81] Scriba GKE. Cyclodextrins in capillary electrophoresis enantioseparations – Recent developments and applications. Journal of Separation Science. 2008;31(11):1991-2011

[82] Contradi S, Vogt C, Rohde E. Separation of enantiomeric barbiturates by capillary electrophoresis using a cyclodextrin containing run buffer. Journal of Chemical Education. 1997;74(9):1122

[83] Kanaka Durga Devi N, Prameela Rani A, Muneer Aved M, SaiKumar K, Kaushik J, Sowjanya V. Cyclodextrins in pharmacy – An overview. Pharmacophore. 2010;1(3):155-165

[84] Tiwari G, Tiwari R, Rai AK. Cyclodextrins in delivery systems: Applications. Journal of Pharmacy & Bioallied Sciences. 2010;2(2):72-79

[85] Das SK, Rajabalaya R, David S, Gani N, Khanam J, Nanda A. Cyclodextrins-the molecular container. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2013;4(2):1694-1720

[86] Chordiya Mayur A, Senthilkumaran K. Cyclodextrin in drug delivery: A review. Research & Reviews In Pharmacy & Pharmaceutical Sciences. 2012;1(1):19-20
[87] Suvarna V, Gujar P, Murahari M. Complexation of phytochemicals with cyclodextrin derivatives – An insight. Biomedicine & Pharmacotherapy. 2017;88:1122-1144

[88] Rasheed A, Kumar CKA, Sravanthi VVNSS. Cyclodextrins as drug carrier molecule: A review. Scientia Pharmaceutica. 2008;76(4):567-598

[89] Challa R, Ahuja A, Ali J, Khar RK. Cyclodextrins in drug delivery: An updated review. AAPS PharmSciTech. 2005;6(2):E329-E357

[90] Gidwani B, Vyas A. A comprehensive review on cyclodextrin-based carriers for delivery of chemotherapeutic cytotoxic anticancer drugs. BioMed Research International. 2015;2015:1-15

[91] Adeoye O, Cabral-Marques H. Cyclodextrin nanosystems in oral drug delivery: A mini review. International Journal of Pharmaceutics 2017. DOI: http://dx.doi.org/doi:10.1016/j.ijpharm.2017.04.050

[92] Tejashri G, Amrita B, Darshana J. Cyclodextrin based nanosponges for pharmaceutical use: A review. Acta Pharmaceutica. 2013;63(3):335-358

[93] Martín del Valle EM. Cyclodextrins and their uses: A review. Process Biochemistry. 2004;39(9):1033-1046

[94] Astray G, Gonzalez-Barreiro C, Mejuto JC, Rial-Otero R, Simal-Gandara J. A review on the use of cyclodextrins in foods. Food Hydrocolloids. 2009;23(7):1631-1640

[95] Fenyvesi É, Vikmon MA, Szente L. Cyclodextrins in food technology and human nutrition: Benefits and limitations. Critical Reviews in Food Science and Nutrition. 2016;56:1981-2004

[96] Zipp H. Cyclodextrins – Novel solutions for the food industry. Food Ingredients Brasil. 2012;22:56

[97] López-Nicolás JM, Rodríguez-Bonilla P, García-Carmona F. Cyclodextrins and antioxidants. Critical Reviews in Food Science and Nutrition. 2014;54(2):251-276

[98] Centini M, Maggiore M, Casolaro M, Andreassi M, Maffei Facino R, Anselmi C. Cyclodextrins as cosmetic delivery systems. Journal of Inclusion Phenomena and Macroyclic Chemistry. 2007;57(1-4):109-112

[99] Buschmann H-J, Schollmeyer E. Applications of cyclodextrins in cosmetic products: A review. Journal of Cosmetic Science. 2002;53(3):185-191

[100] Voncina B, Vivod V. Cyclodextrins in textile nishing. In: Günay M, editor. Eco-Friendly Textile Dyeing and Finishing. Chapter 3. Rijeka: InTech; 2013. pp. 53-75. ISBN: 978-953-51-0892-4

[101] Voncina B. Application of cyclodextrins in textile dyeing. In: Hauser PJ, editor. Textile Dyeing. Chapter 17. Rijeka: InTech; 2013. pp. 373-392

[102] Venturini CDG, Nicolini J, Machado C, Machado VG. Properties and recent applications of cyclodextrins. Quimica Nova. 2008;31(2):360-368
[103] Mosher G, Thompson DO. Complexation: Cyclodextrins. In: Encyclopedia of Pharmaceutical Technology. New York: Marcel Dekker, Inc.; 2007. pp. 671-696

[104] D’Souza VT, Lipkowitz KB. Cyclodextrins: Introduction. Chemical Reviews. 1998;98(5):1741-1742

[105] Szejtli J. Introduction and general overview of cyclodextrin chemistry. Chemical Reviews. 1998;98(97):1743-1753

[106] Szejtli J. The properties and potential uses of cyclodextrin derivatives. Journal of Inclusion Phenomena and Molecular Recognition in Chemistry. 1992;14(1):25-36

[107] Bender ML, Komiyama M. Cyclodextrin chemistry. In: Hafner K, Rees CW, Trost BM, Lehn J-M, von Rague Schleyer P, Zahradnik R, editors. Reactivity and Structure Concepts in Organic Chemistry. Vol. 6. Berlin Heidelberg: Springer-Verlag; 1978. p. 269. ISBN-13: 978-3-642-66844-9. Available from: http://link.springer.com/10.1007/978-3-642-66842-5

[108] Matencio A, García-Carmona F, López-Nicolás JM. The inclusion complex of oxyresveratrol in modified cyclodextrins: A thermodynamic, structural, physicochemical, fluorescent and computational study. Food Chemistry. 2017;232:177-184

[109] Martínez G, Gómez MA. Ciclodextrinas: Complejos de inclusión con polímeros. Revista Iberoamericana de Polímeros. 2007;8(4):300-312

[110] Miller LA, Carrier RL, Ahmed I. Practical considerations in development of solid dosage forms that contain cyclodextrin. Journal of Pharmaceutical Sciences. 2007;96(7):1691-1707

[111] Baker GA, Crane NJ, Mayrhofer RC, Betts TA. Cyclodextrin inclusion complexes with a solvatochromic fluorescent probe. Journal of Chemical Education. 2002;79(10):1261

[112] Valero M, Rodriguez LJ, Velázquez MM. Determination of thermodynamic parameters of the cyclodextrin inclusion processes: An undergraduate physical chemistry lab experiment. Journal of Chemical Education. 1999;76(3):418

[113] Rekharsky MV, Inoue Y. Complexation thermodynamics of cyclodextrins. Chemical Reviews. 1998;98(5):1875-1918

[114] Diaz D, Vargas-Baca I, Gracia-Mora J. Beta-cyclodextrin inclusion complexes with iodine: An advanced and inexpensive undergraduate chemistry experiment. Journal of Chemical Education. 1994;71(8):708

[115] Davies JED, Kemula W, Powell HM, Smith NO. Inclusion compounds – past, present, and future. Journal of Inclusion Phenomena. 1983;1(1):3-44

[116] Prochowicz D, Kornowicz A, Justyniak I, Lewiński J. Metal complexes based on native cyclodextrins: Synthesis and structural diversity. Coordination Chemistry Reviews. 2016;306:331-345

[117] Hong SB, Liu MY, Zhang W, Deng W. Organic reactions catalyzed by cyclodextrin and its derivatives. Chinese Journal of Organic Chemistry. 2015;35(2):325-336
Macaev F, Boldescu V. Cyclodextrins in asymmetric and stereospecific synthesis. Symmetry-Basel. 2015;7(4):1699-1720

Bellia F, La Mendola D, Pedone C, Rizzarelli E, Saviano M, Vecchio G. Selectively functionalized cyclodextrins and their metal complexes. Chemical Society Reviews. 2009;38(9):2756-2781

Norkus E. Metal ion complexes with native cyclodextrins: An overview. Journal of Inclusion Phenomena and Macrocyclic Chemistry. 2009;65(3):237-248

Hapiot F, Tilloy S, Monflier E. Cyclodextrins as supramolecular hosts for organometallic complexes. Chemical Reviews. 2006;106(3):767-781

Li Z, Chen S, Gu Z, Chen J, Wu J. Alpha-cyclodextrin enzymatic production and food applications. Trends in Food Science and Technology. 2014;35(2):151-160

Martina K, Binello A, Lawson D, Jicsinzsky L, Cravotto G. Recent applications of cyclodextrins as food additives and in food processing. Current Nutrition & Food Science. 2013;9(3):167-179

Astray G, Mejuto JC, Morales J, Rial-Otero R, Simal-Gándara J. Factors controlling flavors binding constants to cyclodextrins and their applications in foods. Food Research International. 2010;43(4):1212-1218

Moreira Da-Silva A. Cyclodextrins as food additives and ingredients: Nutraceutical applications. In: Conference Paper. May, 2009. Available from: https://www.researchgate.net/publication/246546437_CYCLODEXTRINS_AS_FOOD_ADDITIVES_AND_INGREDIENTS_NUTRACEUTICAL_APPLICATIONS

Szente L, Szefli J. Cyclodextrins as food ingredients. Trends in Food Science and Technology. 2004;15(3-4):137-142

Yoshii H. Application to food processing of cyclodextrin. Nippon Shokuhin Kagaku Kogaku Kaishi. 2004;51(12):647-655

Loftsson T, Brewster ME. Pharmaceutical applications of cyclodextrins: Basic science and product development. The Journal of Pharmacy and Pharmacology. 2010;62(11):1607-1621

Loftsson T, Duchêne D. Cyclodextrins and their pharmaceutical applications. International Journal of Pharmaceutics. 2007;329(1-2):1-11

Davis ME, Brewster ME. Cyclodextrin-based pharmaceutics: Past, present and future. Nature Reviews. Drug Discovery. 2004;3:1023-1035

Frömming K-H, Szejtli J. Cyclodextrins in pharmacy. In: Davies JED, editor. Topics in Inclusion Science. Vol. 5. Dordrecht-Boston-London: Kluwer Academic Publishers; 1994. p. 233

Antoniuk I, Amiel C. Cyclodextrin-mediated hierarchical self-assembly and its potential in drug delivery applications. Journal of Pharmaceutical Sciences. 2016;105(9):2570-2588
[133] Zheng Y, Wyman IW. Supramolecular nanostructures based on cyclodextrin and poly(ethylene oxide): Syntheses, structural characterizations and applications for drug delivery. Polymer. 2016;8(5):198

[134] Arima H, Hayashi Y, Higashi T, Motoyama K. Recent advances in cyclodextrin delivery techniques. Expert Opinion on Drug Delivery. 2015;12(9):1425-1441

[135] Bonnet V, Gervaise C, Djedaini-Pilard F, Furlan A, Sarazin C. Cyclodextrin nanoassemblies: A promising tool for drug delivery. Drug Discovery Today. 2015;20(9):1120-1126

[136] Nascimento MHM, Akkari ACS, Mariano KCF, Braz ASK, Lombello CB, de Araujo DR. Cyclodextrin-based delivery systems for arthritic diseases: From development to experimental therapeutics. Current Pharmaceutical Design. 2015;21(33):4907-4916

[137] Lakkakula JR, Krause RWM. A vision for cyclodextrin nanoparticles in drug delivery systems and pharmaceutical applications. Nanomedicine (London, England). 2014;9(6):877-894

[138] Zafar N, Fessi H, Elaissari A. Cyclodextrin containing biodegradable particles: From preparation to drug delivery applications. International Journal of Pharmaceutics. 2014;461(1-2):351-366

[139] Zhang J, Ma PX. Cyclodextrin-based supramolecular systems for drug delivery: Recent progress and future perspective. Advanced Drug Delivery Reviews. 2013;65(9):1215-1233

[140] Laza-Knoerr AL, Gref R, Couvreur P. Cyclodextrins for drug delivery. Journal of Drug Targeting. 2010;18(9):645-656

[141] Li J, Loh XJ. Cyclodextrin-based supramolecular architectures: Syntheses, structures, and applications for drug and gene delivery. Advanced Drug Delivery Reviews. 2008;60(9):1000-1017

[142] Vyas A, Saraf S, Saraf S. Cyclodextrin based novel drug delivery systems. Journal of Inclusion Phenomena and Macrocyclic Chemistry. 2008;62(1-2):23-42

[143] Carrier RL, Miller LA, Ahmed I. The utility of cyclodextrins for enhancing oral bioavailability. Journal of Controlled Release. 2007;123(2):78-99

[144] Loftsson T, Vogensen SB, Brewster ME, Konradsdottir F. Effects of cyclodextrins on drug delivery through biological membranes. Journal of Pharmaceutical Sciences. 2007;96(10):2532-2546

[145] Loftsson T, Jarho P, Másson M, Järvinen T. Cyclodextrins in drug delivery. Expert Opinion on Drug Delivery. 2005;2(2):335-351

[146] Arima H, Motoyama K, Higashi T. Potential therapeutic application of dendrimer/cyclodextrin conjugates with targeting ligands as advanced carriers for gene and oligonucleotide drugs. Therapeutic Delivery. 2017;8(4):215-232

[147] Gonzalez-Gaitano G, Isasi JR, Velaz I, Zornoza A. Drug carrier systems based on cyclodextrin supramolecular assemblies and polymers: Present and perspectives. Current Pharmaceutical Design. 2017;23(3):411-432
Duchene D, Cavalli R, Gref R. Cyclodextrin-based polymeric nanoparticles as efficient carriers for anticancer drugs. Current Pharmaceutical Biotechnology. 2016;17(3):248-255

Uekama K, Hirayama F, Irie T. Cyclodextrin drug carrier systems. Chemical Reviews. 1998;98(81):2045-2076

Loftsson T, Brewster ME. Pharmaceutical applications of cyclodextrins: Effects on drug permeation through biological membranes. The Journal of Pharmacy and Pharmacology. 2011;63(9):1119-1135

Oliveri V, Vecchio G. Cyclodextrins as protective agents of protein aggregation: An overview. Chemistry – An Asian Journal. 2016;11(11):1648-1657

Martínez Á, Ortiz Mellet C, García Fernández JM. Cyclodextrin-based multivalent glyco-displays: Covalent and supramolecular conjugates to assess carbohydrate-protein interactions. Chemical Society Reviews. 2013;42(11):4746-4773

Varca GHC, Andréo-Filho N, Lopes PS, Ferraz HG. Cyclodextrins: An overview of the complexation of pharmaceutical proteins. Current Protein & Peptide Science. 2010;11(4):255-263

Gharib R, Greige-Gerges H, Fourmentin S, Charcosset C, Auezova L. Liposomes incorporating cyclodextrin-drug inclusion complexes: Current state of knowledge. Carbohydrate Polymers. 2015;129:175-186

European Medicines Agency. Background Review for Cyclodextrins Used as Excipients – In the Context of the Revision of the Guideline on ‘Excipients in the Label and Package Leaflet of Medicinal Products for Human Use’ (CPMP/463/00 Rev. 1). 2014. pp. 1-17. Available from: www.ema.europa.eu/contact

Loftsson T, Brewster ME. Cyclodextrins as functional excipients: Methods to enhance complexation efficiency. Journal of Pharmaceutical Sciences. 2012;101(9):3019-3032

Akasha AA, Elwahedi MA, Eldeeb AM. Cyclodextrins and their pharmaceutical applications. PharmaTutor Magazine. 2014;2(7):40-46

Loftsson T, Masson M. Cyclodextrins in topical drug formulations: Theory and practice. International Journal of Pharmaceutics. 2001;225(1-2):15-30

Benkovics G, Malanga M, Fenyvesi É. The ‘Visualized’ macrocycles: Chemistry and application of fluorophore tagged cyclodextrins. International Journal of Pharmaceutics. 2017;531(2):689-700

di Cagno M, Pio M. The potential of cyclodextrins as novel active pharmaceutical ingredients: A short overview. Molecules. 2016;22(1):1-14

Shimpi S, Chauhan B, Shimpi P. Cyclodextrins: Application in different routes of drug administration. Acta Pharmaceutica. 2005;55(2):139-156

Irie T, Uekama K. Pharmaceutical applications of cyclodextrins. III. Toxical issues and safety evaluation. Journal of Pharmaceutical Sciences. 1997;86(2):147-162

Leclercq L. Interactions between cyclodextrins and cellular components: Towards greener medical applications? Beilstein Journal of Organic Chemistry. 2016;12:2644-2662
[164] Lima PSS, Lucchese AM, Araujo HG, Menezes PP, Araujo AAS, Quintans LJ, Quintans JSS. Inclusion of terpenes in cyclodextrins: Preparation, characterization and pharmacological approaches. Carbohydrate Polymers. 2016;151:965-987

[165] Takazawa T, Mitsuhashia H, Mertes PM. Sugammadex and rocuronium-induced anaphylaxis. Journal of Anesthesia. 2016;30(2):290-297

[166] Won YJ, Lim BG, Lee DK, Kim H, Kong MH, Lee IO. Sugammadex for reversal of rocuronium-induced neuromuscular blockade in pediatric patients: A systematic review and meta-analysis. Medicine. 2016;95(34):4678

[167] de Oliveira MGB, Guimaraes AG, Araujo AAS, Quintans JSS, Santos MRV, Quintans LJ. Cyclodextrins: Improving the therapeutic response of analgesic drugs: A patent review. Expert Opinion on Therapeutic Patents. 2015;25(8):897-907

[168] Vecseryes M, Fenyesi F, Bacsokay I, Deli MA, Szente L, Fenyesi É. Cyclodextrins, blood-brain barrier, and treatment of neurological diseases. Archives of Medical Research. 2014;45(8):711-729

[169] Luke DR, Tomaszewski K, Damle B, Schlamm HT. Review of the basic and clinical pharmacology of sulfobutylether-beta-cyclodextrin (SBECD). Journal of Pharmaceutical Sciences. 2010;99(8):3291-3301

[170] Welliver M. Cycloextrin introduction to anesthesia practice: Form, function, and application. AANA Journal Course. 2007;75(4):289-296

[171] Abdolmaleki A, Ghasemi F, Ghasemi JB. Computer-aided drug design to explore cyclodextrin therapeutics and biomedical applications. Chemical Biology and Drug Design. 2017;89(2):257-268

[172] Feng RL, Deng PZ, Teng FF, Song ZM. Recent development of copolymeric delivery system for anticancer agents based on cyclodextrin derivatives. Anti-Cancer Agents in Medicinal Chemistry. 2016;16(3):299-308

[173] Radu CD, Parteni O, Ochiuz L. Applications of cyclodextrins in medical textiles – Review. Journal of Controlled Release. 2016;224:146-157

[174] Parrot-Lopez H, Perret F, Bertino-Ghera B. Amphiphilic cyclodextrins and their applications. Preparation of nanoparticles based on amphiphilic cyclodextrins for biomedical applications. Annales Pharmaceutiques Françaises. 2010;68(1):12-26

[175] Smith DKA. supramolecular approach to medicinal chemistry: Medicine beyond the molecule. Journal of Chemical Education. 2005;82(3):393

[176] Szejtli J. Medicinal applications of cyclodextrins. Medicinal Research Reviews. 1994;14(3):353-386

[177] Leudjo Taka A, Pillay K, Yangkou Mbianda X. Nanosponge cyclodextrin polyurethanes and their modification with nanomaterials for the removal of pollutants from waste water: A review. Carbohydrate Polymers. 2017;159:94-107

[178] Han YQ, Zhou WJ, Shen HM, Liu QP, WY Y, Ji HB, She YB. Progress in the immobilization of beta-cyclodextrin and their application in adsorption of environmental pollutants. Chinese Journal of Organic Chemistry. 2016;36(2):248-257
[179] Letort S, Balieu S, Erb W, Gouhier G, Estour F. Interactions of cyclodextrins and their derivatives with toxic organophosphorus compounds. Beilstein Journal of Organic Chemistry. 2016;12:204-228

[180] Crini G, Morcellet M. Synthesis and applications of adsorbents containing cyclodextrins. Journal of Separation Science. 2002;25(13):789-813

[181] Cravotto G, Caporaso M, Jicsinszky L, Martina K. Enabling technologies and green processes in cyclodextrin chemistry. Beilstein Journal of Organic Chemistry. 2016;12(1):278-294

[182] Sharma N, Baldi A. Exploring versatile applications of cyclodextrins: An overview. Drug Delivery. 2016;23(3):729-747

[183] Bhaskara-Amrit UR, Agrawal PB, Warmoeskerken MMCG. Applications of beta-cyclodextrins in textiles. Autex Research Journal. 2011;11(4):94-101

[184] Bilensoy E. Cyclodextrins in pharmaceutics, cosmetics, and biomedicine: Current and future industrial applications. Hoboken, New Jersey: John Wiley & Sons, Inc.; 2011. ISBN: 9780470926819

[185] Grigoriu A, Popescu O. Applications of cyclodextrines in textiles – A review. Buletinul Institutului Politehnic din Iaşi. 2011;11:94-101

[186] Singh M, Sharma R, Banerjee UC. Biotechnological applications of cyclodextrins. Biotechnology Advances. 2002;20(5-6):341-359

[187] Arenskötter M, Folmer F, Llewellyn C, Pardo A, Reinecke F, Trebbi G. Cyclodextrins. An overview. Intensive Program Agriculture: Source of Raw Materials for Industry. Germany: Gent. 2001:1-7. Available from: http://www.oocities.org/florecitafolmer/paper04a.htm

[188] Hedges AR. Industrial applications of cyclodextrins. Chemical Reviews. 1998;98(5):2035-2044

[189] Szejtli J. Utilization of cyclodextrins in industrial products and processes. Journal of Materials Chemistry. 1997;7(4):575-587

[190] Duchene D, Wouessidjewe D. Industrial uses of cyclodextrins and their derivatives. Journal of Coordination Chemistry. 1992;27(1-3):223-236

[191] Saenger W. Cyclodextrin inclusion compounds in research and industry. Angewandte Chemie (International Ed. in English). 1980;19(5):344-362

[192] Mejia-Ariza R, Grana-Suarez L, Verboom W, Huskens J. Cyclodextrin-based supramolecular nanoparticles for biomedical applications. Journal of Materials Chemistry. 2017;5(1):36-52

[193] Swaminathan S, Cavalli R, Trotta F. Cyclodextrin-based nanosponges: A versatile platform for cancer nanotherapeutics development. Wiley Interdisciplinary Reviews. Nanomedicine and Nanobiotechnology. 2016;8(4):579-601
[194] Karoy AH, Wilson LD. Nano-sized cyclodextrin-based molecularly imprinted polymer adsorbents for perfluorinated compounds – A mini-review. Nanomaterials. 2015;5(2):981-1003

[195] Simoes SM, Rey-Rico A, Concheiro A, Alvarez-Lorenzo C. Supramolecular cyclodextrin-based drug nanocarriers. Chemical Communications (Camb). 2015;51(29):6275-6289

[196] Kang Y, Guo K, Li BJ, Zhang S. Nanoassemblies driven by cyclodextrin-based inclusion complexation. Chemical Communications (Camb). 2014;50(76):11083-11092

[197] Concheiro A, Alvarez-Lorenzo C. Chemically cross-linked and grafted cyclodextrin hydrogels: From nanostructures to drug-eluting medical devices. Advanced Drug Delivery Reviews. 2013;65(9):1188-1203

[198] Moya-Ortega MD, Alvarez-Lorenzo C, Concheiro A, Loftsson T. Cyclodextrin-based nanogels for pharmaceutical and biomedical applications. International Journal of Pharmaceutics. 2012;428(1-2):152-163

[199] Purkayastha P, Jaffer SS, Ghosh P. Physicochemical perspective of cyclodextrin nano and microaggregates. Physical Chemistry Chemical Physics. 2012;14(16):5339-5348

[200] Martín-Banderas L, Holgado MA, Venero JL, Álvarez-Fuentes J, Fernández-Arévalo M. Nanostructures for drug delivery to the brain. Current Medicinal Chemistry. 2011;18(34):1-19

[201] Bilensoy E, Hinsic AA. Recent advances and future directions in amphiphilic cyclodextrin nanoparticles. Expert Opinion on Drug Delivery. 2009;6(11):1161-1173

[202] Dodziuk H. Molecules with holes – Cyclodextrins. In: Dodziuk H, editor. Cyclodextrins and Their Complexes: Chemistry, Analytical Methods, Applications. Weinheim: Wiley-VCH Verlag GmbH & Co., KGaA; 2006. pp. 1-30. ISBN: 3-527-31280-3

[203] Mosinger J, Tomankova V, Nemcova I, Zyka J. Cyclodextrins in analytical chemistry. Analytical Letters. 2001;34(12):1979-2004

[204] Armstrong DW. Cyclodextrin in analytical chemistry. In: Huber O, Szejtli J, editors. Proceedings of the Fourth International Symposium on Cyclodextrins. Germany: Springer; 1998. pp. 437-439

[205] Adly FG, Antwi NY, Ghanem A. Cyclodextrin-functionnalized monolithic capillary columns: Preparation and chiral applications. Chirality. 2016;28(2):97-109

[206] Guo JL, Lin YJ, Xiao Y, Crommen J, Jiang ZJ. Recent developments in cyclodextrin functionalized monolithic columns for the enantioseparation of chiral drugs. Journal of Pharmaceutical and Biomedical Analysis. 2016;130:110-125

[207] Al-Othman ZA, Al-Warthan A, Ali I. Advances in enantiomeric resolution on monolithic chiral stationary phases in liquid chromatography and electrochromatography. Journal of Separation Science. 2014;37(9-10):1033-1057

[208] Jáč P, Scriba GKE. Recent advances in electrodriven enantioseparations. Journal of Separation Science. 2013;36(1):52-74
[209] Mandrioli R, Mercolini L, Raggi MA. Chiral analysis of amphetamines, methadone and metabolites in biological samples by electrodriven methods. Electrophoresis. 2011;32(19):2629-2639

[210] Pathak D, Pathak K. Cyclodextrins as chiral discriminators. Indian Drugs. 2008;45(10):765-774

[211] Takahashi AI, Veiga FJB, Ferraz HG. A literature review of cyclodextrin inclusion complexes characterization – Part II: X-ray diffraction, infrared spectroscopy and nuclear magnetic resonance. International Journal of Pharmaceutical Sciences Review and Research. 2012;12(1):8-15

[212] Boccio M, Sayago A, Asuero AGA. bilogarithmic method for the spectrophotometric evaluation of stability constants of 1:1 weak complexes from mole ratio data. International Journal of Pharmaceutics. 2006;318(1-2):70-77

[213] Schneider H-J, Hacket F, Rüdiger V, Ikeda H. NMR studies of cyclodextrins and cyclodextrin complexes. Chemical Reviews. 1998;98(5):1755-1786

[214] Lay S, Ni X, Yu H, Shen S. State-of-the-art applications of cyclodextrins as functional monomers in molecular imprinting techniques: A review. Journal of Separation Science. 2016;39(12):2321-2331

[215] Széjti J. Application of cyclodextrins in the chromatography. Starch-Stärke. 1987;39(10):357-362

[216] Szente L, Széjti J. Non-chromatographic analytical uses of cyclodextrins. Analyst. 1998;123(4):735-741

[217] Liu BW, Zhou H, Zhou ST, Yuan JY. Macromolecules based on recognition between cyclodextrin and guest molecules: Synthesis, properties and functions. European Polymer Journal. 2015;65:63-81

[218] Chen Y, Liu Y. Cyclodextrin-based bioactive supramolecular assemblies. Chemical Society Reviews. 2010;39(2):495-505

[219] Breslow R. Adjusting the lock and adjusting the key in cyclodextrin chemistry. An introduction in biomimetic chemistry. In: Dolphin D, et al., editors. Advances in Chemistry. Washington, DC: American Chemical Society; 1980. pp. 1-15

[220] Zhao QQ, Zhang WX, Wang RM, Wang YT, Ouyang DF. Research advances in molecular modeling in cyclodextrins. Current Pharmaceutical Design. 2017;23(3):522-531

[221] Wenz G, Monflier E. Superstructures with cyclodextrins: Chemistry and applications III. Beilstein Journal of Organic Chemistry. 2016;12:937-938

[222] Chui JKW, Fyles TM. Cyclodextrin ion channels. Organic & Biomolecular Chemistry. 2014;12:3622-3634

[223] Harada A, Takashima Y, Yamaguchi H. Cyclodextrin-based supramolecular polymers. Chemical Society Reviews. 2009;38:875-882
[224] Khan AR, Forgo P, Stine KJ, D’Souza VT. Methods for selective modifications of cyclodextrins. Chemical Reviews. 1998;98(5):1977-1996

[225] Lipkowitz KB. Applications of computational chemistry to the study of cyclodextrins. Chemical Reviews. 1998;98(5):1829-1874

[226] Nepogodiev SA, Kurkov SV, Loftsson T. Cyclodextrins. International Journal of Pharmaceutics. 2013;453(1):167-180

[227] Nepogodiev SA, Stoddart JF. Cyclodextrin-based catenanes and rotaxanes. Chemical Reviews. 1998;98(5):1959-1976

[228] Takahashi K. Organic reactions mediated by cyclodextrins. Chemical Reviews. 1998;98(5):2013-2034
