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An Overview on Cyclodextrin and Its Derivatives Encapsulated Inclusion Complex: Preparation Methods and Influencing Factors

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Abstract
Inclusion Complex formation is supported by non-covalent interaction between host and guest molecules. Cyclodextrins are supramolecular hosts with distinct structural characteristics that can enclose a diverse spectrum of viable compounds. The toroidal shape of CD offers the hydrophobic environment in the cavity where the guest moieties are entrapped which undergoes the physicochemical transformation and results into a superior physical, chemical and biological profiles. This review describes the chemical behavior of pharmaceuticals, both natural and synthetic, as well as other related compounds complexed with cyclodextrins. The study focuses on the commonly employed preparation methods of inclusion complexes and influencing factors to demonstrate host-guest interaction. The study demonstrates the possible stoichiometric combinations of cyclodextrins with the active pharmaceutical and organic molecules. The review also provides instances of synthetic pharmaceuticals that have combined with cyclodextrin to create inclusion products, demonstrating how cyclodextrins can be exploited to create biological substances with novel features and advance therapeutic research.

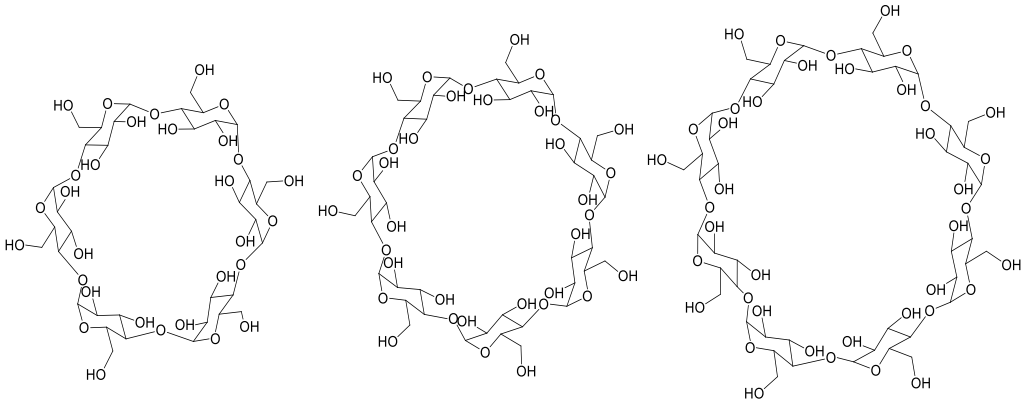
Keyword: Cyclodextrin, β-Cyclodextrin, inclusion products

1.1 Introduction

Villiers originally isolated cyclodextrins (CDs) in 1891 from a culture of Bacillus amylobacter grown on a starch medium. Villiers noticed the crystalline byproduct had similarities to cellulose, thus he gave it the name Cellulosine. Soon after Villiers in 1903, Schardinger identified the bacterium Bacillus macerans, which was used to create cyclodextrins. Schardinger dextrins are so-called because of the scientist's identification of cyclodextrins as a type of cyclic oligosaccharide. Pringsheim's discovery of cyclodextrins' complexing ability came after Schardinger's and marked a significant step forward in the field of cyclodextrin study. Midway through the 1930s (1938), Freudenberg et al., deduced the chemical composition of cyclodextrins. French and Cramer began developing methods for synthesizing and

purifying cyclodextrin complexes in 1950. Szetjli, often referred to as the "Godfather of cyclodextrins," made a significant contribution to this area of study between the years 1970 and 1980.

The α-(1,4)-linked glucopyranose subunits that make up cyclodextrins are the key structural feature of this class of oligosaccharides. Their names include cycloamylose, cyclomaltose, and Schardinger dextrins [1-3]. They form when the enzyme cyclodextrin glucanotransferase (CG Tase) degrades starch, triggering an intramolecular transglycosylation process [4]. The three most abundant CDs are all torus-like macro-rings composed of glucopyranose units; they are crystalline, non-hygroscopic, homogeneous substances. Six glucopyranose units make up the α-cyclodextrin, seven make up the β-cyclodextrin, and eight make up the γ-cyclodextrin Fig. 1.1[5-7].



α -CD **β-CD** **γ-CD**

Fig. 1.1 Structure of α, β and γ Cyclodextrin

Among three types of parent cyclodextrins, β-Cyclodextrin is the most accessible, lowest-priced and generally the most useful.

This review paper introduces the research techniques applied to prepare cyclodextrins-guest inclusion complexes. We also discuss several factors that influence CD complexation.

1.2 Inclusion Complexes

The inherent capacity of cyclodextrins to form inclusion complexes (fig. 1.2) with a variety of compounds is the key to understanding the relevance of these molecules [8]. Through the process of molecular complexation, cyclodextrins are capable of forming solid inclusion complexes (also known as host-guest complexes) with an extremely diverse collection of solid, liquid, and gaseous chemicals. In these particular compounds, the hollow of the cyclodextrin host molecule serves as a storage space for a guest molecule. The formation of a complex is determined by the size of the host cavity as well as the guest molecule [9]. Within the cyclodextrin molecule is a cavity known as the lipophilic cavity. This cavity creates a milieu into which non-polar moieties of the suitable size can penetrate to create inclusion complexes. The development of such inclusion complex does not result in the breaking or formation of any covalent bonds [10]. The discharge of enthalpy-rich molecules of water from within the cavity is the primary mechanism that drives the development of the complex. A more stable lower state [10] is achieved as a result of the displacement of water molecules by even more hydrophobic biomolecules that are present in the solution. This allows for the achievement of an apolar-apolar connection and the reduction of cyclodextrin ring strain [11].

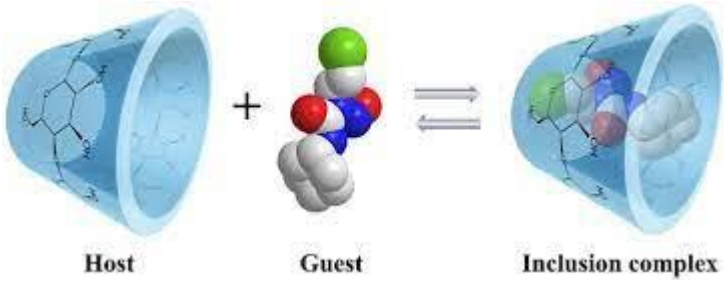


Fig 1.2. Formation of inclusion complex

The attachment of molecules inside the host cyclodextrin is not stable or permanent; rather, it is a dynamic equilibrium between the two parties. The strength of the binding is determined by how well the 'host-guest' complex fits together as well as by the specific local interactions that occur between atoms on the surface.

1.2.1 Inclusion Complexes' Stoichiometry

A 1:1 drug/cyclodextrin, D/CD combination is the most prevalent kind of cyclodextrin complex, and it is represented by

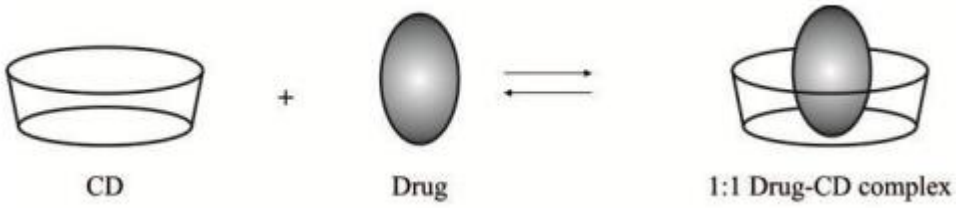


Fig. 1.3 Equilibrium binding of drug and CD to form 1:1 complex

The following equation gives the stoichiometry of the drug/cyclodextrin D/CD inclusion complex [12].

$$D + CD \overset{K_{1:1}}{} D\ CD$$

$K_{1:1}$ values range from around 50 to 2000 M^{-1}, with mean values for α-, β- and γ-CD of 129 M^{-1}, 490 M^{-1}, and 355 M^{-1}, respectively.

The AP type equilibrium phase diagram is the most typical for higher order D/CD complexes, and the most frequent stoichiometry for these complexes is 1:2 D/CD. It is hypothesized that this sort of complex is produced when a second cyclodextrin molecule creates a complex with an already present 1:1 complex [13,14].

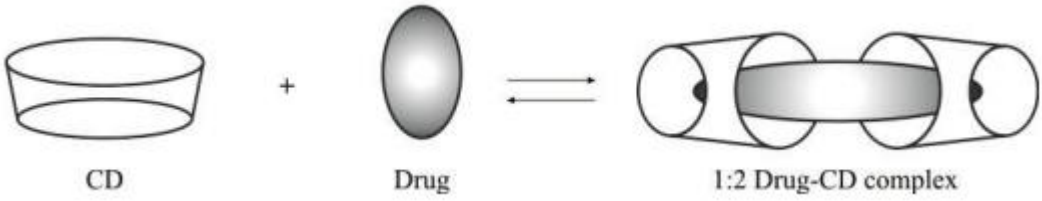


Fig. 1.4 Equilibrium binding of drug and CD to form 1:2 complexes

An inclusion combination of drug and cyclodextrin D/CD with a stoichiometry of 1:2 is represented by the equation

$$D/CD + CD \overset{K_{1:2}}{} D \quad CD_2$$

1.3 Methods of Complexity Enhancement

Inclusion complexes can be formed using a number of different complexation strategies. The many complexation strategies reflect the diversity of therapeutic compounds, formulation components, manufacturing methods, and final products. The following section will discuss various approaches [15].

1.3.1 Physical mixing, milling, co-grinding, and solid phase complexation

The medication and cyclodextrin are combined in a mortar at 1:1 and 1:2 molar ratios, and the mixture is triturated constantly for roughly an hour.

The powdered ingredients are triturated, and then sieved through No. 80 before being dried in a desiccator. Large-scale production of the physical combinations takes just 30 minutes in quick mass granulators. After the powdered combinations are made, they are kept in a dry, temperature-controlled area with a humidity level between 21 and 22 degrees Celsius.

1.3.2. Kneading

A slurry-like consistency is achieved by taking the drug as well as cyclodextrin in varied molar ratios and mixing them well in a mortar with the addition of a small quantity of water while triturating. One hour of continuous trituration is performed. After being air - dried at room temperature, the slurry is ground into a powder and put into a desiccator after having been passed through a No.80 sieve. Granulators are utilized for mass production, and the trituration times range between 15 minutes to an hour, with the humidity kept between 40 and 50 percent throughout. [16]

1.3.3 Co-precipitation

Saturated solutions of cyclodextrin and guest molecule are prepared by adding them to 40-60°C freshwater or a chain length alcohol (such as ethanol or isopropanol). The complicated precipitate is separated using filtration or centrifugation after cooling. The Complexation time in this approach might be anywhere from 24 hours to 48 hours [17].

1.3.4 Assimilation/Precipitation

The active ingredient is combined with cyclodextrin dissolved in an aqueous solution after being dissolved in an alkaline solution. Under constant stirring, a solution of hydrochloric acid is added to the clear solution, and the mixture is neutralized until the equivalence point is reached. Inclusion complex is confirmed to have formed when a white precipitate forms at the equivalency point [18].

1.4 CD Derivatives with Minor Changes

The goal of the modifications made to natural CDs is to make them amorphous or crystalline. Furthermore, after alteration, they should have strong aqueous solubility to provide high concentration, microbiological stability, and physical stability for an acceptable amount of time in free as well as in complex form. Because all CDs (α, β and γ) have interchangeable hydroxyl groups in positions 18, 21, and 24 respectively. The modified CDs are also less harmful when administered via orally or intravenously Thus, there is no upper bound on the number or breadth of potential derivatives. The following enhancements in attributes are accomplished by modifying CDs.

- So that the free and complex forms of the modified CDs are more soluble.
- So that the CD and its visitor feel more connected to one another.
- So that the targeted groups may be fastened to the binding sit

1.4.1. First, let's talk about methylated derivatives

The water solubility of the methylated derivative of β-CD increases after the inclusion of the methyl group. In general, the solubility in water improves up to around 13–14 methyl groups, and then starts to drop off significantly beyond that.

Crystalline 2, 6-di-o-methyl-β-CD has good solubility in cold condition but is insoluble in hot condition; it is the methylated form of β-CD. When compared to other CDs, it is among the most effective solubilizers. One of the most valuable pharmaceutical products is a random methylation of β-CD, which is used in medication development.

1.4.2. Hydroxylated Derivatives

The reaction involving CD as well as propylene oxide in water yields hydroxylated derivatives. Products with 2-hydroxypropyl groups replace the CD's hydroxyl group in the final formulation [20].

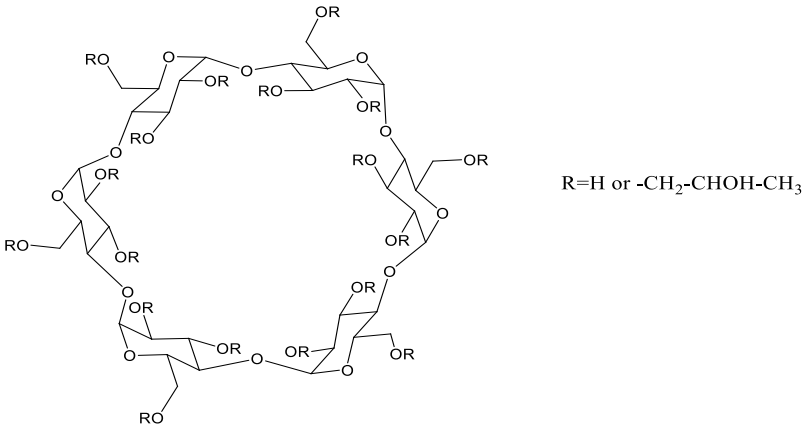


Fig. 1.5 Structure of Hydroxypropyl α-cyclodextrin

1.4.3 An Overview of Sulfoalkylated Derivatives

Aqueous reaction of CD with propane sulfone or butyl sulfone yields sulfopropyl or sulfobutyl derivatives of β -CD. Sulfobutyl-CD is non-crystallizable, highly soluble in water, and has no adverse effects, even when taken in large quantities [21].

1.4.4 Sulfur-containing Derivatives

In dimethyl formamide, CDs are reacted with pyridine-SO3 to produce these derivatives. It has been discovered that these compounds have antiviral, anti-inflammatory, and anti-lipidemic actions, in addition to their anti-angiogenic or anti-proliferative capabilities. They do not cause hemolysis, are not poisonous, and do not damage the kidneys.

In addition to these, numerous additional derivatives are useful in the pharmaceutical industry [22].

1.5 Cyclodextrin complexation to host/drug molecules: influencing factors

Cyclodextrin/drug complex formation is affected by a number of factors.

1.5.1 Disc Formats

The creation and performance of inclusion complexes are vulnerable to the type of CD present. The solubility of medications like albendazole, mebendazole, and ricobendazole was significantly improved by using CDs like hydroxypropyl β-cyclodextrin (HP-β-CD) and methyl beta cyclodextrin (Me-β-CD) as compared to β-cyclodextrin (19). The Diaz et al., have reported that improved trend is consistent values of pharmacological interest were found with β-CD as well as HP β-CD structures only when the effects of α-CD, β-CD, γ-CD, and HP- β -CD on Fenuprofen were studied. According to Mura and colleagues' studies, Methyl beta-CD improves Ketoprofen solubility efficiency over beta-CD.
Hypothesized that, among the three CDs (α-CD, β-CD, and γ-CD) studied; only β-CD exhibited a significant propensity for CD adsorption to cocaine in aqueous system [23].

1.5.2 Cavity Size

The guest needs to fit comfortably inside the CD; hence its cavity size needs to be appropriate. Researchers Arias-Blanco and coworker found that, perhaps the cavity size of beta-CD is adequate enabling complexation of Gliclazide rings, but that of α-CD is insufficient. Researchers extrapolated that partial incorporation of the guests inside the cavity increased solubility due to their investigation of the effect of β -CD on Digitoxin. Akasaka and coworkers have deduced, from their research into the effects of the CDs on macrocyclic substances, that smaller macrocyclic compounds of the lower CDs achieve relative stability, while bigger macrocyclic complexes of higher CDs gain greater stability. Based on their research, the cavity of α-CD is less suited for inclusion and that the improvement of disintegration time is extremely successful with only higher CDs. Prochloro-methazine's solubility is decreased when it interacts with β-CD, HP-β-CD, or Dimethyl beta cyclodextrin (DM β-CD), according to research by Lutka and colleagues. This is because the CD cavity cannot accommodate the promethazine ring [24].

1.5.3 The Influence of Preparation Techniques

Complexation phenomena of medications containing CDs are influenced by their manufacturing methods. Processing techniques such as Co-grinding, kneading, physical mixture, solvent extraction, co-precipitation, spray-drying, as well as freeze-drying are all processes that can disrupt drug/CD complexation. The drug's and CD's unique properties will determine how well they complex. It has been observed by Castillo and colleagues that the freeze-drying approach alone is particularly effective for inclusion complex formation for medications like Albendazole, Mebendazole, Ribendazole and Ketoprofen with CDs [25]. Co-precipitation combined sealed heating have reportedly produced superior dissolving results for Ketoprofen using β -CD and DM- β -CD than kneading has. Spray drying with sealed heating techniques of preparation resulted in improved complex formation in the case of α-CD, β-CD, and γ-CD, and kneading is found to be ineffectual, as stated by scientists who have examined the effect of α-CD, β-CD, and γ-CD on Ibuproxam. Chowdary and colleagues investigated the interaction of Nimesulide with β-CD and found that the kneading method resulted in more drug dissolution than co-evaporation [26]. Palmieri et al. found that for β -CD, HP β -CD, and Methoxybutyrate, the best complexation results were obtained via solid dispersion, kneading was unsuccessful, while spray-drying resulting in complete complexation with a fixed ratio of 1:4 [29]. That spray-drying produced superior dissolving behavior than kneading while working with Oxazepam and DM-β-CD in their study. Using the freeze-drying technique, Pose-Vilarnovo and coworkers found that the dissolution rate of Sulphamethoxazole inclusion complexes with β -CD and HP β -CD was increased. Grinding, physical

mixing, and kneading have been reported to be superior means of dissolution for Glibenclamide in studies examining the effect of β -CD [27]. Researchers found that neutralization improved dissolving performance and overall complex stability compared to typical solvent and kneading procedures while formulating and evaluating beta-CD on Tenoxicam[28].

1.5.4 The Relationship between pH and Ionization State

Sulfobutyl ether beta cyclodextrin (SBE-β-CD) and DY-9760E have been found to interact strongly in the acidic area at pH4 [33], as studied and published by Nagase and colleagues. At a pH of 1, Researchers report that the cationic medication NSC-639829 is more soluble when combined with SBE- beta-CD. In their study with CDs such HP-β -CD, Randomly Methylated β -CD, SBE- beta-CD, Carboxy methyl beta-cyclodextrin (CMβ-CD), and 2-hydroxy-3-trimethyl-ammoniopropyl-beta-cyclodextrin, Researcher found that the solubility of ETH-615 could be increased only with randomly methylated (RM) beta-CD. The difficulty of the highly polar drug [34] entering the CD cavity causes its complexing stability constants to be low at pH5, while those for the less polar anionic version are high at pH 10.
Dalmora and coworkers found that piroxicam complexed well with beta -CD at acidic pH. McCandless et al. discovered that the solubility (mg/ml) of Levemopamil HCl increases by a factor of 3 at basic pH (from 7.88 to 25.62 mg/ml) and by a factor of 325 at basic pH (from 0.0036 to 1.37 mg/ml) [29]. Kim and coworkers investigated the interaction of Ziprasidone mesylate using SBE- beta-CD, and they observed that complexation is favored more with the ion pair than with the dissociated ionic form [35]. According to research from Tros de Ilarduya et al. on Sulindac and β -CD, the non-ionized form of the medication was more amenable to complexation. Unionized Mebendazole is less included than ionized Mebendazole in the inclusion complex formation [30].

1.5.5 Heat or Cold

According to research conducted by Nagase and colleagues, the effect of SBE- β -CD on DY-9760E suggests that the stability constant is barely affected by changes in temperature. Tros de Ilarduya et al. found that the apparent stability characteristic of the Sulindac- β -CD inclusion complex decreases with increasing temperature (35). The binding with phenolphthalein to β -CD, found that the association constant decreased with increasing temperature. A rise in temperature reduces the stability characteristic of the complex [31].

1.5.6 Degree of substitution

Substituent type, number, and location on the parent CD molecule may have a significant impact on the molecule's physicochemical properties, such as its complexation capacity. In case of HP- β -CD, the "degree of substitution" is not a distinguishing feature of the β -CD derivative. Differences in the physicochemical features of HP-CD samples that have the same level of substitution generated under different conditions can result from irregularities in the occupancy of hydroxypropyl groups at various locations on the parent CD molecule. Since this purity of CD can have a significant impact on the final quality of the medicinal product and its marketability [32].

Conclusion:

CDs are important to improve the apparent solubility, rate of dissolution and chemical stability of guest molecule. Inclusion complex with cyclodextrins is the most attractive technique to enhance aqueous

solubility of guest molecules. Innate structural features of CDs like hydrophobic cavity give rise to a host-guest complex. The structure of cyclodextrin has been modified to derivatives to improve water solubility, physiochemical properties and the inclusion capacity of original cyclodextrins. CDs derivatives can encapsulates apolar guest molecule into their cavities with greater ease and hence enhance the solubility of the included guest molecules. Inclusion complex of HPβCD produced a comparatively higher solubility than that of βCD. Different approaches are available to enhance the complex efficiency such as kneading, co-precipitation, neutralization, etc. each methods have their own advantages and some limitations.

REFERENCES:

1. Guendouzi, O., Guendouzi, A., Ouici, H. B., Brahim, H., Boumediene, M., & Elkeurti, M. (2020). A quantum chemical study of encapsulation and stabilization of gallic acid in β-cyclodextrin as a drug delivery system. Canadian Journal of Chemistry, 98(4), 204-214.
2. Siddiqui, A. J., Singh, R., Jahan, S., Alreshidi, M., Hamadou, W. S., Khan, A., ... & Adnan, M. (2022). Enzymes in Food Fermentations. In African Fermented Food Products-New Trends (pp. 101-133). Cham: Springer International Publishing.
3. Ali, K. A., Roy, P., Maity, A., & Chakraborty, P. (2021). Tailor-made cyclodextrin-based nanomaterials as drug carriers. In Tailor-Made and Functionalized Biopolymer Systems (pp. 155-200). Woodhead Publishing.
4. Ali, K. A., Roy, P., & Maity, A. (2021). Pranabesh Chakraborty1 1Division of Pharmaceutics, Department of Pharmaceutical Sciences & Technology, Maulana Abul Kalam Azad University of Technology, Haringhata, West Bengal, India. Tailor-Made and Functionalized Biopolymer Systems: For Drug Delivery and Biomedical Applications, 155.
5. Gloe, T. E. (2016). Carbohydrate Conjugates to Explore Bacterial Adhesion: From Amadori Rearrangement to Surface Functionalization (Doctoral dissertation, Christiana Albertina University of Kiel).
6. Amiri, S., & Amiri, S. (2017). Cyclodextrins: properties and industrial applications. John Wiley & Sons.
7. Apetrei, C. (Ed.). (2016). Natural Sources, Physicochemical Characterization and Applications (Vol. 1). Bentham Science Publishers.
8. Ravindran Maniam, M. M., Loong, Y. H., & Samsudin, H. (2022). Understanding the Formation of β-Cyclodextrin Inclusion Complexes and Their Use in Active Packaging Systems. Starch-Stärke, 74(7-8), 2100304.
9. de la Peña, A. M., Salanas, F., Gómez, M. J., Acedo, M. I., & Pena, M. S. (1993). Absorptiometric and spectrofluorimetric study of the inclusion complexes of 2-naphthyloxyacetic acid and 1-naphthylacetic acid with β-cyclodextrin in aqueous solution. Journal of inclusion phenomena and molecular recognition in chemistry, 15, 131-143.
10. Xiao, Z., Hou, W., Kang, Y., Niu, Y., & Kou, X. (2019). Encapsulation and sustained release properties of watermelon flavor and its characteristic aroma compounds from γ-cyclodextrin inclusion complexes. Food Hydrocolloids, 97, 105202.
11. Zhu, G., Feng, N., Xiao, Z., Zhou, R., & Niu, Y. (2015). Production and pyrolysis characteristics of citral–monochlorotriazinyl-β-cyclodextrin inclusion complex. Journal of Thermal Analysis and Calorimetry, 120, 1811-1817.

12. da Rocha Neto, A. C., da Rocha, A. B. D. O., Maraschin, M., Di Piero, R. M., & Almenar, E. (2018). Factors affecting the entrapment efficiency of β-cyclodextrins and their effects on the formation of inclusion complexes containing essential oils. Food Hydrocolloids, 77, 509-523.
13. Kavetsou, E., Pitterou, I., Katopodi, A., Petridou, G., Adjali, A., Grigorakis, S., & Detsi, A. (2021, December). Preparation, Characterization, and Acetylcholinesterase Inhibitory Ability of the Inclusion Complex of β-Cyclodextrin–Cedar (Juniperus phoenicea) Essential Oil. In Micro (Vol. 1, No. 2, pp. 250-266). Multidisciplinary Digital Publishing Institute.
14. Araújo, L. D. S. S., Lazzara, G., & Chiappisi, L. (2021). Cyclodextrin/surfactant inclusion complexes: an integrated view of their thermodynamic and structural properties. Advances in Colloid and Interface Science, 289, 102375.
15. Bednarek, E., Bocian, W., & Michalska, K. (2019). Nuclear magnetic resonance spectroscopic study of the inclusion complex of (R)-tedizolid with HDAS-β-CD, β-CD, and γ-cyclodextrin in aqueous solution. Journal of Pharmaceutical and Biomedical Analysis, 169, 170-180.
16. Sbârcea, L., Ledeţi, A., Udrescu, L., Văruţ, R. M., Barvinschi, P., Vlase, G., & Ledeţi, I. (2019). Betulonic acid—cyclodextrins inclusion complexes. Journal of Thermal Analysis and Calorimetry, 138, 2787-2797.
17. Raffaini, G., & Ganazzoli, F. (2019). A Molecular Dynamics Study of a Photodynamic Sensitizer for Cancer Cells: Inclusion Complexes of γ-Cyclodextrins with C70. International Journal of Molecular Sciences, 20(19), 4831.
18. Das, S., Nath, S., Singh, T. S., & Chattopadhyay, N. (2020). Cavity size dependent stoichiometry of probe–cyclodextrin complexation: Experimental and molecular docking demonstration. Journal of Photochemistry and Photobiology A: Chemistry, 388, 112158.
19. Mohandoss, S., Atchudan, R., Edison, T. N. J. I., Mandal, T. K., Palanisamy, S., You, S., ... & Lee, Y. R. (2019). Enhanced solubility of guanosine by inclusion complexes with cyclodextrin derivatives: Preparation, characterization, and evaluation. Carbohydrate polymers, 224, 115166.
20. Topuz, F., & Uyar, T. (2022). Advances in the development of cyclodextrin-based nanogels/microgels for biomedical applications: Drug delivery and beyond. Carbohydrate Polymers, 120033.
21. Venuti, V., Corsaro, C., Stancanelli, R., Paciaroni, A., Crupi, V., Tommasini, S., ... & Majolino, D. (2019). Analysis of the thermal fluctuations in inclusion complexes of genistein with β-cyclodextrin derivatives. Chemical Physics, 516, 125-131.
22. Adamiak, M., & Ignaczak, A. (2019). Quantum chemical study of the complexation process of bis-β-D-glucopyranosyl diazacrown derivative with aspirin and paracetamol molecules. Computational and Theoretical Chemistry, 1167, 112591.
23. Mashaqbeh, H., Obaidat, R., & Al-Shar'i, N. (2021). Evaluation and characterization of curcumin-β-cyclodextrin and cyclodextrin-based nanosponge inclusion complexation. Polymers, 13(23), 4073.
24. Mukherjee, D., Singh, P., Singh, S., Roy, D. S., Singha, S., Pal, U., ... & Pal, S. K. (2021). Host assisted molecular recognition by human serum albumin: Study of molecular recognition controlled protein/drug mimic binding in a microfluidic channel. International Journal of Biological Macromolecules, 176, 137-144.
25. Wu, H., Xia, T., Qi, F., Mei, S., Xia, Y., Xu, J. F., & Zhang, X. (2022). A Cleavable Self-Inclusion Conjugate with Enhanced Biocompatibility and Antitumor Bioactivity. CCS Chemistry, 1-7.

26. Al Hujran, T. A., Magharbeh, M. K., Habashneh, A. Y., Al-Dmour, R. S., Aboelela, A., & Tawfeek, H. M. (2022). Insight into the Inclusion Complexation of Fluconazole with Sulfonatocalix [4] naphthalene in Aqueous Solution, Solid-State, and Its Antimycotic Activity. Molecules, 27(14), 4425.
27. Mohammed-Saeid, W., Karoyo, A. H., Verrall, R. E., Wilson, L. D., & Badea, I. (2019). Inclusion complexes of melphalan with gemini-conjugated β-cyclodextrin: Physicochemical properties and chemotherapeutic efficacy in in-vitro tumor models. Pharmaceutics, 11(9), 427.
28. do Nascimento Cavalcante, A., Feitosa, C. M., da Silva Santos, F. P., de Sousa, A. P. R., Júnior, R. D. S. S., de Souza, A. A., ... & Rashed, K. (2019). Elaboration and characterization of the inclusion complex between β-cyclodextrin and the anticholinesterase 2-oleyl-1, 3-dipalmitoyl-glycerol extracted from the seeds of Platonia insignis MART. Journal of Molecular Structure, 1177, 286-301.
29. Rajalakshmi, P., Peter, D. N., & Ananthi, N. (2021). Structure-activity relationship of supramolecular compounds in drug delivery. Mini-Reviews in Organic Chemistry, 18(7), 961-989.
30. Jia, Z., Luo, Y., Barba, F. J., Wu, Y., Ding, W., Xiao, S., ... & Fu, Y. (2022). Effect of β-cyclodextrins on the physical properties and anti-staling mechanisms of corn starch gels during storage. Carbohydrate Polymers, 284, 119187.
31. Wang, K., Li, Y., Zhang, Y., Huang, M., Xu, X., Ho, H., ... & Sun, J. (2022). Improving physicochemical properties of myofibrillar proteins from wooden breast of broiler by diverse glycation strategies. Food Chemistry, 382, 132328.
32. Syed Yaacob, S. F. F., Suwaibatu, M., Raja Jamil, R. Z., Mohamed Zain, N. N., Raoov, M., & Mohd Suah, F. B. (2023). Review of molecular imprinting polymer: Basic characteristics and removal of phenolic contaminants based on the functionalized cyclodextrin monomer. Journal of Chemical Technology & Biotechnology, 98(2), 312-330.
33. Li, T., Guo, R., Zong, Q., & Ling, G. (2022). Application of molecular docking in elaborating molecular mechanisms and interactions of supramolecular cyclodextrin. Carbohydrate Polymers, 276, 118644.
34. Janicka, P., Kaykhaii, M., Płotka-Wasylka, J., & Gębicki, J. (2022). Supramolecular deep eutectic solvents and their applications. Green Chemistry, 24(13), 5035-5045.
35. Leclercq, L. (2016). Interactions between cyclodextrins and cellular components: Towards greener medical applications?. Beilstein journal of organic chemistry, 12(1), 2644-2662.