Cyclodextrin applications in pharmacy, biology, medicine, and environment

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This year marks the 130th anniversary of the discovery of cyclodextrins, biosynthetic cyclic oligosaccharides obtained by enzymatic degradation of starch (Fig. 1) (Morin-Crini et al. 2021). To mark this occasion, the editors of this special issue invited colleagues to write articles describing their own innovative research on cyclodextrins and/or analyzing current knowledge on this subject.

For more than 130 years, cyclodextrins fascinate researchers and industrialists around the world. These substances belong to the family of cage molecules, i.e., the core of their structure is composed of a stable hydrophobic cavity that can encapsulate other compounds with hydrophobic moieties through host-guest interactions (Fig. 2). Cyclodextrins and their derivatives have found applications in many fields such as chemistry, pharmacy, biology, medicine and biomedicine, food, beverage industry, cosmetology and hygiene, chromatography, catalysis, biotechnology, agrochemistry, and remediation (Crini et al. 2018).

This special Issue on “Cyclodextrin Applications in Pharmacy, Biology, Medicine and Environment” consisted of 8 selected works (6 research articles and 2 review papers) from distinguished authors worldwide.

Violetta Mohos et al. investigated the use of insoluble β -cyclodextrin bead polymers to extract 12 mycotoxins from aqueous solutions including beverages (wine and beer samples). Mycotoxins as toxic metabolites of filamentous fungi are common contaminants in numerous beverages and foods. The authors demonstrated that cyclodextrin polymers can effectively extract citrinin, dihydrocitrinone,

sterigmatocystin, zearalanone, α -zearalanol, and β -zearalanol at each buffer tested (pH 3.0, 5.0, and 7.0). Among the mycotoxins tested, only the extraction of ochratoxin A showed pH dependence. The Langmuir and Freundlich isotherms were suitable for the quantitative evaluation of mycotoxin-polymer interactions. The results were explained by the presence of cyclodextrin molecules in the polymer, which allows the formation of inclusion complexes with the mycotoxins. Cyclodextrin-based polymers may be suitable mycotoxin binders for analytical and decontamination purposes (Mohos et al. 2021).

Grégorio Crini et al. proposed to use cyclodextrin-based polymers as adsorbents to treat three alkylphenols, namely, one nonylphenol (4-*n*-NP) and two octylphenols (4-*n*-OP and 4-*tert*-OP), present in both mono- and polycontaminated aqueous solutions by a batch method. Alkylphenols as industrial pollutants are commonly present in wastewater but they are difficult to eliminate by conventional treatment processes, ending up in the sludge of wastewater treatment plants. The experiments were carried out with five cyclodextrin polymers (α -ECP, β -ECP, γ -ECP, α,β,γ -ECP, and HP- β -ECP). Their results showed that all polymers, with the exception of α -ECP, had high adsorption capacities between 60 and 100% of the alkylphenols in the concentration range studied (between 25 and 100 $\mu\text{g/L}$). In all cases, HP- β -ECP has shown the highest removals, regardless of the structure of the molecule. The 4-*tert*-OP compound was the best adsorbed, regardless of the material and the solution studied. The performance remained unchanged after five sorption-regeneration cycles. The main adsorption mechanism of alkylphenols occurring in cyclodextrin polymers was the inclusion within the cyclodextrin cavities. The obtained results proved that cyclodextrin polymers could serve as efficient adsorbents for the removal of alkylphenols from real effluents (Crini et al. 2021).

Alberto Rubin Pedrazzo et al. reported a new, environmentally friendly, and efficient synthesis of cyclodextrin

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Fig. 1 Schematic representations of the three main cyclodextrins, namely α -cyclodextrin, β -cyclodextrin, and γ -cyclodextrin, containing six, seven, and eight glucose units in their structure, respectively, and their dimensions

Fig. 2 Schematic representation of the inclusion phenomena between a cyclodextrin molecule and a guest to form inclusion complexes

nanosponges by means of mechanochemistry involving the application of mechanical forces to drive and control chemical reactions by transferring energy to chemical bonds. The mechanochemical approach involves the use of a twin screw extruder. This chemical reactor has great potential for continuous organic synthesis, as it allows fine temperature control and a continuous process. Cyclodextrin nano-sponges, characterized by a three-dimensional nanostructured network with controlled properties, have shown remarkable contributions in the last 20 years in different applications such as environmental (e.g., as adsorbent for pollutant removal), pharmaceutical (as drug delivery system), and food (for removal of target substances). The eco-design of these nanomaterials opens up new application prospects (Pedrazzo et al. 2021).

Somenath Panda and Sophie Fourmentin proposed cyclodextrin-based supramolecular low melting mixtures as efficient absorbents for volatile organic compounds abatement. Four supramolecular low-melting mixtures, derived from modified cyclodextrins and levulinic acid, were prepared and evaluated for their absorption capability towards five volatile organic compounds, namely acetaldehyde, butanone, dichloromethane, thiophene, and toluene. The vapor-liquid equilibrium partition coefficient values showed multifold reduction from their values in water. The compounds could be desorbed easily by simply heating the absorbent, thereby enabling easy recovery. In addition, the low melting mixtures had excellent recyclability after several absorption/desorption cycles, facilitating their long-term usability. Overall, the easy-to-synthesize, green, low-melting mixtures showed

to combine the encapsulation ability of cyclodextrins with the superior absorption of low-melting mixtures with affinity for hydrophilic as well as hydrophobic molecules, making them versatile absorbents for volatile organic compounds abatement (Panda and Fourmentin 2021).

Asmaa Bouyahya et al. developed a simple and flexible synthetic strategy that opens the way to new hybrid materials useful for eco-friendly, with low cost and short time extraction techniques relevant for green analytical chemistry. This original support is based on an innovative supramolecular tripartite association between an ionic liquid covalently immobilized on a primary β -cyclodextrin rim and an anionic water-soluble polymer. These polyelectrolytes are based on electrostatic interactions between the opposite charges of the ionic liquid and the sodium polystyrene sulfonate. The inclusion properties of the free cavities of the cyclodextrins and the synergic effect of the polymeric matrix were confirmed using three reference guests such as phenolphthalein, *p*-nitrophenol, and 2-anilinonaphthalene-6-sulfonic acid by UV-visible, fluorescent, and NMR spectroscopies. The support has been applied successfully in dialysis devices to extract and concentrated an aromatic model molecule (Bouyahya et al. 2021).

Kazim Köse et al. reviewed new synthesis methods for the preparation of cyclodextrin-based materials and their applications for the removal of target substances such as metals, dyes, and pharmaceuticals. Their comprehensive literature review focused in particular on methods for the chemical modification of cyclodextrins (Köse et al. 2021).

Monika Yadav et al. also reviewed remediation technologies using functionalized cyclodextrin. The authors discussed and critiqued various environmental applications of gels, nanocomposites, and membranes containing cyclodextrin ligands. These new materials coupled with biodegradation or advanced oxidation techniques could help meet the challenges of water pollution (Yadav et al. 2021).

Rodrigue Tchoffo et al. prepared a composite material by polymerization of β -cyclodextrin on the surface of natural hydroxyapatite obtained from bovine bones for a potential application in electrochemistry for the detection of Pb(II). Hydroxyapatite was pre-calcined, treated with $(\text{NH}_4)_2\text{HPO}_4$, calcined, and treated with citric acid. The composite was characterized by XRD, FTIR, and SEM techniques and then used as electrode material for the detection of Pb ions in spring water, well water, river water, and tap water samples, with both effective results in terms of sensitivity and reproducibility (Tchoffo et al. 2021).

We — as editors — would like to thank the authors of this Special Issue for their contribution. Despite a considerable amount of work and an equally large number of industrial products on the market, cyclodextrins continue to attract the interest of both the academic community and industry and there is no doubt that new discoveries and applications are still to come. For example, recent studies on the use of cyclodextrin in virology (protection against Covid) show that these molecules have not yet revealed all their secrets!

References

- Bouyahya A, Sembo-Backonly BS, Favrelle-Huret A, Balieu S, Guillen F, Mesnage V, Karakasyan-Dia C, Lahcini M, Le Cerf D, Gouhier G (2021) New ternary water-soluble support from self-assembly of beta-cyclodextrin-ionic liquid and an anionic polymer for dialysis device. *Environ Sci Pollut Res*. <https://doi.org/10.1007/s11356-021-16374-0>
- Crini G, Bradu C, Fourmentin M, Cosentino C, Ribeiro ARL, Morin-Crini N (2021) Sorption of 4-n-nonylphenol, 4-n-octylphenol and 4-tert-octylphenol on cyclodextrin polymers. *Environ Sci Pollut Res*. <https://doi.org/10.1007/s11356-021-14435-y>
- Crini G, Fourmentin S, Fenyvesi E, Torri G, Fourmentin M, Morin-Crini N (2018) Cyclodextrins, from molecules to applications. *Environ Chem Lett* 16:1361–1375. <https://doi.org/10.1007/s10311-018-0763-2>
- Köse K, Tüysüz M, Aksüt D, Uzun L (2021) Modification of cyclodextrin and use in environmental applications. *Environ Sci Pollut Res*. <https://doi.org/10.1007/s11356-021-15005-y>
- Mohos V, Faisal Z, Fliszár-Nyúl E, Szenté L, Poór M (2021) Testing the extraction of 12 mycotoxins from aqueous solutions by insoluble beta-cyclodextrin bead polymer (2021). *Environ Sci Pollut Res*. <https://doi.org/10.1007/s11356-021-15628-1>
- Morin-Crini N, Fourmentin S, Fenyvesi E, Lichtfouse E, Torri G, Fourmentin M, Crini G (2021) 130 years of cyclodextrin discovery for health, food, agriculture, and the industry: a review. *Environ Chem Lett* 19:2581–2617. <https://doi.org/10.1007/s10311-020-01156-w>
- Panda S, Fourmentin S (2021) Cyclodextrin based supramolecular low melting mixtures: efficient absorbents for volatile organic compounds abatement. *Environ Sci Pollut Res*. <https://doi.org/10.1007/s11356-021-16279-y>
- Pedrazzo AR, Trotta F, Hoti G, Cesano F, Zanetti M (2021) Sustainable mechanochemical synthesis of β -cyclodextrin polymers by twin screw extrusion. *Environ Sci Pollut Res*. <https://doi.org/10.1007/s11356-021-15187-5>
- Tchoffo R, Ngassa GBP, Doungmo G, Kamdem AT, Tonlé IK (2021) Surface functionalization of natural hydroxyapatite by polymerization of β -cyclodextrin: application as electrode material for the electrochemical detection of Pb(II). *Environ Sci Pollut Res*. <https://doi.org/10.1007/s11356-021-15578-8>
- Yadav M, Thakore S, Jadeja R (2021) A review on remediation technologies using functionalized cyclodextrin. *Environ Sci Pollut Res*. <https://doi.org/10.1007/s11356-021-15887-y>

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