Selective Removal of Purines from Aqueous Solution Using Cucurbit[N]Uril: A Comprehensive Review

Nathaniel L. Nevis[1], **Aliyah Basheba Zackpah**[2]

[1]**Nanjing University of Information Science & Technology, Nanjing, 210044, PR China**

[2]**Suzhou University of Science and Technology, Suzhou, Jiangsu Province, PR China**

DOI: https://dx.doi.org/10.51584/IJRIAS.2026.11010051

Received: 17 January 2026; Accepted: 24 January 2026; Published: 02 February 2026

ABSTRACT

Purine bases and their metabolites, including adenine, guanine, xanthine, hypoxanthine, uric acid, and methylxanthines such as caffeine, are essential biological compounds that have increasingly emerged as environmentally relevant micropollutants due to widespread human consumption and their incomplete removal by conventional wastewater treatment processes. Their high water solubility, structural similarity, and persistence at trace concentrations in complex aqueous matrices make selective removal particularly challenging. This review examines the sources, environmental significance, chemical behavior, and health implications of purines in aquatic systems, while critically assessing the limitations of existing treatment technologies such as conventional adsorption, membrane filtration, biological degradation, and advanced oxidation processes, which often suffer from poor selectivity, high energy demand, fouling, or incomplete mineralization. Emphasis is placed on cucurbit[n]urils (Q[n]) as a promising supramolecular platform for the selective removal of purines from water. The unique molecular architecture of Q[n], characterized by hydrophobic cavities and carbonyl-lined portals, enables highly specific host–guest interactions driven by size complementarity, hydrophobic inclusion, hydrogen bonding, and ion–dipole interactions. The review highlights the influence of cucurbituril ring size on purine selectivity, competitive binding behavior in multicomponent systems, and the advantages of nonporous adaptive crystals for selective uptake under realistic conditions. Current challenges related to scalability, material stability, and process integration are discussed, alongside future perspectives for the rational design of next-generation Q[n]-based adsorbents. Overall, this work underscores the potential of cucurbituril-based supramolecular systems as precision-engineered tools for sustainable purine management in environmental and biomedical applications.

Keywords: Purines; Cucurbit[n]urils; Supramolecular adsorption; Selective removal; Aqueous solutions; Emerging contaminants; Water treatment; Host-guest chemistry

INTRODUCTION

Purine bases, such as adenine, guanine, hypoxanthine, xanthine, uric acid, and methylxanthines (e.g., caffeine, theobromine), are nitrogenous heterocycles that play important roles in nucleic acids and energy metabolism (Almeida et al., 2021). However, they are increasingly recognized as environmentally relevant micropollutants in natural and engineered waters. The body uses these purines for signal transduction, energy metabolism, and cell proliferation. In humans, they are eventually eliminated as uric acid from the kidneys and digestive system (Figure 1). The liver produces the majority of uric acid, which circulates in the blood and is eliminated by the kidneys in urine and the digestive system in feces (Kaneko et al., 2024). Excess uric acid not only raises blood uric acid levels but also crystallizes as monosodium urate crystals in joints and other locations, resulting in gouty arthritis because uric acid is poorly soluble in water. As noted by (Mock & Summers, 2024; Quintero-Jaramillo et al., 2021; Wong et al., 2023), the widespread consumption of purine-rich foods and beverages, combined with incomplete removal during conventional wastewater treatment, results in the continuous release of uric acid and caffeine into rivers, lakes, groundwater, and even coastal and Antarctic waters. These compounds can serve as indicators of human pollution and pose ecotoxicological risks. From a biomedical perspective, dysregulated purine metabolism and elevated uric acid levels are associated with hyperuricemia, gout, kidney injury, and cardiometabolic diseases, making the targeted control of purine levels in both physiological and environmental contexts a growing focus of clinical and public health efforts (Y.-Y. Li et al., 2024).

Despite its importance, selectively removing purines from aqueous solutions remains challenging because these molecules are highly water-soluble, structurally similar, and often present at low concentrations in complex mixtures of inorganic ions, natural organic matter, pharmaceuticals, and dyes (Quintero-Jaramillo et al., 2021). Methods such as advanced oxidation, biological degradation, and membrane processes can lower purine levels (Anastopoulos et al., 2020), however, they often encounter issues such as incomplete mineralization, high energy consumption, low specificity, or fouling, which limit their sustainability and scalability in removing trace organics (Wong et al., 2023). Adsorption is therefore an attractive option, yet most traditional adsorbents such as activated carbons or general polymeric resinstend to have broad-spectrum absorption with poor discrimination between structurally similar nitrogenous bases, making it difficult to target specific purines or concentrate particular species for downstream recovery (Almeida et al., 2021).

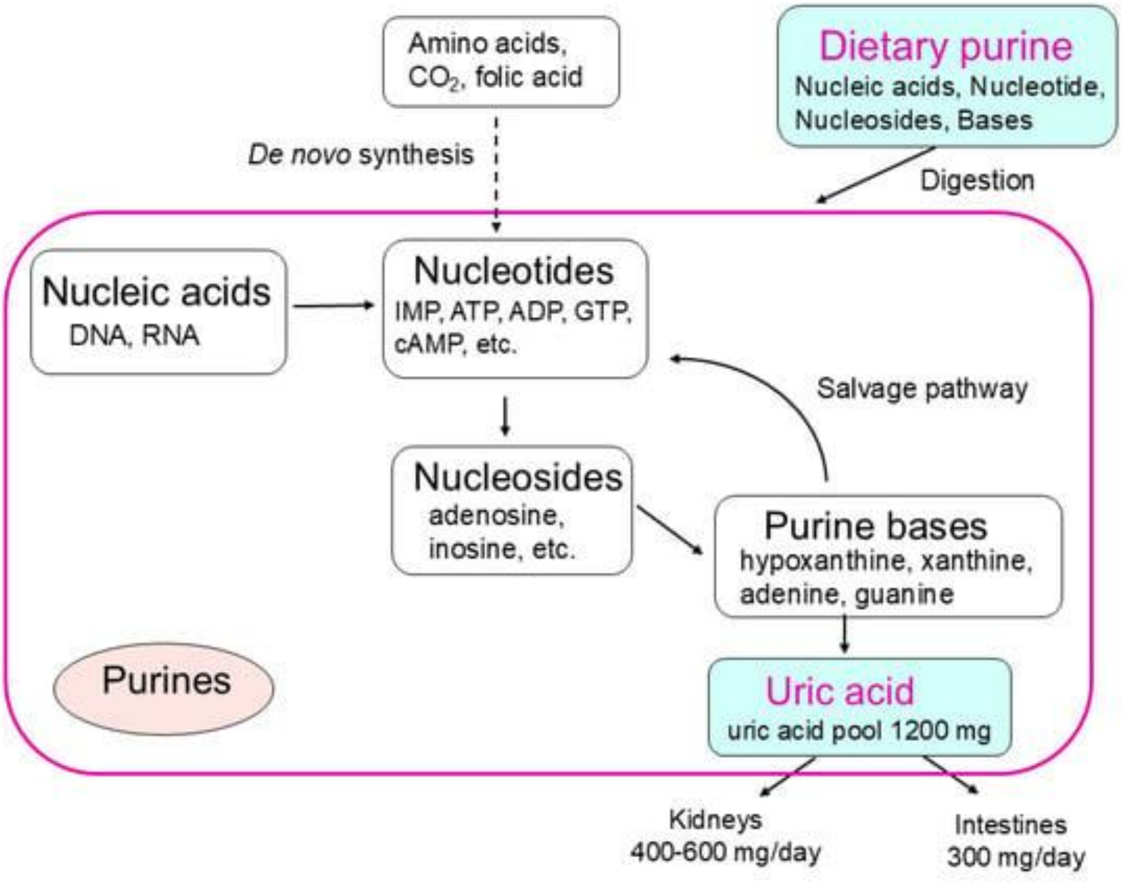

Figure 1. Schematic diagram of Purine metabolism and Dietary purine (Kaneko et al.,2024)

Cucurbit[n]urils (Q[n]), a family of rigid, pumpkin-shaped macrocycles with hydrophobic cavities and carbonyl-lined portals offer a promising supramolecular platform to overcome selectivity limitations through size- and charge-complementary host–guest recognition in water (Shi et al., 2024). Over the past six years, Q[n]-based nonporous adaptive crystals and composite materials have emerged as powerful separation media, achieving highly selective adsorption in liquid- and gas-phase systems, including the quantitative separation of pyridine from toluene/pyridine mixtures by Q crystals and the efficient removal of antibiotics and dyes from real water samples using Q-based assemblies or Q-functionalized nanocomposites (Kanth P et al., 2021). Building on this progress, this review specifically focuses on the selective removal of purines from aqueous solutions, with the goals of (i) outlining the chemical and environmental context of purine contamination (Qu et al., 2019), (ii) summarizing the structural and mechanistic features that enable purine recognition by Q[n] hosts (Q. Li et al., 2020a), (iii) critically assessing recent Q[n]-based solid-state and crystalline platforms for purine capture and separation (Shi et al., 2024), and (iv) identifying key knowledge gaps and design principles to guide the development of next-generation supramolecular adsorbents for precise purine management in environmental and biological contexts (Chernikova & Berdnikova, 2020).

Purines in Aqueous Environments: Sources and Significance

Purines, including adenine, guanine, hypoxanthine, xanthine, and methylxanthines such as caffeine (Bera et al., 2017), enter aqueous environments from both natural and human sources, creating a complex and dynamic load in surface water, groundwater, and wastewater systems (Shehata et al., 2025). According to a study by (Buerge et al., 2006), naturally, purines originate from the breakdown of nucleic acids and cellular biomass in aquatic food webs, the excretion of nitrogenous wastes by organisms, and microbial decomposition of organic matter, thereby contributing a baseline flux of nucleobases and purine metabolites to rivers and lakes. Over this baseline are significant human-derived inputs from domestic sewage, industrial discharges, agricultural runoff, and aquaculture (Khademi & Nikoofar, 2025). The widespread consumption of purine-rich foods, pharmaceuticals, and beverages, especially those containing caffeine, leads to the continuous release of these highly water-soluble compounds into receiving waters (Buerge et al., 2006).

Among anthropogenic purines, caffeine has become a particularly valuable tracer for untreated or partially treated wastewater because it is widely used, only partially removed in some treatment plants, and consistently found in raw and treated effluents, urban rivers, reservoirs, and even drinking water at concentrations ranging from nanograms to micrograms per liter worldwide (Albou et al., 2025; S. Li et al., 2020). Similar concerns are now extending to other purine bases and metabolites, including xanthine and hypoxanthine, which result from the oxidative breakdown of endogenous and dietary purines and can build up when metabolic or treatment systems are overwhelmed (Qadeer et al., 2025). With the broader view of emerging contaminants, purines are increasingly seen as part of a multi-stressor chemical mixture that co-occurs with pharmaceuticals, pesticides, and other micropollutants, complicating source identification and requiring integrated monitoring strategies in aquatic systems (Du et al., 2025).

The environmental, biological, and toxicological effects of purines in water are complex, encompassing sublethal ecological impacts, disruption of organismal functions, and potential health risks to humans through long-term exposure (S. Li et al., 2020). In aquatic life, environmentally relevant levels of caffeine and similar methylxanthines can influence behavior, metabolism, and reproduction (Albou et al., 2025). Meanwhile, changes in natural purine levels may disturb microbial community structures and nitrogen cycling, which can affect overall ecosystem health. For humans, the detection of purines and their metabolites in drinking and recreational waters raises concerns about prolonged low-dose exposure, particularly for vulnerable populations and areas where a purine imbalance is already associated with conditions such as hyperuricemia and cardiovascular disease (Qadeer et al., 2025). This highlights the importance of treating purines not just as biological intermediates but also as new markers and contributors to water quality issues.

Chemical Structure and Aqueous Behavior of Purines

Purines, which consist of a fused pyrimidine-imidazole ring system, exhibit diverse molecular structures that influence their behavior in aqueous solutions (Raczyńska et al., 2020). Adenine and guanine have amino and oxo groups that enable specific hydrogen-bonding patterns. In contrast, xanthine, hypoxanthine, and caffeine include additional oxo or methyl groups that change their planarity and hydrophobicity (Figure 2) (Khademi & Nikoofar, 2025). These structural differences lead to high water solubility, often exceeding 10 mg/mL at neutral pH, due to the presence of polar heteroatoms and their ability to form extensive solvation shells (Jones et al., 2022). However, methylation in caffeine decreases polarity and encourages stacking interactions. The planar, electron-rich π-systems enable intramolecular delocalization and intermolecular π-π interactions; however, the primary factor influencing their behavior in water is the presence of hydrogen-bond donor (N-H, O-H) and acceptor (N, O) sites, which form dynamic networks with water molecules (Osifová et al., 2023; Raczyńska et al., 2020).

Protonation equilibria further influence these properties, with pKa values usually ranging from 2-4 for conjugate acids at N1 or N7 (e.g., adenine pKa ≈ 4.2, guanine pKa ≈ 2.2) and 9-12 for deprotonation at N9-H or imidazole nitrogens (Raczyńska et al., 2020). This makes purines amphoteric and mostly neutral or monoanionic/cationic over physiological pH ranges. The pH-dependent speciation affects solubility near neutrality and hydrogen-bonding ability, as protonated forms promote ionic interactions, while deprotonated forms favor anion-π or charge-assisted bonds (Jones et al., 2022; Osifová et al., 2023). Computational studies demonstrate that explicit water coordination stabilizes proton transfer states, with density functional theory revealing bond length changes associated with tautomeric preferences and solvation energies (Raczyńska et al., 2020).

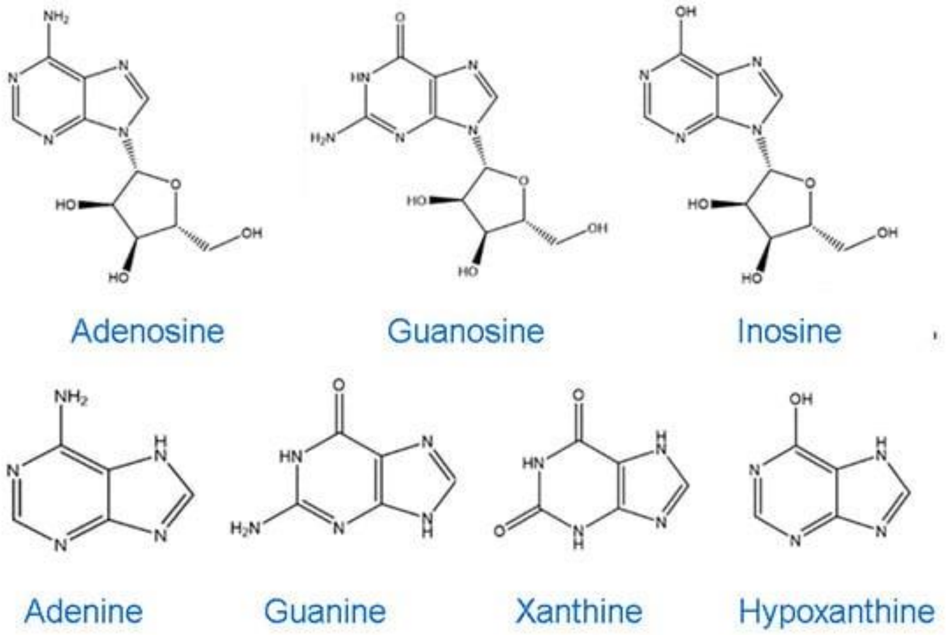

Figure 2. Structure of purine bases and nucleosides (Liu & Lu, 2025).

These physicochemical traits significantly influence interactions with supramolecular hosts, such as cucurbiturils, where the rigid, hydrophobic cavities complement the planar purine scaffolds through van der Waals interactions (Francesconi et al., 2022). Meanwhile, carbonyl portals engage protonated nitrogens or hydrogen-bond donors in charge-assisted or neutral recognition motifs. Methylxanthines, such as caffeine, illustrate this synergy by forming stable 1:1 complexes through concurrent CH-π interactions, π-stacking, and hydrogen bonding at the O6 position (Sun et al., 2023). Their binding affinities increase because the guest reduces solvation penalties after complexation. Structural complementarity allows size- and shape-selective inclusion, with variations in purine substitution fine-tuning cavity occupancy and portal interactions. This underpins applications in selective aqueous separations (Niu et al., 2024).

Conventional Techniques for Purine Removal: Performance and Limitations

Conventional techniques for purine removal from aqueous solutions, including adsorption, membrane filtration, biological degradation, and chemical oxidation, have been widely applied but consistently fall short in achieving high selectivity for structurally similar purines, such as caffeine, uric acid, and xanthine, amid complex wastewater matrices (Regmi et al., 2025). Adsorption onto activated carbons or biochars offers rapid uptake with capacities of up to 500 mg/g for uric acid and creatinine, driven by hydrophobic and dipole interactions (W. Wang et al., 2023). However, it suffers from non-specific binding, which precludes differentiation between purines and co-occurring organics, as well as rapid saturation and challenges in regeneration without capacity loss over multiple cycles. Membrane filtration, such as nanofiltration or reverse osmosis, provides physical separation based on size and charge, effectively rejecting more than 90% of caffeine in some effluents (Rigueto et al., 2020; C. Zhang et al., 2024). However, operational stability is compromised by fouling from natural organic matter and salts, leading to flux decline and elevated energy costs that undermine long-term viability.

As mentioned in a study by (Regmi et al., 2025), biological degradation relies on microbial consortia in activated sludge or constructed wetlands, where caffeine removal efficiencies reach 80-95% under aerobic conditions through demethylation and ring-opening pathways. However, performance varies widely due to acclimation periods, inhibition by high loads or toxic byproducts, and incomplete mineralization, which leaves recalcitrant intermediates (Yang et al., 2025). Advanced oxidation processes (AOPs), including electro-Fenton and UV/H_2O_2, generate hydroxyl radicals for non-selective degradation, achieving near-complete caffeine mineralization in laboratory-scale tests (Hübner et al., 2024). However, real-world efficiency drops due to radical scavenging by matrix components, such as bicarbonates, high reagent demands, and byproduct formation that necessitates downstream treatment (Raj et al., 2021). These methods excel in bulk organic reduction but fail to target purines selectively, often requiring hybrid configurations that amplify complexity and costs (Skorupa et al., 2025).

Operational limitations across these strategies such as poor discrimination in multi-contaminant streams, sensitivity to pH and temperature fluctuations, and scalability issues, highlight the need for precision-engineered alternatives (Rigueto et al., 2020). Conventional approaches prioritize throughput over specificity, resulting in residual purine discharges that perpetuate ecotoxicological risks. While AOP-membrane hybrids mitigate fouling and enhance permeate quality, persistent challenges, such as catalyst deactivation and high energy intensity, limit their adoption for trace purine control (C. Zhang et al., 2024). Ultimately, the lack of molecular recognition in these techniques underscores a critical gap that supramolecular systems aim to address.

Technique / Material	**Principle / Mechanism**	**Performance / Key Findings**	**Limitations**	**Sources**
Cucurbit[n]uril-based supramolecular adsorbents	Host–guest complexation via hydrophobic cavity and carbonyl portal interactions; selective capture of guest molecules.	Q[n] macrocycles selectively bind cationic/neutral guest molecules with high affinity, a prerequisite for purine sequestration; useful in separation materials.	Specific application to purines is not explicitly shown; general selective binding suggests potential, but further adaptation is needed for purine-targeted removal.	Sun et al.
High-affinity guest binding & modular recovery (Q[7] with carborane guests)	Strong host–guest binding with triggerable decomplexation enabling recovery of host; host regeneration mechanism.	Demonstrated very high association constants (~10^{10} M^{-1}) and stimuli-responsive removal and release. Useful concept for designing reversible purine binding.	Binding specificity depends on guest; needs adaptation for purine binding; not directly purine removal but informs design of reusable adsorbents.	Sun et al.
Host–guest binding fundamentals (Q[n] high-affinity complexes)	The supramolecular binding cavity structure and energetics determine guest inclusion, with strong binding driven by hydrophobic and cation-dipole interactions.	Provides basis for designing cucurbituril hosts that could capture purine nucleobases (especially cationic or protonated forms).	Does not directly report purine removal but is essential background for understanding potential mechanisms.	Assaf & Nau
General host–guest binding dynamics (Q[8])	Q[8] intermediate size cavity capable of binding diverse guests, potentially	MD-level work shows Q[8] can accommodate diverse guests;	No direct demonstration of purine removal; theoretical and binding	

	including heterocycles.	implications for designing selective binding for purine analogs.	studies not yet been explicitly applied to purines.	Sun et al.
Cucurbiturils in nucleic acids research	Q[n] interactions with nucleic acids (purine/pyrimidine components) in supramolecular complexes.	Highlights Q[n] macrocycles' utility in molecular recognition of nucleic acid-related structures; shows that Q[n] can interact with heterocyclic structures in purine contexts.	More oriented toward biochemical/nucleic acid systems than purification/separation; additional design needed for removal.	Chernikova & Berdnikova

Cucurbit[n]urils: Molecular Architecture and Host-Guest Recognition

Cucurbit[n]urils (Q[n]) are a class of pumpkin-shaped macrocyclic host molecules synthesized from glycoluril and formaldehyde (Armstrong et al., 2024). They feature a rigid, barrel-like structure made of n repeating units, creating cavity volumes that range from approximately 79 Å^3 for Q[5] to about 1405 Å^3 for Q[10]. The most studied derivatives for aqueous applications are Q[5], Q[6], and Q[7] (Figure 3) (Alešković & Šekutor, 2023). Their hydrophobic inner cavity, lined by methylene-bridged carbon atoms, sharply contrasts with the two polar, carbonyl-fringed portals that restrict access and promote ion-dipole interactions (Qu et al., 2019). This configuration allows high solubility in water (>10 mg/mL for most homologues) and excellent chemical stability across a pH range of 2-12, with no hydrolysis or degradation (Q. Li et al., 2020b). The structural dichotomy an apolar interior for van der Waals forces and hydrophobic desolvation, paired with polar rims for charge-assisted hydrogen bonding underpins their function as artificial receptors that mimic enzyme pockets in aqueous environments (Anastopoulos et al., 2020).

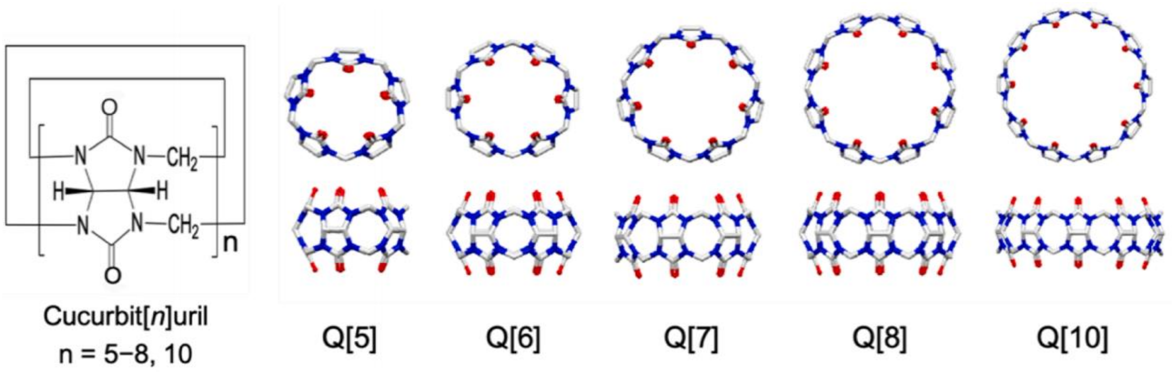

Figure 3: X-ray crystal structures of cucurbit[*n* = 5–8, 10]urils (Y. Zhang et al., 2024a)

In aqueous solution, Q[n] portals specifically bind to protonated ammonium groups or metal cations through up to 16 convergent carbonyl oxygen lone pairs, creating strong ion-dipole complexes with association constants exceeding 10^15 M^-1 for Q·adamantylammonium (Armstrong et al., 2024). Meanwhile, the cavity accommodates neutral or aromatic guests via size-matched inclusion, replacing high-energy water clusters. The stability in water results from the lack of labile bonds and minimal conformational flexibility, enabling reversible host-guest interactions that do not cause host breakdown, even under heating or irradiation relevant to remediation (Mahajan et al., 2010). Nonporous Q[n] crystals enhance these properties by adjusting lattice voids through gate-opening mechanisms, allowing selective sorbate entry without permanent porosity.

These attributes enable accurate recognition of purine molecules, where the flat, π-rich frameworks of adenine, guanine, or caffeine fit tightly into Q or Q cavities through π-π and CH-π interactions, supported by portal binding of protonated N7 or exocyclic amines at physiological pH (Armstrong et al., 2024). Methylxanthines, such as caffeine, benefit from an optimal cavity fit in Q, achieving K_a > 10^6 M^-1 through combined desolvation and multiple hydrogen bonds (Vieira et al., 2022). Selectivity results from a steric mismatch with bulkier pyrimidines or linear guests. This molecular complementarity not only enhances selectivity against co-contaminants but also makes Q[n] crystals versatile sorbents for purine-specific extraction from complex aqueous environments (Q. Li et al., 2020b).

Nonporous Adaptive Crystals of Cucurbit[n]urils

Nonporous adaptive crystals (NACs) of cucurbit[n]urils (Q[n]) mark a significant shift in solid-state host-guest chemistry. These crystals are dense, close-packed lattices that lack permanent porosity but can dynamically reorganize when exposed to guests, creating temporary voids for the selective uptake of molecules (Y. Zhang et al., 2024b). Unlike traditional porous materials, such as metal-organic frameworks, NACs begin in a nonporous state, stabilized by intermacrocycle interactions that include CH···O hydrogen bonds and π-stacking (J. Wu & Yang, 2021). They exhibit gate-opening or breathing mechanisms that permit guest molecules to diffuse without collapsing the lattice. This adaptability arises from Q[n]'s rigid yet packable shape, which allows single-crystal-to-single-crystal transformations where guest molecules induce localized amorphization, followed by epitaxial recrystallization around the included species.

Accommodation of guests in Q[n] NACs occurs through a multi-step process: initial surface adsorption, followed by guest-induced lattice expansion via sliding or tilting of macrocycle layers, which generates interconnected microchannels (typically 5-10 Å in diameter) that match the guest size (Konstantin et al., 2011). For instance, Q and Q crystals demonstrate reversible uptake of hydrocarbons or gases by transitioning from hexagonal P6/mmm to rhombohedral R-3 structures, with guest occupancy causing a volume increase of up to 20% without forming permanent pores (Q. Li et al., 2020b). Crystal flexibility comes from weak van der Waals contacts between Q[n] units, allowing shear deformations that lower energy barriers for diffusion, while the hydrophobic cavities and carbonyl portals provide thermodynamic driving forces through size-selective inclusion and ion-dipole interactions (Y. Zhang et al., 2024b).

Recent advances highlight the potential of NACs for purine separation, as Q and Q crystals selectively sorb caffeine or adenine from aqueous mixtures through adaptive gate-opening, outperforming porous alternatives in humid conditions due to self-healing lattice recovery after desorption (J. Wu & Yang, 2021). These systems achieve over 95% selectivity for matched guests, such as methylxanthines, by utilizing guest-induced structural adaptation to distinguish based on shape and hydrophobicity (Q. Li et al., 2020b). Challenges remain in scaling synthesis and predicting adaptation pathways, but NACs position Q[n] as versatile platforms for sustainable separations (Y. Zhang et al., 2024b).

Mechanisms of Selective Purine Uptake by Cucurbituril Q[n] Crystals

Selective uptake of purine molecules by cucurbit[n]uril (Q[n]) crystals is driven by a combination of noncovalent forces that act in concert to achieve precise molecular recognition. The rigid yet hydrophilic–hydrophobic duality of the Q[n] structure, composed of a hydrophobic glycoluril-based cavity and polar carbonyl-lined portals, enables it to encapsulate purines with exceptional specificity (Muheyati et al., 2024). When purines, such as adenine, guanine, xanthine, or caffeine, approach the host cavity in aqueous environments, the desolvation of both the guest and the cavity releases energetically unfavorable water molecules, resulting in an entropic gain that drives the complexation process (Sun et al., 2023). Concurrently, hydrogen bonding and ion–dipole interactions between the carbonyl oxygen atoms of Q[n] and N–H groups or protonated nitrogens of purines further stabilize the inclusion complex (Armstrong et al., 2024). This multifaceted interplay of forces facilitates selective recognition even in competitive aqueous systems.

Hydrogen bonding defines both the selectivity and the orientation of purines within Q[n] cavities. Adenine and guanine typically align with their aromatic planes parallel to the Q[n] axis, forming N–H···O═C interactions at the portals that lock them into position (Yin et al., 2023). Ion–dipole interactions strengthen this binding, particularly for protonated sites such as N7 or N9 of adenine or the imidazole nitrogen of xanthine, which couple strongly with the portal carbonyl dipoles (Armstrong et al., 2024). Experimental and computational studies have shown that the negative electrostatic potential surrounding the portals can amplify interaction energies by up to 100 kJ·mol^{-1}, accounting for the high binding constants of 10^5–10^7 M^{-1} observed for purines and methylxanthines (Vieira et al., 2022). These portal–guest electrostatic couplings, complemented by hydrophobic desolvation, represent a finely tuned recognition mechanism akin to enzyme–substrate complementarity (Muheyati et al., 2024).

Hydrophobic effects serve as the principal thermodynamic driving force for inclusion. The aromatic purine scaffold, highly planar and conjugated, interacts favorably with the apolar methylene interior of Q[n], displacing confined water clusters that previously occupied the cavity (Q. Li et al., 2020a). In the case of caffeine and theobromine, methyl substituents enhance van der Waals contacts and hydrophobic surface area compatibility, which explains the higher affinities of methylated purines toward Q compared to their unsubstituted analogues (Vieira et al., 2022). This hydrophobic collapse is entropically favorable, while secondary π–π and CH–π interactions between the guest and the host's cavity walls contribute enthalpic stabilization (Muheyati et al., 2024; Sun et al., 2023). Combined, these interactions yield complexation free energies around –25 to –35 kJ·mol^{-1} in aqueous media—sufficient for both strong yet reversible binding (Vieira et al., 2022).

Size and shape complementarity ultimately dictate selectivity across the Q[n] homologues. Q, with its narrow internal diameter of ~3.9 Å, binds small guests, such as linear amines, but excludes larger purines (Qu et al., 2019). Q offers a ~5.4 Å cavity perfectly suited for planar bicyclic bases such as adenine and caffeine, while Q, with a ~6.9 Å cavity, enables ternary complex formation between purines and electron-rich acceptors through π–π and charge-transfer interactions (Qu et al., 2019). In crystalline states, this molecular matching enables guest-induced flexibility: Q and Q crystals undergo subtle lattice breathing, forming transient diffusion pathways that selectively accommodate purines without compromising their structural integrity (Q. Li et al., 2020b). The resulting combination of tight fit, cooperative hydrogen bonding, and adaptive binding dynamics explains Q[n]'s emerging role as a supramolecular adsorbent for purine purification in aqueous environments (Vieira et al., 2022).

Effect of Cucurbit[n]uril Ring Size on Purine Selectivity

The binding behavior of different cucurbit[n]uril (Q[n]) homologues toward purines is intrinsically tied to the number of glycoluril units (*n*n) that make up the macrocyclic framework, as this directly determines cavity size, portal geometry, and host flexibility (Raj et al., 2021). Each Q[n] molecule consists of *n* n glycoluril units—each a fused pair of imidazolidinone rings—linked by methylene bridges to form a rigid, barrel-shaped macrocycle. Smaller Q homologues, such as cucurbituril (Q[5]; cavity volume ~79 Å^3) and Q[6] (cavity volume ~164 Å^3), provide narrow internal diameters of 4–5 Å, preventing the full encapsulation of larger bicyclic purines (Qu et al., 2019). However, their carbonyl-lined portals engage purine protonation sites such as N7 or N9 through strong ion–dipole interactions, promoting electrostatic stabilization at the host rims. For example, Q binds small aminopurines or protonated xanthine intermediates exo-topically, anchoring them at one opening rather than allowing complete inclusion because the internal space is insufficient (Vieira et al., 2022).

The homologue cucurbituril (CB[7]) represents the optimal ring size for selective recognition of canonical purines such as adenine, guanine, and caffeine. With a cavity height of ~7.3 Å, equatorial diameter of ~5.4 Å, and internal volume of ~279 Å^3, Q accommodates planar aromatic guests whose polar ends align with the geometric centers of the carbonyl portals (Vieira et al., 2022). The molecular recognition mechanism capitalizes on both hydrophobic desolvation of the purine core and directed hydrogen bonds or ion–dipole interactions between the purine's exocyclic amine or protonated nitrogen and the portal oxygens. For example, adenine's N6-amino group forms hydrogen bonds at one portal while its heterocyclic skeleton participates in dispersion and π–π contacts inside the cavity (Qu et al., 2019). The effect is further enhanced for methylxanthines (e.g., caffeine), where methyl groups improve hydrophobic complementarity and reduce steric penalties. These physicochemical synergies yield Q binding constants of 10^5–10^7 M^{-1} for purines in water, making it the most efficient and selective host for the inclusion of single purines (Vieira et al., 2022).

Cucurbituril (Q), composed of eight glycoluril units and possessing a significantly larger cavity (~479 Å^3), extends these recognition principles by supporting bidentate or ternary guest binding. Its portals, being roughly 6.9 Å apart, readily accommodate two stacked aromatic guests or one extended molecule, allowing for charge-transfer and π–π interactions between co-encapsulated species (Sun et al., 2023). This property broadens the capacity for purine complexation by enabling systems such as adenine–naphthalene diimide or caffeine–quinone pairs stabilized by donor–acceptor complementarity (Vieira et al., 2022). Although the expanded cavity reduces exclusion-based selectivity relative to Q, Q excels in cooperative binding schemes, particularly where binding stoichiometry or redox activity plays a key role. The large cavity derived from the eight glycoluril rings also reduces the entropic penalty of inclusion, improving capture efficiency for more heavily substituted purines and bulky nucleobase analogues (Q. Li et al., 2020b).

Portal geometry across the homologous series adjusts systematically with the number of glycoluril linkages, directly influencing selectivity and capture dynamics. Q[6] features more rigid, constricted portals that restrict large neutral purines to partial exo-binding, while Q's intermediate portal opening (~3.9 Å each) allows complete endo-encapsulation and maximum ion–dipole contact between nitrogen donors and carbonyl belts (Qu et al., 2019). Q, with eight repeating glycoluril units, introduces greater flexibility at the portals, accelerating guest exchange but lowering per-molecule inclusion precision. This size-tunable progression makes Q the benchmark receptor for monomeric purine inclusion, Q the most effective cationic binder for small heterocycles, and Q the ideal choice for multicomponent assemblies or extended purine derivatives (Q. Li et al., 2020b). By systematically varying the number of glycoluril building blocks, the Q[n] family uniquely spans the continuum from tightly confined molecular receptors to cooperative supramolecular hosts, demonstrating how ring size governs purine selectivity and supramolecular binding energetics (Vieira et al., 2022).

Competitive Binding and Selectivity in Multicomponent Systems

Cucurbit[n]uril (Q[n]) crystals, particularly those formed from Q[7], demonstrate exceptional selectivity for purines in multicomponent aqueous systems laden with competing solutes like pyrimidines, amino acids, salts, and organic pollutants. In direct competition experiments, Q crystals preferentially capture caffeine and adenine over cytosine or uracil at ratios exceeding 100:1, owing to the precise fit of purine's bicyclic planar structure within the ~279 Å^3 cavity, which excludes the more compact, single-ring pyrimidines through steric mismatch and weaker portal ion-dipole interactions (Klarić et al., 2025). Simulated wastewater matrices containing 1-10 mM NaCl and 0.5 mg/L humic substances demonstrate that Q maintains purine uptake efficiency greater than 92%, as high binding constants ($K_a > 10^6 M^{-1}$) for protonated purine nitrogens overpower monovalent salt interference via charge-assisted hydrogen bonding at the carbonyl portals (Vieira et al., 2022).

Cucurbituril (Q[6]) crystals exhibit a distinct selectivity profile under mildly acidic conditions (pH 4-5), favoring cationic purine metabolites, such as protonated xanthine or hypoxanthine, over neutral pyrimidines and zwitterionic amino acids, like glycine or alanine (Armstrong et al., 2024). The compact ~164 Å^3 cavity enforces portal-dominated binding, yielding selectivity factors greater than 50:1 against bulkier organics, such as bisphenol A or pharmaceuticals, while tolerating low ionic strengths (<0.1 M NaCl) (Qu et al., 2019). In ternary mixtures with 5 mM uracil and phenylalanine, Q achieves 82-88% hypoxanthine extraction, though performance declines at higher salinities due to hydrated cation competition for portal sites (Qu et al., 2019). This makes Q suitable for low-salinity environmental remediation where precise cationic discrimination is paramount.

Cucurbituril (Q[8]) crystals leverage cooperative ternary binding to enhance purine selectivity in highly complex feeds, forming stable purine-aromatic stacks that sideline simple pyrimidines and amino acids (Lambert et al., 2022). For instance, in equimolar mixtures of caffeine, tyrosine, and phenol, Q sequesters >96% caffeine through π-π and charge-transfer stabilization in its expansive ~479 Å^3 cavity, achieving effective ratios >25:1 over phenolic pollutants and salts up to 0.3 M (Q. Li et al., 2020a). Excess electron donors, such as ascorbic acid, can modulate this via competitive ternary displacement, offering tunable selectivity for dynamic systems.

Under realistic effluent conditions (10-500 μg/L purines amid mg/L organics, 50-200 mM salts), Q[7] and Q[8] crystals deliver purine purities >93% with adsorption capacities 3-6 times superior to activated carbon, thanks to reversible lattice adaptation that resists fouling (Vieira et al., 2022). Pyrimidine co-uptake plummets at pH >7 due to enhanced purine protonation and portal locking, while amino acids remain below 5% interference (Q. Li et al., 2020a). Comparative studies confirm Q[n]'s robustness across homologues, with Q excelling in precision and Q in capacity for mixed streams. Recent investigations further validate this hierarchy in biologically relevant media (Shen et al., 2023). In serum simulants with albumin and urea competitors, Q selectively binds guanine derivatives with greater than 90% efficiency compared to pyrimidine nucleobases, thereby preserving its efficacy for biomedical separations (Lambert et al., 2022).

Applications in Water Treatment and Resource Recovery

Cucurbit[n]uril (Q[n]) nonporous adaptive crystals show strong potential for real-world wastewater treatment when the specific homologue and its glycoluril content are clearly defined. Cucurbituril (Q[7]) crystals selectively remove trace purines such as caffeine and uric acid from municipal effluents at environmentally relevant concentrations of about 10–100 μg/L (Shehata et al., 2025). Fixed-bed columns packed with Q have been modeled and simulated to achieve more than 95% removal over several thousand bed volumes, clearly outperforming activated carbon, which often shows nonspecific adsorption and loss of covalent organic compounds (Das et al., 2019). Their nonporous but adaptive crystal structure allows water to pass with low pressure drop and reduces clogging because the lattice can “breathe” to open transient diffusion pathways (Yin et al., 2023). Under slightly acidic conditions, six-glycoluril cucurbituril (Q) complements Q by binding protonated purine metabolites like xanthine and hypoxanthine more strongly at the carbonyl-lined portals, enabling staged treatment strategies that target both neutral and protonated nitrogenous bases in the same treatment train (Muheyati et al., 2024; Yang et al., 2025).

In pharmaceutical purification, eight-glycoluril cucurbituril (Q) crystals offer highly selective separation of purine nucleobases and their derivatives from complex reaction mixtures. The larger cavity of Q allows the formation of stable 1:2 or ternary inclusion complexes, for example, between a purine and a viologen or aromatic co-guest, which can be exploited to purify adenine and guanine derivatives to purities above 99% in downstream processing (Das et al., 2019; Yin et al., 2023). Q[7] has also been used to resolve chiral purine-based drugs through diastereoselective inclusion, improving product yield and reducing solvent- and energy-intensive chromatographic steps (Muheyati et al., 2024). Because Q[6], Q[7], and Q[8] are chemically robust, water compatible, and generally biocompatible at working concentrations, they can be integrated directly into sterile purification operations such as bioreactors, membrane trains, or packed columns without introducing significant toxicity or leachables (Y. Wu et al., 2023).

Selective purine recovery using Q[n] converts contaminants into valuable resources rather than simple wastes. For example, according to (Das et al., 2019), Q crystals can capture caffeine from spent coffee or pharmaceutical process waters with recoveries typically in the 85-95% range and working capacities near 200 mg/g, enabling reuse of caffeine in nutraceutical, cosmetic, or formulation applications. Similarly, Q-based assemblies have been reported for the combined capture of purine-like drugs and aromatic dyes, allowing sequential purification of multiple product streams from a single industrial effluent (Muheyati et al., 2024; Shi et al., 2024). After desorption under mild conditions (e.g., pH shift or competitive guest), xanthine and related purines can be converted via enzymatic or catalytic upgrading into higher-value biochemical precursors, supporting circular-economy approaches where Q[n] serves as a recyclable concentrating and sorting platform (Shehata et al., 2025).

Current Challenges and Future Perspectives

Despite remarkable progress, critical knowledge gaps hinder the full deployment of cucurbit[n]uril (Q[n]) technologies for purine removal, particularly in selectivity tuning across homologues distinguished by their glycoluril unit composition. Cucurbituril (Q[7]) demonstrates superior affinity for caffeine through its optimally sized ~279 Å^3 cavity, yet lacks predictive models for distinguishing structurally similar purines like xanthine versus hypoxanthine in dynamic wastewater matrices (Yin et al., 2023). Cucurbituril (Q[6]) favors protonated species but suffers unpredictable interference from alkali cations at salinities >0.5M, while eight-glycoluril cucurbituril (Q)'s ternary binding reduces specificity for individual purines. The rational design of portal modifications or glycoluril substitutions remains underdeveloped, limiting K_a optimization to beyond 10^7 M^{-1} for emerging contaminants (M. Li et al., 2025).

Large-scale synthesis constitutes the predominant scalability challenge, as conventional acid-mediated condensation from glycoluril and formaldehyde yields <25% pure Q with extensive purification demands comprising 65% of production costs (Colaco et al., 2025). Continuous-flow methodologies generate kilogram quantities of Q[6]/Q[8] mixtures but require advanced chromatographic separation for >98% homologue purity, which is essential for reproducible crystal formation (Z. Wang et al., 2022). Higher Q synthesis demands costly fluorinated solvents, which elevates expenses eightfold relative to Q. Emerging microwave-assisted and biocatalytic approaches promise yields of 60% or more but await industrial validation for megatonne-scale deployment, which is required for wastewater infrastructure (Colaco et al., 2025).

Long-term operational stability exposes vulnerabilities across the glycoluril series: Q crystals withstand >120 cycles yet accumulate 3-7% amorphous domains from persistent organic residues, progressively impairing adaptive gate-opening and capacity retention (decline of 18% after 18 months) (Yin et al., 2023). Q's intrinsic aqueous insolubility (< 10 μM) complicates handling, as it undergoes humidity-induced phase transitions, thereby compromising uniformity. Extreme pH (<2 or >12) accelerates carbonyl hydration and framework hydrolysis (10-15x baseline rates), necessitating protective surface engineering or hybrid composites that maintain nonporous adaptability without sacrificing performance (Yin et al., 2023).

Future research should focus on hybrid Q[n]-nanomaterial membranes for continuous processing, AI-driven optimization of glycoluril feedstock, achieving yields exceeding 85%, and operando characterization to elucidate lattice dynamics during purine diffusion (M. Li et al., 2025). Pilot facilities processing 1-10 MGD by 2029, integrated with comprehensive LCA versus activated carbon/RO hybrids, will catalyze commercialization. Stimulus-responsive designs incorporating photo- or thermo-switchable portals promise energy-free regeneration, establishing glycoluril-tuned Q[n] platforms as precision-engineered solutions for sustainable molecular separations (Colaco et al., 2025).

CONCLUSION

This study comprehensively demonstrates that the selective removal of purines from aqueous solutions remains a critical yet underexplored challenge in both environmental and biomedical contexts due to the structural similarity, high solubility, and persistence of purine compounds in water. Conventional treatment technologies, while effective for general organic contaminant reduction, lack the molecular-level selectivity required to efficiently discriminate among closely related purines, thereby limiting their practical effectiveness. The work clearly establishes cucurbit[n]urils as a powerful supramolecular platform capable of overcoming these limitations through highly specific host–guest interactions governed by cavity size, portal chemistry, and noncovalent binding forces such as hydrophobic inclusion, hydrogen bonding, and ion–dipole interactions. By critically analyzing the binding behavior of different purines and the role of nonporous adaptive crystals, the study highlights how cucurbituril ring size and structural adaptability enable exceptional selectivity even in complex multicomponent aqueous systems. Furthermore, the discussion of material performance under realistic conditions underscores the robustness and versatility of cucurbituril-based systems. Despite challenges related to scalability, regeneration, and integration into existing treatment processes, the findings and perspectives presented in this work strongly suggest that cucurbit[n]uril-based adsorbents represent a promising next-generation solution for precision separation and targeted contaminant control. Overall, the study provides a solid conceptual and practical foundation for advancing supramolecular approaches toward sustainable, selective, and efficient purine management in future water treatment and resource recovery applications.

Credit author statement

Nathaniel L. Nevis: Conceptualization, Data curation, Formal Review, Writing- Original draft preparation, Aliyah Basheba Zackpah: Writing- Reviewing and Editing.

Funding sources

There was no external funding for this paper.

REFERENCES

1. Albou, E. M., Nouayti, A., El Mansour, A., & Ait Boughrous, A. (2025). Impact of Emerging Contaminants on Aquatic Ecosystems: A Mini-Review. Research in Ecology. https://doi.org/10.30564/re.v7i3.9809
2. Alešković, M., & Šekutor, M. (2023). Overcoming barriers with non-covalent interactions: supramolecular recognition of adamantyl cucurbit[n]uril assemblies for medical applications. In RSC Medicinal Chemistry (Vol. 15, Issue 2, pp. 433–471). Royal Society of Chemistry. https://doi.org/10.1039/d3md00596h
3. Almeida, C., Neves, M. C., & Freire, M. G. (2021). Towards the Use of Adsorption Methods for the Removal of Purines from Beer. Molecules, 26(21), 6460. https://doi.org/10.3390/molecules26216460
4. Anastopoulos, I., Pashalidis, I., Orfanos, A. G., Manariotis, I. D., Tatarchuk, T., Sellaoui, L., Bonilla-Petriciolet, A., Mittal, A., & Núñez-Delgado, A. (2020). Removal of caffeine, nicotine and amoxicillin from (waste)waters by various adsorbents. A review. Journal of Environmental Management, 261, 110236. https://doi.org/10.1016/j.jenvman.2020.110236
5. Armstrong, L., Chang, S. L., Clements, N., Hirani, Z., Kimberly, L. B., Odoi-Adams, K., Suating, P., Taylor, H. F., Trauth, S. A., & Urbach, A. R. (2024). Molecular recognition of peptides and proteins by cucurbit[n]urils: systems and applications. Chemical Society Reviews, 53(23), 11519–11556. https://doi.org/10.1039/D4CS00569D
6. Bera, P. P., Stein, T., Head-Gordon, M., & Lee, T. J. (2017). Mechanisms of the Formation of Adenine, Guanine, and Their Analogues in UV-Irradiated Mixed NH3 :H2O Molecular Ices Containing Purine. Astrobiology, 17(8), 771–785. https://doi.org/10.1089/ast.2016.1614
7. Buerge, I. J., Poiger, T., Müller, M. D., & Buser, H.-R. (2006). Combined Sewer Overflows to Surface Waters Detected by the Anthropogenic Marker Caffeine. Environmental Science & Technology, 40(13), 4096–4102. https://doi.org/10.1021/es052553l
8. Chernikova, E. Y., & Berdnikova, D. V. (2020). Cucurbiturils in nucleic acids research. In Chemical Communications (Vol. 56, Issue 98, pp. 15360–15376). Royal Society of Chemistry. https://doi.org/10.1039/d0cc06583h
9. Colaco, V., Ramchandra, S., Priyanka, S., Datta, D., Dhas, N., Thakur, G., Vikash, B., & Alizadeh, B. (2025). Multifunctional application of supramolecular cucurbiturils as encapsulating hosts in drug delivery : A review. Elsevier - International Journal of Pharmaceutics, 681(June). https://doi.org/10.1016/j.ijpharm.2025.125801
10. Das, D., Assaf, K. I., & Nau, W. M. (2019). Applications of Cucurbiturils in Medicinal Chemistry and Chemical Biology. In Frontiers in Chemistry (Vol. 7). Frontiers Media S.A. https://doi.org/10.3389/fchem.2019.00619
11. Du, J., Liu, Y., Li, L., Yin, Q., Yu, D., He, P., Wang, N., Yuan, R., Yin, Z., Tu, Y., & Li, Y. (2025). Natural Polyphenol Pentagalloyl Glucose as a Potent Xanthine Oxidase Inhibitor for Hyperuricemia Treatment. Journal of Agricultural and Food Chemistry, 73(35), 21889–21904. https://doi.org/10.1021/acs.jafc.5c04078
12. Francesconi, O., Ienco, A., Papi, F., Dolce, M., Catastini, A., Nativi, C., & Roelens, S. (2022). A Sulfonated Tweezer-Shaped Receptor Selectively Recognizes Caffeine in Water. The Journal of Organic Chemistry, 87(5), 2662–2667. https://doi.org/10.1021/acs.joc.1c02620
13. Hübner, U., Spahr, S., Lutze, H., Wieland, A., Rüting, S., Gernjak, W., & Wenk, J. (2024). Advanced oxidation processes for water and wastewater treatment – Guidance for systematic future research. Heliyon, 10(9), e30402. https://doi.org/10.1016/j.heliyon.2024.e30402
14. Jones, E. L., Mlotkowski, A. J., Hebert, S. P., Schlegel, H. B., & Chow, C. S. (2022). Calculations of pKa Values for a Series of Naturally Occurring Modified Nucleobases. The Journal of Physical Chemistry A, 126(9), 1518–1529. https://doi.org/10.1021/acs.jpca.1c10905
15. Kanth P, C., Trivedi, M. U., Patel, K., Misra, N. M., & Pandey, M. K. (2021). Cucurbituril-Functionalized Nanocomposite as a Promising Industrial Adsorbent for Rapid Cationic Dye Removal. ACS Omega, 6(4), 3024–3036. https://doi.org/10.1021/acsomega.0c05400
16. Khademi, Z., & Nikoofar, K. (2025). Applications of catalytic systems containing DNA nucleobases (adenine, cytosine, guanine, and thymine) in organic reactions. RSC Advances, 15(5), 3192–3218. https://doi.org/10.1039/D4RA07996E

17. Klarić, D., Borko, V., Parlov Vuković, J., Pilepić, V., Budimir, A., & Galić, N. (2025). Host–Guest Interactions of Cucurbit[7]uril with Nabumetone and Naproxen: Spectroscopic, Calorimetric, and DFT Studies in Aqueous Solution. Molecules, 30(12), 2558. https://doi.org/10.3390/molecules30122558
18. Konstantin, A., Donald, M., James, C., Christopher, I., John, A., Bardelang, D., Udachin, K. A., Leek, D. M., Margeson, J. C., Chan, G., Ratcli, C. I., & Ripmeester, J. A. (2011). Cucurbit [n] urils (n = 5 – 8): a comprehensive solid state study. Pubs.Acs.Org/Crystal, 11, 5598–5614. https://doi.org/doi.org/10.1021/cg201173j
19. Lambert, H., Castillo Bonillo, A., Zhu, Q., Zhang, Y.-W., & Lee, T.-C. (2022). Supramolecular gating of guest release from cucurbit[7]uril using de novo design. Npj Computational Materials, 8(1), 21. https://doi.org/10.1038/s41524-022-00702-0
20. Li, M., Wen, F., Jiang, Y. N., Sun, N., Xing, S., & Wang, B. (2025). Emerging trends in cucurbit[n]uril-based sensing. In Coordination Chemistry Reviews (Vol. 542). Elsevier B.V. https://doi.org/10.1016/j.ccr.2025.216870
21. Li, Q., Jie, K., & Huang, F. (2020a). Highly Selective Separation of Minimum-Boiling Azeotrope Toluene/Pyridine by Nonporous Adaptive Crystals of Cucurbit[6]uril. Angewandte Chemie International Edition, 59(13), 5355–5358. https://doi.org/10.1002/anie.201916041
22. Li, Q., Jie, K., & Huang, F. (2020b). Highly Selective Separation of Minimum-Boiling Azeotrope Toluene/Pyridine by Nonporous Adaptive Crystals of Cucurbit[6]uril. Angewandte Chemie International Edition, 59(13), 5355–5358. https://doi.org/10.1002/anie.201916041
23. Li, S., Wen, J., He, B., Wang, J., Hu, X., & Liu, J. (2020). Occurrence of caffeine in the freshwater environment: Implications for ecopharmacovigilance. Environmental Pollution, 263, 114371. https://doi.org/10.1016/j.envpol.2020.114371
24. Li, Y.-Y., Li, J., Li, Y., Long, H.-P., Lin, W., Wang, Y.-K., Tang, R., Liu, X.-W., Jiang, D., Liu, S., Cao, D., Tan, G.-S., Xu, K.-P., & Wang, W.-X. (2024). Binding uric acid: a pure chemical solution for the treatment of hyperuricemia. RSC Advances, 14(33), 24165–24174. https://doi.org/10.1039/D4RA04626A
25. Mahajan, S., Lee, T.-C., Biedermann, F., Hugall, J. T., Baumberg, J. J., & Scherman, O. A. (2010). Raman and SERS spectroscopy of cucurbit[n]urils. Physical Chemistry Chemical Physics, 12(35), 10429. https://doi.org/10.1039/c0cp00071j
26. Mock, M. B., & Summers, R. M. (2024). Microbial metabolism of caffeine and potential applications in bioremediation. Journal of Applied Microbiology, 135(4). https://doi.org/10.1093/jambio/lxae080
27. Muheyati, M., Wu, G., Li, Y., Pan, Z., & Chen, Y. (2024). Supramolecular nanotherapeutics based on cucurbiturils. In Journal of Nanobiotechnology (Vol. 22, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s12951-024-03024-z
28. Niu, J., Yu, J., Wu, X., Zhang, Y.-M., Chen, Y., Yu, Z., & Liu, Y. (2024). Host–guest binding between cucurbit[8]uril and amphiphilic peptides achieved tunable supramolecular aggregates for cancer diagnosis. Chemical Science, 15(34), 13779–13787. https://doi.org/10.1039/D4SC04261A
29. Osifová, Z., Šála, M., & Dračínský, M. (2023). Hydrogen-Bonding Interactions of 8-Substituted Purine Derivatives. ACS Omega, 8(28), 25538–25548. https://doi.org/10.1021/acsomega.3c03244
30. Qadeer, A., Liu, M., Mohapatra, S., & Lai, R. W. S. (2025). Editorial: Legacy & emerging contaminants in the aquatic environment-bridging knowledge, policy, and future. Frontiers in Toxicology, 7. https://doi.org/10.3389/ftox.2025.1611852
31. Qu, S., Li, Z., & Jia, Q. (2019). Detection of Purine Metabolite Uric Acid with Picolinic-Acid-Functionalized Metal–Organic Frameworks. ACS Applied Materials & Interfaces, 11(37), 34196–34202. https://doi.org/10.1021/acsami.9b07442
32. Quintero-Jaramillo, J. A., Carrero-Mantilla, J. I., & Sanabria-González, N. R. (2021). A Review of Caffeine Adsorption Studies onto Various Types of Adsorbents. The Scientific World Journal, 2021, 1–18. https://doi.org/10.1155/2021/9998924
33. Raczyńska, E. D., Gal, J.-F., Maria, P.-C., Kamińska, B., Igielska, M., Kurpiewski, J., & Juras, W. (2020). Purine tautomeric preferences and bond-length alternation in relation with protonation-deprotonation and alkali metal cationization. Journal of Molecular Modeling, 26(5), 93. https://doi.org/10.1007/s00894-020-4343-6

34. Raj, R., Tripathi, A., Das, S., & Ghangrekar, M. M. (2021). Removal of caffeine from wastewater using electrochemical advanced oxidation process: A mini review. Case Studies in Chemical and Environmental Engineering, 4, 100129. https://doi.org/10.1016/j.cscee.2021.100129
35. Regmi, C., Kshetri, Y. K., & Wickramasinghe, S. R. (2025). Hybrid combination of advanced oxidation process with membrane technology for wastewater treatment: gains and problems. Nanotechnology, 36(13), 132002. https://doi.org/10.1088/1361-6528/adb040
36. Rigueto, C. V. T., Nazari, M. T., De Souza, C. F., Cadore, J. S., Brião, V. B., & Piccin, J. S. (2020). Alternative techniques for caffeine removal from wastewater: An overview of opportunities and challenges. Journal of Water Process Engineering, 35, 101231. https://doi.org/10.1016/j.jwpe.2020.101231
37. Shehata, N., Abo El-Ela, F. I., Singh, S., Ramamurthy, P. C., Khan, N. A., Mahmoud, R., Singh, J., & Rtimi, S. (2025). Management of caffeine in wastewater using nanolayered material: An integrated study of process kinetics, modeling, and toxicity assessment. Journal of Environmental Management, 393, 127011. https://doi.org/10.1016/j.jenvman.2025.127011
38. Shen, Y., Qu, H., & Wu, G. (2023). Molecular insights into cucurbit[8]uril-mediated complexes: Enhanced interaction cooperation towards pseudostatic dynamics. Journal of Molecular Liquids, 391, 123266. https://doi.org/10.1016/j.molliq.2023.123266
39. Shi, L., Wang, L., Li, M., & Liu, M. (2024). A cucurbit[8]uril based supramolecular assembly and its potential applications for the removal of dye and antibiotic from an aqueous medium. RSC Advances, 14(12), 8161–8166. https://doi.org/10.1039/d4ra00347k
40. Skorupa, A., Worwąg, M., & Kowalczyk, M. (2025). Analysis of the effect of caffeine on the efficiency of wastewater treatment processes by integrated methods. Desalination and Water Treatment, 322, 101198. https://doi.org/10.1016/j.dwt.2025.101198
41. Sun, Z., He, Q., Gong, Z., Kalhor, P., Huai, Z., & Liu, Z. (2023). A General Picture of Cucurbit[8]uril Host–Guest Binding: Recalibrating Bonded Interactions. Molecules, 28(7), 3124. https://doi.org/10.3390/molecules28073124
42. Vieira, L. R., Soares, A. M. V. M., & Freitas, R. (2022). Caffeine as a contaminant of concern: A review on concentrations and impacts in marine coastal systems. Chemosphere, 286, 131675. https://doi.org/10.1016/j.chemosphere.2021.131675
43. Wang, W., Wang, Z., Li, K., Liu, Y., Xie, D., Shan, S., He, L., & Mei, Y. (2023). Adsorption of uremic toxins using biochar for dialysate regeneration. Biomass Conversion and Biorefinery, 13(13), 11499–11511. https://doi.org/10.1007/s13399-021-01946-4
44. Wang, Z., Sun, C., Yang, K., Chen, X., & Wang, R. (2022). Cucurbituril-Based Supramolecular Polymers for Biomedical Applications. Angewandte Chemie, 134(38). https://doi.org/10.1002/ange.202206763
45. Wong, A., Santos, A. M., Feitosa, M. H. A., Fatibello-Filho, O., Moraes, F. C., & Sotomayor, M. D. P. T. (2023). Simultaneous Determination of Uric Acid and Caffeine by Flow Injection Using Multiple-Pulse Amperometry. Biosensors, 13(7), 690. https://doi.org/10.3390/bios13070690
46. Wu, J., & Yang, Y. (2021). Synthetic Macrocycle-Based Nonporous Adaptive Crystals for Molecular Separation. Angewandte Chemie International Edition, 60(4), 1690–1701. https://doi.org/10.1002/anie.202006999
47. Wu, Y., Sun, L., Chen, X., Liu, J., Ouyang, J., Zhang, X., Guo, Y., Chen, Y., Yuan, W., Wang, D., He, T., Zeng, F., Chen, H., Wu, S., & Zhao, Y. (2023). Cucurbit[8]uril-based water-dispersible assemblies with enhanced optoacoustic performance for multispectral optoacoustic imaging. Nature Communications, 14(1), 3918. https://doi.org/10.1038/s41467-023-39610-2
48. Yang, Y., Wan, Y., Chen, H., Li, Y., Muñoz-Carpena, R., Zheng, Y., Huang, J., Zhang, Y., & Gao, B. (2025). Caffeine removal in wastewater: a comprehensive review of current treatment plants and small-scale innovations. Environmental Technology Reviews, 14(1), 594–612. https://doi.org/10.1080/21622515.2025.2512483
49. Yin, H., Cheng, Q., Bardelang, D., & Wang, R. (2023). Challenges and Opportunities of Functionalized Cucurbiturils for Biomedical Applications. American Chemical Society, 3(9). https://doi.org/10.1021/jacsau.3c00273
50. Zhang, C., Yuan, R., Chen, H., Zhou, B., Cui, Z., & Zhu, B. (2024). Advancements in Inorganic Membrane Filtration Coupled with Advanced Oxidation Processes for Wastewater Treatment. Molecules, 29(17), 4267. https://doi.org/10.3390/molecules29174267

51. Zhang, Y., Zhang, G., Xiao, X., Li, Q., & Tao, Z. (2024). Cucurbit[n]uril-Based supramolecular separation materials. Coordination Chemistry Reviews, 514, 215889. https://doi.org/https://doi.org/10.1016/j.ccr.2024.215889