

Design strategies and recent advances in cellulase-mimetic solid acid catalysts

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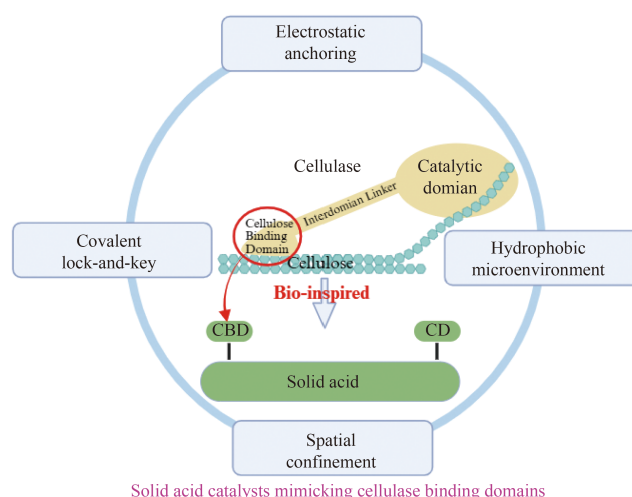
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Abstract: The dense crystalline structure and limited accessibility of cellulose severely hinder its efficient catalytic conversion. In response, biomimetic solid acid catalysts inspired by cellulase binding domains (CBDs) have emerged as a promising strategy to enhance cellulose hydrolysis by mimicking the substrate recognition and enrichment functions of natural enzymes. This review systematically summarizes recent advances in the design of CBD-mimetic solid acids based on four representative strategies: electrostatic anchoring, hydrophobic microenvironment engineering, spatial confinement and covalent lock-and-key mechanisms. The underlying principles of these approaches, including substrate-specific recognition, local concentration enhancement, and synergistic “adsorption-catalysis” effects, are critically discussed to elucidate their contributions in improving catalytic affinity, selectivity, and durability. Despite significant progress, challenges such as mass-transfer resistance and insufficient structural robustness remain in complex biomass conversion systems. Looking forward, the integration of sub-enzymatic materials, such as carbon quantum dots (CQDs), into biomimetic catalysts offers new opportunities to achieve efficient, recyclable and hierarchically organized catalytic systems, thereby providing a powerful route for the sustainable valorization of cellulose and other lignocellulosic resources.

Key words: biomimetic cellulase; solid acid catalyst; binding domain; biomass conversion



Cellulose is the most widely distributed natural polymer in the biosphere and is the basic framework of plant cell walls, with an annual production exceeding 50 billion tons globally^[1]. Its unique linear β -1,4-glucan structure not only confers excellent stability but also makes it a core resource for producing sustainable fuels, high-value chemicals, and advanced materials, making it one of the most promising biopolymers. Cellulose consists of alternating highly

ordered crystalline regions and loosely arranged amorphous regions. The efficient hydrolysis of cellulose, which involves the interaction between these regions, is a key step in its industrial utilization^[2]. Using single-molecule carbohydrate-binding module (CBM) probes and atomic force microscopy (AFM), Zhang et al.^[3] discovered that the amorphous regions of cellulose are the initial attack sites of enzymatic and acid catalysis. Ai et al.^[4] further verified and

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expanded this mechanism through comparative experiments on cellulose synthase CesaA mutants and overexpressing transgenic materials. Currently, the industrial processes mainly rely on microbial cellulase systems, which typically involve the synergistic effect of endoglucanases, exoglucanases, and β -glucosidases to accomplish cellulose hydrolysis^[5]. A canonical cellulase has a multi-domain structure, including a cellulose binding domain (CBD), a catalytic domain (CD), and an interdomain linker connecting them^[6–7]. The CBD enhances enzyme-substrate binding efficiency by interacting with cellulose's hydrophobic crystalline surface through aromatic residues (such as Tyr and Trp) *via* CH– π interactions, and by forming hydrogen bonds with hydroxyl groups on hydrophilic surfaces. The active site of CD usually contains two carboxyl residues (commonly Glu or Asp) forming a synergistic carboxylate ion pair ($-\text{COOH}/-\text{COO}^-$), where one acts as a proton donor and the other as a nucleophile or stabilizer, enabling efficient glycosidic bond cleavage. This multi-domain synergistic mechanism is considered critical to the high catalytic efficiency of cellulases.

Enzyme catalysis has advantages including mild reaction conditions, low pollution, minimal equipment demands, and high product selectivity. However, limited by high substrate requirements, high formulation costs, and difficulties in recycling, the industrial application of cellulases in biomass conversion is severely restricted^[8]. Therefore, biomimetic catalytic strategies have attracted increasing attention, aiming to mimic the efficient catalytic mechanisms of natural cellulases and combine the stability and easy recyclability of solid materials to construct cellulase-mimetic catalysts capable of overcoming these limitations. Biomimetic catalysis seeks to emulate the essential features of enzymatic systems, namely, high substrate affinity, exceptional catalytic efficiency, and precise product selectivity^[9]. Solid acids that can provide protons (Brønsted acids) or accept electron pairs (Lewis acids) are important materials in cellulase-mimetic research^[10]. To overcome the high cost and low stability of enzymes, as well as the insufficient affinity and mass transfer limitations of solid acids, biomimetic solid acid catalysts that simulate the structure and function of natural cellulases have become a hotspot in biomass catalysis research in recent years^[11–12].

Currently, the research on cellulase-mimetic solid acid catalysts primarily focuses on mimicking the catalytic domain (CD). By introducing or modulating acidic functional groups on the solid acid surface to simulate the bifunctional mechanism of the $-\text{COOH}/-\text{COO}^-$ conjugate acid-base pair, various efficient catalytic systems have been constructed, significantly enhancing the activity, selectivity, and mildness of cellulose hydrolysis. However, this strategy fails to address the key bottlenecks of substrate adsorption and interfacial mass transfer, and remains inadequate in enhancing affinity toward natural cellulose. Therefore, mimicking the cellulase binding domain (CBD) to improve substrate recognition and binding has become an important direction in developing high-performance biomimetic

catalysts^[5]. Natural CBDs achieve efficient anchoring to cellulose through multiple interactions, including electrostatic forces, hydrophobic stacking^[13–14], hydrogen bonds^[15–16], van der Waals forces^[13,17–19] and structural complementarity^[17,19]. These interactions not only facilitate the enrichment of enzyme molecules at the substrate surface but also disrupt the supramolecularly ordered structure of cellulose, thereby optimizing the local microenvironment for hydrolysis. The specific binding mechanisms of different CBD families offer diverse molecular templates for the rational design of biomimetic catalysts. This review comprehensively summarizes four representative CBD-mimetic strategies, including electrostatic anchoring, hydrophobic interaction engineering, spatial confinement, and covalent lock-and-key construction, highlighting their underlying mechanisms, research progress, and current challenges. By elucidating these structure–function relationships, the review provides theoretical guidance and technological insights for developing high-performance cellulase-mimetic solid acid catalysts for efficient cellulose valorization.

1 Cellulase-mimetic solid acid catalysts based on electrostatic anchoring

The biomimetic principle of electrostatic anchoring-type solid acid catalysts is inspired by the interactions between charged residues (e.g., Arg⁺, Lys⁺) in cellulase binding domains (CBDs) and the electrostatic microdomains on the cellulose surface (Figure 1). The core design concept involves charge topology matching, in which the spatial arrangement of charged groups (such as $-\text{SO}_3^-$ and $-\text{NR}_3^+$) on the catalyst surface is engineered to complement the local charge distribution of cellulose^[15,20]. A second principle is electrostatic-hydrogen bond synergism, where electrostatic attraction governs the binding orientation while hydrogen bonds stabilize the molecular conformation, thereby reinforcing the catalyst-substrate interactions with cellulose's functional groups and chemical linkages^[21–22]. Moreover, dynamic enrichment effects induced by electrostatic attraction markedly increase the local concentration of catalytic sites at the solid-solid interface, enhancing the binding constant by 2–3 orders of magnitude^[16]. These cooperative mechanisms collectively disrupt the supramolecularly ordered structure of cellulose^[21] and establish a high-concentration reactive microenvironment at the interface^[22–23], thereby facilitating subsequent hydrolytic and catalytic transformations.

In a typical electrostatic-driven design, Akiyama et al.^[23] introduced sulfonic acid groups ($-\text{SO}_3\text{H}$) onto a MIL-101-type porous coordination polymer (PCP) framework to mimic the CBD. Protons (H^+) from the ionization of sulfonic acid groups interact with the hydroxyl oxygen of cellulose, forming charge complementarity that is cooperatively stabilized by hydrogen bonds, thereby achieving directional adsorption.

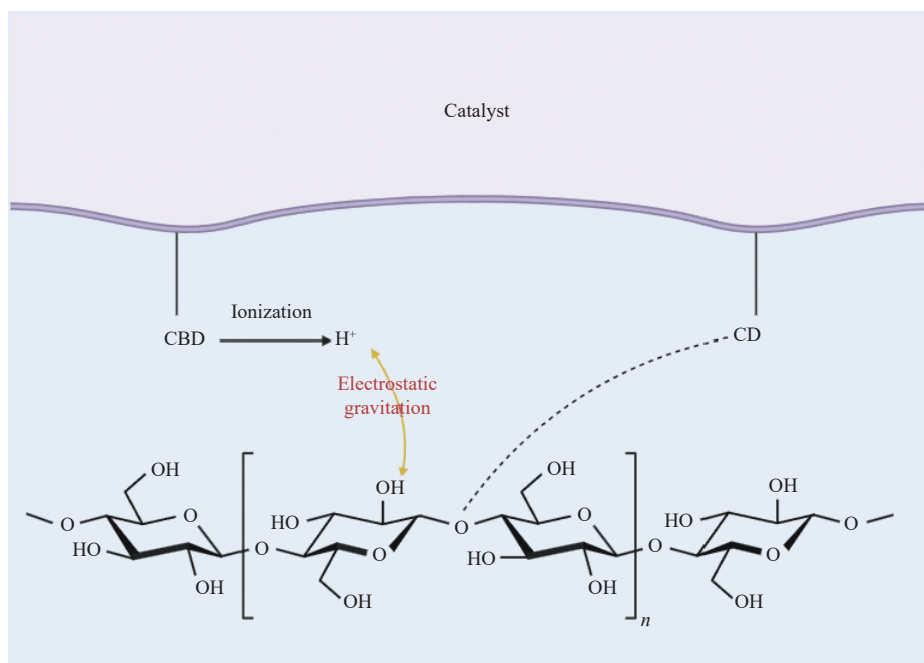


Fig. 1 Mechanism of cellulose binding by the CBD-mimetic domain in an electrostatic anchoring-type cellulase-mimetic solid acid catalyst

The confinement effect of the PCP pores (≈ 3 nm in diameter) enhances the local electrostatic field, disrupting the supramolecular order of cellulose (e.g., crystalline regions) and promoting the dissociation of chain segments to generate cellobiose. At the same time, densely arranged sulfonic acid groups (acid density 1.8 mmol/g) in the rigid pore channels simulate the charged residues of the enzyme CBD, achieving stable adsorption-catalysis *via* dynamic electrostatic matching. This catalyst shows high selectivity for glucose/cellobiose production without byproducts and could be reused 13 times without activity loss, outperforming commercial sulfonic acid resins. This research shows that densely arranged charged groups mimicking the CBD achieve efficient binding and catalysis through electrostatic interactions.

Yang et al.^[24] designed sulfonated magnetic reduced graphene oxide (Fe₃O₄-RGO-SO₃H), utilizing the hydroxyl groups retained in the reduced graphene oxide (RGO) as a CBD-mimetic structure. These hydroxyl groups form directional hydrogen bonds with the oxygen atoms of the β-1,4-glycosidic bonds in the cellulose chain, anchoring the cellulose conformation precisely and achieving electrostatic complementarity. This interaction facilitates the tight adsorption of cellulose chains onto the catalyst surface, which disrupts supramolecular ordered barriers (e.g. crystalline regions) and increases the local substrate concentration, as evidenced by a 20% cellobiose adsorption rate. Meanwhile, the hydrophobic skeleton of RGO and its residual oxygen-containing groups (e.g., carboxyl) synergistically create an optimized interface microenvironment. This enhanced electrostatic matching strengthens substrate adsorption, as shown by controlled experiments excluding a dominant role for -SO₃H/-COOH groups. This study introduces the synergism of hydrogen bonding based on electrostatic forces, strategically using the

hydroxyl groups of the carrier to achieve precise anchoring of the conformation, thereby enhancing both the directionality and strength of binding.

Verma et al.^[25] constructed a multi-functionalized graphene oxide with sulfonic acid ($-\text{SO}_3\text{H}$), carboxyl ($-\text{COOH}$) and hydroxyl ($-\text{OH}$) groups, serving as a multi-functional synergistic CBD mimic. Its mechanism of action involves three main aspects: Polar groups form hydrogen bonds with the hydroxyl groups of cellulose, weakening the hydrogen bonds between cellulose chains and enabling directional adsorption; Graphene, with a thickness of 3.4 Å, physically penetrates the cellulose with interlayer spacing of 7.0–8.0 Å, disrupting the crystalline regions of cellulose; and acid-adsorption synergy, wherein $-\text{COOH}$ provides a Brønsted acidic site for glycosidic bond hydrolysis, $-\text{SO}_3\text{H}$ enhances the acidity, and $-\text{OH}/-\text{COOH}$ facilitates substrate adsorption (contrast experiments confirmed that the activity of $\text{G-SO}_3\text{H}$ drops dramatically in the absence of oxygen-containing groups). This design achieved a cellulose conversion rate of 98% (catalyst/substrate ratio 1 : 1, Table 1), with an apparent activation energy of only 12 kJ/mol, much lower than the 170 kJ/mol for sulfuric acid, and exhibits excellent magnetic separation and cycle stability. These results demonstrate the significant potential of multi-functional synergy in overcoming the crystalline barriers of cellulose.

The introduction of flexible groups with both catalytic and binding domain functions in solid acids has attracted significant attention in recent years. Zhang et al.^[26] constructed a biomimetic system by grafting an ionic liquid 1-(trimethoxypopylsilane)-3-methylimidazolium chloride (IL group) onto the surface of bamboo charcoal sulfonic acid (BC-SO₃H), integrating both binding and catalytic functions. The flexible IL chains disrupt the cellulose

network through hydrogen bonding, mimicking the “dynamic decrystallization” function of the enzyme CBD, and generate intramolecular synergy with the catalytic domain ($-\text{SO}_3\text{H}$): Cl^- from the IL forms hydrogen bonds with $-\text{SO}_3\text{H}$, promoting H^+ dissociation and enhancing acid strength. This catalyst exhibited remarkable activity at 80°C , with a cellulose hydrolysis turnover number (TON) of 1.47, far surpassing the 0.61 of unmodified $\text{BC}-\text{SO}_3\text{H}$. At 90°C , in cooperation with the ionic liquid $[\text{BMIM}]\text{Cl}$, its TON value further increased to 6.23. Meanwhile, the spatial adaptability of flexible IL chain overcame the lignin barrier, enabling the catalyst to achieve a TON value of 2.53 for ZnCl_2 -pretreated bamboo (Table 1). The catalyst also demonstrated excellent cycle stability, with minimal loss of $-\text{SO}_3\text{H}$ and 100% retention of the IL group, significantly outperforming the unmodified catalyst. This study not only mimicked the dynamic decrystallization function of the enzyme CBD, but also tightly coupled adsorption and catalysis through the synergy of IL's Cl^- and $-\text{SO}_3\text{H}$, representing the frontier development direction for electrostatic anchoring-type cellulase-mimetic solid acid catalysts.

Electrostatic anchoring-type cellulase-mimetic solid acid catalysts effectively disrupt the crystalline barriers of cellulose through charge topology matching, electrostatic-hydrogen bond synergism, and dynamic enrichment effects, creating a high-concentration reaction environment at the interface for efficient and stable catalysis. Future development could focus on the design of multifunctional flexible chains to strengthen the binding-catalysis coupling, the application of external field coordination to enhance reaction efficiency, and the implementation of green, low-cost structural adjustments to promote large-scale applications. However, challenges remain, including achieving high selectivity adsorption of catalysts and reactants in complex biomass conversion systems, as well

as addressing the costs and stability of grafting flexible groups.

2 Cellulase-mimetic solid acid catalysts based on hydrophobic interaction

Hydrophobic interactions represent core mechanisms for cellulose binding by natural cellulase CBDs, a fundamentally entropy-driven process^[27]. When hydrophobic amino acid residues (such as Trp, Tyr, Met, etc.) on the surface of the CBD approach the hydrophobic regions of the cellulose chain, ordered water molecules at the interface are displaced and released, resulting in an increase in system entropy and thereby driving the binding^[27–28]. This process is typically accompanied by van der Waals interactions^[29] and can disrupt the hydrogen bonding network within cellulose, reducing its crystallinity^[13]. Therefore, CBDs can stably adsorb onto the cellulose surface, facilitating the catalytic domain effectively approach to the substrate, thereby enhancing hydrolysis efficiency^[30].

Early biomimetic designs directly utilize the intrinsic hydrophobicity of carrier materials to enhance cellulose adsorption, as shown in Figure 2. Onda et al.^[31] used activated carbon as the carrier, introducing sulfonic acid groups as the catalytic domain and employing the graphitized carbon layer of the carrier as the binding domain. The graphitized carbon layer anchors cellulose through hydrophobic interactions, displacing water molecules to form an entropy-driven microenvironment that increases the contact probability between the substrate and the catalyst. Its rigid planar structure mimics the aromatic ring of tryptophan in the enzyme CBD, providing a durable adsorption interface that remains stable under hydrothermal conditions.

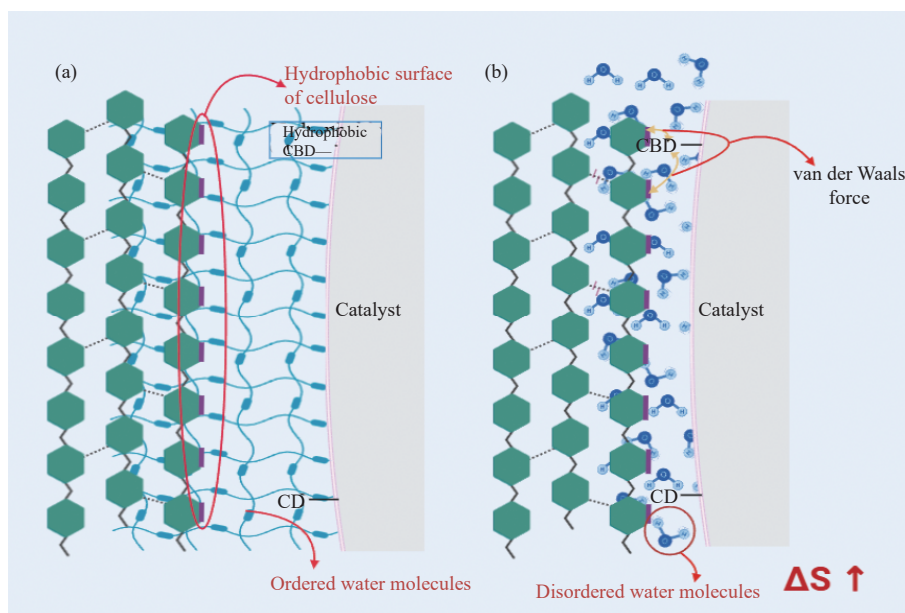


Fig. 2 Mechanism of cellulose binding by the CBD-mimetic domain in a hydrophobic microenvironment-type cellulase-mimetic solid acid catalyst

Furthermore, the rigid plane and sulfonic acid group (SO_3H) form a spatial match, achieving 90% hydrolysis selectivity. In contrast, hydrophilic zeolite carriers have low activity due to hydration and are prone to collapse. Later research shifted to optimizing nanostructures. Chung et al.^[32] constructed mesoporous carbon nanoparticles (MCN), whose graphitized framework binds glucan through hydrophobic $\text{CH}-\pi$ interactions, with mesoporous channels (3.2 nm) forming a confined hydrophobic space. The adsorption is entropy-driven process with long-chain glucans preferentially binding, achieving an adsorption capacity of 303 mg/g, which is 27 times that of non-porous carbon. Dornath et al.^[33] designed a sulfonic acid-functionalized three-dimensional ordered mesoporous carbon ($\text{SO}_3\text{H}-3\text{DOM}$), in which hydrophobic aromatic domains selectively bind long-chain glucans (adsorption capacity 3.9 times that of glucose), and increase the unit area adsorption by molecule tightly stacking (Table 1). For branched glucans containing $\alpha(1\rightarrow6)$ bonds, some glucose units hang outside the carbon surface, mimicking the flexible anchoring effect of the CBD hydrophobic pocket on cellulose chains. Entropy remains the dominant factor; stronger surface hydrophobicity lead to more significant release of water molecules. However, excessive loading of sulfonic acid groups can weaken hydrophobicity and reduce adsorption efficiency.

At the molecular level, simulating CBD residues with specific hydrophobic groups has provided significant insights. Molecules such as indole and methylene blue have shown that aromatic structures not only effectively replicate the hydrophobic recognition of cellulose binding domains but also reveal entropy-driven mechanisms and temperature-dependent adsorption behavior^[34]. The fused bicyclic structure of indole enhances hydrophobic contact and van der Waals interactions, demonstrating the sensitivity of binding strength to molecular structure. Meanwhile, methylene blue achieves nearly irreversible binding at high temperatures through the stacking of multiple aromatic rings, illustrating the potential of multiple aromatic domains in constructing stable hydrophobic interfaces. These results suggest that rational control over the planarity and substitution effects of aromatic groups could be a key path for molecular-level biomimetic design. Meanwhile, the composite strategy of hydrophobic interfaces with hydrophilic backbones further expands the design possibilities. Silica/carbon nanocomposites demonstrate that a “hydrophobic-hydrophilic” dual-functional interface can balance efficient adsorption and structural stability, while the mesopore confinement effect significantly enhances substrate contact and catalytic kinetics^[35]. This indicates that merely enhancing hydrophobicity is inadequate for solving problems of long-term stability and controllability, instead, the development of multi-scale coupling strategies that integrate molecular recognition with macroscopic structures will become a core direction for future design.

The frontier in developing hydrophobic interaction-type

cellulase-mimetic solid acid catalysts lies in the precise integration of a deep understanding of hydrophobic mechanisms with catalytic functions. The two-stage research by the Yabushita's team provides a representative paradigm: their early work revealed that the aromatic framework of carbon materials facilitates entropy-driven cellulose binding through $\text{CH}-\pi$ interactions and the repulsion of interfacial water molecules, thereby clarifying the dominant role of hydrophobic interfaces^[36]. In subsequent research, they introduced micropore confinement and weak acid sites into zeolite-templated carbon, constructing a synergistic “hydrophobic framework + catalytic function” system, which not only replicated the enrichment mechanism of CBD hydrophobic pocket but also conferred directional catalytic capability^[37]. This approach demonstrates an evolution from mechanistic insight to functional coupling, suggesting that future designs should establish more refined structure-function synergies between molecular recognition and activity regulation to achieve efficient and selective cellulose conversion.

Overall, hydrophobic interaction-type cellulase-mimetic solid acid catalysts excel in their ability to effectively replicate the hydrophobic pocket mechanism of natural cellulase CBDs. By leveraging $\text{CH}-\pi$ interactions between the aromatic carbon framework and the hydrophobic crystalline surface of cellulose, coupled with the repulsion of interfacial water molecules, these catalysts achieve entropy-driven efficient substrate binding. This interaction not only significantly enhances the selective adsorption and enrichment of long-chain glucans, but also reduces the crystallinity of cellulose and mass transfer resistance, thereby improving catalytic efficiency. In recent years, research in this area have expanded from focusing on a single hydrophobic interface to a synergistic “hydrophobic framework + functional site” system. For instance, by introducing weak acid sites or constructing nanopore confined structures within the carbon framework, materials have been endowed with dual capabilities for directional catalysis and substrate recognition. The future development of such catalysts are likely to involve fine-tuning hydrophobic domains at the molecular level, synergistic design with acidic/metallic sites, as well as the construction of stable and scalable multi-scale pore structures. However, several challenges remain, including how to maintain the hydrophobic-dominated mechanism without weakening acidity by over-functionalization, how to ensure structural stability under high-temperature hydrothermal conditions, and how to balance selectivity with general applicability in complex biomass substrates.

3 Cellulase-mimetic solid acid catalysts based on spatial confinement

Spatial confinement-type cellulase-mimetic solid acid catalysts capture and locally concentrate cellulose chains through nanopores, significantly increasing the effective

substrate concentration at catalytic sites. At the same time, the confined environment induces the exposure of chain segment conformations and suppresses side reactions, thereby mimicking the synergy of “binding domain-catalytic domain” in natural cellulases and enhancing the integration of “adsorption-catalysis” process^[38]. Zhang et al.^[16] confirmed the adsorption preference of CBD for cellulose through quartz crystal microbalance experiments, further validating the critical role of spatial confinement in substrate enrichment during hydrolysis. In recent years, the “spatial confinement” strategy has been significantly expanded in the design of solid acid catalysts, with researchers precisely adjusting pore size and surface chemistry to efficiently enrich cellulose within the pores and improve its accessibility to active sites. Similar to the hydrophobic pockets of natural enzymes, this confined environment not only strengthens the “adsorption-catalysis” integration process but may also impart chain length or conformation selectivity, providing new strategies to overcome the bottlenecks in cellulose hydrolysis rate and product selectivity (Figure 3).

Lai et al.^[39] proposed a biomimetic design based on mesoporous confinement adsorption, which is a direct application of the spatial confinement biomimetic principle. Using magnetic mesoporous silica ($\text{Fe}_3\text{O}_4\text{-SBA-SO}_3\text{H}$) as the carrier, their mesoporous channels (4.8 nm) are highly matched with the cellulose chain diameter, enabling physical capture driven by spatial steric effects. The high specific surface area ($464 \text{ m}^2/\text{g}$) provides dense binding sites, achieving a cellulose adsorption capacity equivalent to the production of 390 mg of glucose per gram of catalyst. The catalytic-adsorption synergistic effect is also

remarkable, for the high concentration (2.2 mmol/mL) of sulfonic acid groups ($-\text{SO}_3\text{H}$) in the pores forming a locally high-acidic environment that promotes cellulose hydrolysis. Furthermore, spatial confinement “locks” cellulose chains inside the pores, prolonging their contact time with acid sites and significantly enhancing the hydrolysis efficiency of β -1,4-glycosidic bonds. Control experiments showed that non-porous materials have negligible catalytic activity, highlighting the critical role of pore size control in substrate binding and reaction. More importantly, the magnetic response characteristics of the carrier enable the efficient catalyst recovery from complex mixtures, solving the problem of solid-solid separation. This work not only provides experimental validation for spatial confinement biomimicry but also offers valuable insights for developing solid acid materials with both high catalytic efficiency and recyclability.

After confirming the important role of mesopore confinement, researchers have extended this strategy to advanced carbon-based materials. Pang et al.^[40] employed high-temperature sulfonated ordered mesoporous carbon (CMK-3- SO_3H -250) to achieve precise matching of pore size with cellulose chains, and leveraged a hydrophobic/hydrophilic balance to promote the entry of cellulose chain segments into the pores. The combined effects of confined environment and local high acid concentration drove efficient cellulose hydrolysis, significantly increasing glucose yield to 74.3% (Table 1). Compared to the <5% yield observed in microporous carbon with low specific surface area, it highlighted the critical role of mesoporous structures in physical enrichment and catalysis performance.

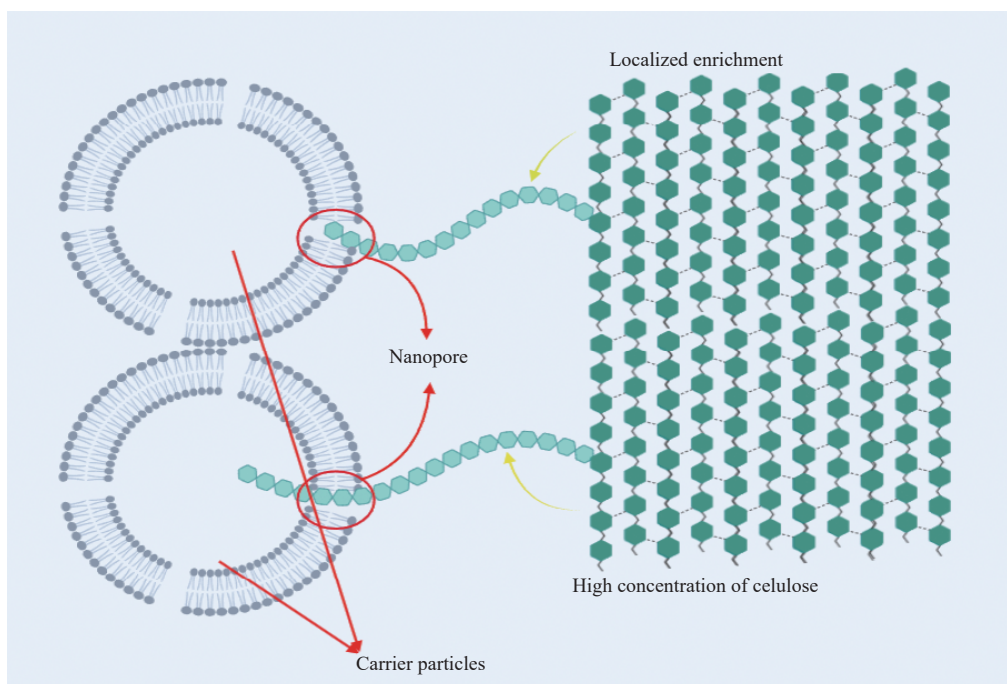


Fig. 3 Mechanism of cellulose binding by the CBD-mimetic domain in a spatial confinement-type cellulase-mimetic solid acid catalyst

Subsequently, the concept of spatial confinement was extended to non-porous nanogap structures, achieving deep functional integration. Sugano et al.^[41] combined hydrophobic adsorption and acid catalysis using carboxylated carbon nanotubes (COOH-CNT). The intrinsic hydrophobicity and the nanoscale confined space of CNTs efficiently trapped cellulose crystals, with adsorption capacity over three times that of natural CBD. At the same time, the carboxyl groups directly serve as catalytic sites, concentrating the local substrate level and compressing the interaction distance to enzymatic precision, significantly overcoming the mass transfer limitation in conventional solid acids. Although its specific activity is still lower than that of natural enzymes, this integrated “adsorption-catalysis” design provides an advanced paradigm for spatial confinement biomimicry and demonstrates the unique potential of nanomaterials in reconstructing “enzyme pocket” functions.

In summary, spatial confinement-type cellulase-mimetic solid acid catalysts capture and locally enrich cellulose chains through nanopores or nanogaps, effectively increasing the concentration of the substrate at the catalytic sites. At the same time, they induce the exposure of chain segment conformations and suppress side reactions, thereby mimicking the “binding domain-catalytic domain” synergy in natural enzymes. This design not only replicates the substrate enrichment and directional catalysis mechanisms of enzymes but also achieves selectivity for chain length and conformation through pore size matching, surface functionalization, and hydrophobic/hydrophilic balance regulation, thereby overcoming the bottlenecks in conventional solid acids, such as inefficient mass transfer and unselective hydrolysis. The future development direction is expected to focus on precise control of pore size

distribution, integration of multifunctional sites and innovation of nanostructures, to better mimic the dynamic adaptability and synergy of natural enzyme pockets. However, challenges remain, including maintaining the stability of the confined structures under high temperature and complex reaction conditions, and achieving precise, scalable and cost-effective fabrication of these structures for industrial application.

4 Cellulase-mimetic solid acid catalysts based on covalent lock-and-key

The mechanism of covalent lock-and-key catalysts is based on the reversible esterification reaction between boric acid and *cis*-diols in sugars, enabling selective recognition, spatial anchoring, and catalytic coupling at the molecular level^[42]. Boric acid forms three- or four-coordinate boronate esters with glucose residues (Figure 4), which not only specifically “hook” sugar units but also amplify the affinity through synergistic multivalent binding, leading to efficient substrate enrichment. The coordination process induces local conformational constraints and electron rearrangements, making adjacent glycosidic bonds more prone to forming oxocarbenium-like intermediates and lowering the energy barrier for bond cleavage. When the recognition site is closely adjacent to the acid site, the substrate is precisely pulled into the catalytic center, enabling efficient proton transfer or nucleophilic attack, thereby significantly improving the reaction rate and selectivity. The dynamic reversibility of the boronate ester bonds ensures a “binding-catalysis-release” cycle, with its reversible nature guaranteeing the catalyst regeneration after the reaction.

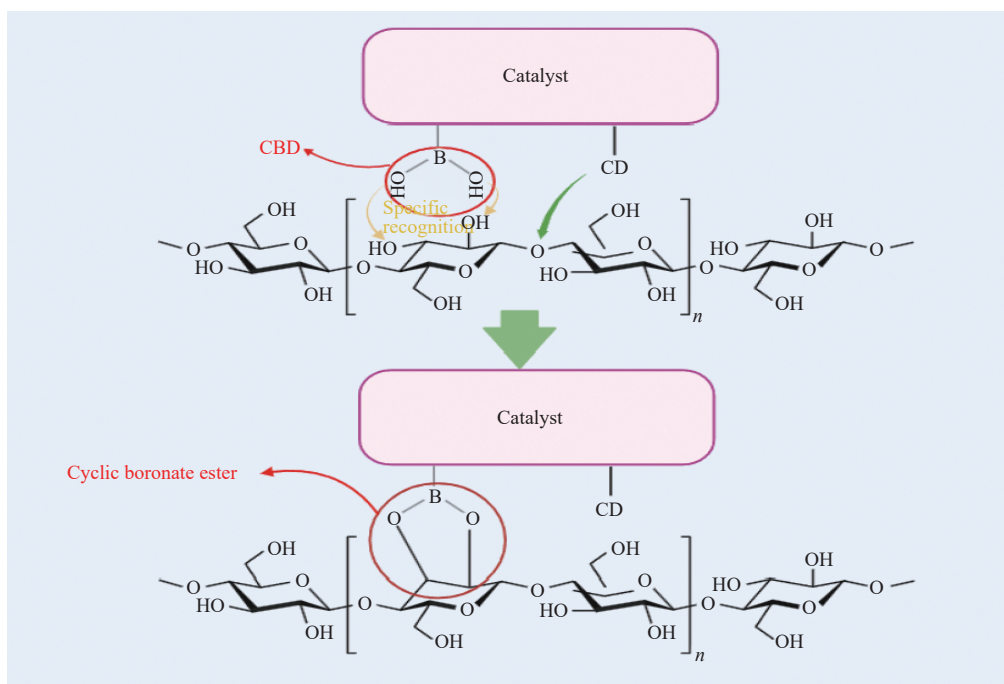


Fig. 4 Mechanism of cellulose binding by the CBD-mimetic domain in a covalent lock-and-key-type cellulase-mimetic solid acid catalyst

To enhance the coordination efficiency in aqueous phases, the pK_a of boric acid is often adjusted, and recognition sites are localized or arrayed in hydrophobic environments to minimize water interference; spatial optimization of the arrangement of recognition and catalytic sites amplifies the neighboring effect, effectively replicating the three-stage synergy of “recognition-binding-catalysis” in natural enzymes at the molecular level.

Based on the covalent lock-and-key principle, Yang et al.^[43] constructed a bifunctional porous polymer using naphthylboronic acid as the monomer. The polymer employs the boronic acid groups ($-B(OH)_2$) on its surface as cellulose binding domains, achieving efficient binding through covalent bond-mediated specific adsorption. Under

acidic hydrolysis conditions, the boric acid groups react with the *cis*-diol units on the cellulose chains to form a reversible five-membered cyclic neutral boronate ester structure, in which the boron atom forms a B–O–C bond with the oxygen atoms from two adjacent hydroxyl groups in cellulose. This cyclic boronate ester is both rigid and dynamically reversible, enabling the active sites to regenerate after hydrolysis. This covalent anchoring significantly enhances catalytic efficiency, yielding 94.6% glucose from microcrystalline cellulose after 48 h of hydrolysis (Table 1), nearly three times that of the unfunctionalized control group (31.8%) and substantially higher than the average yield of conventional solid acid catalysts (7.7%).

Table 1 CD, CBD, binding mechanism, substrate, reaction conditions, and yields of different catalysts

Catalyst	CD	CBD	Binding mechanism	Substrate	Conditions	Catalytic performance
Cr-MIL101-SO ₃ H ^[21]	–SO ₃ H	–SO ₃ H	electrostatic anchoring	cellulose	393 K, 3 h, in water	5.3% (total sugar)
Fe ₃ O ₄ -RGO-SO ₃ H ^[22]	–COOH, –SO ₃ H	–OH	electrostatic anchoring	Avicel	423 K, 5 h, in water	> 28% (total sugar)
Fe-GO-SO ₃ H ^[23]	–COOH, –SO ₃ H	–OH, –COOH	electrostatic anchoring	MCC	348 K, 24 h, in water	96% (total sugar)
BC-SO ₃ H-IL ^[24]	–SO ₃ H	IL groups	electrostatic anchoring	cellulose	363 K, 2 h, in [BMIM]Cl/H ₂ O, MW irradiation	64.6% (total sugar)
AC-SO ₃ H ^[29]	–SO ₃ H	hydrophobic carbon plane	hydrophobic microenvironment	ball-milled Avicel	423 K, 24 h, in water	30% (total sugar)
MCN ^[32]	–	mesoporous carbon surface	hydrophobic microenvironment	long-chain glucans	room temperature, in aqueous phase	solely adsorptive for long-chain glucans (303 mg/g)
SO ₃ H-3D0m carbon ^[33]	–SO ₃ H	aromatic carbon domain	hydrophobic microenvironment	mixed glucan oligomers	393 K, 2 h, in water	long-chain glucan adsorption (3.9× glucose capacity)
K26 ^[36]	oxygenated functional groups	hydrophobic aromatic carbon framework	hydrophobic microenvironment	ball-milled cellulose	413 K, 24 h, in water	entropically driven adsorption ($\Delta S_{ads}^{\circ} = +23.5$ J/mol·K)
ZTC ^[37]	carboxylic acid groups	microporous carbon surface	hydrophobic microenvironment	cellulose	453 K, 3 h, in water	87% (glucose)
Fe ₃ O ₄ -SBA-SO ₃ H ^[39]	–SO ₃ H	mesoporous silica channels	spatial confinement	corn cob	423 K, 3 h, in water	45% (total sugar)
AC-N-SO ₃ H-250 ^[40]	–SO ₃ H	carbon surface	spatial confinement	ball-milled cellulose	423 K, 24 h, in water	74.3% (total sugar)
CMK-3-SO ₃ H-250 ^[40]	–SO ₃ H	ordered mesoporous carbon	spatial confinement	ball-milled cellulose	423 K, 24 h, in water	94.4% (total sugar)
COOH-CNT ^[41]	–COOH	carbon nanotube backbone	spatial confinement	cellobiose	pH = 3.0, room temperature, in buffer	superior adsorption (3× natural CBD)
S2 ^[43]	–SO ₃ H	–B(OH) ₂	covalent lock-and-key	ACC	393 K, 48 h, in water	94.6% (glucose)
S2 ^[43]	–SO ₃ H	–B(OH) ₂	covalent lock-and-key	ball-milled ACC	393 K, 24 h, in water	94.9% (glucose)
BR-Catalyst ^[44]	iron-liquid environment	–B(OH) ₂	covalent lock-and-key	microcrystalline α -cellulose	353K, 5 h, in [BMIM]Cl	95% (glucose)
BP-Catalyst ^[45]	–COOH	–B(OH) ₂	covalent lock-and-key	pretreated MCC	473 K, 4 h, in water	64.1% (total sugar)

Moreover, the catalyst maintains 74.6% glucose yield after four reuse cycles (Table 1), significantly outperforming the design based on hydrogen bond adsorption (35.7%). These results fully validate the advantages of “lock-and-key” binding in overcoming cellulose crystallinity barriers and maintaining stability.

To further improve reaction homogeneity and efficiency, researchers have gradually expanded from multiphase systems to precise molecular-level designs. Zhu et al.^[44] designed an ionic liquid-boronic acid conjugate compound (Boronic Acid-Phosphonium Catalyst, BR-Catalyst), in which the boric acid group can specifically bind to the C₂-C₃ *cis*-diol sites of glucose units in cellulose chain under neutral conditions. The formation of the boric acid-cellulose complex was directly confirmed by ¹¹B NMR spectroscopy ($\delta = -1.1$). Thanks to the dissolving effect of the ionic liquid and the synergistic hydrogenation of Ru nanoparticles, the rate of cellulose hydrolysis to glucose conversion reached 95%, followed by a 94% yield of the hydrogenation to sorbitol (Table 1), far exceeding the conversion rate without BR-Catalyst (15%). This series of studies not only reveals the unique mechanism of covalent “lock-and-key” binding in overcoming cellulose recalcitrance but also demonstrates its evolution from porous polymers to molecular conjugates, highlighting the broad prospects of covalent lock-and-key cellulase-mimetic solid acid catalysts in precise and renewable catalysis.

In summary, covalent lock-and-key cellulase-mimetic solid acid catalysts form reversible cyclic structures with boric acid and other reagents to achieve specific recognition and stable anchoring of cellulose chains, effectively overcoming their crystallinity barriers while providing both high efficiency and recyclability. Compared to traditional strategies based on hydrogen bonds or physical adsorption, this approach demonstrates stronger binding strength and superior cycling stability, achieving significant breakthroughs in cellulose hydrolysis and its derivative conversion. Future development are expected to focus on molecular-level precision design, such as ionic liquid-boronic acid conjugates and synergistic catalysis with nanometals, to enhance reaction homogeneity, product selectivity, and energy efficiency. At the same time, the combination of *in situ* characterization and computational simulations will help clarify the synergistic mechanisms between dynamic covalent binding and catalytic sites. The main challenges lie in the stability of boric acid-based groups in complex reaction environments, selective recognition of non-cellulose by-products, and the scalability and cost control of catalysts at an industrial scale. Solving these issues will be crucial for translating this technology from the laboratory research to practical applications.

5 Conclusions and perspectives

This review comprehensively summarizes recent progress in the development of cellulase-mimetic solid acid catalysts,

with a focus on the roles and mechanisms of biomimetic strategies, including covalent lock-and-key, hydrophobic microenvironments, spatial confinement, and electrostatic anchoring in enhancing cellulose binding specificity and catalytic efficiency. These approaches successfully emulate the key functions of the natural cellulase binding domain (CBD). Notably, the intrinsic preference of cellulase CBDs for amorphous cellulose regions provides a “precise navigation” effect, directing the catalyst toward structurally accessible and reactive sites within the cellulose supramolecular framework and thereby enabling efficient substrate enrichment. By recurrence this molecular recognition and targeting mechanism, the discussed biomimetic strategies effectively enhance substrate activation and interfacial catalysis efficiency, leading to significant improvements in both activity and selectivity of solid acid catalysts. The promising opportunities in the future exist in overcoming the limitations of macro-reaction environments, particularly by utilizing sub-enzymatic materials such as carbon quantum dots (CQDs) to achieve the transition from surface to bulk phases, and by combining multifunctionality and traceability to promote the design of efficient, recyclable catalytic systems, thus opening new pathways for the efficient conversion of biomass.

Declaration of Competing Interest

The authors declare no conflict of interest.

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仿纤维素酶固体酸催化剂结合域设计与研究进展

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摘 要: 纤维素结晶致密、生物和化学催化剂可及性差, 限制了其高效转化。近年来, 仿纤维素酶固体酸催化剂通过模拟酶结合域(CBD)的识别与富集功能, 显著提升了纤维素水解效率。本工作综述了静电锚定、疏水微环境、空间限域和共价锁钥等典型仿生策略, 阐明了其在底物特异识别、局部富集及“吸附-催化”协同中的效果及作用机理。研究表明, 这些策略有效改善了固体酸的亲和力和选择性, 并在葡萄糖产率与循环稳定性方面取得突破。然而, 其在复杂生物质转化体系中仍受限于传质瓶颈和结构稳定性不足。展望未来, 碳量子点等亚酶尺度材料有望实现吸附-催化一体化并突破固-固传质障碍, 为构建高效可循环利用的纤维素转化催化体系提供新思路。

关键词: 仿纤维素酶; 固体酸催化剂; 结合域; 生物质转化

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