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Pancatalytic biomaterials enable inflammation-related disease intervention

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Inflammatory disease (ID) is an umbrella term encompassing all conditions where both acute and chronic inflammation serve as the central pathogenic mechanism, imposing a profound global health burden due to the high morbidity, mortality, and socioeconomic impact of these conditions. These pathologies are unified by dysregulated inflammatory cascades, oxidative stress, and immune microenvironment imbalances, which drive progressive tissue damage and organ dysfunction. Conventional therapies, including immunosuppressants and anti-inflammatory agents, often provide only palliative relief, fail to address root causes, and carry the risk of systemic toxicity. The emerging pancatalytic biomaterial based approach, which involves the holistic management of preparation (P) of the catalyst, activation (A) of the biological effect and nontoxic treatment (N) of diseases, offers a transformative paradigm for precision management of ID. These pancatalytic biomaterials constitute the operational foundation of pancatalytic therapy, a multidisciplinary framework that integrates catalytic biomaterials with catalytic biology and catalytic medicine to systematically orchestrate pathological processes *via* the P–A–N framework, ultimately redefining therapeutic strategies from toxic therapy to nontoxic treatment. This review systematically investigates the rational design of pancatalytic biomaterials, classifying them into inorganic, organic, and organic/inorganic hybrid systems based on the composition. The therapeutic applications of pancatalytic biomaterials across cardiovascular, neurological, respiratory, sensory and other systems are comprehensively summarized. Finally, the current challenges in this field are discussed, and future developments and trends in employing pancatalytic biomaterials for inflammatory disease treatment are projected, thereby advancing further research and clinical translation.

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1. Introduction

Inflammation-related diseases (IDs) encompass a broad spectrum of pathological conditions in which persistent or dysregulated inflammatory responses serve as major drivers of disease development and progression.[1–3] Inflammation itself is an essential physiological process, acting as a frontline defense to eliminate infectious agents, repair tissue damage, and restore homeostasis following injury or infection.[4,5] This process is typically characterized by a well-orchestrated sequence of events, beginning with rapid onset, a subsequent pro-inflammatory phase, and ultimately, a transition to resolution that supports tissue healing and functional recovery.[6,7] However, disruptions in this finely tuned response, such as excessive activation or failure to resolve inflammation, can result in chronic or misdirected immune activity, which is central to the pathogenesis of a variety of IDs.[8] Examples of such disorders include inflammatory bowel disease (IBD), hepatitis, atherosclerosis (AS), hypertension, multiple sclerosis (MS), uveitis, sensorineural hearing loss (SNHL), and neurodegenerative diseases.[9] These conditions, though clinically diverse, display common pathological hallmarks: sustained immune activation, persistent oxidative stress, and an imbalance in tissue homeostasis that leads to ongoing injury and impaired function.[10]

At the molecular level, chronic inflammation is often triggered and perpetuated by the continuous presence of danger signals, either from invading pathogens (pathogen-associated molecular patterns (PAMPs)) or from host tissue damage-associated molecular patterns (DAMPs). These signals activate innate immune cells, prompting them to release a range of mediators including cytokines, chemokines, proteases, and reactive oxygen species (ROS), which together propagate the inflammatory cycle.[11,12] Under normal circumstances, such immune responses are essential for clearing threats and restoring tissue integrity. However, when these mechanisms become excessive or dysregulated, they can initiate a self-amplifying cascade, resulting in widespread tissue damage, decreased

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immune tolerance, and ultimately the progression of inflammatory diseases.[13,14] Understanding the dynamic relationship between inflammation and tissue homeostasis has paved the way for targeted strategies to modulate pathological inflammation. Conventional anti-inflammatory therapies such as corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and biological agents targeting key cytokines remain the mainstay of treatment. Nevertheless, these therapeutic approaches are frequently limited by low specificity, rapid elimination, and potential off-target effects, often requiring high doses that may compromise safety and efficacy.[15] These limitations highlight the need for more precise and innovative interventions, including emerging approaches that leverage nanobiotechnology and stimuli-responsive biomaterials, to achieve more effective management of IDs.

To address these limitations in current anti-inflammatory therapies, we propose a novel therapeutic paradigm termed pancatalysis, which fundamentally differs from traditional catalysis in both scope and mechanism.[16] While conventional catalysis focuses primarily on accelerating isolated chemical reactions under controlled conditions, pancatalysis is realized through the development of advanced biomaterials that synergistically integrate three key components to achieve physiological modulation: (1) catalytic biomaterials are engineered to catalyze biochemical reactions triggered by endogenous stimuli (*e.g.*, H_2O_2, glucose, glutathione, lactic acid) or external stimuli (*e.g.*, light, ultrasound, electric/magnetic fields);[17] (2) catalytic biology involves modulating biological molecules (*e.g.*, proteins, lipids, nucleic acids) and pathways (*e.g.*, oxidative stress, cell death, metabolism) using catalytic biomaterials;[18] and (3) catalytic medicine focuses on precisely regulating reactions at disease sites for targeted therapy and diagnostics with minimal side effects, contrasting with traditional catalysis' lack of therapeutic specificity.[19,20] The operational foundation of this strategy is the P–A–N framework (preparation–activation–nontoxic treatment), which coordinates material design with biological response to achieve multi-level therapeutic outcomes, representing a level of systemic integration that conventional catalytic systems typically lack as they focus primarily on reaction efficiency.

Pancatalytic biomaterials, constituting both the operational foundation and physical embodiment of the pancatalysis

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paradigm, herald a transformative paradigm shift in ID treatment. Pancatalytic biomaterials, ranging from inorganic biomaterials to organic systems and even to organic/inorganic hybrid types, are engineered to trigger the specific biological effects by initiating catalytic chemical reactions, ultimately achieving nontoxic disease treatment. For instance, V_2C MXenes exhibit multi-enzyme catalytic properties, neutralizing ROS and restoring redox balance in neurodegenerative models,[21] while melanin-based composites resolve myocardial infarction (MI) microenvironments through proton-coupled electron transfer.[22] By harnessing disease-specific stimuli such as pathological pH, hypoxia, or ROS overproduction, these catalytic biomaterials activate therapeutic cascades only at target sites, minimizing off-target effects. Central to this approach is the ''Preparation of the catalyst, Activation of the biological effect and Nontoxic treatment of diseases'' (P–A–N), which guides the design, fabrication and biomedical application of pancatalytic biomaterials.[16,23] The P–A–N framework is exemplified by engineered GaHCF nanoabsorption catalysts (GaHCF NACs) for AS and $CaSi_2$ nanosheets for rheumatoid arthritis (RA).[24,25] In AS, GaHCF's preparation optimizes iron-binding affinity, while its activation phase sequesters pathologic iron and scavenges ROS to resolve ferroptosis–inflammation cycles; nontoxic treatment repurposes iron for diagnostic signaling. For RA, the preparation of calcium disilicide nanoparticles (CSNs) involves liquid exfoliation, while their activation phase hydrolyzes them in inflamed joints to release H_2 for ROS scavenging and form bone-repairing calcium phosphate. The nontoxic treatment exhibits excellent biocompatibility and therapeutic performance in anti-inflammation and bone mineralization. These examples illustrate how the P–A–N framework enables the development of sophisticated therapeutic platforms capable of addressing the multifaceted nature of inflammatory diseases. By integrating material design with biological response modulation, pancatalytic biomaterials represent a significant advancement over conventional anti-inflammatory therapies, offering targeted, multi-modal intervention against the complex pathophysiology of inflammation.

This review systematically examines the emerging paradigm of pancatalytic biomaterials for inflammatory disease treatment through a multidisciplinary lens integrating materials science, biology and clinical medicine. We present a detailed design and classification of pancatalytic biomaterials based on their catalytic mechanisms and composition, with particular focus on their design principles under the P–A–N framework. The review thoroughly investigates their therapeutic applications across multiple physiological systems affected by chronic inflammation, such as cardiovascular, neurological, respiratory and sensory systems (Fig. 1). Special emphasis is placed on elucidating the structure–function relationships that enable these materials to simultaneously target oxidative stress, immune dysregulation and tissue damage, the key pathological drivers of inflammatory diseases. Finally, we critically analyze current translational challenges and outline future research directions to accelerate the clinical implementation of these innovative biomaterials for inflammatory disease management.

2. Design and classification of pancatalytic biomaterials

Pancatalytic biomaterials are a class of engineered materials designed to catalyze specific biochemical reactions, thereby modulating inflammatory pathways and providing targeted therapeutic interventions for IDs. These materials are classified into three main categories based on their composition and properties: inorganic, organic, and organic/inorganic hybrid catalytic biomaterials.

2.1 Design of pancatalytic biomaterials

Catalyzing specific biochemical reactions. The emerging catalytic biomaterials are designed to respond to both endogenous biological signals and external stimuli, thereby catalyzing specific biochemical reactions for personalized therapeutic interventions.[17] Of these catalytic functions, scavenging ROS is particularly crucial in inflammatory diseases where oxidative stress plays a pathogenic role. Pancatalytic biomaterials are frequently engineered to mimic the catalytic activities of endogenous enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), or are designed to directly scavenge ROS, which are critical for redox balance and inflammation control. By tailoring nanoscale structure and surface chemistry, these materials exhibit enzyme-like kinetics, enabling efficient scavenging of ROS in pathological microenvironments. Compared to natural enzymes, artificial nanozymes offer greater stability and sustained activity, providing targeted redox modulation and attenuating inflammation-associated oxidative stress, thus holding promise for advanced therapeutic interventions. For example, hexacyanoferrate nanocatalysts (CaH NCs) extend this paradigm by integrating multi-enzyme mimetic properties (SOD, CAT, GPx, and peroxidase) to regulate mitochondrial dysfunction and neuroinflammation in autism spectrum disorder.[26] Similarly, amyloid fibril-templated ceria nanozymes demonstrate cascaded SOD-CAT-like catalysis with optimized Ce^{3+}/Ce^{4+} ratios, synergistically alleviating oxidative stress, hypoxia, and hyperinflammation in diabetic wounds through glucose oxidase-coupled hydrogel microneedles.[27]

Biocompatibility and biodegradability. Ensuring the safety of biomaterials requires that these materials either undergo biodegradation into nontoxic byproducts or remain biologically inert within the body. Biocompatibility refers to the absence of cytotoxicity or adverse immune responses, such as inflammation or allergy, from both the intact material and its degradation products. Biodegradability allows materials to be broken down under physiological conditions into substances that can be efficiently cleared, thereby reducing the risk of bioaccumulation and minimizing long-term toxicity. For materials that are non-degradable, chemical stability and minimal biological reactivity are essential to avoid undesired interactions with tissues and organs. These criteria form the basis for evaluating the clinical applicability of novel nanomaterials. For instance, pH-responsive MoO_{3-x} nanourchins rapidly biodegrade into renal-clearable molybdate ions under physiological conditions (pH 7.4), eliminating off-target catalytic activity in healthy

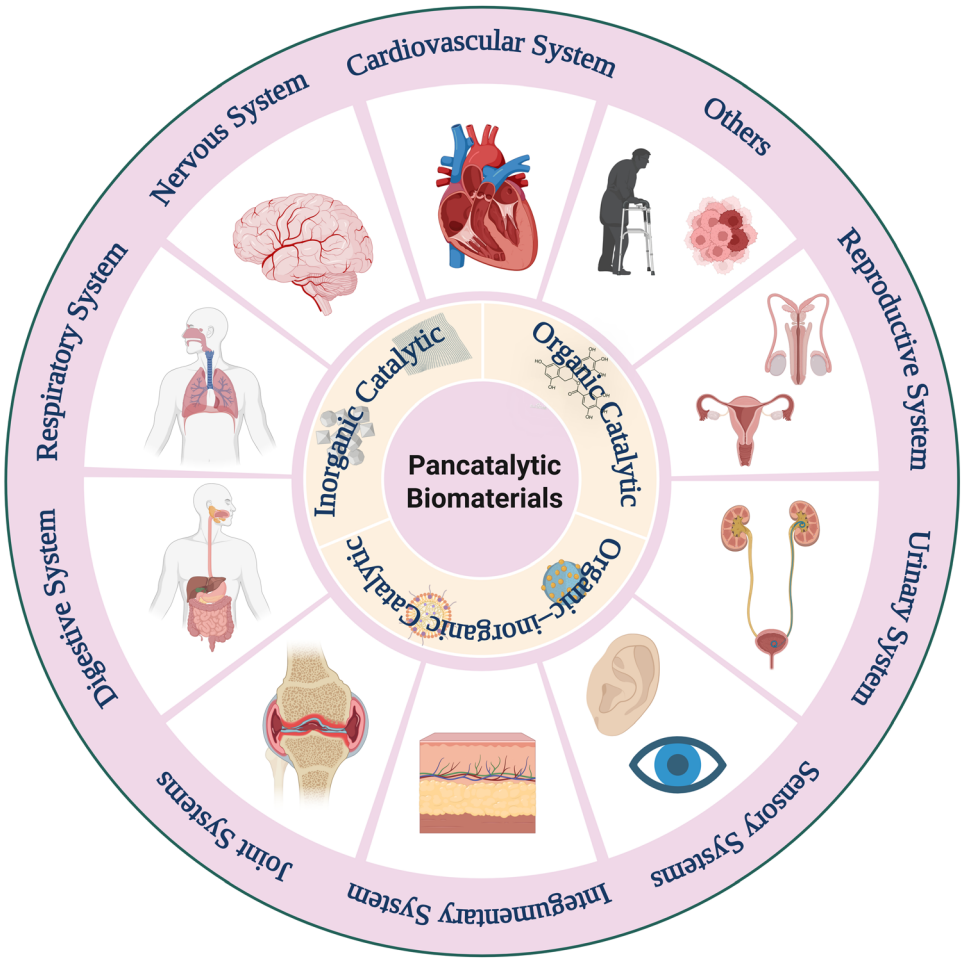

Fig. 1 Schematic representation of pancatalytic biomaterials classified as inorganic, organic, and organic/inorganic hybrids, highlighting their therapeutic applications for inflammatory diseases across multiple organ systems, including cardiovascular, nervous, respiratory, digestive, joint, integumentary, sensory, urinary, and reproductive systems. Created with https://BioRender.com.

tissues while retaining tumor-specific enzymatic effects in acidic microenvironments.[28] Meanwhile, zinc sulfide-based nanozymes leverage the intrinsic biocompatibility of zinc, degrading to release thiolate ligands that accelerate bioorthogonal catalysis while ensuring metabolic clearance of zinc ions.[29] These designs exemplify how controlled degradation pathways mitigate bioaccumulation risks and align with the imperative for clinically translatable, safety-first nanotherapies.

Targeting and activation mechanisms. The precision of anti-inflammatory therapy is typically enhanced by employing pancatalytic biomaterials engineered for targeted delivery and stimuli-responsive activation. Such materials are designed to accumulate preferentially at pathological sites based on physicochemical properties, including particle size, surface charge, and the presence of affinity ligands.[30] Therapeutic activity is then selectively triggered by specific microenvironmental cues, such as acidic pH, elevated ROS, or increased expression of certain enzymes. This strategy improves local efficacy while reducing systemic side effects, contributing to the optimization of therapeutic outcomes in inflammatory diseases.[31,32] For example, in IBD therapy, inflamed colon-targeted antioxidant nanotherapeutics are constructed by functionalizing mesoporous silica nanoparticles (MSNs) with ROS-scavenging ceria nanoparticles (Ce NPs), followed by poly(acrylic acid) coating to enable electrostatic targeting of inflamed colon tissues.[33] In MI, Fe-Cur@TA nanozymes are modified with tannic acid, enabling them to specifically bind to cardiac elastin and collagen for preferential localization in damaged heart regions.[34] These targeting strategies enhance local drug concentration and allow microenvironment-responsive activation, thereby improving therapeutic precision in various diseases.

Multifunctionality. Pancatalytic biomaterials bring together various functions, combining therapy, diagnosis, and regeneration into one cohesive platform. This holistic approach enables better disease management, where real-time monitoring of therapeutic actions is possible, and regenerative processes can be supported effectively. By utilizing these combined properties, these biomaterials can target specific pathological signals and help track the effectiveness of treatments, thereby improving clinical results. This multifunctionality marks an important step forward in biomedical engineering, offering new ways to tackle the complexities of managing diseases

compared to traditional therapies. For instance, in treating acute liver failure, researchers have developed a ROS-sensitive nanozyme-augmented photoacoustic nanoprobe that allows for early diagnosis and timely nanocatalytic therapy.[35] This innovative system pairs the imaging capabilities of near-infrared agents with the catalytic actions of ceria nanozymes, enabling real-time monitoring of ROS and addressing oxidative stress at the injury site simultaneously. In a similar vein, using Mn_3O_4 nanozymes to engineer stem cells for MI therapy boosts their therapeutic impact by enhancing ROS scavenging capabilities and allows for tracking *via* magnetic resonance imaging.[36] These multifunctional strategies illustrate how pancatalytic biomaterials can synergize various treatment approaches, leading to more effective healthcare solutions across different diseases.

2.2 Classification of pancatalytic biomaterials

In the field of anti-inflammatory therapy, pancatalytic biomaterials have attracted significant attention due to their ability to precisely modulate disease microenvironments, catalytically eliminate ROS, and regulate immune responses. Based on differences in composition and functional properties, these materials are mainly classified into three categories: inorganic, organic, and organic/inorganic hybrid systems. Inorganic catalytic materials, with their outstanding multi-enzyme-mimetic activities and stability, exhibit remarkable advantages in antioxidation and inflammation regulation; organic materials emphasize biocompatibility and structural tunability, often achieving efficient anti-inflammatory effects by mimicking natural enzyme functions or through self-assembly; and hybrid systems integrate the catalytic activity of inorganic components with the adaptability of organic constituents, enabling multifunctional and precise regulation. The following sections will discuss representative materials from each category of pancatalytic biomaterials and recent advances in their applications for IDs.

Inorganic catalytic biomaterials are widely studied due to their exceptional catalytic efficiency, stability, and tunable redox properties. Cerium oxide (CeO_2) nanoparticles exemplify this category, mimicking SOD and CAT activities through Ce^{3+}/Ce^{4+} redox cycling. These nanoparticles effectively scavenge ROS in IBD and MI models.[22,33] Prussian blue analogs (*e.g.*, GaHCF) further demonstrate therapeutic potential by sequestering excess iron in atherosclerotic plaques, disrupting ferroptosis–inflammation interactions while enabling non-invasive photoacoustic imaging.[24] Advanced materials like V_2C MXenes exhibit multi-enzyme mimetic properties (SOD, CAT, GPx), providing broad-spectrum antioxidant protection in neurodegenerative and inflammatory diseases.[21] Additionally, black phosphorus nanosheets (BPNSs) catalyze ROS degradation to promote tissue repair.[37]

Organic catalytic biomaterials comprise both purely organic systems and organic-based hybrid constructs, such as natural polyphenols (including quercetin, resveratrol, and tannic acid), synthetic conducting polymers (like polypyrrole and polyaniline), polysaccharide derivatives (*e.g.*, chitosan, alginate), artificial antioxidant polymers, supramolecular organic frameworks, and engineered enzyme systems like antioxidant enzyme-loaded polymersomes. These materials are engineered to mimic natural enzyme activities or exhibit direct ROS-scavenging capabilities, regulate redox homeostasis, and facilitate targeted drug delivery, making them highly versatile for biomedical applications.[38] These materials bridge the gap between natural antioxidant enzymes (SOD, CAT) and chemical antioxidants (vitamin C), combining their advantages while overcoming limitations such as poor enzyme stability and transient antioxidant effects. Moreover, engineered modifications of natural enzymes can effectively compensate for their inherent limitations. Recent advances include ROS-responsive polyion complex vesicles (PICsomes) encapsulating catalase, where engineered semipermeable membranes enhance enzyme stability and enable sustained redox regulation through cysteamine-mediated GSH biosynthesis. The results further demonstrate significant long blood circulation of PICsomes loaded with catalase and strong protection effects against bloodstream oxidative stress, paving the way for the further development of truly effective *in vivo* therapeutics.[39] This innovative approach not only addresses the stability issues of natural enzymes but also provides sustained catalytic activity and targeted delivery, representing a significant advancement in biomimetic antioxidant therapy. A notable example is the development of CAT-loaded nanogels (CAT-NGs) for neutrophilic asthma treatment, where chitosan-based nanogels significantly improved CAT stability and bioavailability while endowing additional antibacterial properties. This system demonstrated enhanced therapeutic efficacy in alleviating airway inflammation and oxidative stress through efficient ROS scavenging and inhibition of NOD-like receptor family pyrin domain containing 3/nuclear factor kappa-light-chain-enhancer of activated B cells (NLRP3/NF-κB) pathways.[40] For chemical antioxidants like vitamin C, vitamin C–lipid nanoassemblies effectively address IBD treatment challenges. Through fatty acid conjugation, these self-assembling nanoparticles enhance vitamin C's stability and enable targeted delivery to inflamed colon tissues. In mouse models, they demonstrate significant ROS scavenging and disease mitigation. When combined with budesonide, they provide synergistic anti-inflammatory effects while maintaining immune function and gut microbiome balance, overcoming vitamin C's inherent pharmacokinetic limitations.[41] These examples collectively demonstrate how advanced material engineering can optimize both enzymatic and non-enzymatic antioxidant systems for improved therapeutic outcomes.

Among them, polydopamine (PDA) and epigallocatechin gallate (EGCG) are particularly prominent. PDA, inspired by mussel adhesive proteins, possesses abundant catechol groups that endow it with CAT- and SOD-like activities, enabling effective scavenging of ROS, modulation of inflammatory responses, and promotion of tissue repair. PDA-based platforms have demonstrated significant protective effects in neural injury and degenerative disease models by reducing oxidative stress and enhancing neuronal survival.[42,43] EGCG, a key polyphenol found in green tea, can self-assemble or co-assemble into nanoparticles, substantially improving its inherent antioxidant and anti-inflammatory capabilities. When incorporated into advanced

delivery systems, EGCG-based nanomaterials have shown efficacy in alleviating radiation-induced skin injury, suppressing tissue inflammation, and accelerating wound healing.[44] Together, these examples demonstrate the broad therapeutic promise of organic catalytic biomaterials in precisely regulating oxidative stress and inflammation, and in promoting the repair of damaged tissues across various disease models. Their structural diversity and multifunctionality highlight their potential for future clinical translation in the treatment of inflammatory, neurodegenerative, and other oxidative stress-related conditions.

Hybrid systems are engineered to combine the robust catalytic activity and redox properties of inorganic materials with the structural versatility, biocompatibility, and functional tunability of organic components, enabling multifunctional and highly precise therapeutic interventions. By integrating these complementary characteristics, such systems can achieve enhanced catalytic efficiency, controlled drug delivery, responsive targeting, and adaptive interactions with complex biological environments.[38] MOFs, such as Ce-MOFs, deliver dexamethasone while scavenging ROS in uveitis, leveraging their porous structures for controlled drug release.[45] Biomimetic nanosystems like Fe-Cur@TA nanozymes merge Fe^{3+}–curcumin coordination for ROS scavenging with tannic acid-mediated cardiac targeting, effectively disrupting the inflammation-free radical cycle in MI.[34] Similarly, melanin-based composite nanomedicines (MCN) integrate PDA, Prussian blue, and Ce_xO_y to neutralize ROS cascades in ischemic heart disease, showcasing synergistic catalytic and regenerative effects.[22]

3. Applications of pancatalytic biomaterials in inflammation-related disease

The remarkable versatility of pancatalytic biomaterials is demonstrated by their broad therapeutic applications across multiple physiological systems affected by inflammatory diseases, as systematically summarized in Table 1. These advanced materials, categorized as inorganic, organic, and hybrid systems, have been successfully engineered to target specific inflammatory pathologies through their unique catalytic properties. The table highlights representative examples of pancatalytic biomaterials that have shown efficacy in diverse disease models, ranging from cardiovascular disorders (*e.g.*, GaHCF NACs for atherosclerosis) to neurological conditions (*e.g.*, IP6@GCA/AP for Alzheimer's disease), respiratory diseases (*e.g.*, CAT-NGs for neutrophilic asthma), and beyond. In the following sections, each representative example listed in the table will be analyzed through the lens of the P–A–N framework, with detailed discussions on how the preparation, activation, and nontoxic treatment components are specifically engineered for different disease applications.

3.1 Cardiovascular system

Cardiovascular diseases (CVDs), encompassing atherosclerosis, thrombosis, myocardial/cerebral infarction, and subsequent ischemia-reperfusion injury, represent a major global health threat.[66–68] According to the World Health Organization (WHO), CVDs account for approximately 17.9 million deaths annually worldwide.[69] These conditions not only drive high mortality but also cause severe disabilities, such as heart failure following MI or motor dysfunction post-stroke, imposing a profound socioeconomic burden. CVDs encompass ischemic or hemorrhagic disorders affecting the brain, heart, and systemic vasculature, predominantly arising from multifactorial etiologies such as AS, hypertension, dyslipidemia, and increased blood viscosity.[67] Clinically, these conditions manifest with elevated rates of morbidity, mortality, disability, and recurrence, frequently resulting in multiorgan complications.

AS, characterized by chronic inflammation and vascular dysfunction, underlies the pathogenesis of CVDs, and is marked by the formation of lipid-rich plaques on arterial walls.[69,70] These plaques arise from lipid deposition and inflammatory activation, initiating with endothelial dysfunction that permits low-density lipoprotein (LDL) infiltration into the subendothelial space. Oxidative modification converts LDL to oxidized LDL (ox-LDL), triggering monocyte recruitment and differentiation into macrophages.[71] Macrophages engulf ox-LDL to form foam cells, which accumulate in the arterial intima, perpetuating chronic inflammation and releasing cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α).[72,73] Subsequently, vascular smooth muscle cells migrate to the intimal layer, undergo aberrant proliferation, and secrete extracellular matrix components such as collagen and elastin, collectively contributing to the formation and stabilization of fibrous caps. As lipid cores expand, inflammatory cell infiltration intensifies, and fibrous tissue hyperplasia progresses, arterial walls undergo progressive thickening and calcification, culminating in luminal narrowing and the development of mature atherosclerotic plaques.[74] Notably, rupture or erosion of vulnerable plaques may trigger thrombus formation, leading to acute vascular occlusion and subsequent ischemic events such as MI or stroke, which remain the leading causes of global mortality. Current clinical strategies primarily focus on restoring blood flow *via* thrombolysis or percutaneous coronary intervention. However, rapid reperfusion often induces oxidative stress-mediated tissue damage, a phenomenon termed ischemia-reperfusion injury, which paradoxically complicates therapeutic outcomes.[75–77] Hypertension induces endothelial damage through mechanical stress (such as elevated shear forces) and biochemical pathways (such as overactivation of the renin–angiotensin system). This exacerbates the progression of CVD and thus accelerates atherosclerosis.[78]

In response to these challenges, new biomaterials, particularly pancatalytic biomaterials, show innovative potential. By integrating multi-modal response characteristics (such as pH, ROS, angiotensin converting enzyme), these materials can accurately identify the pathological microenvironment of CVD and achieve integrated diagnosis and treatment.

AS, a chronic inflammatory disease characterized by lipid-rich plaque formation in arterial walls, poses a significant global health burden due to its progression to life-threatening

Table 1 Representative pancatalytic biomaterials for inflammatory diseases across physiological systems, including material classification, animal models, and targeted diseases

System	Pancatalytic biomaterials	Classification	Animal model	Type of IDs	Ref.
Cardiovascular	GaHCF NACs	Inorganic	High-fat diet-fed ApoE/− mice	Atherosclerosis	24
Cardiovascular	MCN	Organic/inorganic	MI model in mice	Myocardial infarction	22
Cardiovascular	Pt@LF	Organic/inorganic	Ischemic stroke in mice	Stroke	46
Cardiovascular	CaHF NPs	Inorganic	Stress-induced hypertension in mice	Hypertension	47
Nervous	IP6@GCA/AP	Organic/inorganic	5 × FAD mice	Alzheimer's disease	48
Nervous	ATB NPs	Organic/inorganic	Preformed fibril induced PD mice	Parkinson's disease	49
Nervous	$MnFe_2O_4$ NPs	Inorganic	HD model in mice	Huntington's disease	50
Nervous	MSN-CeNPs	Inorganic	Experimental autoimmune encephalomyelitis in mice	Multiple sclerosis	51
Respiratory	PEG@CS/ BPQDs-AM NPs	Organic/inorganic	The mice after cigarette smoking and *P. aeruginosa* infection	Chronic obstructive pulmonary disease	52
Respiratory	CAT-NGs	Organic	Mice infected with NTHi and subjected to OVA	Neutrophilic asthma	40
Digestive	RuCo nanosheets	Inorganic	DSS-induced IBD model in mice	Inflammatory bowel disease	53
Digestive	mRNA LNPs	Organic	Liver fibrosis mouse models	Metabolic dysfunction-associated steatohepatitis	54
Joint	$CaSi_2$	Inorganic	Adjuvant-induced arthritis mice	Rheumatoid arthritis	25
Joint	BPNSs	Inorganic	ACLT in rats	Osteoarthritis	37
Integumentary	Cu/Zn-MOF	Organic/inorganic	MC903-induced AD-like mouse model	Atopic dermatitis	55
Integumentary	FeN_4O_2-SACs	Inorganic	IMQ-induced psoriasiform model in mice	Psoriasis	56
Sensory	Gel/Mn/NAC/PDA	Organic/inorganic	Cisplatin-induced ototoxicity model in mice	Sensorineural hearing loss	57
Sensory	Cs@P/CeO_2	Organic/inorganic	BAK-induced DED model in mice	Dry eye disease	45
Sensory	DSP@Ce-MOFs F127 hydrogel	Organic/inorganic	Endotoxin-induced uveitis in mice	Uveitis	58
Sensory	MLPGa	Organic/inorganic	*C. albicans*-infected fungal keratitis model in mice	Fungal keratitis	59
Urinary	$Pt_{5.65}S$	Inorganic	Cisplatin-induced AKI in mice	Acute kidney injury	60
Urinary	DEC	Organic/inorganic	CFT073-induced UTIs in mice	Urinary tract infections	61
Reproductive	FeLab	Organic/inorganic	*C. albicans*-induced vaginitis in mice	Candida vaginitis	62
Reproductive	TPDA NPs	Organic	LPS-induced acute prostatitis mouse models	Prostatitis	63
Others	DNA-pDHN	Organic	4T1 tumor-bearing mouse models	Tumor	64
Others	UPDA NPs	Organic	DOX-induced senescence in mice	Aging	65

cardiovascular events such as MI and stroke.[79–81] Central to its pathology is the development of unstable ''vulnerable plaques'', which feature thin fibrous caps, necrotic cores enriched with oxidized lipids, and intraplaque hemorrhage. These plaques are prone to rupture, driven by the cell death mechanism and sustained inflammation.[82,83] Despite advances in pharmacotherapy, current strategies including iron chelators (*e.g.*, deferoxamine), ferroptosis inhibitors (*e.g.*, ferrostatin-1), and anti-inflammatory biologics (*e.g.*, canakinumab) face critical limitations.[84–87] High costs, systemic toxicity (*e.g.*, increased infection risk with interleukin inhibitors), and the need for polypharmacy to compensate for single-target inefficacy hinder clinical translation. Moreover, conventional therapies fail to address the spatial coexistence of cell death, oxidative stress, and chronic inflammation within plaques, underscoring the need for multifunctional interventions.[88] Pancatalytic biomaterials address these challenges through integrated preparation (P), activation (A), and nontoxic treatment (N). Engineered GaHCF NACs exemplify this approach, leveraging their catalytic properties to achieve multifaceted therapeutic effects. During preparation, GaHCF NACs are designed with gallium's iron-mimetic properties to ensure structural stability and high iron-binding affinity. In the activation phase, they dynamically capture excess iron and scavenge reactive oxygen/nitrogen species (RONS), disrupting ferroptosis and lipid peroxidation while repolarizing macrophages toward anti-inflammatory M2 phenotypes. This dual catalytic action reduces necrotic core expansion and enhances fibrous cap stability. The nontoxic treatment phase leverages GaHCF NACs' *in situ* photoacoustic signaling capability, which converts sequestered iron into diagnostic signals for real-time plaque monitoring. By neutralizing pathologic iron while utilizing it for theranostics, GaHCF NACs circumvent systemic toxicity and enhance biocompatibility (Fig. 2(a)). This tripartite strategy of synergistic material design, catalytic microenvironment modulation, and self-monitoring functionality demonstrates how pancatalysis holistically resolves the iron–inflammation–oxidation axis, offering a paradigm for precision treatment of inflammatory CVDs.[24]

MI, a critical manifestation of CVDs, remains a leading cause of global mortality. Despite advancements in preventive strategies, approximately 50 million individuals suffer from MI annually.[68,76,80] The pathological progression of MI is tightly regulated by the dynamic myocardial infarction microenvironment (MIM), a tripartite system dominated by hypoxia, acidosis (pH 6.5–6.8), and redox imbalance due to excessive ROS.[89–91] These interconnected perturbations disrupt cardiomyocyte survival pathways, exacerbate mitochondrial dysfunction, and drive inflammatory cascades, ultimately leading to fibrotic scarring and irreversible cardiac damage.[92–94] Current clinical interventions, such as reperfusion therapy, paradoxically

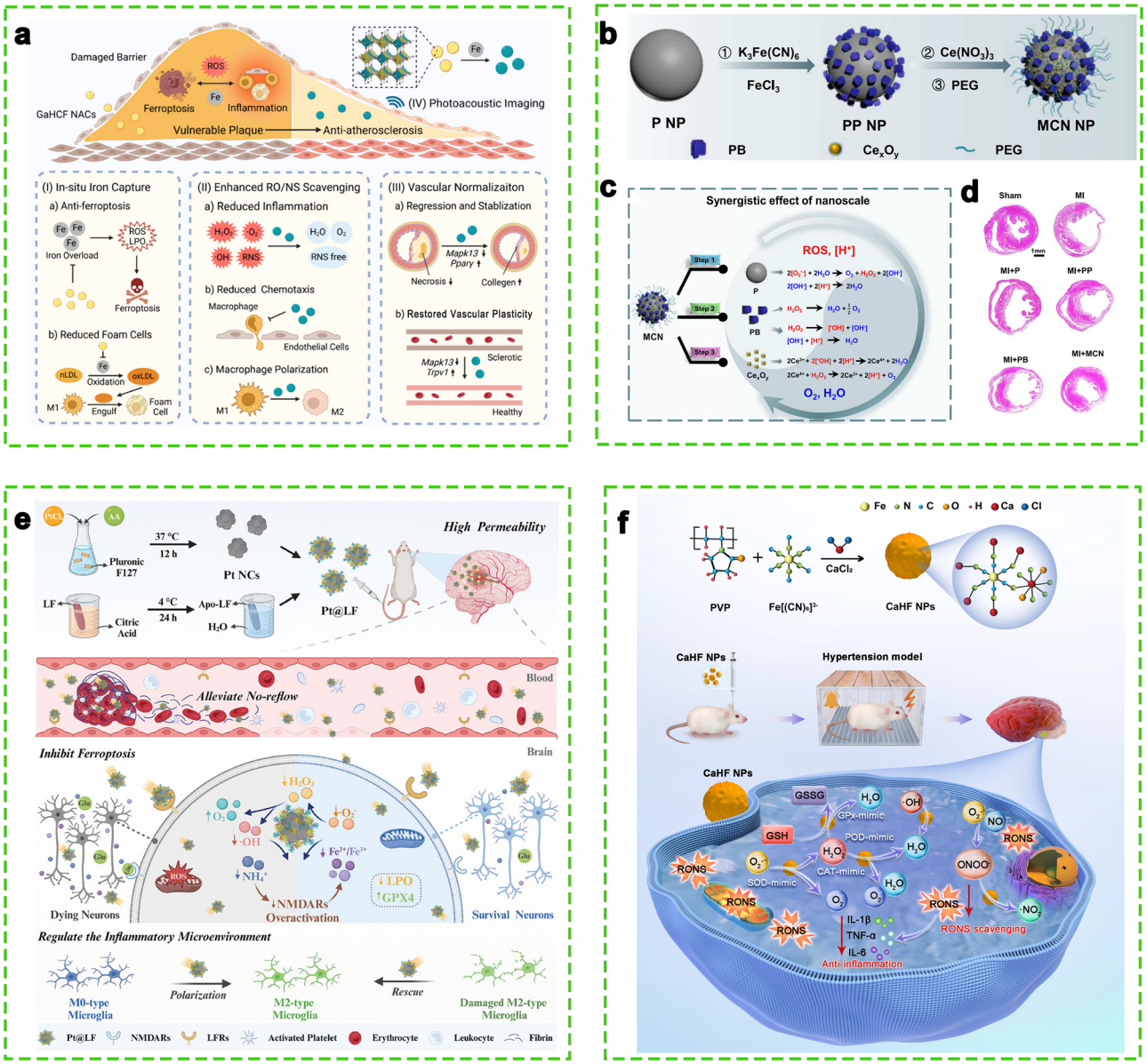

Fig. 2 Pancatalytic biomaterials for the treatment of cardiovascular disease. (a) GaHCF NACs for AS treatment *via* the P–A–N framework. Reproduced with permission.[24] Copyright 2025 American Chemical Society. (b) Diagram illustrating the synthesis process of MCN. Reproduced with permission.[22] Copyright 2024, Springer Nature. (c) Diagrammatic representation emphasizing the role of MCN in ameliorating hypoxic conditions. Reproduced with permission.[22] Copyright 2024, Springer Nature. (d) Representative images of HE staining on day 28 after MI. Reproduced with permission.[22] Copyright 2024, Springer Nature. (e) Pt@LF nanomotor for stroke treatment *via* the P–A–N framework. Reproduced with permission.[46] 2024 Wiley-VCH GmbH. (f) CaHF NPs for hypertension treatment *via* the P–A–N framework. Reproduced with permission.[47] Copyright 2023 Elsevier Ltd. All rights reserved.

aggravate oxidative stress and fail to prevent ischemia-reperfusion injury, underscoring the urgent need for novel therapeutic paradigms.[95] Pancatalytic biomaterials break this deadlock through holistic catalytic management spanning preparation (P), activation (A), and nontoxic treatment (N). MCN exemplifies this enzyme-inspired catalytic paradigm. During preparation, MCN synergistically assembles PDA, Prussian blue, and cerium oxide into a multi-catalytic nanoarchitecture mimicking enzymatic cooperativity (Fig. 2(b)). In the activation phase, it employs proton-coupled electron transfer and redox catalytic cycling to convert pathologic H^+, ROS, and hypoxia into O_2 and H_2O through self-sustained catalytic cascades, simultaneously resolving acidosis, quenching oxidative stress, and restoring oxygen homeostasis (Fig. 2(c)). These catalytic actions dismantle the MIM's vicious cycle while polarizing macrophages toward anti-inflammatory phenotypes. The nontoxic treatment phase leverages MCN's endogenous components and clinically validated materials to ensure localized metabolically catalytic activity and safe clearance, eliminating off-target risks (Fig. 2(d)).[22]

Stroke ranks as the second leading global cause of death and the third contributor to chronic disability, with half of survivors facing lifelong functional impairment.[96] Projections indicate a

1.5-fold increase in stroke-related mortality by 2050 compared to 2020, driven by aging populations and insufficient therapeutic advancements.[79,97,98] The ischemic penumbra, a salvageable region surrounding the irreversibly damaged core, faces dual threats: energy failure from hypoperfusion and ''no-reflow'' phenomena caused by microthrombi and pericyte-mediated vasoconstriction, which impede drug delivery. Current clinical strategies rely on thrombolytics like recombinant tissue-type plasminogen activator (rt-PA), but their narrow therapeutic window (<4.5 hours) limits applicability, while delayed interventions (*e.g.*, antithrombotics or neuroprotectants) exhibit diminished efficacy.[99,100] Clinical limitations stem from three interrelated barriers: (1) inadequate penetration of therapeutics into hypoxic regions due to microvascular occlusion and blood–brain barrier (BBB) dysfunction;[101] (2) the inability of monotherapies (*e.g.*, ROS scavengers or iron chelators) to address the ferroptosis–excitotoxicity axis;[102] and (3) systemic toxicity risks from non-targeted drug distribution.[103] Pancatalytic biomaterials address these gaps through the P–A–N framework. The Pt@LF nanomotor exemplifies this paradigm (Fig. 2(e)). During preparation, platinum nanoclusters (Pt NCs) are functionalized with apo-lactoferrin (Apo-LF), combining Pt's dual CAT-like and NH^{4+} scavenging activities with Apo-LF's iron-chelating capacity and BBB-targeting capability *via* lactoferrin receptor binding. In the activation phase, Pt NCs convert pathologic ROS into O_2, mitigating lipid peroxidation and restoring redox balance, while Apo-LF sequesters excess iron to inhibit ferroptosis drivers. Simultaneously, NH^{4+} clearance prevents *N*-methyl-D-aspartic acid receptors' overactivation, breaking the excitotoxicity vicious cycle. The nanomotor's self-propelling motion enhances penetration through occluded microvessels, enabling mechanical thrombolysis and targeted delivery to the penumbra. For nontoxic treatment, Apo-LF's endogenous origin and Pt's metabolic stability ensure biocompatibility, minimizing off-target effects. By synchronously modulating iron homeostasis, redox imbalance, and neuroinflammation, Pt@LF reprograms the ischemic microenvironment, polarizing microglia toward anti-inflammatory phenotypes and reducing infarct volume.[46]

Hypertension, affecting over 1.28 billion individuals globally in 2019 and projected to rise to 1.56 billion by 2025, represents a critical public health challenge due to its strong association with cardiovascular, cerebrovascular, and renal complications.[104,105] The pathogenesis is intricately linked to oxidative stress and neuroinflammation driven by RONS, including superoxide anion ($^{\bullet}O_2^-$), hydrogen peroxide (H_2O_2), hydroxyl radicals ($^{\bullet}OH$), nitric oxide (NO), and peroxynitrite ($ONOO^-$).[106–108] In the rostral ventrolateral medulla, a key regulator of sympathetic nervous activity, RONS overproduction originates from nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX) and mitochondrial dysfunction. These reactive molecules disrupt redox balance, amplify sympathetic excitability, and reduce NO bioavailability, converting its neuroprotective role into a cytotoxic one through $ONOO^-$ formation under hypoxic conditions.[109] Concurrently, microglia, the brain's resident immune cells, shift to a proinflammatory state in response to RONS, releasing cytokines that further exacerbate NOX-mediated ROS generation, DNA damage, and neuronal apoptosis. This self-reinforcing vicious cycle underscores the interplay between oxidative stress, neuroinflammation, and sympathetic overactivation in sustaining hypertensive pathology.[110,111]

Despite advances in understanding hypertensive pathophysiology, clinical management of hypertension continues to face significant challenges, including poor patient adherence to lifelong medication, drug-related side effects (*e.g.*, hypotension, renal impairment), and the complexity of managing comorbidities (*e.g.*, diabetes, chronic kidney disease). Additionally, limited efficacy of lifestyle interventions and the prevalence of resistant hypertension further complicate sustained blood pressure control.[112] Pancatalytic biomaterials bridge these gaps through integrated preparation (P), activation (A), and nontoxic treatment (N). Calcium hexacyanoferrate (III) nanoparticles (CaHF NPs) exemplify this holistic catalytic system (Fig. 2(f)). During preparation, ultrasmall CaHF NPs are engineered to mimic SOD, CAT, GPx, and POD activities, creating a multi-enzyme catalytic capacity for broad-spectrum RONS neutralization. In the preparation phase, ultrasmall CaHF NPs are rationally engineered with multi-enzyme mimetic activities, including SOD, POD, GPx, and CAT, to enable efficient scavenging of diverse RONS. During the activation phase, these nanoparticles are triggered by the pathological microenvironment, where elevated RONS and neuroinflammation drive hypertension progression; CaHF NPs catalytically convert harmful species such as H_2O_2, $^{\bullet}O_2^-$, $^{\bullet}OH$, and NO into harmless molecules, thereby alleviating oxidative stress, suppressing inflammation, and reducing neuronal apoptosis. In the nontoxic treatment phase, CaHF NPs demonstrate high biocompatibility and minimal side effects, overcoming the stability and safety limitations of natural enzymes and traditional nanozymes. CaHF NPs exemplify how concerted catalytic engineering resolves the interconnected drivers of hypertension.[47]

3.2 Nervous system

Neuroinflammation is a complex immune response of the central nervous system (CNS) to harmful stimuli such as infection, ischemia, or trauma.[113] Its core characteristics include excessive activation of glial cells (microglia and astrocytes), elevated release of cytokines (pro-inflammatory cytokines, chemokines, and ROS), migration of peripheral immune cells, and localized tissue damage.[114] Under physiological conditions, neuroinflammation maintains brain homeostasis by clearing pathogens and repairing damaged tissues. However, chronic or dysregulated inflammatory responses trigger neuronal injury and degeneration, serving as a central driving factor for neurodegenerative diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and multiple sclerosis (MS).[114]

Neuroinflammation is a complex process driven by the interplay of central and peripheral immune components within the CNS. At its core, this mechanism involves the activation of resident glial cells, notably microglia and astrocytes, which dynamically regulate inflammatory responses. Microglia, the primary immune sentinels of the CNS, exhibit functional

plasticity by polarizing into pro-inflammatory M1 phenotypes or anti-inflammatory M2 phenotypes. M1 microglia exacerbate neurotoxicity through excessive release of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and TNF-α, along with ROS, while M2 microglia promote tissue repair *via* anti-inflammatory mediators like interleukin-10 (IL-10). Similarly, astrocytes adopt reactive states classified as neurotoxic A1 or neuroprotective A2 subtypes, influencing neuroinflammation through cytokine production, metabolic regulation, and BBB modulation. The infiltration of peripheral immune cells, including neutrophils, monocytes, and lymphocytes, further amplifies CNS inflammation. Neutrophils disrupt BBB integrity through the release of proteases and the formation of neutrophil extracellular traps, while monocytes differentiate into macrophages that interact with microglia to shape inflammatory outcomes. Cytokines such as IL-6, interleukin-23, and granulocyte-macrophage colony-stimulating factor act as critical signaling molecules, activating pathways like Janus kinase-signal transducer and activator of transcription (JAK-STAT) and mitogen-activated protein kinase (MAPK) to coordinate immune responses. Chronic dysregulation of these processes leads to sustained inflammation, contributing to neurodegenerative pathologies.

Neuroinflammation is characterized by a dynamic interplay of central and peripheral immune mechanisms triggered by pathogens, injury, or stress.[113] Central to this process are microglia, the CNS-resident immune cells, which exhibit dual functional polarization into pro-inflammatory M1 or anti-inflammatory M2 phenotypes.[115] M1 microglia, activated *via* Toll-like receptors (TLRs) and interferon-γ signaling, release cytotoxic mediators such as IL-1β, TNF-α, and ROS, exacerbating neuronal damage.[116] Conversely, M2 microglia promote tissue repair through anti-inflammatory cytokines including IL-10 and transforming growth factor-beta (TGF-β), as well as various growth factors. Astrocytes similarly adopt reactive states, namely, neurotoxic A1 or protective A2 subtypes, regulated by pathways including NF-κB, MAPK, and JAK/STAT3.[117,118] Reactive astrocytes influence neuroinflammation by modulating cytokine release, BBB integrity, and metabolic support, though chronic activation disrupts neuronal homeostasis and amplifies neurodegeneration.[119–122] Peripheral immune cells, such as neutrophils and monocytes, infiltrate the CNS under pathological conditions.[123] Neutrophils compromise the BBB *via* proteases and extracellular traps, while monocytes differentiate into macrophages that interact with microglia, shaping inflammatory outcomes.[124,125] Cytokines like IL-6, IL-1β, and TNF, produced by glial cells and infiltrating leukocytes, activate signaling pathways (*e.g.*, JAK-STAT, MAPK) to propagate inflammation.[126] Persistent dysregulation of these interactions, marked by sustained cytokine release, glial hyperactivation, and immune cell influx, drives chronic neuroinflammation, contributing to neurodegenerative disorders.

The intricate pathological networks of neurodegenerative diseases, such as glial cell phenotypic imbalance and oxidative-inflammatory cycles, urgently require multi-target synergistic intervention strategies. Pancatalytic biomaterials, which integrate biocatalysis (*e.g.*, enzyme-mimetic activity), material catalysis (*e.g.*, ROS-scavenging nanozymes), and medical regulation (*e.g.*, targeted delivery), achieve holistic management through the P–A–N framework. For example, AD as a representative neurodegenerative disorder is pathologically characterized by β-amyloid (Aβ) plaque deposition, neurofibrillary tangles caused by tau hyperphosphorylation, chronic inflammation, and neuronal apoptosis.[127] While conventional single-target therapies like Aβ-targeting antibodies (*e.g.*, Aducanumab) partially clear plaques, they fail to address the complex interplay of multiple pathological pathways in AD, underscoring the necessity for multi-target synergistic therapies.[128] Recently, a supramolecular assembly-based platform strategy (IP6@GCA/AP) has achieved systemic intervention in AD pathology through dynamic modular design (Fig. 3(a)). Key mechanisms include the following: guanidinium-modified calixarene (GCA) inhibits fibril formation and disassembles pre-existing fibrils *via* strong interactions between guanidinium groups and negatively charged residues (aspartate/glutamate) on Aβ42; its low hydration energy enhances microglial phagocytosis and clearance of Aβ. Ascorbyl palmitate (AP), acting as an antioxidant, alleviates oxidative stress in the AD brain by scavenging ROS, thereby mitigating inflammation; its hydroxyl groups form heteromultivalent bonds with GCA, enhancing binding affinity to Aβ. Dipotassium phytate (IP6), precisely released *via* a biomarker displacement activation strategy, inhibits β-secretase activity to reduce Aβ production.[48]

PD is a neurodegenerative disorder centered on the degeneration of dopaminergic neurons in the substantia nigra pars compacta and striatal dopamine (DA) depletion.[129] Clinically manifested as motor dysfunction and cognitive impairment, its pathology is closely associated with α-synuclein (α-syn) aggregates forming Lewy bodies, which directly induce neuronal toxicity and exacerbate pathological progression by suppressing autophagy systems such as chaperone-mediated autophagy (CMA).[129–131] Current PD treatments, such as levodopa and DA agonists, alleviate symptoms by boosting DA levels but cannot regenerate degenerated neurons or enable precise spatial modulation in the substantia nigra, failing to halt disease progression.[132,133] While deep brain stimulation (DBS) activates neurons *via* external stimuli (*e.g.*, near-infrared light), it necessitates permanent device implantation, risking infections and hardware complications.[134] Optogenetic DBS alternatives avoid implants but rely on viral-mediated gene delivery for light-sensitive proteins, raising safety issues linked to genetic manipulation.[135] To address this, researchers developed a wireless photothermal-driven DBS nanosystem (Au@TRPV1@β-syn NPs, ATB NPs). ATB NPs exemplify the P–A–N paradigm by synergizing photothermal energy conversion, targeted biological modulation, and protein homeostasis restoration (Fig. 3(b)). The nanosystem is composed of gold nanoshells (AuNSs) for near-infrared (NIR, 808 nm) light-to-heat conversion, transient receptor potential vanilloid family member 1 (TRPV1) antibodies conjugated to AuNSs to anchor specifically to DA neurons in the substantia nigra (SN), and β-synuclein (β-syn) peptides linked *via* NIR-responsive bonds for competitive binding to the hydrophobic

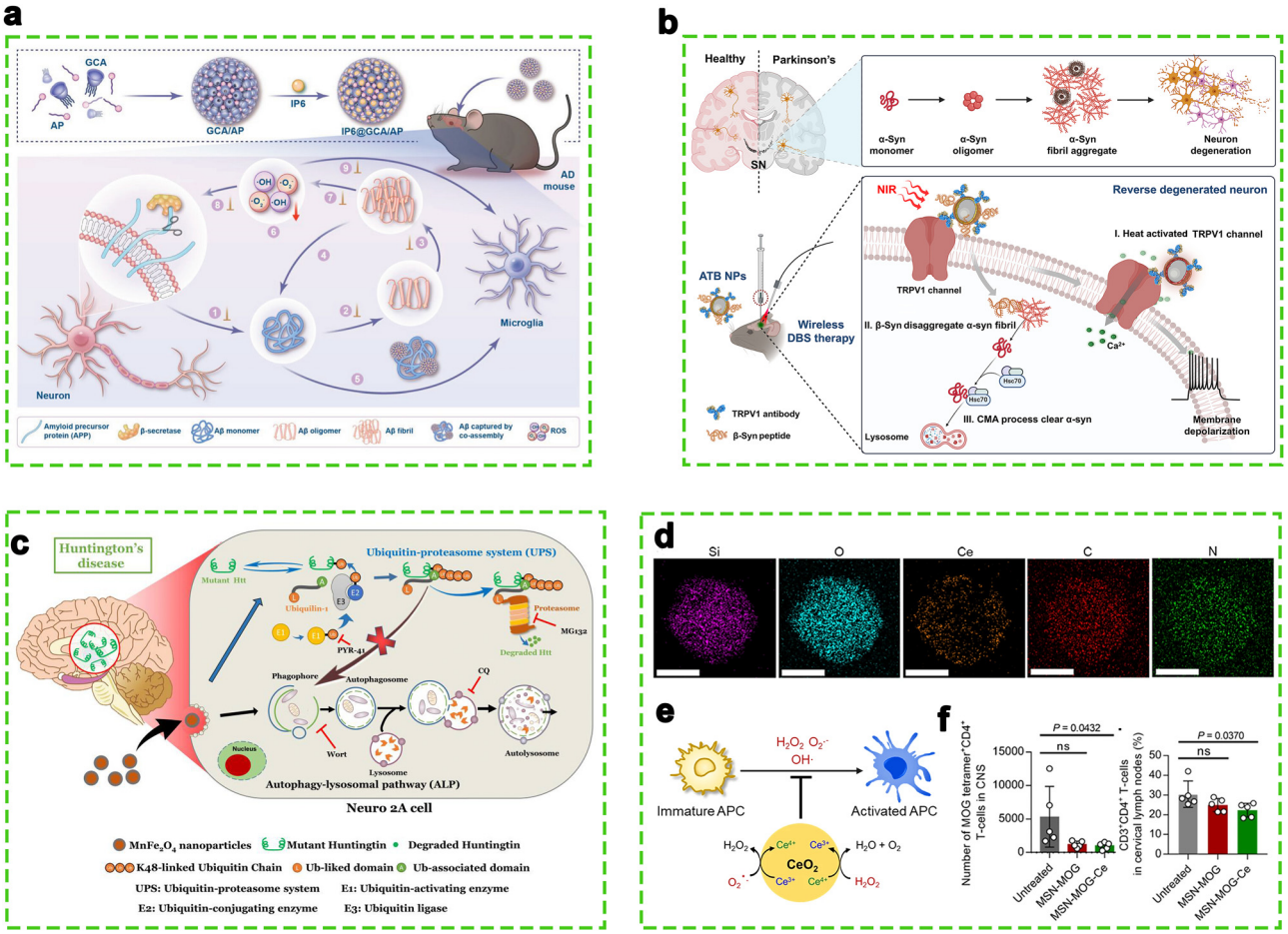

Fig. 3 Pancatalytic biomaterials for the treatment of nervous system diseases. (a) IP6@GCA/AP for AD treatment *via* the P–A–N framework. Reproduced with permission.[48] Copyright 2024 Wiley-VCH GmbH. (b) ATB NPs for PD treatment *via* the P–A–N framework. Reproduced with permission.[49] Copyright 2025, The American Association for the Advancement of Science. (c) $MnFe_2O_4$ NPs for HD treatment *via* the P–A–N framework. Reproduced with permission.[50] Copyright 2019 Elsevier Ltd. All rights reserved. (d) Energy dispersive X-ray spectroscopy elemental mapping. Reproduced with permission.[51] Copyright 2022, Springer Nature. (e) Scheme demonstrates the catalytic property of CeNPs to scavenge intracellular ROS for the suppression of APC activation. Reproduced with permission.[51] Copyright 2022, Springer Nature. (f) The number and frequency of $CD3^+CD4^+$ T cells infiltrating the spinal cord and the frequency of $CD3^+CD4^+$ T cells in cervical lymph nodes on day 31. Reproduced with permission.[51] Copyright 2022, Springer Nature.

regions of α-syn. Following stereotaxic delivery to the SN, ATB NPs localize on DA neurons through TRPV1 targeting. Upon pulsed NIR irradiation, the nanosystem acts as a nanoantenna to convert light into localized heat, which simultaneously activates TRPV1 channels to induce Ca^{2+} influx and restore DA neuronal activity while triggering the release of β-syn peptides to disrupt α-syn fibrils. The heat further stimulates CMA to enhance lysosomal clearance of pathological α-syn preformed fibrils. This spatiotemporally controlled process elevates striatal DA levels, degrades toxic aggregates, and reverses motor deficits in PD mice, achieving these outcomes without the invasive risks associated with DBS. By integrating physical energy transduction with biological pathway regulation, ATB NPs demonstrate the transformative potential of pancatalytic biomaterials in precision neuromodulation and neurodegenerative disease therapy.[49]

HD is an autosomal dominant neurodegenerative disorder caused by abnormal polyglutamine (polyQ) expansion (CAG repeats >35) in the N-terminal region of huntingtin (Htt) protein.[136] Its core pathology involves toxic aggregation of mutant Htt (mHtt), leading to neuronal dysfunction, motor impairments, short-term memory deficits, and progressive death.[137] $MnFe_2O_4$ nanoparticles (NPs) exemplify a pancatalytic biomaterial strategy for HD therapy through the P–A–N framework. During the preparation phase, biocompatible $MnFe_2O_4$ NPs are synthesized *via* a simple method and delivered to neuronal cells stably expressing mutant huntingtin with 74 polyglutamine repeats (mHtt-Q74). In the activation phase, these NPs selectively enhance K48-linked ubiquitination of mHtt-Q74, directing its recognition by the ubiquitin receptor ubiquilin-1 (not p62/SQSTM1) for targeted degradation *via* the ubiquitin-proteasome system (UPS), bypassing autophagy-lysosomal pathways. This UPS-specific activation overcomes prior limitations of nanomaterials relying solely on autophagy. In the nontoxic treatment phase, $MnFe_2O_4$ NPs achieve precise clearance of toxic mHtt-Q74 aggregates without compromising wild-type protein function or inducing cytotoxicity, effectively

restoring proteostasis (Fig. 3(c)). This work pioneers the use of nanomaterials to exploit UPS-mediated degradation for HD, offering a novel therapeutic avenue for polyglutamine expansion disorders.[50]

MS is a neuroinflammatory autoimmune disorder characterized by autoreactive $CD4^+$ T cell-mediated demyelination and axonal damage in the CNS, leading to progressive motor dysfunction.[138] Existing treatment regimens for MS primarily achieve transient alleviation of chronic neuropathic symptoms while carrying the risk of systemic immune compromise.[139] To address this, a pancatalytic biomaterial-based immunosuppressive vaccine (MSN-CeNPs) integrates catalytic material design and immunomodulatory functions under the P–A–N framework. In the preparation phase, MSNs are engineered with high antigen-loading capacity to deliver self-antigens to splenic antigen-presenting cells (APCs), while surface-conjugate CeNPs provide catalytic ROS-scavenging activity *via* redox cycle-mediated antioxidant mimicry (*e.g.*, SOD/CAT-like activity) (Fig. 3(d)). During activation, CeNPs catalytically neutralize inflammatory ROS in the microenvironment, synergizing with antigen-loaded MSNs to reprogram APCs into a tolerogenic phenotype marked by reduced costimulatory molecule (CD80/CD86) expression and anti-inflammatory cytokine secretion (Fig. 3(e)). This catalytic remodeling of APCs drives naïve T cell differentiation into $Foxp3^+$ regulatory T cells (Tregs) rather than pathogenic Th1/Th17 subsets, establishing antigen-specific immune tolerance. In the nontoxic treatment phase, the expanded Treg population suppresses autoreactive $CD4^+$ T cell infiltration into the CNS, halting demyelination and mitigating late-stage experimental autoimmune encephalomyelitis without systemic immunosuppression (Fig. 3(f)). By coupling catalytic material properties (ROS elimination) with biological immunomodulation (APC/Treg axis), this strategy exemplifies the transformative potential of pancatalytic biomaterials in resolving chronic neuroinflammation through spatially confined, toxicity-free therapeutic catalysis.[51]

3.3 Respiratory system

Inflammatory respiratory diseases represent a significant component of the global disease burden, with their development closely linked to multifaceted environmental and genetic risk factors.[140] Exogenous stimuli such as environmental pollutants (*e.g.*, PM2.5), cigarette smoke, and pathogenic microbial infections trigger chronic inflammatory responses, leading to progressive damage to airways and pulmonary parenchyma.[141] Chronic inflammatory disorders, including asthma and chronic obstructive pulmonary disease (COPD), are characterized by high recurrence rates and disability, significantly impairing patients' quality of life. Infectious diseases like bacterial pneumonia and tuberculosis face escalating therapeutic challenges due to the spread of drug-resistant strains and immune evasion mechanisms. Notably, fibrotic conditions such as idiopathic pulmonary fibrosis exhibit pathological progression intertwined with persistent inflammatory microenvironments, manifesting as inflammatory-fibrotic transitions.[142]

The shared pathological mechanisms of these diseases stem from dysregulated inflammatory response networks. PAMPs or DAMPs activate pattern recognition receptors (*e.g.*, TLRs) on alveolar macrophages and airway epithelial cells, initiating NF-κB and MAPK signaling pathways.[143] This cascade drives excessive release of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) and chemokines (C–X–C motif ligand 8, CXCL8; C–C motif ligand 2, CCL2).[144,145] Recruitment of neutrophils and monocytes amplifies inflammatory cascades, with tissue destruction mediated by elastase and matrix metalloproteinases.[146] Oxidative stress perpetuates a vicious cycle: ROS overproduction directly damages epithelial barriers and activates the NLRP3 inflammasome, promoting IL-1β maturation. Th2 immune polarization dominates allergic inflammation, where interleukin-4, interleukin-5, and interleukin-13 induce goblet cell hyperplasia and immunoglobulin E production and eosinophil infiltration, driving airway hyperresponsiveness.[147] In chronic inflammation, dysfunctional Tregs and sustained activation of pro-inflammatory M1 macrophages jointly sustain pathological processes.[148,149]

COPD, ranked as the third leading global cause of mortality, imposes a substantial burden on public health through progressive airway obstruction, emphysema, and irreversible airflow limitation.[148] Cigarette smoke remains the primary etiological driver, yet persistent airway inflammation persists even after smoking cessation, highlighting the complexity of its pathogenesis.[150] COPD progression is critically mediated by dysregulated alveolar macrophage polarization in response to environmental triggers.[145] M1 macrophages, activated by Th1 signals, exacerbate inflammation *via* overproduction of NO, TNF-α, IL-6, and CCL2, driving tissue destruction.[144] Conversely, M2 macrophages, regulated by Th2 cytokines (IL-4/IL-13), promote anti-inflammatory responses and tissue repair through Arg1/TGF-β upregulation. However, the imbalance between M1-driven inflammation and M2-mediated repair mechanisms underpins chronic pathological changes, including airway remodeling and fibrosis.[144] Current therapeutic strategies, such as inhaled corticosteroids and long-acting bronchodilators, offer symptomatic relief but fail to reverse structural damage or halt disease progression, particularly in advanced emphysema.[151] These limitations underscore the urgent need for innovative therapeutic strategies capable of targeting the root causes of COPD pathology while overcoming anatomical and biochemical barriers in the respiratory tract. The PEG@CS/BPQDs-AM NPs exemplify a pancatalytic strategy for COPD therapy by integrating sequential catalytic processes into a unified therapeutic platform. This system addresses the challenges of mucus barrier penetration and controlled drug release through rationally engineered biomaterial interactions. The chitosan core, functionalized with polyethylene glycol (PEG), leverages its inherent mucoadhesive properties to adhere to the negatively charged pulmonary epithelium while enhancing mucus penetration *via* PEG-mediated hydrophilicity, a critical step in overcoming airway defenses. Embedded black phosphorus quantum dots (BPQDs) serve as catalytic triggers, where their gradual autoxidation generates phosphate

ions and protons, inducing localized dissociation of the PEG@CS matrix. This self-regulated degradation not only ensures precise spatiotemporal release of anti-inflammatory macrophages at diseased sites but also disrupts pathogenic biofilms through reactive species generation, synergistically enhancing therapeutic efficacy. The pancatalytic framework is further realized by BPQDs' inherent biocompatibility and biodegradability, ensuring nontoxic metabolic clearance post-treatment (Fig. 4(a)). By orchestrating material preparation (P), activation of the bio-effect (A), and nontoxic treatment (N), this system demonstrates holistic management of COPD pathology, offering a paradigm for designing multifunctional biomaterials that harmonize catalytic processes with biological precision.[52]

Asthma, a chronic respiratory disease marked by airway inflammation, bronchoconstriction, and mucus overproduction, affects over 300 million people globally, with rising prevalence linked to genetic-environmental interactions.[152,153] Neutrophilic asthma, a severe subtype resistant to corticosteroids and associated with bacterial colonization (*e.g.*, *NTHi*, *S. aureus*), represents 5–20% of cases but accounts for 50–80% of asthma-related healthcare burden due to high hospitalization and mortality.[154,155] Pathological mechanisms involve oxidative stress from excessive ROS generated by pollutants, allergens, and inflammatory cells *via* Nox2-derived superoxide, which transforms into damaging H_2O_2 and downstream radicals (*e.g.*, $^{\bullet}OH$, HOCl), worsening airway hyperresponsiveness and remodeling.[156–158] While CAT demonstrates potent H_2O_2-neutralizing capacity, its clinical utility is hampered by rapid degradation and poor bioavailability.[159] Current therapies, including corticosteroids and bronchodilators, inadequately address ROS-driven pathology, particularly in neutrophilic variants, necessitating innovative strategies to enhance antioxidant delivery and bacterial clearance.[160] The CAT-loaded nanogels (CAT-NGs) embody a pancatalytic approach by integrating catalytic ROS scavenging with multifunctional biomaterial engineering. Composed of chitosan–arginine–maleimide conjugates crosslinked with citric acid and ε-polylysine, these nanogels protect CAT from enzymatic degradation while leveraging their mucoadhesive properties for targeted airway delivery. The system operates through sequential catalytic processes, where ionic crosslinking during preparation ensures structural stability, while the antibacterial ε-polylysine shell activates biofilm disruption to counteract infection-associated neutrophilic inflammation (Fig. 4(b)). Upon inhalation, CAT-NGs neutralize H_2O_2 *via* enzymatic catalysis, interrupting ROS propagation and suppressing NLRP3/NF-κB signaling pathways, a nontoxic intervention that concurrently alleviates oxidative stress and inflammation. This holistic strategy not only preserves CAT's catalytic efficiency but also addresses comorbid bacterial challenges, demonstrating how pancatalytic biomaterials synchronize material design, biological activation, and therapeutic precision to redefine asthma management.[40]

3.4 Digestive system

Inflammatory gastrointestinal diseases represent a heterogeneous group of disorders characterized by chronic inflammation of the digestive tract, severely compromising patients' quality of life and long-term health outcomes.[161] Among these, IBD and metabolic dysfunction-associated steatohepatitis (MASH) stand as two prototypical pathological entities.[162] IBD patients frequently suffer from persistent intestinal inflammation, leading to chronic diarrhea, malabsorption, progressive malnutrition, weight loss, and growth retardation in pediatric populations. Prolonged mucosal damage significantly elevates the risk of colorectal cancer, with severe cases necessitating

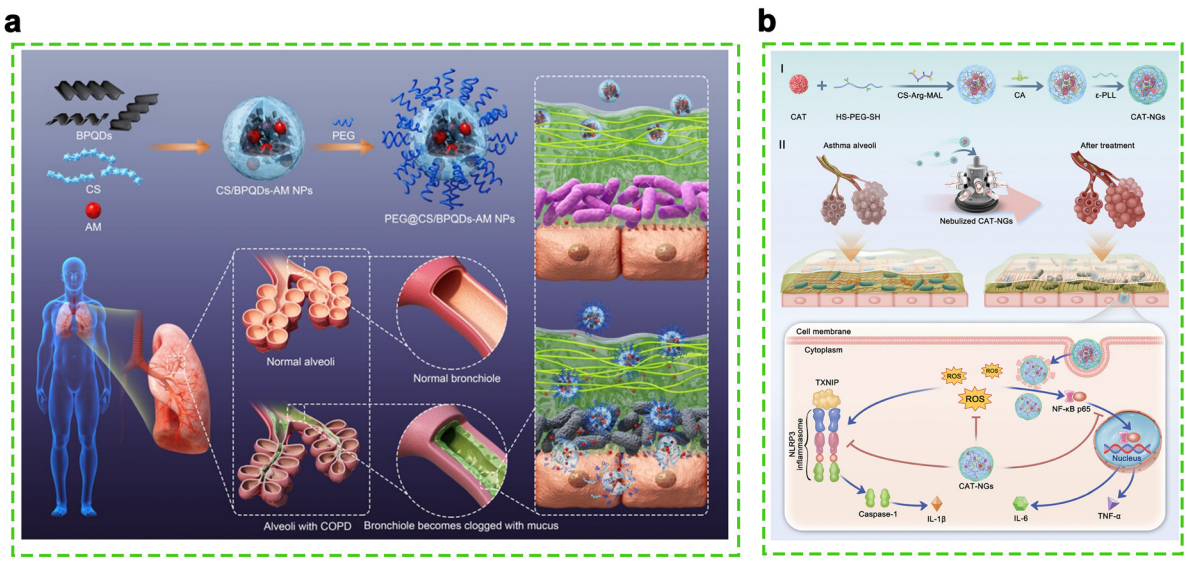

Fig. 4 Pancatalytic biomaterials for the treatment of respiratory system diseases. (a) PEG@CS/BPQDs-AM NPs for COPD treatment *via* the P–A–N framework. Reproduced with permission.[52] Copyright 2020 Wiley-VCH GmbH. (b) CAT-NGs for asthma treatment *via* the P–A–N framework. Reproduced with permission.[40] Copyright 2024 Wiley-VCH GmbH.

surgical resection of affected bowel segments.[163,164] MASH, on the other hand, is defined by metabolic dysregulation-driven hepatic inflammation and fibrosis, placing patients at heightened risk of end-stage liver diseases such as cirrhosis, hepatic decompensation, and hepatocellular carcinoma.[165] Both conditions are further complicated by extraintestinal systemic manifestations, including arthritis, uveitis, and erythema nodosum, which amplify patients' physical and psychological burden.[166]

Inflammatory bowel diseases (IBDs), encompassing Crohn's disease (CD) and ulcerative colitis (UC), represent chronic and relapsing inflammatory disorders of the gastrointestinal tract, imposing substantial burden on global healthcare systems and patient well-being.[167] Characterized by heterogeneous pathology, CD manifests as transmural, discontinuous inflammation across the entire gastrointestinal tract, predominantly targeting the ileum and colon, while UC is restricted to continuous mucosal inflammation in the colon and rectum.[168,169] Both subtypes severely compromise patients' quality of life, with elevated risks of colorectal cancer, systemic complications, and mortality, underscoring their clinical urgency.[170] The global prevalence of IBD has surged, affecting over 3.5 million individuals globally, driven by complex interactions among genetic susceptibility, environmental triggers (*e.g.*, dietary shifts, psychological stress), and microbial dysbiosis.[171–174] Despite advances in identifying these contributing factors, the precise etiology remains elusive, hindering the development of curative therapies.

Current management strategies predominantly rely on immunosuppressive agents, corticosteroids, and biologics such as anti-TNF monoclonal antibodies, which aim to attenuate aberrant immune activation and promote mucosal healing.[175,176] However, therapeutic efficacy is inconsistent, with up to 30% of patients exhibiting primary non-response to anti-TNF agents and 30–40% developing secondary resistance over time, necessitating escalated dosing or alternative regimens, which amplify the risk of infections and malignancies.[177–180] Surgical interventions, though employed in severe cases, are limited by prolonged recovery, recurrence, and functional impairments. Conventional drug delivery systems, including pH-responsive or enzyme-triggered formulations, face challenges in overcoming the colon's hostile microenvironment, marked by fluctuating pH, enzymatic degradation, mucus barriers, and microbial activity, leading to premature drug release or inadequate targeting.[181] These limitations highlight the unmet need for advanced biomaterial-based platforms capable of precise, sustained drug delivery to inflamed tissues while minimizing systemic toxicity.

To address these critical gaps, RuCo nanosheets have emerged as a promising pancatalytic approach for IBD treatment through integrated preparation, activation, and nontoxic action. In the preparation phase, bimetallic RuCo nanosheets are synthesized *via* solvothermal methods, leveraging ruthenium's acid resistance and cobalt's biocompatibility to optimize stability and catalytic efficiency. Their electronic structure modulation, driven by electronegativity differences, enhances dual enzyme-like activities (SOD and CAT), validated by density functional theory calculations. During activation, RuCo nanosheets catalytically scavenge ROS *via* SOD-like and CAT-like cascades, disrupting NF-κB signaling and suppressing proinflammatory cytokine release. This mitigates intestinal barrier damage and dysbiosis, addressing IBD's core pathology. The nontoxic treatment phase is ensured by cobalt's physiological relevance and ruthenium's gastric stability, enabling oral delivery with minimal systemic exposure (Fig. 5(a)). Preclinical studies demonstrate significant anti-inflammatory efficacy without adverse effects, highlighting targeted ROS neutralization and sustained catalytic activity in the gastrointestinal tract. By unifying material design, catalytic bioactivity, and biocompatibility, RuCo nanosheets embody pancatalysis, offering a robust, orally administrable strategy for IBD management.[53]

MASH, a severe subtype of metabolic dysfunction-associated steatotic liver disease, has emerged as a global health crisis driven by chronic caloric excess, genetic susceptibility, and metabolic dysregulation.[182] Characterized by hepatic steatosis, lobular inflammation, hepatocyte injury, and progressive fibrosis, MASH significantly elevates the risk of cirrhosis, hepatocellular carcinoma, and liver-related mortality, while imposing a growing burden on healthcare systems worldwide. Its pathophysiology involves a complex interplay of lipotoxicity, mitochondrial dysfunction, oxidative stress, and dysregulated immune responses.[182] Lipid nanoparticles (LNPs) function as pancatalytic biomaterials in MASH therapy through a holistic strategy integrating preparation, activation, and nontoxic targeting (Fig. 5(b)). The preparation phase involves engineering LNPs with retinoid derivatives (*e.g.*, all-*trans* retinoic acid) to enhance fibrotic liver targeting. These ligands bind retinol-binding protein-4 (RBP-4) on activated hepatic stellate cells (HSCs), with carboxylic retinoids optimizing LNP surface rearrangement for improved RBP-4 affinity and cellular uptake. This design achieves a ~10-fold increase in mRNA delivery efficacy compared to conventional LNPs. In the activation phase, LNPs deliver mRNA encoding therapeutic proteins like relaxin, an anti-fibrotic agent targeting the TGF-β pathway, fused to a collagen-binding domain (CBD) for exopolysaccharide-rich extracellular matrix (ECM) anchoring. This fusion enables ~80% hepatic retention, ensuring sustained local activity to suppress HSC activation and ECM deposition. Finally, the nontoxic treatment phase minimizes systemic exposure by combining RBP-4-mediated targeting and CBD-driven ECM anchoring, reducing off-target effects while maintaining therapeutic efficacy. Validated in preclinical MASH models, this pancatalytic approach exemplifies precise catalyst design, bioactivity amplification, and nontoxic treatment, offering a transformative framework for fibrosis treatment.[54]

3.5 Joint systems

Osteoarthritis (OA) and rheumatoid arthritis (RA), two prevalent forms of chronic inflammatory arthritis, collectively impose substantial burden on global health due to their progressive destruction of synovial joints and irreversible functional impairment. While OA primarily stems from mechanical wear-and-tear of articular cartilage, RA arises from autoimmune-driven synovial tissue attacks, though both culminate in a vicious

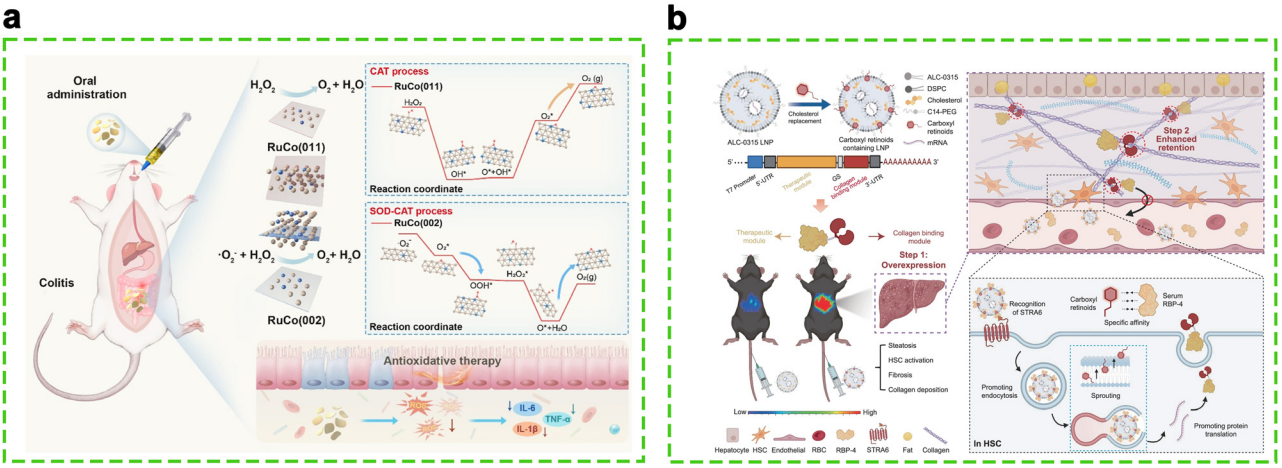

Fig. 5 Pancatalytic biomaterials for the treatment of digestive system diseases. (a) RuCo nanosheets for IBD treatment *via* the P–A–N framework. Reproduced with permission.[53] Copyright 2025 American Chemical Society. (b) LNPs function as pancatalytic biomaterials in metabolic dysfunction-associated MASH. Reproduced with permission.[54] Copyright 2024 Springer Nature.

cycle of joint degradation and disability.[183] The pathological difference lies in their destructive patterns: RA predominantly induces synovial hyperplasia and superficial osteochondral erosion through autoimmune inflammation, whereas OA triggers extensive structural breakdown penetrating deep into subchondral bone layers.[72] Shared between these disorders is the establishment of a chronically inflamed microenvironment characterized by hyperactivated immune cell infiltration and sustained pro-inflammatory cytokine storms, collectively termed the "inflammatory arthritic cascade".[184] Clinically, this manifests as progressive joint space narrowing, bony ankylosis, and eventual deformity with mobility loss. Current therapeutic regimens, including anti-inflammatories, disease-modifying anti-rheumatic drugs (DMARDs), and immunosuppressants, merely alleviate symptoms while failing to halt disease progression, often causing side effects upon prolonged administration.[185] These limitations underscore the urgent need for targeted therapies capable of resolving localized inflammation without compromising systemic immunity, a challenge being addressed by emerging pancatalytic biomaterial strategies.

RA, a chronic autoimmune disorder affecting ≈0.5–1.0% of the global population, leads to debilitating joint inflammation, bone erosion, and progressive deformity, severely compromising patients' quality of life.[186,187] Its pathogenesis involves misguided immune attacks on synovial tissues, triggering a self-perpetuating cycle of oxidative stress and inflammatory cascades.[187] Excessive ROS not only damage bone and cartilage but also polarize macrophages toward pro-inflammatory M1 phenotypes, amplifying cytokine storms (*e.g.*, IL-6, TNF-α) that exacerbate the inflammatory cascades. Current clinical strategies, including NSAIDs, glucocorticoids, DMARDs like methotrexate, and biologics such as TNF-α/IL-6 inhibitors, face critical limitations. While these agents temporarily suppress inflammation, they often cause systemic toxicities (*e.g.*, gastrointestinal bleeding, osteoporosis) or exhibit inadequate therapeutic durability.[188,189] High costs and variable patient responses further restrict the accessibility and efficacy of advanced biologics. A central challenge lies in reconciling targeted immunomodulation with tissue regeneration, as conventional therapies fail to address both inflammatory dysregulation and structural joint repair.

The pancatalytic biomaterial platform, exemplified by calcium phosphate particles (CAPs) derived from hydrolyzed CSNs, offers a holistic solution by integrating catalytic and quasi-catalytic processes. In the preparation (P) phase, CSNs are engineered through liquid exfoliation of bulk $CaSi_2$, ensuring controlled hydrolysis kinetics (Fig. 6(a)-i and ii). Upon reaching inflamed joints, CSNs undergo activation (A) *via* hydrolysis, releasing hydrogen gas (H_2) to scavenge ROS, alkaline $Ca(OH)_2$ to inhibit osteoclast activity, and Ca^{2+}/SiO_2 precursors for CAP formation. The catalytic H_2 neutralizes oxidative stress while modulating macrophage polarization, breaking the ROS–inflammation feedback loop (Fig. 6(b)-i–iii). Simultaneously, localized alkalinity disrupts osteoclastic bone resorption, and endogenous Ca^{2+}/phosphate interactions drive the nontoxic treatment (N) phase by mineralizing CAPs, which promote osteogenic repair without exogenous toxicity (Fig. 6(c)). This tripartite pancatalytic strategy, synchronizing antioxidant, anti-inflammatory, and bone-remodeling actions, addresses RA's multifaceted pathology. By leveraging self-sustaining catalytic cascades and biocompatible byproducts, the system circumvents systemic side effects while achieving sustained therapeutic outcomes, embodying the pancatalysis principle of holistic disease management through material-catalyzed biological modulation.[25]

OA, a prevalent degenerative joint disorder affecting over 52 million adults in the U.S. alone, imposes significant socioeconomic burden due to its association with chronic pain, cartilage destruction, and progressive joint dysfunction.[190] While traditionally viewed as a cartilage-centric disease, OA is now recognized as a whole-joint pathology involving synovial inflammation, subchondral bone remodeling, and osteophyte

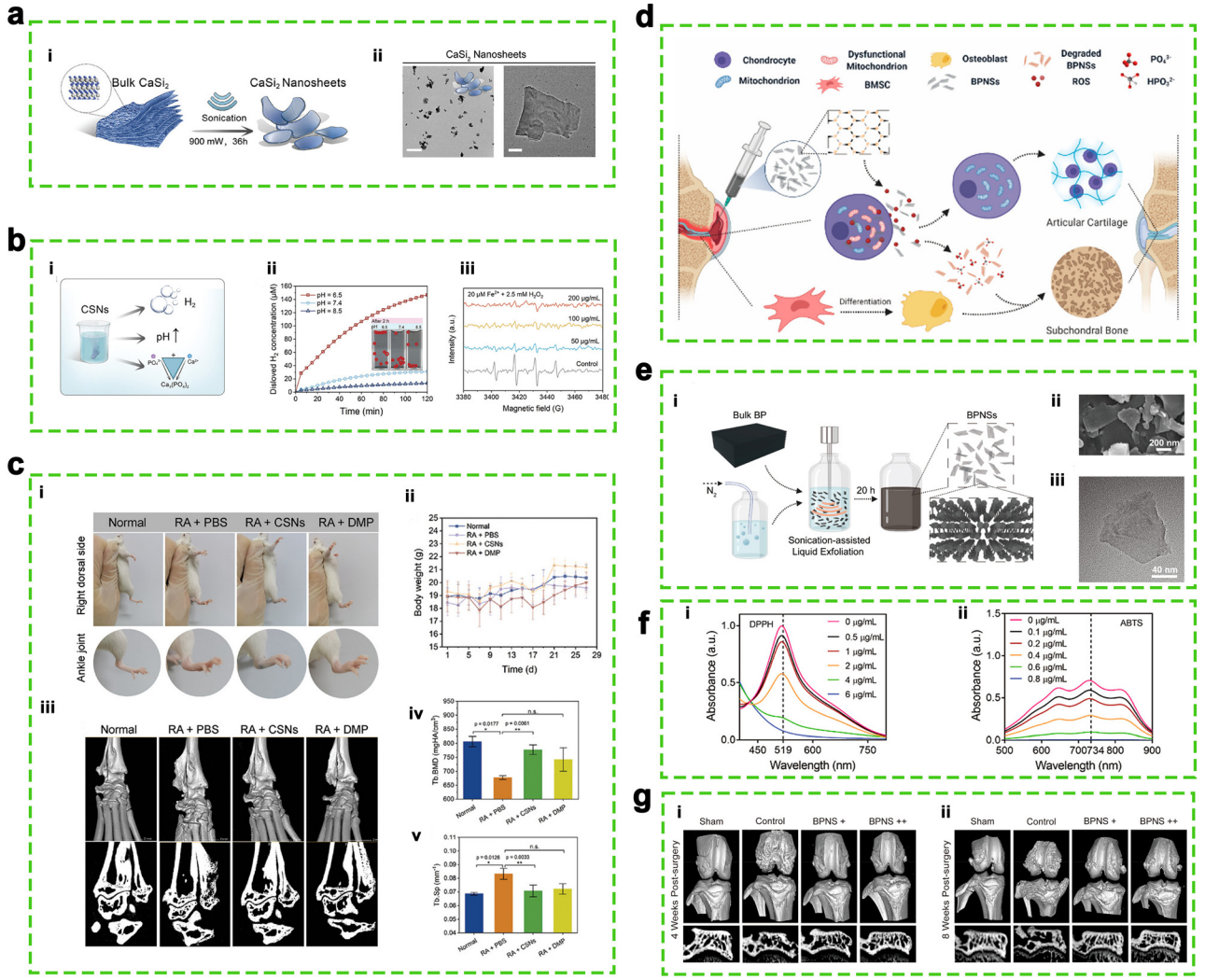

Fig. 6 Pancatalytic biomaterials for the treatment of joint system diseases. (a-i) Schematic representation of CSNs fabricated from bulk calcium disilicide (BCS) through ultrasonic-assisted exfoliation. (a-ii) TEM image of CSNs with uniform size. Scale bar: 500 nm. (b-i) Schematic representation of the reaction product from the hydrolysis of CSNs. (b-ii) Photograph and quantitative measurements of hydrogen gas produced by CSNs reacting with H_2O at different pH values. (b-iii) Electron spin resonance analysis of CSNs in the presence of Fe^{2+} (20 μm) and H_2O_2 (2.5 mm). (c-i) Representative photographs of the ankle joint of mice from different groups. (c-ii) body weight curves of mice subject to different treatments. Data are expressed as means ± SD (N = 5). (c-iii) Representative 3D-reconstructed micro-CT images of right ankle joints of mice from different groups on day 27. Histomorphometric micro-CT analysis of bone microstructure. (c-iv) Tb.BMD and (c-v) Tb.Sp for right ankle joints of mice from different groups on day 27. Data are expressed as means ± SD (N = 4). Reproduced with permission.[25] Copyright 2024 Wiley-VCH GmbH. (d) BPNSs for OA treatment *via* the P–A–N framework. (e-i) Synthesis of BPNSs through a modified sonication-assisted liquid exfoliation method. Representative (e-ii) SEM and (e-iii) TEM images of BPNSs. The scavenging activity of BPNSs toward three typical free radicals was monitored *via* UV-vis spectroscopy and quantitatively analyzed: (f-i) DPPH and (f-ii) ABTS. (g) Representative three-dimensional reconstruction images of differently treated rat knees at weeks 4 and 8 (upper row) and coronal micro-CT images of the rat medial tibial plateau in different groups (lower row). Reproduced with permission.[37] Copyright 2023 American Chemical Society.

formation.[191] Central to its progression is a self-amplifying cycle of oxidative stress and mitochondrial dysfunction in chondrocytes, where defective mitochondria generate excessive ROS that exacerbate cartilage degradation, ATP depletion, and apoptotic cascades.[192–194] Subchondral bone alterations further complicate OA pathogenesis, shifting from early-stage bone resorption to late-stage sclerosis, with evidence suggesting that restoring subchondral bone architecture could potentially reverse disease progression.[195–197] While non-surgical approaches like medication and physical therapy can alleviate pain and preserve joint function to improve quality of life, they remain limited to symptom control and fail to target core pathological processes such as cartilage degeneration and synovial inflammation. More importantly, current therapies cannot effectively halt disease progression or achieve tissue repair, and this fundamental limitation of "addressing symptoms without resolving the root cause" significantly hinders the overall efficacy of OA treatment.[198]

The pancatalytic biomaterial approach, exemplified by BPNSs, addresses OA's multifaceted pathology through integrated catalytic processes (Fig. 6(d)). In the preparation (P) phase, BPNSs are engineered *via* liquid-phase exfoliation of bulk black phosphorus, leveraging weak van der Waals

interactions to create atomically thin 2D structures with inherent biocompatibility (Fig. 6(e)). Upon reaching OA-affected joints, BPNSs undergo activation (A) through surface oxidation, where their unique electronic structure enables catalytic ROS scavenging *via* electron transfer reactions, neutralizing free radicals while suppressing pro-inflammatory macrophage polarization (Fig. 6(f)). This antioxidant activity disrupts the ROS-mitochondrial dysfunction cycle, preserving chondrocyte viability and cartilage homeostasis. Simultaneously, BPNSs' degradation products, primarily phosphorus oxides, initiate nontoxic treatment (N) by promoting subchondral bone regeneration through phosphate ion release, which stimulates osteogenic mineralization without exogenous toxicity (Fig. 6(g)). This dual-action mechanism concurrently targets oxidative stress in cartilage and bone remodeling in subchondral regions, embodying the pancatalysis principle of harmonizing catalytic bioactivity (ROS elimination) with quasi-catalytic biological processes (bone regeneration). By coupling material-driven catalytic ROS neutralization with physiologically guided tissue repair, BPNSs achieve holistic OA management that surpasses conventional symptom-focused therapies, demonstrating how pancatalytic systems can synchronize disease-modifying interventions across multiple pathological axes.[37]

3.6 Integumentary system

Skin inflammatory diseases affect a significant portion of the population, with estimates suggesting that 20–25% of the population are impacted by chronic, non-communicable forms.[199] Specific conditions show varying prevalence: atopic dermatitis (AD) affects up to 30% of children and 2–10% of adults, while psoriasis impacts 2–3% of the population.[200] Hidradenitis suppurativa ranges from 0.2 to 0.4% on average, with higher rates in certain demographics like 1.3% in African Americans.[199] These diseases significantly impair quality of life, with AD linked to sleep disturbances and mental health issues like depression and suicide risk, and psoriasis associated with cardiovascular comorbidities, reducing life expectancy by about 15 years in severe cases.[201]

AD represents a chronic inflammatory skin disorder marked by persistent pruritus, epidermal barrier dysfunction, and immune dysregulation, imposing substantial physical, psychological, and socioeconomic burden globally.[202–204] Predominantly emerging in early childhood but increasingly prevalent in adults, AD significantly compromises quality of life for patients and caregivers while elevating the risk of comorbidities such as allergic diseases, cardiovascular disorders, and mental health conditions.[205–209] Its pathogenesis involves multifaceted interactions among genetic predisposition, epidermal barrier impairment, immune hyperactivation (particularly Th2-driven inflammation), and oxidative stress.[210] Chronic inflammation in AD exacerbates ROS accumulation, which further disrupts barrier integrity, perpetuates pruritus through the itch–scratch cycle, and amplifies inflammatory cascades.[211] Despite current therapies targeting anti-inflammatory pathways, allergen avoidance, and phototherapy, limitations persist, including incomplete efficacy, systemic side effects, and the need for prolonged monitoring, especially in pediatric populations. These challenges underscore the demand for novel strategies that address the root mechanisms of AD, particularly oxidative-antioxidant imbalances and immune dysregulation.[212] In this context, pancatalytic biomaterials like the copper/zinc metal–organic framework (Cu/Zn-MOF) offer a holistic therapeutic approach by integrating catalytic preparation (P), activation (A) of the bio-effect, and nontoxic treatment (N). Cu/Zn-MOF mimics the dual-site synergistic action of natural antioxidant enzymes such as SOD and GPx, which are deficient in AD patients. By replicating the histidine-bridged Cu–Zn bimetallic coordination found in CuZn-SOD, this biomaterial scavenges ROS through catalytic dismutation of superoxide radicals, thereby restoring redox homeostasis (Fig. 7(a) and (b)). Furthermore, Cu/Zn-MOF suppresses Fcγ receptor-mediated phagocytic signaling, a pathway implicated in immune complex-driven inflammation, thereby mitigating chronic inflammatory responses in AD lesions (Fig. 7(c)). The pancatalytic strategy not only addresses oxidative stress but also modulates immune hyperactivity without relying on conventional immunosuppressants, aligning with the need for safer, multitarget therapies. By bridging catalytic material design with disease-specific mechanisms, this approach exemplifies the translation of biomimetic catalysis into clinical applications, offering a paradigm for managing complex inflammatory skin disorders through redox regulation and immune pathway modulation.[55]

Psoriasis is a chronic inflammatory skin disorder characterized by recurrent erythematous plaques, abnormal keratinocyte proliferation, and dysregulated immune responses, affecting approximately 3% of the global population.[213–216] Its high recurrence rate (approximately 90%) and association with systemic comorbidities, including CVDs and diabetes, impose substantial physical, psychological, and socioeconomic burden.[217] Pathologically, excessive ROS accumulation driven by oxidative-antioxidative imbalance amplifies inflammatory cytokine release, perpetuates keratinocyte hyperproliferation, and sustains chronic inflammation.[218–220] Current therapies, such as immunosuppressants and biologics, often fail to address root causes, leading to relapse post-treatment, increased infection risks, and potential carcinogenicity. These limitations highlight the urgent need for therapies that target oxidative stress and immune dysregulation without compromising long-term safety.[221–223] The pancatalytic approach using biomimetic iron single-atom catalysts (FeN_4O_2-SACs) offers a holistic strategy by integrating catalyst preparation (P), activation (A) of the bio-effect, and nontoxic treatment (N) of diseases. FeN_4O_2-SACs mimic the catalytic centers of multiple natural antioxidant enzymes, including SOD, CAT, and ascorbate peroxidase, through their atomically dispersed FeN_4O_2 coordination structure. This design enables broad-spectrum ROS scavenging *via* catalytic dismutation of $^{\bullet}O_2^-$ and H_2O_2, restoring redox homeostasis in psoriatic lesions (Fig. 7(d) and (e)). By suppressing ROS-driven inflammatory cascades and keratinocyte hyperproliferation, FeN_4O_2-SACs alleviate symptoms and reduce relapse rates, outperforming conventional treatments like calcipotriol (Fig. 7(f)). Mechanistically, FeN_4O_2-SACs upregulate estrogen receptor 1, a key protein downregulated in psoriasis, thereby

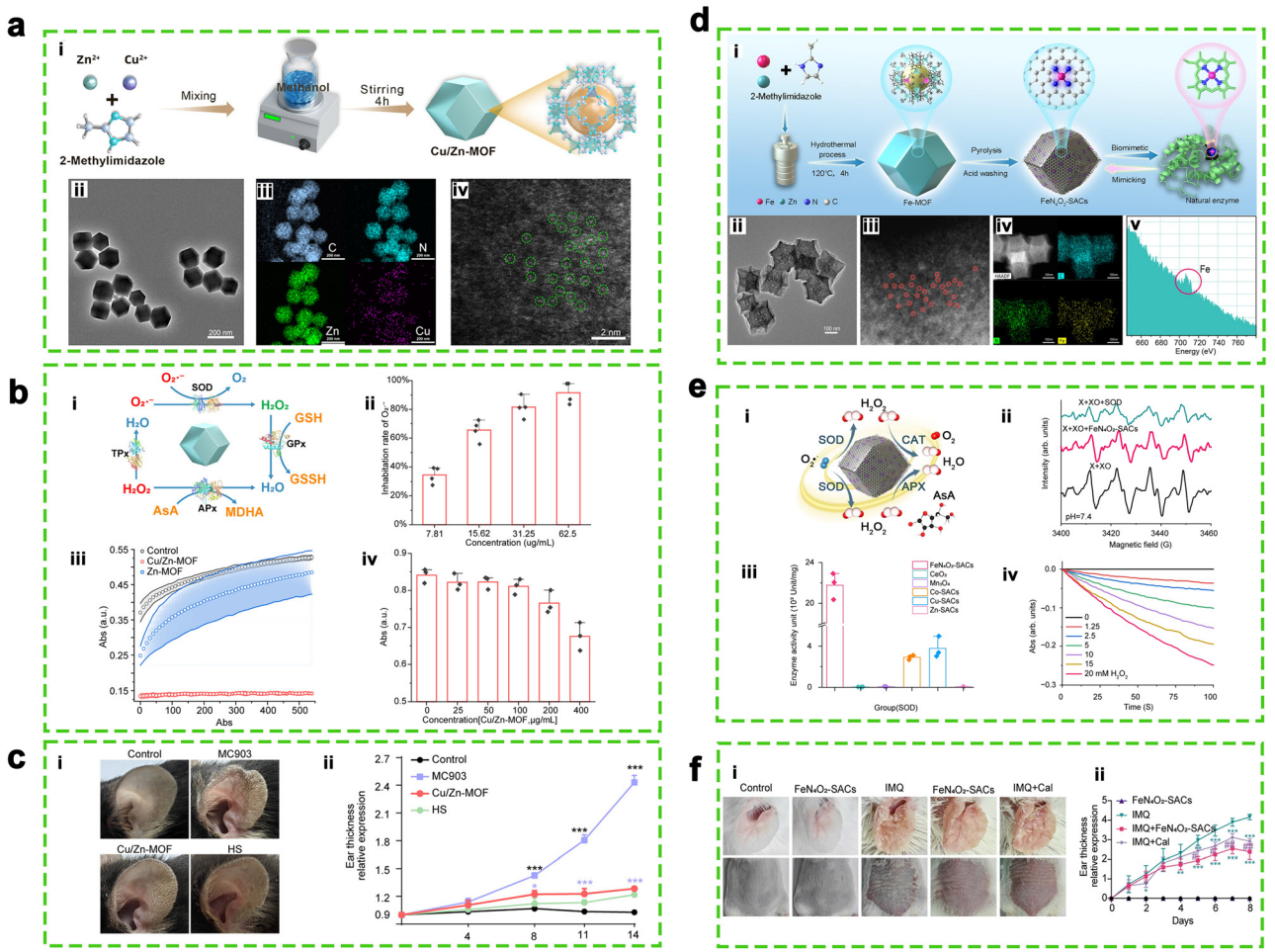

Fig. 7 Pancatalytic biomaterials for the treatment of integumentary system diseases. (a-i) Schematic illustration of Cu/Zn-MOF synthesis. (a-ii) TEM images of Cu/Zn-MOF. (a-iii) Element mapping displaying the distribution of C, N, Zn, and Cu. (a-iv) AC-HAADF-STEM image of Cu/Zn-MOF. (b-i) Schematic illustration of the ROS cascade clearance of Cu/Zn-MOF. (b-ii) SOD-like performance of Cu/Zn-MOF under various concentrations. (b-iii) GPx-like activity evaluation of Cu/Zn-MOF. (iv) TPx-like activity analysis by Cu/Zn-MOF concentration-dependent cysteine (0.2 mM) depletion in the presence of H_2O_2. (c-i) Images of skin lesions after 14-day induction (n = 4 samples/group). (c-ii) Quantification of ear thickness. Reproduced with permission.[55] Copyright 2024 American Chemical Society. (d-i) Synthetic process of biomimetic FeN_4O_2-SACs. (d-ii) TEM image of FeN_4O_2-SACs. (d-iii) AC HAADF-STEM image of FeN_4O_2-SACs, with single iron atoms marked using red circles. n = 3 samples with similar results. (d-iv) HAADF-STEM image and the corresponding EDX mappings of FeN_4O_2-SACs: C, blue; N, green; Fe, yellow. (d-v) EELS atomic spectrum of Fe elements in FeN_4O_2-SACs. The element-specific absorption edge is highlighted by a red circle. (e-i) Schematic illustration of ROS clearance by FeN_4O_2-SACs. (e-ii) ESR spectra of FeN_4O_2-SACs and natural SOD for $O_2^{\bullet-}$ clearance at pH = 7.4 (X: xanthine; XO: xanthine oxidase). (e-iii) Comparison of SOD-like activities between FeN_4O_2-SACs and control materials CeO_2, Mn_3O_4, Co-SACs, Cu-SACs and Zn-SACs by WST-8 colorimetric analysis. (e-iv) CAT-like assay for eliminating varied concentrations of H_2O_2 using 125 μg ml^{-1} FeN_4O_2-SACs by UV absorption tests. (f-i) Representative images of lesions on day 8, n = 4 samples per group. (f-ii) Quantification of ear thickness. Reproduced with permission.[56] Copyright 2023, Springer Nature.

modulating inflammatory pathways and enhancing therapeutic durability. The pancatalytic framework not only addresses oxidative stress through enzyme-like catalysis but also ensures biocompatibility and sustained efficacy, exemplifying a multi-target, non-immunosuppressive strategy for managing psoriasis. This biomimetic approach bridges atomic-level catalyst design with disease-specific mechanisms, advancing catalytic therapy as a paradigm for inflammatory skin disorders.[56]

3.7 Sensory systems

The sensory system serves as the body's primary network for environmental perception, integrating organs such as the eyes, ears, nose, tongue, and skin to mediate vision, hearing, smell, taste, and tactile functions.[224] Ocular and auditory systems are particularly critical for information processing and quality of life; inflammatory disorders in these systems, including conjunctivitis (conjunctival inflammation), keratitis (corneal inflammation), uveitis (uveal tract inflammation), and dry eye syndrome, often induce symptoms such as chronic irritation, photophobia, and progressive vision deterioration.[225] In the auditory domain, SNHL, frequently associated with labyrinthitis (inner ear inflammation), manifests as sudden hearing impairment, tinnitus, and balance disturbances.[226] Beyond direct sensory dysfunction, these conditions exert profound

systemic impacts: visual deficits may restrict social engagement and exacerbate psychological distress, while auditory impairments amplify communication barriers, fostering social isolation and depression.[227] Chronic inflammation in untreated cases precipitates irreversible complications, including corneal scarring, secondary glaucoma, and persistent vestibular dysfunction, severely compromising occupational productivity and functional independence.[228] Therapeutic strategies emphasize early intervention with anti-inflammatory agents or surgical approaches to mitigate long-term sequelae, highlighting the urgency of targeted therapies to address sensory system inflammations in clinical practice.

SNHL, a major global public health issue, severely compromises social communication and imposes significant socioeconomic burden due to irreversible hair cell (HC) loss and spiral ganglion neuron damage caused by factors such as noise exposure, genetic mutations, aging, and ototoxic drugs like cisplatin.[229–231] Cisplatin-induced ototoxicity is characterized by progressive and irreversible hearing impairment, primarily driven by oxidative stress-triggered inflammatory cascades and metabolic disturbances, while current clinical interventions (*e.g.*, hearing aids or cochlear implants) are limited by invasiveness, high costs, and inability to repair cellular damage.[232–234] To address these challenges, the Zr-MOF-Mn composite, guided by the pancatalysis strategy (P–A–N), offers a synergistic therapeutic approach Fig. 8(a). The Zr-MOF-framework, engineered with tunable mesopores, serves as a carrier to integrate Mn-TCPP (a superoxide dismutase-mimetic enzyme) and *N*-acetyl-L-cysteine-derived carbonized polymer dots (NAC CPDs), leveraging its high surface area and biocompatibility for efficient enzyme delivery. Mn-TCPP scavenges ROS *via* Mn^{3+}/Mn^{4+} redox cycling, while NAC CPDs enhance chemical stability and prolong antioxidant efficacy. Upon crossing the round window membrane into the cochlea, the composite targets HC mitochondria to eliminate ROS, thereby suppressing pathological HIF-1α accumulation, reversing glycolysis-dominated metabolic reprogramming, and restoring oxidative phosphorylation. Simultaneously, it inhibits BAX-mediated mitochondrial outer membrane permeabilization and mtDNA leakage, blocking caspase-dependent apoptosis and NLRP3 inflammasome activation. To ensure sustained therapeutic action and minimize systemic toxicity, PDA-coated GelMA hydrogel microcapsules

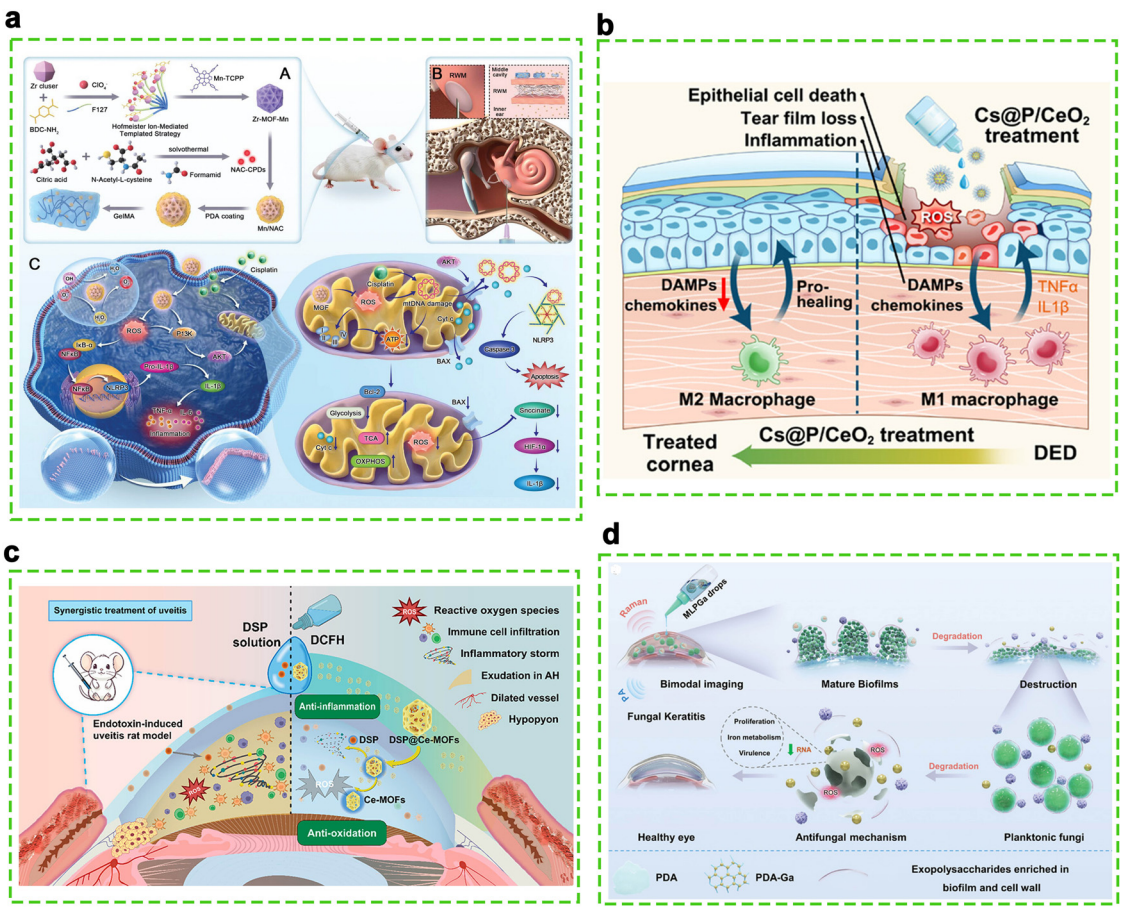

Fig. 8 Pancatalytic biomaterials for the treatment of sensory system diseases. (a) Treatment of SHLH based on Zr-MOF-Mn composite materials *via* the P–A–N framework. Reproduced with permission.[57] Copyright 2024 Wiley-VCH GmbH. (b) Cs@P/CeO_2 for DED treatment *via* the P–A–N framework. Reproduced with permission.[45] Copyright 2024 American Chemical Society. (c) DCFH system for uveitis treatment *via* the P–A–N framework. Reproduced with permission.[58] Copyright 2023 American Chemical Society. (d) MLPGa nanosystem for fungal keratitis treatment *via* the P–A–N framework. Reproduced with permission.[59] Copyright 2022 Wiley-VCH GmbH.

are employed, which enable controlled drug release, extending local antioxidant effects within the cochlea. This pancatalysis-driven system achieves mitochondrial homeostasis restoration and immune microenvironment modulation, providing a multifunctional ''ROS scavenging–apoptosis inhibition–anti-inflammation'' paradigm that overcomes the limitations of conventional therapies for cisplatin-induced SNHL.[57]

Dry eye disease (DED), a prevalent global ocular surface disorder affecting approximately one-third of the population, manifests as chronic ocular discomfort, visual impairment, and diminished quality of life due to tear film instability, sustained inflammation, and corneal microenvironment imbalance.[235,236] Its pathogenesis involves complex interactions among intrinsic and extrinsic factors, including oxidative stress–inflammation vicious cycles, where excessive ROS amplify inflammatory signaling, exacerbating epithelial damage and immune dysregulation.[237–240] Conventional therapies, such as artificial tears and immunosuppressants (*e.g.*, cyclosporine A), provide only transient symptom relief and face limitations like low bioavailability, local irritation, and an inability to simultaneously target oxidative stress and inflammatory pathways.[241] Addressing these challenges, the Cs@P/CeO_2 composite, guided by the pancatalysis strategy (P–A–N), offers a synergistic therapeutic approach (Fig. 8(b)). The CeO_2 nanozyme core, engineered with oxygen vacancies enabling Ce^{3+}/Ce^{4+} redox cycling, provides self-regenerative antioxidative capacity. PEG surface modification enhances biocompatibility and hydrophilicity, while cyclosporine A (CsA) loading integrates immunomodulatory functionality. Upon ocular administration, Cs@P/CeO_2 penetrates the ocular surface to scavenge ROS, disrupt the oxidative stress–inflammation cascade, and suppress T-cell-mediated hyperimmunity. Single-cell sequencing reveals its capacity to reprogram the corneal microenvironment by polarizing macrophages from pro-inflammatory (M1) to pro-repair (M2) phenotypes, promoting epithelial regeneration, and fine-tuning immune–epithelial crosstalk for tissue homeostasis. The PEG shell minimizes systemic toxicity and extends corneal retention, enabling sustained drug release, while the self-renewing antioxidative activity of nanoceria ensures long-term efficacy. By holistically integrating catalytic ROS scavenging, immunomodulation, and biocompatible delivery, Cs@P/CeO_2 exemplifies the pancatalysis-driven paradigm, overcoming the limitations of single-target therapies and offering a ''ROS elimination–inhibition of inflammation–tissue repair'' strategy for DED and related oxidative stress–inflammatory disorders.[45]

Uveitis, a spectrum of immune-mediated ocular disorders affecting the uveal tract and adjacent tissues, manifests as ocular pain, redness, photophobia, and vision-threatening complications, contributing to 10–20% of blindness cases in the United States due to recurrent inflammation and secondary damage.[242,243] Its pathogenesis involves dysregulated immune responses intertwined with oxidative stress, where excessive ROS and NO overproduction disrupt the blood–aqueous barrier, induce lipid peroxidation in iris epithelial cells and photoreceptor mitochondria, and amplify inflammatory cascades.[244–246] Current first-line therapies, such as corticosteroids (*e.g.*, dexamethasone sodium phosphate, DSP), face limitations including incomplete efficacy (*e.g.*, 25% non-response rate in clinical trials) and adverse effects like intraocular pressure elevation.[247,248] Moreover, conventional drug delivery routes, noninvasive eye drops with low bioavailability or invasive methods risking infection, fail to ensure sustained therapeutic concentrations. To address these challenges, the DSP@Ce-MOFs F127 hydrogel (DCFH) system, guided by the pancatalysis strategy (P–A–N), integrates multifunctional biomaterials for synergistic therapy (Fig. 8(c)). Preparation (P): cerium-based metal–organic frameworks (Ce-MOFs) are engineered as porous carriers with dual functionality, ROS scavenging *via* Ce^{3+}/Ce^{4+} redox cycling and high-capacity DSP loading due to their large surface area. Activation (A): Ce-MOFs demonstrate dual functionality through their ROS-scavenging capacity and porous structure that enables efficient DSP loading/release, while the F127 hydrogel enhances ocular retention and sustained drug delivery. Nontoxic treatment (N): the DCFH system achieves therapeutic efficacy by synergistically reducing oxidative stress and inflammation, while its ocular biocompatibility ensures safe application without adverse effects.[58]

Fungal keratitis, a leading cause of corneal blindness in developing countries, is characterized by severe infections (*e.g.*, *Candida albicans*) that induce corneal opacity, pain, hypopyon, and irreversible vision loss.[249,250] Its pathogenesis involves fungal biofilm formation and exopolysaccharide-rich extracellular matrix (ECM), particularly β-1,3-glucan, which act as permeation barriers to shield pathogens from antifungal agents.[251,252] Biofilms exhibit innate resistance, requiring drug concentrations up to 1000-fold higher than those effective against planktonic fungi, rendering conventional topical antifungals (*e.g.*, azoles) inadequate due to poor penetration and limited efficacy. Furthermore, the biofilm-associated ECM promotes fungal adherence and immune evasion, exacerbating treatment challenges.[253,254] Current therapies fail to address both biofilm disruption and metabolic interference, highlighting the need for multifunctional strategies that degrade exopolysaccharides while enhancing antifungal potency. Guided by the pancatalysis framework (P–A–N), the lyticase and gallium ions co-integrated nanosystem (MLPGa) integrates catalytic degradation of fungal barriers and metal-ion-mediated antifungal activity (Fig. 8(d)). Preparation (P): the system employs PDA-modified mesoporous silica nanoparticles as carriers, co-loading lyticase (a β-1,3-glucanase) and gallium ions (Ga^{3+}). Lyticase enzymatically degrades β-1,3-glucan in fungal cell walls and biofilms, while Ga^{3+} mimics iron to disrupt fungal metabolic pathways. Activation (A): upon application, lyticase catalytically hydrolyzes exopolysaccharides, dismantling biofilm integrity and exposing embedded fungi. Concurrently, Ga^{3+} penetrates the compromised fungal cells, acting as a ''Trojan horse'' to interfere with iron-dependent enzymes, induce metabolic dysfunction, and generate cytotoxic ROS. This dual action synergistically eliminates both planktonic fungi and resilient biofilms. Nontoxic treatment (N): the PDA coating enhances biocompatibility and enables real-time Raman monitoring of Ga^{3+} release, ensuring controlled ion delivery to minimize off-target toxicity. By combining enzymatic biofilm

disruption, Ga^{3+}-mediated metabolic interference, and biocompatible monitoring, MLPGa exemplifies a pancatalysis approach, holistically addressing fungal resistance mechanisms while prioritizing safety. This strategy overcomes the limitations of single-target antifungals, offering a ''barrier degradation–metabolic disruption–toxicity mitigation'' paradigm for fungal keratitis and other biofilm-associated infections.[59]

3.8 Urinary system

The urinary system is highly susceptible to a variety of IDs, including acute kidney injury (AKI) and urinary tract infections (UTIs).[255,256] These conditions are not only among the most prevalent and recurrent clinical problems, but they also carry a profound risk of progressing to chronic kidney disease, organ dysfunction, or severe systemic complications. The complexity of these diseases lies in their multifactorial pathogenesis, including ischemic and oxidative insults or persistent bacterial colonization and inflammation.[257] The high morbidity and mortality associated with these diseases, together with their tendency to cause chronic disability, underscore the urgency of developing more effective and targeted therapeutic strategies.

For AKI, which is characterized by a sudden decline in renal function and a high risk of progression to chronic kidney disease, the major pathophysiological trigger is renal ischemia/reperfusion injury, leading to excessive generation of ROS and mitochondrial dysfunction in renal proximal tubule cells.[258,259] Despite the protective role of irisin, a myokine that promotes mitochondrial biogenesis and oxidative metabolism, its clinical application is severely limited by instability in circulation, short half-life, and poor kidney targeting.[260] The $Pt_{5.65}S$ pre-nanozyme demonstrates pancatalytic biomaterial properties for AKI treatment by implementing the P–A–N framework through its unique design and multimodal therapeutic actions (Fig. 9(a)). Engineered *via* Ptzyme–Na_2S reaction during the preparation phase, this ultra-small nanoparticle remains catalytically inert under normal physiological conditions. The activation mechanism involves two distinct but complementary therapeutic pathways (Fig. 9(b)-i and ii). First, the system releases H_2S gas which mediates critical biological effects through sulfation of NF-κB/Ικκβ, effectively suppressing inflammatory signaling cascades while concurrently enhancing Nrf2-mediated antioxidant pathways. Second, the nanoparticle exhibits pH-triggered broad-spectrum ROS/RNS scavenging capacity by demonstrating both SOD-like and CAT-like enzymatic activities specifically in the acidic/inflammatory AKI microenvironment (Fig. 9(b)-iii). The system ensures nontoxic treatment through renal-clearable dimensions and conditional activation that prevents off-target effects, while combining exogenous nanozyme catalysis with endogenous H_2S signaling for synergistic oxidative stress and inflammation regulation (Fig. 9(c)).[60] This integrated approach exemplifies pancatalysis by simultaneously addressing multiple pathological factors (oxidative stress, inflammation, and cellular damage) through coordinated material design, microenvironment-responsive activation, and biosafety features tailored for AKI management.

Similarly, UTIs represent one of the most prevalent bacterial infections worldwide, frequently caused by uropathogenic *Escherichia coli* (UPEC) *via* FimH-mediated adhesion to urinary tract epithelial cells.[261] The persistent colonization by UPEC and subsequent inflammatory response result in substantial tissue injury and high recurrence rates. While anti-adhesive glycomimetic agents have been developed to mimic the innate defense mechanism of uromodulin, they often fail to address the accompanying inflammation and oxidative stress, and the excessive use of antibiotics exacerbates inflammation and promotes resistance.[262] To overcome these challenges, a bioinspired dextran-modified ceria nanozyme (DEC) has been constructed, offering integrated anti-adhesive and anti-inflammatory properties under the P–A–N framework (Fig. 9(d)). In the preparation phase, ultrasmall ceria nanoparticles are modified with Food and Drug Administration (FDA)-approved dextran, which provides multivalent binding sites mimicking uromodulin glycans for efficient FimH targeting and bacterial capture (Fig. 9(e)-i). In the activation phase, DEC exhibits dual-functionality at the infected site: dextran inhibits UPEC adhesion and colonization, while the ceria core acts as an antioxidant nanozyme, scavenging ROS and suppressing local inflammation triggered by bacterial toxins such as lipopolysaccharides (Fig. 9(e)-i and ii). Finally, in the nontoxic treatment phase, both components of DEC demonstrate high biocompatibility and are safely metabolized, avoiding the drawbacks of antibiotics such as resistance development and secondary inflammatory injury (Fig. 9(f)). This integrated, staged strategy significantly enhances therapeutic efficacy and biosafety in UTI management. Together, these advances in pancatalytic biomaterials employing a preparation–activation–nontoxic treatment paradigm offer a promising and versatile platform for the precise and safe treatment of IDs of the urinary system.[61]

3.9 Reproductive system

Candida vaginitis, a prevalent gynecological inflammatory disorder caused by *Candida albicans* infection,[263] affects approximately 75% of women globally during their lifetime, with 5–8% developing recurrent infections.[264] This condition is characterized by vaginal dysbiosis, local inflammatory responses with epithelial cell damage, and high recurrence rates due to limitations of conventional therapies.[265] Current antifungal agents such as clotrimazole and fluconazole demonstrate significant shortcomings including fungistatic rather than fungicidal activity, disruption of normal vaginal microbiota, mucosal damage, and pH imbalance exacerbating recurrence risks.[265–267] The FeLab system (rGO@FeS_2/Lactobacillus@HA hydrogel) exemplifies an innovative pancatalytic therapeutic strategy based on the P–A–N framework (Fig. 10(a)). In the preparation phase, the system co-encapsulates peroxidase-mimetic rGO@FeS_2 nanozymes with probiotic Lactobacillus within a hyaluronic acid hydrogel matrix, enabling pathogen-responsive release through hyaluronidase degradation (Fig. 10(b)-i). During activation, the system simultaneously achieves physiological vaginal pH restoration (4–4.5) through probiotic lactic acid production and targeted pathogen elimination *via* nanozyme-catalyzed conversion of

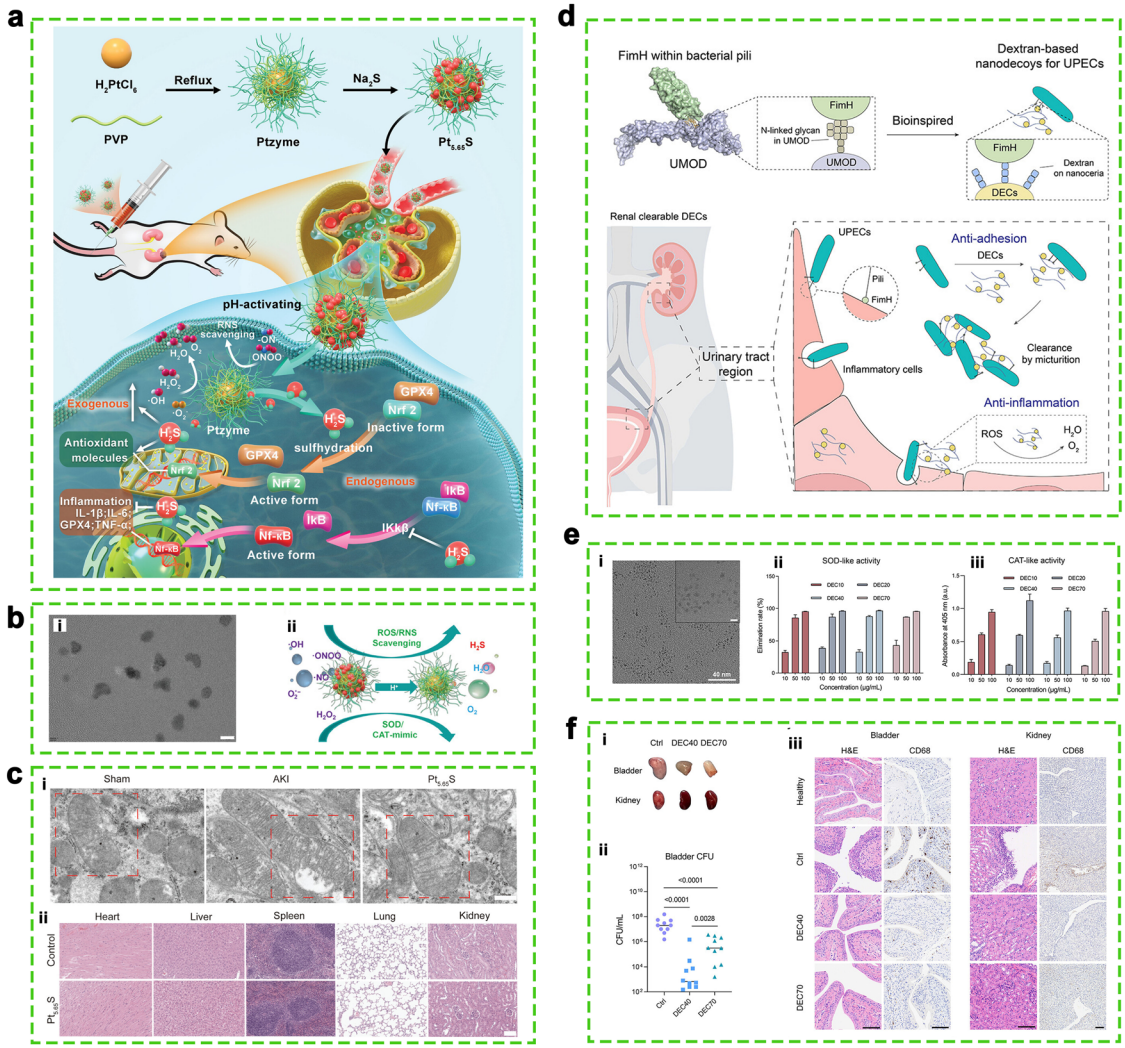

Fig. 9 Pancatalytic biomaterials for the treatment of urinary system diseases. (a) $Pt_{5.65}S$ pre-nanozyme for AKI *via* the P–A–N framework. (b-i) TEM image of the $Pt_{5.65}S$ pre-nanozyme (scale bar = 5 nm). (b-ii) Schematic illustration of $Pt_{5.65}S$ pre-nanozyme pH active antioxidative activities and release of H_2S. (c-i) TEM images of mitochondria in the kidney from each group. The red box in the figure depicts representative TEM images showing the morphology of mitochondria under different conditions. Scale bar = 500 μm. (c-ii) HE staining of the heart, liver, spleen, lung, and kidney. Scale bar = 100 μm. Reproduced with permission.[60] Copyright 2024 Advanced Science published by Wiley-VCH GmbH. (d) DEC for UTIs *via* the P–A–N framework. (e-i) TEM images of DEX-CeO_2. (e-ii) SOD-like activities of DECs. (e-iii) CAT-like activities of DECs. (f) In the repeated UTI model, representative images of bladders and kidneys with/without treatment are shown in (i), and (ii) total bladder and (iii) kidney bacterial counts were determined after homogenization. Reproduced with permission.[61] Copyright 2024 American Chemical Society.

bacterial-derived H_2O_2 into hydroxyl radicals (Fig. 10(b)-ii and iii). During the nontoxic treatment phase, the system effectively eradicates *C. albicans* while preserving beneficial flora, achieves localized therapeutic action that protects mucosal cells, and through probiotic colonization reestablishes a healthy microbiota, thereby significantly reducing recurrence rates (Fig. 10(c)).[62] This integrated system demonstrates synergistic catalytic antimicrobial activity and ecological modulation, offering an effective and safe precision therapy that establishes a new paradigm for treating reproductive system inflammatory diseases.

Chronic prostatitis represents a significant global health concern, accounting for over 90% of prostatitis cases with a prevalence of 8.2% worldwide.[268] This condition is characterized by persistent inflammatory reactions in the prostate gland, leading to elevated expression of pro-inflammatory cytokines such as IL-1β and TNF-α.[269] A key pathological feature is the excessive generation of reactive RO/NSs, including hydroxyl radicals $^{\bullet}OH$, $^{\bullet}O_2^-$, H_2O_2, $NO^{\bullet}$, and $ONOO^-$, which disrupt redox homeostasis and induce oxidative stress.[270] These pathological changes not only contribute to typical clinical symptoms but also lead to mitochondrial dysfunction and tissue damage. Of particular concern is the established link between chronic prostatitis and more severe complications – long-term oxidative stress and inflammation promote epigenetic alterations that increase the risk of developing prostatic intraepithelial neoplasia and prostate cancer (PCa), the second most common cancer in men globally.[271] Additionally, chronic prostatitis significantly impacts male

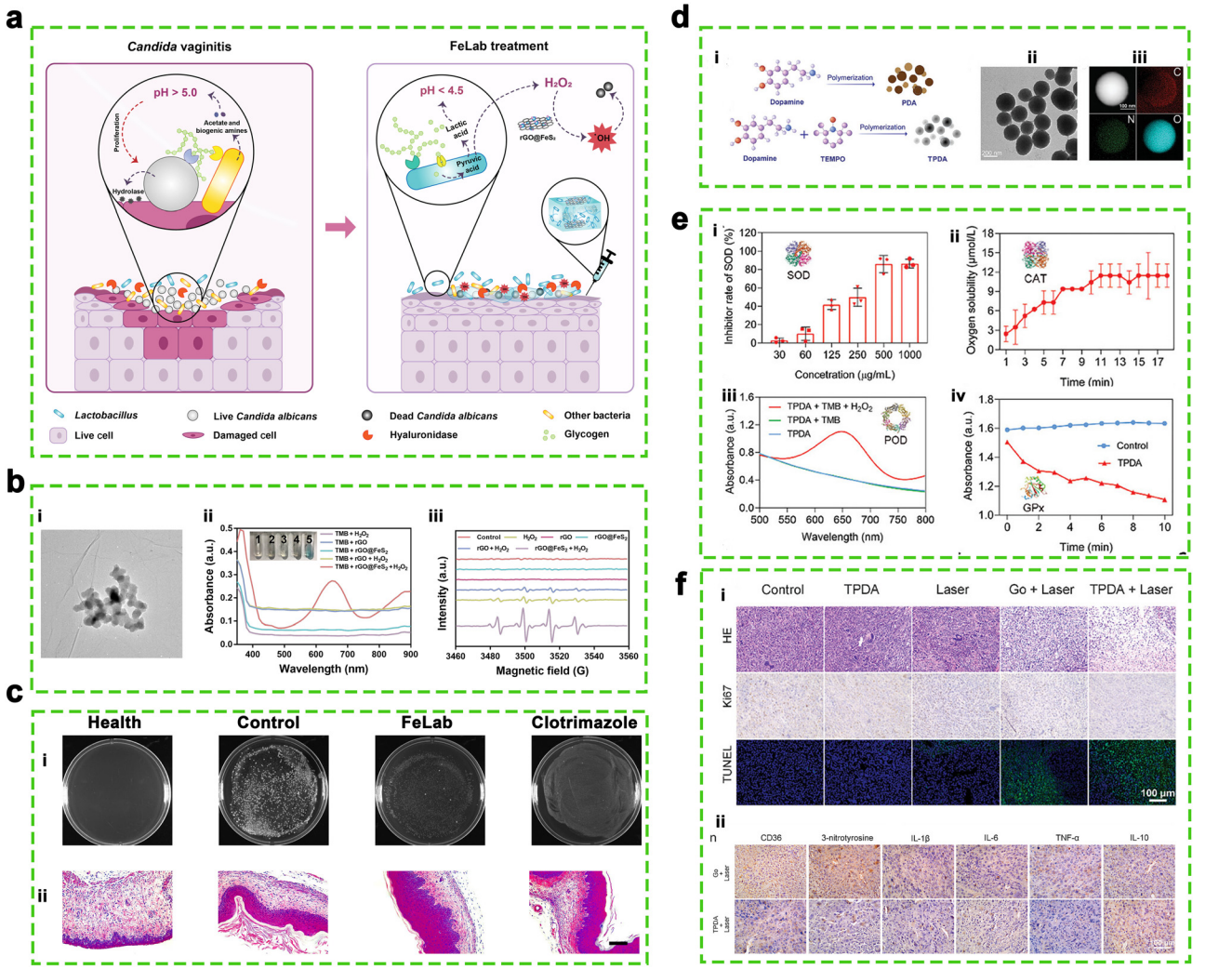

Fig. 10 Pancatalytic biomaterials for the treatment of reproductive system diseases. (a) rGO@FeS_2 for candida vaginitis *via* the P–A–N framework. (b-i) TEM images of rGO@FeS_2. (b-ii) Ultraviolet-visible absorption spectra and the corresponding color changes of TMB in different reaction systems. (b-iii) EPR monitoring the generation of $^{\bullet}OH$ by rGO@FeS_2 in the presence of H_2O_2 in a pH 4.5 HAc–NaAc buffer after 5 min of incubation. (c-i) Digital images of *C. albicans* colonies in the vaginal washes in different groups. (c-ii) H&E-staining images of the vaginal tissue in different groups. (d-i) Schematic illustration of TPDA NP and PDA NP preparation. Reproduced with permission.[62] Copyright 2023, The American Association for the Advancement of Science. (d-ii) TEM image of TPDA NPs. (d-iii) Scanning transmission electron microscopy images with EDS mapping of C, N, and O elemental signals of TPDA NPs. (e-i) SOD-like activity of TPDA NPs. (e-ii) CAT-like ability of TPDA NPs. (e-iii) POD-like ability of TPDA NPs. (e-iv) GPx-like ability of TPDA NPs. (f-i) H&E, Ki-67, and TUNEL staining results of the tumors from different groups. (f-ii) The IHC results of CD36, 3-nitrotyrosine, IL-1β, IL-6, TNF-α, and IL-10 expression in the tumors from the two groups of GO NSs under 808 nm laser irradiation and TPDA NPs under 808 nm laser irradiation. Reproduced with permission.[63] Copyright 2024 Wiley-VCH GmbH.

reproductive health, often causing sexual dysfunction and fertility issues.[272]

Current clinical management of chronic prostatitis encounters multiple challenges, with conventional anti-inflammatory therapies often inducing undesirable systemic side effects and immune modulators potentially provoking unpredictable or excessive immune responses. Moreover, existing treatments fail to adequately address the root cause of oxidative stress or provide comprehensive protection against cancer development. The clinical challenge is further compounded by the need for therapies that can simultaneously manage inflammation, prevent malignant transformation, and preserve reproductive function without causing adverse effects. These unmet medical needs highlight the urgent requirement for innovative treatment strategies that can target multiple pathological pathways in prostate diseases while maintaining an acceptable safety profile. Their therapeutic action follows a P–A–N framework where during preparation, donor–acceptor pairs are constructed to optimize catalytic and photothermal properties (Fig. 10(d)). The activation phase involves catalytic elimination of RO/NSs to restore redox balance coupled with downregulation of CD36 expression to inhibit NF-κB signaling, thereby alleviating inflammation and improving sexual function in experimental autoimmune prostatitis models (Fig. 10(e)). For

nontoxic treatment, the system leverages the inherent biocompatibility of polydopamine and 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) derivatives while enabling photothermal ablation of cancerous lesions (Fig. 10(f)).[63] This integrated approach simultaneously addresses prostatitis symptoms, prevents malignant transformation, and preserves reproductive function, representing a significant advancement over conventional monotherapeutic strategies. The unique combination of catalytic ROS scavenging and photothermal capabilities positions tetramethylpiperidine-1-oxyl doped polydopamine nanoparticles (TPDA NPs) as a promising therapeutic platform for comprehensive prostate disease management.

3.10 Others

Photothermal therapy (PTT) has emerged as a promising tumor treatment modality due to its precise spatiotemporal control and low invasiveness.[273] However, the therapeutic efficacy of PTT is significantly compromised by its inherent inflammatory side effects.[274] During treatment, localized hyperthermia induces substantial heat stress that triggers a cascade of detrimental biological responses.[275] This includes rapid overproduction of ROS, necrotic cell death, and subsequent activation of immune cells. The resulting inflammatory cascade leads to excessive secretion of proinflammatory cytokines (TNF-α, IL-6, IL-1β) and formation of neutrophil extracellular traps, creating an immunosuppressive microenvironment that paradoxically promotes tumor recurrence and metastasis.[276] Current PTT approaches face critical limitations in addressing these issues, as they typically focus solely on thermal ablation while neglecting the consequential inflammatory responses, or employ passive anti-inflammatory strategies that only act after inflammatory cascades are already established. To address these

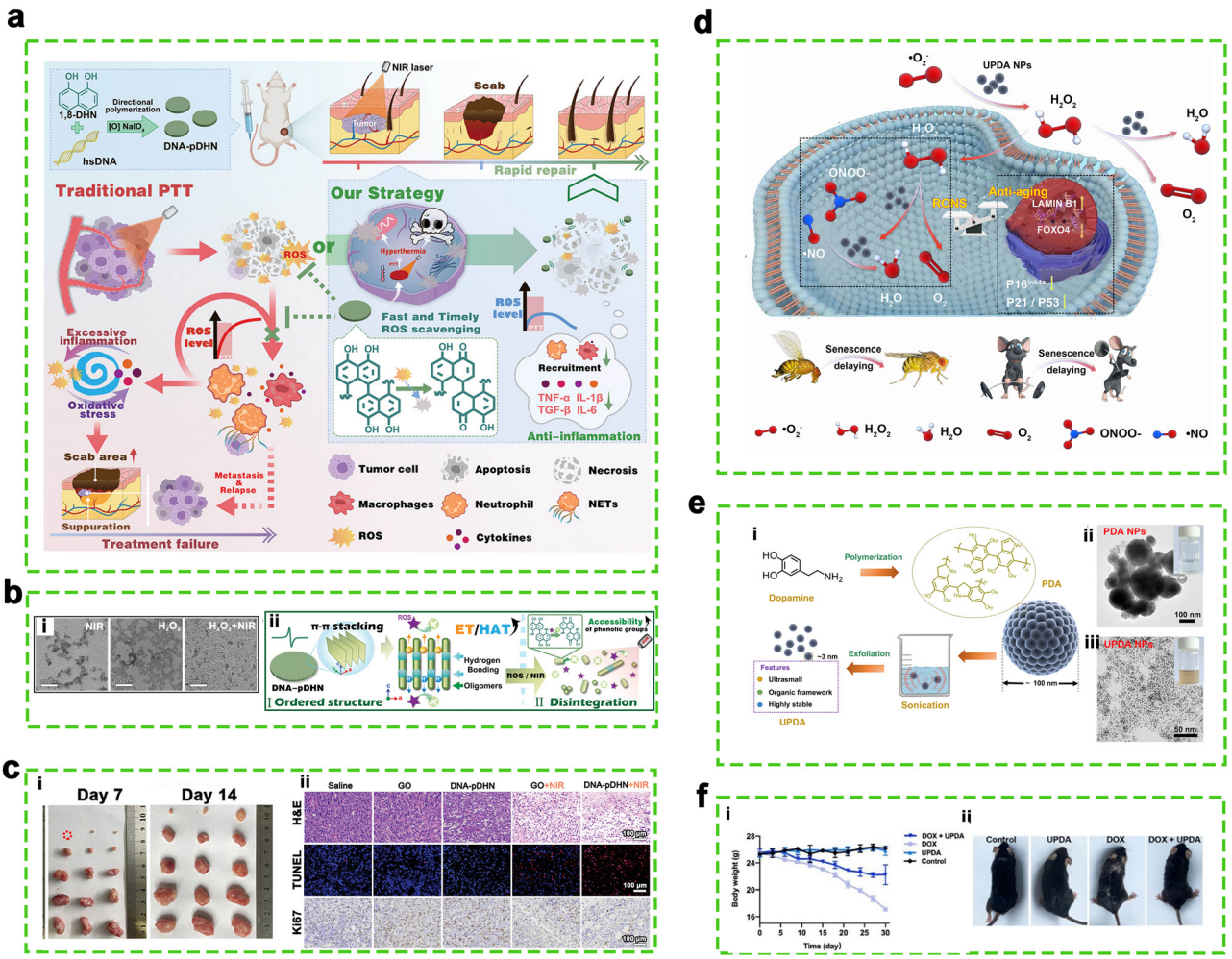

Fig. 11 Pancatalytic biomaterials for the treatment of other diseases. (a) DNA-pDHN nanodisks for tumor *via* the P–A–N framework. (b-i) AFM and TEM images of DNA-pDHN. (b-ii) TEM images of DNA-pDHN nanodisks after different treatments. (c-i) Photograph of the tumors collected from different groups of mice after treatment. (c-ii) H&E, Ki67, and TUNEL staining of tumor tissues on day 14. Reproduced with permission.[64] Copyright 2023 Wiley-VCH GmbH. (d) UPDA NPs for tumor *via* the P–A–N framework. (e-i) The step-by-step production and key physical features of UPDA NPs. (e-ii) A representative TEM image of PDA NPs. The inset is a representative photograph of PDA NPs dispersed in deionized water. (e-iii) A representative TEM image of UPDA NPs. (f-i) Weight changes of mice after different treatments. (f-ii) Representative fur appearances of mice receiving different treatments. Reproduced with permission.[65] Copyright Published by Elsevier Ltd.

challenges, DNA-guided allomelanin nanodisks (DNA-pDHN) were developed as innovative pancatalytic biomaterials. The system operates through a preparation–activation–nontoxic treatment (P–A–N) framework (Fig. 11(a)). In the preparation phase, DHN oligomers are precisely organized into optimized nanostructures (Fig. 11(b)-i). During activation, the nanodisks demonstrate dual photothermal conversion and ROS scavenging capabilities (Fig. 11(b)-ii). This leads to nontoxic treatment outcomes including inflammation control and tumor suppression (Fig. 11(c)). The DNA-pDHN system represents a significant advance in PTT by simultaneously addressing both tumor ablation and inflammatory consequences through integrated catalytic mechanisms.[64]

The aging process is marked by a state of persistent, low-grade systemic inflammation, which occurs alongside cellular senescence, decline in immune function (immunosenescence), impaired organ performance, and the onset of age-associated pathologies.[277,278] Senescent cells release a complex mixture of signaling molecules, collectively termed the senescence-associated secretory phenotype (SASP), which includes cytokines, chemokines, and growth factors. These SASP components not only sustain chronic inflammatory conditions but also propagate senescence to neighboring healthy cells through paracrine signaling.[279] Concurrently, prolonged inflammation accelerates the aging of immune cells, diminishing their functional capacity and impairing their ability to eliminate senescent cells and inflammatory mediators. This establishes a self-perpetuating cycle in which inflammation drives senescence, and senescence, in turn, exacerbates inflammation. Persistently high levels of inflammatory mediators in critical organs, such as the bone marrow, liver, and lungs, contribute to progressive tissue damage and the development of age-related disorders. Given these observations, chronic inflammation is now regarded as an intrinsic contributor to the aging process, and targeting inflammatory pathways may represent a viable therapeutic approach for mitigating age-related decline.[280] Recent studies demonstrate that oxidative stress serves as a key molecular link between inflammation and senescence, creating a vicious cycle that accelerates aging. Ultra-small polydopamine nanoparticles (UPDA NPs) represent a paradigm of pancatalytic biomaterials for anti-aging therapy that comprehensively embodies the P–A–N framework (Fig. 11(d)). Engineered through liquid-phase exfoliation, UPDA NPs mimic the cascade activities of natural antioxidant enzymes (CAT/SOD), with their ultrasmall size significantly enhancing radical-scavenging efficiency by maximizing electron-donating capacity and reactive species contact area (Fig. 11(e)). In aging-related microenvironments, these nanoparticles demonstrate broad-spectrum catalytic activation, effectively dismutating $^{\bullet}O_2^-$ to H_2O_2/O_2 (SOD-like activity), decomposing H_2O_2 into H_2O/O_2 (CAT-like activity), and directly neutralizing $^{\bullet}OH$, $^{\bullet}NO$, and $ONOO^-$, thereby disrupting the oxidative stress–senescence vicious cycle at the molecular level. The system ensures nontoxic treatment through its biocompatible polydopamine matrix and renal-clearable dimensions, while transcriptomic analysis reveals additional anti-senescence effects mediated *via* NF-κB pathway regulation (Fig. 11(f)). This integrated approach showcases how UPDA NPs synergize catalytic RONS elimination with systemic safety, offering a clinically translatable strategy that holistically addresses aging through synchronized material design (preparation), pathological microenvironment remodeling (activation), and metabolic safety (nontoxic treatment).[65]

4. Conclusion and perspectives

Pancatalytic biomaterials represent an emerging and transformative paradigm in the treatment of IDs. These engineered materials are defined by their integration of principles from catalytic biology and catalytic medicine, enabling holistic modulation of pathological microenvironments. Within the P–A–N framework, pancatalytic biomaterials function to catalyze specific bio-effects. In inflammatory diseases, their core function lies in either mimicking natural enzymatic activities (*e.g.*, SOD, CAT, GPx) or demonstrating direct ROS-scavenging capabilities, while exhibiting stimuli-responsive catalytic behavior (*e.g.*, to pH, ROS, hypoxia), thereby executing multi-modal bioeffects like oxidative stress regulation, immune cell phenotype reprogramming, inflammation resolution, and tissue homeostasis restoration. The rational design and application of these materials are guided by the P–A–N framework, ensuring targeted action, efficacy, and biocompatibility.

Based on composition and properties, pancatalytic biomaterials are broadly categorized into three main classes: inorganic materials (*e.g.*, CeO_2, V_2C MXenes, BPNSs), valued for their robust catalytic efficiency and stability; organic materials (*e.g.*, PDA, EGCG), prized for their inherent biocompatibility, structural tunability, and ability to mimic natural enzymes; and organic/inorganic hybrid systems (*e.g.*, metal–organic frameworks, melanin-based composites), which synergistically combine the catalytic potency of inorganic components with the functional versatility and biocompatibility of organic elements. Key characteristics underpinning their therapeutic potential include inherent enzyme-mimetic activities, stimuli-responsiveness for spatiotemporal control, biocompatibility, biodegradability (or controlled metabolic clearance), targeted delivery mechanisms, and inherent multifunctionality allowing theranostic integration. Pancatalytic biomaterials demonstrate broad therapeutic applicability across multiple physiological systems affected by chronic inflammation. They exhibit significant potential in managing inflammatory diseases of the cardiovascular system, nervous system, respiratory system, digestive system, joint system, integumentary system, sensory system, urinary system, reproductive system, and other inflammation-related disorders.

While pancatalytic biomaterials demonstrate substantial therapeutic potential, a critical examination of the P–A–N framework reveals key limitations that must be overcome to realize their full clinical impact. The P–A–N framework, while providing a systematic approach for designing pancatalytic biomaterials, exhibits several inherent limitations that become particularly apparent during clinical translation. The framework's current implementation struggles to adequately account

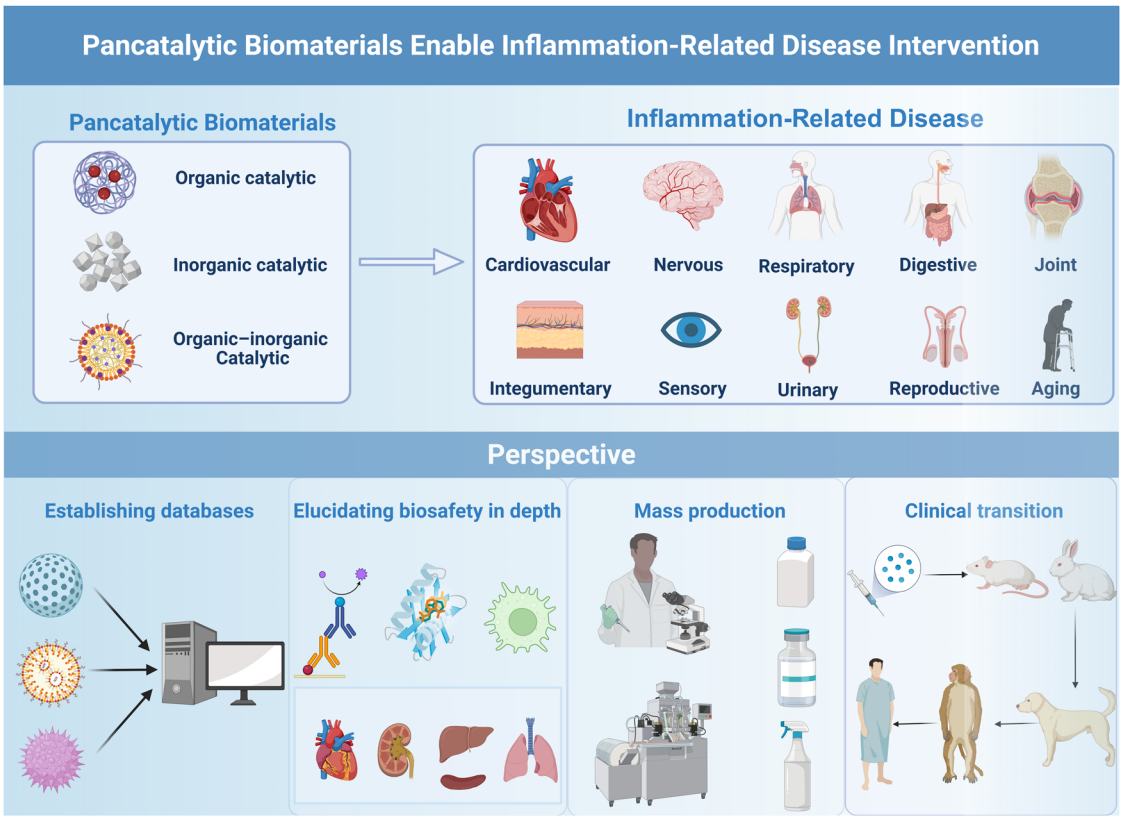

Fig. 12 Summary of the current applications and the future developments of pancatalytic materials. Created with https://BioRender.com.

for the dynamic complexity of inflammatory microenvironments, where rapid fluctuations in biochemical markers and substantial spatial heterogeneity often exceed the operational ranges of stimulus-responsive systems, compromising the reliability of the activation phase. Furthermore, the interdependent nature of the preparation, activation, and nontoxic treatment components creates fundamental optimization challenges, where enhancements in catalytic activity frequently come at the expense of biocompatibility, while modifications to improve safety profiles may inadvertently diminish therapeutic efficacy. These limitations are compounded by significant translational gaps between controlled laboratory models and clinical reality, including species-specific metabolic differences and oversimplified disease representations that fail to capture the complexity of human inflammatory conditions. The framework also lacks robust quantitative guidelines for balancing the competing demands of its three components, particularly in multicatalytic systems designed to address complex, multifactorial inflammatory pathologies. These challenges are most pronounced under chronic inflammatory conditions, where the extended duration of treatment and evolving disease states place exceptional demands on material stability and long-term biocompatibility. These identified limitations, rather than diminishing the framework's value, serve as strategic waypoints guiding the next phase of innovation. The identified limitations of the P–A–N framework, while presenting significant challenges, highlight critical opportunities for advancing pancatalytic biomaterials. This versatile therapeutic platform has demonstrated efficacy across diverse inflammation-related pathologies through multiple breakthroughs, yet remains in its developmental infancy. Systematic solutions must now be developed to overcome these challenges and enable clinical translation (Fig. 12).

4.1. Establishing comprehensive databases

The development of comprehensive databases integrating catalytic performance parameters and disease-specific biomarkers represents a critical frontier in advancing pancatalytic biomaterials for inflammatory diseases. These repositories must systematically characterize catalytic profiles while enabling AI-driven prediction of novel therapeutic pathways. By correlating catalytic signatures with the distinct pathological microenvironments characteristic of chronic inflammation, such as varying pH gradients, ROS profiles, and immune cell distributions, these databases can facilitate personalized biomaterial design tailored to specific inflammatory conditions. The integration of computational modeling with big data analytics allows for intelligent screening of material properties (including size, surface charge, and catalytic kinetics) while predicting their behavior in complex biological systems. This data-driven approach is particularly crucial given the need to balance multienzyme catalytic efficiency with fundamental biocompatibility requirements when targeting inflammatory microenvironments. Advanced machine learning algorithms, trained on both material

performance data and clinical outcomes, can optimize catalyst design for specific inflammatory pathologies while accounting for critical safety parameters.

Recent successful applications highlight the pivotal role of machine learning and high-throughput screening methodologies: (1) machine learning-assisted identification of RuO_2 nanoparticles that combine photothermal tumor ablation with catalase-mimicking anti-inflammatory activity through systematic analysis of structure–activity relationships, demonstrating synergistic therapeutic effects in tumor microenvironments;[281] and (2) high-throughput screening-derived $SrDy_2O4$ nanozymes that simultaneously scavenge ROS, modulate gut microbiota through selective bacterial regulation, and provide diagnostic imaging capabilities for ulcerative colitis treatment, showcasing multifunctional therapeutic potential.[282] These cases exemplify how machine learning-driven prediction and high-throughput experimental screening in integrated databases synergistically guide the rational design of pancatalytic biomaterials for specific inflammatory conditions. Building on these proof-of-concept demonstrations, such systematic databases promise to transform current empirical approaches into precision platforms for developing next-generation anti-inflammatory therapies. By codifying the relationships between material properties and biological outcomes, these knowledge bases enable the rational design of therapeutics that simultaneously address catalytic potency, microenvironmental responsiveness, and biosafety – ultimately enabling tailored interventions for diverse inflammation-related diseases.

4.2. Elucidating biosafety mechanisms in depth

The clinical translation of pancatalytic biomaterials presents significant biosafety challenges that require comprehensive investigation. While preliminary studies indicate acceptable biocompatibility for certain materials, critical gaps remain in understanding their long-term biological interactions and metabolic fate. Recent advances in material design have introduced innovative strategies to enhance biosafety. For instance, non-metallic catalytic biomaterials like evodiamine, a natural compound with chemotherapeutic and peroxidase-like activity, show promise. When co-delivered with ICG in liposomal nanoparticles, this system enables synergistic chemotherapy/CDT/PDT effects against oral cancer while maintaining excellent biosafety, highlighting the potential of metal-free catalytic systems.[283] Similarly, researchers have developed ultrasmall, biodegradable materials such as monodispersed CoS_2 nanoclusters. Their loosely stacked structure provides abundant catalytic sites for efficient Fenton-like reactions, converting H_2O_2 into cytotoxic ·OH in tumors.[284] These nanoclusters rapidly dissociate into excretable ions, with toxicological studies confirming minimal toxicity.

The path to clinical translation requires resolving several key challenges. The complex relationship between material properties (surface characteristics, composition, structure) and biological systems raises concerns about inflammatory responses, immune activation, and potential toxicity from degradation byproducts. Current safety assessments are hindered by the lack of standardized evaluation protocols for nanomaterials, particularly regarding their metabolic pathways and tissue-specific accumulation. Thorough preclinical testing must evaluate blood compatibility, multi-organ histopathology, immune responses, biodegradation kinetics, and clearance mechanisms across multiple biological models, including large animals that better approximate human physiology. Key parameters such as optimal dosing, administration routes, and exposure duration need careful optimization to balance therapeutic efficacy with safety. The development of novel catalytic materials with enhanced biocompatibility and controlled degradation profiles, combined with rigorous safety validation through multidisciplinary approaches, will be crucial for advancing these therapies toward clinical applications while ensuring patient safety. This requires establishing comprehensive safety profiles through systematic preclinical studies to gain regulatory approval and build confidence for clinical use.

4.3. Mass production

Mass production of pancatalytic materials faces significant hurdles despite their cost-effective lab-scale synthesis, as complex fabrication procedures and specialized equipment impede scalable manufacturing. Key challenges include the technical difficulty in scaling up ultrasmall or composite nanocatalysts, low stability leading to oxidation during storage, and reliance on toxic solvents that pose contamination risks. Recent breakthroughs in bacterial extracellular vesicle (BEV) production systems offer promising solutions to these challenges. The EXODUS platform (T-2800/H-600) represents a cutting-edge automated system that integrates ultrasound-assisted nanofiltration technology to achieve high-throughput, GMP-compliant isolation of BEVs (20–400 nm) with remarkable purity and batch-to-batch consistency. Notably, these naturally derived BEVs demonstrate potent ROS scavenging capabilities, making them promising candidates for anti-inflammatory applications.[285,286] Their unique lipid bilayer structure enables efficient loading of therapeutic cargo. Similarly, the development of EGCG polymer colloidal spheres through an innovative combination of ternary condensation reactions and ethanol-mediated nanoprecipitation has demonstrated exceptional drug loading capacities (up to 86% for paclitaxel) while preserving catalytic activity. The integration of continuous microfluidic processing (5 mL min^{-1}) in this system ensures precise control over particle characteristics (PDI < 0.2, size < 200 nm), addressing critical challenges in nanoparticle manufacturing consistency.[287]

To enable the clinical translation of pancatalytic materials, standardized protocols must be developed that incorporate lessons from these successful examples, focusing on reproducible synthesis under mild, green conditions while eliminating organic solvent residues and ensuring rigorous quality control of physical properties (size, morphology, surface chemistry). Production processes must be further optimized through collaborative efforts across academia, industry, and regulatory bodies to establish comprehensive manufacturing guidelines that address cost reduction, workflow simplification, and stringent

quality control requirements that can effectively bridge the gap between bench-scale innovation and clinical deployment.

4.4. Clinical translation

The clinical translation of pancatalytic biomaterials requires establishing robust evaluation systems and comprehensive clinical validation. Current preclinical models often show limited predictive value for human therapeutic outcomes, highlighting the need for more physiologically relevant testing platforms across multiple biological systems. Thorough clinical investigations must systematically assess safety profiles, treatment efficacy, and long-term performance to build a solid evidence base for regulatory approval. Successful implementation will depend on collaborative efforts between research institutions, clinical centers, and industry partners to bridge the gap between laboratory development and practical applications. Parallel educational initiatives should enhance the understanding of these novel therapies among medical professionals and patients. By addressing these fundamental aspects through coordinated research and development strategies, pancatalytic biomaterials can progress toward becoming clinically viable solutions for managing complex inflammatory conditions.

Building upon these critical considerations, sustained multidisciplinary efforts must be directed toward achieving fundamental breakthroughs in pancatalytic biomaterials to establish this innovative approach as a frontline therapeutic strategy for inflammatory diseases. While significant challenges remain in database establishment, biosafety elucidation, mass production, and clinical translation, these hurdles precisely define the roadmap for future research and development. Through systematic optimization of the P–A–N framework and standardization of interdisciplinary evaluation protocols, pancatalytic biomaterials are poised to revolutionize inflammatory disease management by synergizing targeted catalytic efficacy with enhanced biocompatibility. We anticipate that continued innovation in bioinspired material design, coupled with advanced manufacturing technologies and rigorous clinical validation, will accelerate the transition of these smart therapeutic systems from laboratory breakthroughs to clinical reality. The convergence of materials science, nanotechnology, and immunology embodied by pancatalytic biomaterials promises to open new frontiers in precision medicine, ultimately delivering safer and more effective treatments for patients suffering from inflammatory conditions worldwide.

Author contributions

Xiaoyan Jiang: investigation, data curation, visualization, writing – original draft. Yu Chen: conceptualization, funding acquisition, supervision, writing – review & editing.

Conflicts of interest

There are no conflicts to declare.

Abbreviations

ID	Inflammatory disease
P	Preparation
A	Activation
N	Nontoxic treatment
IDs	Inflammation-related diseases
P–A–N	Preparation of the catalyst, activation of the biological effect and nontoxic treatment of diseases
IBD	Inflammatory bowel disease
AS	Atherosclerosis
MS	Multiple sclerosis
SNHL	Sensorineural hearing loss
PAMPs	Pathogen-associated molecular patterns
DAMPs	Damage-associated molecular patterns
ROS	Reactive oxygen species
NSAIDs	Nonsteroidal anti-inflammatory drugs
GaHCF NACs	GaHCF nanoabsorption catalysts
MI	Myocardial infarction
RA	Rheumatoid arthritis
CSNs	Calcium disilicide nanoparticles
SOD	Superoxide dismutase
CAT	Catalase
GPx	Glutathione peroxidase
CaH NCs	Hexacyanoferrate nanocatalysts
CeO_2	Cerium oxide
Ce NPs	Ceria nanoparticles
MSNs	Mesoporous silica nanoparticles
BPNSs	Black phosphorus nanosheets
PDA	Polydopamine
PICsomes	Polyion complex vesicles
EGCG	Epigallocatechin gallate
MCN	Melanin-based composites
CVDs	Cardiovascular diseases
WHO	World Health Organization
LDL	Low-density lipoprotein
ox-LDL	Oxidized LDL
IL-6	Interleukin-6
TNF-α	Tumor necrosis factor-α
RONS	Reactive oxygen/nitrogen species
MIM	Myocardial infarction microenvironment
Pt NCs	Platinum nanoclusters
BBB	Blood–brain barrier
Apo-LF	Apo-lactoferrin
$^{\bullet}O_2^-$	Superoxide anion
H_2O_2	Hydrogen peroxide
$^{\bullet}OH$	Hydroxyl radicals
NO	Nitric oxide
$ONOO^-$	Peroxynitrite
NADPH	Nicotinamide adenine dinucleotide phosphate
NOX	NADPH oxidase
CaHF NPs	Calcium hexacyanoferrate(III) nanoparticles
CNS	Central nervous system
AD	Alzheimer's disease

PD	Parkinson's disease
HD	Huntington's disease
MS	Multiple sclerosis
IL-1β	Interleukin-1β
NLRP3	NOD-like receptor family pyrin domain containing 3
NF-κB	Nuclear factor kappa-light-chain-enhancer of activated B cells
IL-10	Interleukin-10
JAK-STAT	Janus kinase-signal transducer and activator of transcription
MAPK	Mitogen-activated protein kinase
TLRs	Toll-like receptors
TGF-β	Transforming growth factor-beta
Aβ	β-Amyloid
GCA	Guanidinium-modified calixarene
AP	Ascorbyl palmitate
IP6	Dipotassium phytate
DA	Dopamine
α-syn	α-Synuclein
CMA	Chaperone-mediated autophagy
DBS	Deep brain stimulation
TRPV1	Transient receptor potential vanilloid family member 1
SN	Substantia nigra
β-syn	β-Synuclein
polyQ	Polyglutamine
Htt	Huntingtin
mHtt	Mutant Htt
NPs	Nanoparticles
mHtt-Q74	74 polyglutamine repeats
UPS	Ubiquitin-proteasome system
APCs	Antigen-presenting cells
COPD	Chronic obstructive pulmonary disease
CXCL8	C–X–C motif ligand 8
CCL2	C–C motif ligand 2
PEG	Polyethylene glycol
BPQDs	Black phosphorus quantum dots
CAT-NGs	CAT-loaded nanogels
MASH	Metabolic dysfunction-associated steatohepatitis
IBDs	Inflammatory bowel diseases
CD	Crohn's disease
UC	Ulcerative colitis
LNPs	Lipid nanoparticles
RBP-4	Retinol-binding protein-4
HSCs	Hepatic stellate cells
CBD	Collagen-binding domain
ECM	Exopolysaccharide-rich extracellular matrix
OA	Osteoarthritis
RA	Rheumatoid arthritis
DMARDs	Disease-modifying anti-rheumatic drugs
CAPs	Calcium phosphate particles
H_2	Hydrogen gas
AD	Atopic dermatitis
HC	Hair cell
NAC CPDs	*N*-Acetyl-L-cysteine-derived carbonized polymer dots
BAX	BCL2-associated X protein
DED	Dry eye disease
DSP	Dexamethasone sodium phosphate
AKI	Acute kidney injury
UTIs	Urinary tract infections
UPEC	Uropathogenic *Escherichia coli*
DEC	Dextran-modified ceria nanozyme
FDA	Food and Drug Administration
PCa	Prostate cancer
TEMPO	2,2,6,6-Tetramethylpiperidine-1-oxyl
TPDA NPs	Tetramethylpiperidine-1-oxyl doped polydopamine nanoparticles
PTT	Photothermal therapy
DNA-pDHN	DNA-guided allomelanin nanodisks
Cur	Curcumin
TA	Tannic acid
DSS	Dextran sulfate sodium
FAD	Familial Alzheimer's disease
ACLT	Anterior cruciate ligament transection
SASP	Senescence-associated secretory phenotype
BAK	Benzalkonium chloride
UPDA NPs	Ultra-small polydopamine nanoparticles
DCFH	DSP@Ce-MOFs F127 hydrogel
MLPGa	Lyticase and gallium ions co-integrated nanosystem

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

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