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A Review

Biohybrid molecules: Integrating natural and synthetic components for advanced biochemical applications

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Biohybrid molecules, a fusion of natural and synthetic components, represent a significant leap in biochemical technology. These innovative molecules harness the unique properties of both their natural and synthetic constituents, enabling new possibilities in advanced biochemical applications. The integration of biological and artificial elements offers enhanced functionality, stability, and versatility, paving the way for groundbreaking advancements in areas such as drug delivery, diagnostics, and bioengineering. This approach not only bridges the gap between biology and chemistry but also opens up new frontiers in the development of smart, responsive systems tailored for specific biomedical purposes. This could revolutionize regenerative medicine, offering new hope for patients in need of transplants or tissue repairs. The development of biohybrid molecules is still in its early stages, but the promise they hold is immense. As technology advances and our understanding of molecular interactions deepens, the potential for biohybrids to transform healthcare, environmental science, and even industrial processes becomes increasingly tangible. There is significant potential for future research to unlock these possibilities, where the boundaries between natural and synthetic components are seamlessly integratedfor the betterment of society.

Keywords: Biohybrid molecules, Gold particles, Nanomaterials, PEGylation

Introduction

The field of biohybrid molecules has gained considerable attention in recent years as a promising approach to bridging the gap between biological and synthetic systems. By integrating the inherent specificity and functionality of natural biomolecules with the versatility and robustness of synthetic materials, researchers have created novel systems capable of addressing a wide range of challenges in biotechnology and medicine[1]. Biohybrid molecules offer a powerful combination of the best attributes from both worlds natural biomolecules, such as proteins, peptides, and nucleic acids, provide specificity and bioactivity, while synthetic components contribute enhanced stability, tunability, and ease of production[2]. This unique combination opens new possibilities for drug delivery, diagnostics, biosensing, catalysis, and tissue engineering.

One area where biohybrid molecules have shown great promise is in drug delivery systems. For example, conjugating proteins with synthetic polymers has led to the development of more stable drug carriers capable of prolonging circulation time and enhancing the delivery of therapeutic agents to specific targets. Polyethylene glycol (PEG) conjugation, or PEGylation, of therapeutic proteins has been a particularly successful approach[3]. PEGylation improves protein stability and reduces immunogenicity, allowing drugs such as PEGylated interferons to be used in the treatment of hepatitis C with increased efficacy and fewer side effects. Similarly, biohybrid nanocarriers incorporating synthetic polymers with peptide-based targeting ligands have been developed to achieve targeted delivery of anticancer drugs to tumor tissues, thereby reducing off-target effects and enhancing therapeutic outcomes.

Biohybrid molecules also play an essential role in biosensing and diagnostics. A notable example is the integration of aptamers single-stranded DNA or RNA molecules that can bind to specific targets with nanomaterials such as gold nanoparticles or carbon nanotubes to create highly sensitive biosensors[4]. These biohybrid sensors have demonstrated exceptional sensitivity and selectivity for detecting

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various biomolecules, ranging from small metabolites to complex proteins, with applications in clinical diagnostics and environmental monitoring[5]. One well-known example is the use of aptamer-functionalized gold nanoparticles for the detection of thrombin, a protein involved in blood clotting. This biohybrid sensor exhibits colorimetric changes upon binding to thrombin, providing a simple and effective tool for detecting coagulation-related disorders.

In the field of biocatalysis, biohybrid molecules have enabled the development of highly efficient and versatile catalytic systems. Enzyme-polymer hybrids, for instance, have been synthesized to improve enzyme stability under harsh reaction conditions. The conjugation of enzymes with synthetic polymers, such as poly (N-isopropylacrylamide), has been shown to enhance their thermal and pH stability, enabling their use in non-aqueous or high-temperature environments. Such biohybrid catalysts have applications in industrial processes, where conventional enzymes might lose activity or denature[6]. The integration of enzymes with synthetic nanomaterials has also led to the development of nano biocatalysts with enhanced catalytic efficiency and recyclability, opening new possibilities for sustainable industrial biotransformation's.

Despite these advances, the development of biohybrid molecules is not without challenges. Issues such as ensuring biocompatibility, avoiding immune responses, and achieving large-scale production remain significant hurdles. For example, while PEGylation improves protein stability, it can sometimes lead to the formation of anti-PEG antibodies, which may reduce therapeutic efficacy. Addressing these challenges requires a deep understanding of both the biological and synthetic components involved, as well as innovative strategies for optimizing their interactions.

The aim of this review is to provide a comprehensive overview of the current state of biohybrid molecules, with a focus on their design, synthesis, and diverse applications. By examining specific examples from recent research, such as PEGylated drugs, aptamer-nanomaterial biosensors, and enzyme-polymer hybrids, we highlight the ways in which biohybrid molecules are transforming modern biochemistry and medicine. Furthermore, we discuss the challenges that need to be addressed to unlock the full potential of these hybrid systems, particularly in terms of stability, biocompatibility, and scalability[7]. Ultimately, biohybrid molecules represent an exciting frontier in biochemical research, with the potential to revolutionize the development of tailored biochemical tools and therapeutic strategies.

Conjugation of enzymes with synthetic polymers

The conjugation of enzymes with synthetic polymers has emerged as a powerful strategy to enhance enzyme stability, activity, and functional versatility for a range of biochemical and industrial applications. Enzyme-polymer conjugation typically involves covalently attaching synthetic polymers to enzyme molecules, providing improved physical and chemical properties while preserving or even enhancing enzymatic activity[8]. This approach aims to address some of the inherent limitations of enzymes, such as their sensitivity to environmental changes (*e.g.*, temperature, pH, and solvents) and their susceptibility to denaturation or degradation (Fig. 1).

One prominent example of enzyme-polymer conjugation is the attachment of polyethylene glycol (PEG) to enzymes, a process known as PEGylation. PEGylation has been widely used to enhance enzyme stability, prolong enzyme half-life, and reduce immunogenicity in therapeutic and industrial applications. For instance, PEGylated uricase, an enzyme used to treat gout by breaking down uric acid, exhibits significantly improved stability and a reduced immune response compared to its native form[9]. PEGylated uricase, also known as pegloticase, is used to treat chronic gout in adults and hyperuricemia in patients with hematologic malignancies. It has has several advantages, including nontoxic, long half life**,** reduced immunogenicity and well tolerated[10]. The PEGylated version of the enzyme, known commercially as Krystexxa, has been approved for use in treating chronic gout, particularly in patients who are refractory to conventional treatments.

Another example involves the conjugation of enzymes with temperature-responsive polymers, such as poly (N-isopropylacrylamide) (PNIPAM). PNIPAM is a thermos responsive polymer that

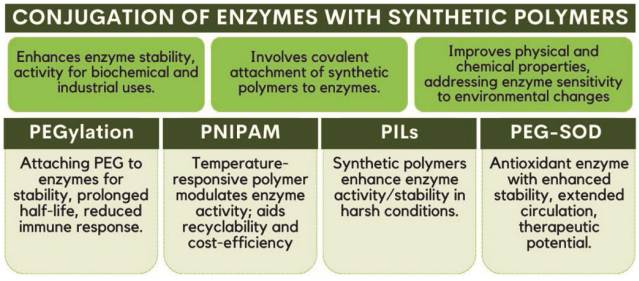

Fig. 1 — Conjugation of enzymes with synthetic polymers

undergoes a phase transition at a specific temperature, which makes enzyme-PNIPAM conjugates highly attractive for applications requiring temperature-dependent control. For instance, conjugation of PNIPAM with β-galactosidase, an enzyme used for lactose hydrolysis, allows for enzyme activity to be modulated based on temperature changes[11]. At temperatures below the phase transition point, the polymer is soluble, allowing the enzyme to be active in aqueous media. However, above the transition temperature, the polymer becomes insoluble, facilitating easy recovery of the enzyme through precipitation. This property is particularly useful in industrial settings where enzyme recyclability and cost efficiency are critical. PNIPAM is used to create cell sheet surfaces for cell culturing, used in drug delivery systems, as nanocarriers, thermogels and pH-sensitive drug delivery systems, also used in tissue engineering applications, wound dressings, gel actuators (convert external stimuli into mechanical motion) and PNIPAM-based thin films can be used as nano-switches[12].

Another notable example is the conjugation of enzymes with poly (ionic liquids) (PILs), which are synthetic polymers based on ionic liquids. PILs have many medical and biomedical applications, including to create antimicrobial membranes that are effective against bacteria like *E. coli, S. aureus*, and *C. albicans*. PIL membranes can be used to treat skin wounds, reducing inflammation, can be used in drug delivery, as nanocomposites, gas membranes, smart surfaces and as catalysts[13]. These enzyme-PIL conjugates have shown promise in catalyzing reactions under harsh chemical conditions, such as in organic solvents. The immobilization of lipase enzymes on PILs has been found to improve enzyme activity and stability in non-aqueous media, making them highly suitable for use in biodiesel production and other organic syntheses. The enhanced catalytic efficiency of enzyme-PIL conjugates is attributed to the unique properties of ionic liquids, including their ability to maintain enzyme structure and stability while minimizing substrate and product inhibition.

Polymer-enzyme conjugates have also found applications in biomedical fields. For example, the conjugation of superoxide dismutase (SOD), an antioxidant enzyme, with PEG has been used to enhance the enzyme's stability and circulation time for treating oxidative stress-related diseases. SOD is an important enzyme for scavenging reactive oxygen species (ROS) in the body, but its therapeutic application is limited due to rapid degradation[13]. PEG-SOD conjugates, however, exhibit extended blood circulation, enhanced protection against ROS, and increased therapeutic potential in conditions such as arthritis and neurodegenerative diseases.

Furthermore, enzyme conjugation with hydrophilic polymers, such as polyvinyl alcohol (PVA) or polyacrylamide, has been utilized for the development of biocatalytic hydrogels, which are used in biosensing and bioreactor applications. Polymer-based hydrogel drug delivery systems (DDS) offer sustained, controlled drug release, maintaining therapeutic levels and preventing sudden fluctuations that may impair treatment. By extending release duration, these hydrogels enhance bioavailability and reduce dosing frequency, supporting patient compliance. Additionally, targeted delivery to specific tissues is achievable by incorporating targeting ligands or modifying hydrogel properties, minimizing systemic exposure and off-target effects while maximizing therapeutic efficacy[14]. These hydrogels provide a protective microenvironment that maintains enzyme activity while facilitating substrate diffusion. For instance, glucose oxidase (GOx) conjugated with PVA in hydrogel form has been used to develop glucose sensors, which have applications in medical diagnostics for monitoring blood glucose levels in diabetic patients.

Overall, the conjugation of enzymes with synthetic polymers holds immense potential in enhancing enzyme performance for both industrial and biomedical applications. By improving enzyme stability, reusability, and adaptability to different environments, enzyme-polymer conjugates address many of the limitations faced by free enzymes, paving the way for more efficient and cost-effective processes in diverse fields, ranging from pharmaceutical and chemical industries to environmental and medical applications.

Integration of enzymes with synthetic nanomaterials

The integration of enzymes with synthetic nanomaterials represents an exciting area of research, offering enhanced functionality and versatility to overcome the limitations associated with free enzymes, such as instability and reduced activity under harsh conditions. Synthetic nanomaterials, including nanoparticles, nanotubes, and nanofibers,

provide a suitable platform to immobilize enzymes, preserving their native conformation and activity while enabling easy recovery and reuse. Recent advancements in the synthesis and characterization of nanoparticles, along with the discovery of unique properties in certain classes of nanomaterials, have sparked increased interest in their potential use as carriers for enzyme-based drugs. Current research in this area has focused on developing enzyme-nanomaterial conjugates for various applications, ranging from industrial catalysis and environmental remediation to biosensing and therapeutic purposes (Fig. 2).

A prominent example of this approach is the immobilization of enzymes on gold nanoparticles (AuNPs). Gold nanoparticles provide a large surface area, high biocompatibility, and tunable surface properties, making them ideal candidates for enzyme immobilization. Enzyme-AuNP conjugates have been widely studied for biosensing applications. For example, glucose oxidase (GOx) immobilized on AuNPs has been used to develop highly sensitive glucose biosensors[15]. These enzyme-nanomaterial conjugates exhibit enhanced electron transfer between the enzyme and the electrode, leading to improved sensor performance. Such sensors have shown promise in continuous monitoring of glucose levels in diabetic patients, offering rapid and accurate glucose measurements.

Another area of current research involves the conjugation of enzymes with magnetic nanoparticles (MNPs). MNPs allow for easy separation of enzymes from reaction mixtures by applying an external magnetic field, making them ideal for biocatalysis applications. Lipase immobilized on magnetic nanoparticles has been used for the production of biodiesel from vegetable oils, where the magnetic properties facilitate the easy recovery and reuse of the enzyme, improving cost efficiency[16]. Lipase immobilized on magnetic nanoparticles has various pharmaceutical and industrial applications, including biocatalysis, where it enhances stability and selectivity; nanobiocatalysts, as in the use of magnetic nanoparticles to immobilize *Thermomyces*

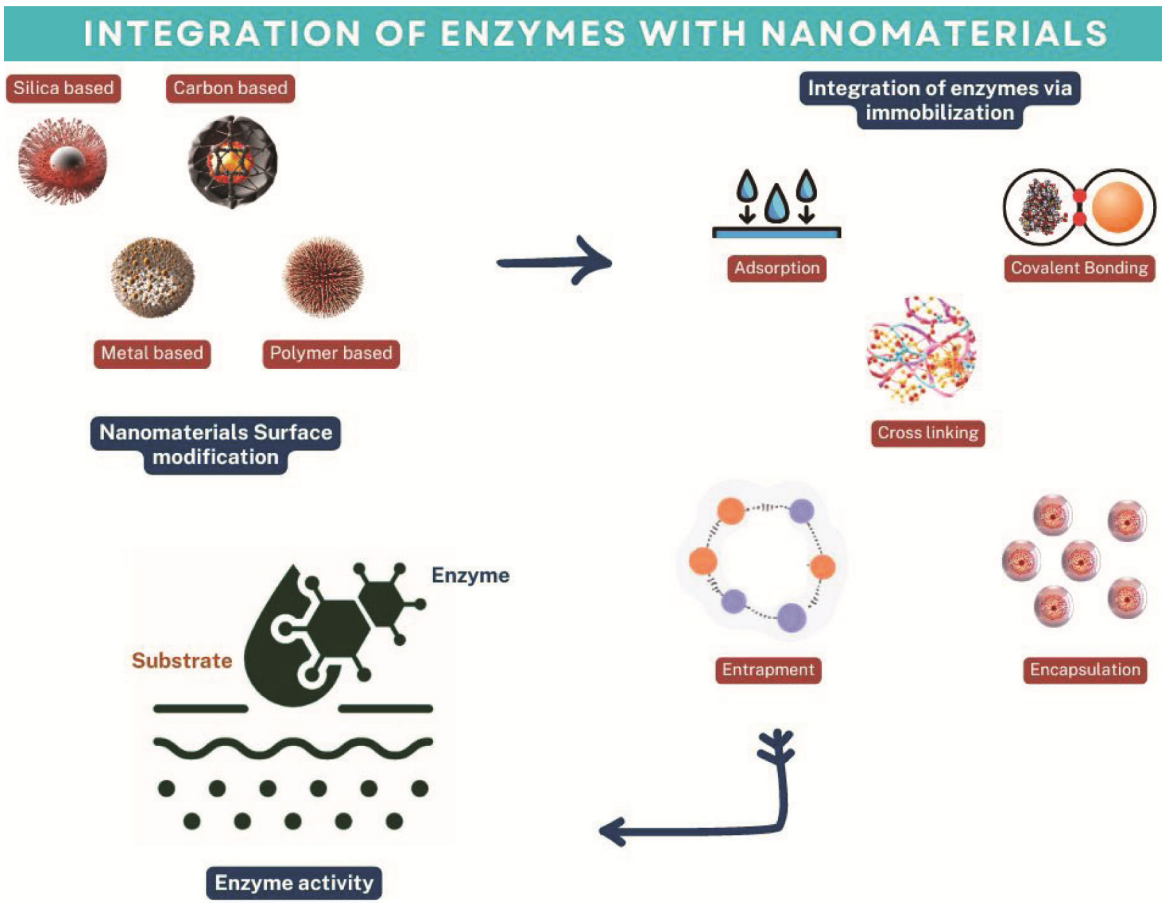

Fig. 2 — Integration of enzymes with nanomaterials

lanuginosus lipase for ester synthesis; antibacterial activity, such as *Candida rugosa* lipase immobilized on nanoparticles to combat *Staphylococcus aureus;* and improved enzyme reusability, reducing operational costs. The large surface-area-to-volume ratio of magnetic nanoparticles also allows for high enzyme loading. The properties of magnetic nanoparticles, including size and morphology, depend on their synthesis method and conditions[17]. Additionally, peroxidase enzymes immobilized on magnetic nanoparticles have been studied for their application in wastewater treatment, enabling efficient degradation of toxic dyes and pollutants in the environment.

Carbon-based nanomaterials, such as carbon nanotubes (CNTs) and graphene, have also been widely explored for enzyme immobilization. Carbon nanotubes, with their high surface area and electrical conductivity, are particularly advantageous for developing electrochemical biosensors. CNTs have a wide range of medicinal and pharmaceutical applications, including targeted drug and gene delivery to specific cells, reducing side effects; facilitating gene therapy by delivering DNA sequences; promoting tissue regeneration; serving in diagnostic and analytical biosensors; enhancing photo-therapy platforms; enabling the separation of chiral drugs; assisting in the extraction and analysis of drugs and pollutants; exhibiting antioxidant properties; and acting as ultrasound contrast agents in bio imaging[18]. For instance, horseradish peroxidase (HRP) conjugated with CNTs has been used for hydrogen peroxide detection, demonstrating enhanced sensitivity and rapid response due to efficient electron transfer. Graphene oxide (GO), with its excellent mechanical properties and large surface area, has also been utilized to immobilize enzymes for biocatalysis. Enzyme-GO conjugates have been applied in various biochemical reactions, showing improved stability and catalytic efficiency under challenging conditions.

Current research has also expanded to developing enzyme conjugates with metal-organic frameworks (MOFs), which are porous crystalline materials with high surface area and tunable pore sizes. MOFs have various medicinal and pharmaceutical applications, including controlled drug delivery for conditions like cancer and pain management, imaging as contrast agents, theranostics for personalized treatment combining drug targeting and imaging, regenerative medicine when integrated with biomedical materials, and detoxification[19]. MOFs provide a stable environment for enzyme immobilization while allowing easy access to substrates. For example, catalase enzymes have been immobilized on MOFs for applications in antioxidant therapies, providing enhanced enzyme stability and protection from proteolytic degradation.

Future research focusing on the integration of enzymes with synthetic nanomaterials seeks to tackle various challenges. These include ensuring biocompatibility, minimizing enzyme leaching from nanomaterials, and enhancing enzyme activity across diverse environmental conditions. A promising direction for the future involves creating multi-enzyme nanomaterial systems, where multiple enzymes are co-immobilized on a single nanomaterial platform to facilitate cascade reactions[20]. This strategy has the potential to greatly enhance the efficiency of intricate biochemical processes, particularly those needed for metabolic engineering or synthetic biology applications.

Another promising direction is the development of stimuli-responsive enzyme-nanomaterial conjugates, where enzyme activity can be controlled by external stimuli, such as temperature, pH, or light. For example, light-responsive nanoparticles can be used to activate or deactivate enzymes, enabling precise spatiotemporal control over enzymatic reactions. Such systems could have significant implications in drug delivery and on-demand therapeutic applications.

Additionally, advances in nanofabrication techniques are expected to lead to the development of more sophisticated enzyme-nanomaterial systems, with better control over enzyme orientation, loading, and stability. The use of biocompatible nanomaterials (Table 1), such as silica nanoparticles and biodegradable polymers, is also anticipated to expand, particularly in biomedical applications, where enzyme-nanomaterial conjugates could serve as targeted drug delivery vehicles or as therapeutic agents for treating diseases, including cancer and neurodegenerative disorders.

In conclusion, the integration of enzymes with synthetic nanomaterials has made significant progress, enhanced enzyme functionality and extending their applications across multiple domains. Future research holds great promise in further optimizing these systems to improve efficiency, stability, and control, thereby unlocking new opportunities in industrial biocatalysis, environmental remediation, and biomedical innovation.

Table 1 — Information of biocompatible nanomaterials

Nanomaterial Type	Properties	Applications
Gold Nanoparticles (AuNPs)	Large surface area, high biocompatibility, tunable surface properties	Drug delivery, biosensing, medical diagnostics
Silver Nanoparticles (AgNPs)	Antimicrobial, high conductivity	Wound dressings, coatings, medical devices
Magnetic Nanoparticles (Fe3O4)	Magnetic properties, biocompatibility	Magnetic resonance imaging (MRI), hyperthermia therapy
Quantum Dots	Fluorescent, tunable emission	Bioimaging, diagnostics
Liposomes	Biodegradable, encapsulate drugs	Drug delivery, gene therapy
Carbon Nanotubes (CNTs)	High strength, electrical conductivity	Tissue engineering, biosensors
Polymeric Nanoparticles	Biodegradable, customizable	Drug delivery, imaging
Silica Nanoparticles	Biocompatible, porous	Drug delivery, imaging
Hydrogel Nanoparticles	High water content, biocompatibility	Tissue engineering, drug delivery

Current research: Applications in treatment

Enzyme-nanomaterial hybrids for enhanced therapeutics

One of the key areas of current research is the development of enzyme-nanomaterial hybrids for enhanced therapeutic interventions. Enzymes, due to their catalytic efficiency, play an essential role in many biological processes, but their inherent instability limits their practical application. The conjugation of enzymes with synthetic nanomaterials like nanoparticles or polymeric matrices provides a stable environment, improving enzyme activity, stability, and usability in harsh conditions (Fig. 3).

A notable example is the use of catalase immobilized on gold nanoparticles for antioxidant therapy. Catalase breaks down hydrogen peroxide, a reactive oxygen species (ROS), into water and oxygen, thereby reducing oxidative stress that is implicated in several diseases, including neurodegenerative disorders like Parkinson's and Alzheimer's disease. Catalase-gold nanoparticle hybrids show enhanced enzyme stability and activity in physiological environments, making them suitable for delivering therapeutic effects *in vivo*. Gold nanoparticles (AuNPs) can also be used to eradicate tumour cells by producing oxidative stress and reactive oxygen species (ROS), used as an X-ray imaging agent for cancer diagnosis and therapy and also used to treat inflammation-associated diseases by delivering catalase to macrophages, which metabolizes hydrogen peroxide[21].

DNA-synthetic polymer hybrids for targeted gene therapy

Another active area of research is the development of DNA-synthetic polymer hybrids for gene therapy. DNA-based therapeutics have been recognized for their potential in treating genetic disorders; however, their clinical use is limited by issues like poor stability

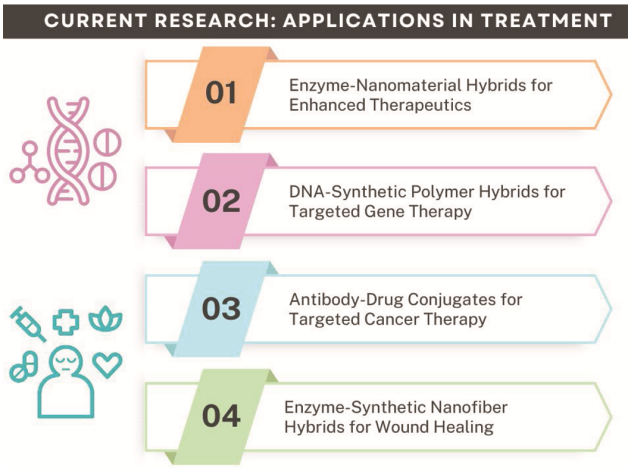

Fig. 3 — Current Research: Applications in Treatment and Diagnostics

in the bloodstream and low cellular uptake. Synthetic polymers like polyethyleneimine (PEI) and poly (lactic-co-glycolic acid) (PLGA) are widely used to enhance the delivery efficiency and stability of DNA[22].

For instance, plasmid DNA encoding therapeutic genes can be conjugated with PEI to form stable polyplexes. These complexes protect DNA from degradation by nucleases and facilitate endosomal escape, leading to higher gene transfection efficiency. DNA-PEI hybrids have been used in clinical trials for the treatment of cancers by encoding tumor suppressor genes that can specifically target cancer cells, thereby reducing tumor growth without affecting healthy tissues. Such hybrid systems are a promising advancement in gene therapy, addressing issues of targeting, stability, and safety [23]. DNA-PEI hybrids are primarily used for gene delivery, leveraging the ability of the cationic polymer PEI (polyethyleneimine) to condense and efficiently deliver DNA into cells, making it a key component in non-viral gene therapy applications like introducing

therapeutic genes into target tissues to treat diseases like cancer or genetic disorders. Important applications of DNA-PEI hybrids are Transfection in research, Gene therapy development, cancer treatment and used to deliver small interfering RNAs (siRNAs) to silence specific genes by complexing with them, offering potential for disease treatment[24].

Antibody-drug conjugates for targeted cancer therapy

The combination of monoclonal antibodies with synthetic cytotoxic drugs is another example of successful integration of natural and synthetic components. Antibody-drug conjugates (ADCs) consist of an antibody linked to a cytotoxic drug, providing targeted delivery of chemotherapy agents specifically to cancer cells, thereby minimizing damage to normal cells.

An example is Brentuximab Vedotin, an FDA-approved ADC for the treatment of Hodgkin lymphoma, systemic anaplastic large cell lymphoma, peripheral T-cell lymphoma, primary cutaneous anaplastic large cell lymphoma, CD30-expressing mycosis fungoides). Brentuximab uses an antibody that targets the CD30 receptor on the surface of lymphoma cells and delivers a potent cytotoxic agent, MMAE, directly to the cancer cells[25]. Brentuximab vedotin is used in combination with other chemotherapy in paediatric patients 2 years or older as first treatment for Hodgkin lymphoma. Brentuximab vedotin injection is in a class of medications called antibody-drug conjugates. It works by killing cancer cells. This targeted approach has shown a high therapeutic effect with fewer side effects compared to conventional chemotherapy. ADCs represent a rapidly growing field, with multiple conjugates in various stages of clinical trials for treating different cancers, and highlight the potential of biohybrid systems in personalized medicine.

Enzyme-synthetic nanofiber hybrids for wound healing

The integration of enzymes with synthetic nanofibers has also found significant applications in wound healing. Nanofibers provide a scaffold-like structure, allowing for the controlled release of bioactive agents[18], while enzymes can promote tissue regeneration and antimicrobial activity. A notable example is lysozyme immobilized on electro spun polycaprolactone (PCL) nanofibers. Polycaprolactone (PCL) nanofibers are preferred polymer for long-term drug delivery because of its slow degradation rate. It's also compatible with a wide range of drugs. PCL is used in tissue engineering applications for the regeneration of bone, nerve, and cardiovascular tissue. It is also used in wound dressing applications, used to restore injured myocardium cells and increase blood supply in injured myocardium and for three-dimensional bioprinting[26]. Lysozyme is an antimicrobial enzyme capable of breaking down bacterial cell walls, and its conjugation with PCL nanofibers enables sustained enzyme release, promoting wound healing while preventing bacterial infections.

These hybrids wound dressings are particularly advantageous in chronic wounds, such as diabetic foot ulcers, where persistent infections delay the healing process. The combination of synthetic nanofibers and enzymes offers a biocompatible, controlled, and effective approach to wound treatment, reducing the frequency of dressing changes and promoting faster healing.

Future scope: Possible directions and opportunities

Development of multi-functional biohybrid platforms

A promising direction for future research involves the development of multi-functional biohybrid platforms that can perform several tasks simultaneously (Fig. 4). For example, integrating enzyme-loaded nanomaterials with imaging agents could create theragnostic platforms that can be used for both therapy and diagnosis. Enzyme-AuNP hybrids have been investigated for combining catalytic activity with photothermal properties, enabling cancer treatment and real-time monitoring via imaging.

Multi-functional biohybrid platforms could also integrate different enzymes to form cascade reactions, similar to metabolic pathways in cells[27]. Such systems could be used for advanced biocatalysis in industrial settings, where the synthesis of complex molecules requires multiple enzymatic steps. By immobilizing these enzymes in close proximity on a synthetic scaffold, researchers aim to improve reaction efficiency and reduce unwanted side products.

Stimuli-responsive biohybrid systems for on-demand therapy

The future of biohybrid molecules lies in their ability to respond to environmental changes or external stimuli, offering on-demand therapeutic

Fig. 4 — Future Research: Emerging directions and prospects

interventions. Stimuli-responsive hybrids, in which enzyme or drug activity can be triggered by pH, temperature, light, or magnetic fields, are gaining attention for their potential to provide targeted and controlled therapeutic effects[28]. For instance, enzyme-nanomaterial hybrids that respond to changes in the tumor microenvironment, such as low pH or high ROS levels, could selectively activate enzymes to produce cytotoxic agents directly in the tumor tissue, minimizing systemic toxicity.

Light-responsive enzyme systems are also being explored for their potential in non-invasive therapies. By using photoactive nanoparticles conjugated to enzymes, light irradiation can trigger enzyme activity in specific regions, allowing for precise spatial control of therapeutic effects[29]. Such systems hold great promise in cancer treatment, enabling localized therapy that minimizes damage to surrounding healthy tissues.

Integration of artificial intelligence for biohybrid design

Future research will likely incorporate artificial intelligence (AI) and machine learning (ML) to accelerate the discovery and optimization of biohybrid molecules. AI can predict optimal combinations of natural and synthetic components, simulate their interactions, and identify the best candidates for specific applications. For example, machine learning algorithms can be used to predict the stability, activity, and interaction of enzyme-nanomaterial hybrids, allowing for rapid prototyping and reducing the trial-and-error aspect of experimental research[30].

AI-driven approaches could also aid in the personalized design of biohybrid systems for therapeutic applications, taking into account patient-specific factors such as genetic makeup, immune response, and disease progression. By integrating AI into biohybrid research, researchers hope to develop more effective, personalized, and precise treatment strategies.

Biodegradable and biocompatible biohybrid materials for sustainable medical applications

The use of biodegradable and biocompatible synthetic materials is a major focus of future research, particularly in the context of developing sustainable biomedical applications. Traditional synthetic materials, such as metallic nanoparticles, pose challenges related to long-term toxicity and biocompatibility[31]. To address these challenges, future research will focus on using biodegradable polymers like poly (lactic acid) (PLA) and poly (glycolic acid) (PGA) for biohybrid systems.

These biopolymers can be used as scaffolds for enzyme or drug delivery, offering controlled release and eventual breakdown into non-toxic byproducts. For example, PLA-based nanoparticles conjugated with enzymes are being studied for targeted drug delivery systems that degrade after fulfilling their therapeutic purpose, thereby reducing the risk of long-term toxicity and environmental impact. Such biodegradable biohybrid systems could transform drug delivery and tissue engineering, providing safe and effective treatment options while minimizing adverse effects[32].

Conclusion

The integration of natural and synthetic components for advanced biochemical applications has demonstrated significant potential in enhancing therapeutic efficacy, developing novel diagnostics, and improving industrial biocatalysis. Current

research has paved the way for biohybrid systems that offer improved stability, targeted delivery, and multi-functional capabilities. However, challenges such as biocompatibility, scalability, and precise control over biohybrid interactions remain to be addressed.

Future scope is likely to focus on developing multi-functional, stimuli-responsive biohybrid systems that offer on-demand and personalized therapeutic effects. The use of AI to accelerate the design of biohybrid molecules, combined with the development of biodegradable materials, promises to lead to more effective, sustainable, and safer biomedical applications. Integrating natural biomolecules with synthetic materials represents a transformative approach in biochemistry and biotechnology, providing innovative solutions for addressing current challenges and unlocking new opportunities for research and application.

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Conflict of interest

The authors declare no conflict of interest.

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