

Next-Generation Metal–Organic Frameworks: Shaping the Future of Steroid Compound Management

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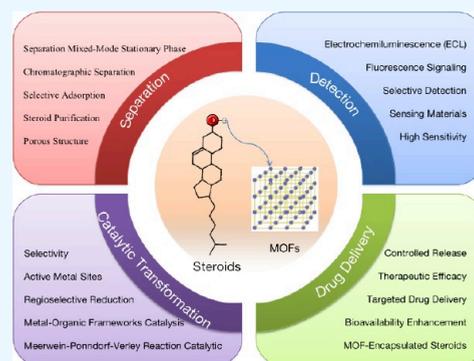
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ABSTRACT: Metal–Organic Frameworks (MOFs), as a new type of porous material, have attracted widespread attention in the fields of chemistry, materials science, and biomedicine owing to their unique structural characteristics and potential for functionalization. This review summarizes the latest research progress of MOFs in the field of steroid compounds, including the latest research progress of MOFs in the purification and separation of steroids, sensing and detection, catalytic transformation, and drug delivery. First, we explore how the porous structure and chemical functionalization of MOFs achieve efficient separation and purification of steroid compounds. Second, the high sensitivity and selectivity of MOFs as sensing materials in steroid detection, as well as their application potential in actual sample analysis, are analyzed. Furthermore, the role of MOFs in steroid catalytic transformation reactions is discussed, including their performance as catalysts or catalyst carriers. Finally, we focus on the innovative applications of MOFs in drug delivery systems, especially their advantages in controlled release and targeted drug delivery. This article also explores the future development trends and application prospects of MOFs in the field of steroids, highlighting the challenges and opportunities in material design, functionalization strategies, and practical implementations. Through this review, we aim to provide a comprehensive theoretical basis and practical guidance for further research and application of MOFs in the field of steroids.



1. INTRODUCTION

Steroids, also known as steroidal compounds, are natural or synthetic compounds that possess a steroidal ring structure. They exhibit a variety of biological activities,¹ such as antitumor, antiviral, antibacterial, and antioxidant properties. Steroids can serve as insecticides, aromatase inhibitors, α -reductase inhibitors, and neuromuscular blocking agents, and are widely used in fields like medicine, food, and cosmetics.² A search using “steroids” as the keyword from January 2014 to August 2024, as shown in Figure 1, reveals that the top 5 most frequent keywords are covid-19, testosterone, steroid, corticosteroids, and treatment (Figure 1). Due to their stable chemical structure, good lipid solubility, and the ability to effectively penetrate biological cell membranes and bind with specific receptors,³ steroidal drugs are commonly used for anti-inflammatory and immunosuppressive purposes. For instance, sex hormone drugs are used in hormone replacement therapy, and steroidal antibiotics are used for infectious disease treatment. Some athletes often use a type of anabolic steroid,⁴ which is also a kind of steroid, but taking large amounts can be very harmful to the body. Therefore, steroids are listed as banned substances and can be detected in urine. Steroids are also a class of endocrine disruptors that can adversely affect the environment and pose risks to organisms even at very low

concentrations. Hence, the development, analysis, detection, and application of steroid compounds are all very important.⁵

The detection methods for steroid hormones are mainly divided into two categories of detection methods: immunoassay and chromatography. Immunoassays are suitable only for analyzing a few hormones and have drawbacks such as complex processing, long operation cycles, poor reproducibility and accuracy, high cross-reactivity rates, and a tendency to produce false-positive results. Chromatography–mass spectrometry has been developed to achieve high-sensitivity detection of steroid with different structural characteristics. Under current trends, sample preparation is increasingly inclined toward miniaturized versions of classic extraction techniques, which are typically faster, simpler, and more environmentally friendly. In this context, solid-phase microextraction (SPME) has emerged as a solvent-free or solvent-minimized approach. It is widely used for sample extraction and purification, serving as an effective

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Figure 3. Global publications in the research field of MOFs.

the performance of the enzyme.²⁴ The porous structure, large surface area and excellent stability of MOF. It can also reduce the mass transfer resistance and improve the adsorption capacity, recognition ability, thermal stability, separation efficiency and reusability of the polymer.²⁵

From 2014 to 2024, the top 100 countries/regions in the world in terms of research output in the field of metal–organic frameworks (MOFs) are shown in Figure 3. The country/region with the most publications in this field is China (7777 articles, 50.23%), followed by the United States of America (2808 articles, 18.14%) and India (942 articles, 6.08%) in second and third place, with an average annual publication volume of 1401 articles. The peak year for publications was 2023 with 2785 articles, and the fastest growth rate was in 2018 at 39.09%, indicating that this field is developing rapidly in this field and that it is in a phase of swift ascent.

In the field of steroid detection, MOFs have garnered widespread attention due to the adaptability of their design and the finetuning of the pore structures. These characteristics endow MOFs with great potential in separation, enrichment, and sensing, especially for steroid analysis in complex biological samples. However, despite the broad application prospects of MOFs in this field, there are relatively few review articles on the use of MOFs in steroid detection to date, which limits a comprehensive understanding and application of MOFs in this area. This review aims to provide an overview of the advancements in MOF-based approaches for steroid compound management. It summarizes the structural characteristics of MOF and the application for steroid separation, detection and sensing. Additionally, its role in facilitating catalytic transformations during steroid synthesis, as well as enhancing the stability and bioavailability of steroid molecules in vivo, is discussed. Furthermore, it highlights current challenges and explores the potential future directions for integrating MOFs into practical steroid management systems, paving the way for more efficient and sustainable practices in this area.

2. STRUCTURAL CHARACTERISTICS OF MOFS

MOFs are a type of crystalline porous material with a periodic network structure, formed through the self-assembly of

inorganic metal centers (metal ions or metal clusters) and bridging organic ligands.^{26,27} Through the selection of various metal centers and organic ligands, over 20,000 types of MOF materials have been synthesized to date.²⁸ MOFs are primarily formed by coordination bonds between metal centers and organic ligands. At the same time, other binding interactions also exist within MOFs and play important roles in their structures, such as hydrogen bonding, van der Waals forces, and π – π stacking.²⁹ MOF materials possess many unique characteristics, including crystalline structures, high specific surface areas, tunable sizes, and multifunctionality.

2.1. Crystalline Properties and High Surface Area.

The metal nodes of MOFs are typically composed of metal ions (such as Zn^{2+} , Cu^{2+} , Fe^{3+} , etc.) or metal-oxo clusters (such as Zn_4O , $\text{Al}_{12}\text{O}_{12}$, etc.), while the organic linkers are often multidentate ligands like dicarboxylic acids, tricarboxylic acids, tetracarboxylic acids, etc. By rationally combining metal nodes with organic linkers, a variety of topological structures can be constructed, such as cubes, octahedra, dodecahedra, etc., hence MOFs generally possess a high degree of crystallinity. As a typical crystalline porous material with periodic uniform channels, MOFs offer the possibility for precise molecular sieving.^{30,31} Nitschke and colleagues reported a Cu_6L_4 pseudo-octahedral metal–organic cage that can encapsulate long-arm drug molecules such as fluorinated steroids, like fluocortolone. The Cu_6L_4 cage binds and encapsulates the fluorinated steroid guest molecules within a tetrahedral structure but does not bind nonfluorinated steroids, providing a foundation for the separation of steroid compounds.³² Due to their regular porous structure, a variety of pore sizes, and pore volumes, metal–organic frameworks (MOFs) possess the excellent property of having a large surface area. MIL-101 (Cr) is a mesoporous MOF based on chromium terephthalate, with pore diameters of 29 and 34 Å, and a pore volume of approximately 1.8 cm^3/g . The surface area can reach over 3000 m^2/g ,³³ making it widely used in the adsorption and separation of samples. For instance, MIL-101 (Cr) has been utilized for the direct extraction of estrone (E1), 17 β -estradiol (E2), estriol (E3), and 17 α -ethynylestradiol (EE2). A new two-step technique that combines ultrasound-assisted emulsification microextraction (USEME) and microsolid-phase extraction (μ -

SPE) has been established for the extraction of these estrogens.³⁴

2.2. Adjustable Pore Size. The precise control of pore size in MOFs can be achieved by adjusting the synthesis conditions, such as the type of metal ions, the kind of ligands, the solvent, and the temperature. For instance, altering the radius of metal ions or selecting organic ligands with different rigidities and lengths can significantly affect the size and shape of the MOF's pores. Post-treatment techniques like solvent exchange, chemical modification, and thermal treatment can also effectively adjust the pore size of MOFs. Solvent exchange, for example, can remove template molecules formed during the synthesis process, thereby altering the pore size. Some MOFs possess a dynamic pore structure, referred to as "breathing" MOFs. These MOFs can change their pore size in response to external environmental changes, such as pressure, temperature, and atmosphere, offering the possibility of flexible application under variable conditions.³⁵

2.3. Multifunctionality. By introducing functional groups such as hydroxyl, carboxyl, and amine onto the surface of MOFs, their surface chemical properties can be significantly altered, thereby enhancing their performance in specific applications. The mixed assembly technique, which involves combining different types of metal ions and ligands to form MOFs, can create materials with multifunctional surfaces.^{36–38} Amino-functionalized aluminum-based metal–organic framework mesoporous nanorods Al-MOFs@NH₂ can serve as SPE adsorbents for the selective extraction and enrichment of trace hydrocortisone (HC) in pharmaceutical wastewater, revealing its potential value in capturing and removing steroid hormones in environmental water bodies.³⁹ Wang et al. prepared a porous carbon material embedded with iron (MIL-53-C) through the direct carbonization of MIL-53, which has a high surface area and good magnetic properties. Utilizing it as a magnetic solid-phase extraction adsorbent, they established a simple and efficient method for the magnetic solid-phase extraction-high-performance liquid chromatography ultraviolet detection of three sex hormones (methyltestosterone, testosterone propionate, and nandrolone phenpropionate) in water and human urine samples.^{40,41}

2.4. Catalytic Activity. Metal–Organic Framework (MOF) nanozymes catalyze specific chemical reactions by providing functional sites in the reaction process that are similar to the active centers of natural enzymes, thereby mimicking the catalytic mechanisms of natural enzymes.⁴² MOFs achieve functionalization for a variety of catalytic reactions by introducing different metal ions and organic ligands. For instance, metal ions can act as redox catalysts, while organic ligands can offer proton transfer sites.⁴³ The high surface area and porous structure of MOFs enable the enrichment of reactants at the interface, thus enhancing reaction rate and selectivity. Synergy between different metal ions and ligands can further enhance catalytic performance.⁴⁴ The (Zr) (Zr)UiO-66(NH₂)/SiO₂ hybrid material has been tested as an efficient and reusable heterogeneous catalyst for the synthesis of steroid derivatives. In steroid conversion reactions, there is a clear correlation between the catalytic activity of the dispersed Zr sites within the confined MOF and the loading amount on mesoporous SiO₂.⁴⁵

3. RESEARCH APPLICATIONS OF MOFS IN THE FIELD OF STEROID COMPOUNDS

Due to the highly ordered porous structure of MOFs, their large surface area, composition diversity, facile synthesis and tunable pore structures, MOFs have demonstrated significant potential for applications in adsorption, catalysis, sensing, energy storage, and more. In recent years, substantial progress has been made in the research on the detection, separation, catalytic transformation, and drug delivery of steroid compounds using MOFs.⁴⁶

3.1. Separation of Steroid Compounds. MOFs possess highly tunable pore structures and surface chemical properties, enabling the selective separation of steroid compounds through physical adsorption⁴⁷ and chemical bonding.⁴⁸ Guocan Zheng and colleagues used a composite of in situ synthesized three-dimensional mesoporous graphene (3D-MG) and zirconium-based metal–organic frameworks (MOFs), denoted as MG@UiO-66, as an adsorbent and matrix in Surface-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (SALDI-TOF MS) for the detection of steroids.⁴⁹ Ali Azari et al. employed a novel method utilizing Fe₃O₄@NH₂-MIL88B nanorods (NRs.) as an efficient adsorbent for the removal of dexamethasone from aqueous solutions; the surface's rich π electrons, amino groups (–NH₂), and acidic carboxyl groups (–COOH) play a significant role in the adsorption mechanism of dexamethasone (Figure 4).⁵⁰

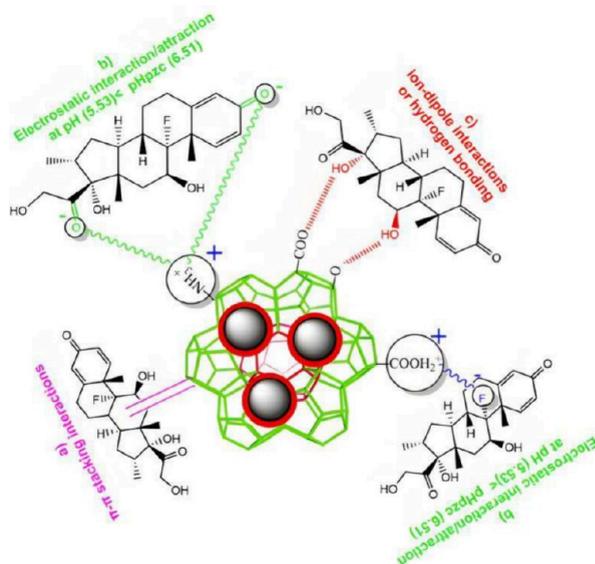


Figure 4. Possible mechanism of dexamethasone adsorption on Fe₃O₄@NH₂-MIL_{88B} NRs. Reprinted with permission from ref 48. Copyright [Scientific Reports 2023].

In 2016, Gomaa et al. modified the zeolitic imidazolate framework-8 (ZIF-8) with a polytetrafluoroethylene (PTFE) double-layer microfiltration membrane and tested the removal characteristics of the modified membrane using progesterone as a model pollutant. Compared with the unmodified membrane, the adsorption capacity of the membrane increased by nearly 40%, and the water permeability almost doubled. After three regeneration cycles, the membrane maintained its original removal efficiency at around 95%, making it a promising candidate for further development as a continuous

membrane adsorption material for water purification (Figure 5).⁵¹

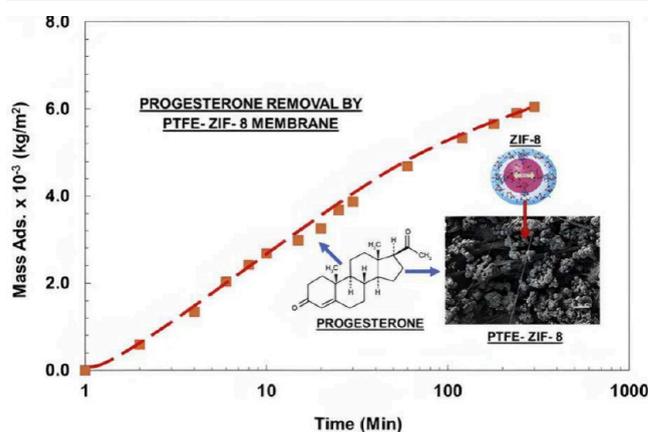


Figure 5. Adsorption capacity of progesterone on PTFE-ZIF-8. Reprinted with permission from ref 51. Copyright [Chemical Engineering Journal 2016].

To meet the growing demand for the analysis of real samples, the development of multifunctional mixed-mode stationary phase materials is of great significance. In 2021, Qiao et al. grafted MOF-74 nanocrystals onto the surface of carboxyl-functionalized silica gel, using 2,5-dihydroxyterephthalic acid as the organic ligand and nickel as the metal center. The packed MOF-74@SiO₂ column exhibited hydrophilic/reversed-phase mixed-mode retention characteristics. Compared with commercial C8 columns or silica-based columns, the MOF-74@SiO₂ column demonstrated significant separation selectivity for polycyclic aromatic hydrocarbons, phenolic compounds, and polar sulfonamide compounds within short separation times, successfully applied in the separation and detection of illegally added glucocorticoids in children's facial creams.⁵²

In 2024, Tang et al. for the first time synthesized an intriguing mixed-mode silica-based stationary phase using the room-temperature synthesized and highly stable zeolitic imidazolate framework-67 (ZIF-67) in combination with an amphiphilic polymer hydrogel. The amphiphilic polymer hydrogel and ZIF-67 exhibited remarkable synergistic effects in enhancing separation capability and the applicability of the stationary phase. Experimental results showed that the ZIF-67/hydrogel@SiO₂ stationary phase could be applied to various chromatographic separation modes, demonstrating excellent resolution and separation selectivity for polycyclic aromatic hydrocarbons, steroid hormones, nucleosides, B vitamins, sulfonamide drugs, benzoic acids, and dinitrobenzene isomers (Figure 6).⁵³

3.2. Detection of Steroid Compounds. Steroid compounds are of great significance in clinical, food, and environmental analysis. Simultaneously, their crucial physiological functions in organisms and widespread applications in medications underscore the importance of efficient and accurate detection. However, detecting steroid compounds poses challenges due to their low concentrations in complex matrices and high background interference.

Due to the advantages of easily modifiable surfaces, MOF-based extraction techniques can effectively enrich steroid compounds in real samples, significantly improving the detection limits of methods such as liquid chromatography and mass spectrometry. Wang et al. prepared aluminum-based metal-organic frameworks (Al-MOFs@NH₂), which have stable mesoporous structures, large specific surface areas, and abundant binding sites. Through hydrogen bonding and hydrophobic interactions, these materials significantly increased the adsorption capacity for hydrocortisone (HC). Al-MOFs@NH₂ can be used as a selective adsorbent for the extraction and enrichment of trace amounts of HC, enabling the detection of steroid compounds in pharmaceutical wastewater.⁵⁴

Moreover, combining MOFs with other materials possessing high adsorption performance can enhance their hydrophobicity

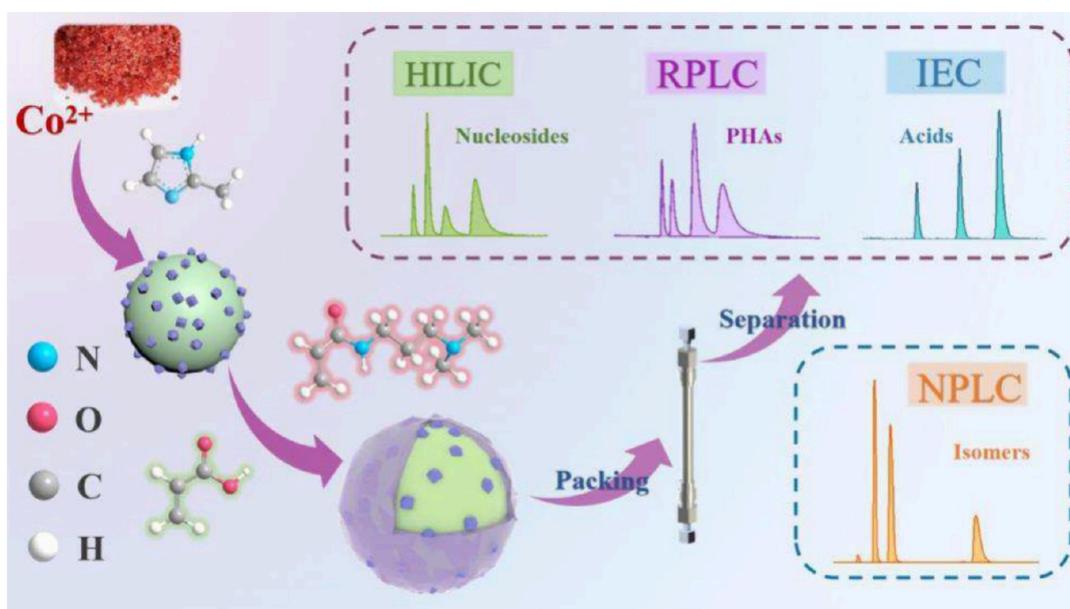


Figure 6. Chromatographic separation using ZIF-67/Hydrogel@SiO₂ as a stationary phase. Reprinted with permission from ref 53. Copyright [Separation and Purification Technology 2024]

Table 1. MOFs as SPE Adsorbents for the Detection of Steroid Compounds

MOFs	Steroid Compounds	Limits of Detection (LODs)	Mass Spectrometry (MS) Type	Sample	Reference
Al-MOFs@NH ₂	Hydrocortisone	$0.5 \times 10^{-3} \mu\text{g mL}^{-1}$	High Performance Liquid Chromatography (HPLC)	Pharmaceutical wastewater	54
MG@UiO-66	Testosterone, Methyltestosterone, Androstenedione, Estrone	3–15 nM L ⁻¹	SALDI-TOF MS	Water Samples	56
MIL-101(Cr)	Estrone	0.954 ng L ⁻¹	Ultrahigh performance liquid chromatography-MS/MS (UHPLC-MS/MS)	Water Samples	34
MIL-101(Cr)-NH ₂	Progesterone	0.02 ng mL ⁻¹	Direct analysis in real-time MS (DART-MS)	Water and Artificial Urine Samples	57
UiO-66(Zr)	Androgens, Progestogens	2.0 ng L ⁻¹	Liquid Chromatography-MS/MS (LC-MS/MS)	Water Samples	58
UiO-67	Progestogens	0.06–0.30 ng L ⁻¹	HPLC-MS	Milk	59
ZIF-8-GOS	Five Sex Hormones	0.52–2.11 $\mu\text{g L}^{-1}$	HPLC	Milk and Dairy Products	60

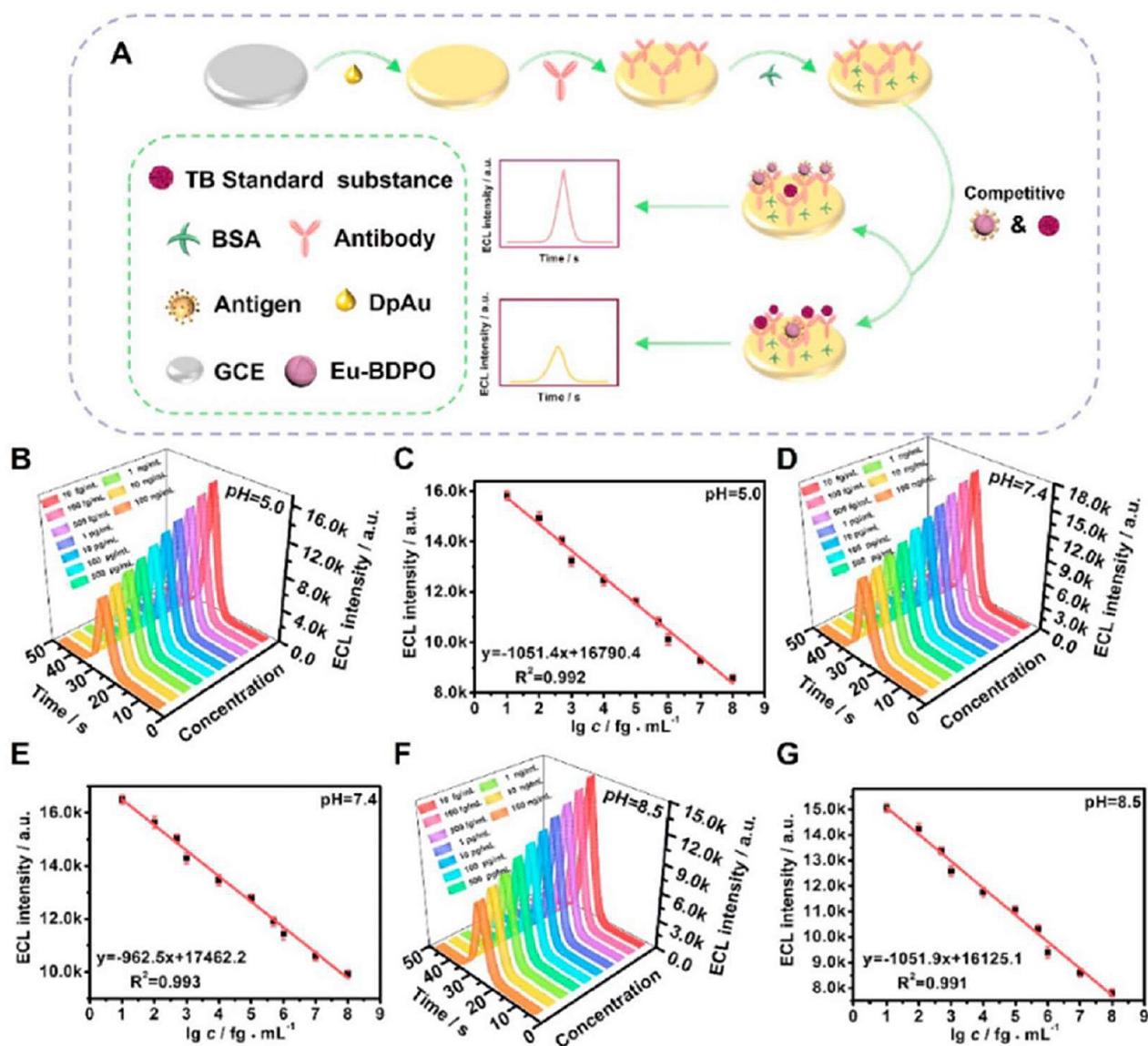


Figure 7. (A) The fabrication process of the competitive ECL biosensor. ECL intensity–time curves with a wide concentration range of 10 fg/mL to 100 ng/mL under different pH conditions: (B) 5.0, (D) 7.4 and (F) 8.5. The corresponding linear equation of the TB standard substance concentrations and ECL signals under different pH conditions: (C) 5.0, (E) 7.4 and (G) 8.5. Reprinted with permission from ref 64. Copyright [Analytical and Bioanalytical Chemistry 2018].

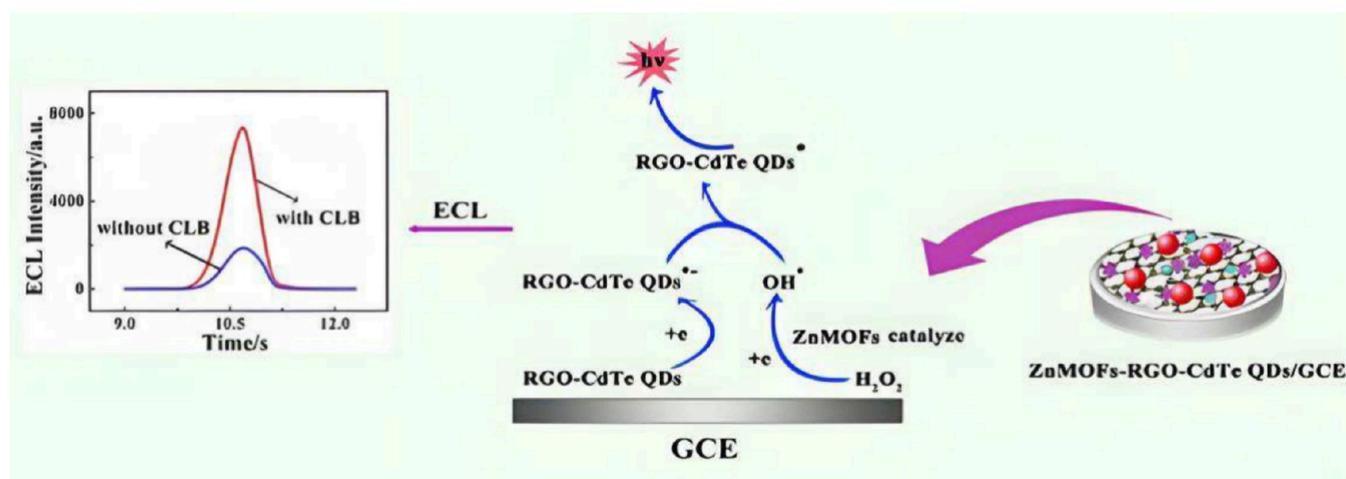


Figure 8. Detection mechanism of an electrochemiluminescence sensor for clenbuterol using ZnMOF-RGO-CdTe quantum dots (QDs). Reprinted with permission from ref 61. Copyright [Biosensors & Bioelectronics 2023].

and achieve better synergistic effects.⁵⁵ Liu et al. synthesized a graphene-based metal–organic framework composite, MG@UiO-66, which demonstrated excellent enrichment capabilities for steroid compounds. This material was combined with SALDI-TOF MS to enable highly sensitive and rapid detection of steroids in environmental water samples.⁵⁶

Table 1 below showcases the latest advancements in the utilization of MOFs as a novel and efficient solid-phase extraction (SPE) adsorbent for mass spectrometry detection of steroid compounds, revealing their application potential and challenges in steroid detection.

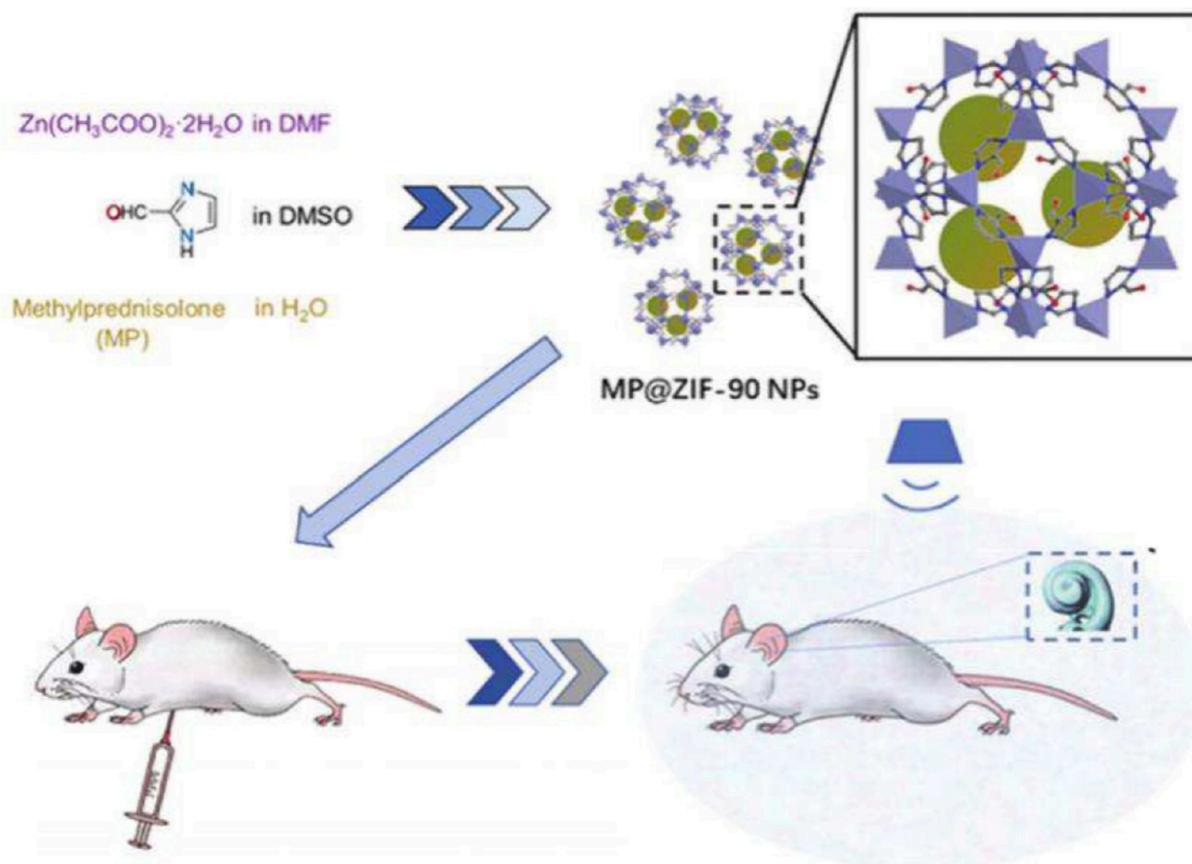
3.3. Sensing of Steroid Compounds. MOFs, due to their unique structural properties, can serve as excellent sensing materials for the detection of steroid compounds. In the sensing detection of compounds, MOFs achieve high sensitivity and selectivity toward target molecules primarily through signals such as fluorescence, color changes, and electrochemical responses.⁶⁰ For instance, Wu et al. constructed an efficient biosensor (electrochemical luminescence, ECL) with a wide pH range using Eu-MOF (Eu-BDPO) with acid and alkali resistance properties as the luminescent material, enabling trace detection of trenbolone (TB). This method offers a more practical and sensitive approach for monitoring steroid estrogens, thus high and steady ECL signals of Eu-MOF were acquired under different environments with pH = 1.0–14.0.⁶¹ Liu et al. used an amino-functionalized metal–organic framework (UiO-66-NH₂, U₆NH₂) as a carrier, embedded gold nanoparticles (AuNPs) on its surface, and immobilized cholesterol oxidase (ChOx). Then, using cholesterol as the template molecule, they synthesized molecularly imprinted polymers (MIPs). The resulting U₆NH₂@AuNPs-ChOx@MIPs could effectively and selectively detect cholesterol in blood using a colorimetric method. With a limit of detection (LOD) = 2.4 mM, while the normal level of blood cholesterol should be less than 5.18 mM.⁶² Wei et al. employed a zinc-based metal–organic framework with metal–ligand charge transfer properties as an efficient ECL probe for trace detection of trenbolone. They also used prepared Ag@Fe bimetallic nanocrystals as a coreactant accelerator. Its unique core–shell structure and inherent synergistic catalytic mechanism efficiently activated S₂O₈²⁻, enhancing ECL emission (Figure 7).⁶³

Clenbuterol (CLB), with long-term use harmful to human health, has been listed by the World Anti-Doping Agency (WADA). In 2018, Chen et al. developed a novel electrochemical luminescence (ECL) sensor using a hybrid material based on zinc metal–organic frameworks, reduced graphene oxide, and cadmium telluride quantum dots (ZnMOF-RGO-CdTe QDs) for the detection of CLB. The combination of ZnMOFs and RGO-CdTe QDs endowed the sensor with high sensitivity toward CLB detection, where the intensity of the ECL signal increased with the increase in CLB concentration (Figure 8).⁶⁴

3.4. Catalytic Transformation of Steroid Compounds. Rich metal active sites and porous structure make MOFs an efficient catalyst, exhibiting exceptional catalytic performance in the transformation reactions of steroid compounds.⁶⁵ Zr-containing MOF-808 can selectively reduce steroidal ketones to the corresponding hydroxysteroids through the Meerwein-Ponndorf-Verley (MPV) reaction, enabling the one-step diastereoselective synthesis of 17 α -hydroxy derivatives as a homogeneous catalyst. Besides excellent stability and reusability, MOF-808 also demonstrates good chemical selectivity (only the ketone group is reduced even in the presence of other reducible groups such as C=C bonds) and regioselectivity (only the 17-position ketone group is reduced in 3,17-sterone, while the 3-ketone group remains largely unchanged). The diastereoselectivity of this process is controlled by the confinement within the MOF cavity, where the Zr⁴⁺ active sites are located.⁶⁶

3.5. Drug Delivery of Steroid Compounds. The high specific surface area, adjustable pore size, and functionalizable framework structure of MOFs can significantly enhance the properties of steroid compounds. MOFs provide a novel platform for the encapsulation, delivery, and controlled release of steroid compounds.⁶⁷ By precisely controlling the pore environment of MOFs, specific interactions with steroid molecules can be achieved, potentially improving their stability, bioavailability, and therapeutic effects.^{68,69}

Noise-induced hearing loss (NIHL) is associated with both acute and chronic noise exposure. The application of steroid hormones is a first-line treatment option for NIHL. However, high doses of steroid hormones in vivo are necessary to maintain their efficacy and can cause side effects such as headaches and osteoporosis. Xu et al. developed an inner ear



Inner Ear Therapy using MP@ZIF-90 NPs

Hearing Protection against Noise-induced Hearing Loss

Figure 9. Schematic illustration of the preparation of MP@ZIF-8 for inner ear therapy. Reprinted with permission from ref 70. Copyright [Nanoscale 2020].

steroid hormone delivery system based on zeolitic imidazolate frameworks (ZIFs). Methylprednisolone (MP) was encapsulated in ZIF-90 nanoparticles (NPs), resulting in MP@ZIF-90 NPs, which showed good biocompatibility and stability at a pH of 7.4. After intraperitoneal injection, ZIF-90 effectively protected the drug in the peripheral blood circulation, enabling it to cross the blood-labyrinth barrier (BLB) into the inner ear for slow drug release. Auditory brainstem response (ABR) test results indicated that MP@ZIF-90 provided better protection against noise-induced damage in mice compared to free MP and MP encapsulated in ZIF-8 (MP@ZIF-8). Importantly, the inner ears of mice treated with MP@ZIF-90 during noise exposure showed no defects and had low nephrotoxicity (Figure 9).⁷⁰

Rong Gui designed a novel nanoparticle drug delivery system with a core–shell structure, termed *Pm*-GCH. This system comprises a core consisting of glycyrrhizic acid (G) and hydrocortisone (H) loaded with calcium ions (Ca^{2+}), encapsulated within a shell of platelet membrane (*Pm*) vesicles. In an inflammatory acidic environment, GCH gradually degrades, releasing glycyrrhizic acid and hydrocortisone. Due to glycyrrhizic acid's ability to inhibit the inactivation of hydrocortisone, it suppresses the activity of phospholipase A2 (PLA2) and the classical activation pathway of complement C2, thereby blocking the production of inflammatory factors and exerting an anti-inflammatory effect. Consequently, this enhances the therapeutic efficacy of

hydrocortisone in the treatment of steroid-resistant nephrotic syndrome (SRNS) (Figure 10).⁷¹

In 2024, Steunou et al. described the design of a novel anti-inflammatory nanomedicine, termed Au@MIL, which was synthesized through a one-pot, cost-effective, and environmentally friendly method. This nanomedicine combines a benchmark porous iron(III) carboxylate MOF, specifically MIL-100(Fe), with glutathione-protected gold nanoclusters (i.e., Au25SSG18 NCs). With a high drug-loading capacity for the glucocorticoid dexamethasone phosphate (DexP), this nanocarrier exhibits low toxicity and remarkable colloidal stability. The drug-loaded Au@MIL nanocarrier demonstrates potent anti-inflammatory activity, fostering a deeper understanding of the molecular and cellular events involved in the inflammatory process (Figure 11).⁷²

Zhang et al. have developed a bilateral microneedle patch for the delivery of dexamethasone (DXMS) and paeoniflorin (Pae) encapsulated within a cyclodextrin-based metal–organic framework (CD-MOF). Each microneedle base is equipped with NaH particles. Upon intranasal administration, the microneedles are propelled into the nasal mucosa by hydrogen gas generated from NaH, which then swells to form a hydrogel for sustained drug release. This addresses the challenges of traditional intranasal delivery methods for allergic rhinitis treatments, such as adverse nasal ciliary clearance and the nasal mucosal barrier. The newly designed device significantly enhances the therapeutic effect of the drugs, and the hydrogen

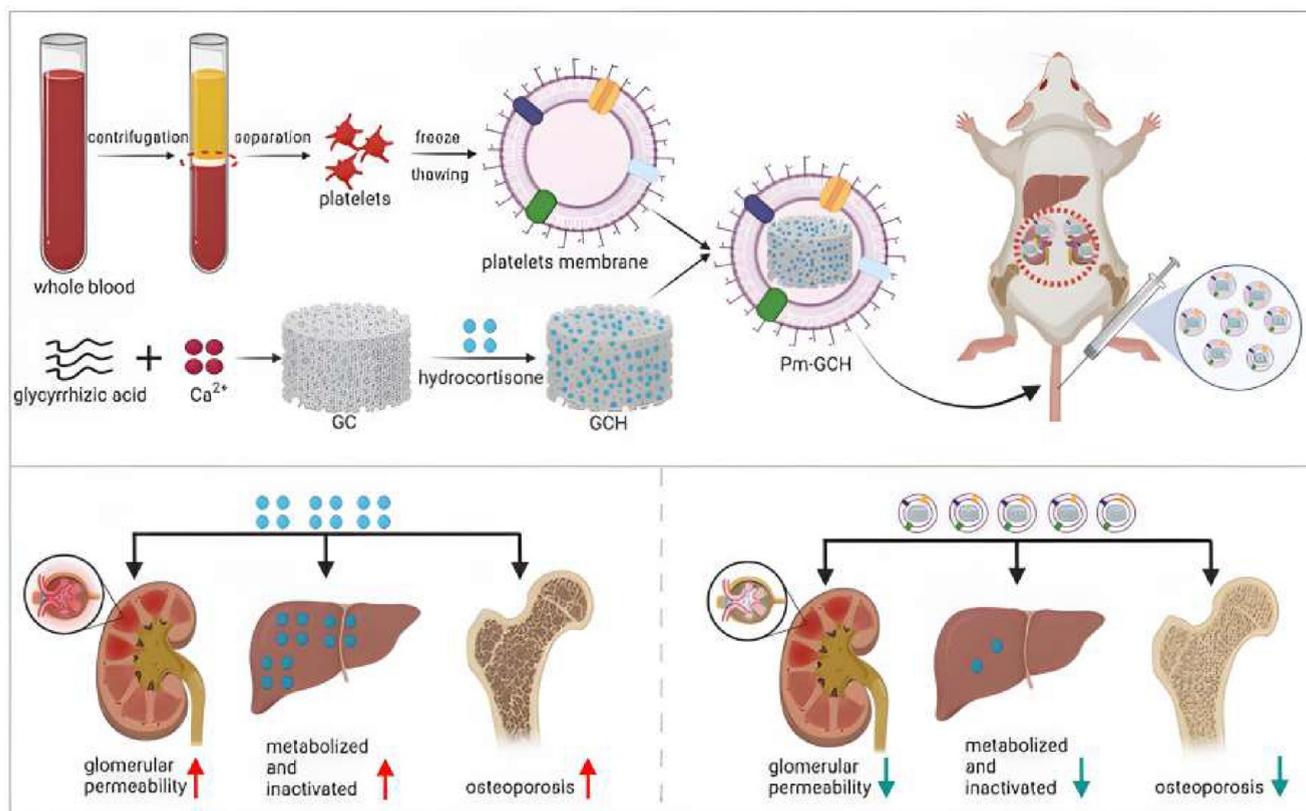


Figure 10. Construction of Pm-GCH and its targeted therapeutic mechanism in SRNS by inhibiting inflammation and osteoporosis. Reprinted with permission from ref 71. Copyright [Journal of Nanobiotechnology 2021].

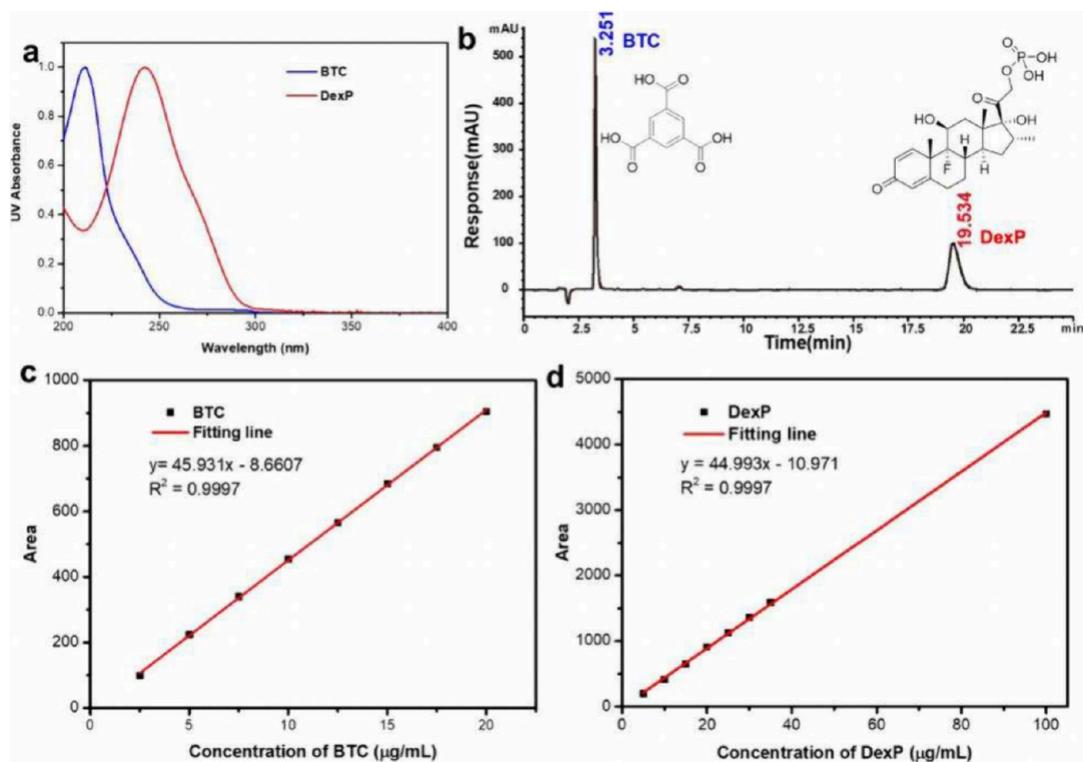


Figure 11. (a) UV-vis spectra and (b) HPLC chromatogram (insert: molecular structure) of 1,3,5-trimesic acid (BTC) and DexP, (c, d) calibration curves of (c) 1,3,5-BTC and (d) DexP in water by HPLC. Reprinted with permission from ref 71. Copyright [Nanoscale 2024].

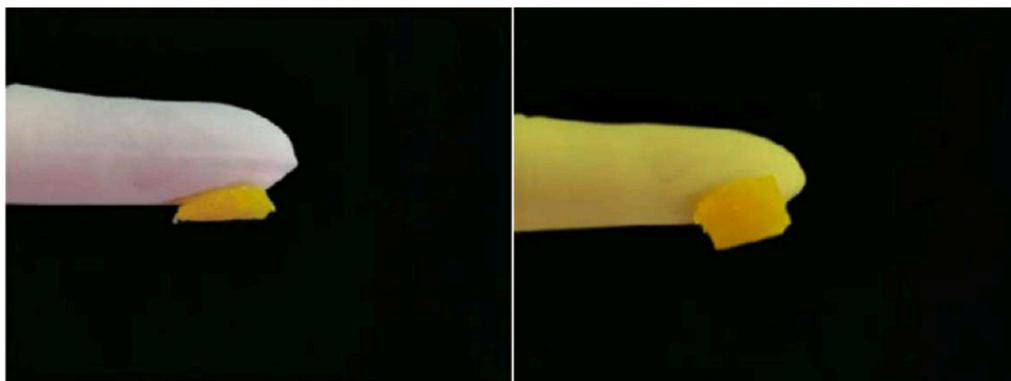


Figure 12. Wetted psyllium seed gum (PSG)/xanthan gum (XG)/polyvinylpyrrolidone (PVP) showed the adhesive property. Reprinted with permission from ref 73. Copyright [Advanced Healthcare Materials 2022]

gas produced by NaH may have potential adjuvant therapeutic effects, providing a promising solution to reduce the clinical abuse of glucocorticoids (Figure 12).⁷³

4. CONCLUSION AND PROSPECTS

MOFs, as a novel class of multifunctional materials, have demonstrated immense potential for applications in the separation, detection, catalytic conversion, and drug delivery of steroid compounds. However, MOFs still face several challenges in practical applications, such as stability in aqueous solutions, synthesis costs, and scalability issues. Future research should focus on developing more stable and efficient MOFs materials, while exploring their expanded applications in biomedicine, drug development, and other fields.

4.1. Precise Monitoring and Dynamic Regulation. The development of a new generation of MOFs-based sensors should prioritize real-time monitoring and dynamic analysis of steroid compounds within biological systems. These sensors should possess high sensitivity and selectivity, enabling precise tracking of steroid compound changes during biological processes, thereby providing crucial information for understanding their roles in biological pathways and metabolism. Furthermore, exploring the potential of MOFs in regulating steroid compound homeostasis, such as through smart responsive materials that enable drug release in the presence of specific biomarkers, is also essential.

4.2. Fluorescence Imaging and Therapeutic Strategies Across Biological Barriers. Addressing the limitations of fluorescent probes in biological applications, MOFs with red-shifted absorption properties, particularly in the second near-infrared window, should be designed to enhance penetration capabilities in biological tissues. This will facilitate the use of MOFs in deep tissue imaging and photodynamic therapy. Additionally, developing multifunctional MOFs nano-platforms that integrate diagnostic imaging with therapeutic functions, such as combining photothermal therapy, chemotherapy, and gene therapy, could offer novel strategies for treating complex diseases like cancer.

4.3. Stability Optimization and Environmentally Responsive Design. To address the stability challenges that MOFs may encounter in biological environments, such as photobleaching, pH sensitivity, and enzymatic degradation, novel MOFs materials should be developed. Through structural optimization and surface modification, the stability and durability of MOFs in complex biological environments can be improved. Furthermore, designing environmentally

responsive MOFs that enable controlled drug release in specific biological microenvironments, such as tumor microenvironments or inflammatory regions, can enhance therapeutic efficacy while reducing side effects.

Future research directions should focus on the following areas: **Personalized Medicine**, developing MOFs that can be customized to individual patient needs, such as designing MOFs to release specific drugs based on a patient's genetic profile or disease state; **Combination Therapies**, exploring the use of MOFs to deliver multiple drugs simultaneously to achieve synergistic effects, which could be particularly beneficial in treating multidrug-resistant cancers; **Environmental Applications**, creating MOFs for environmental remediation, such as removing endocrine-disrupting chemicals from water sources to mitigate the impact of steroid compounds on ecosystems; and **Regenerative Medicine**, investigating the potential of MOFs to deliver growth factors or other bioactive molecules to promote tissue repair and regeneration. Through these focused efforts, it is anticipated that the applications of MOFs in the field of steroid compounds will continue to overcome existing limitations, enabling more precise monitoring, more effective treatments, and broader clinical applications.

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