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## A Mini Overview of Biomedical Utilization of Zeolitic Imidazolate Frameworks

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**Abstract:** Zeolitic Imidazolate Frameworks (ZIFs) are a type of metal-organic framework (MOF) composed of imidazole ligands and zinc ions. They have been identified as a promising platform for developing theranostics, including nanocarriers for drug delivery and fluorescent molecules. ZIF materials are suitable matrices for encapsulating enzymes, medicinal molecules, and nanoparticles due to their high biocompatibility. Moreover, these compounds are susceptible to degradation in acidic conditions or in the presence of competing ligands, rendering them a valuable basis for constructing sensitive theranostic systems. ZIF showed identical physiochemical characteristics, which facilitated the evaluation of size-dependent biological components of the organisms. ZIFs exhibit potential for diverse biological applications such as bioimaging, biosensing, drug delivery, and theranostic. This review will focus on the biomedical applications of ZIFs, including biosensing, drug delivery, bioimaging, and theranostic applications.

**Keywords:** ZIF; Bioimaging; Biosensing; Drug delivery; Theranostic

### 1. INTRODUCTION

MOFs are crystalline porous materials that combine inorganic and organic components [1,2]. ZIFs are a subclass of MOFs. ZIF showed comparable physiochemical characteristics, offering benefits for evaluating their size-dependent biological aspects. ZIFs are feasible for several biomedical applications (see Fig. 1). ZIFs possess intriguing theranostic properties, which make them a flexible platform for applications that combine diagnostic and therapeutic functions [3]. The porous nature of ZIFs enables detection of various biomolecules, such as enzymes, antibodies, DNA etc. Encapsulation enhances the activity and sensitivity of biomolecules in biosensing by providing a stable and regulated environment for these frameworks [4]. ZIFs also show intriguing bioimaging capabilities. ZIFs can be utilized as imaging contrast agents due to inclusion of magnetic nanoparticles in these. ZIFs' porous nature allows for high loading capacities of various imaging agents, which in turn increases signal intensity and imaging sensitivity. ZIFs can be utilized as T<sub>2</sub> contrast agent [5], T<sub>1</sub>-T<sub>2</sub> dual-mode contrast agent [6] of magnetic resonance imaging (MRI).

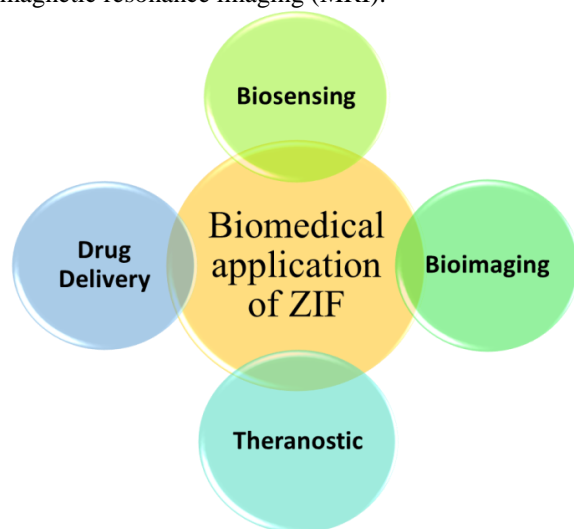


Fig. 1. Diverse biomedical utilization of ZIFs

ZIFs are designed with a precise network of channels and holes that can store different drugs. This porosity enables the ZIF to effectively encapsulate therapeutic compounds, allowing for high drug loading capacities. ZIF has been used cargo encapsulation. Once incorporated into the MOF during synthesis, the cargoes cannot easily disperse out via the tiny windows and are only dispersed upon MOF decomposition, despite the pores being huge enough to accommodate even relatively large biomolecules and drugs. ZIF-8 naturally works as a pH-triggered release mechanism since it is stable in neutral aqueous settings and progressively degrades in mildly acidic circumstances. In recent years, proteins, camptothecin (CPT), and inorganic particles have all been encapsulated using ZIF-8[7]. ZIF has the potential to provide selectivity and permanence in in vivo therapies without compromising the operational activity of DNA plasmids. Doxorubicin hydrochloride (DOX) was placed into a ZrO<sub>2</sub> shell, and then ZIF-8 NPs, composed of Zn<sup>2+</sup> and 2-methylimidazolate (2-H-MeIm) ligands, were used to coat the NPs. ZIF-8/DOX@ZrO<sub>2</sub>@Ionic liquid has shown superior performance in Computed Tomography (CT) imaging. For PET imaging-guided tumor treatment, theranostic ZIF demonstrates a quick, simple, and entirely aqueous method [8]. In this review, we will discuss about the biomedical applications of ZIFs.

### 2. BIOSENSING

ZIFs are perfect for biosensing applications due to their distinctive features. ZIFs' porous structure makes it possible to encapsulate other biomolecules like enzymes, antibodies, or DNA. The biomolecules' activity and sensitivity in biosensing are increased by this encapsulation, which offers a stable and regulated environment for them. ZIF-8 matrix and Glucose (Glu) oxidase-anchored gold nanoclusters (GOD-AuNCs) can be used to create a capillary-based fluorimetric system for measuring glucose in the human blood. The GOD-catalyzed generation of hydrogen peroxide might cause the fluorescence to fade proportionally to the Glu concentrations when Glu was added by self-driven sampling. [9], Glassy carbon electrode (GCE) combined

with ZIF-67 exhibited excellent catalytic activity in glucose oxidation. In the meanwhile, a unique Ag@ZIF-67 nanocomposite was created using a sequential deposition-reduction approach to extend the electrocatalytic performance of the customized electrode. Again, the Ag@ZIF-67/GCE demonstrated increased catalytic activity for the oxidation of glucose [10]. A non-enzymatic glucose sensor made of ZIF-67 hollow nanoprisms (ZIF-67 HNPs) is possible. For guest molecules to enter and exit the MOF crystals quickly, a rapid diffusion channel is provided by the interparticle holes of hollow structure. The electrocatalytic performance of these nanostructured MOF-based sensors for glucose oxidation in an alkaline solution is extremely good [11]. At room temperature, polyhedral Co-based zeolite imidazole frame [Co(mim)<sub>2</sub>]<sub>n</sub> (abbreviated as ZIF-67; mim = 2-methylimidazole) exists in situ incorporated on both sides of physically exfoliated graphene nanosheets (GSs), and sandwich like GS@ZIF-67 hybrids with an ordered nanostructure are efficiently utilized for the measurement of glucose in the serums of human with excellent outcomes [12]. The combination of glucose oxidase (GOx) and gold nanoparticles (AuNPs) in the pore space of a ZIF-8 nanocomposite displays remarkable stability with low-level glucose detection in H<sub>2</sub>O medium by employing a significantly minimal concentration of GOx (about 62 µg per mL) [13]. In addition to exhibiting peroxidase-like activity, the combination of NiPd hollow nanoparticles and glucose oxidase (GOx), denoted as (GOx@ZIF-8(NiPd)), could also catalyze the oxidation of Glu. Additionally, GOx@ZIF-8(NiPd)/GCE demonstrated excellent electrochemical performance regarding glucose as well as significant electrocatalytic activity for ORR[14]. The ZIF-8 plated Fe<sub>3</sub>O<sub>4</sub>/PPy magnetic nanocomposite (Fe<sub>3</sub>O<sub>4</sub>/PPy@ZIF-8) with its strong conductivity and huge surface area demonstrated exceptional electro detection capability for glucose [15]. Ni<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>@ZIF-67/GCE demonstrated very high sensitiveness of 2783 µA mM<sup>-1</sup> cm<sup>-2</sup> with a broad linear range (1.0 µM - 4.0 mM), and a low LOD of 0.7 µM at a S/N ratio of 3. It has also been shown that Ni<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>@ZIF-67/GCE may be used to sense glucose in serum of human with excellent recoveries (about 92-109%) [16]. Cu/Co-ZIF nanoflake arrays upon carbon cloth exhibit high selectivity, reproducibility, and real-world applicability, pointing to its potential for use in enzyme-free glucose monitoring. With a great sensitivity of 1.03 mAmm<sup>-1</sup>cm<sup>-2</sup>, the Cu/Co-ZIF-20 electrode exhibits a broad linear range (0.05 mM - 6.0 mM) [17]. The ZIF-N 2 customized screen-printed carbon electrode's nonenzymatic glucose sensing capabilities, including long time stability, selectivity, and repeatability, were also shown to be extraordinary[18]. Moreover, Ag NPs/ZIF-67 @CNT [19], Enzyme-Loaded Hemin/G-Quadruplex-Modified ZIF-90 [20], Nickel decorated ZIF-8 derived Carbon Nanoframe [21], composite of ZIF-8, glucose oxidase and gold nanocluster [22], ZIF-67 derived porous Co<sub>3</sub>O<sub>4</sub> hollow nanopolyhedrons [23], Mn<sub>3</sub>O<sub>4</sub>@ZIF-67 on carbon cloth [24] can contribute in sensing glucose. So, these can be applied in glucose sensors. Both enzyme-based and enzyme-free processes are possible for the sensing of glucose by ZIF nanomaterials. ZIF-8 MOFs

[25], ZIF-67 [26], 3D ZIF-8/PDA Photonic Crystal has been used in the biosensors for blood component detection [27]. Cysteine (Cys) is an amino acid that contains sulfur and has several important biological activities in the human body. Recently, trace Cys was monitored in HeLa cells using fluorimetric test strips utilizing ZIFs and Au-Ag NCs. These nanospheres were first applied on test strips then further coated with ZIF-8 using a vacuum-aided quick dehydration approach with very hydrophobic patterns. The ZIF-8 coating, which was used to create the test strips, has increased the fluorescence, storage, and environmental stabilities. AuNCs/β-Gal/GOx@ZIF-8 is capable of detecting lactose present in samples of lactose-free milk. In favor of fast and precise sensing, the quenching rate of AuNCs/β-Gal/GOx@ZIF-8 was enhanced to 3.4 times that of the free AuNCs/β-Gal/GOx system. This was made possible by the higher local concentration of the fluorescent probe and the quenching agent [28]. Uric acid (UA) is a naturally occurring waste product produced during the digestion of purine-containing meals. In urine, uric acid may be found using ZIF-11. In a pH 7 buffered aqueous solutions, this electrode catalyzes the oxidation of UA while exhibiting a 70 mV reduction in overpotential contrasted to a glassy carbon electrode. Using differential pulse-anodic stripping voltammetry (DP-ASV), the oxidation current of UA against concentration displays excellent linearity band of 20-540 µM (R=0.998) and has a LOD of 0.48 µM while S/N is 3. [29]. The detection limits of the glucose and uric acid sensors based on porous Co<sub>3</sub>O<sub>4</sub> hollow nanopolyhedrons, which were developed using ZIF-67, are both down to 100 nM, which is far higher than the sensitivity needed for non-invasive identification of glucose as well as uric acid, found in tears [23]. A nanoprobe with a ZIF encapsulated CuNC and nitrogen-doped CDs as spherical nanocomposites (CD@ZIF-CuNC) has been effectively utilized for measuring UA, which is catalyzed by uricase to create hydrogen peroxide, with a LOD of 0.33 µM and a linear range of 1-30 µM [30]. L-tryptophan (L-Trp), uric acid (UA), and Dopamine (DA) may be measured using a version of the Ni-ZIF-8/N S-CNTs/CS composite on a glassy carbon electrode. With broad linear ranges of 5~850 µM, 1~600 µM and 8~500 µM and minimal detection limits of 0.69, 0.41, and 0.93 µM, respectively, Ni-ZIF-8/N S-CNTs/CS/GCE demonstrated exceptional electrocatalytic activity for the electrochemical responses of L-Trp, UA, and DA [31] The synchronous voltammetric measurement of DA and UA occurred using a Co(II)-based ZIF-67 and graphene oxide (GO) electrodeposited over a glassy carbon electrode (GCE), usually at working potentials of 0.11 and 0.25 V (vs. SCE) [32]. ZIF-67/rGO also senses dopamine as well as H<sub>2</sub>O<sub>2</sub>[33]. With the simultaneous voltammetric measurement of uric acid (URA) and acetaminophen (ACE) using cetyltrimethylammonium bromide (CTAB) as a differentiating agent, a ZIF-67/g-C<sub>3</sub>N<sub>4</sub> composite was used as a modifying agent for a glassy carbon electrode. The detection limits for a ACE and URA in human urine are 0.053 and 0.052 µM, respectively, due to the linear relationship between the oxidation peak currents of ACE and URA and the concentration range of 0.2 - 6.5 µM [34]. Moreover, urea can be detected using cobalt zeolitic imidazolate

framework (Co-ZIF)-nickel microwires (NiMWs) [35]. and ZIF-8/urease [36]. Harmful Cholesterol present in human body could be sensed using HRP@ZIF-8 nanocomposite [37], AuNCs/ChOx@ZIF-8/PEI nanocomplexes [38] and Pd@ZIF-8 [39]. Synuclein oligomers such as Alpha-Synuclein can be detected by CoMnZIF@CNF nanohybrid [40]. ZIF-67 [41] and ZIF-67 derived NiCo LDH can be utilized as enzyme free lactate sensor for human body [42]. Moreover, silica@ZIF-8 can sense atropine [43] and bimetallic ZIF/carbon nanofibers (CoMnZIF-CNF) composite can sense adrenaline [44]. Ascorbic acid can be sensed using ZIF-8/Pt NPs/GCE sensor [45], AA-imprinted poly(o-PD)/ZIF-67/CC [46] and C-dots/ZIF-8/MnO<sub>2</sub> [47]. ZIF-67 derivatives such as ZIF-67/AgNWs Nanocomposite have the ability to sense Folic Acid [48] and EDAPbCl<sub>4</sub>@ZIF-67 has the ability to detect protocatechuic acid [49]. Additionally, ZIF-8 can even detect virus DNA such as HIV-1 [50]. Biosensors based on ZIF have been created for a diversity of applications, comprising the detection of disease biomarkers, environmental monitoring, and food safety. ZIFs are excellent candidates for the construction of extremely sensitive and selective biosensors in a variety of academic and industrial settings due to their remarkable biosensing capabilities as well as their adaptability and tenability (see Fig. 2).

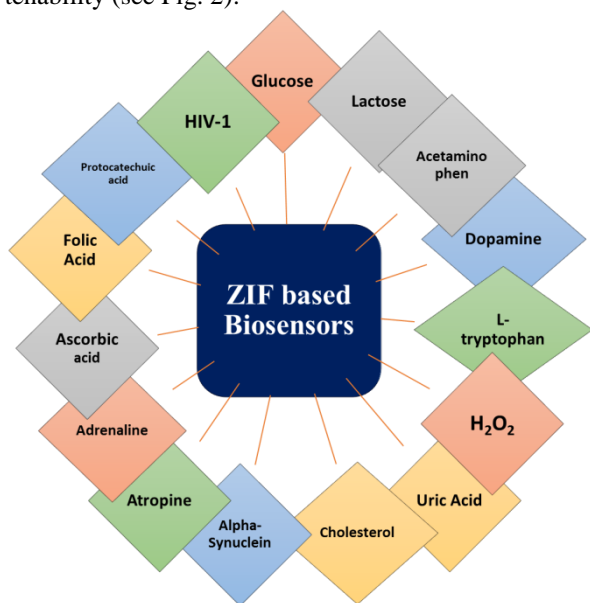


Fig. 2. Diagram on sensing applications of ZIFs

### 3. BIOIMAGING

In addition to having outstanding biosensing characteristics, ZIFs also show intriguing bioimaging capabilities. Bioimaging is the study of biological structures or processes at the cellular or molecular level with a focus on their visibility and characterization. ZIFs are a novel family of materials that have special qualities that make them appropriate for bioimaging applications. The capacity of ZIFs to contain imaging or contrast chemicals inside their porous structure is one of its main benefits in bioimaging. Among other things, these imaging agents may be magnetic nanoparticles or fluorescent dyes. Due to the porous structure of ZIFs, these imaging agents may be loaded to high loading capacities, resulting in increased signal intensity and higher imaging sensitivity.

In PTT and chemotherapy, LA-AuNR/ZIF-8, which contains Zn<sup>2+</sup> and 2-H-MeIM components, is applied where BALB/c mice with the H22 tumor are used as the animal model. Another MOF, ZIF-8/DOX@ZrO<sub>2</sub>@IL, with the same imaging technique and construction as LA-AuNR/ZIF-8, is employed in chemotherapy and microwave thermal therapy with H22 tumor-bearing mice as the model. When it comes to component matters, DOX loaded AZIF-8 also exhibits similarities. It is utilized in chemotherapy, and its imaging technique and model are, respectively, PET and 4T1 tumor-bearing mice [8]. Gd-DTPA@ZIF-8 nanoparticles have shown excellent biocompatibility and stability. Gd-DTPA@ZIF-8 NPs perform as a contrasting agent to improve T1-weighted MRI imaging at a mouse tumor location. The haemolysis percentage was much lower than the 5% needed by the pharmacopoeia for the utilization of materials as potential medicines when the highest concentration of Gd-DTPAb@ZIF-8 NPs was 400 lg mL<sup>-1</sup>. This proves the Gd-DTPAb @ZIF-8 NPs may be used in vivo and have acceptable biocompatibility. The impact of the Gd-DTPAb @ZIF-8 NPs on the development of 4T1 and human umbilical vein endothelial cells (HUVEC) was examined using the MTT technique in order to further assess the cytotoxicity of the Gd-DTPAb @ZIF8 NPs. Over 75% of 4T1 and HUVEC cells survived after 24 hours incubation in Gd-DTPAb @ZIF-8 nanomaterial culture media having 0, 12.5, 25, 50, 100, and 200 lg mL<sup>-1</sup> of Gd-DTPA, indicating that Gd-DTPAb @ZIF-8 nanomaterial containing medium displayed a nearly insignificant toxicity to both cell types over the test conditions applied. The Gd-DTPAb @ZIF-8 NPs' outstanding biocompatibility and suitability for in vivo imaging investigations were thus further shown. The porous nanomaterial ZIF-8 was effectively adsorbed with Gd-DTPA, resulting in Gd-DTPA@ZIF-8 NPs with a satisfactory reduction rate for usage as a T<sub>1</sub> MR contrasting agent. According to the investigational findings, Gd-DTPA@ZIF-8 has a relaxation rate that is almost six times greater than that of Gd-DTPA [51]. Fe<sub>3</sub>O<sub>4</sub>-ZIF-8 and other ZIF nanomaterials have shown their viability as MRI contrast materials for in-vivo bioimaging. Fe<sub>3</sub>O<sub>4</sub>-ZIF-8 can be employed in sensitive tumor imaging. Any substance used as an MRI contrast agent must possess magnetic properties. Fe<sub>3</sub>O<sub>4</sub> within this composite has sufficient magnetic properties to make it effective as an MRI contrast agent [5]. Furthermore, T<sub>1</sub> contrasting agent tiny Fe<sub>3</sub>O<sub>4</sub> nanoparticles were assembled into T<sub>2</sub> contrasting agent (Fe<sub>3</sub>O<sub>4</sub>-ZIF-8) clusters using pH- and GSH-responsive ZIF-8 as the matrix. T<sub>2</sub> signal changed to T<sub>1</sub> signal because of the disintegration of Fe<sub>3</sub>O<sub>4</sub>-ZIF-8 and the release of tiny Fe<sub>3</sub>O<sub>4</sub> nanoparticles caused by the acidic GSH and pH [52]. The ZIF-8 structure disintegrates as the pH decreases, altering the capability for T<sub>2</sub> to T<sub>1</sub> contrast. This framework has been demonstrated to respond to glutathione (GSH) similarly [53]. ZIF-8's 2-methylimidazololate, whose strong 19F MRI signal exhibits an intriguing pH dependence property, was partially replaced with 19F MRI nanoprobe, which show great promise as a 19F MRI contrast material for stimuli-responsive imaging with high depth of penetration and low background [54]. In a nutshell ZIFs have excellent bioimaging capabilities because of their

high stability, adjustable optical and magnetic characteristics, and capacity to encapsulate imaging agents. These features make ZIFs a viable type of materials for developing bioimaging methods, allowing more accurate viewing and comprehension of biological processes at the molecular and cellular levels.

#### 4. DRUG DELIVERY

ZIFs are shown to have excellent drug delivery capabilities, and they have a lot of promise for controlled and targeted drug release. ZIFs have a well-defined network of holes and channels that can hold a variety of medicinal compounds. Due to the hypotoxicity of  $Zn^{2+}$  and the comparatively wide pore cavities, porous nMOFs, such as zinc-based nMOFs, have drawn increasing interest in the drug delivery area. The ZIF-8, made of zinc ions and 2-methylimidazolate, is one of these materials that offers a fresh way to deliver drugs molecules [55]. The mineralization of ZIF-8 has been investigated using biomimicry. Numerous DNA, enzymes, and proteins have been used, resulting in the creation of new holes inside the framework of biomacromolecules. By simply changing the pH, it is possible to readily remove the biomineralized ZIFs layer while retaining the natural activity of the liberated biomacromolecules. As a result, it helps in medication delivery [56]. The in-situ encapsulation approach considerably improved the drug loading efficiency of the ZIFs, as shown by the comparative study of ZIF-8, which was encapsulated with caffeine for the investigation of caffeine release. However, when both ex-situ and in situ encapsulation procedures were used, it was shown that the drug release pattern and the amount of caffeine that came out from the ZIFs were similar. It was discovered that the caffeine-containing ZIFs displayed two different kinds of physisorption-based interactions. More specifically, these interactions comprised hydrogen bonds between the carbonyl groups in the caffeine molecules and the ZIF-8's imidazole methyl groups as well as van der Waals forces among the caffeine and these groups. The interactions caused the ZIFs' rate of caffeine emission to slow down [57]. ZIF-8 combined with 5-Fu has improved drug delivery capabilities. 50% of the medication was first released from ZIF-8, and the stable release in PBS persisted for 7 days [55]. Moreover, ZIF-8 can react to the acidic conditions of the tumor microenvironment (TME) and undergo degradation, thereby facilitating effective drug delivery [58]. Rat serum albumin was attached to ZIF-90 for a magnetic field-induced stimuli-responsive anticancer medication delivery under MRI monitoring. The blood circulation and water suspension of the nanoparticles were enhanced by the protein conjugation to ZIF-90. Moreover, a precisely designed magnetic ZIF-90 nanoparticle may release drugs when exposed to an extremely low frequency alternating magnetic field (ELF-AMF). The implanted  $Gd_2O_3$  or  $Fe_3O_4$  nanoparticles function as efficient MRI tracers for prospective drug delivery imaging to assure accuracy. When ZIF-90 nanoparticles are utilized as drug carriers, the size of the particles has to be further decreased in order to enhance endocytosis performance. ZIF-90 then displayed a successful drug delivery outcome [59]. As a result of its porous structure, stimuli-responsive

behavior, tunability, and biocompatibility, ZIFs have excellent drug transport capabilities. ZIFs are strong candidates for the creation of cutting-edge drug delivery systems that provide controlled release, targeted therapy, and increased effectiveness in the treatment of a variety of illnesses because of these attributes.

#### 5. THERANOSTIC

ZIFs have intriguing theranostic qualities that make them a flexible platform for applications that mix therapeutic and diagnostic uses. The term of "theranostics" refers to the fusion of therapeutic and diagnostic capabilities into a single system that enables the simultaneous management and monitoring of illnesses [60]. For chemotherapy medicine utilization, a large dosage is required, which has serious adverse effects. Co-delivery platform of 2 distinct chemical medications based on nanoscale ZIF-90, not only minimized drug toxicity, but also produced excellent therapeutic synergy. ZIF-90 was selected as the framework for the MOFs for its large surface area and outstanding biocompatibility. This co-delivery system was created by connecting DOX to its outer layer of nanoscale ZIF-90 and simultaneously embedding 5-FU in the pores of the framework. Furthermore, the ZIF-90 framework was unstable at low pH whereas it showed greater stability at high pH. Because of the acidic environment at tumor locations, 5-FU@ZIF-90-DOX was able to deliver DOX and 5-Fu to specific cancer cells while also controlling their release [61]. Theranostic nanostructures based on genes, such as pEGFP-C1@ZIF-8 and pEGFP-C1@ZIF-8-polymer, are effective in encapsulating plasmid DNA (pDNA) and delivering genes intracellularly. The two of the foregoing included pEGFP-C1, a pDNA expressing improved green fluorescent protein. By using a biomimetic mineralization technique, pEGFP-C1 was embedded into ZIF-8 MOF for the pEGFP-C1@ZIF-8 system, having a loading content of nearly 2.5%. Additionally, in vivo antitumor studies revealed that 60 nm DOX@AZIF-8 showed a significant PET imaging result, better biosafety, significant tumor accumulation, and enhanced therapeutic efficacy in 4T1 tumor-carrying mice, opening new opportunities to create ZIFs of the ideal size for cancer theranostics [8]. Arsenic trioxide was introduced into the ZIF shell to show how the drug delivery mechanism worked. Through a postsynthetic ligand exchange, the drug was added to the framework with a loading of 53 mg of as per 1 g (or 70 mg of  $As_2O_3/1$  g). Two distinct pH levels 7.4 and 6.0 of phosphate buffered saline were used to study the drug excretion. The porous ZIF-8 shell completely and quickly disintegrated at pH 6, causing a full release of drugs. The findings of the in vitro cytotoxicity assays revealed that at moderate doses, neither the fibroblasts nor the chosen cancer cell lines were significantly harmed by the drug-free nanocarrier. For theragnostic applications,  $Fe_3O_4$ -MOF core-shell nanoparticles and  $Fe_3O_4$ -ZIF-8 are very useful [62]. PTB (photothermal bacterium) @ZIF-90/MB demonstrated preferred tumor-targeted capacity and improved photothermal tumor ablation ability. Gene therapy is self-sufficient using  $Zn^{2+}$  ions-specific DNzyme loaded ZIF-8 MOF nanoplatfoms. This Nano system demonstrated effective intracellular transport and pH-sensitive DNA

enzyme molecule release, which resulted in the DNA enzyme mediated suppression of EGR-1 and produced the mRNA cleavage-induced gene therapy. ZIF-8 nanohybrids that respond to pH for controlled cancer treatment. Fluorescein camptothecin (CPT), which has a negative charge, was electrostatically adsorbate into the ZIF-8 nanohybrids. The acidic specified target was what determined how well the pH-responsive release worked. When compared to cells untreated with CPT, the cells treated with CPT-ZIF-8 displayed more cytotoxicity. Again, the final core-shell built nanoplatfrom, known as DOX/Fe-G@Z, was created by mineralizing the DOX/Fe-G with a thin ZIF-8 MOF shell. It seems that DOX/Fe-G@Z completely reduced tumor development due to the combined effects of chemotherapy and gene therapy suggests that the nanoplatfrom allowed for MRI-guided combination chemotherapy and gene therapy treatment [7]. After loading the anticancer medication DOX, ZIF-8 NPs were employed for covering the ZrO<sub>2</sub> shell. Because of the ZrO<sub>2</sub> shell's encapsulation, ZIF-8@ZrO<sub>2</sub> exhibited negligible toxicity to L929 cells and mice in both in vitro and in vivo toxicity assessment outcomes. The microwave thermal impact of ZIF-8/DOX@ZrO<sub>2</sub>@IL nanocomposites have been shown to function under microwave irradiation due to the excellent microwave sensitivity of IL. In addition, T<sub>2</sub>-weighted MRI, FL imaging, and CT imaging using Fe<sub>3</sub>O<sub>4</sub>@PAA/AuNCs/ZIF-8 NPs for cancer detection and treatment were supported by in vivo anticancer experiments. NPs@ZIF-8@Au NR-DOX, a multifunctional heterodimer based on ZIF-8 and many NPs, is used for OI, CT, and photoacoustic imaging (PAI) imaging as well as cancer treatment using chemotherapy and PTT in mice carrying HeLa tumors. NPs@ZIF-8@Au NR-DOX with a diameter of about 140 nm were created as bearers to load DOX, Ag<sub>2</sub>S, Ag<sub>2</sub>Se, or UCNPs in ZIF-8 and Au NR@PEG on the surface. Due to ZIF-8's propensity to degrade, these carriers may continually release pharmaceuticals and nanoplatfroms under acidic circumstances. Through synergetic PTT, in vivo investigations revealed that such a heterodimer has exceptional OI, PA, and CT imaging capabilities as well as a full tumor-elimination impact without overt side effects, serving as a useful benchmark for tumor treatment [8]. On the whole, ZIFs have strong theranostic qualities, giving them a suitable foundation for the creation of cutting-edge treatments that combine treatment and monitoring tasks. Their porous nature, stimuli-responsive behavior, tunability, and compatibility with diagnostic components all increase their potential to advance customized medicine and enhance patient care.

## 6. CONCLUSION

In conclusion, ZIFs have been shown to be very adaptable materials with extraordinary capabilities in the scopes of theranostics, bioimaging, drug delivery, and biosensing. They have shown to have exceptional sensitivity and selectivity and have been effectively used in the construction of biosensors for a variety of applications. ZIFs are excellent choices for academic and industrial biosensing applications due to their versatility and tunability. Due to their great stability, changeable optical and magnetic characteristics, and

capacity to contain imaging agents, ZIFs also have remarkable bioimaging capabilities, providing accurate viewing and comprehension of biological processes at the molecular and cellular levels. Due to its porous structure, stimuli-responsive behavior, tunability, and biocompatibility, ZIFs also excel in drug delivery applications, providing controlled release, targeted therapy, and increased treatment effectiveness. Overall, ZIFs have excellent theranostic properties that serve as a firm platform for the creation of sophisticated therapies that combine therapeutic and monitoring activities, eventually developing personalized medicine and enhancing patient care.

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