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Advanced porous materials for antimicrobial treatment

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Abstract
Infectious diseases are a global public health concern generated by uncontrolled uses of antimicrobials resulting in multidrug-resistant (MDR) pathogens. The antimicrobial resistance (AMR) has made explicit the ineffective action of the current medicines and vaccines. Rapid diagnosis and effective treatment are the keys to reduce the capacity of MDR pathogens spreading very fast, avoiding high socioeconomic impact, severe and prolonged illness and death. Advanced porous materials have emerged as promising alternatives to the conventional diagnoses and therapy due to their low-cost production, high biocompatibility, adjustable porous structure, large surface area, easy surface functionalization and capacity of loading high drugs amount. In this review, we first highlighted the current strategies to fight against infectious diseases. Then, we introduce the main advanced porous materials used in infectious diseases, including mesoporous silica nanoparticles (MSNs), porous silicon nanoparticles (PSiNPs), metal–organic frameworks (MOFs), covalent–organic frameworks (COFs), hydrogen-bonded organic frameworks (HOFs) and porous carbon materials. The strategies to fabricate these materials and their characterization for the application in the recent years for antimicrobial treatment is also discussed. Finally, we present an overview outlook and challenges on the future application of such materials for infectious diseases.

KEYWORDS
antimicrobial applications, Infectious diseases, organic-based frameworks materials, porous carbon materials, silica-based porous materials
1 | INTRODUCTION

Infectious diseases have been considered one of the global healthcare threats due to the overuse and misuse of antimicrobials that generate an enhancement of the multidrug-resistant (MDR) pathogens, including bacteria, viruses, fungi and parasites. The MDR occurs when the microorganism does not respond to the current antimicrobials making difficult the infections treatment. Low access to sanitation, hygiene and absence of clean water reduces the population healthcare control, rising the risk of spreading the disease until high levels of contamination, severe illness and death.\(^\text{[1–5]}\)

According to the World Health Organization (WHO), the MDR pathogens are among the top 10 health concerns worldwide, which lead to high morbidity and mortality rates. The deaths related to the MDR pathogens are estimated to reach up to 10 million of people until 2050.\(^\text{[5–7]}\) Without effective control and prevention, the MDR pathogens increase the socioeconomic impact in the endemic regions by affecting the productivity of the patients and directly the healthcare systems, prolonging their intensive care and, consequently, increasing the costs in the hospitals. In addition, medical surgeries like cesarean sections and organ transplantsations are riskier due to the absence of effective treatment of MDR pathogens.\(^\text{[5–7]}\)

Antibiotics like ciprofloxacin usually applied for urinary tract infections treatment have exhibited resistance rates by the \textit{Escherichia coli} and \textit{Klebsiella pneumoniae} of up to 92.9\% and 79.4\%, respectively. Methicillin-resistant \textit{Staphylococcus aureus} (MRSA) have made people 64\% more sensitive to severe illness and death. Resistance to antivirals like antiretroviral drugs (ARV) has been detected in people with human immunodeficiency virus (HIV), generating drug-resistant HIV pathogens. Invasive fungal infections including \textit{Candida auris} have shown fast spreading and increasing resistance to fluconazole and amphotericin B, whereas drug-resistant parasites have comprised one of the highest threats to malaria control.\(^\text{[5,8]}\)

Considering the aforementioned medical problems, porous materials appear as low-cost and tailorable structures to reduce the misuse of antimicrobials. New approaches based on functional porous materials can be an effective way to struggle against the global spread of the infectious diseases. Porous materials present several adjustable physicochemical properties, such as pore size, shape and structure, reflecting in high surface area and pore volume in addition to chemical and physical stabilities, low density and highly functional surfaces.\(^\text{[9,10]}\) Specifically, nanosized porous materials, including mesoporous silica nanoparticles,\(^\text{[11]}\) porous silicon nanoparticles,\(^\text{[12]}\) metal–organic frameworks (MOFs),\(^\text{[13]}\) covalent–organic frameworks (COFs),\(^\text{[14]}\) hydrogen-bounded organic frameworks (HOFs)\(^\text{[15]}\) and porous carbon materials\(^\text{[11]}\) have attracted great attention as advanced nanotools for biomedical applications. These porous structures can act as excellent antimicrobial platforms alone or in association with other molecules or structures. The high surface area, porosity and the easy surface functionalization may favor high interactions with the microbial membranes inducing oxidative stress, physical contact destruction, effective release of antimicrobials besides photo-induced antimicrobial activity.\(^\text{[6,16]}\)

In this review, we described the current strategies to tackle the infectious diseases like bacteria, viruses, fungi and parasites. Then, we highlighted the main advanced porous structures, including silica-based porous materials, MOFs, COFs, HOFs and porous carbon materials, and we report on the current progress towards the treatment of the infectious diseases. Taking into account the lack of currently effective treatment, further perspectives and challenges concerning the treatment of AMR pathogens are discussed at the end of this review, expecting to inspire new approaches to design precise nanomedicines based on such porous materials to fight against infectious diseases.

2 | CURRENT STRATEGIES TO FIGHT AGAINST INFECTIOUS DISEASES

Microbial diseases have been considering a high health threatening to the modern world due to the capacity of pathogenic microorganisms like bacteria, viruses, fungi and parasites to acquire MDR, leading to high mutation levels, severe infections and high mortality. As a result of AMR, the current treatment became ineffective with the infections persisting in the living beings, enhancing the risk of fast and wide spread to the others.\(^\text{[1–3,8,16]}\) Besides the antibiotics applications and some available vaccines, other current approaches are described to fight against MDR pathogens such as natural antimicrobial drugs (plant-based ones), antimicrobial peptides (AMPs), phages and metal-based nanoparticles (Figure 1).\(^\text{[8,17,18]}\)

Plants can produce phytochemicals that are small molecules essential in the growth but also in their protection against pathogenic microorganisms. These compounds are known as secondary metabolites and have been studied for their potential application as anti-inflammatory,\(^\text{[19,20]}\) anti-oxidant,\(^\text{[19,20]}\) anti-cancer,\(^\text{[21–24]}\) and antimicrobials.\(^\text{[17,24–26]}\) Flavonoids, alkaloids, tannins, saponins, cardenolides, terpenoids, and phytosteroids are the most of promising source of natural-based drugs.\(^\text{[22–24]}\) These plant-based compounds associated with antibiotics have shown synergistic antimicrobial therapy due to their mechanisms of action like inhibition of enzymes...
FIGURE 1 Current strategies applied for antimicrobial infection control. Created using Biorender.com.

that inactivate drugs and the inhibition of active sites modification in MDR pathogens.\[22–24\] Other important mechanisms comprise the permeability enhancement, cell membrane lysis, imbalance of intracellular metabolism, inhibition of efflux pumps, increased ions flow, and inhibition of DNA/RNA transcription.\[22–24\] Although several secondary metabolites have been reported in literature, only few of them have been approved by the Food and Drugs Administration (FDA), such as paclitaxel, reserpine, colchicine, codeine, and capsaicin.\[17,22–26\] Few FDA approval may be attributed to their issues like poor aqueous solubility, low bioavailability and specificity.\[17,22–26\]

AMPs are also a current approach to tackle infectious diseases. They are biomacromolecules composed of 10–50 amino acids that are capable of combating MDR pathogens by blocking intracellular targets or provoking extracellular imbalance leading to cell lysis and death.\[17,27,28\] The presence of amino acids with high positive charges and the α-helix and β-sheet stable structures make AMPs potential choice for clinical antimicrobial therapy.\[8,29\] Despite being an alternative to the commercial antimicrobials, AMPs therapeutic are still limited due to their low metabolic stability, poor pharmacological properties besides their expensive production. Chemical modifications and association with carriers are important approaches to overcome these problems and improve AMPs application.\[17,27,28\]

Phages are another approach to combat MDR pathogens. They are viruses that can target bacteria and act effectively against biofilms, encoding enzymes that can infect and disrupt the cell wall.\[17,30\] Bacteriophages show fast and selective action against bacteria besides low probability to generate resistant pathogens. The efficacy of phage therapy application has been described in preclinical and also clinical cases make them personalized tools to fight against MDR bacteria.\[17,30,31\] The disadvantages of this potential therapy are the antiphage defense system and the restriction mutation of phages.\[17,32\]

Nanoparticles (NPs) are the most versatile and appealing materials to fight against infectious diseases. They exhibit unique physicochemical properties that can be adjustable according to the demand. The antimicrobial activity of the NPs depends on their size, morphology, surface charge and possible interaction with the microbial pathogens.\[8,17,33\] Current, several metal-based NPs like silver, gold, copper, copper oxide, iron oxide, titanium dioxide, zinc oxide, and so on, have been explored for antimicrobial applications in textiles, contaminated water, food industry, biomedicine and so on.\[8,17,33\] Destabilization and destruction of cell membrane, reactive oxygen species (ROS) generation, disruption of electron transfer chains, metabolic pathway interference, inhibition of DNA or RNA replication, and promotion of cell apoptosis have been described as NPs action mechanisms against microbials.\[8,17,33,34\] However, the metal-based NPs application remain a challenge regarding to their bio-compatibility and efficacy for diseases treatment. More and deeper in vivo studies and the association of theses nanoparticles with multifunctional carriers are essential to improve their applicability and reduce possible side effects.\[8,17,33\]

Despite the prevention, treatment available and the current approaches to combat MDR pathogens, most of them lack of good bioavailability and targeting function against infectious diseases. In light of this, besides the need of more surveillance programs and government intervention, research towards multifunctional porous materials and new formulations design are essential for early diagnostics and effective infectious disease treatment.

3 | ADVANCED POROUS MATERIALS

Porous materials are networks of periodic or non-ordered pore structure or voids exhibiting low density and high specific surface area. The porous materials can be classified according to the their pore sizes including microporous (smaller than 2 nm), mesoporous (from 2 to 50 nm) and macroporous (from 50 to 1000 nm).\[19,10\] These unique characteristics allied with the tunable pore size, shape, composition and high surface functionality make them current and potential materials for several applications in catalysis,\[35,36\] energy storage\[37–39\] and
biomedical[12,40–42] fields. Table 1 depicts some current advanced porous materials as antimicrobial agents.

3.1 | The bioinspired nanostructures and size, shape and porosity impact on antimicrobial activity

The design of bioinspired nanostructures has emerged as a potential antimicrobial material to fight against pathogenic microorganisms.[43,44] The high surface area, hydrophilicity or hydrophobicity, well-organized and flexible nanostructures from plants and insects’ origin show antimicrobial action by physical contact and adhesion to certain microorganism’s cell walls disrupting them and provoking the microorganism’s death.[43,44] The antimicrobial action of pristine nanostructures depends on their parameters such as size, shape and porosity.[10,45] The size and shape of the nanostructures can affect the interaction with the microorganisms. Surface roughness can increase the physical contact and adhesion to the bacterial wall altering their membrane surface tension generating damage.[43,44,46] Distinct pore size and structure from advanced nanomaterials impact directly in their specific surface area and the loading and delivery of antimicrobial drugs.[45–47] In general, the pore size can be tuned according to the kind of template or ligands used to fabricate the porous structures. Small pore size materials can load small molecules and promote sustained release. Large pore size favors the loading of high drugs amount but also provide fast drug release.[45–47] The pores structures can also affect the drug release rate. Interconnected and non-organized pores structures can provide faster drug release than organized pores structures.[45–47] However, most of the pristine bioinspired and porous nanostructures do not show 100% efficacy against biofilms and MDR pathogen, which can be improved by exploring their surface chemistry to reach smart and targeted porous materials for efficient antimicrobial treatment.

Abbreviations: MIC, minimum inhibitory concentration; MSN-C and MSN-R, Calcinated and refluxed mesoporous silica nanoparticles; LYC-loaded MSNs, Lycopene-loaded mesoporous silica nanoparticles; NF-MSNs, non-functionalized-mesoporous silica nanoparticles; AF-MSNs, after functionalized-mesoporous silica nanoparticles; NF-MSN/VA and AF-MSN/VA, vancomycin-loaded non-functionalized and functionalized mesoporous silica nanoparticles; PSI NPs, porous silicon nanoparticles; PSI NPs-VA, vancomycin-loaded porous silicon nanoparticles; CARG-PSI NPs-VA, 9-amino acid cyclic peptide CARGGLKSC functionalized vancomycin-loaded porous silicon nanoparticles; F-siRF5, small interfering ribonucleic acid-loaded fusogenic porous silicon nanoparticles; F-siRF5-CRV, C-Ahx-CRVLRSGC peptide conjugated small interfering RNA-loaded fusogenic porous silicon nanoparticles; T-705@MSN, favipiravir-loaded mesoporous silica nanoparticles; T-705@MSN-RVG, a glycopeptide of the rabies virus functionalized favipiravir-loaded mesoporous silica nanoparticles; Ag$_2$(HBTC)[im], silver ions-contained metal–organic frameworks; Ag$_2$(HBTC)[im]-Polyactic acid (PLA) fibrous mat, silver ions-contained metal–organic frameworks into the polyactic acid-based polymer; Ag@MOF, silver nanoparticles-contained cyclodextrin metal–organic framework; Ag@MOF@PDA NPs, polydopamine-coated silver nanoparticles-contained cyclodextrin metal–organic framework; MOF@PDA, polydopamine-coated cyclodextrin metal–organic framework; AgNPs, silver nanoparticles; COF TGTP, guanidyl cation-contained covalent–organic framework; Ag/COF TGTP particles, silver nanoparticles-anchored guanidyl cation-contained covalent–organic framework; DhaTph–, porphyrin-based covalent-organic frameworks; IBU@DhaTph–, ibuprofen-encapsulated porphyrin-based covalent-organic frameworks; HOF-101-F@PVDF-HFP and HOF-101-H@PVDF-HFP, hydrogen-bonded organic framework-contained poly(vinylidene fluoride-co-hexafluoro-propylene) nanofibers; PFC-33, anionic hydrogen-bonded organic frameworks; polyHOF, anionic hydrogen-bonded organic frameworks co-polymerized with α,ω-diacyloyl poly(ethylene glycol); RHPC, rice husk based porous carbon; RH-Ag, silver nanoparticles-loaded rice husk based porous carbon; N/A, not applicable; LED, light-emitting diode.

3.2 | Silica-based porous materials (MSNs and PSiNPs)

Despite various porous materials currently available for therapeutic purposes, the silica-based ones exhibit excellent biocompatibility, low immunogenicity and cheap production. Its controllable physicochemical characteristics like high surface-to-volume ratio, large pore volume and surface area can positively influence its biological behavior and increases its loading capacity. As a result, small and large molecules can be adsorbed onto or delivery from these materials. Additionally, its tunable morphology, size and pores structure can maximize cellular uptake and biomedical applications.[60–62] It is also worth mentioning that the silan group (-Si-OH) available onto its porous/surface allow the functionalization with targeting ligands and stimuli-responsive gatekeepers, making
TABLE 1 Application of the advanced porous materials as antimicrobial agents.

<table>
<thead>
<tr>
<th>Porous material type</th>
<th>Size</th>
<th>In vitro antimicrobial effect</th>
<th>Materials injection dosage</th>
<th>In vivo antimicrobial effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcinated and refluxed MSNs (MSN-C and MSN-R, respectively) and LYC-loaded MSNs</td>
<td>Average particle size of 70 nm</td>
<td>MIC value for Clinical-azole resistant strain were 500 µg mL⁻¹ for MSN-C and LYC whereas no activity were detected for MSN-R and MSN@LYC For ATCC 18804 strain the MIC were 500 µg mL⁻¹ for MSN-C and LYC, 1000 µg mL⁻¹ for MSN-R, and no activity was observed for MSN@LYC</td>
<td>N/A</td>
<td>N/A</td>
<td>[54]</td>
</tr>
<tr>
<td>NF-MSNs, AF-MSNs, NF-MSN/VA and NF-MSN/VA</td>
<td>NF-MSNs, AF-MSNs and NF-MSN/VA exhibited average size of 160, 165 and 179 nm, respectively</td>
<td>MIC value: NF-MSN: 500 µg mL⁻¹; AF-MSN: 125 µg mL⁻¹; NF-MSN/VA: 15.6 µg mL⁻¹; AF-MSN@VA: 3.9 µg mL⁻¹</td>
<td>N/A</td>
<td>N/A</td>
<td>[49]</td>
</tr>
<tr>
<td>PsiNPs, PSiNPs-VA and CARG-PSiNPs-VA</td>
<td>Average size of 180 nm</td>
<td>From S. aureus model the dosage of free VA were 9 and 15 mg kg⁻¹. For the CARG-PSiNPs-VA the dosage was 1 mg kg⁻¹</td>
<td>N/A</td>
<td>N/A</td>
<td>[50]</td>
</tr>
<tr>
<td>PSiNPs, F-siIRF5 and F-siIRF5-CRV</td>
<td>Average size of the PSiNPs, F-siIRF5 and F-siIRF5-CRV were 50, 75 and 225 nm, respectively</td>
<td>For 100 and 145 mg kg⁻¹ for the vancomycin and tobramycin (both controls) and 100 mg kg⁻¹ for all nanosystems</td>
<td>N/A</td>
<td>MRSA model: F-siLuc-CRV over 1 × 10¹⁰ CFU g⁻¹; free VA and NF-siIRF5-CRV: &gt; 1 × 10⁹ CFU g⁻¹ and F-siIRF5-CRV: &lt; 6 × 10² CFU g⁻¹ Pulmonary model: tobramycin, F-siLuc-CRV and NF-siIRF5-CRV: all showed &gt; 1 × 10⁹ CFU g⁻¹; F-siIRF5-CRV: 1 × 10² CFU g⁻¹,</td>
<td>[51]</td>
</tr>
<tr>
<td>MSN, T-705@MSN and T-705@MSN-RVG</td>
<td>MSN, T-705@MSN and T-705@MSN-RVG with average size of 120, 168 and 238 nm, respectively</td>
<td>T-705 reduced virus titer from 6 Log FFU mL⁻¹ to 1.5 Log FFU mL⁻¹</td>
<td>The dosage of T-705@MSN-RVG was 2 mg mL⁻¹</td>
<td>The survival of mice treated with the T-705@MSN-RVG where higher (77%) when compared with the infection control (only 23%)</td>
<td>[52]</td>
</tr>
<tr>
<td>Ag₂[HBTC][im] and Ag₂[HBTC][im]-Polyactic acid (PLA) fibrous mat</td>
<td>Average size of 500 and 600 nm for Ag₂[HBTC][im] and Ag₂[HBTC][im]-Polyactic acid (PLA) fibrous mat, respectively</td>
<td>More than 95% bacterial growth inhibition rate for against E. coli and P. aeruginosa (Gram-negative) or S. aureus and M. smegmatis (Gram-positive bacteria)</td>
<td>N/A</td>
<td>The wound healing ratio can be up 99.9%, which indicated the excellent antibacterial capacity of the Ag₂[HBTC][im]-Polyactic acid (PLA) fibrous mat</td>
<td>[53]</td>
</tr>
<tr>
<td>Ag@MOF, MOF@PDA and Ag@MOF@PDA NPs</td>
<td>The hydrodynamic particle sizes of Ag@MOF, MOF@PDA, and Ag@MOF@PDA were 152.7, 206.8, and 208.2 nm, respectively</td>
<td>Near infrared (808 nm) laser-mediated combination therapy killed more than 95% of the bacteria and eradicate 96% of the biofilm biomass (at 500 µg mL⁻¹ for all nanosystems)</td>
<td>N/A</td>
<td>The combined therapy can eliminate the bacterial-infection-induced biofilm and effectively ablate the bacterial, achieving better and faster wound healing with minimal biotoxicity</td>
<td>[54]</td>
</tr>
<tr>
<td>AgNPs, COF₁₉₇₅P and Ag/COF₁₉₇₅P particles</td>
<td>The average size of AgNPs, COF₁₉₇₅P and Ag/COF₁₉₇₅P particles were about 200, 850 and 950 nm, respectively</td>
<td>The inhibition rate of Ag/COF₁₉₇₅P for Staphylococcus aureus and Escherichia coli were 100% (50 and 100 µg mL⁻¹ for S. aureus and E. coli, respectively). The average hemolysis rate was less than 5% for the Ag/COF₁₉₇₅P, suggesting good biocompatibility</td>
<td>N/A</td>
<td>N/A</td>
<td>[55]</td>
</tr>
</tbody>
</table>

(Continues)
possible to design multifunctional and targeted therapeutic approaches to reduce drug side effects and improve its efficacy for diagnosis and therapy.\textsuperscript{[61]}

In light of this, mesoporous silica nanoparticles (MSNs) and porous silicon nanoparticles (PSiNPs) comprise the most studied porous materials for biomedical applications.\textsuperscript{[62]} While MSNs are formed by a porous network inside a silicon oxide matrix, PSiNPs consist of the crystalline silicon skeleton traversed by nanosized pores, those crystalline silicon domains act as quantum dots, conferring intrinsic photoluminescence to the PSiNPs.\textsuperscript{[63,64]} Moreover, MSNs are currently produced by bottom-up approach whereas PSiNPs fabrication occur mainly by the top-down one.\textsuperscript{[60,64]}

Although MSNs are commonly synthesized by modified Stöber method (a sol–gel method), the aerosol-assisted synthesis, soft templating (single micelle templating, microemulsion templating and vesicle templating) and hard templating (metal or metal oxide nanoparticle encapsulated MSNs and polymer bead templating) are currently applied for their fabrication.\textsuperscript{[1,65]} For PSiNPs production, electrochemical anodizing and stain etching are the most used ones, followed by other approaches like chemical vapor etching, chemical stain etching, laser-induced etching, reactive ion (plasma) etching, metal-assisted etching and, spark processing.\textsuperscript{[64,66,67]} Although there are few reports in the literature, PSiNPs can also be synthetized by bottom-up approach despite the easy oxidation and hydration of the Si precursors.\textsuperscript{[66]}

It is worth highlighting the surface chemistry of both nanoparticles, which make them versatile porous materials for the antimicrobial applications. As previously mentioned, MSNs display silanol groups onto their surface, ready for binding or interaction with specific molecules improving their range of application.\textsuperscript{[60,68]} Moreover, the native PSiNPs have an anodized surface containing Si hydrides groups (\(-\text{Si-H}_x, x = 1–3\)), which confer a wide control of surface chemistry via several methods of modification. Thermal oxidation, thermal carbonization and hydrosilylation processes can be performed to reach more
FIGURE 2 (A) Schematic representation of the MSN@LYC application process in the larvae; Kaplan-Meier survival curve of G. mellonella larvaefor MSN-C (B) and MSN-R (C).\(^{[48]}\)

stable, hydrophilic or hydrophobic PSiNPs for a broad range of applications from optoelectronics devices to biomedical purposes.\(^{[60,64,69]}\)

3.2.1 Mesoporous silica nanoparticles (MSNs)

As a result of the major problem in the treatment of vulvovaginal candidiasis (VVC) related to the growing resistance to common antifungals used in therapy, our research group evaluated the potential of Lycopene (LYC)-loaded MSNs (MSN@LYC) (Figure 2A), a carotenoid extracted from tomatoes, against VVC disease. In this study, the MSNs were synthesized by the modified Stöber method followed by two distinct methods of purification; acid reflux (MSN-R) and calcination (MSN-C). In the minimum inhibitory concentration (MIC) used to evaluate the in vitro antifungal activity, both MSN-R and MSN-C showed some antifungal activities, which make them attractive vehicles for the VVC and other antifungal treatment. In addition, these results suggest that the nanocarriers are used to potentialize antifungal drugs via synergistic effect against fungal diseases. Through the minimum fungicide concentration (MFC) determination, both nanosystems also displayed fungistatic action. Finally, the toxicity of both bare nanoparticles was evaluated in an alternative in vivo model in Galleria Mellonella larvae and the evaluated dosage range (2000–125 mg kg\(^{-1}\)) did not cause death or toxicity (Figure 2B,C). These findings make the MSNs potential nanotools for further antifungal studies and treatment.\(^{[48]}\)

Combating biofilms formation in medical devices is also a challenging issue since it is a virulence factor that can lead to the development of drug resistance. In order to prevent biofilms formation in bone implants, Rahaman et al.\(^{[49]}\) also developed mesoporous silica-based nanosystems. The nanoparticles were synthesized
by the Stöber method and amino-functionalized with 3-aminopropyltriethoxysilane (APTES). According to the authors, the APTES-modified MSNs not only increases the vancomycin (VA) encapsulation efficiency but also acted as targeting ligand for improving electrostatic interactions with the negatively charged bacterial cell membrane. The dynamic light scattering (DLS) analysis confirmed that after the functionalization, the MSNs were positively charged with around +30.5 mV. After VA loading, the ZP was +33.3 mV. The non-functionalized MSNs (NF-MSNs), functionalized MSNs (AF-MSNs) and VA-loaded functionalized MSNs (AF-MSN/VA) exhibited average hydrodynamic size of 160.6, 165.1 and 179.1 nm, respectively. Additionally, Fourier transformed infrared spectroscopy (FTIR) analysis depicted the characteristic bands of the silica network for all samples, and, for AF-MSNs peaks at 1360, 1630 and 1520 cm$^{-1}$ were assigned to C-N stretching, and NH$_2$ deformation, respectively, which indicated that functionalization was achieved satisfactorily. These results were corroborated by energy-dispersive X-ray spectroscopy since the AF-MSNs displayed higher amounts of nitrogen and carbon when compared to the NF-MSNs. Cytotoxicity studies were performed for four types of nanosystems; non-functionalized and functionalized MSNs (NF-MSNs and AF-MSNs, respectively) and VA-loaded non-functionalized and functionalized MSNs (NF-MSN/VA and AF-MSN/VA, respectively) using MG-63 cells. According to the results, the APTES functionalization provided better biocompatibility for the MSNs, since the survival of cells treated with the AF-MSNs were significantly higher than NF-MSNs in all evaluated conditions. Additionally, the in vitro antibacterial activity against *Staphylococcus aureus* using AF-MSN/VA (MIC value of 3.9 µg mL$^{-1}$) displayed better activity in preventing and combating biofilm when compared to the NF-MSN/VA (MIC value of 15.63 µg mL$^{-1}$). The results suggest that the fabricated functional AF-MSN/VA are nanotools for preventing infections in post-implant surgeries.

In order to circumvent the limitation of drug delivery through the blood-brain barrier (BBB) to combat neurotropic viruses like rabies virus, poliovirus and Zika virus, Ren et al.$^{[52]}$ developed packaging favipiravir (T-705)-loaded MSNs functionalized with a glycopeptide of the rabies virus (RVG). The average size of the nanosystems was verified during its manufacture by transmission electron microscopy (TEM) analysis. The results showed that MSN, T-705@MSN and T-705@MSN-RVG with average size of 120, 168 and 238 nm, respectively. In in vitro cytotoxicity tests performed in neuroblastoma cells, at concentrations lower than 2 mg mL$^{-1}$ of the T-705@MSN-RVG, no significant difference in viability was detected. In an in vivo model of vesicular stomatitis virus infection, from brain sections analyzed by fluorescence microscopy, the T-705@MSN-RVG was delivered into the brain of mice, with the same cellular distribution as the virus. As for therapeutic efficacy, a significant difference was observed in the survival of mice treated with the T-705@MSN-RVG (77% of survival) when compared with the infection control group (only 23% of survival). Moreover, the authors evaluated changes in inflammation and viral load through CD45 detection and a lower intensity was observed in the group treated with the T-705@MSN-RVG and a decrease in viral RNA in the brain regarding to the infection control group. In view of these results, the authors considered the T-705@MSN-RVG a promising platform for the treatment of neurotropic viruses.

### 3.2.2 Porous silicon nanoparticles (PSiNPs)

In order to get around the antimicrobial resistance issue, Hussain et al.$^{[50]}$ synthesized PSiNPs by electrochemical etch and subsequently incorporated vancomycin (VA) through self-sealing method, resulting in the formation of calcium silicate, trapping the drug without changing the particle structure. From the TEM images the authors observed that before the self-sealing process the particles showed open porosity, while after this process the porous structure was more occluded, with thicker pore walls, suggesting that the reaction with calcium ions occurred. Firstly, 9-amino acid cyclic peptide CARGGLKSC (CARG) was screened by phage display in *S. aureus*-induced pneumonia in an in vivo model as a targeting agent to achieve functional PSiNPs for antimicrobial purposes. The VA-loaded PSiNPs was modified with 3-(ethoxydimethyl)-propylamine and then functionalized by maleimide chemistry aiming to bind the CARG to the PSiNPs-VA. The use of CARG as a targeted ligand increased the PSiNPs-VA activity besides reducing the required dose and consequently decreasing the side effects, since 1 mg kg$^{-1}$ of PSiNPs-VA was 100% effective, compared to 9 mg kg$^{-1}$ of free VA, which was only partially effective. It is worth mentioning that the CARG-PSiNPs-VA proved to be specific to *S. aureus* in vitro, but not to the *P. aeruginosa*. In addition, the in vivo tests carried out in mice showed the accumulation of the CARG-PSiNPs-VA in the lungs and skin of infected animals, but not in tissues infected by *P. aeruginosa*. Furthermore, CARG-PSiNPs-VA in vivo activity was superior in suppressing infections (100% of recovery) when compared with the PSiNPs-VA and free VA (33% of survival). In conclusion, the choice of specific peptides and their association with antibiotics-loaded PSiNPs can improve the biocompatibility and efficacy of the multifunctional nanocarriers for a broad of infectious diseases treatment.

In order to avoid MDR, Kim et al.$^{[51]}$ described an interesting approach to design immunotherapeutic...
nansystems aiming to prevent antimicrobial mutations. In this sense, the authors synthesized PSiNPs (by electrochemical etching) and promoted the incorporation of siRNA inside the porous structure. The fusogenic nanosystem was achieved by coating the siRNA-PSiNPs with lipid structure using 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC), 1,2-distearoyl-sn-glycerol-3-phosphoethanolamine-polylethylene glycol (DSPE-PEG), and 1,2-dioleoyl-3-trimethylammonium-propane (DOTAP). The maleimide-terminated nanoplatform was conjugated to the CRV peptide (C-Ahx-CRVLRSGSC) to target macrophages in the infection site (Figure 3A). The multifunctional nanosystem proposes to deliver siRNA against the irf5 gene, stopping pro-inflammatory signals in the M1 phenotype. From DLS analysis, the PSiNPs, F-siIRF5 and F-siIRF5-CRV exhibited average hydrodynamic size of 50, 75 and 225 nm, respectively, confirming the PSiNPs modification. The silencing effect in J774a.1 macrophages in vitro of the F-siIRF5-CRV and F-siIRF5-CRV were 86% and 45%, respectively (Figure 3B). Moreover, the time of silencing effect was also evaluated 7 days post-transfection in J774a.1 macrophages (Figure 3C). The degree of gene expression increased from 55% to 90% for NF-siIRF5-CRV whereas for the F-siIRF5-CRV the gene expression was below 50%, increasing from 14% to 37%. These results

![Figure 3](https://onlinelibrary.wiley.com/doi/10.1002/nano.202300114)
indicate that the multifunctional F-siIRF5-CRV nanosystem was more effective and need less often dosing than the other ones. The engineered nanosystem not only induced 80% of gene silencing in activated macrophages in an in vivo methicillin-resistant *S. aureus* (MRSA) muscle infection experiment performed in Balb/C mice but also showed the excessive inflammatory response, improving the therapeutic outcome in vivo (Figure 3D). In addition, a *P. aeruginosa* pneumonia model was carried out with the same type of animal and the results were in accordance with the previous one (Figure 3E). Additionally, in both models the developed nanosystem significantly reduced the number of CFUs. From the model with MRSA, the non-fusogenic nanosystems showed more than $1 \times 10^9$ CFU g$^{-1}$, whereas the fusogenic one presented fewer than $6 \times 10^2$ CFU g$^{-1}$. In the pulmonary model, while the non-fusogenic nanosystem displayed fewer than $1 \times 10^{12}$ CFU g$^{-1}$, the fusogenic one showed $1 \times 10^2$ CFU g$^{-1}$. In view of this, the authors concluded that the engineered nanosystem was able to significantly reduce the expression of the irf5 gene in macrophages, which significantly improved the therapy, regardless of the strain used, making this a promising approach for infectious disease treatment.

### 3.3 Metal-organic frameworks (MOFs)

MOFs are a series of compounds based on the formation of metal ions or metal clusters and their coordinated organic ligands.\[70,71\] This particular and long-range ordered structure endows MOF-based materials unique characteristics, such as the tunable porous channels, the outstanding biodegradation or the multiple spatial shapes.\[72,73\] Meanwhile these characteristics prosper the studies and applications of MOFs in many different research fields, for example, water treatment,\[74,75\] energy storage,\[76,77\] sensors,\[78,79\] electrocatalysis.\[72,80,81\] Furthermore, with the development and other discovered merits,\[82-84\] for example, excellent biocompatibility and biodegradability, non- or low-toxicity and controlled morphology size, and easy surface modification, they have been widely applied in biomedical research,\[85-87\] such as drug delivery,\[88,89\] cancer therapy\[82,90\] and especially, antibacterial.\[84,91\]

Metal-based or Metal ions-based materials, represented by Ag or Ag$^+$, are one of the most well-known and investigated agents against the bacterial.\[84,87,92\] Therefore, as a metal ions-based materials, MOFs have natural and pronounced antibacterial properties.\[13,73\] Besides the mentioned Ag$^+$-based MOFs, such as the Zn$^{2+}$-based MOFs, Cu$^{2+}$-based MOFs, Fe$^{3+}$/Fe$^{2+}$ MOFs also have been studied for their antibacterial effect.\[13,91\] In generally, the antibacterial effects of the released metal ions from the MOFs, which can be the inherent ions or loaded ions, can be ascribed to following reasons:\[93\] (1) The exterior metal ions can interact with bacterium membranes and then induce the cell membrane disruption; (2) The intracellularly entered metal ions can inactivate the intracellular proteins, cause Deoxyribonucleic Acid (DNA) damage, impede the metabolism, or induce the generation of the reactive oxygen species (ROS);\[73\] (3) In addition to the metal ions, some special organic ligands with antibacterial effect, for example, imidazole\[94\] or hydrazine benzoate,\[95\] can be another fundamental building block to form the MOFs against bacterium.\[91\] Similar to inherent metal ions, with the degradation of MOFs, the antimicrobials can be released and kill the bacterial; (4) Besides, the porous structure and the high porosity give MOFs capacity to load the antibacterial agents, no matter another metal ions or antibacterial molecules, working as a therapeutic agents carrier.\[96\] The loaded agents can be controlled released upon the stimulus after the adjustable modification; and (5) Some of the MOFs can be used as photosensitizer to generate the ROS for the antibacterial effect.\[93\] Below we list two typical specific research to illustrate the antibacterial effect of MOFs.

To avoid the possible side effects from the excessive antibiotic abuse, Zhang et al. utilized the silver ions-MOFs with the capacity to gradually release strongly antibacterial Ag$^+$ ions to replace the antibiotics as the antibacterial agent to develop an antibacterial wound dressing, Ag$_2$[HBTC][im]-Polyactic acid (PA) fibrous mat.\[53\] This synthesized fibrous mat was prepared by the electrospinning technology, which can easily embed and the silver ions-MOFs into the PA-based polymer. Furthermore, as the matrix materials of the wound dressing, the biocompatible PA polymer not only can prevent the easy detachment of the MOFs and also can help accelerate the wound exudates absorption and hemostasis. The characterization results showed the prepared fibrous mat processes excellent water and thermal stability, up to 300°C. The in vitro antibacterial experiments indicated that the electrospun fibrous mat has outstanding broad-spectrum antibacterial effect, no matter against the Gram-negative or Gram-positive bacterial, with more than 95% bacterial growth inhibition rate (Figure 4A–D). Moreover, the in vivo exponential results showed that as an antibacterial wound dressing, the wound healing ratio can be up 99.9%, much higher than other comparison groups, which indicated the excellent antibacterial capacity of the slowly released silver ions and the resemble structure to the extracellular matrix. This fabricated fibrous mat provides an important reference for the development of subsequent antibiotic-free wound dressing.

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**FIGURE 4** In vitro and in vivo antibacterial effect of the MOFs-based therapeutic platforms. A, Growth curve of 1-PLA against *Escherichia coli*. B, Growth curve of 1-PLA against *Pseudomonas*. C, Growth curve of 1-PLA against *Staphylococcus aureus*. D, Growth curve of 1-PLA against *Mycobacterium smegmatis*. E, In vivo antibacterial process timeline and the representative pictures of the infected wounds healing process during the treatment. F, IL-6 and TNF-α levels in the serum during the treatment. G, In vivo antibiofilm process timeline and the representative pictures of the biofilm infected wounds healing process during the treatment. Reprinted with permission.[53,54] Copyright 2020 and 2023, Elsevier and John Wiley and Sons, respectively.
The mature biofilm and antibiotics abuse are two of the main reasons of the bacterial drug-resistance growth, among which the biofilm can work as the bacterial protector by limiting the penetration depth of the antibacterial agents, possibly increasing the drug-resistance or finally causing the failure of antibacterial agents, such as the antibiotics and the metal ions. To develop an innovative therapeutic system which can eradicate the biofilms and kill the bacterial effectively, He et al. fabricated ultrafine silver nanoparticles (NPs)-contained cyclodextrin MOFs and then encapsulated the polydopamine (PDA) as coating shell to form the Ag@MOF@PDA NPs with photothermal effect. The experimental results showed that under 808 nm laser irradiation, the synthesized MOFs-based NPs can effectively converted light energy into heat energy with 36.7% photothermal conversion efficacy. Then these NPs generate local hypothermia to disrupt the biofilm integrity and controllably accelerating the release of the silver ions into the effective concentration and penetrating deeper against bacterial, enabling synergic photothermal/chemical antibacterial effect. The in vitro experimental results showed that with laser-mediated combination therapy, 76% biofilm biomass and 95% bacterial were eradicated or killed and the temperature-induced silver ions also promoted the ROS generation. Moreover, the in vivo experiments showed that the combined therapy can significantly eliminate the bacterial-infection-induced biofilm and effectively ablate the bacterial, achieving better and faster wound healing in a biosafe way (Figure 4E–G).

3.4 | Covalent–organic frameworks (COFs)

Unlike the MOFs, COFs are constructed on the covalent bonds between the light elements, such as C, H, O and N. Normally, compared with most MOFs, the stability of COFs is higher due to the strong connection between the organic ligands. Even in an acid condition, pH from 1 to 5, some COFs still can keep stable. In addition, due to their high hydrolytic stability, COFs can be recycled and then reused with normal purification process, for example, centrifuge or filtration. Meanwhile, similar to MOFs, COFs have very organized and periodic structure makes them crystalline and tunable, which enables the possibility to control and endow the composition and multi functions in the predictable method during the COFs design. Moreover, the high porosity and large surface area entitle the COFs applications in biomedicine, such as cancer treatment, drug delivery, biosensing and antimicrobial. As for the antibacterial research, especially for the antibiotic-resistant bacterial, although in the COFs construction, normally no metal ions are involved, but some organic ligands, which are capable to link to metal ions can be introducted into the composition of the COFs skeleton, such as porphyrin or bipyridine, for fighting against bacterial. Besides the loaded metal ions, the porous structure also allow the COFs to load or encapsulate other antibacterial agents, such as antibiotics. Additionally, many COFs with conjugation system also can fabricated as photocatalytic agents for the light-induced photothermal or photodynamic antibacterial applications, for example, porphyrin-based COFs, boron-based COFs or acridine-based COFs.

The agglomeration and decomposition of the Ag NPs caused by the high surface energy, the antibacterial effect will be lessened and the burst release of the silver ions also can be cytotoxic, rising the health risk. To avoid this problem and prolong the stability of the single Au NPs, Zhang et al. used the guanidyl cation-contained COFs to deposit and anchor the Ag NPs, forming the Ag/COF@TGTP particles for antimicrobial research (Figure 5A). The characterization results showed that the COFs as carrier can improve the AgNPs stability, better the water dispersion and then guarantee the AgNPs biosafety. Moreover, the cationic COFs as the AgNPs carrier and matrix material can sustainably release the silver ions and also facilitate the adherence of the Ag/COF@TGTP to Gram-negative bacterial. The in vitro antibacterial results showed that no matter to Gram-positive or Gram-negative bacterial, the synthesized Ag/COF@TGTP have excellent antibacterial efficiency (Figure 5B,C). To Escherichia coli, inhibition rate of Ag/COF@TGTP (100 µg mL$^{-1}$) was 100% and to Staphylococcus aureus, inhibition rate of Ag/COF@TGTP (50 µg mL$^{-1}$) was 100%, both better than comparison groups, achieving broad-spectrum antibacterial effect. Ding et al. fabricated a self-standing, flexible and robust porphyrin-based COFs membrane encapsulated ibuprofen (so-called IBU@DhaTph membrane), and then the derived band-aid like dressing combined with hollow medical tape was also prepared for wound healing. The aims was to develop a new wound dressing that processes both high antibacterial effect and also can be used for anti-inflammation to help accelerate the wound healing, based on the drug loading capacity of COFs and via interfacial polymerization and impregnation. The experimental results showed that the ibuprofen can be released controllably at body temperature. Meanwhile, under visible light or natural sunlight irradiation, ROS were generated with high efficiency, indicating the photodynamic function of the COFs-based membrane. The in vitro antibacterial experiments demonstrated that after illumination, the fabricated membrane exhibited excellent synergistic photodynamic/chemical antibacterial effect and the anti-inflammatory effect whether with or without light.
FIGURE 5 Antibacterial effect of the COFs-based therapeutic platforms. A, Scheme of the Ag/COF\textsubscript{TGGP} particles preparation. B, In vitro \textit{E. coli} counting experiment of the AgNPs, COF\textsubscript{TGGP} and Ag/COF\textsubscript{TGGP}. C, In vitro \textit{S. aureus} counting experiment of the AgNPs, COF\textsubscript{TGGP} and Ag/COF\textsubscript{TGGP}. D, Representative pictures of the Staphylococcus aureus infected wounds healing process during the in vivo antibacterial treatment process. (E) \textit{S. aureus} infected wounds size curve during the in vivo antibacterial treatment process. F, The survival rate of the derived \textit{S. aureus} from the infected wounds. Reprinted with permission\textsuperscript{[55]} Copyright 2022, Elsevier B.V.
After 3 hour of visible light irradiation, the *Staphylococcus aureus* and *Escherichia coli* survival rates were 4.3% and 6.2%, respectively. Furthermore, the in vivo antibacterial and wound healing experiment showed the synergistic antibacterial effect of the COFs-membrane derived wound dressing, even just upon the natural sunlight illumination (Figure 5D–F). 4 days after the bacterial infection and the combined treatments, the *S. aureus* mortality in COFs-membrane derived wound dressing reached 100% and the scar disappeared within 14 days, further exhibiting their excellent antinfec tion and tissue repair capacity.

### 3.5 Hydrogen-bonded organic frameworks (HOFs)

Besides the MOFs and COFs, another current hotspot porous materials mainly constructed by the organic ligands are HOFs, which are assembled through hydrogen bonds.[119] Similar to the previous two organic frameworks, the structure of HOFs also can be predesigned to control the needed spatial configuration. Based on that, through the introduction of the firm molecules and the composition units with hydrogen-bond, HOFs with stable, open and porous structure can obtained, which endow HOFs with high surface area and the capacity to load other agents, such as molecular drugs.[120,121] Moreover, since hydrogen-bonds are flexible and reversible, HOFs are highly crystalline and it is much easier and greener to controllably fabricate and purify HOFs when compared with MOFs or COFs, for example, simple evaporation crystallization or gas diffusion.[119] Furthermore, it is precisely because the preparation method and healing process are much easier, which makes the reproducibility and the recycling ability of HOFs higher and the single crystals cultivation and acquirement more facile.[115,120] In addition, similar to the COFs, since no metal ions are involved in the intrinsic construction, HOFs possesses an advantage in terms of density and biotoxicity.[119] Besides, the HOFs may be more suitable to develop the dynamic frameworks-based materials compared with MOFs and COFs because the weak hydrogen bond in HOFs.[122] Based on the mentioned advantages, HOFs have become the research hotspot in many fields, such as biomedicine, gas storage, sensing or catalysis.[115,123–126]

To develop new antimicrobial agents and also to avoid possible side effects of the metal ions and the abuse of antibiotics when applied against microorganism, Wang et al. synthesized a series of broad-spectrum antimicrobial nanofibers based on photoactive HOFs and poly(vinylidene fluoride-co-hexafluoro-propylene) through the simple and low cost electrospinning method.[57] These nanofibers called HOF@PVDF-HFP (including HOF-101-F@PVDF-HFP and HOF-101-H@PVDF-HFP) with uniformly embedded HOFs of rod-like nanocrystals. The characterization results indicated that the nanofibers can generate ROS under 520 nm light-emitting diode (LED) irradiation with singlet oxygen yield up to 63 mmol g⁻¹. After the ROS generation capacity was verified, the in vitro antibacterial experiments further demonstrated that under illumination for 5 minutes, more than 90% *Escherichia coli* were killed (Figure 6A). Furthermore, the following in vitro anti-virus indicated that after 10 minutes illumination, more than 90% of the *Vesicular stomatitis* and the *Herpes* viruses can be sterilized (Figure 6B). Meanwhile, the in vitro anti-fungi experiments demonstrated that under 2.5 minutes illumination, the fungitoxicity of the nanofibers to *Candida albicans* can be up to around 55% and that to *Candida auris* also can reach around 40% (Figure 6C). This work highlighted a novel way for the following antimicrobial materials development.

The new functional groups introduction into the prepared HOFs structure usually led to the formation of new hydrogen bonds, which will change the original topology and possibly cause the loss and lack of the designed rationality and functionality of the HOFs. To overcome this obstacle, Liu et al. adopted the method of directly integrating the functional groups into basic HOFs structure to prepare an anionic HOFs, PFC-33 (Figure 6D).[58] In the PFC-33 structure, porphyrin used as the photosensitizer were integrated into the backbone and a commercial quaternary ammonium biocide were incorporated as the counterions, which will interact with the ionic backbone, endowing the controlled release of the biocide. The characterization results exhibited that in the physiological environment with high ions conditions, the porosity and the electrostatic interaction can induce the release of the antibacterial agents, biocide, in a controllable way. Meanwhile, the experiments also verified that under 650 nm LED irradiation, the ROS were generated, demonstrating their capacity for the photodynamic antibacterial capacity. Furthermore, for easy and better antibacterial applications, the carboxyl groups on the PFC-33 were used to fabricate the HOF membrane, named with polyHOF, through the post synthetic modification and following polymerization. The in vitro antibacterial experimental results showed that after the irradiation, the *Escherichia coli* inhibition ratios of PFC-33 can be up to 76.1% and that of polyHOF can reach to 59.4% (Figures 6E,F), demonstrating their excellent photodynamic/chemical combined antibacterial effect.
3.6 | Porous carbon materials

Besides the organic ligands-based materials, a wide variety of porous carbon materials also attract the attention of the researchers and have become the hotspot in different fields, for example, catalysis, antibiotic removal, drug delivery, phototherapy, gas adsorption, or electrochemical applications due to their interesting properties such as adjustable pore structures, large surface area, special optical characteristics, and high chemical inertness. Moreover, since the porous carbon materials also have excellent physiological properties, for example, facilitation of the ROS generation and the resulting oxidative stress, the capacity to destruct the microbial membrane, and preliminary verified high biological safety, porous carbon materials have been investigated for the antimicrobial studies. The common porous carbon materials for antibacterial research mainly includes carbon nanotubes, fullerenes, graphene,
To overcome the self-aggregation of the AgNPs for better antibacterial effect and also to minimize the possible environment pollution from the disposed rice husk (RH), Cui et al. utilized the RH to prepare the porous carbon materials as the carrier to load the AgNPs on the surface in a simple and low cost way to RH-Ag composites for the antimicrobial investigation (Figure 7A). The characterization results showed the RH-Ag exhibited higher sustainable silver ions release characteristics compared with AgNPs. With this slower silver ions release capacity, the possible side effects from the silver ions are avoided and the antimicrobial behaviors can be prolonged. The in vitro antibacterial experiments demonstrated that at 25 µg mL⁻¹, the *Escherichia coli* growth can be completely inhibited much better than pristine Ag NPs (Figure 7B). Furthermore, the cell morphology observation by field emission scanning electron microscopy (FESEM) showed that the cell wall of the *E. coli* treated with RH-Ag was damaged and the observed translucent shell also indicates that the RH-Ag can dilapidate the cytoplasmic membrane and cause the leakage of the content of the cells and the cell death (Figure 7C–E). Besides, the cytotoxicity assay verified the biocompatibility of the RH-Ag to human skin keratinocytes cells.

4 | CONCLUSION AND FUTURE PERSPECTIVES

The multi-drug resistant (MDR) pathogens have been increased faster than the design of effective treatments against them, leading to a serious global healthcare concern. The fast spreading of the infectious diseases as demonstrated by the COVID-19 pandemic increases the urgency for early diagnostic and new therapies. Advanced porous materials are versatile structures capable to be molded according to the needs to effectively eliminate the target microbial. Adjustable pore size and surface functionality have allowed the fabrication of multifunctional platform either for the release of antimicrobial molecules or for associated phototherapy.

Silica-based porous materials, MOFs, COFs, HOFs and carbon porous materials have shown great potential as nanotools for antimicrobial treatment, although only few examples have been currently described in the literature. Additionally, the current progress towards the design of these advanced porous materials for antimicrobial treatment are mainly focused on in vitro antimicrobial evaluation with only few examples in vivo reported so far. Moreover, there is a lack of studies regarding the infectious diseases caused by parasites and fungi, being still considered neglected disease, which attract few interests of the public authorities and researchers.
While several studies have been devoted to MSNs, MOFs, COFs, and carbon porous materials in pre-clinical evaluation for cancer therapy, deeper in vivo studies are essential to understand the biodistribution and biosafety of the current advanced porous materials to reach effective infectious disease treatment and, ultimately, be translated to clinical trials.

The future outlooks are based on the design of multifunctional porous materials that can perform simultaneous diagnostic and therapy, as well as their scale-up production from the lab-to-bench. The enhancement of targeting possibilities and efficiency may be the key for improving the treatment efficacy. Furthermore, the association of real-monitoring molecules or compounds with the advanced porous materials comprises a powerful diagnostic tool that allow better evaluation and the understanding of the multifunctional systems behavior face to the preclinical assays even facilitate the way to eventually reach clinical applications.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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