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Nanoengineered biomaterials for anticancer and antimicrobial drug targeting

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Nanoengineered biomaterials have been shown to possess enhanced physicochemical and biological properties, leading to their increasingly widespread use for diverse biomedical applications, particularly targeting cancer and microbial infections.

This themed issue collection in *Material Advances* focuses on the potential role of nanoengineered biomaterials for anticancer and antimicrobial applications. The broad research areas relating to this topic include: nano-phytotherapeutics, biogenic nano-biomaterials, cancer therapeutic approaches, antimicrobial therapeutic approaches, nano-biomaterials based sensors, overcoming drug resistance, redox biology mechanism, photothermal and photodynamic therapy, toxicological and drug-polymer stability studies, clinical and pre-clinical aspects. In this thematic issue, 6 review articles and 11 research articles, a total of 17 articles, are published, which primarily focus on the potential role of diverse nanoengineered biomaterials in anticancer and antimicrobial applications with improved theragnostic applications.

The first section of our introduction primarily focuses on the work of

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researchers reporting anticancer applications of various biomaterial-based strategies. Biomaterials, conventionally are natural or synthetic materials that interact with biological systems for supporting, enhancing, or substituting damaged tissues or biological functions. Biomaterials-based platforms, developed using mostly nanoparticles, polymers, lipids or hydrogels, have shown great potential in advanced drug delivery systems applicable for oral, pulmonary, transdermal, nasal, and ocular drug targeting. Biomaterials deliver a highly versatile theranostic strategy to produce distinct macro and microenvironments, and employ cells and/or tissues *in vitro* and *in vivo*. These advanced biomaterial-based theranostic strategies have shown potential implications for treating chronic disease conditions, particular cancer, and microbial infections. In cancer theranostics, researchers have reported that the microenvironment plays a vital role in cancer cases and biomaterials efficiently offer a platform to engineer the microenvironments (*in vitro* and *in vivo*). In addition, nanoengineered biomaterials have been particularly helpful due to their tunable size, biocompatibility, biodegradability, targetability, improved release properties, ability to load both hydrophobic and hydrophilic bioactives and/or drugs. These properties have allowed to significantly enhance the effectiveness of numerous novel anticancer therapeutic strategies, particularly immunotherapies (*e.g.* cancer nanovaccines), or combined therapeutic strategies combining immunotherapy with photothermal, photodynamic and/or radiotherapy strategies. The ability of nanoengineered biomaterials to generate distinct microenvironments makes it more likely to have an impact on both the discovery and clinical translation progression in cancer management.[1,2]

Abodunrin *et al.* reported various challenges associated with photodynamic therapy (PDT) and possible ways to overcome these challenges using metal organic frameworks (MOFs) and their nanoscale MOFs (NMOFs). These MOFs and NMOFs, composed of organic ligands and inorganic metal components, formed into well-ordered systems, are useful as photosensitizers (PS) in PDT. They also summarized the advantages of MOFs-based platforms for PDT and also the significance of the design strategy of MOFs in PDT for effective cancer management (**https://doi.org/10.1039/D4MA00425F**). Similarly, the current development and applications of nanotechnology-driven MOF-based PS for photodynamic cancer therapy, antibacterial and wound healing management was discussed by Pattnaik *et al.* (**https://doi.org/10.1039/D4MA00376D**). In their work they highlighted the current progression and challenges of various MOF-altered multifunctional agents for PDT, light-activating mechanisms of PDT and their potential role in the demolition of targeted pathogens, leading to enhanced therapeutic applications. Dias *et al.* summarized the theragnostic potentials of poly(3,4-ethylenedioxythiophene) nanoparticles (PED-NPs) probably due to their superior biocompatibility, electrical, and thermal features for collective imaging, controlled drug release properties and localized photothermal excision. However, they also reported that researchers need to put in additional effort for focusing on the development of prognostic preclinical models, ascendable manufacturing approaches and clinical collaborations, to enable transformation of PED-NPs from the laboratory to clinical applications, particularly for fabricating personalized cancer nanomedicines (**https://doi.org/10.1039/D4MA00260A**).

In another work, Shi *et al.* highlighted the advances of combinatorial strategies (prodrug and nanoparticle-based drug delivery systems) over the use of nanomedicines alone, primarily in cancer therapy. They focused on the recent fabrication strategies and advances in the field of prodrug-mediated nanocarriers for numerous cancer therapeutic approaches dealing with the tumor microenvironment, with emphasis on chemotherapy and immunotherapy (**https://doi.org/10.1039/D3MA01132A**). Puri and co-workers reported the plant-mediated synthesis approaches of selenium nanoparticles (SeNPs), and their biomedical applications. They also summarized the various approaches of SeNP functionalization. Also, highlighted the prospect for targeted drug delivery for improved cancer theranostics (**https://doi.org/10.1039/D3MA01126G**).

Injectable hydrogels are another type of biomaterial with potential as a drug delivery tool due to their distinctive features such as biodegradability, biocompatibility, porous structure, higher water content, binding affinity to biological fluids, and superior flexibility. Das *et al.* have reported the conventional approaches for synthesizing the biological characteristics of diverse natural cationic polymers and injectable hydrogels fabricated from them. They also discussed distinguished studies on natural cationic polymer-based hydrogel-mediated systems for anticancer therapy, focusing on major molecular insights, therapeutic methods, pharmacological action, and

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pre-clinical/clinical implications (https://doi.org/10.1039/D3MA00484H). Ariraman *et al.* synthesized thermostable and biocompatible quercetin-loaded nanoarchaeosomes of particle size (53.5 ± 1 nm), drug loading (99 ± 0.2%) and sustained release behavior, which exhibited potential *in vitro* anticancer effects against MCF-7 breast cancer cells. They reported that the major anticancer mechanism involved cell death in cancerous cells due to reactive oxygen species (ROS) generation, and triggering of necroptosis with cell cycle arrest at the G0/G1 phase (https://doi.org/10.1039/D4MA00258J).

Moloudi *et al.* synthesized liposomes using a thin-film hydration technique for co-delivery of berberine (BBR) and citrate gold nanoparticles (GNPs), forming berberine and citrate gold nanoparticles co-loaded liposomes (BGLs) of size 100 nm, as a new photosensitizing agent for effective PDT against lung cancer (A549) spheroid cells. Results demonstrated that BGLs significantly induced cytotoxicity against A549 cells, possibly due to ROS generation, with decreased cell viability of spheroids up to 34.12%. Thus, these materials could potentially act as a nanotheranostic agent for tumor and cancer management (https://doi.org/10.1039/D4MA00286E). In another work, Mougkogiannis and Adamatzky reported the effective outcome of alterations in the growing spike train dynamics and electrical signalling of polyaniline nanomaterials hybridized with proteinoids under diverse optical stimulation frequencies. The findings of their study demonstrated potential for building adaptive, brain-stimulated computer systems by displaying extrinsic monitoring over the network's self-systematized dynamics (https://doi.org/10.1039/D4MA00253A). Yang *et al.* fabricated graphene oxide-based nanosheets coated over periodic mesoporous organosilica, followed by coating with glucose oxidase to form a nanocatalyst complex, which significantly catalyzed hydrogen peroxide and exhibited effective photothermal therapy ensuring notable antitumor efficiency with no noticeable systemic toxicity (https://doi.org/10.1039/D4MA00109E).

Zhou *et al.* designed a temperature-responsive liposomal system composed of bismuth nanosheets (photothermal agents) and multiple model drugs (5-fluorouracil and metformin) to exert the synergistic combined effects of PDT with chemotherapy. The results of *in vitro* and *in vivo* studies revealed the excellent antitumor effects of this combined system (https://doi.org/10.1039/D3MA01060K). Paul *et al.* prepared pH-responsive hydrogels co-loaded with doxorubicin (a chemotherapeutic drug) and zinc phthalocyanine (a phototherapeutic drug) to establish a synergistic chemo–phototherapeutic combinatorial strategy. These hydrogels exhibited anti-cancer effects against the treated MCF-7 cells. The mechanism involved laser-mediated ROS generation due to zinc phthalocyanine (https://doi.org/10.1039/D3MA00900A).

This second section of our introduction primarily focuses on the work of researchers reporting antimicrobial applications of various biomaterial-based strategies. Apart from anticancer and antitumor applications, the nanoengineered biomaterials have also exhibited their potential role as antimicrobial agents, particularly antibacterial applications targeting a wide-range of bacterial strains. Antibacterial biomaterials such as polycationic polymers, biomaterial-mediated non-antibiotic therapeutic regimens (bacteriophages, peptides, enzymes) and their nanoforms, have potentially enhanced the probabilities of effective management of bacterial infections and also antibiotic-resistant circumstances. Biomaterials can release the active pharmaceutical agents and/or biomolecules to the targeted sites with sustained release behavior, leading to improved therapeutic effects with reduced systemic adverse effects. Further, the biomaterial-based delivery systems can efficiently protect the antibacterial drug moieties from enzymatic degradation and deactivating factors within the body. Additionally, biomaterials have the potential for allowing simultaneous delivery of two or more therapeutic agents, possibly enhancing the overall therapeutic efficacy.[3]

Dong *et al.* designed *in situ* hydrogels composed of 4-arm-poly(ethylene glycol) succinimidyl and ε-poly-L-lysine (an antibacterial peptide) which allowed quick crosslinking under physiological conditions deprived of any extra crosslinking agents. The hydrogels have excellent water absorption and retention ability which supports their wound healing abilities. These hydrogels showed superior biocompatibility and also exhibited admirable antibacterial activity *in vitro* as well as *in vivo* in a rat model (https://doi.org/10.1039/D4MA00287C). Alkaabi *et al.* explored the dual-potential of Safranal-loaded iron-mediated metal–organic frameworks (MOFs, MIL-88B(Fe)) as a novel therapeutic strategy for treating liver cancer (HepG2 liver cancer cell lines). Additionally, this system exerted potential antibacterial effects against *Escherichia coli* and *Lactobacillus* strains. The anticipated mechanism of action of these systems for dual therapeutic activity was possibly due to effective release of the Safranal and ferric ions within the cells (https://doi.org/10.1039/D4MA00345D). Gupta *et al.* synthesized a copolymer comprised of jeffamine, piperazine, and bisphenol-a-diglycidyl ether, and reported their effect on the effective prevention of microbial colonization. These excellent stability and resilience of the material even after several washing cycles, signified prolonged efficiency and also exhibited antibacterial effects against *Escherichia coli*, *Staphylococcus aureus*, *Mycobacterium smegmatis* and *Candida albicans* (https://doi.org/10.1039/D4MA00393D). Zhang *et al.* reported an economical and effective one-step method to produce cetrimonium bromide deposited polycaprolactone-based nanofibres using coaxial electrospinning. The nanofibres exhibited antiviral effects against SARS-CoV-2 and respiratory syncytial virus, and also antibacterial effects against *Staphylococcus aureus* and *Pseudomonas aeruginosa* bacterial strains (https://doi.org/10.1039/D4MA00125G).

Rathore *et al.* synthesized zinc oxide nanoparticles (ZnO-NPs) through a sol–gel technique and further crystallized it using an annealing strategy. These crystalline ZnO-NPs (21 nm size) showed superior photoluminescence effects as well as antibacterial effects against *Bacillus subtilis*, *Escherichia coli* and *Pseudonomas* bacterial strains (https://doi.org/10.1039/D3MA01096A).

Nanoengineered biomaterials-mediated therapeutic strategies can significantly

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improve the effectiveness of existing chemotherapeutic and antimicrobial agents by aiding sustained and targeted release of encapsulated drugs and/or biomolecules, leading to superior efficacy and reduced toxicities. These strategies have been found to be helpful to increase stability and overall bioactivity of the therapeutic agents, enabling co-delivery of other agents (imaging, photosensitizers, cross-linkers and others) and by controlling the local microenvironment, and thus are also useful as potential diagnostic tools. Thus, fabrication of nanoengineered biomaterials-mediated carriers can be a potential theragnostic tool for efficient anticancer and antimicrobial applications. However, in future various preclinical and clinical studies are essentially required for their translational applications.

Finally, we extend our sincere appreciation to the entire editorial team of *Materials Advances* for their invaluable support and collaboration in successfully bringing this themed collection to completion. We hope that this thematic issue will create interesting reading for a wide-group of researchers working worldwide on diverse types of biomaterials to establish their potential anticancer and antimicrobial applications.

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