

Biomedical Applications of Sonocatalysis: Current Advancements and Future Perspectives

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Abstract: A separate area of sonochemistry known as “sonocatalysis” makes use of the interaction between solid catalysts and ultrasonic (US) to speed up and improve the selectivity of chemical reactions. Sonocatalysis is a non-traditional catalytic activation technique that can open up new activation routes and drastically change reaction processes that are normally not possible with conventional catalysis. This unique approach provides new opportunities to facilitate reactions under milder conditions, with the potential to improve both selectivity and overall efficiency. The applications of sonocatalysis are broad, encompassing environmental remediation, sonodynamic therapy, and biomass conversion. Across these applications, the underlying mechanisms of sonocatalysis and the specific interactions between solid catalysts and US are the key factors driving the enhanced reaction activity. This article introduces the design concepts of specific sonocatalytic therapies based on nanomedicines. Furthermore, based on different treatment principles and therapeutic diversity, representative paradigms of nanomedicine-assisted or enhanced sonocatalytic therapies are elaborated in detail. This review offers an updated and comprehensive retrospective of the nano-sonocatalytic biomedical field and thoroughly explores the progress of various sonocatalytic approaches for disease treatment. Finally, an in-depth discussion of the current challenges and future prospects is presented. It is highly anticipated that the rational combination of nanomedicines and clinical sonocatalytic therapy will promote the emergence and establishment of a new branch in sonocatalytic biomedicine.

Keywords: ultrasound; nanomedicine; catalytic biomaterials; sonocatalysis; disease therapy

1. Introduction

Sonochemistry represents a highly dynamic and rapidly evolving field dedicated to exploring the unique effects of ultrasound (US) on chemical systems, which carries profound implications across industrial, environmental, and biomedical domains [1–3]. Recently, the capacity of US to potentiate diverse chemical processes has propelled its application in areas encompassing US-assisted extraction, crystallization, chemical synthesis, advanced material fabrication, and noninvasive therapeutics [4–6]. US is essentially inaudible to the human ear because it is an acoustic wave with frequencies from 20 kHz to 20 MHz [7]. Inspired by nature, humans have seen animals like dolphins and bats using ultrasonic echolocation for underwater and nocturnal navigation. Researchers have traditionally developed advanced acoustic technologies, such as bathymetric mapping devices and marine sonar systems for fish detection, based on these biological principles [8].



Sonocatalysis has recently become an important branch of sonochemistry. It improves system efficiency by adding solid catalysts into an ultrasonic field. Once in this field, these solid catalysts interact with US-generated radicals. They also absorb local cavitation energy. This process makes the chemical reactions easier to control both thermodynamically and kinetically [9,10]. Researchers often apply this method to environmental cleanup. For example, they use semiconductors like titanium dioxide (TiO_2) or zinc oxide (ZnO). These materials work well with acoustic waves to break down pollutants in water [11,12]. Combining US with solid catalysts offers two main benefits. First, it greatly speeds up the breakdown of tough organic contaminants, such as dyes and drugs. Second, it lowers the overall energy needed for the process [13]. Early research mostly used this technology to clean up the environment. Today, however, the focus is moving toward precision biomedicine [14,15]. Scientists are adjusting acoustic parameters and building bio-responsive catalysts. Through these changes, they have successfully adapted this non-invasive technique for new medical treatments [16,17].

Over the years, scientists have optimized US parameters for broader medical applications [18,19]. Beyond standard diagnostic imaging, US now functions as a versatile application. The medical community widely adopts this technology. It is non-invasive, cost-effective, safe, and provides real-time feedback. Recently, developments in nanotechnology have reshaped US-based biomedicine [20,21]. Researchers frequently introduce multifunctional micro- and nano-platforms into ultrasound systems. Combining these advanced materials with acoustic waves greatly improves medical outcomes. This approach offers reliable tools for precision diagnostics, targeted therapies, and personalized theranostics [19,22].

Building upon these diverse applications, the integration of sonocatalysis into biomedical engineering has yielded a series of highly innovative therapeutic paradigms [23,24]. For example, researchers use engineered sonocatalysts for cancer and infectious diseases [25]. Upon US activation, they not only generate lethal reactive oxygen species (ROS) to eradicate deep-seated tumors or drug-resistant biofilms but also catalyze local biochemical reactions to reshape hostile pathological microenvironments, such as relieving tumor hypoxia [26,27]. Furthermore, piezocatalytic biomaterials also offer new tools for tissue engineering and nerve repair [28,29]. Sound waves apply mechanical stress to these materials. The materials then change this stress into small electrical signals. These signals act like natural bioelectric fields in the body. As a result, they help bones grow faster and assist in healing nerves [30]. Furthermore, researchers design sonocatalytic platforms as smart drug carriers. These systems allow for precise, on-demand drug release directly at the disease site [31,32].

While preclinical studies are promising, the clinical use of biomedical sonocatalysis remains a major challenge. This perspective summarizes recent progress in sonocatalyst design and its applications in biomedical engineering. The following sections highlight specific case studies. We explain how acoustic energy works in targeted therapy, regenerative medicine, and drug delivery (Figure 1). We then discuss current technical challenges. We focus on biocompatibility, energy conversion rates, and safety issues in deep tissues. By outlining future research needs, we aim to promote cross-field teamwork and help move sonocatalytic nanomedicine toward clinical practice.

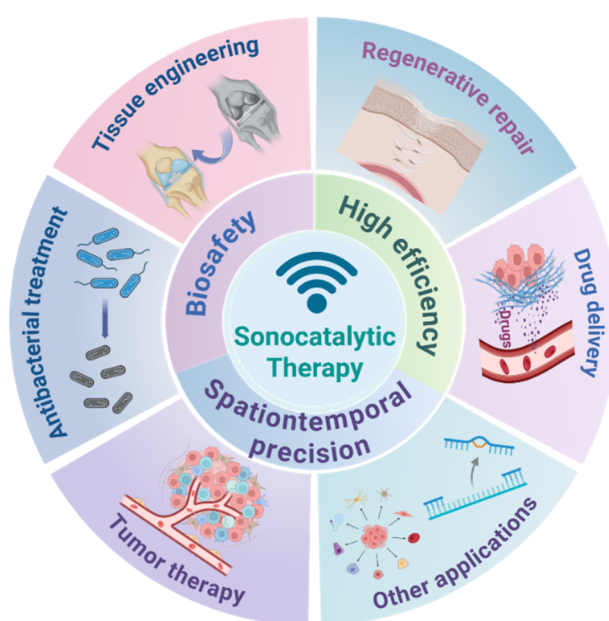


Figure 1. Schematic of the basic mechanism of sonocatalytic therapy and its biomedical applications. Created with BioRender.com.

2. Applications

2.1. Tumor Therapy

Sonodynamic therapy advancement depends on producing strong ROS using US-responsive sonocatalysts. However, existing therapies are often hindered by low ROS yields resulting from sluggish charge transfer operations and poorly defined active sites. To circumvent these challenges, Liu and colleagues designed an *in situ* oxygen vacancy (O_v) modified Pd-TiO₂ sonocatalyst featuring spatially separated dual reactive sites. This architectural design successfully optimizes overall charge dynamics and amplifies ROS generation [33]. Mechanistic studies show that US-induced O_v acts exactly as an electron pump, precisely directing electron transfer from titanium dioxide (TiO₂) to palladium, mitigating the interfacial barrier, and activating the intersystem transport channel connecting palladium and titanium (Figure 2A). This organized intracellular charge redistribution systematically modulates the d-band center of palladium. As a result, the electron-abundant palladium sites are established as the principal operational centers for adsorbing and activating oxygen to produce singlet oxygen. The molecular mechanisms underlying the charge transfer cascade and pivotal active regions in US-activated Pd-TiO₂ systems are revealed in this elegant study, providing a rational blueprint for engineering sonocatalytic materials. A recent study showed tumor suppression using 2D ZnIn₂S₄ nanosheets with indium vacancies [34]. This structural modification serves to effectively sequester excited electrons and holes. While pristine ZnIn₂S₄ exhibits a highly periodic electrostatic potential, the engineered vacancies effectively disrupt this intrinsic symmetric field. Such an electronic perturbation not only drives the simultaneous separation and mobilization of charge carriers but also severely restricts their recombination. Finally, this ROS causes tumor cell pyroptosis through the ROS/NLRP3/caspase 1/GSDMD pathway (Figure 2B).

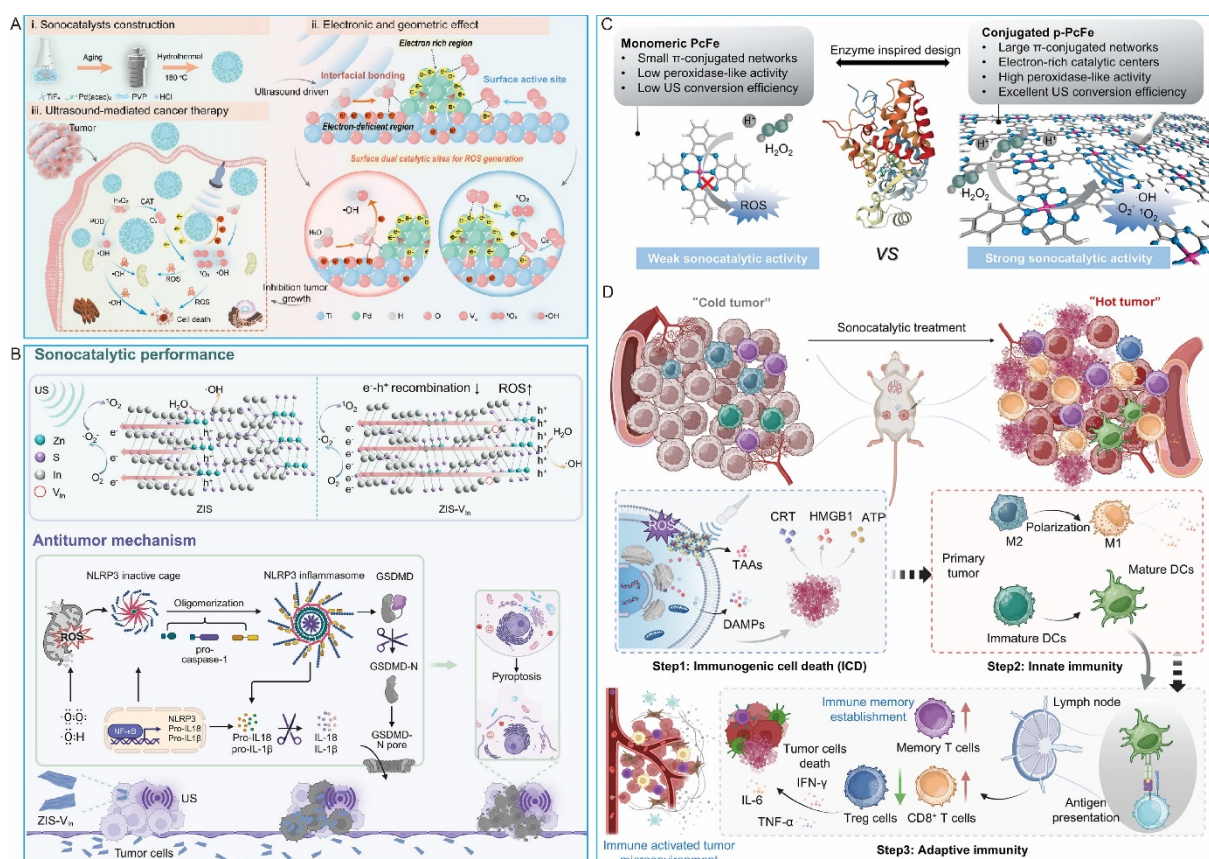


Figure 2. (A) Preparation of Pd-TiO₂ sonocatalysts and their catalytic mechanisms in tumor treatment [33]. Copyright 2026, Wiley-VCH. (B) US-activated therapeutic mechanism of ZnIn₂S₄ nanostructures [34]. Copyright 2025, Wiley-VCH. (C) Structural features and enzymatic activities of p-PcFe compared to bare molecules. (D) p-PcFe formulation stimulates antitumor immunity to overcome local immunosuppression [35]. Copyright 2025, Wiley-VCH.

The rational design of smart sonocatalytic materials capable of modulating both innate and adaptive immune responses significant advancement in contemporary tumor immunotherapy. Taking inspiration from the naturally occurring heme structure within peroxidases, Li and coworkers have created a biomimetic polymeric iron

phthalocyanine network [35]. The developed sonocatalyst enables targeted immunotherapy for breast cancer. Structurally, the polymer features an extended π -conjugation system, electron-rich active centers, and a d- π orbital delocalization. Due to these electronic properties, the material exhibits high peroxidase-mimicking activity and efficient acoustic energy conversion in the tumor microenvironment (TME), leading to the generation of ROS (Figure 2C,D). Hydrogen therapy is a promising cancer treatment. It remodels the TME and disrupts cancer cell mitochondria, leading to energy depletion and cell death. To amplify this therapeutic efficacy, researchers recently developed the sonocatalyst named as BPM, which was explicitly tailored to catalyze the simultaneous generation of molecular hydrogen and oxygen directly within the tumor matrix. Architecturally, the mesocrystalline lattice of BPM integrates bismuth fluoride, polyoxometalates, and molybdenum carbide [36]. This ternary compositional synergy drastically improves charge carrier separation and speeds up electron transfer kinetics upon US excitation, thereby driving highly efficient catalytic water splitting. This platform effectively induces deadly oxidative stress while simultaneously reducing local hypoxia by coordinating the localized evolution of two therapeutic gases in conjunction with glutathione (GSH) depletion. This orchestrated cascade fundamentally shatters mitochondrial networks and restrains malignant metabolic pathways. Furthermore, by encouraging dendritic cell maturation, stimulating T lymphocytes, and promoting macrophage polarization toward the tumoricidal M1 phenotype, this dynamic system actively reverses local immunosuppression and collectively orchestrates strong systemic antitumor immunity.

2.2. Against Bacterial Infection

Severe bacterial infections critically hinder tissue repair by causing chronic unhealed wounds. Currently, clinical management relies heavily on massive antibiotic usage [37], which inevitably provokes antimicrobial resistance, highlighting the need for alternative therapies [38,39]. Emerging as an innovative noninvasive modality, piezocatalytic therapy driven by sonosensitizers offers excellent spatiotemporal control and deep biological tissues [40]. Upon US stimulation, these sonosensitizers undergo spontaneous polarization, driving the spatial separation of electrons and holes. These charge carriers engage in redox reactions with water or oxygen, yielding abundant ROS to kill bacterial pathogens (Figure 3A) [28]. To further enhance the efficacy of US-driven therapies, recent research has focused on specific clinical challenges, such as diabetic ulcers. A primary impediment in diabetic wounds is recurrent bacterial colonization. To address this, antibacterial dynamic therapy facilitated by US-responsive nanozymes has emerged to disrupt pathogen redox homeostasis (Figure 3B) [41]. However, to maximize ROS production in these complex microenvironments, material structures must be optimized. Therefore, rationally engineering heterojunctions with a direct Z-scheme configuration has been employed. This structural design significantly augments charge separation efficiency and prolongs charge carrier lifetimes, which increases the ROS quantum yield to normalize the diabetic wound microenvironment (Figure 3C) [42].

Beyond simply eradicating bacteria, ideal antibacterial materials should concurrently promote tissue regeneration. Addressing this dual requirement, an artificial nanozyme constructed from metalloporphyrin networks (Polypor) was developed. Mechanistic studies revealed that Polypor not only exerts sonodynamic antibacterial effects but also actively modulates fibroblast and vascular endothelial growth factor signaling. This dual-function intervention accelerates localized angiogenesis and collagen remodeling, thereby reprogramming the infected wound microenvironment [43]. Finally, to combat highly stubborn multidrug-resistant (MDR) infections, synergistic mechanisms beyond conventional ROS generation are required. For instance, the integration of Fe(III)-siderophore-purpurin nanosideromycin (FSP) provides active targeting capabilities to detect infection sites. Upon localization, the US-triggered ROS burst, combined with iron overload, initiates a ferroptosis-like bacterial killing pathway. This integrated targeting and synergistic mechanism results in the complete eradication of MDR PA-induced pyomyositis [44].

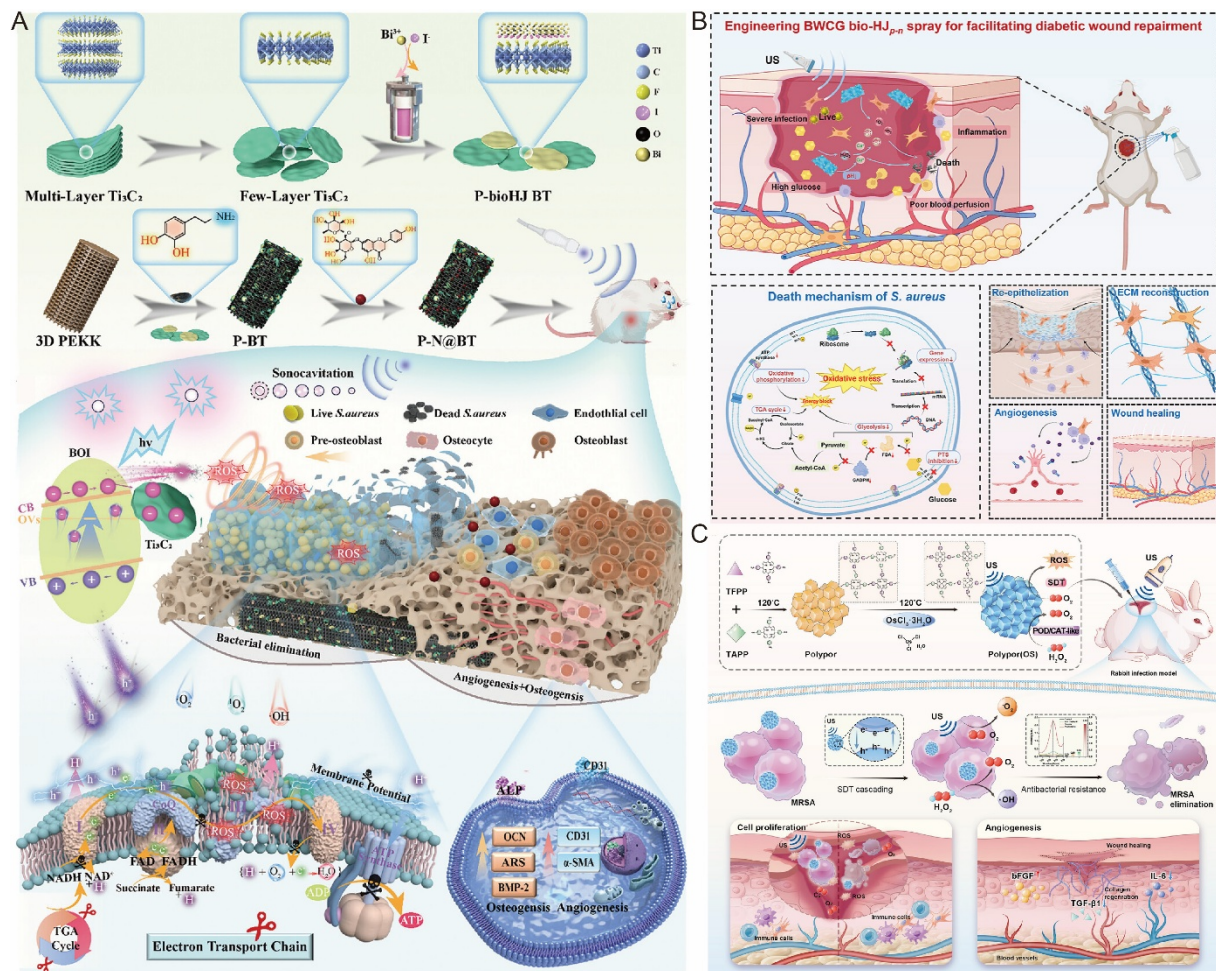


Figure 3. (A) Preparation process and sonocatalytic mechanism of the responsive bio-heterojunction [28]. Copyright 2025, Wiley-VCH. (B) Process for developing BWCG *p-n* heterojunction sprays to accelerate diabetic wound closure [42]. Copyright 2025, Elsevier. (C) Visual summary explaining how oxidative treatments driven by US waves promote tissue recovery during bacterial infections [43]. Copyright 2025, Wiley-VCH.

2.3. Tissue Engineering and Regenerative Repair

US acts as a mechanical wave, dispersing energy into the surrounding medium while applying strong physical stresses to biological structures. In the field of tissue engineering, acoustic radiation forces are highly useful for controlling the precise alignment, controlled aggregation, and spatial displacement of cells or microparticles [45,46]. Furthermore, acoustic streaming is triggered by the viscous attenuation of acoustic energy, which creates directed fluidic currents. These convective fluxes, which are propelled by drag forces, not only speed up the mass transit of nutrients and cellular payloads but also control the local velocity gradients that determine the regional resuspension or concentrated cell gathering. As a result, these biomechanical processes powered by sound are effective instruments for the morphogenesis of functioning living tissues [47,48]. The construction of engineered tissues mainly requires cells, scaffolds, and active signals. A successful engineered tissue should work like the natural one. It needs to help cells attach, grow, and differentiate, while responding to local changes [49]. To do this, scaffolds must have suitable structures, such as proper pores and mechanical strength. They also need enough binding sites to control cell functions.

Osteosarcoma represents a highly aggressive skeletal malignancy predominantly afflicting pediatric and adolescent populations. Although disease management typically requires limb salvage surgeries combined with comprehensive chemotherapy and radiotherapy, severe therapeutic resistance frequently precipitates fatal tumor recurrence and necessitates repeated surgical interventions [50,51]. Currently, while 3D printed calcium phosphate scaffolds exhibit considerable potential for skeletal repair, they critically fail to simultaneously eradicate residual malignant tissue and intelligently adapt to dynamic local microenvironments [52,53]. Following surgical interventions, tumor recurrence and persistent inflammation trigger excessive hydrogen peroxide (H₂O₂) accumulation alongside severe hypoxia. This pathological condition profoundly disrupts local redox homeostasis and heavily obstructs subsequent bone regeneration. Furthermore, conventional biocatalytic materials remain

fundamentally incapable of distinctively converting H_2O_2 into ROS for tumor ablation or into vital oxygen for subsequent tissue repair [54,55]. To resolve this formidable challenge, recent research introduced an US-activated biocatalytic 3D printed scaffold designated as HS-ICTO (Figure 4A). This sophisticated platform incorporates a titanium dioxide substrate uniquely modified with specific coordination linkages of TiO_2 and iridium (Ir). This precise chemical arrangement yields specialized nanoparticles exhibiting diverse enzymatic characteristics, which are subsequently integrated into a hydroxyapatite framework. Within the acidic tumor region, US activation induces massive ROS generation and radical GSH depletion, decisively driving malignant cell apoptosis. Conversely, within normal bone defect areas, this smart scaffold immediately converts excessive H_2O_2 directly into O_2 . This conversion effectively alleviates severe oxidative stress and vigorously promotes the osteogenic differentiation of stem cells, thereby executing an intelligent sequential therapeutic paradigm [56]. In an additional remarkable investigation, researchers successfully engineered an acoustically dynamic 4D biological scaffold by meticulously integrating exfoliated black phosphorus (BP) nanosheets and a specific nitric oxide (NO) donor onto a 3D printed bioactive glass (BG) framework, yielding an advanced composite specifically designated as BP-GSNO-BG (Figure 4B). This integrated platform effectively utilizes external US irradiation to activate the inherent piezoelectric properties of the internal BP, thereby continuously producing abundant ROS. Simultaneously, this targeted acoustic energy forcefully triggers the donor molecules to release dramatically high concentrations of NO. These two potent chemical agents collaborate synergistically to execute profound biological cytotoxicity against surrounding malignant cells. Beyond generating exceptional tumoricidal effects, the inherent biodegradation byproducts derived from BP combine harmoniously with physiologically low continuous concentrations of NO to significantly accelerate localized bone regeneration during subsequent healing phases [57].

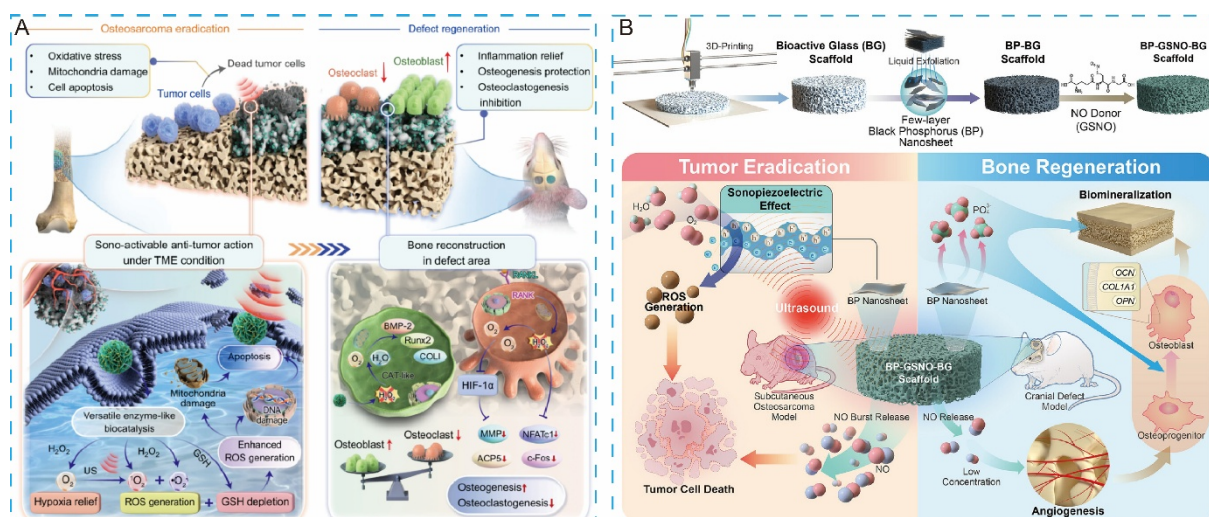


Figure 4. (A) 3D-printed US-responsive biocatalytic scaffolds for limb-salvaging bone cancer treatment [56]. Copyright 2025, Nature. (B) Diagram showing a constructed matrix containing BP, GSNO, and BG that responds to US. It is designed to merge sonopiezoelectric treatments for bone tumors with skeletal tissue regrowth [57]. Copyright 2025, Wiley-VCH.

2.4. Other Types of Sonocatalysis and Applications

The spatiotemporal precision of targeted US has prompted research into wider biomedical applications, even if clinical evaluations of acoustic medicine mostly concentrate on ROS creation for tumor eradication or tissue regeneration [58]. Catalytic biomaterials are being used for microenvironmental modulation in autoimmune diseases, localized thrombolysis in cardiovascular illnesses, and wireless deep brain electrostimulation in neurological disorders using acoustic mechanical energy [59,60]. However, realizing these interventions is often hindered by the limitations of traditional sonodynamic agents, such as specific semiconductor bandgap requirements and long-term biosafety concerns. This necessitates the development of alternative acoustic activation paradigms.

To address these limitations, sono-tribocatalytic therapy (STT) has emerged as a novel modality. Unlike conventional systems that require specific bandgap energies, STT utilizes interfacial friction and subsequent triboelectrification driven by acoustic cavitation. For instance, studies have demonstrated that ultrasonic mechanical agitation can generate surface charges on nanostructures, such as iron oxyhydroxide nanorods. These tribocatalytically induced charges interact with dissolved oxygen and surrounding aqueous environments to initiate

downstream redox reactions [61]. This mechanochemical activation process maintains exceptional material recyclability while producing quantities of cytotoxic radicals, which can lead to mitochondrial dysfunction and trigger the inflammatory cell death pathways known as PANoptosis (Figure 5A). Consequently, STT bypasses traditional semiconductor constraints, offering a different approach for acoustic therapeutics.

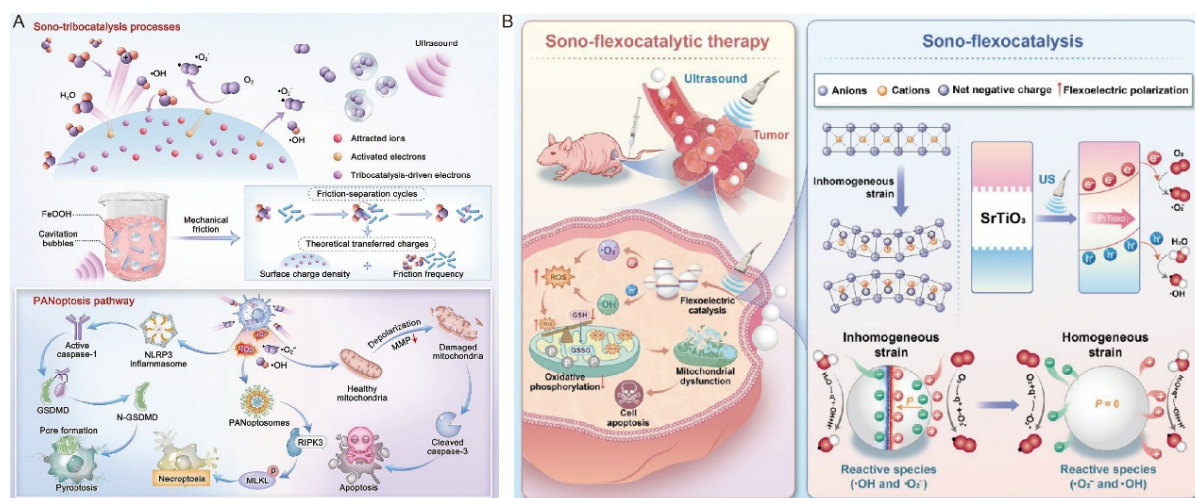


Figure 5. (A) Mechanism of tribocatalytic cancer therapy using FeOOH nanocatalysts. The STT process generates excessive ROS, inducing DNA and mitochondrial damage, which triggers PANoptosome assembly and subsequent PANoptosis [61]. Copyright 2026, Elsevier. (B) Schematic of SrTiO₃ nanoflexocatalyst-mediated sono-flexocatalytic tumor therapy [62]. Copyright 2026, Wiley-VCH.

In addition to friction-based charge generation, sono-flexocatalytic has also been explored as a complementary mechanism. Traditionally, piezocatalytic applications in biomedicine have been limited to materials with noncentrosymmetric crystal architectures, restricting material selection. To overcome this structural barrier, recent studies have introduced centrosymmetric biomaterials, such as strontium titanate nanocatalysts. These nanoparticles undergo acoustic mechanical stress during continuous US irradiation, which causes localized strain gradients that promote flexoelectric polarization and charge carrier separation. Superoxide anions and hydroxyl radicals are produced when this process starts surface redox reactions (Figure 5B). Sono-flexocatalysis eliminates the need for noncentrosymmetry by using strain gradient-induced flexoelectricity, which increases the pool of possible nanotherapeutics.

3. Future Perspective

Biomedical sonocatalysis has advanced into previously unheard-of therapeutic domains thanks to the synergistic confluence of nanotechnology and acoustic medicine, yet the difficult path from preclinical proof of concept to true clinical translation is still in its early stages. Sonodynamic tumor eradication, sonopiezocatalytic tissue regeneration, and the discovery of a novel sono-tribocatalytic process are just a few of the amazing discoveries that have mostly been proven in highly controlled laboratory settings or in crude mouse models. Researchers must methodically address a number of crucial scientific and engineering constraints in order to successfully cross the difficult translational gap toward human clinical trials. The precise optimization of catalytic material designs, the thorough understanding of intricate biological interactions, and the strategic creation of acoustic delivery systems should be the primary focus of future research projects.

The most important of these difficulties is the strict balance between exceptional catalytic efficiency and complete systemic biosafety. Nowadays, obtaining strong sonocatalytic performance often necessitates extremely complex compositional engineering, heavily depending on rigid inorganic lattices or heavy transition metals (such as titanium, tungsten, or tellurium-based nanostructures, which frequently lack known biological clearance pathways). However, in order to avoid harmful extended buildup within the hepatic and splenic reticuloendothelial networks, biological systems require nanotherapeutics to have perfect biodegradability and quick renal clearance pathways. In order to precisely predict material degradation kinetics and identify highly biocompatible organic elements or endogenous metabolic metal ions (such as iron, calcium, magnesium, or readily hydrolyzable metal-organic frameworks), future material design paradigms must make use of sophisticated computational modeling and machine learning algorithms. Furthermore, strictly standardizing the structural fabrication processes is mathematically imperative to ensure immense batch reproducibility under Good Manufacturing Practice (GMP) standards.

Beyond intelligent material design, rapid multidisciplinary involvement is required to precisely manage acoustic energy transmission within extremely complex and physiologically varied human tissues. Human anatomy has enormous acoustic attenuation barriers, significantly reflecting and dispersing ultrasonic waves at tissue interfaces and dense cortical bone structures, in contrast to tiny animal models. Innovative hardware is needed for the next generation of acoustic therapy to ensure that enough mechanical energy reaches deep-seated diseased targets without causing unintentional thermal damage to nearby healthy organs. Standardizing US parameters is necessary for clinical translation in order to precisely balance the danger of off-target cavitation with the cavitation threshold for deep-tissue penetration. Highly concentrated acoustic transmitters and sophisticated spatial imaging modalities must be smoothly integrated by engineers. Simultaneously, the development of small wearable ultrasonic transducers that can provide precisely continuous and strictly dosed acoustic mechanical stimulation will significantly change the management of chronic diseases, especially for long-term tasks like sustained neurostimulation and skeletal tissue engineering.

Lastly, scientists need to radically change the focus of their research from merely surface-level cellular death to the deep coordination of systemic biological networks. Large-scale molecular cascades that go much beyond localized oxidation are invariably triggered by the acoustic mechanical stress and abundant ROS produced during sonocatalysis. Comprehensive utilization of cutting-edge transcriptome sequencing and enhanced spatial metabolomics is urgently required to thoroughly characterize the intricate dynamic reciprocal relationships between sonocatalysts, localized immune cell populations, and global metabolic homeostasis. Ultimately, the future of sonocatalytic biomedicine entirely depends on seamless interdisciplinary collaboration. By organically uniting material scientists, rigorous biological immunologists, innovative acoustic engineers, and highly experienced clinical physicians, this exceptionally dynamic field will undoubtedly shatter existing therapeutic boundaries and establish a paradigm in precision noninvasive medicine.

Author Contributions

X.S. and S.L.: contributed equally to this work; X.S. and S.L.: wrote the manuscript; X.S.: illustrated the figures; C.L. and H.F.: revised the manuscript. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement

Not Applicable.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

During the preparation of this work, the authors used Gemini 3 Pro Thinking to polish the language. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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