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The Role of Infrasound and Audible Acoustic Sound in Modulating Wound Healing: A Systematic Review

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ABSTRACT

This systematic review evaluates the therapeutic effects of infrasound (1–20 Hz) and low-frequency audible sound (20 Hz–20 kHz) on wound healing, with a focus on cell migration, tissue regeneration, and bone repair. A comprehensive literature search across PubMed, Scopus, and Google Scholar was conducted to synthesise current data on these acoustic frequencies' impact on cellular functions. Key findings indicate that infrasound enhances bone growth and osteogenic differentiation of bone marrow stem cells, significantly accelerating fracture healing by increasing bone mineral density. Low-frequency sound at 100 Hz promotes fibroblast migration and alters cell morphology through actin restructuring, with effects varying by horizontal versus vertical vibrations. Additionally, frequencies of 10 and 20 kHz stimulate epidermal wound healing in mice by activating keratinocyte functions. These results highlight the potential of specific acoustic frequencies as non-invasive, cost-effective wound treatment options, particularly for bone regeneration and chronic wounds. Further research is recommended to refine acoustic parameters and validate clinical applications to establish therapeutic protocols.

1 | Introduction

1.1 | Rationale

Wound healing is a complex, multifaceted process involving the coordinated efforts of various cell types to restore tissue integrity following injury. Mechanotransduction, the process by which cells perceive and respond to mechanical forces, plays a critical role in regulating the wound healing cascade: mechanical stimuli, such as tension, compression, and shear stress, can profoundly influence cellular behaviour, including proliferation, migration, and differentiation [1, 2]. These mechanical stimuli are particularly significant in bone tissue. Osteocytes, interconnected through the lacunocanalicular network, experience shear forces as interstitial fluid flows through this system. Mechanosensors detect these forces, transmitting signals through the cytoskeleton and activating key transcription regulators, such as RUNX2, which are crucial for osteoblastic differentiation [3].

In recent years, the application of acoustic waves has emerged as a promising therapeutic approach for enhancing wound healing, with numerous studies demonstrating the ability of ultrasound (> 20 kHz) to modulate cellular processes and promote

Abbreviations: BMC, bone mineral content; BMD, bone mineral density; BMSCs, bone marrow mesenchymal stem cells; CGRP, calcitonin gene-related peptide; ECM, extracellular matrix; LSPL, low sound pressure level; MDCK, Madin–Darby canine kidney cells; NIH-3T3, National Institutes of Health 3T3 fibroblast cell line; NPY, neuropeptide Y; pQCT, peripheral quantitative computed tomography; SAWs, surface acoustic waves; TEWL, transepidermal water loss.

Aryna C. Armand and Matin Bikaran have contributed equally to this work.

Summary

- Successful wound healing relies on the regulation of cellular migration, tissue regeneration, and mechanotransduction processes influenced by external stimuli like acoustic waves.
- This systematic review aims to assess the effects of low-frequency acoustic stimulation, specifically infrasound (1–20 Hz) and low-frequency audible sound (20 Hz–20 kHz), on wound healing, focusing on its impact on cell migration, bone regeneration, and fibroblast activity. Studies from PubMed, Scopus, and Google Scholar were included to provide a comprehensive analysis.
- Results show that infrasound enhances bone growth and osteogenic differentiation, while low-frequency audible sound at 100 Hz boosts fibroblast migration, and frequencies at 10 and 20 kHz accelerate epidermal healing by affecting keratinocyte activity.

tissue regeneration [4–6]. While ultrasound offers increasing potential for wound healing and cell growth, it is not without risks. Some studies have reported possible adverse effects, such as cell damage and death, particularly in the lower < 10 MHz ultrasound range, if parameters are not properly controlled [4, 6].

While the therapeutic potential of ultrasound in wound healing has been well documented, there is a growing body of evidence suggesting that lower frequency acoustic stimulation, particularly infrasound (1–20 Hz) and audible sound (20 Hz–20 kHz), may also have significant effects on cellular behaviour and tissue regeneration. A systematic review of the current literature on the effects of infrasound and audible acoustic waves (1 Hz–20 kHz) on cell migration and wound healing is necessary to synthesise existing knowledge, identify knowledge gaps, and guide future research in this promising field to open new avenues for non-invasive therapeutic interventions.

1.2 | Objectives

This systematic review aims to:

1. Synthesise the current understanding of the mechanisms by which infrasound (1–20 Hz) influences cell migration and the wound healing process
2. Synthesise the current understanding of the mechanisms by which audible acoustic waves (20 Hz–20 kHz) influence cell migration and the wound healing process
3. Identify knowledge gaps and areas for future research in the clinical application of low-frequency acoustic stimulation for wound healing therapies.

By addressing these objectives, this review seeks to provide a systematic overview of the potential therapeutic applications of infrasound and low-frequency acoustic stimulation in wound healing, laying the groundwork for future clinical applications and research directions.

2 | Materials and Methods

2.1 | Eligibility Criteria

This review included studies that investigated the effects of lower frequency sound (1–20 kHz) on various aspects of wound healing processes. Eligible studies encompassed experimental and review articles focusing on epithelial growth, bone regeneration, mesenchymal stem cell proliferation, cytoskeletal remodelling, nuclear positioning, and other relevant processes involved in tissue repair. Studies that exclusively examined ultrasound (frequencies > 20 kHz) were excluded. No restrictions were placed on publication dates; however, priority was given to more recent literature (> 2007) to ensure the relevance of findings.

2.2 | Information Sources

A comprehensive literature search was conducted across multiple databases, including:

- NCBI PubMed (Date: 7/13/24; 7/27/24; 7/28/24, 9/3/24, 9/22/24, and 10/8/24).
- Scopus (Date: 7/13/24; 7/27/24; 7/28/24, 9/3/24, and 10/8/24).
- Google Scholar (Date: 7/13/24; 7/27/24; 7/28/24, 9/3/24, and 10/8/24).
- ChatGPT 4o (though verified by reviewers for accuracy with self-search prior to use) (Date: 7/13/24, 7/27/24, 7/28/24, 9/3/24, and 10/8/24).

2.3 | Search Strategy

This systematic review was conducted in accordance with the PRISMA guidelines, ensuring transparency and rigour in the reporting of review methods and findings (Figure 1). The search strategy employed in PubMed involved the use of specific keywords and phrases, including:

- "Infrasound AND healing"
- "Infrasound AND cell growth"
- "Infrasound AND bone growth"
- "Wound healing AND low frequency sound waves"
- "Cell migration AND low frequency sound"
- "Cell migration AND acoustic sound"
- "Acoustic vibration and Fibroblast"
- "Acoustic waves and cell migration"

English language was a limit for inclusion in this review. Additionally, priority was given to more recent literature (> 2007) to ensure relevance of findings.

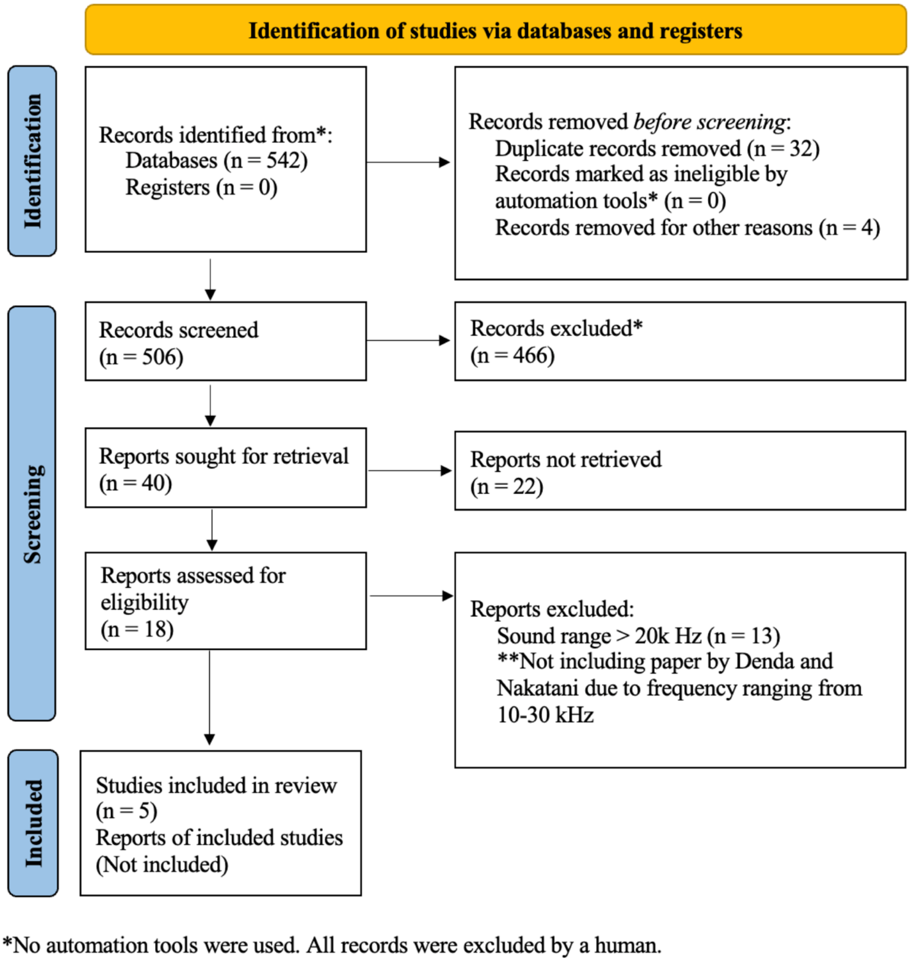

FIGURE 1 | PRISMA 2020 flow diagram. For new systematic reviews which included searches of databases and registers only. The screening process excluded 466 studies from the initial 506 identified based on title review. Studies referencing ultrasound, as well as those involving infrasound or acoustic sound applied in non-wound healing therapies, were omitted. This process further excluded 22 studies that mentioned "acoustic sound" in their titles but did not encompass the proper frequency range of 20–20 kHz within the text. Ultimately, five studies were selected for review in this paper, as they met the required frequency criteria. Notably, one study with a reported range of 10–30 kHz was included despite its slightly broader scope, as further investigation revealed a specific focus on 20 kHz within its findings.

2.4 | Selection Process

Studies were screened and selected based on predefined eligibility criteria, focusing on the appropriate sound frequency range and relevant outcomes related to tissue repair, such as cell migration, wound healing, and bone regeneration/growth/behaviour. Both reviewers independently screened titles and abstracts, followed by a full-text review of relevant literature. Any disagreements regarding study inclusion were resolved through discussion, referencing the review objectives to reach a consensus.

2.5 | Data Collection Process

Data extraction was performed collaboratively by the reviewers. Aryna Armand led the extraction process, focusing on information pertinent to the review's objectives. The extracted data were subsequently reviewed and discussed with Matin Bikaran to ensure accuracy and relevance. No discrepancies arose during this process.

2.5.1 | Data Items

Data items extracted from the included studies encompassed:

- Study characteristics (e.g., authors, year of publication, and study design).
- Details on sound frequency and type of acoustic stimulation used.
- Outcomes measures (e.g., cell migration rates, wound healing metrics, and bone regeneration indicators).
- Mechanistic insights related to cellular responses to acoustic stimulation.

2.6 | Study Risk of Bias Assessment

The risk of bias was not formally assessed in this review due to the diverse methodologies employed across the included studies. However, the reviewers acknowledged potential biases inherent in the included studies, such as small sample sizes or a lack of control groups.

2.7 | Effect Measures

No effect measures were applicable to the synthesis and/or presentation of results.

2.8 | Synthesis Methods

No statistical methods were utilised in synthesising the data, as the review focused on qualitative analysis of the findings from the included studies. The synthesis involved summarising key themes and outcomes related to the effects of infrasound and low-frequency acoustic stimulation on wound healing processes.

2.9 | Ethical Considerations

This systematic review did not involve any direct research on human subjects. All studies included in this review adhered to ethical guidelines for animal or human research as described in their respective publications. Any clinical or in vivo studies referenced in this review obtained the necessary ethical approvals from their institutional review boards, and informed consent was obtained from human participants where applicable.

2.10 | Animal Investigations

This systematic review references several studies involving animal models, specifically those investigating the effects of infrasound and acoustic stimulation on bone regeneration and wound healing. All animal investigations cited in this review were conducted in accordance with ethical guidelines for the care and use of animals in scientific research. The animal studies followed protocols approved by institutional animal care and use committees (IACUC) to ensure humane treatment of the animals.

2.11 | Statistics

As this is a systematic review, no new statistical analysis was performed by the authors. The included studies employed appropriate statistical methods for their respective experimental designs, including analysis of variance (ANOVA), *t*-tests, and regression analysis, to assess the significance of their findings. The quality and statistical rigour of each study were carefully considered during the literature selection process to ensure robust data synthesis.

3 | Results

3.1 | Study Selection

A comprehensive literature search was conducted to identify relevant studies examining the effects of infrasound and low-frequency audible acoustic stimulation on wound healing. After removing duplicates, studies were screened based on their titles and abstracts to determine their relevance to the review objectives. Eligible studies were then assessed in full text to confirm their inclusion based on predefined criteria. The selection process involved both reviewers, who independently evaluated the studies and resolved disagreements through discussion.

3.2 | Study Characteristics

The characteristics of the included studies are summarised in Table 1. Three studies, Long et al., He and Fan, and Enomoto et al., examined infrasound, while two studies, Mohammed et al. and Denda and Nakatani, evaluated audible acoustic sound. Three studies (two infrasound and one acoustic sound) were in vitro using cell-based experiments, while two studies (one infrasound and one acoustic sound) were in vivo using animal models. These studies varied in design and focus, examining different aspects of wound healing influenced by infrasound, and low-frequency acoustic stimulation.

3.3 | Effects of Infrasound on Wound Healing

Infrasound has been investigated for its potential biological effects, particularly in the context of wound healing and tissue regeneration. While some studies highlight its association with psychological and emotional discomfort [7, 8], recent research has focused on its physiological impact, suggesting infrasound may positively influence bone growth, remodelling, and the proliferation of osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) [9, 10].

Long et al. conducted a study investigating the effects of low sound pressure level (LSPL) infrasound on bone fracture healing in rats [9]. In their study, researchers exposed stabilised femoral defected rats to low sound pressure levels at 12–20 Hz (< 90 dB) for 30 min twice every day for 6 weeks and monitored their fracture healing with radiography. They then assessed callus development by measuring the change in the fracture gap over time with peripheral quantitative tomography (pQCT) and the progression of mineralization in the femur by measuring the area of higher density callus within the fracture gap. They found that the infrasound group demonstrated a more consistent and smoother fracture healing and modelling process, as evidenced by radiographs and histomorphology. Notably, the infrasound group showed significantly higher average bone mineral content (BMC) and bone mineral density (BMD) compared to the control group. Immunofluorescence assays revealed increased expression of calcitonin gene-related peptide (CGRP) (a physiological bone metabolism regulator) and decreased innervation of Neuropeptide Y (an antiosteogenic factor NPY) after 2 weeks in the local microenvironment of the infrasound group.

Building on these findings, He and Fan explored the direct effects of infrasound on BMSCs, which play a crucial role in bone regeneration [10]. BMSCs from rat tibia and femur were extracted after exposing BMSCs to infrasound for a duration ranging from 10 min to 2 h. Following this treatment, cells were counted to evaluate proliferation, while apoptosis was measured by quantifying Annexin V in the culture. They demonstrated that infrasound at 16 Hz and 90 dB for 60 min significantly increased

TABLE 1 | Notable study characteristics and findings.

Study	Year	Study design	Sound frequency	Cell type/tissue	Outcomes measured
Long et al.	2013	In vivo	16 Hz	Bone (rat model)	Bone density and osteogenesis
He and Fan	2014	In vitro	16 Hz	Bone marrow mesenchymal stem cells (rat)	Proliferation, osteogenic differentiation, and mineralization
Mohammed et al.	2016	In vitro	100 Hz	Fibroblasts (human and murine)	Migration distance and morphological changes
Enomoto et al.	2020	In vitro	11.2 Hz	Fibroblasts (murine)	Migration distance, glucose consumption, and nuclear shape
Denda and Nakatani	2010	In vivo	10–30 kHz[a]	Epidermis (murine)	Transepidermal water loss and lamellar body secretion

[a]This study utilised sounds at 30 kHz, which is beyond the predetermined range of this review.

the proliferation and osteogenic differentiation of BMSCs and reduced the rate of apoptosis in vitro. The same duration of infrasound exposure also upregulated the mRNA and protein expression of survivin, an anti-apoptotic protein.

The results indicate that infrasound exposure has measurable effects on bone growth and remodelling, as evidenced by enhanced BMC and BMD in vivo and increased proliferation and differentiation of BMSCs in vitro.

3.4 | Effects of Low-Frequency Audible Acoustic Stimulation

The field of acoustic stimulation for wound healing is still in its nascent stages, with limited studies exploring the effects of low-frequency sound on cellular behaviour and tissue regeneration. Despite the scarcity of research, the few studies conducted thus far have shown promising results, highlighting the potential of this approach to influence wound healing processes.

Recent studies have demonstrated that low-frequency acoustic stimulation can significantly influence cell behaviour, particularly in the context of cell migration and wound healing [11–13]. Mohammed et al. provided foundational evidence on the effects of acoustic vibration on fibroblast cell migration [11]. In this study, a speaker-based system was applied to the underside of the cell culture plates to mechanically stimulate human lung and murine areolar/adipose fibroblast cells. They reported that after 5 min of mechanical stimulation via low-frequency acoustic vibrations, particularly at 100 Hz, there was a significant enhancement in the mean migration distance of fibroblasts measured via differential interference contrast microscopy up to 4 h after stimulation. Interestingly, higher frequencies (200 Hz and 1600 Hz) showed less pronounced effects, indicating a frequency-dependent response. The research further demonstrated that acoustic vibration induced changes in cell morphology, particularly actin restructuring, promoting the formation of filopodia and lamellipodia, which play a vital role in environmental sensing and cell migration.

Enomoto et al. furthered these studies by investigating the effect of directional wave propagation on cellular movement [12]. They used a rubber insert in a culture dish to create a gap between fibroblasts, and after removing the insert, the cells were exposed to vibrational stimulation at 11.2 Hz, either orthogonal or parallel to the gap. The migration distance, represented by the remaining gap size, was measured after 24 h of vibrational stimulation. Results showed that vibration orthogonal to the wound gap (horizontal vibration) enhanced the collective migration distance, glucose consumption, and altered nuclear shape and orientation in response to 11.2 Hz at 2 V [12]. Conversely, vertical vibrations parallel to the gap slowed the migration rate and glucose consumption. These results point to the directionality of the acoustic wave playing a role in the speed of cell migration.

Finally, Denda and Nakatani explored the effects of sound frequencies between 10 and 30 kHz on skin barrier recovery [13]. After disrupting the skin barrier of hairless mice using tape stripping, the mice were then exposed to sound frequencies of 10, 20, and 30 kHz for 1 h. The sound pressure levels and distances from the sound source were varied to assess their impact on barrier recovery via transepidermal water loss (TEWL). They found that all tested frequencies significantly accelerated skin barrier recovery, with 20 kHz (the upper of acoustic sound) being the most effective. Further, at 20 kHz, higher sound pressure levels (88 dB) and shorter distances between the speaker and skin (up to 3 cm) showed to result in significant acceleration in barrier recovery. Electron microscopy was used to observe lamellar body secretion, which is indicative of epidermal permeability barrier homeostasis. Overall, they concluded that the specific sound frequencies, particularly 20 kHz, can enhance skin barrier recovery by modulating epidermal keratinocyte activity.

Collectively, these studies provide evidence that low-frequency acoustic waves impact key factors in wound healing, such as cell migration and morphology in vitro, and skin barrier recovery in vivo.

3.5 | Summary of Findings

Results of this review are summarised below and visualised in Figure 2.

3.6 | Infrasound (1–20 Hz)

- Improvement in fracture healing in vivo:
  - Low sound pressure level (LSPL) infrasound has been found to improve fracture healing in rat models.
  - The infrasound group showed significantly higher BMC and BMD compared to the control group. Increased expression of CGRP and decreased innervation of Neuropeptide Y (NPY) after 2 weeks were also observed, suggesting modulation of a neuro-osteogenic network.
- Promotion of bone growth and osteogenic differentiation in vitro:
  - Infrasound has been shown to promote in vitro bone growth and the osteogenic differentiation of BMSCs derived from rat models.

3.7 | Acoustic Audible Sound (20 Hz–20 kHz)

- Enhancement of fibroblast cell migration in vitro:
  - Low-frequency audible acoustic stimulation, particularly at 100 Hz, has been shown to significantly enhance human and murine fibroblast cell migration in vitro.
  - Acoustic vibration at 100 Hz induced changes in human and murine cell morphology in vitro, including the formation of filopodia and lamellipodia, which are essential for cell migration and environmental sensing.
- Directional influence on cell migration in vitro:
  - Horizontal vibrations (orthogonal to the wound gap) have been found to enhance collective migration distance, glucose consumption, and alter nuclear shape and orientation of murine fibroblasts in vitro.
  - Vertical vibrations (parallel to the wound gap) slowed the migration rate and glucose consumption, indicating that the directionality of the acoustic wave plays a significant role in the cellular responses of murine fibroblasts in vitro.
- Acceleration of skin barrier recovery in vivo:
  - Exposure of murine epidermis to 10 kHz and 20 kHz, particularly to 20 kHz with higher sound pressure levels (88 dB) and shorter distances between the speaker and skin (up to 3 cm), significantly accelerated skin barrier recovery by modulating epidermal keratinocyte activity in vivo.
  - Lamellar body secretion, indicative of epidermal permeability barrier homeostasis, was observed via electron microscopy, further supporting the role of 20 kHz in enhancing skin repair mechanisms.

4 | Discussion

4.1 | Implications of Infrasound and Low-Frequency Acoustic Stimulation

Our systematic review has revealed intriguing potential for both infrasound and low-frequency audible acoustic stimulation in wound healing and tissue regeneration. The findings suggest that these acoustic interventions could offer novel, non-invasive approaches to modulating cellular behaviour and enhancing healing processes.

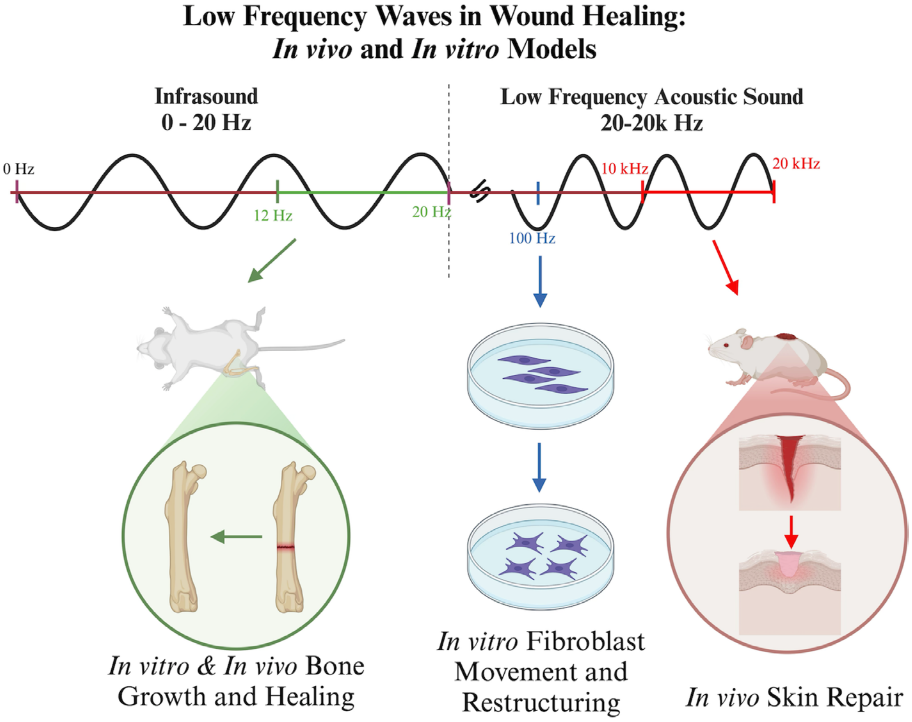

FIGURE 2 | Low frequency waves in wound healing. Infrasound (0–20 Hz) and low-frequency audible sound (20–20 kHz) enhance wound healing by promoting bone growth, cell migration, and skin repair in preclinical studies. These findings highlight early-stage research exploring acoustic wave applications in regenerative medicine, with further investigation required to assess clinical viability (created in BioRender. Bikaran, M. (2025), https://BioRender.com/n53c439).

In the realm of infrasound (1–20 Hz), the studies by Long et al. and He and Fan point to promising applications in bone healing and regeneration. The observed improvements in fracture healing, increased bone mineral content and density, and enhanced osteogenic differentiation of BMSCs suggest that infrasound could be particularly beneficial in orthopaedic contexts. The modulation of the neuro-osteogenic network opens up interesting avenues for exploring the interplay between acoustic stimulation and neurological factors in bone healing.

These findings have significant implications for the treatment of complex wounds involving bone tissue, such as in cases of severe trauma, chronic wounds that extend to the bone, and even osteoporosis/osteomalacia. Perhaps among osteoporotic populations who are unable to partake in heavy-weight bearing exercises, the application of infrasound waves has the potential to initiate mechanotransduction and mimic mechanical stress necessary for both indirect and direct bone healing, potentially accelerating healing in these challenging cases. Moreover, the observed effects on BMSC proliferation and differentiation suggest that infrasound might be leveraged to enhance stem cell-based therapies in regenerative medicine. By considering the timing when BMSCs exhibit peak activity during the fracture healing process, we may enhance their function through the application of infrasound.

Another target population may include individuals with neglected malunion fractures after surgical intervention. Infrasound therapy may potentially act as a non-invasive alternative to osteotomy in the treatment of malunion. Given the promising results on the proliferative effects of infrasound on BMSCs, further investigation on the potential impact of infrasound on the migration and proliferation of epithelial fibroblasts is warranted.

Turning to low-frequency audible acoustic stimulation (20 Hz–20 kHz), the work of Mohammed et al. and Enomoto et al. highlights the potential for manipulating cell migration and wound closure. The enhancement of fibroblast migration, particularly at specific frequencies, suggests that acoustic stimulation could be fine-tuned to accelerate wound healing processes. The observed changes in cell morphology indicate that acoustic stimulation may be influencing fundamental cellular mechanisms involved in migration and environmental sensing.

The directional effects observed by Enomoto et al. are particularly intriguing, as they suggest that the orientation of acoustic waves relative to a wound could be a crucial factor in treatment efficacy. This finding opens up possibilities for highly targeted acoustic therapies, where the direction and frequency of stimulation could be optimised based on wound geometry and desired healing outcomes.

Finally, Denda and Nakatani's findings suggest that specific sound frequencies can modulate epidermal keratinocyte activity, leading to improved skin barrier recovery. This has potential therapeutic applications in wound healing, where enhancing skin barrier function can accelerate healing and reduce the risk of infection.

While these findings are promising, it is important to note that the field is still in its early stages. The observed effects are complex and likely involve multiple cellular and molecular pathways. The frequency-dependent nature of the responses underscores the need for careful optimisation of acoustic parameters in any potential therapeutic applications. Furthermore, the variability in cellular responses highlights the importance of considering cell type-specific effects in future research and potential clinical applications.

As we continue to unravel the mechanisms by which acoustic stimulation influences cellular behaviour, we may uncover new paradigms for wound treatment that complement or enhance existing therapies. The non-invasive nature of acoustic stimulation makes it a particularly attractive avenue for further research, with potential applications ranging from accelerating healing in acute wounds to managing chronic wound conditions.

4.2 | Limitations and Future Directions

Significant knowledge gaps persist in our understanding of infrasound and audible acoustic wave effects on wound healing. There is limited investigation into the underlying mechanisms, particularly for lower frequency acoustic stimulation, and an incomplete understanding of the molecular pathways involved in mechanotransduction across different frequency ranges. Additionally, there is a lack of comprehensive studies on how infrasound and audible acoustic waves influence cell morphology, gene expression, and extracellular matrix (ECM) composition. Furthermore, all studies indicated small sample sizes and limited generalisability to humans, highlighting the need for larger, rigorously designed clinical trials.

To address these limitations and advance the field, future research should focus on adopting a multidisciplinary approach to examine the effects of infrasound and acoustic waves on cellular processes. This includes exploring potential mechanotransduction pathways specific to different frequency ranges and analysing changes in cell stiffness, cytoskeletal organisation, and the production of key ECM components in response to various acoustic parameters. Investigating a broader range of frequencies and intensities, including pulsating versus constant and intermittent versus long-term stimulation, will also be crucial for developing optimised treatment protocols.

By demonstrating significant effects on cellular migration, differentiation, and tissue regeneration, these modalities offer a promising, non-invasive approach that could transform clinical wound care. In particular, the ability of infrasound to enhance bone growth and remodelling suggests potential applications for treating complex wounds involving bone, such as fractures and orthopaedic injuries, as well as chronic bone generation conditions like osteoporosis and osteomalacia. Similarly, the enhancement of fibroblast migration and keratinocyte modulation through audible acoustic waves may present a novel method for accelerating wound closure, particularly in chronic wound cases such as diabetic ulcers and pressure sores or in those with limited mobility.

Given their non-invasive nature and demonstrated efficacy in both in vitro and in vivo models, acoustic stimulation offers a unique therapeutic advantage over more invasive or high-risk methods. With proper optimisation of frequency and wave direction, acoustic therapy could be safely administered in outpatient or even at-home settings, making it a cost-effective option for patients with chronic wounds or those at risk of slow healing. Future research should focus on bridging the gap between preclinical findings and human trials, with the aim of developing tailored acoustic treatments that address the specific needs of various wound types and patient populations. The next critical step is clinical validation through well-designed trials that assess safety, efficacy, and practical implementation in a medical setting.

By integrating acoustic stimulation into clinical practice, the potential exists to significantly improve healing outcomes, reduce treatment costs, and enhance patient quality of life.

4.3 | Limitations of the Review Process

First, search strategy limitations include potential database restrictions and the possibility of missing relevant studies not published in English or those outside selected time frames, impacting the comprehensiveness of the findings. Bias in study selection may also be a factor, as publication bias could skew the data towards studies reporting positive effects, given the lack of unpublished or null-result studies in this area. Additionally, data synthesis constraints arose from the heterogeneity among studies in methodologies, sound frequencies, and biological models, hindering the ability to conduct quantitative meta-analysis and requiring reliance on qualitative synthesis. Reviewer expertise in acoustics and cellular biology, while thorough, may also limit interpretations of findings from niche fields. Transparently acknowledging these limitations enhances the clarity regarding the boundaries within which the review's findings should be interpreted.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

This systematic review did not generate any new data. All data analyzed in this review are derived from previously published studies, which are cited within the manuscript. No additional data are available.

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