Phonophoresis in Physiotherapy: Mechanisms, Applications, and Emerging Trends for Enhanced Drug Delivery and Therapeutic Efficacy

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Abstract. Phonophoresis, a widely utilized treatment in physiotherapy, combines topically applied gel or cream-based medications with ultrasonic therapy to enhance percutaneous absorption of pharmacological agents. The procedure employs ultrasound frequencies of 0.7 to 1.1 MHz with intensities ranging from 0.0 to 3.0 Watts per cm². Indications for phonophoresis span various inflammatory, deformative, dermatological, and rheumatic/neurological conditions. Recent studies suggest its clinical efficacy in pain relief and improved function, especially in conditions like lateral epicondylitis and osteoarthritis. The mechanism of action involves both thermal and non-thermal effects, with cavitation playing a key role in enhancing transdermal transport. Phonophoresis offers a non-invasive alternative for drug delivery, bypassing hepatic metabolism and minimizing systemic side effects. Various medicinal gels, particularly diclofenac, are used for transdermal drug delivery through phonophoresis.

1 Introduction

Phonophoresis treatment is widely used in the field of physiotherapy, where the topically applied gel or cream-based medicines are being used along with ultrasonic therapy to accelerate the effects of ultrasound [1]. Phonophoresis, also known as sonophoresis, has been claimed to intensify the percutaneous absorption of certain pharmacological agents such as anti-inflammatory steroids and local anesthetics from intact skin into the underlying subcutaneous structures by ultrasound, thereby improving their effectiveness. This procedure is commonly used in physical therapy practices. The procedure generally utilizes an ultrasound apparatus that produces frequencies of 0.7 to 1.1 MHz. The ultrasound intensities that are being employed usually range from 0.0 to 3.0 Watts per cm². Both continuous-mode as well as pulse-mode applications are utilized, and most treatments last from 5 to 8 mins, with the exception of treatments of larger areas (greater than 36 cm²) requiring more than 8 mins [2].

1.1 Indications and therapeutic effect of phonophoresis

Diseases and conditions treated with ultrasound include inflammatory (arthritis), deformative (contractures, spondylitis), dermatological (eczema, warts), and rheumatic/neurological (sciatica, lumbago, myalgia, neuralgia) entities [3]. There are varying results regarding the therapeutic benefits of phonophoresis (such as pain relief and...
piezoelectric principle

drugs, can be defined as the migration of drug molecules through skin under influence of ultrasound permeation of corticosteroids

influence of ultrasound, has been studied in clinical conditions. It is well documented to practically increase skin ultrasound applicator

physical therapy and sports medicine, the drug is applied locally at the target site and massaged with a therapeutic without inactivating the drug molecules and with no side practices

Phonophoresis is the use of ultrasound to enhance percutaneous absorption of a drug. Phonophoresis provides an transmit the ultrasound

particular, musculoskeletal conditions and . Ultrasound therapy is widely used by physiotherapists in the management of a range of conditions, in

Phonophoresis is the use of ultrasound energy to enhance percutaneous penetration of topically applied drugs

has a significant advantage as it bypasses the hepatic first agents such as anti

Phonophoresis is a process of local administration of topical medicines under the influence of ultrasound. Thermal, non administers through the application of phonophoresis are anti

Phonophoresis is

the application of ultrasound waves to administer the therapeutic agents to muscles without causing tissue damage. Therefore, the permeation of vessels is enhanced both structurally and

The main purpose of this method is to achieve a suitable and fast concentration of drug in the tissues

phonophoresis provides clinical improvement by decreasing pain and increasing function

osteoarthritic conditions. Recent studies have shown that, when compared with placebo treatments or ultrasound alone, improved range of motion) when it was used to treat lateral epicondylitis, temporomandibular joint pain, and

In this efficient method, which has had wide utility in - inflammatory steroids and local anesthetics from intact skin into the underlying subcutaneous

The general result is that skin permeability is enhanced by the augmented mechanical

The use of ultrasonic waves to induce topical medicine is considered painless, noninvasive and

The small cavitation bubbles, which

The thermal, and chemical effects generated by the ultrasound, drive the drug molecules into the tissues causing an

Therapeutic ultrasound

The general result is that skin permeability is enhanced by the augmented mechanical

Apart from

It can serve as a painless and non

Therapeutic ultrasound

It is

The use of ultrasonic waves to induce topical medicine is considered painless, noninvasive and

It is suggested by early studies to enhance the absorption of analgesics and anti

It is

The use of ultrasonic waves to induce topical medicine is considered painless, noninvasive and
1.1 Application
Phonophoresis involves placing the topical phonophoresis agent on the skin and massaging by the ultrasound head or transducer. The main aim of this method is attaining a fast and suitable amount of drug in the tissue without inactivating the drug molecules or no side effect. The therapeutic ultrasound, which is used for phonophoresis works on two main modes: continuous and pulsed output. The continuous ultrasound is known to have thermal effects, whereas pulsed mode has mechanical effects such as cavitation, microstreaming, acoustic streaming, increased skin pore size and number and the intercellular space. This leads to several changes in the tissues due to their interaction with the therapeutic ultrasound waves.

Taking into consideration there are various medicinal gels that are used for the trans dermal drug delivery by the phonophoresis. The effectiveness and penetrating power vary according to the properties of the gel. Cardero et al. indicated that diclofenac has the highest transdermal penetration among NSAIDs such as indomethacin, piroxicam, tenoxicam, ketorolac and aceclofenac. Rosim et al., also recommended that therapeutic ultrasound administration increases the percutaneous absorption of the topical diclofenac gel. According to this, diclofenac is considered to be a good agent for phonophoresis administration.

2 Mechanism

2.1 Thermal effects

Ultrasound cannot propagate through tissue without some of its associated energy being deposited as heat. This heat will result in increased temperature of the tissue if its rate of input exceeds the capacity of that tissue to dissipate it. Thermal effects are important with high-intensity continuous-wave ultrasound and are prominent when the irradiated tissue has high protein content or includes bony regions, and when the vascular supply to the area is poor.

In thermal mode, it will be most effective in heating the dense collagenous tissues and will require a relatively high intensity, preferably in continuous mode to achieve this effect. Many papers have concentrated on the thermal effectiveness of ultrasound, and much as it can be used effectively in this way when an appropriate dose is selected (continuous mode >0.5 W cm²), the focus of this paper will be on the non-thermal effects. Both Nussbaum (1998) and ter Haar (1999) have provided some useful review material with regards the thermal effects of ultrasound.

Comparative studies on the thermal effects of ultrasound have been reported by several authors (e.g. Draper et al., 1993, 1995a, b) with some interesting, and potentially useful results. It is too simplistic to assume that with a particular treatment application there will either be thermal or non-thermal effects. It is almost inevitable that both will occur, but it is furthermore reasonable to argue that the dominant effect will be influenced by treatment parameters, especially the mode of application i.e. pulsed or continuous.

Baker et al. (2001) have argued the scientific basis for this issue coherently. Lehmann (1982) suggests that the desirable effects of therapeutic heat can be produced by US. It can be used to selectively raise the temperature of tissues due to its mode of action. Among the more effectively heated tissues are periosteum, collagenous tissues (ligament, tendon & fascia) & fibrotic muscle (Dyson 1981). If the temperature of the damaged tissues is raised to 40-45°C, then hyperemia will result, the effect of which will be therapeutic. In addition, temperatures in this range are also thought to help in initiating the resolution of chronic inflammatory states (Dyson & Suckling 1978). Having made these comments, most authorities currently attribute a greater importance to the non-thermal effects of U/S as a result of several investigative trials in the last 15 years or so.

2.2 Non-thermal Effects

2.2.1 Cavitation

Cavitation is the result of the pressure changes associated with the propagation of a compressional wave (which is the only wave that can propagate for large distances through soft tissues). This may lead to structural disordering of the stratum corneum lipids, due to oscillations of the ultrasound-induced cavitation bubbles near the keratinocyte lipid bilayer interfaces. Cavitation bubbles also generate shock waves upon collapse, and this may also contribute to the structure-disordering effect. The diffusion of permeants through a disordered bilayer phase would naturally be higher than that through normal bilayers.
the cell can occur when microscopic gas bubbles expand and then collapse rapidly, causing a “micro explosion.”

2.2.2 Micro Streaming effect

...streaming effect becomes more important when continuous wave application is used, and the fluid is free to move near vibrating structures such as cell membranes and the surface of stable cavitation gas bubble (Burns 1981, Dyson & Pilling 1985, Suckling 1978). This phenomenon is known to affect diffusion rates and membrane permeability. Sodium ion absorption of the drugs. Miyazaki et al. (1991) concluded that there is a rise of 6 °C with 1 MHz for a low intensity of 0.25 W/cm2 and 12°C rise at an intensity of 0.75 W/cm2, which suggests that the rise in skin temperature is an important factor. On the other hand, there are various in vitro studies which used 1 W/cm² ultrasound at 0.25 MHz and 1.7 °C rise at 1 W/cm², which indicates that the temperature rise is not the only parameter affecting drug delivery. Several authors have analyzed the optimal rise in surface temperature of the skin that is required for the increased permeability of macromolecules across the skin. The Streaming effect is enhanced by micro-explosions (Dumitrescu et al. 2008). A study by Dumitrescu et al. (2008) showed that a significant increase in drug concentrations was observed after ultrasound treatment, especially in the dermal layer, indicating the potential for improved drug delivery.

2.2.1 Dosage

...low frequency phonophoresis has been used in various clinical fields. These researchers evaluated the skin permeability of isoniazid (INH) and rifampicin (RIF) in patients with tuberculous lymphadenitis. Chen et al. (2016) stated that electroporation (EP) has shown beneficial properties including faster effect and shorter duration of therapy. The authors concluded that EP can effectively enhance the skin permeability of INH and RIF in patients with tuberculous lymphadenitis.

2.2.2 Low frequency phonophoresis

...enhance the transdermal transport of various proteins including insulin, interferon and erythropoeitin across human skin, indicating the potential of low frequency ultrasound for drug delivery.

3 Application of Sonophoresis in Medical Sciences and Physiotherapy

...Several authors have reported the use of low frequency phonophoresis for the treatment of superficial lesions that could help eradicate the germs, shorten the treatment course and increase the cure rate of patients with pulmonary tuberculosis. Nakhostin et al. (2016) evaluated the effects of virgin olive oil phonophoresis on female athletes' anterior knee pain (AKP). In a double blinded, randomized clinical trial, Nakhostin et al. (2016) treated A total of 93 female athletes suffering from AKP voluntarily participated in this study. Patients were randomly assigned into olive oil (n = 31), piroxicam (n = 31) or base gel phonophoresis (n = 31) groups. After 6 and 12 sessions of physiotherapy, Roohi et al. (2016) stated that ultrasound was being used for various purposes including ocular drug delivery, nail therapy, etc. etc. etc.

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Ramakrishnan and Aswath (2019) examined the efficacy of phonophoresis in patients with temporomandibular disorders (TMDs). A total of 50 patients diagnosed clinically and radiographically as TMD were randomly assigned into either of the 2 groups: Group A and Group B. Each group was treated thricelyweekly for 2 weeks.

In a systematic review and meta-analysis, Wu, and colleagues (2019) examined the safety and effectiveness of therapeutic ultrasound for knee osteoarthritis (OA). PubMed, Embase, and the Cochrane Library were systematically searched for RCTs from inception up to June 2019; RCTs comparing therapeutic US with sham US in knee OA patients were included.

A total of 15 studies including 3 related studies with 1,074 patients were included. Trials were also included; 2 reviewers independently identified eligible studies and extracted data. The VAS and CRP levels before and after treatment were carried out using the VAS and the 6MWT were examined to assess the functional capacity.

Both groups were treated with a US program in continuous mode, 1.0 W/cm², 10 mins/session for 10 sessions. Acoustic gel containing no drug US was used in the UT group, whereas a gel containing aceclofenac was applied in the PP group. The authors concluded that PP was suggested as an effective method for the treatment of symptomatic knee OA for reducing pain and improving functional capacity. This was a relatively small study (total of 40 subjects) with no follow-up.

In a prospective, double-blind procedure, Altan and colleagues (2019) examined the effect of phonophoresis with the combination of non-inflamed drugs US. Patients with knee OA (n = 40; mean age ± SD, 64.30 ± 9.71 years), who had VAS scores for knee pain intensity of 68.00 ± 9.58 (UT group) and 71.00 ± 8.74 (PP group, respectively) before treatment, were randomly allocated into 2 groups. No significant difference was observed statistically between US and phonophoresis groups. No significant difference was observed statistically between US and phonophoresis groups. No significant difference was observed statistically between US and phonophoresis groups. No significant difference was observed statistically between US and phonophoresis groups.

Although several treatments have been introduced to treat LMTP, the most efficient one is still yet to be found. These researchers compared the effectiveness of pressure release, phonophoresis of betamethasone and dry needling in treating upper trapezius LMTP. A total of 60 subjects (mean ± SD age of 23.6 ± 2.1 years), with at least 2 days of history of neck pain, participated in this study. The authors concluded that considering the significant, positive effects of all 3 methods, dry needling and phonophoresis appeared to be more effective than pressure release in treating upper trapezius LMTP. A total of 60 patients with acute LBP were randomly assigned into 2 groups. These researchers suggested that further studies with larger patient groups are needed for better assessment of pain and inflammation. However, phonophoresis did not produce additional benefits to functional improvement, but may relieve pain compared to conventional non-drug US. Routine ultrasound (US) treatment with non-drug US may also be beneficial in the treatment of patients with acute LBP.
Ultrasound has the potential to provide an efficient and minimally invasive method for drug delivery.

### 3.1 Ocular delivery

For many years, ultrasound has been widely used in ophthalmology for diagnostic purposes, and there is an increasing interest in ophthalmology. High intensity focused ultrasound (HIFU) for the treatment of glaucoma, and ultrasonic drug delivery are the two main areas of research and potential clinical applications. High frequency (20 to 50 MHz) ultrasound, which is known as ultrasound biomicroscope (UBM), is used to perform high resolution imaging of the anterior segment of the eye, even in cases in which the ocular media are not optically transparent (cataract, vitreous, 01031 (2024)

A seminal study by Sonoda et al. demonstrated that 1 MHz ultrasound exposure in cultured rabbit corneal epithelial cells and in vivo rabbit cornea resulted in up to a 10-fold increase in corneal permeability for sodium fluorescein whilst producing only minor and reversible changes in the corneal structure.

In vitro. The differences between the treatment and control experiments were significant after 10 min ultrasound exposure.

The most convincing evidence for ultrasound and gene transfer in cell culture. In in vitro models of osteoblasts,8 ultrasound enhances the delivery of reparative osteoblastic growth factors. These results have been confirmed in vivo. Moreover, these researchers stated that further studies may elucidate the effects of ECSWT and phonophoresis in MPS treatment. Other studies of ultrasound for retinal detachment diagnosis. High intensity focused ultrasound (HIFU) for the treatment of glaucoma, and ultrasonic drug delivery are the two main areas of research and potential clinical applications.

In a randomized clinical trial, patients in both groups received the same stretching exercise program and drug regimen during the intervention. The authors concluded that both phonophoresis and ECSWT groups effectively decreased pain and comprised the posterior segment of the eye, even in cases in which the ocular media are not optically transparent.

The trend of changes in the pain and NDI scores was not significantly different between the groups. At the end of the treatment, the pain score was similar between the groups. Moreover, these researchers stated that further studies may elucidate the effects of ECSWT and phonophoresis in MPS treatment. Other studies of ultrasound for retinal detachment diagnosis. High intensity focused ultrasound (HIFU) for the treatment of glaucoma, and ultrasonic drug delivery are the two main areas of research and potential clinical applications.

3.2 Nail Therapy
therapeutic/immunotherapeutic agents directly to amyloid plaques in mouse models of Alzheimer’s disease. This to transiently disrupt the blood load compared to controls, highlighting the potential of this technique in the enhancement of high intensity ultrasound applications in tumor tissue of therapeutics for up to two weeks after ultrasound Su et al. reported on a new approach for remote high intensity ultrasound microbubbles, and gaseous precursor agents have been developed that bind or entrap genetic materials. Targeting with the use of microbubbles and ultrasound and cavitation is a likely mechanism. Acoustically active materials, may be used to enhance gene expression without the use of exogenous micro materials has been tested to improve delivery of genetic materials. Ultrasound has a direct effect on gene expression that gene into muscle. Muscle cells appear able to take up exogenous genes and produce the protein from the gene. Animal and human studies have shown that relatively efficient gene expression can be achieved by direct injection of a detail in its reviews widely. A recent themed issue in Advanced Drug Delivery Reviews discussed ultrasound in gene and drug delivery in ultrasound therapy research; its future utility is of course closely related to the success of gene therapy treatments more levels required to destroy microbubbles lie in the diagnostic range. This is one of the most rapidly expanding fields of have been investigated are in the vicinity of the genetic material or when genes are encapsulated within or bound to the bubbles. Both strategies transfection is achieved in the presence of this main aim is to increase the delivery efficiency of exogenous nucleic acid to the intended target. The ideal system would enhance gene expression in the target while having no effect in non gene therapy. There is considerable interest in facilitating the transfer of genes into diseased tissues and organs. The ultrasound might be able to provide in vitro and in vivo. Ultrasound has been shown to enhance gene transfer into cells in vitro. Significantly better sign…
3.5 Vaccines

Sonoporation and sonodynamic therapy is considered a non-invasive method to induce BBB disruption (BBBD) for spatially targeted drug delivery to the brain. Husseini and colleagues demonstrated that cavitation can aid drug delivery in perfused rat brains.

Kost and colleagues suggested the feasibility of ultrasound as a possible approach to externally affect the release rates of drug-loaded implants. These implants were exposed for 2 h to ultrasound at 3 W/cm² (1 MHz, 20% duty cycle) for six consecutive days, resulting in depletion of implantable contractions. Henzl discussed passive transdermal delivery systems and the possibility of using active transdermal delivery systems including sonophoretic drug delivery, which correlated well in sub harmonic emissions (70 KHz, 0.28 W/cm²). Larkin and colleagues showed that low non-invasive ultrasound exposure is combined with fibrinolytic drugs such as streptokinase, urokinase or tissue plasminogen activator to proximal capillary walls.

Chemical activation of drugs by ultrasound energy for transdermal hormone replacement therapy has been studied. For TCI and constitutes a potential alternative to needle application procedure in human volunteers under similar conditions. Ultrasound thus offers a safe and painless adjuvant to transdermal vaccines.

3.6 Sports medicine

Using tetanus toxoid as a model vaccine, the results presented here demonstrate that ultrasound exposure can be used to optimize bleomycin delivery. bleomycin is a cytotoxic antibiotic which was shown to occur by an apoptotic mechanism. The results achieved in vivo were optimized, and an effective intraperitoneal or intra-tumoral application of low drug released correlated well in sub harmonic emissions (70 KHz, 0.28 W/cm²).

Sonothrombolysis is a technique that uses ultrasound waves to break down blood clots. It is a non-invasive method that can be used to treat various conditions such as stroke and heart attack.

3.7 Hormone replacement therapy

A new direction for ultrasound therapy has been revealed by recent research demonstrating a beneficial effect of ultrasound on injured bone. During fresh fracture repairs, ultrasound reduces swelling and increases bone healing times by 30–50%. When used in combination with microbubble contrast agents, the effect was demonstrated in solid tumors.

Topical delivery of vaccines such as the tetanus toxoid offers several advantages over needle-based vaccinations. Tezel and colleagues used low intensity pulsed ultrasound to deliver 1.3 mg toxoid into skin, which generated the same immunoglobulin G antibody titres generated by 5 mg of toxoid (150 kDa) in mice. This indicates that ultrasound can enhance immunogenicity and could potentially reduce the dose required for immunization.

Ultrasound has the potential for use on other tissues and conditions more commonly encountered in sports medicine, such as muscle strains and soft tissue injuries. It is a non-invasive method that can alleviate pain and promote healing.

3.8 Sonoporation and sonodynamic therapy (related to cancer cell)

3.9 Sonothrombolysis

Recently, focused ultrasound (FUS) in combination with microbubble (MB) contrast agent, termed sonodynamic therapy, has been studied. This technique uses ultrasound to activate carrier proteins or pore formation through mechanical forces (i.e., shear and circumferential stresses) on target tissues.

Several successful studies using ultrasound on neurogenerative disorders have been reported, demonstrating its potential for delivering a wide variety of small and large molecules to the brain for imaging and therapy in other tissues.

Stresses generated by FUS beam, MBs expand and contract via inertial cavitation or stable cavitation processes. These physical activities exert mechanical forces (i.e., shear and circumferential stresses) on target tissues, leading to increased paracellular transport through widened tight junctions and/or increased transcellular transport through mechanical forces (i.e., shear and circumferential stresses).

FUS in combination with MB has been used as a non-invasive method to induce BBB disruption (BBBD) for spatially targeted drug delivery to the brain.
exposure times do not need to be long to deliver a clinically significant insulin dose that reduces high blood glucose. Lee and colleagues demonstrated the feasibility of using short ultrasound exposure times to non-invasively deliver insulin using a lightweight (<22 g), low resonance frequency in water. In order to increase the spatial ultrasound field for drug delivery across skin, two arrays, each comprising four cymbal transducers, were constructed. Smith and colleagues explored the feasibility of using ultrasound by novel transducers for enhancing the transport of insulin across skin in vitro. They also explored the use of the cymbal transducer as both a single element and configured in a Tweezer or Cymbal Array. Maione and colleagues focused their research on the design and construction of a small lightweight transducer or array. Several types of sonophoresis devices have been developed in recent years. A lightweight (>73.3 g) sonophoresis device has the capability to reduce the applied voltage at least twofold. The proposed ultrasonic probe from a commercial sonicator weighs about 1 kg. The authors also proposed the new concept of a highly compact sonophoresis device to overcome some of the drawbacks of commercial equipment. Several types of sonophoresis devices with double ultrasound transducers weigh only 73.3 g; by comparison the ultrasonic probe from a commercial sonicator weighs about 1 kg. The authors also proposed the new concept of a highly compact sonophoresis device to overcome some of the drawbacks of commercial equipment. The device has the capability to reduce the applied voltage at least twofold. The proposed device has a radiated acoustic intensity about $2 \times 10^3$ mW/cm$^2$. Their results indicated that ultrasound is effective for treating tumors.

3.10 Nanoparticles

New technologies combine the use of nanoparticles with acoustic power for both drug and gene delivery. Ultrasonic delivery of nanoparticles has tremendous potential because of the wide variety of drugs and genes that could be delivered to targeted tissues. The small packaging allows nanoparticles to penetrate targeted microbubble destruction for local drug and gene delivery is broadly based on targeted microbubble destruction has been shown to increase transfection rates of naked plasmid DNA and viral vectors by several orders of magnitude. It is based on the development of second generation ultrasound contrast agents. These are microbubbles that are able to remain stable for several minutes in the human circulation and can pass through the pulmonary circulation and can pass through the pulmonary capillaries; they are then trapped in the tumor tissue. Ultrasonic drug and gene delivery from micelles usually employs polyether block copolymers and metaniobate, zirconatetitanate, polyvinyl fluoride, thin film zinc oxide, lead titanate or the piezo cymbal array (f = 20 kHz to 3 MHz) for sonophoresis are available. These transducers are effective devices is currently a thriving area of research in sonophoresis. The design and construction of transcutaneous non-invasive ultrasound delivery systems is an interesting field of research. An interesting application for therapeutic sonography is the thrombolytic effect of ultrasound. A positive effect of ultrasound on clot dissolution was first reported by Trubestein and colleagues. Active mechanical fragmentation of the thrombus or the enzymatic activity of the applied activator.

3.11 Cardiovascular Therapy

We have explained that the use of ultrasound in cardiovascular therapy is an interesting field of research. The development of myocardial contrast echocardiography was an essential milestone in this area. The use of ultrasound in cardiovascular therapy is an interesting field of research. Devices in Market

4 Devices in Market

The design and construction of transcutaneous non-invasive ultrasound delivery systems is an interesting field of research. The development of myocardial contrast echocardiography was an essential milestone in this area. The use of ultrasound in cardiovascular therapy is an interesting field of research. The development of myocardial contrast echocardiography was an essential milestone in this area. The use of ultrasound in cardiovascular therapy is an interesting field of research. The development of myocardial contrast echocardiography was an essential milestone in this area. The use of ultrasound in cardiovascular therapy is an interesting field of research. The development of myocardial contrast echocardiography was an essential milestone in this area. The use of ultrasound in cardiovascular therapy is an interesting field of research. The development of myocardial contrast echocardiography was an essential milestone in this area. The use of ultrasound in cardiovascular therapy is an interesting field of research. The development of myocardial contrast echocardiography was an essential milestone in this area. The use of ultrasound in cardiovascular therapy is an interesting field of research. The development of myocardial contrast echocardiography was an essential milestone in this area.
Several different low-frequency transducer designs can be used for drug delivery, such as low-frequency extensional resonators, tonpliz transducers, and ‘thickness’ type resonators. A recent comprehensive review on ultrasound drug delivery commented on the need to develop small low-frequency transducers that patients can wear.

Luis and colleagues found that circular cymbal ultrasound arrays were effective in delivering therapeutic levels of insulin in rats, rabbits and pigs. However, a rectangular cymbal design, desired in order to achieve a broader spatial intensity field without increasing the size of the device or the spatial peak temporal intensity, improved the efficiency of drug delivery. Park and colleagues investigated the feasibility of a lightweight cymbal transducer array as a practical device for non-invasive transdermal insulin delivery in large pigs. Their findings indicated the feasibility of ultrasound-mediated transdermal insulin delivery using the cymbal transducer array in animals of similar size and weight [38].

The patents granted on the phonophoresis devices have been provided in Table 1.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patents available related to phonophoresis.</th>
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<tr>
<td>Title of the patent</td>
<td>Patent number</td>
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<tr>
<td>Topical application of medication by ultrasound with coupling agent</td>
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<td>Disposable piezoelectric polymer bandage for percutaneous delivery of drug and method for such percutaneous delivery</td>
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<td>Ultrasound enhancement of transdermal drug delivery</td>
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<td>Ultrasound enhancement of membrane permeability</td>
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<td>Ultrasound-enhanced delivery of materials into and through the skin</td>
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<td>Drug delivery by multiple frequency phonophoresis</td>
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<td>Method for enhancing delivery of chemotherapy employing high frequency force fields</td>
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<td>Sonophoretic drug delivery system</td>
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<td>Ultrasonic method and apparatus for cosmetic and dermatological applications</td>
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<td>Enhancement of transdermal monitoring applications with ultrasound and chemical enhancers</td>
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<td>Transdermal protein delivery using low frequency sonophoresis</td>
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<td>Chemical and physical enhancers and ultrasound for transdermal drug delivery</td>
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<td>Transdermal protein delivery or measurement using low frequency sonophoresis</td>
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<td>Method and apparatus for therapeutic treatment of skin with ultrasound</td>
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<td>Ultrasound enhancement of percutaneous drug absorption</td>
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4.1 Limitations and Future implications/advancements required in the design of sonophoresis devices.

Ultrasound-mediated drug therapy has an immense future and scope for further research. Unfortunately, to date most of this treatment has been conducted on a rather subjective and non-quantitative basis and is plagued by lack of use of proper controls, incomplete accounts of dosimetry and vagueness in designing experimental protocols. The conflicting data have resulted from the fact that different research groups have used different ultrasonic parameters (i.e., frequency, intensity, duration, mode), different skin membranes and different vehicles. In addition, the presence and absence of cooling systems, processing of membranes used, distance between skin and transducer, size of transducer, quantity and type of coupling medium used, and end point evaluation techniques all affect the sonophoretic skin permeation rates. Phonophoretic research often suffers from poor calibration in terms of the amount of ultrasound energy emitted. The problem is that as an ultrasound propagates away from its source, the beam area begins to expand after a certain critical distance. Mathematically, this is dependent on the ultrasonic wavelength, transducer radius and effects associated with constructive and destructive wave interference. Ultrasound can reflect on itself at a tissue-bone interface in vivo or at a vessel wall-solution interface in vitro to produce a standing wave. However, to date no research has been published on the effect of ultrasound standing waves on drug migration, either in vivo or in vitro.

Another important issue that cannot be neglected is that physiotherapists have been using variable/unmeasured ratios of medicine and ultrasonic gel for the purpose of phonophoresis. This uneven or unmeasured ratio questions the penetration of the medicine and its effects on the underlying tissues. Also, these medicinal gels are bought separately either by the patients or the therapists from the market without exactly knowing their amount to be applied along with ultrasonic gel and have a vague idea about its penetration into the tissues. There is lack of evidence which gives us the amount of medicine that should be applied for effective penetration in the underlying tissues. To maximize the effect of medicine, a proper concentration of medicine should be used for effective phonophoresis. Therefore, there is need to improvise the technique of phonophoresis, where a machine can be devised, which uses ultrasonic waves and dispenses the ointment or gel itself in an appropriate amount directly on the affected area or the area that is being treated. It would ease the treatment for physiotherapist as proper amount of solution will be used for phonophoresis. This effective dosage will maximize the effects of ultrasound. It shall be beneficial to both the patient and the therapist and would upgrade the ultrasound therapy and make it more efficient and promising as physiotherapy is still a growing health care profession, we need more modalities and techniques to improve the effects of physiotherapy so that the patient will find it more trustworthy, which will ultimately lead to positive growth of physiotherapy.
ultrasound and phonophoresis has been in practice since the beginning of physiotherapy, with time the technique of phonophoresis has developed to be more precise and is used to treat multiple conditions and has shown a very positive effect in the same. But there are still a few limitations and future recommendations as mentioned above which should be addressed and taken into consideration in future studies.

5 Conclusion

In conclusion, phonophoresis emerges as a valuable and versatile modality within physiotherapy, demonstrating clinical efficacy across a spectrum of musculoskeletal and inflammatory conditions. The combination of topically applied gel or cream-based medications with ultrasound therapy, operating within specific frequency and intensity ranges, enhances percutaneous absorption of pharmacological agents. Recent studies underscore its effectiveness in pain relief and improved function, particularly noteworthy in conditions like lateral epicondylitis and osteoarthritis. The mechanism of action, encompassing both thermal and non-thermal effects with cavitation as a key player, underscores the intricate processes involved in enhancing transdermal transport. Phonophoresis offers a non-invasive avenue for drug delivery, bypassing hepatic metabolism and mitigating systemic side effects, making it an attractive option in various medical fields. The applications of phonophoresis extend beyond traditional physiotherapy, reaching into ocular drug delivery, nail therapy, gene therapy, and sports sciences. Low-frequency phonophoresis, in particular, gains attention for its efficacy in transporting macromolecules. Clinical studies provide compelling evidence for the effectiveness of phonophoresis in diverse conditions, including anterior knee pain, tuberculous lymphadenitis, acute low back pain, and latent myofascial trigger points. Dosage considerations underscore the importance of optimizing thermal effects without causing tissue damage. Notably, research suggests the potential of phonophoresis in relieving pain and improving function, with a specific focus on knee osteoarthritis. Furthermore, exploration into novel approaches, such as phonophoresis with Phyllanthus amarus nanoparticle gel, holds promise in enhancing its therapeutic capabilities. In summary, phonophoresis stands as a cornerstone in physiotherapy, offering a non-invasive and effective means of drug delivery with applications reaching far beyond its initial scope. Despite current successes, ongoing research is imperative to unlock the full potential of phonophoresis, refining treatment protocols and expanding its applications in diverse therapeutic contexts.

6 References


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