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Review Article

A Review On: Ultrasound In Pharmaceutics

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ABSTRACT

Ultrasound is composed of mechanical sound waves that originate from molecular movements that oscillate in a propagation medium. The waves have a very high frequency, equal to approximately 20 kHz, divided into two categories (i.e., low-intensity and high-intensity waves) and cannot be perceived by the human ear. Ultrasound waves are emitted from an ultrasound transducer. The choice of frequency of the transducer is important as higher frequencies give increased spatial resolution. Ultrasound is an imaging test that uses sound waves to make pictures of organs, tissues, and other structures inside your body. Ultrasound device, basically, consists of transducer, transmits, pulse generator, compensating, amplifiers, the control unit for focusing, digital processor and system for display. The various types of ultrasounds used for human's life, Food Industry, agriculture, veterinary science like, abdominal ultrasound, trans-vaginal ultrasound, obstetricsultrasound,3D ultrasound, transrectal, endoscopic, pelvic, breat, etc. Depending on its intensity, ultrasound is used for the activation or deactivation of enzymes, mixing and homogenization, emulsification, dispersion, preservation, stabilization, dissolution and crystallization, hydrogenation, tenderization of meat, ripening, ageing and oxidation, and as an adjuvant for solid-liquid extraction for maceration to accelerate and to improve the extraction of active ingredients from different matrices.

INTRODUCTION

Ultrasound can be defined as the sound waves with frequencies more than the upper audible limit of human hearing capacity. Have you ever wondered how bats can travel so smoothly in the dark. One shall be surprised to know that they do it with the help of sound waves! Bats are able to avoid any obstruction even on pitch-black nights through the help of these waves that are inaudible to the human ear. These sound waves have a much greater frequency and form a type of sound called ultrasound(1) . Pharmaceutics is the branch of pharmacy that deals with all aspects of the process to turn a new chemical entity (NIC) into appropriate medication. Pharmaceutics deals with

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the formation of pure substances into dosage forms such as capsule, injection, suppository, cream, ointment, eyedrops, inhaler, nasal spray etc(2) . The major mechanical effect of ultrasound is provided when the power is high enough to cause cavitation(3) . Ultrasound is made up of mechanical sound waves that originate from molecular movement that oscillate in a propagation medium. The waves have a very high frequency, equal to approximately 20 kHz, are divided into two categories i.e., low intensity and high intensity waves, and cannot be perceived by the human ear(4) . Ultrasound device, basically, consists of transducer, transmitter, pulse generator, compensating, amplifiers, the control unit for focussing, digital processor and system for display (5). Ultrasound technology is an environmentally friendly technology that hardly ever causes thermal damage to raw materials. Strong processing conditions of traditional technology often accelerate the rate of quality deterioration, and microbes are the safety hazard of ready-to-eat foods (6) . Several theoretical concepts for ultrasound propagation, including the Biot theory and various scattering theories, have been modified or developed to help explain how ultrasound velocity and attenuation depend on the composition and structural characteristics of cancellous bone (7) . For swine, ultrasound has been used for over 30 years and has been shown to significantly increase the accuracy of predicting body composition (8) . There is a chance to use ultrasounds as an effective intensifying and accelerating factor in the drying process. Available technical solutions have demonstrated the ability to prevent the loss of essential bioactive components that naturally occur in fruits and vegetables. The impact of key parameters and ultrasound technology on drying kinetics and food quality was discussed in this study, which provides a state-of-the-art overview of the application of ultrasound technology in the drying of food products, including ultrasound pre- treatment and ultrasound assisted drying (9) . Sono Bioleaching, also known as the use of ultrasound in bioleaching, is a method that has been shown to accelerate the rate and volume of metal extraction (10) . In the past few years, there has been an increase in the use of ultrasound-assisted extraction (UAE) to prepare environmental and food samples for analysis of a variety of contaminants, including organic compounds (pesticides, drugs, polycyclic aromatic hydrocarbons, polyhalogenated flame retardants, etc.) and heavy metals (11). (12) The propagation of ultrasound in a medium produces various physical and chemical effects, and these effects have been harnessed to improve the efficiency of various food processing operations. Ultrasonic processing is a novel and promising technology in the food industry (12) . Although ultrasonography is useful in detecting intrauterine pregnancy, the use of ultrasound in the diagnosis of heterotopic pregnancy has been reviewed in the international literature between 1979 and 1984 (13) . An emerging and promising technology in tissue engineering, three-dimensional (3D) bioprinting allows for the precise alignment of self- assembly cell spheroids used as bioink following droplet ejection from the bioprinter (14) .This review discusses the unified findings from patients with coronavirus disease (COVID-19), as well as from the avian (H7N9) and H1N1 influenza epidemics, and highlights the ultrasound findings reported from various studies and case reports (15) . Ultrasonic energy can be used to inactivate many enzymes by causing cavitation and acoustic streaming in the liquid medium, which are sufficient mechanical, thermal, and chemical effects to do so (16) . Application of ultrasound can affect the size and morphology of the crystals, crystallisation time, and the crystallinity of the zeolites. The observations show that application of ultrasound can shorten the crystallisation time. The use of ultrasonics in the

textile industry is reviewed, including the identification of processes which could benefit from ultrasound (17) . New families of power ultrasonic transducers have been developed in recent years to meet actual needs, which contributes to the implementation of power ultrasound of application in many fields such as the chemical industry, food industry, and manufacturing. The major challenges for the power ultrasound application in real situations are the design and development of specific power ultrasonic systems for large- scale operations (18) . Although the concept of using ultrasound during the tableting of pharmaceutical powders is new, the use of ultrasound- assisted compression of materials has long been known in the metallurgy, plastic, and ceramic industries (19) .When ultrasound (US) irradiation is applied to the skin, it increases its permeability (sonophoresis) and allows the delivery of various substances into and through the skin. However, the stratum corneum acts as a barrier that limits the penetration of substances to the skin. This makes transdermal drug delivery an appealing alternative to the conventional drug delivery methods of oral administration and injections (20) .

Mechanism of ultrasound:

Ultrasound waves are emitted from an ultrasound transducer. The choice of frequency of the transducer is important as higher frequencies give increased spatial resolution (i.e., smaller objects can be resolved) but the depth over which useful information can be obtained is reduced (21) .

Research on the effects of ultrasound on biological materials can be seen as bioeffect studies, which may result in risk evaluations for diagnostic ultrasound applications as well as therapeutic applications. However, an understanding of the interaction of ultrasound with tissue provides the scientific basis for image production, therapeutic applications, and risk assessment. On the other hand, the study of how tissue affects the ultrasound wave can be viewed as the basis for diagnostic ultrasound imaging (22) . After outlining the two main mechanisms-heating and cavitation-that result from ultrasonic propagation, the impact of conduction, perfusion, and beam geometry on the ultimate temperature rise in the heating case has been highlighted (23) . Attenuation of ultrasonic waves propagating through a medium is caused by coherent scattering, which includes diffraction, refraction, and reflection of the acoustic wave at tissue boundaries, in addition to absorption and scattering within a specific tissue (24)

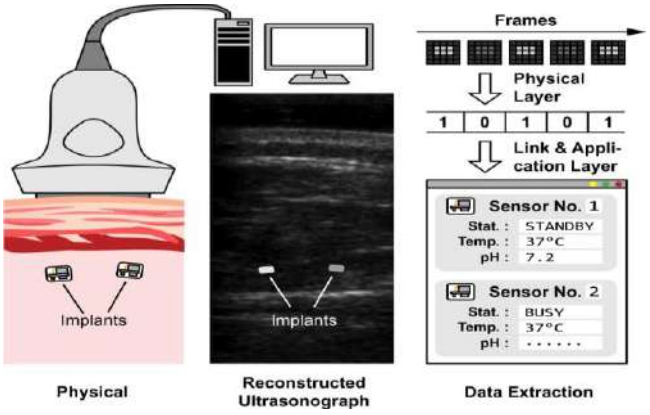

Fig no.1: mechanism of ultra sonography

Types of ultrasounds :

1. Abdominal ultrasonography

An abdominal ultrasound is a non-invasive procedure used to assess the organs and structures within the abdomen. This includes the liver, gallbladder, pancreas, bile ducts, spleen, and abdominal aorta.

2. Transvaginal ultrasound

Transvaginal ultrasound is an examination of the female pelvis. It helps to see if there is any abnormality in the uterus (womb), cervix (the neck of the womb), endometrium (lining of the womb), fallopian tubes, ovaries, bladder or the pelvic cavity.

3. Obstetric ultrasonography.

Obstetric ultrasonography, or prenatal ultrasound, is the use of medical ultrasonography in pregnancy, in which sound waves are used to

create real-time visual images of the developing embryo or foetus in the uterus.

4. 3D ultrasound

They let you see your baby's face for the first time. Some doctors like 3D and 4D ultrasounds because they can show certain birth defects.

5. Echocardiogram

A test of the action of the heart using ultrasound waves to produce a visual display, for the diagnosis or monitoring of heart disease.

6. Transrectal ultrasonography

Transrectal ultrasound (TRUS) is a 5- to 15-minute outpatient procedure that uses sound waves to create a video image of the prostate gland.

7. Abdomen ultrasound

An abdominal ultrasound is a non-invasive procedure used to assess the organs and structures within the abdomen. This includes the liver, gallbladder, pancreas, bile ducts, spleen, and abdominal aorta.

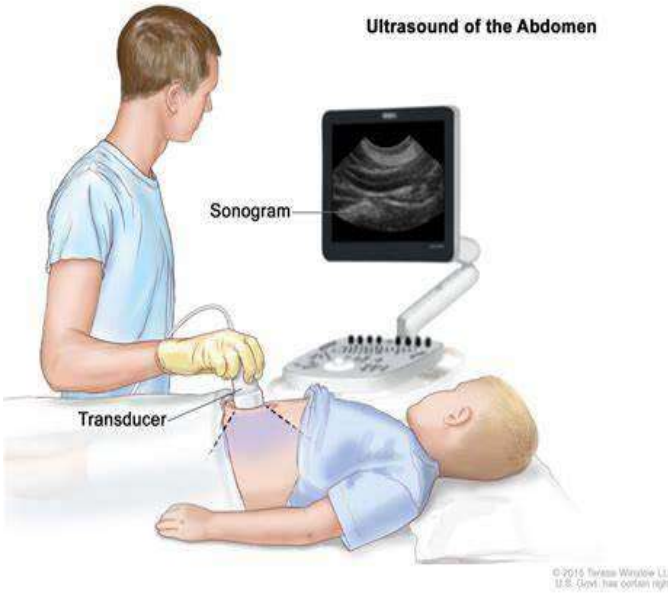

Fig no.2: ultrasound of the abdomen

8. Endoscopic ultrasound

Endoscopic ultrasound or echo-endoscopy is a medical procedure in which endoscopy is combined with ultrasound to obtain images of the internal organs in the chest, abdomen and colon. It can be used to visualise the walls of these organs, or to look at adjacent structures.

9. Pelvic Ultrasound

A pelvic ultrasound is a non-invasive diagnostic exam that produces images that are used to assess organs and structures within the female pelvis.

10. Breast ultrasound

Breast ultrasound uses sound waves and their echoes to make computer pictures of the inside of the breast. It can show certain breast changes, like fluid-filled cysts.

11. Fetal echocardiography

Foetal echocardiography is a specialised ultrasound test performed during pregnancy to evaluate the position, size, structure, function and rhythm of the unborn baby's heart.

12. Transesophageal echocardiogram

A transoesophageal echocardiogram (TEE) uses echocardiography to assess the structure and function of the heart. During the procedure, a transducer (like a microphone) sends out ultrasonic sound waves.

13. Nuchal scan

nuchal translucency scan is an ultrasound scan that measures your baby's nuchal translucency — a fluid-filled space behind your baby's neck.

14. Transcranial Doppler

Transcranial doppler ultrasound (TCD) is a diagnostic test. It measures blood flow to and within the brain.

15. Doppler effect

Doppler ultrasound is a special type of ultrasound which is used to look at blood flow.

16. Carotid ultrasonography

Carotid ultrasound can show whether plaque buildup has narrowed one or both of your carotid arteries and reduced blood flow to your brain.

17. Renal ultrasonography

Renal ultrasonography is the examination of one or both kidneys using medical ultrasound. Ultrasonography of the kidneys is essential in the

diagnosis and management of kidney-related diseases.(25)

Principle of ultrasound in pharmaceutics:

A subfield of acoustics known as ultrasound deals with inaudible waves that are higher than 20 kHz. The field of ultrasound, which includes both low- and high-intensity waves, is currently thought to be developing and expanding and has a wide range of applications. In particular, the application of ultrasound is very promising in the field of food technology because it is a non- ionising, non-contaminating green mechanical energy that ensures sustainability of processes. Nevertheless, the introduction of ultrasonic technology in the food industry is sluggish, possibly because of the discipline's limited dispersion in the food industry (26) .Various elastography techniques have been applied to a wide range of tissues and diseases. The accuracy and reliability of these techniques vary depending on the pathology, patient-based factors, and ultrasonography operator-based factors. Ultrasound elastography measures tissue mechanical properties by monitoring the response of tissue to acoustic energy (27) . The use of ultrasound in orthopaedics is growing as a result of technological advancements. Ultrasound is generated by a piezoelectric effect and requires matter for propagation; depending on the properties of matter, the propagation velocity varies and the images are the overall result of the interaction of reflection, refraction, absorption, scattering, transmission, and attenuation. The transducer is the most crucial device, and it varies depending on the array of piezoelectric elements (28) .The Doppler technique is based on the idea that ultrasonic echoes reflected from moving targets have a frequency shift that is proportional to velocity. Targets moving away from the transducer produce echoes with a reduced centre frequency, while targets moving toward it have an increased centre frequency. This frequency shift is known as the "Doppler shift (29) .

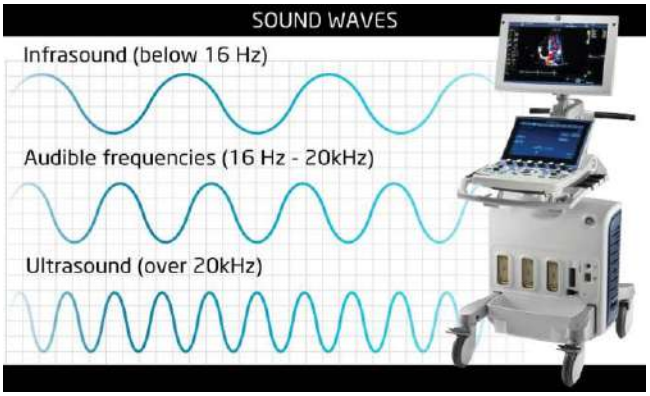

Fig no.3: Different sound waves

Role of ultrasound in different processes:

1. **Role of ultrasound in molecular imaging**

Ultrasound has received less attention than other imaging modalities for molecular imaging, but it has a number of potential benefits: it is inexpensive, readily available, portable, and can image structure and function with less sedation than other modalities, making it arguably the most physiological modality and enabling convenient cardiac studies in small animals. High frame rates of over 200 frames per second are achievable on current commercial systems (30) .

2. **Role of ultrasound in assessment of male fertility**

Ultrasonography (US) is a widely used and well-tolerated imaging modality for evaluating pathologic conditions of the testes. Recent advances in US applications and post- processing have created new opportunities for the structural and functional analysis of testicular tissue, and thus, male fertility .(31)

3. **Role of ultrasound in breast cancer screening**

The gold standard for screening for breast cancer is mammography; however, as patients and healthcare providers become more aware of the limitations of mammography, particularly in dense breasts, supplemental screening with ultrasound and magnetic resonance imaging has been increasing. The roles of both in screening need to be re-examined. This article reviews the feasibility, usefulness, and efficacy of ultrasound

as a screening tool for the early detection of occult breast cancer. (32)

4. Role of ultrasound in dengue fever

This investigation included 128 patients (2-9 years old) who had a clinical suspicion of dengue fever; serological testing was done to confirm the diagnosis; 40 patients tested negative for dengue fever and were subsequently removed from the study. The goals of the investigation were to ascertain whether ultrasonography is a valuable addition to clinical and laboratory profiles in the diagnosis of dengue fever or dengue haemorrhagic fever, as well as whether ultrasonography is helpful in predicting the severity of the illness (33)

5. Role of ultrasound in low back pain

Low back pain is one of the most common musculoskeletal conditions in the world. One major challenge for clinicians is the lack of objective assessment modalities; while CT and MRI are commonly used, they are not sensitive enough to distinguish abnormalities between patients with low back pain and healthy individuals. Instead, the disease can only be partially understood by using real-time ultrasound, which measures the anisotropic nature of muscles, which is altered in function, while scans only provide structural assessment (34).

6. Role of ultrasound in acute appendicitis

Acute appendicitis is the most common surgical abdominal emergency, with a lifetime prevalence of one in seven[1]. The diagnosis is primarily clinical, but because of a variety of presentations, it is accurate in up to 80% of patients. Due to the serious consequences of missing diagnoses, common surgical practice has been to operate on cases that raise doubts rather than wait and see until the diagnosis is certain, leading to a negative appendectomy rate of 20 to 30% and being deemed acceptable; however, this practice is currently being questioned in the context of quality assurance. The removal of a normal appendix is not a benign procedure, and negative appendicectomy carries a definitive morbidity (35)

7. Role of ultrasound in Sono crystallization

Power ultrasound is applied as a mechanical aid to blend and cavities the medium during the process of salting-out crystallisation. Sono crystallization is widely used to control nucleation and, thus, improve the product quality. For this purpose, power ultrasound is turned on within the metastable zone during the crystallisation process. Sono crystallization can reduce induction time and increase nucleation rate. Can initiate crystallisation at lower supersaturation (36)(37)(38) .

Advantages of Ultrasound:

a) Advantages of ultrasound in imaging

1. Pulsed acoustic waves are transmitted and received by a hand-held transducer in medical ultrasound imaging. This is a well-established technology that is utilised extensively globally (39) .
2. For the purpose of evaluating biological processes at the molecular level, targeted contrast-enhanced ultrasound, or molecular ultrasound, is a newly developed imaging technique that combines ultrasound technology with innovative molecularly-targeted ultrasound contrast agents(40).
3. Ultrasound is becoming a practical imaging modality for the diagnosis and evaluation of the musculoskeletal system. Its benefits include affordability, ease of use, and multiplanar capability(41).
4. Early cancer detection, functional imaging, and molecular imaging are among the possible clinical uses of ultrasound-mediated biphotonic imaging (42) .
5. Real-time ultrasound imaging is widely used in medicine today. It offers a convenient, affordable, and safe way to examine a variety of organs and tissues (43) .

b) Advantages of ultrasound in medicine

1. The use of high frequency sound in physical therapy has gained support lately.
2. According to clinical reports, ultrasonic therapy is recommended when heat treatment is necessary (44) .
3. Ultrasound beams with high intensity can be directed deep into the body, causing damage only to the focal volume and not to the surrounding or adjacent tissues, (45) .
4. It is safer than diagnostic methods like X-rays and CT scans because patients are not exposed to ionising radiation and the procedures are typically painless and don't involve needles, injections, or incisions (46) .
5. This eliminates the risks associated with invasive procedures and makes it safe and comfortable for patients. Moreover, ultrasound is portable and can be used in clinics, at the patient's bedside, or even in remote locations. Its instantaneous results allow for timely diagnosis and treatment decisions (47) .

c) Advantages of ultrasound in therapy

1. The clinical management of benign and malignant diseases makes use of hyperthermia (HT) (48).
2. The benefits of ultrasonography include its non- invasive nature, its deep bodily penetration, its focus and precise control (49)
3. English lingual stops, vowels, sibilants, and liquids have all been treated with ultrasonic technology thanks to a number of small-scale studies involving adults and adolescents with accented speech, residual speech impairment, and severe hearing loss (50).
4. Ultrasound (US) waves have demonstrated encouraging results for various types of wounds. The key benefits of US treatment for wounds include high penetration into the wound bed, excellent steering and focus ability, and no recognized negative effects (51).

d) Advantages of ultrasound in assisted extraction

1. Ultrasound-assisted extraction (UAE) with high penetration into the wound bed and high steer has garnered increasing interest because it is a useful technique for the quick extraction of several compounds from food and environmental samples, with extraction efficiency on par with traditional methods (52) .
2. Main benefits and drawbacks of ultrasonic systems used for extraction; ultrasound-assisted extraction (UAE) of bioactive compounds using aqueous solutions; in particular, the phenomenon of cavitation in heterogeneous media is addressed (53) .
3. This technology can be used directly to change the properties of the final product or the process, or indirectly to monitor processes that minimise certain disadvantages or enhance certain benefits in the fabrication of products (54) .

Disadvantage of ultrasound:

1. The invasiveness of these techniques usually precludes their use in research with subjects who are asymptomatic(55) .
2. There is no description of how to use ultrasonography to locate the sacral hiatus for caudal epidural injections, and it is inaccurate (56) .
3. In the right situations, contrast-enhanced ultrasound gives nephrologists the framework they need to decide on this cutting-edge imaging test (57) .
4. the use of ultrasound in various diagnostic contexts (58) .
5. We are unable to obtain image information from ultrasound regarding the depth of the inserted needle (59) .

6. The limitation of ultrasonography is its reliance on subjective evaluation of the images that are displayed. Standardising examination conditions, such as using a quantitative method to assess tissue reflectivity, can help minimise differences between observers as well as within them (60)
7. Certain issues and developmental disorders that ultrasound cannot detect at all may yield inaccurate results (61) .
8. The consumer may be harmed by the free radicals created during cavitation. Ultrasound may have a chemical effect that results in component degradation, discoloration, and an off-flavour (62).
9. Extended exposure to low- intensity ultrasonography may result in superficial skin burns (63).
10. Ultrasound waves have the potential to cause minor tissue heating as well as small gas pockets (cavitation) in bodily fluids or tissues; the long-term effects of these effects are yet to be determined (64) .
11. Radiography has several drawbacks, including depth compression, poor density discrimination, and insensitivity to minute amounts of peritoneal fluid (65) .
12. Gas-filled or bony tissues cannot be scanned with ultrasonography because the gas and bone "shadow" any organs that are located beyond them and the sound beam is completely reflected at soft tissue/gas interfaces and absorbed at soft tissue/bone interfaces (66).
13. degree of bubble destruction, a poor-quality tissue image, and a decreased resolution of local contrast Reduced MI can cause issues with depth penetration. Low MI techniques have two effects: first, they elicit harmonic US waves; second, they prevent bubbles from popping (67) .
14. Health effects like skin reddening and hair loss that could happen following a significant acute exposure to ionising radiation (68) .
15. The signal dropout behind calcium because the ultrasonic beam cannot pass through calcium. The inability of intravascular ultrasound to visualise the vessel's deeper structures is another issue that arises frequently (69) .

Uses of Ultrasound:

1. They are achieving this by creating technology that can produce, detect, and process ultrasonic waves for use in solids, liquids, and air searches (70) .
2. Power ultrasound has been applied to improve sterilisation, affect enzyme activity, and affect the way living cells develop (71) .
3. The ultrasound can be used as extraction, crystallisation, freezing, emulsification, filtration, and drying can all be aided by ultrasound (2) .
4. Trend in analytical chemistry: ultrasonic devices are becoming more and more trusted by analytical chemists who use them to assist in steps ranging from sampling through to detection. Their uses range from the most basic use for cleaning to facilitating or making possible different steps of the analytical process- particularly those involved in sample preparation (72) .
5. In an effort to prevent this morbidity, real-time ultrasound guidance for line placement has been developed (73) .
6. Using this device clinically is no more challenging than using traditional immersion ultrasonography (74) .
7. Breast ultrasound is used routinely as an adjunct to mammography to help differentiate benign from malignant lesions (75) .
8. The use of ultrasound to speed up reactions and eliminate fungi, bacteria, and viruses in agricultural settings (76) .

9. Use of intestinal ultrasound for the detection of IBD and its complications, and discusses its use in the management of patients with IBD (77) .
10. Over the past few decades, the use of ultrasound for thyroid cancer has changed significantly. With the advent of high-frequency linear array transducers and the computer- enhanced imaging capabilities of contemporary portable ultrasound equipment, ultrasound has become indispensable for thyroid gland examinations since the late 1960s (78) .

Fig no.4: ultrasound in different field

Future prospects of ultrasound:

1. At-Home Ultrasound Use Will be Approved for Some Applications Life-saving innovations such as electrocardiograms (ECG) have become consumer devices for highly specific use cases (e.g., Apple Watch monitoring risks for atrial fibrillation). Patient- centred ultrasound imaging has already become a crucial part of gynaecology, with companies such as Turtle Health enabling at-home exams to speed up fertility planning and treatments. This will soon spread to many chronic conditions, obstetrics, and wellness applications (79) .
2. Ultrasound Technology Will Become Smaller Than Your Watch I see ultrasound taking on a variety of form factors, from patches to pucks, to probes the size of pens, to tiny transducers -all of which are tailored to the specific users and use cases the solution is intended to serve. The future of ultrasound is one in which its full potential to transform patient care is reached-but only if practitioners embrace it and use it. Handheld ultrasound is breaking traditional barriers for medical imaging modalities, such as wireless capabilities and portability (79).
3. Ultrasound Training will be Part of Most Medical School ProgramsUltrasound Education Will Be Included in Most Medical School Programs: Traditionally, ultrasound imaging training has taken years to become proficient at both using the system and interpreting the images. However, as Al makes ultrasound easier to use and more clinicians are trained to use it, the use of ultrasound will grow exponentially. During their program, medical students will continue to have greater access to handheld ultrasound systems.
4. The optimization of therapeutic efficacy and reduction of systemic toxicity, particularly in the case of cytotoxic drugs, require targeted delivery of therapeutics to specific tissues. A variety of strategies are currently being developed for systemically administered drug delivery, and one such strategy is ultrasound-controlled targeting, a non-invasive technique in which ultrasonic waves penetrate through tissue and stimulate gas-filled microbubbles, leading to bubble rupture and biophysical effects that drive the delivery of attached cargo to surrounding cells. The drug delivery capabilities of ultrasonic- sensitive microbubbles are significantly increased when nanocarrier particles are affixed to the bubble surface, and cargo loading is dictated by the physicochemical (80).
5. In the context of amyotrophic lateral sclerosis, the possibility of utilizing cutting-edge

methods like CRISPR-Cas9 gene editing, stem cell technology, and low-intensity focused ultrasound to facilitate the transport of non-viral vectors to the central nervous system for customized gene therapy is briefly addressed (81).

CONCLUSION

They concluded that prolonged induction is associated with a small increased risk of infectious morbidity. An ultrasound is an imaging test that uses sound waves to make pictures of organs, tissues, and other structures inside your body. It allows your health care provider to see into your body without surgery. Ultrasound imaging is highly focused on the acoustic impedances of various mediums. The waves of sound that are reflected back to the detector in the transductor are converted in to graphs and then to a clear 2D 3D 4Dimage. It helps diagnose the causes of pain, swelling and infection in the body's internal organs and to examine an unborn child (fetus) in pregnant women Ultrasound has been used to diagnose obstructed labor, non-cephalic presentation, single or multiple pregnancy, incomplete miscarriage, molar pregnancy, ectopic pregnancy, fatal abnormality, intrauterine growth restriction and placenta. Ultrasound treatments help to relieve pain, increase blood flow, reduce swelling and inflammation, and promote tissue healing.

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