

Low Frequency, Ultrasonically-Induced Acoustic Therapy with Biostimulation

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Low frequency ultrasound produces change in a liquid medium through the generation and subsequent destruction of cavitation bubbles. Ultrasound is propagated via a series of compression and rarefaction waves induced in the molecules of the medium through which it passes. At certain frequencies, rarefaction cycle may exceed the attractive forces of the molecules of the liquid, and cavitation bubbles will form. Such bubbles propagate by a process known as rectified diffusion where small amounts of vapor from the medium enter the bubble during its expansion phase and are not fully expelled during compression. The bubbles propagate over a period of a few cycles to an equilibrium size for the particular frequency applied. It is the dynamics of these bubbles when they collapse in succeeding compression cycles that generate the energy for the chemical and mechanical effect. Cavitation bubble collapse is a phenomenon induced throughout the liquid by the energy in sound. In aqueous systems at the ultrasonic frequency of 20 kHz, each cavitation bubble collapse acts as a localized "hotspot" generating temperatures of about 4,000 K and pressures in excess of 1,000 atmospheres (1).

The cavitation bubble has a variety of actions within the liquid medium depending upon the type of system in which it is generated. These systems can be divided into homogeneous, heterogeneous solid/liquid, and heterogeneous liquid/liquid.

In homogeneous liquid-phase reactions, the bulk liquid immediately surrounding the bubble where the rapid collapse of the bubble generates kinetic energy which

produces mechanical effects, the bubble, itself, will be subjected to extreme conditions of temperature and pressure on collapse leading to chemical events.

In peeling modality, unlike cavitation bubble collapse in bulk liquid, collapse of a cavitation bubble on or near the surface is asymmetrical because the surface provides resistance to the liquid flow from that side. The result is an inrush of liquid predominately from the side of the bubble remote from the surface resulting in a powerful liquid jet being formed, targeted at the surface. The effect is equivalent to high pressured jetting and is the reason that ultrasound is effective for cleaning. This effect can also activate solid catalysts and increase the mass and heat transfer to the surface by disruption of the interfacial boundary layers (2).

Biostimulation causes changes in Na^+/H^+ ratio and increases in the Na^+/K^+ -ATPase activity, which in turn has an effect on Ca^{++} flux. The Ca^{++} flux affects the level of cyclic nucleotides, which modulate DNA and RNA synthesis, which modulates cell proliferation (3). There may also be an activation of enzymes in the mitochondria which causes a cascade of molecular events leading to the response. Calcium ions are intracellular messengers in many signal-transducing systems. The intracellular level of calcium must be kept low because phosphate esters are prevalent, and calcium phosphates are very insoluble. Cytosolic level of calcium in unexcited cells is several orders of magnitude less than the extracellular concentration. Thus, the cytosolic calcium concentration can be abruptly raised for signaling purposes by transiently opening calcium channels in the plasma membrane or in the intracellular membrane. (4-11).

There is another property of ultrasound which has important therapeutic

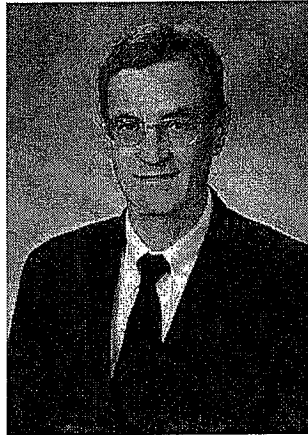
implications. There exists a threshold ultrasound energy below which the effect of ultrasound on skin conductivity cannot be detected, and beyond the threshold value, the conductivity increases with the energy density. In other words, regardless of the intensity, higher than the acoustical cavitation threshold intensity, exposure time and duty cycle used, the effect of ultrasound on skin permeability is similar if the total energy density delivered to the skin is maintained constant (12). The threshold energy density for affecting skin permeability is approximately 222 J/cm^2 and may depend on other ultrasonic parameters such as frequency. The threshold energy value probably reflects the ultrasound energy required to induce minimal structural changes in the skin sufficient to induce a measurable change in skin conductivity. The magnitude of the threshold may depend on the skin itself and may vary between different skin types.

The magnitude of acoustical cavitation can be detected by the presence of subharmonic response (13).

In the present study, the equipment used was the Dermasound with D₂O and distilled water ultrasound media. Approximately 1000 patient were employed in this study. The study parameters utilized were split face, matched pairs, and crossover study. The conditions studied were acne (704), acne rosacea (200), tinea corporis (30), tinea capitis (30), psoriasis (20), hemangioma (10), hamartoma (3), and port wine nevus (3).

The results of this study were as follows: acne patients 98% improved, acne rosacea 90% improved, tinea corporis 100% improved, tinea capitis 100% improved, psoriasis 100% improved, hemangioma 100% improved, hamartoma 100% improved, and port wine nevus 100% improved. Further studies are currently being performed.

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References

1. A. A. Atchley, L.A. Crum, Acoustic cavitation and bubble dynamics, in: K.S. Suslick (Ed), *Ultrasound: its Chemical, Physical, and Biological Effects*, VCH, New York, 1988, pp. 1-64.
2. J.R. Federick. in: *Ultrasound Engineering*, John Wiley, New York, 1980.
3. Smith, K.C. (ed) (1989). *The Science of Photobiology*, 2nd ed. Plenum Press, NY.
4. Whitfield, J.F., Boynton, A.L., MacManus, J.P., Rixon, R.K., Sikorska, M., Tsang, B., Walker, P.R., and Swierenga, S.H.H. (1980). The roles of calcium and cyclic AMP in cell proliferation. *Growth Regulation by Ion Fluxes* (ed. Leffert, H.I.) *Annals of the New York Academy of Sciences* 339, 216-240.
5. Watson, J.D., Hopkins, N.H., Roberts, J.W., Steitz, J.A., and Weiner, A.M. (1987). *Molecular Biology of the Gene* 4th ed. Vol II, Chapter 25, The Control of Cell Proliferation, pp. 962-1005. Benjamin/Cummings, Menlo Park, CA.
6. Stryer, L (1988) *Biochemistry* 3rd edn. pp. 975-1004, Freeman and Company, NY.
7. Tsien, R.W., Hess, P., McCleskey, E.W. and Rosenberg, R.L (1987). Calcium channels: Mechanism of selectivity, permeation, and block. *Annual Reviews in Biophysics Biophysical Chemistry*, 16, 265-290.
8. Tsien, R.W., Lipscombe, D., Madison, D.V., Bley, K.R., and Fox, A.P. (1988). Multiple types of neuronal calcium channels and their selective modulation. *Trends in Neuroscience* 11, 431-437.
9. Berridge, M.J. (1990) Calcium oscillators. *Journal of Biological Chemistry* 265, 9583-9586.
10. Robinson, K.R. and McCaig, C. (1980) Electrical fields, calcium gradients, and cell growth. *Growth Regulation by Ion Fluxes* (ed Leffert, H I) *Annals of the New York Academy of Sciences* 339, 132-138.
11. Findl, E. (1987). Membrane transduction of low energy level fields and the Ca⁺⁺ hypothesis. *Mechanistic Approaches to Interactions of Electric and Electromagnetic Fields with Living Systems* (ed Black, M. and Findl, E.) pp. 15-38, Plenum Press, NY.
12. Mitragotri, S., Farrell, J., Tang, H., Terahara, T., Kost, J., and Langer, R. (2000). Determination of threshold energy dose for ultrasound-induced transdermal drug transport. *Journal of Controlled Release* 63 pp. 41 -52.
13. J. Liu, T.N, Lewis, M.R. Prausnitz, Non-invasive assessment and control of ultrasound-induced membrane permeabilization, *Pharm. Res.* 15 (1998) 918-923.

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PUBLICATIONS (Not Complete):

1. DeBartolo, Hansel M. Jr., M.D., VaoHeerden, Jonathan, M. B., F.R.C.S., Lynn, Hugh, M.D., Norris, Donald, M.D., A Torsion of the spleen, a case report@ *Mayo Clinic Proceedings*, Nov. 1973, Vol. 48.
2. DeBartolo, Hansel M. Jr., M.D., A Cause of hypertension@ *Illinois Medical Journal*, February, 1975.
3. DeBartolo, Hansel M. Jr., M.D., A The physiological basis of sleep: a historical review @ *Bulletin Geisinger Medical Center*, 27:48-55. May, 1975.
4. DeBartolo, Hansel M. Jr., M.D., A cause of hypertension@ *Bulletin*, Geisinger Medical Center, 27:58-59, May, 1975.
5. DeBartolo, Hansel M. Jr., M.D., Jonathan A. VanHeerden, M.B., F.R.C.S., A. Meckels diverticulum@ *Annals of Surgery*, 183:30-33, January, 1976.