REVIEW ARTICLE

ULTRASONICS IN PHARMACY AND ALLIED SCIENCES

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Introduction

Although nearly forty years have passed since ultrasonic acoustic waves were first used for submarine detection, it is only in recent years that the science of ultrasonics has made its impact on a wide and varied field of research and industrial applications. The literature on the subject, large and scattered as it is, contains references to such diverse uses as ultrasonic soldering and laundering, the modulation of light beams in television systems, the measurement of physical properties of gases and liquids, and echo depth sounding. These and many other interesting applications are outside the scope of the present article which is concerned mainly with the pharmaceutical and allied uses, both actual and potential.

Acoustic vibrations are usually divided into two classes according to frequency. Oscillations with frequencies less than 10 to 20 kc./second are referred to as sonics or audible sound, and those with greater frequencies as ultrasonics or inaudible sound. A frequency of about 10 to 14 kc./second represents the upper limit of audible perception in the adult of the human species, although some animals appear to be receptive to higher frequencies. Whereas audible sound waves of more than a few watts power output cause discomfort and may become unbearable, power outputs of the order of hundreds of watts are readily available from ultrasonic generators designed for high intensity work without apparent harmful effect on the operator. It is important to bear in mind that the laws of sound which are valid for the audible range are also true for ultrasonics, although in the latter case other effects appear which have not been observed in the audible range. While these effects appear to be due mainly to the higher frequencies (or shorter wavelengths), some, particularly the biological and chemical actions, have become evident only because of the relative ease of producing extremely large amplitudes of sound at those frequencies. Although wavelength appears to play some part in biological reactions, a direct correlation has not yet been established and most of the evidence points to sound intensity as one of the most important parameters.

It is convenient at this point briefly to mention one or two fundamentals regarding the propagation and properties of sound vibrations. When a sound wave travels through a given medium the individual particles of that medium execute simple harmonic motion. That is, each particle vibrates backwards and forwards across its normal position of rest. This vibration is said to be longitudinal if it is in the same direction as the propagation of the sound, and transverse if at right angles. Liquids and gases support only longitudinal vibrations whereas solids may support

both. The maximum displacement of each particle from its rest position is called the amplitude, and the total number of excursions per second is known as the frequency. The distance between two particles with the same magnitude and direction of displacement is the wavelength. The velocity of propagation (V), the wavelength (λ), and the frequency (f), are related in the expression $V = f\lambda$. The velocity of propagation is a physical constant of the medium while the wavelength and the frequency are not. Hence if a sound wave travels from one medium at a given velocity to another medium with a different velocity, the wavelength will change but the frequency will remain constant since the latter is determined by the sound source. Table 1 shows the velocity of sound in some commonly used liquids[1].

TABLE I

Liquid	Temperature °C	Density g./ml.	Velocity of sound m./second
Acetone	20	0·790	1190
Benzene	20	0·879	1324
Carbon tetrachloride	25	1·595	926
Chloroform	20	1·488	1002
Ethanol	20	0·789	1168
Transformer oil	25	0·880	1350
Castor oil	25	0·969	1477
Water	25	0·997	1497
Xylol	22	0·877	1352

If the physical properties of the medium are taken into account it is possible to consider the sound wave as an alternating pressure phenomenon. The sound pressure variation with time at any given point in the medium is given by $p = P \sin (2\pi f t)$, where P is the pressure amplitude or maximum pressure obtained at a given point, p is the instantaneous pressure at any time t, and f is the frequency. This pressure variation may be either positive or negative; hence, in a given medium, two points a half wavelength apart may have a pressure difference of twice the maximum pressure or pressure amplitude. These large pressure differences appear to account for many of the biological and chemical actions of ultrasonics. Sound intensity, which is not to be confused with sound pressure, is defined as the energy which passes through unit area in unit time. It is usually measured in watts per square centimetre.

Acceleration and Cavitation

Two prime phenomena, acceleration of particles or molecules, and cavitation, are evident when a liquid is irradiated by high intensity ultrasonics. It is generally accepted that the biological and chemical actions may be explained in terms of these phenomena. The acceleration of particles in the propagating medium is truly enormous. For example, if a sound intensity of about 10 W/sq. cm. is delivered into water at a frequency of about 500 kc./second, a pressure amplitude of $5{\cdot}4 \times 10^6$ dynes/sq. cm., or about 5·4 atmospheres is obtained. Thus the pressure alternates between + 5·4 and − 5·4 atmospheres 500,000 times a second. The amplitude of vibration of the individual water molecules is $1{\cdot}16 \times$

10^{-5} cm., but the acceleration of these particles is $1{\cdot}14 \times 10^8$ cm., or about 1000 km/second^2; this is about 10^5 greater than the acceleration due to gravity. It seems probable that these large accelerations may be largely responsible for the disruption of large molecules referred to later.

If a source of ultrasound is immersed in a trough of cold liquid, say water, and the intensity slowly increased, a point occurs at and beyond which the water becomes violently agitated and appears to boil although still cool. The generally accepted explanation of this phenomenon is that the bubbles appear to be formed by the coalescence of minute dissolved gas nuclei as they move towards the nodes of the wave system. In addition the large negative pressures and hence the large stresses in the liquid cause the latter literally to be torn apart with the formation of hollows or cavities. This is referred to as cavitation. The cavities become filled with dissolved gas or the vapour of the surrounding medium, and on their subsequent collapse produce local pressures of the order of thousands of atmospheres. High local temperatures probably exist as well as tremendous local agitation and it seems possible that electrical potentials are formed in the process.

Two major factors which seem to influence the acoustic intensity required to produce cavitation in any liquid are external pressure and viscosity. In general the higher the viscosity the greater the intensity required. Similarly, if the external pressure upon the liquid is raised so must be the intensity of the applied acoustic beam in order that cavitation may occur. These points are important as it appears that most of the biological and chemical effects are not evident in the absence of cavitation.

The rudimentary principles outlined above are sufficient to indicate that ultrasonics are capable of producing great forces. Small wonder that the subject has been of interest to workers in many fields.

Consideration may now be given to the methods used for producing and applying these forces, bearing in mind that in most of the applications considered in this article the test material is irradiated in solution or suspension in a liquid medium. The propagation of ultrasonic waves in gaseous or solid media is a different problem.

Production of Ultrasonics

Although ultrasonic waves may be produced by, for example, spark discharges, for practical purposes generators of ultrasonics in liquids may be divided into three types, (1) the Pohlmann Whistle, (2) the Magnetostriction Generator, (3) the Piezo-electric Generator.

The Pohlmann Whistle (Fig. 1).—This apparatus[2] and its modifications[3] consist of a nozzle from which a high pressure jet of liquid impinges upon a thin steel blade, which then vibrates at its natural frequency, transmitting the oscillations to the liquid in which it is immersed. A pump is required to drive the jet. For the emulsification of two immiscible liquids the nozzle and blade are immersed in a tank containing one phase, the second phase being forced through the nozzle into the first. The emulsion so formed is re-cycled through the system. (Fig. 2). A frequency of up to about 30 kc./second is obtained with this type of

generator, which therefore operates at the lower end of the ultrasonic spectrum. It has the advantage of comparative cheapness and further research may well produce an apparatus suitable for the large scale production of emulsions, to which end its use is probably limited.

The Magnetostriction Generator. (Fig. 3).—Some ferromagnetic materials such as nickel contract when placed in a magnetic field. A nickel rod, tube or laminate[4] placed inside a solenoid through which flows an alternating current will therefore vibrate in its longitudinal axis. the vibration being strongest when the frequency of this current corresponds to the natural frequency of the material. Ultrasonic waves are transmitted to the liquid in which the rod is immersed, providing, of course,

FIG. 1. The Pohlmann whistle.
1. Nozzle. 2. Blade.

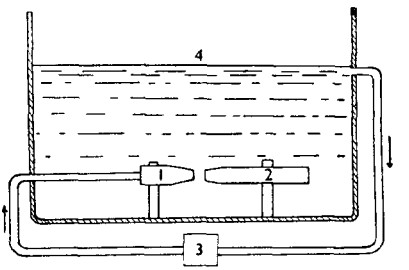

FIG. 2. The Pohlmann whistle as an ultrasonic emulsifier.
1. Nozzle. 2. Blade. 3. Pump. 4. Emulsion.

that the exciting current frequency and the natural frequency of the rod are in the ultrasonic range. The normal frequency range for this type of apparatus is up to about 50 kc./second but laminates have been produced which operate at frequencies of up to 200 kc./second. Eddy current heating produces losses, and another disadvantage is fatigue in the metal which lowers efficiency. This part of the apparatus is, however, readily replaceable. The dimensions of this apparatus are limited by the mechanical properties of the magnetostriction material and as yet it has not been scaled for industrial use. It is nevertheless a useful tool for small scale work and research. Intensities of up to 25 W/sq. cm. cross sectional area of rod have been developed in a commercial model[5]. This type of apparatus forms the basis for the ultrasonic soldering iron.

The Piezo-electric Generator.—In 1880 Pierre and Jacques Curie discovered that certain crystals such as quartz, tourmaline and Rochelle salt exhibited electrical charges upon their surfaces when subjected to mechanical pressure—the so-called "piezo-electric effect." The converse effect, namely that the application of an electrical field of force produces an expansion or contraction of the crystal, was predicted from thermodynamic considerations and later experimentally confirmed by the Curies, and forms the basis upon which the so-called "crystal generators" work. These generators are capable of producing ultrasonic vibrations at much higher frequencies and higher intensities than the types previously mentioned. For this reason many of the investigations into the biological effects

of such vibrations have been carried out with piezo-electric generators[6]. Figure 4 shows the theoretical circuit diagram of a typical apparatus. The crystal, which is supplied with radiofrequency current at high voltage by a valve oscillator (usually a modified Hartley circuit), expands and contracts in sympathy with the applied electric field and transmits vibrations to the surrounding medium in which it is immersed. Maximum intensity is obtained when the frequency of the applied alternating field is the same as the natural or resonant frequency of the crystal, such a condition usually being obtained by tuning the oscillator to the crystal frequency. The upper limit of ultrasonic frequency is determined in particular by the physical properties and type of crystal used. Experiments have been

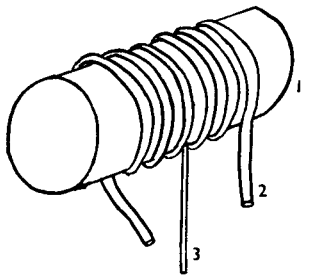

FIG. 3. Magnetostriction device.
1. Nickel rod. 2. Coil through which passes high frequency current. 3. Clamp.

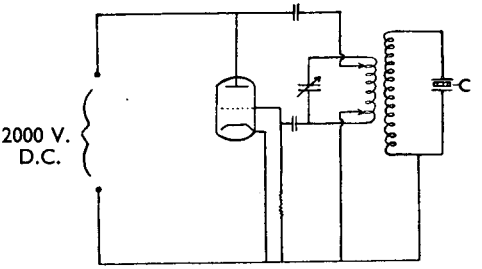

FIG. 4. Theoretical diagram of a typical piezo-electric generator. C. Quartz-crystal.

made with barium titanate[7] and titanate ceramics[8], but quartz is generally used in the form of an X-cut disc with silver electrodes sputtered on to each face. The mechanical strength of piezo-electric crystals has been investigated[9]. If the radiofrequency *current* is too large the crystal may be shattered; power is therefore best applied at high voltage and low current values. However, the higher the frequency the thinner the quartz disc and hence the closer together the electrodes on the crystal surfaces. With the high voltages used (up to 50 to 60 kilovolts in some cases) insulation, arcing and crystal fracture become major problems. Mounting in transformer oil assists in many cases but other ingenious methods of crystal mounting have been devised[10,11,12–21], some[22] for the direct irradiation of aqueous liquids, others for the concentration of the ultrasonic beam by means of spherical mirrors[23–25], or curved quartz crystals[26–28]. Lenses have been used for focussing and "transmission plates" of calculated thickness have been developed[29] for the low loss transmission of ultrasonic energy from one medium to another.

The efficiency of the crystal alone ranges from about 75 to 90 per cent. i.e., about 75 to 90 per cent. of the electrical energy supplied to the crystal is converted into acoustic energy. However the overall efficiency of the whole apparatus including the oscillator is about 20 to 40 per cent., which is about the same order as for the magnetostriction generator. Power levels of up to 500 to 1000 watts have been obtained but at these levels the production of heat in the bath becomes a source of trouble.

The piezo-electric generator, producing as it does high frequency waves of high intensity, has been much used for the irradiation of biological material, for it is at high intensities that many of the now well known effects appear to be exhibited.

Applications

The types of problem within the compass indicated by the title of this article to which ultrasonic acoustic waves have been applied are numerous. They may conveniently be considered under two headings, (1) *Biological* and (2) *Chemical and Physical.*

Biological Applications.—A number of review articles are available on the biological effects of ultrasonic irradiation (e.g., Crawford[5], Dognon and Biancani[30]) and these provide a useful introduction to the subject as a whole, although the latter is now outdated in some respects. In general, the biological material is suspended in an aqueous medium, such as distilled water or normal saline solution, in a tube or ampoule which is placed close to the piezo-electric crystal in a suitable liquid medium such as water or transformer oil. The ultrasonic vibrations propagated by the crystal in this medium are transmitted through the bottom of the tube or ampoule into the suspension. (Fig. 5).

The first observations of the biological action of ultrasonics were made by Langevin in 1917 who noted the sensation of heat produced in the hand when immersed in a liquid irradiated with ultrasonic vibrations. The initial loss of powers of orientation was observed in fish irradiated in a tank of water, further treatment resulting in temporary paralysis which passed off when the beam was switched off. More prolonged exposure resulted in death. Some years later Wood and Loomis[31] reported the destructive action on infusoria and Johnson[32] found that at high intensities a suspension of *Paramœcium* entirely and almost instantaneously disappeared. Harvey and Loomis[33] destroyed certain luminous bacteria, and Williams and Gaines[34] on *E. coli*, Beckwith and Olsen[35] on yeast and Hopwood[36] on vaccinia virus, demonstrated the lethal action of ultrasound on micro-organisms. The effect on yeast[37] appears to be greater with more prolonged exposure but to remain inferior to that exhibited on bacteria. The causative agents of anthrax, dysentery and whooping cough have been destroyed, also *Staphylococcus aureus* and *E. coli*[38,39,40,41]. Grabar and Rouyer[42] at the Pasteur Institute in Paris obtained a 40 per cent. mortality rate on *B. paradysenteriæ* using a low power generator, but a 98 per cent. death rate with one of higher power. Their experiments on a number of bacteria are of interest. Thick suspensions of the micro-organisms in Ringer's solution, normal saline solution or isotonic phosphate solution were placed in a tube of 4 cm. diameter, the bottom being closed by a cellophane membrane. The tube was placed in water over the quartz crystal with the base about 1 cm. from this, and so centred as to obtain maximum agitation within the suspension. An acoustic intensity of 31 W/sq. cm. was produced at the crystal surface and the frequency used was either 320 or 680 kc./second. The suspension was irradiated for definite periods of time, at the completion of which counts were made by plating out suitable

dilutions. Their results are reproduced in Table II. The authors suggest that the mortality rates shown for *B. anthracis* and *B. megatherium* are below the true level because of the liberation of individuals, arising from dis-aggregation of the chains, each giving rise to a colony when plated out. Even so the mortality rate approaches 100 per cent. in three cases. Laporte

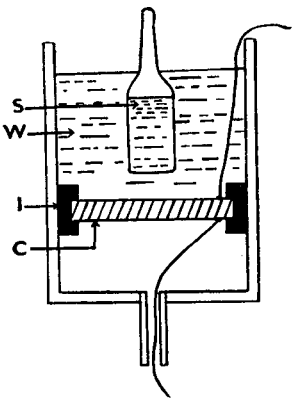

FIG. 5. Quartz crystal and irradiation chamber.

C. Crystal. W. Water
I. Insulation. S. Specimen

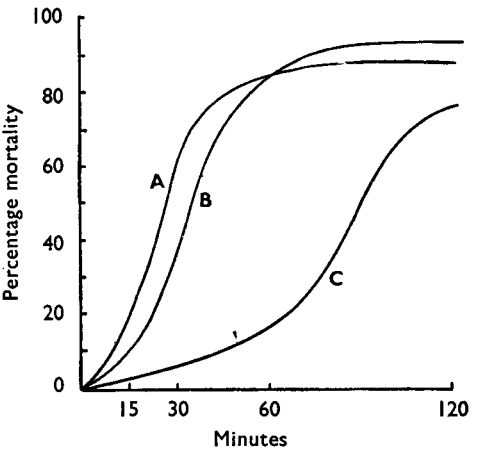

FIG. 6. *Myco. tuberculosis*; percentage mortality of different strains during irradiation with ultrasonics.

A. B.C.G. B. M.6. C. L.A.

and Loiseleur[43] have reported different effects with different strains of *Myco. tuberculosis*, BCG, M6 and LA. Young cultures of age 10 to 15 hours were used, and the results (Fig. 6) show that the rate of disintegration is a function of the time of irradiation. Loiseleur[44] has drawn attention to the similarity of these curves to those obtained by Latarjet[45] by irradiation with ultra-violet light. From results obtained with *E. coli*, Horwood,

TABLE II

Organism	Concentration per ml.	Percentage mortality	Time of exposure minutes	Frequency kilocycles
B. paradysenteriæ	$6{\cdot}2 \times 10^8$	98·0	30	320
B. anthracis	$3{\cdot}5 \times 10^9$	97·5	45	"
B. megatherium, Multilat strain ..	$4{\cdot}4 \times 10^8$	99·7	45	"
Staphylococcus aureus	$40{\cdot}2 \times 10^9$	90·4	45	"
Myco. tuberculosis, BCG strain ..	$3{\cdot}8 \times 10^9$	75·0	75	"
B. dysenteriæ Shigæ	$120{\cdot}8 \times 10^9$	88·0	30	680
Saccharomyces ellipsoideus	$1{\cdot}3 \times 10^9$	85·0	30	"

Norton and Minch[46] have suggested that the bactericidal effect of ultrasonics is a logarithmic function of time of exposure, and that old cultures are more susceptible than young ones.

An important advance has been the extraction of microbial contents[42] and endotoxins[47]. Suspensions of bacteria in distilled water are disintegrated by ultrasonic vibrations. The thick suspensions clear, are centrifuged to throw down the cellular debris and the clear supernatant liquid is filtered through a collodion membrane.

Vaccinia virus[48] and tobacco mosaic virus[49,50] have also been destroyed, and certain bacterial suspensions, after some irradiation, have been shown to remain agglutinable by their anti-sera, but the type of agglutination is modified[51]. Bacteriophage of varying size from 75 mμ to 21 mμ has been destroyed, but the effect was less evident in the size range 8 to 12 mμ[52]. By means of high speed cinematography Harvey and Loomis[53] found that sea urchin's eggs were disintegrated in less than 1/1200th of a second, this being the interval of time between successive frames on the film.

Because of the exploratory nature of this work no cases appear to have been reported in which all the variables of the system have been defined and measured. Hence it is difficult to evaluate much of the research and also to obtain reproducible results. It is even more difficult to make critical comparisons. For example, the measurement of ultrasonic energy actually dissipated within the specimen tube has not proved possible to date, although the use of a transistor to measure small rises in temperature may assist in this problem. The ultrasonic energy is not necessarily distributed evenly throughout the beam. Boyle *et al.*[54] have shown that the greater portion of the energy generated is concentrated in a central diffraction beam arising at a distance from the crystal determined by its radius and frequency and having an angular spread which is also a function of these quantities. Wood and Loomis[6] point out that only when the distance between the vibrating source and the floor of the radiation chamber or tube is an integral number of half wavelengths is the intensity of the radiation a maximum. However, Smith and Stumpf[55] suggest that under these conditions coupling may result which alters the natural frequency of the crystal. Boyle and Rawlinson[56] report that the thickness of this floor is critical in relation to the amount of energy transmitted to the bacterial suspension. Interfering secondary wave trains are also set up from the vibrating walls of the container[57]. The control of heat generated by ultrasonic irradiation is of major importance in experiments with bacteria, for the latter might be destroyed by the heat alone or the action of the waves might be modified. The crystal frequency also varies with temperature. The provision of cooling coils or the addition of ice to the liquid in which the crystal is immersed have been found useful, but a system of thermostatic control seems to be indicated. The type, age and concentration of the bacterial suspension, the medium used and the methods adopted for the determination of the population appear to require definition. Attempts to solve problems of control in quantitative studies of bactericidal effects[58] have not yet succeeded however.

Nevertheless, certain inferences may be drawn from the papers considered above. Most workers e.g.[59,60,61] are of the opinion that the death of biological material is caused by disruption of the cells which electron microscopy shows does occur[62], and protein denaturation probably plays a

part[60]. Oxidation does not appear to be responsible as lethal effects are still observed in the presence of gases other than dissolved air[52,63], although one author[44] suggests that oxygen may play a part. Cavitation does not appear to take place in the absence of dissolved gases and death of the organisms seems not to occur in the absence of this phenomenon. According to Marinesco[64], the disintegration of micro-organisms is caused by the differences in pressure which exist between the nodes and crests of the ultrasonic wave system. These positions are separated by half a wavelength, being closer together when the frequency is greater. This may imply a more effective action at higher frequencies. It is not yet possible to examine this latter hypothesis as present high power generators are limited to an upper frequency limit of about 1 to 3 megacycles/second, imposed by the physical properties and design of the quartz crystal. Examination of many other piezo-electric materials seems to be indicated with a view to raising this limit to much higher frequencies. It appears to be more probable, however, that the large disruptive forces produced by rapidly varying pressures and particle accelerations, previously referred to, play the major part in the lethal activity of ultrasonic waves.

These lethal effects are of interest to pharmacists from the point of view of their possible use as a method for the sterilisation of injections. Most of the bacterial suspensions used so far have consisted of fairly large populations. The results obtained by repetition on small concentrations would probably be interesting, as would the examination of the bacteria not destroyed. The influence of the waves on the medicaments present in the injection would require investigation in each instance in view of the chemical and physical effects reviewed below. Once the variable factors concerned in the application of ultrasonic energy have been defined and controlled, a large scale investigation along these lines appears to be indicated. From the industrial point of view, the major difficulty is one of economics in view of the length of time of irradiation which appears to be necessary and the fact that only one ampoule could be treated at a time with present apparatus. If the time factor could be greatly reduced commercial application may prove to be a worthwhile proposition. Sufficient evidence seems to be presented in the foregoing papers to suggest a fruitful field of research in this direction.

Of interest in the botanical field is the stimulation of plant growth by the treatment of seeds, although a decrease in percentage germination has been recorded by one author[65]. Successful results have been claimed in the treatment of rheumatism and sciatica[66,67]. This may be due to the thermal or vibratory effects or a combination of both. An apparatus for under water massage has been described[68]. The effect of high frequency sound waves on heart muscle and other irritable tissues has been investigated[69]. Ultrasonics have also been applied to problems connected with water purification[70]. In the gastronomic field, the application to the more rapid ripening of cheese and ageing of wines will probably horrify the gourmet.

Chemical and Physical Applications.—The catalogue describing a well-known ultrasonic generator[71] contains, amongst others, a list of the following applications:—induction of molecular rearrangement,

homogenisation of milk, acceleration of chemical reactions, transformation of chemical compounds, flocculation of suspended particles in liquids, emulsification of oil and water[65,72] and mercury and water, increasing the rate of oxidation reactions, dextrinisation of starch, decomposition of gums and gelatin. Oxidation of potassium iodide, hydrogen sulphide and carbon tetrachloride have been demonstrated and the first of these has been used, together with starch, in an attempt to obtain a colorimetric estimation of ultrasonic energy. High polymers have been broken[74] at their co-valent bonds[75]. Other applications are the formation of colloids[76] and their coagulation[77], and the formation of fine grain particles during precipitation. The latter may prove useful in the preparation of photographic emulsions. The clotting time of fibrinogen and the molecular distribution of hæmocyanin have been shown to be considerably modified[78]. Albumin has been split into its component amino-acids and these amino-acids themselves further degraded. Preferential disruption appears to occur in amino-acids containing a cyclic structure (e.g., tryptophane, tyrosine, histidine) and the formation of aspartic acid from histidine is claimed[79]. An interesting and useful feature of these degradations is that the usual methods of acid or alkali hydrolysis are not required and hence the products are obtained in a pure state, no extraneous chemicals having been added.

Critical evaluation of much of this work is difficult for the same reasons which apply to the biological research. The amount of ultrasonic energy required to produce the above effects is not always determined and the operating frequency of the apparatus is sometimes not given. Anomalies occur which require explanation. For example, the emulsification of mercury and water does not require cavitation[72], but these emulsions are not so stable as those of the oil-in-water type which are only produced in the presence of cavitation. Most immiscible liquids are emulsified by ultrasonic irradiation even in the absence of an emulsifying agent. Emulsions may, on the other hand, be cracked by ultrasonics. It seems probable that minute droplets of one phase, formed by the violent disruptive effects of the waves, are thrown into the other phase. If these droplets are sufficiently small an emulsion results. However, the immense forces of acceleration produced in these particles increase their chance of collision and consequent coalescence. This may explain the apparent anomaly.

There seems little doubt that the fracture of macro-molecules is due to these forces of acceleration giving rise to large frictional forces between the macro-molecule and the molecules of the solvent. Presumably, the larger the macro-molecule the greater is its inertia and hence its liability to fracture. Mark[75] has calculated the order of size of these forces when acting on certain bonds and shown them to be greater than the forces of chemical combination. Photochemical reactions have been observed and Frenkel[80] has attempted to explain these by suggesting the formation of electrical charges of opposite sign on opposite walls of the cavitation bubbles. The bubble then acts as a condenser and under certain conditions it is possible that flash over occurs with the production of light,

mainly in the ultra-violet region. Luminescence has been observed to occur in liquids in the dark.

In order to account for oxidation reactions many workers (e.g., Wheyl and Marboe[81]) consider that the aqueous medium is split into oxygen and hydrogen atoms which are electrically charged or chemically unsaturated and hence highly reactive. Peroxides and free hydroxyl groups may also be formed. It is possible to explain the acceleration of so many chemical reactions by postulating the breakdown of the Nernst diffusion layer.

Conclusion

That the science of ultrasonics has come to stay there is no doubt; that it is still in its infancy cannot be denied. Most of the research dealt with in this article can only be considered as exploratory in nature. Considerable pioneer work remains to be done, particularly in the fields of control and measurement of the ultrasonic radiation. It is essential first to establish suitable conditions under which reproducible results are possible. The development of more versatile apparatus capable of producing higher frequencies may produce interesting results, but it is well to bear in mind that solution of problems in this direction may bring new difficulties. For instance, the absorption of ultrasonic energy by a liquid increases as the square of the frequency. Less penetration and greater heat generation will follow.

From a purely pharmaceutical point of view, the following future possibilities suggest themselves:—decreased times for extraction processes, sterilisation of injections and surgical instruments, the breakdown of complex plant constituents without the addition of reagents for the purpose of the elucidation of structure, the investigation of thixotropic substances and gels. The identification of liquids by the measurement of the velocity of ultrasound propagated in them is already possible[72]; the measurement of absorption may also be used, and the technique can be applied to the differentiation of chemical isomers. The velocity of sound in a mixture of liquids depends upon the exact composition of the mixture; here is a pointer to the automatic control of reactions in a continuous system. No doubt many other possible uses will occur to the reader.

My thanks are due to Mr. R. G. Atkinson, F.P.S., for drawing my attention to some of the Russian literature which he kindly undertook to translate. Most of the literature search was conducted whilst the author held an appointment as Assistant Lecturer in Pharmacy at the University of Manchester under Professor H. Brindle, M.Sc., F.R.I.C., F.P.S., to whom thanks are due for his interest and encouragement.

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