# 1 Ultrasonic homogenization

## 1.1 Homogenization

## 1.2 INTRODUCTION

Homogeneity and heterogeneity are concepts relating to the uniformity or lack thereof in a substance. In 1899 Auguste Gaulin obtained a patent on his homogenizer. The patent consisted of a 3 piston pump in which product was forced through one or more hair like tubes under pressure. At the World's Fair in Paris in 1900, Auguste Gaulin exhibited his invention a process for "treating" milk. According to the literature and publications of that time, the word ""homogenized" was first used to describe milk treated by the Gaulin machine. Therefore, the terms "homogenization" and "homogenizer" historically relate to the process and equipment developed by Gaulin. The homogenizer basically consists of a positive-displacement pump to which is attached a homogenizing valve assembly. The pump forces fluids through the homogenizing valve under pressure. The term "homogenization" refers to the process or action that occurs within the homogenizing valve assembly.

## 1.3 FIELD OF HOMOGENIZING

The field of homogenizing encompasses a very broad area. Homogenizing, may mean doing one or more of the following, blending, mixing, disrupting, emulsifying, dispersing, stirring etc. The current processes or methods of homogenizing can be broken down into three (3) major categories, **Pressure**, **Mechanical** and **Ultrasonic**.

### 1.3.1 High-pressure homogenizers

High-pressure homogenizers works by forcing cell suspensions through a very narrow channel or orifice under pressure. Subsequently, and depending on the type of high-pressure homogenizer, they may or may not impinge at high velocity on a hard-impact ring or against another high-velocity stream of cells coming from the opposite direction. Machines which include the impingement design are more effective than those which do not. Disruption of the cell wall occurs by a combination of the large pressure drop, highly focused turbulent eddies, and strong shearing forces. The rate of cell disruption is proportional to approximately the third power of the turbulent velocity of the product flowing through the homogenizer channel, which in turn is directly proportional to the applied pressure. Thus, the higher the pressure, the higher the efficiency of disruption per pass through the machine. The operating parameters which effect the efficiency of high-pressure homogenizers are as follows:

- Pressure
- Temperature
- Number of passes
- Valve and impingement design
- Flow rate

The supremacy of high-pressure homogenizers for disruption of microorganisms is now being challenged by bead mill homogenizers. Still, in terms of throughput, the largest industrial models of high-pressure homogenizers outperform bead mills. Because the process generates heat, the sample, piston and cylinder are usually pre-cooled. Most high-pressure homogenizers used for homogenization were adapted from commercial equipment designed to produce emulsions and homogenates in the food and pharmaceutical industries. Considerable heat can be generated during operation of these homogenizers and therefore a heat exchanger attached to the outlet port is essential.

## 1.3.2 MECHANICAL HOMOGENIZERS

Mechanical homogenizers can be broken down into two (2) separate categories, a) rotor-stator homogenizers and b) blade type homogenizers.

### 1.3.2.1 a) ROTOR-STATOR HOMOGENIZERS

Rotor-stator homogenizers (also called colloid mills or Willems homogenizers) generally outperform cutting blade-type blenders. However, the homogenized sample is contaminated with minute glass and stainless steel particles and the abrasive wear to the rotor-stator homogenizer is unacceptably high. The only thing that ultrasonic and mechanical (rotor-stator) homogenizing have in common is that both methods generate and use to some degree cavitation. Cavitation is defined as the formation and collapse of low-pressure vapor cavities in a flowing liquid. Cavitation is generated as you move a solid object through a liquid at a high rate of speed. In ultrasonic the object being moved is the probe which is being vibrated at a very high rate of speed generating cavitation. In mechanical homogenizing (rotor-stator) the blade (rotor) is being moved through the liquid at a high rate of speed generating cavitation. Since most rotor-stator homogenizers have an open configuration, the product is repeatedly recirculated. The process is fast and depending on the toughness of the tissue sample, desired results will usually be obtained in 15-120 seconds. The variables to be optimized for maximum efficiency are as follows:

- Design and size of rotor-stator (generator)
- Rotor tip speed
- Initial size of sample
- Viscosity of medium
- Time of processing or flow rate
- Volume of medium and concentration of sample
- Shape of vessel and positioning of rotor-stator

The capacity of the rotor-stator should be matched to the viscosity and volume of the medium and with the type and amount of material to be processed. The speed and efficiency of homogenization is greatly degraded by using too small a homogenizer, and the volume range over which a given homogenizer rotor-stator size will function efficiently is only about 10 fold.

#### 1.3.2.2 b) BLADE TYPE HOMOGENIZERS

Although less efficient than rotor-stator homogenizers, blade homogenizers (also called blenders) have been used for many years to produce fine brie and extracts from plant and animal tissue.

### 1.3.3 1) ULTRASONIC HOMOGENIZING

One widely used method to homogenize is ultrasonic disruption. These devices work by generating intense sonic pressure waves in a liquid media. The pressure waves cause streaming in the liquid and, under the right conditions, rapid formation of micro-bubbles which grow and coalesce until they reach their resonant size, vibrate violently, and eventually collapse. This phenomenon is called cavitation. The implosion of the vapor phase bubbles generates a shock wave with sufficient energy to break covalent bonds. Shear from the imploding cavitation bubbles as well as from eddying induced by the vibrating sonic transducer disrupt cells. There are several external variables which must be optimized to achieve efficient material disruption. These variables are as follows:

- Tip amplitude and intensity

- Temperature
- material concentration
- Pressure
- Vessel capacity and shape

Modem ultrasonic processors use piezoelectric generators made of lead zirconate titanate crystals. The vibrations are transmitted down a titanium metal horn or probe tuned to make the processor unit resonate at 15-25 kHz. The rated power of ultrasonic processors vary from 10 to 700 Watts. Low power output does not necessarily mean that the cell disintegrator is less powerful because lower power transducers are generally matched to probes having smaller tips. It is the power density at the tip that counts. Higher output power is required to maintain the desired amplitude and intensity under conditions of increased load such as high viscosity or pressure. The larger the horn, the more power is required to drive it and the larger the volume of sample that can be processed. On the other hand, larger ultrasonic disintegrators generate considerable heat during operation and will necessitate aggressive external cooling of the sample. Typical maximum tip amplitudes are 30-250 urn and resultant output intensities are in the range of 200-2000 W/square cm. The temperature of the sample suspension should be as low as possible. In addition to addressing the usual concerns about temperature liability of proteins, low media temperatures promote high-intensity shock front propagation. So ideally, the temperature of the ultrasonicated fluid should be kept just above its freezing point. The ultrasonic disintegrator generates considerable heat during processing and this complicates matters. Disruption can also be enhanced by increased hydrostatic pressure (typically 15-60 psi) and increased viscosity, providing the ultrasonic processor has sufficient power to overcome the increased load demand and the associated sample heating problems can be solved. The tip should not be placed so shallow in the vessel as to allow foaming. Antifoaming agents or other materials which lower surface tension should be avoided. Finally, one must keep in mind that free radicals are formed in ultrasonic processes and that they are capable of reading with biological material such as proteins, polysaccharides, or nucleic acids. Damage by oxidative free radicals can be minimized by including scavengers like cysteine, dithiothreitol, or other SH compounds in the media or by saturating the sample with a protective atmosphere of helium or hydrogen gas. For practical reasons, the tip diameter of ultrasonic horns cannot exceed about 3 inches. This sets a limit on the scale-up of these devices. While standard sized ultrasonic disrupters have been adapted to continuous operation by placing the probe tip in a chamber through which a stream of cells flow, cooling and free radical release present problems.

## 1.4 Different type of homogenizers

Homogenizer are classified in different groups including:

- High Speed Blender
- High Pressure Homogenizers
- Colloid Mill
- High Shear Dispersers
- Ultrasonic Disruptor
- Membrane Homogenizers

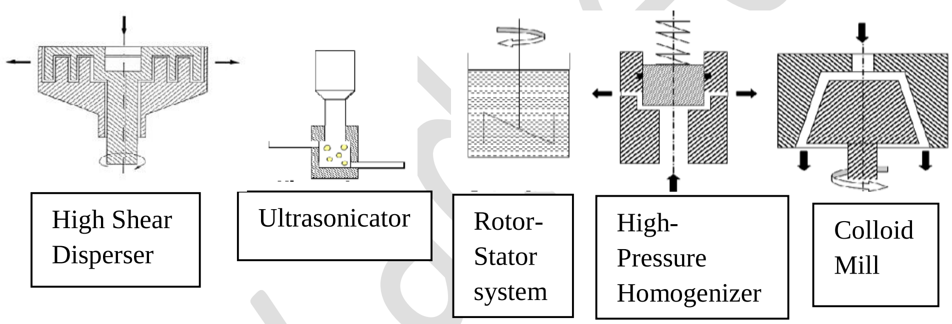


Figure 1-1 Different Type of Homogenizer

## 1.5 Impact of Homogenization by Sonication

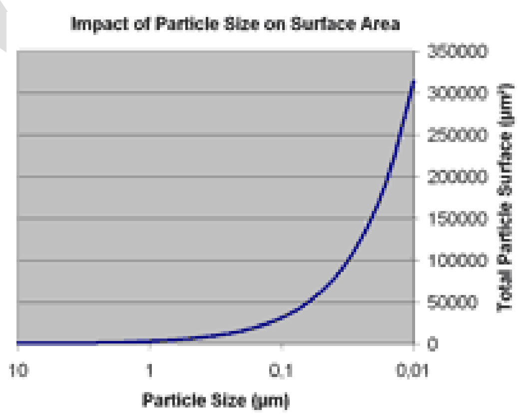


Figure 1-2 Impact of Particle size on surface Area

When ultrasonic processors are used as homogenizers, the objective is to reduce small particles in a liquid to improve uniformity and stability. These particles (disperse phase) can be either solids or liquids. A reduction in the mean diameter of the particles increases the number of individual particles. This leads to a reduction of the average particle distance and increases the particle surface area. Fig 2 shows the correlation between individual particle diameter and total surface area. Surface area and average particle distance can influence the rheology of a liquid.

If there is a difference in specific gravity between the particles and the liquid, the homogeneity of the mixture can influence the stability of the dispersion. If the particle size is similar for the majority of the particles, the tendency to agglomerate during settling or rising reduces, because the similar particles have a similar speed of rising or settling.

## 1.6 Process Parameters of Ultrasoication

• Frequency

- ✓ Size of cavitational bubbles decreases with increasing frequency
- ✓ A minimum pressure drop is required to initiate cavitation below critical wave intensities, almost no droplet disruption
- ✓ Above the critical pressure, direct relationship between applied intensity and achievable particle size

• Sonication time

- ✓ Disruption and stabilization are kinetic events, thus, a minimum sonication time is required to achieve droplet disruption

• Hydrostatic pressure

- ✓ Initially, improved emulsification (up to 5 bar), above 5 bar, decreased efficiency

• Dissolved gas concentration

- ✓ Increased number of cavitational events but reduced intensity of cavitational collapse due to dampening

• Viscosity & Temperature

- ✓ Influences droplet disruption

## 1.7 Advantages of Ultrasonic Homogenizing

Ultrasonic homogenizing is very efficient for the reduction of soft and hard particles. When liquids are exposed to intense ultrasonication sound waves propagate through the liquid causing alternating high-pressure and low-pressure cycles. During the low-pressure cycle, high-intensity small vacuum bubbles are created in the liquid, as the liquid vapor pressure is attained.

When the bubbles reach a certain size, they collapse violently during a high-pressure cycle. During this implosion very high pressures and high speed liquid jets are generated locally. The resulting currents and turbulences disrupt particle agglomerates and lead to violent collisions between individual particles.

One major advantage of ultrasonic homogenizers is the low number of wetted and moving parts. This reduces frictional wear and cleaning time. There are only two wetted parts: The sonotrode and the flow cell. Both have simple geometries and no small or hidden orifices.

Another advantage is the exact control over the operational parameters influencing the cavitation. As amplitude and pressure are the most influential parameters, the wide operational range of each parameter allows for very gentle to very destructive processing.

The adjusted amplitude will be maintained under all operational conditions. This makes ultrasonication controllable and repeatable. Sonication under identical operational parameters will yield consistent and reproducible results. This is important for the quality of the produced material and for the scale-up of process results from the lab to the production level.

## 1.8 Field of Ultrasonic Homogenizer Usage:

### 1.8.1 Emulsifications

Water in oil emulsions are well suited for sonication because there is little danger of the sample being ruined by inversion and the process is considerably faster than traditional mixing methods. The cosmetic industry uses Ultrasonic Homogenization for liquid make-up in order to disperse the pigments uniformly. It is also widely used by lotion and toothpaste manufacturers as the final product has a much longer shelf life and is a higher quality product.

### 1.8.2 Environmental

Sonication is used in environmental testing labs for testing of water, soil and sediment samples. Testing that was done prior to Ultrasonic Homogenization was very time consuming and required high volumes of solvents. The use of Ultrasonics cut the testing time by many hours down to 5-10 minutes making the environmental labs more efficient and reduced solvent waste products.

### 1.8.3 Pharmaceutical

Pharmaceutical research covers a wide range of applications for Ultrasonics. Common uses are mixing of powders and solutions, the making of smaller crystals for drug compounds, and degassing samples. The production of liposomes or lipid vesicles that are used to study mechanisms for drug discovery are also critical in this industry along with putting complex compounds into solution for analysis via chromatography.

### 1.8.4 Focused Cleaning

This may be the least well known application for Ultrasonic Homogenizers. In an Ultrasonic Bath the strength of the sonication waves are limited for this type of application. It takes much more time to clean items in a bath than it would if using a probe type Ultrasonic. The benefits of this are apparent when trying to clean items with very small openings such as needle or wire dies and electronic components as the energy can be focused and directed by moving the probe.

## 1.9 Ultrasonic specific Applications

### 1.9.1 Ultrasonic Homogenizing

Ultrasonic homogenizer are used to reduce small particles in a liquid to improve uniformity and stability. These particles (disperse phase) can be either solids or liquids. Ultrasonic homogenizing is very efficient for the reduction of soft and hard particles.


Figure 1-3 Effect of Ultrasonic in Hemogenization

### 1.9.2 Ultrasonic Dispersing and Deagglomeration

Ultrasonic dispersing and deagglomeration of powder particles generates single-dispersed particles. The dispersing and deagglomeration of solids into liquids is an important application of ultrasonic devices. Ultrasonic cavitation generates high shear forces that break particle agglomerates into single dispersed particles. The mixing of powders into liquids is a common step in the formulation of various products, such as paint, ink, shampoo, beverages, or polishing media. The individual particles are held together by attraction forces of various physical and chemical nature, including van der Waals forces and liquid surface tension. The attraction forces must be overcome on order to deagglomerate and disperse the particles into liquid media. For the dispersing and deagglomeration of powders in liquids, high intensity ultrasonication is an interesting alternative to high pressure homogenizers and rotor-stator-mixers.

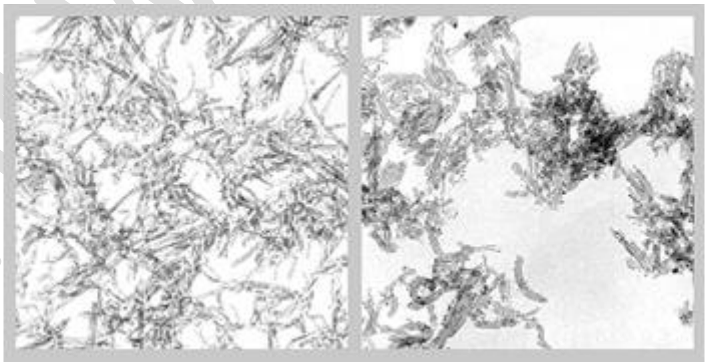

Figure 1-4 Effect of Ultrasonic in Deagglomeration

### 1.9.3 Ultrasonic Emulsifying

Ultrasonication is an effective means for emulsification. A wide range of intermediate and consumer products, such as cosmetics and skin lotions, pharmaceutical ointments, varnishes, paints and lubricants and fuels are based wholly or in part of emulsions. Emulsions are dispersions of two or more immiscible liquids. Highly intensive ultrasound supplies the power needed to disperse a liquid phase (dispersed phase) in small droplets in a second phase (continuous phase). In the dispersing zone, imploding cavitation bubbles cause intensive shock waves in the surrounding liquid and result in the formation of liquid jets of high liquid velocity. At appropriate energy density levels, ultrasound can well achieve a mean droplet sizes below 1 micron (micro-emulsion).

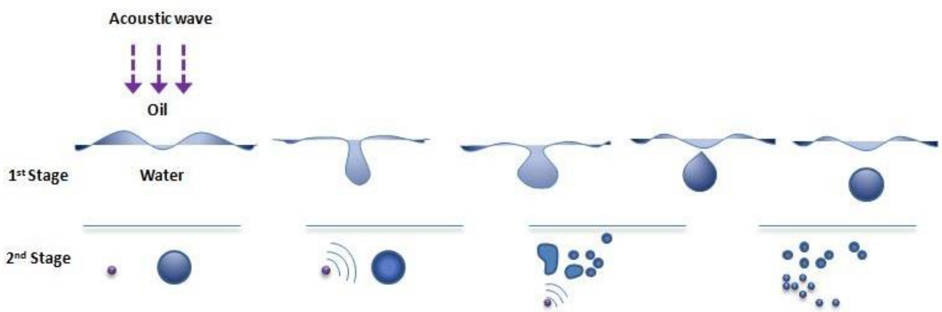


Figure 1-5 Effect of Ultrasonic in Emulidyfing

Ultrasound emulsification occurs when one liquid dispersed into another immiscible liquid under the influence of an acoustic field. The acoustically-formed emulsions have been surprisingly been discovered to possess an unusual stability even without the presence of an emulsifier. Furthermore, the mean droplet size of resulting emulsions is extremely small and generally falls into the submicron region. In an ultrasonic field, the intense shock waves produced in the surrounding liquid caused by imploding cavitation bubbles and the formation of liquid jets at high velocity were responsible for the formation of emulsion droplets. In normal circumstances, a two-stage ultrasound emulsification mechanism of liquid-liquid system can be used to explain the influence of ultrasound energy on droplet formation and disruption

The first stage primarily involves a synergistic action of interfacial waves of acoustic field and Rayleigh-Taylor instability, which eventually lead to the eruption of the oil phase into water medium to form the initial larger droplets.

The second stage is based on the deformation and subsequent break-up of these larger droplets into submicron range due to the impact of cavitation-induced shock waves generated near the interface when subjected to an acoustic field.

In the emulsification process, ultrasound had emerged as an excellent yet powerful emulsifying tool as compared to that of other mechanical alternatives in terms of obtaining a smaller droplet size. Additionally, under the same conditions, in the case of producing a nanoemulsion with desired diameter, the required amount of surfactant was significantly reduced; the energy consumption was considerably lower than other classical mechanical devices. It would, then, appear that ultrasound emulsification may be used in place of high-pressure homogenization and microfluidization as it is capable of achieving similar local power densities with lower operating costs, if a suitable treatment chamber is used.

### 1.9.4 Ultrasonic Wet-Milling and Grinding

Ultrasonic milling of solid materials is an efficient means for the wet-milling and micro-grinding of particles. In particular for the manufacturing of superfine-size slurries, ultrasound has many advantages, when compared with common size reduction equipment, such as: colloid mills (e.g. ball mills, bead mills), disc mills or jet mills. Ultrasonication allows for the processing of high-concentration and high-viscosity slurries – therefore reducing the volume to be processed. Ultrasonic milling is suitable for processing micron-size and nano-size materials, such as ceramics, alumina trihydrate, barium sulphate, calcium carbonate and metal oxides.

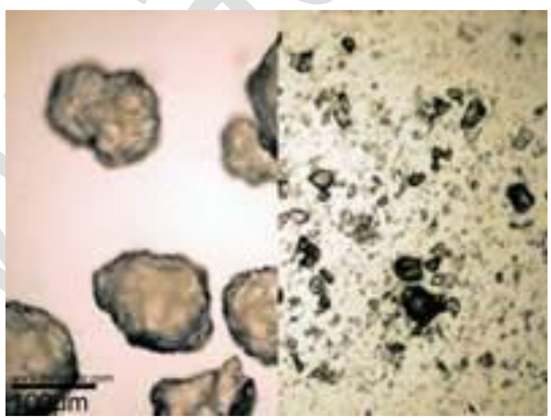

**Figure 1-6 Effect of Ultrasonic in milling of material**

### 1.9.5 Ultrasonic Cell Disintegration

Ultrasonically assisted extraction of compounds from herbs using an ultrasonic processor can disintegrate fibrous, cellulosic material into fine particles and break the walls of the cell structure.

This releases more of the intra-cellular material, such as starch or sugar into the liquid. In addition to that the cell wall material is being broken into small debris.

This effect can be used for fermentation, digestion and other conversion processes of organic matter. After milling and grinding, ultrasonication makes more of the intra-cellular material e.g. starch as well as the cell wall debris available to the enzymes that convert starch into sugars. It does also increase the surface area exposed to the enzymes during liquefaction or saccharification. This does typically increase the speed and yield of yeast fermentation and other conversion processes, e.g. to boost the ethanol production from biomass.

Figure 1-7 Ussage of Ultrasonic in Cell Disintegration

### 1.9.6 Ultrasonic Cell Extraction

The extraction of enzymes and proteins stored in cells and subcellular particles is an effective application of high-intensity ultrasound, as the extraction of organic compounds contained within the body of plants and seeds by a solvent can be significantly improved. Ultrasound has a potential benefit in the extraction and isolation of novel potentially bioactive components, e.g. from non-utilized by-product streams formed in current processes.

Figure 1-8 Ussage of Ultrasonic in Cell extraction

### 1.9.7 Sonochemical Application of Ultrasonics

The mechanism causing sonochemical effects in liquids is the phenomenon of acoustic cavitation. The sonochemical effects to chemical reactions and processes include increase in reaction speed and/or output, more efficient energy usage, performance improvement of phase transfer catalysts, activation of metals and solids or increase in the reactivity of reagents or catalysts.

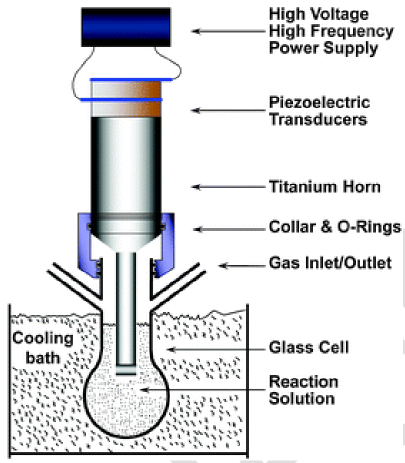


Figure 1-9 Schematic of Sonochemical Process

### 1.9.8 Ultrasonic Transesterification of Oil to Biodiesel

Ultrasonication increases the chemical reaction speed and yield of the transesterification of vegetable oils and animal fats into biodiesel. This allows changing the production from batch processing to continuous flow processing and it reduces investment and operational costs. The manufacturing of biodiesel from vegetable oils or animal fats, involves the base-catalyzed transesterification of fatty acids with methanol or ethanol to give the corresponding methyl esters or ethyl esters. Ultrasonication can achieve a biodiesel yield in excess of 99%. Ultrasound reduces the processing time and the separation time significantly.

### 1.9.9 Ultrasonic Degassing of Liquids

Ultrasonic degassing of oil is an interesting application of ultrasonic devices. In this case the ultrasound removes small suspended gas-bubbles from the liquid and reduces the level of dissolved gas below the natural equilibrium level.

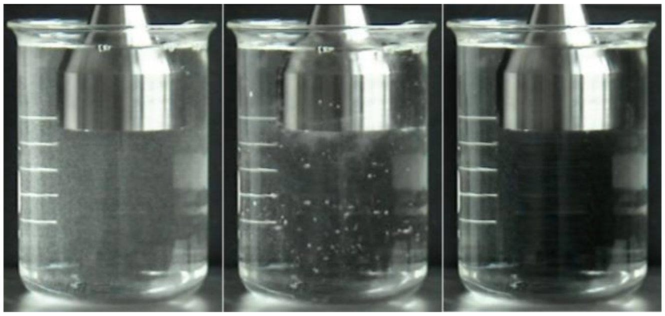

Figure 1-10 Degassing

### 1.9.10 Sonication of Bottles and Cans for Leak Detection

The instantaneous release of carbon dioxide is the decisive effect of ultrasonic leakage tests of containers filled with carbonated beverages.

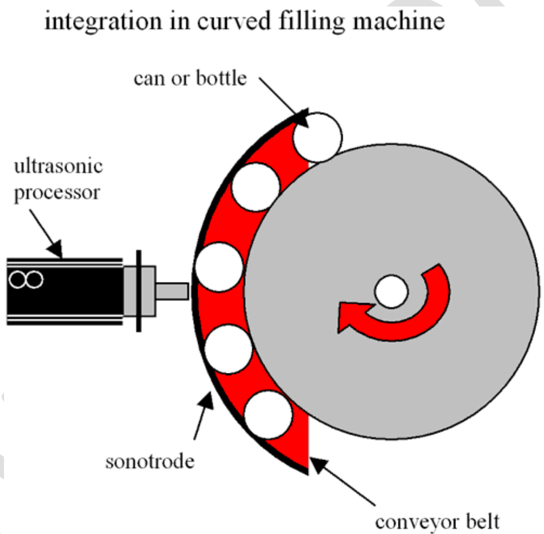


Figure 1-11 Ultrasonic Performance in Quality control

### 1.9.11 Ultrasonic Wire, Cable and Strip Cleaning

Ultrasonic cleaning is an environmentally friendly alternative for the cleaning of continuous materials, such as wire and cable, tape or tubes. The effect of the cavitation generated by the ultrasonic power removes lubrication residues like oil or grease, soaps, stearates or dust.