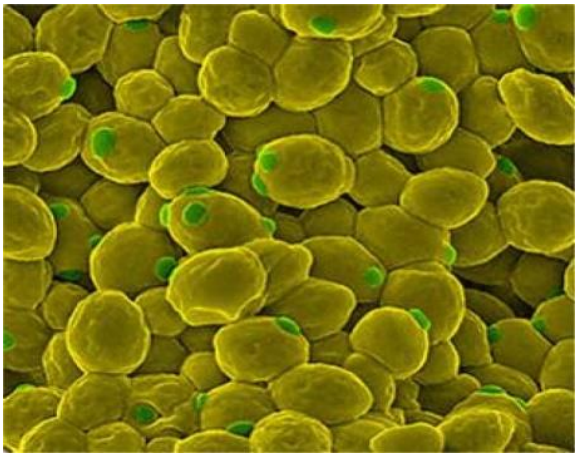
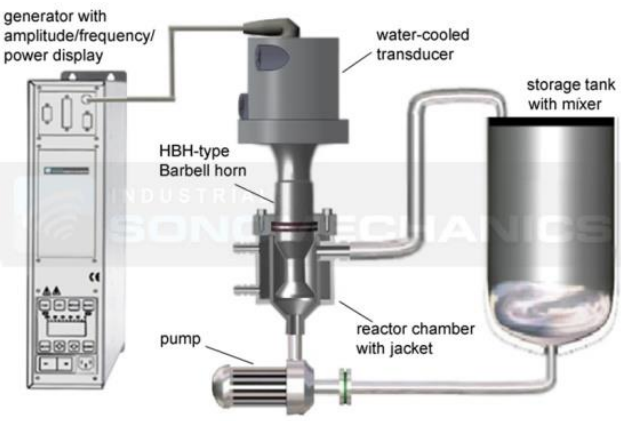
CELL DISRUPTION (LYSIS) FOR RECOMBINANT PROTEIN PRODUCTION

Industrial Sonomechanics (ISM) offers laboratory, bench and industrial-scale high-amplitude ultrasonic processors, which can be used for efficient cell disruption. The processors are based on our patented Barbell Horn Ultrasonic Technology (BHUT), which makes it possible to directly implement laboratory accomplishments in a production environment, guaranteeing reproducible and predictable results at any scale.



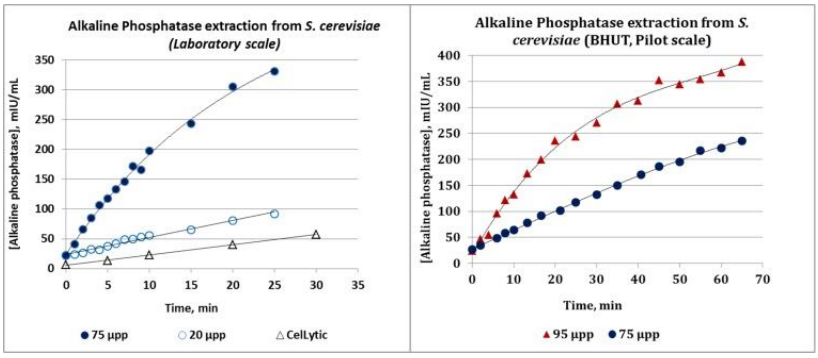
BACKGROUND

Cell disruption (lysis) is an important step in recombinant protein production procedures. Ultrasonic cell disruption (lysing with ultrasound) has been the laboratory-scale method of choice for this application for several decades. The process requires high ultrasonic amplitudes to be applied to cell suspensions, producing extreme shear forces. The shear forces are the result of intense ultrasonic cavitation, which creates violently and asymmetrically imploding vacuum bubbles and causes micro-jets that rupture cell walls. However, due to limitations of conventional ultrasonic technology, this method's industrial implementation has not been possible without reducing ultrasonic amplitudes, diminishing the intensity of cavitation-generated shear forces and, therefore, compromising the efficiency of the lysis process. These limitations have been overcome with BHUT, which, as explained below, permits constructing industrial-scale ultrasonic cell disruptors with the same lysis efficiency as the laboratory devices, while offering much higher productivities.



Why ISM's Ultrasonic Technology?

Conventional ultrasonic liquid processing systems comprise acoustic horns that reduce their diameters in the output direction and can only provide high ultrasonic amplitudes when their output tips are small. Process scale-up requires switching to horns with larger output tip diameters, able to output the ultrasonic energy into greater volumes of processed liquids, while still maintaining high amplitudes. If, however, the output tip diameter of a conventional horn is increased to an industrially acceptable size, its maximum vibration amplitude becomes significantly lower and insufficient for cell disruption. The use of conventional high-amplitude ultrasonic processors is, therefore, limited to laboratory investigations that cannot be directly scaled-up. ISM has successfully overcome this limitation by developing BHUT, which permits constructing pilot and industrial-scale ultrasonic processors able to generate extremely high amplitudes and operate continuously. Our industrial cell disruption equipment is compact, requires very little technical support and includes only two wetted parts (HBH-type Barbell horn and Reactor chamber) with easy access for cleaning.



Cell Disruption of S. Cerevisiae Yeast

In order to illustrate the ability of BHUT-based processors to produce excipient nanocrystals, a sonofragmentation experiment was conducted using our bench-scale ultrasonic liquid processor, BSP-1200. The processor was configured in the flow-through arrangement, as shown in the above schematic.

The initial excipient crystals with the mean particle size diameter (d50) of 15.4 micrometers were suspended in 1 L of an organic solvent at the concentration of 5 % by mass. No surfactants or any other agents were used. The suspension was stirred in the storage tank as it recirculated through the reactor chamber at the rate of 4 L/min for 2 hours. The reactor chamber was equipped with an HBH-type Barbell horn having the diameter of 32 mm and vibrating at the amplitude of 90 microns. The temperature of the suspension was maintained at 25 C throughout the procedure by running chilled water through the temperature control jacket on the reactor chamber.

The results presented above show that after 2 hours of ultrasonic exposure, the required mean particle size of about 0.4 micrometers (400 nanometers) was obtained. For commercial-scale production, the procedure can be transferred to the ISP-3000 industrial ultrasonic processor, which would allow productivity to increase by a factor of 5.

Ultrasound is a simple and effective technique for producing excipient nanocrystals. With the use of BHUT, the process is directly scalable, making it possible to implement laboratory accomplishments in an industrial production environment.

The data presented above was collected in collaboration with Allied Innovative Systems, LLC (ALLIS).

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