CELL DISRUPTION BY HIGH-INTENSITY ULTRASOUND - A POTENTIAL INDUSTRIAL-SCALE TECHNIQUE
Cell Disruption

• Many biologically interesting molecules are produced by culturing in bacterial or yeast cells
  • Antibodies
  • Enzymes
  • Hormones
  • Cytokines
  • Clotting factors
  • Vaccines

• Cell disruption (lysis) is a method for releasing biological molecules from inside a cell
• Global sales for biopharmaceutical proteins ~ $170 Billion
Current Industrial Technologies

High Pressure Homogenization (HPH)

Diagram showing the process of high pressure homogenization with labeled parts: Feed, Seat, Impact ring, Valve, and Homogenized product.
High Pressure Homogenization (HPH)

- Currently the main method (90% of the market)
- Used for bacteria and yeast disruption

**Drawbacks:**
- Pre-processing by non-mechanical techniques
- Heating
- Consumes a lot of energy, damageable valves, expensive maintenance
Current Industrial Technologies

Wet Media Milling (WMM)
Wet Media Milling

- Mills are less popular within pharmaceutical industry (<10% of the market)
- Media occupies 80-90% of the packed volume
- Frequently used in combination with chemical disruptors
- Drawbacks: significant protein denaturation because of high temperature and/or excessive shear, wear of the grinding media
• Ultrasonic cell disruption is a laboratory standard

Sonication vs. Other Methods


Figure 3. Relationship between the selectivity of product release and the ease of product recovery for various disruption techniques based on literature reports.
Conventional Ultrasonic Technology

Ultrasonic Cell Disruption – HIGH AMPLITUDES ARE REQUIRED

- High-Quality Product
- Low-Cost Equipment
- Simple Aseptic Processing
- Selective Extraction

NOT SCALABLE
Barbell Horn Ultrasonic Technology

- Scale up without lowering the amplitudes

Scale-up Factor $= 2\left(\frac{D_{hbh}}{D_{ch}}\right)^2 \approx 25 - 50$
Barbell Horn Ultrasonic Technology

ISP-3000 Ultrasonic Processor
Ultrasonic Disruption of *S. cerevisiae*

**Laboratory scale – LSP-500**

LSP-500 ULTRASONIC PROCESSOR
Batch Setup with CH-type Horn

CH-type horn, $\varnothing = 12.7$ mm

**Bench scale – BSP-1200**

HBH-type horn, $\varnothing = 32$ mm
Sonication Versus Chemical Extraction, Laboratory Scale (45 ml)

Total protein extraction from *S. cerevisiae* (Laboratory scale)

- 3 ml/min
- 4.5 ml/min

Ultrasonic amplitude is important!
Sonication with BHUT, Bench Scale (1500 ml)

Total protein extraction from *S. cerevisiae* (BHUT, Pilot scale)

- 50 ml/min
- 25 ml/min

Alkaline Phosphatase extraction from *S. cerevisiae* (BHUT, Pilot scale)

- 90 ml/min
- 30 ml/min

Ultrasonic amplitude is important!
CONCLUSIONS

• BHUT – effective for cell disruption
• High amplitudes are essential
• Directly scalable

• Proven laboratory standard method can now be taken to the production scale
THANK YOU

Q&A