Pharmaceutical and cosmetic products

High Pressure Processing (HPP) is a **non-thermal technology for pasteurisation** and macromolecule modification that can be applied to a wide variety of products. It can be extensively used in the pharmaceutical and cosmetics industry.

Target products are introduced into a high pressure vessel in their final flexible package, and subjected to a high level of hydrostatic pressure (up to 6000 bar- 600 MPa- 87,000 psi). Product shape and integrity remains unchanged. HPP is an all natural, clean and environmentally friendly technology. High Pressure Processing equipment works with electricity and water. Furthermore water is only the pressure transmitting fluid and thus can be recycled.

HPP applications in cosmetic and pharmaceutical products

- Cold pasteurisation technique: keeps functional properties and activity of thermosensitive components unchanged.
- Drastically reduces the overall microbiological contaminant flora, extending the shelf life of products.
- Allows development of additive-free, natural products.
- Reduces allergenicity due to modifications of 3D structure of proteins.
- Allows a wide range of HPP processed products: liquid and semisolid, lotions, emulsions...

New vaccines

HPP is an alternative to thermal or chemical processes used in the production of vaccines. HPP inactivates the viruses that later will be used as protection against some illnesses, for example, Rift Valley Fever. It has been proved that vaccines elaborated through HPP are much more protective than those elaborated using chemical processes.

Another application of HPP technology is the development of antitumor vaccines through inactivation of tumor cells while keeping its immunogenicity.

New medicaments

HPP has become a real alternative to increase medicament's process yield, specially the ones made up of recombinant proteins. HPP increases the bioavailability of some hydrophobic components through the formation of nano-capsules of protein.

Cosmetics

- Product hygienisation.
- Provides the opportunity to develop additive-free, natural products.
- Extends product shelf life.
- Process-sensitive compounds (vitamins etc.) maintain their functional properties after HPP.
- Keeps the structure of emulsions.
- Enables the development of new emulsions, with new textures and characteristics.
- Allows development of protein/polysaccharide gels which are of interest to the pharmaceutical industry.

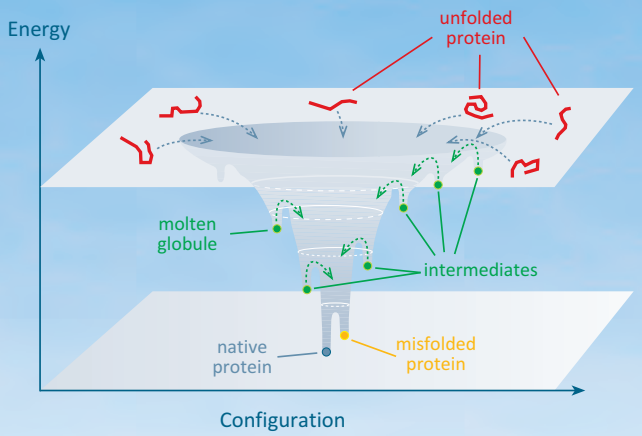
Hypoallergenic products

HPP can be used in the inactivation of allergens (e.g. Hypoallergenic rice), through the modification of secondary, tertiary and quaternary structure of proteins.

Effects and benefits

Renaturation of recombinant proteins and Improved Product Safety

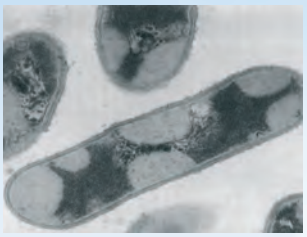
- Refolding of synthetic recombinant proteins (PreEMT™) that couldn't reach the desired conformation during traditional production process.
- Refolds proteins at conditions that favor the native protein, improving process yields and decreasing unit costs.
- Scaleable in the cGMP setting.
- Increases the homogenicity of the final product by decreasing Non-native aggregates.



Radford S., "Protein folding: Progress made and promises ahead", Trends in Biochemical Sciences, V25, 611-618, 2000

Listeria monocytogenes

Before HPP



After HPP

From Mackey *et al.*, in Letters in Applied Microbiology, Vol. 19 - 6, p. 429–432, December 1994.

Increases the product shelf life

- Reduces several logs of spoiling micro-organisms by exposing the packed product up to 600 MPa/87000psi for a period of time from 1 to 5 minutes.
- Increases protein stability of the final product.

Some examples of HPP proteins refolded under pressure

Protein	Type	Solubilization Yield	Activity Yield	Comparison to chaotropic based refolding yield	Best-case high pressure refolding condition	Reference
Bikunin	Kuniz-type protease inhibitor	100%	100%	55%	2000 bar, pH 8, 25ºC 24h, slow depresurization	*Seefeldt et al, Protein science, v13, 2639-2650 (2004)*
Lysozime	Hydrolase	90%	80%	80% at lower protein concentration	2000 bar, pH 8. 50h, depresurization 10 bar/min	*St. John et al, Biotechnology progress, v18,565-571, (2002)*
IL-1ra	Interleukin receptor antagonist	60%	60%	Not tested	1500 bar, pH 7, 31ºC, rapid depresurization	*Seefeldt et al, Journal of biotechnology and bioengineering (in press)*
Malaria pdf48	Unknown	>95%	Activity confirmed	<1%	2650 bar, pH 10.5, despresurization 10 bar/min	*Seefeldt, dep. of chemical and biological engineering thesis (2004)*
BaroFold Fab	Antibody Fragment	>95%	40% at 8 g/L	No Refolding Achieved	2000 bar, pH 9.0, 4h	*BaroFold, www.barofold.com*

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Enero 2012

Natural Safety