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ProductInformation

α-Lactalbumin from bovine milk

Product Number L 5385 Storage Temperature -0 °C

Product Description

CAS Number: 9051-29-0 Molecular Weight: 14,175^{1,2} pl: approximately 4.5³ λ_{max} : 280 nm⁴ Extinction coefficient: E^{1%} = 20.1 (280 nm, phosphate buffer (5.2 g/L NaH₂PO₄ + 7.7 g/L Na₂HPO₄ in water))⁴

 α -Lactalbumin is a small, globular, whey protein that has been found in all milk studied to date. It is a metalloprotein of approximately 14 kDa produced in the mammary glands.⁵ It consists of a single polypeptide chain with 8 cysteines which form 4 disulfide bridges.⁶ α -Lactalbumin binds several metal ions, including calcium, which is thought to play a role in the regeneration of native α -lactalbumin from the reduced, denatured form.⁷ α -Lactalbumin also has a distinct zinc binding site that is thought to play a role in the binding of the lactose synthase complex.⁵

α-Lactalbumin regulates lactose biosynthesis by forming the lactose synthase complex with $β(1\rightarrow 4)$ galactosyltransferase, which typically processes proteins in various secretory cells by transferring galactosyl groups from UDP-galactose to glycoproteins containing N-acetylglucosamine. In the lactating mammary gland, the specificity of $β(1\rightarrow 4)$ galactosyltransferase is modulated by interaction with α-lactalbumin, which increases its affinity and specificity for glucose.⁸ The complex then converts UDP-galactose and glucose to lactose and UDP. This reaction takes place in the Golgi lumen and requires Mn²⁺ ions.

Proteolytic digestion of α -lactalbumin by trypsin and chymotrypsin yields three peptides with bactericidal properties. These polypeptides have been shown to inhibit the growth of Gram-positive bacteria. In addition, a folding variant of α -lactalbumin was also shown to have bactericidal activity against various

strains of *Streptococcus pneumoniae*.⁹ Interestingly, native α -lactalbumin can be converted to the active bactericidal form by ion exchange chromatography in the presence of a cofactor from human milk casein, a C18:1 fatty acid. α -Lactalbumin posseses several classes of fatty acid binding sites indicating normal interactions with fatty acids may explain the multiple roles this protein possesses.¹⁰

A mulitmeric form of α -lactalbumin has also been described as potent a Ca2+-elevating and apoptosisinducing agent with broad, yet selective, cytotoxic activity, killing all transformed, embryonic, and lymphoid cells tested,^{11,12} leaving mature, normal epithelial cells intact. This multimeric form appears to exist in milk. These oligomers have been shown to possess a molten-like globule state, a conformational change when compared to native α -lactalbumin. Multimeric α -lactalbumin was shown to bind to the cell surface, enter the cytoplasm, and accumulate in cell nuclei,¹² consistent with its ability to induce apoptosis. In addition, caspases were activated by aggregated α -lactal burnin and direct interaction of these multimers with mitochondria leads to the release of cytochrome c, which may be an important step in the initiation of the caspase cascade, and hence, induction of apoptosis, in these cells.¹³

In addition, it appears that both monomeric and multimeric α -lactalbumin can bind human milk oligonucleotides of various lengths.¹⁴ This interaction was shown to block both the cytostatic and cytotoxic effects of α -lactalbumin.¹⁵ This suggests that oligonucleotides secreted from mammary cells can serve as factors of regulation of the physiological state of mammary gland cells. Moreover, these oligonucleotides could control the cytotoxic potential of milk.

This product is prepared from raw, unpasteurized milk and contains saturating levels of calcium.¹⁶

Precautions and Disclaimer

For Laboratory Use Only. Not for drug, household or other uses.

Preparation Instructions

This product is soluble in water (50 mg/ml), yielding a clear to slightly hazy, colorless to faint yellow solution.

References

- Vanaman, T. C., et al., The disulfide bonds of bovine α-lactalbumin. J. Biol. Chem., 245(17), 4583-4590 (1970).
- Smith, R. D., et al., New developments in biochemical mass spectrometry: electrospray ionization. Anal. Chem., 62(9), 882-899 (1990).
- Zittle, C. A., Solubility transformation of alphalactalbumin. Arch. Biochem. Biophys., 64, 144-51 (1956).
- Kronman, M. J. and Andreotti, R. E., Inter- and Intramolecular Interactions of α-Lactalbumin. I. The Apparent Heterogeneity at Acid pH. Biochemistry, **3**, 1145 (1964).
- Ren, J., et al., α-lactalbumin possesses a distinct zinc binding site. J. Biol. Chem., 268(26), 19292-19298 (1993).
- Brew, K., et al., Comparison of the amino acid sequence of bovine α-lactalbumin and hens egg white lysozyme. J. Biol. Chem., **242(16)**, 3747-3749 (1967).
- 7. Veprintsev, D. B., et al., Cooperative thermal transitions of bovine and human apo- α -lactalbumins: evidence for a new intermediate state. FEBS Lett., **412(3)**, 625-628 (1997).

- Hill, R. L., and Brew, K., Lactose synthetase. Adv. Enzymol. Relat. Areas Mol. Biol., 43, 411-490 (1975).
- Hakansson, A., et al., A folding variant of α-lactalbumin with bactericidal activity against *Streptococcus pneumoniae*. Mol. Microbiol., **35(3)**, 589–600 (2000).
- 10. Cawthern, K. M., et al., Interactions of α -lactalbumin with fatty acids and spin label analogs. J. Biol. Chem., **272(49)**, 30812–30816 (1997).
- Hakansson, A., et al., Apoptosis induced by a human milk protein. Proc. Natl. Acad. Sci. USA, 92(17), 8064–8068 (1995).
- 12. Svensson, M., et al., Molecular characterization of α -lactalbumin folding variants that induce apoptosis in tumor cells. J. Biol. Chem., **274(10)**, 6388-6396 (1999).
- Köhler, C., et al., Protease activation in apoptosis induced by MAL. Exp. Cell. Res., 249(2), 260-268 (1999).
- Kit, I., et al., Preparations of human α-lactalbumin, inducing apoptosis of transformed cells, contain ribooligonucleotides [Article in Russian]. Dokl. Akad. Nauk., **360(3)**, 406–408 (1998).
- Kit, Y. Y., et al., Endogenous oligonucleotides of human milk and their possible biological function. Biochemistry (Mosc.), 64, 1067–1072 (1999).
- Hiraoka, Y., et al., α-lactalbumin: a calcium metalloprotein. Biochem. Biophys. Res. Commun., 95(3), 1098-1104 (1980).

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