

Product Information

α_2 -Macroglobulin from human plasma

Product Number **M 6159**
 Storage Temperature $-20\text{ }^\circ\text{C}$

Product Description

α_2 -Macroglobulin inhibits all classes of endoproteases. The protease cleaves the α_2 -macroglobulin at a "bait" sequence changing the conformation of the α_2 -macroglobulin. A thioester bond is hydrolyzed that mediates the covalent binding of α_2 -macroglobulin to the protease.¹

α_2 -Macroglobulin is found in normal plasma at a concentration of 220–230 mg/dl accounting for 3–5% of the total plasma protein. Conditions such as kidney and liver diseases, and diabetes can elevate this level.²

The protease/ α_2 -macroglobulin balance plays an important role in mediating inflammation-associated tissue destruction. Serum levels of

α_2 -macroglobulin and protease/ α_2 -macroglobulin complexes are increased in patients with sepsis, emphysema, periodontitis, rheumatoid arthritis, and other inflammatory diseases. It is hypothesized that the oxidant inactivation of α_2 -macroglobulin contributes to tissue destruction in inflammation. α_2 -Macroglobulin has been implicated as a genetic risk factor for late-onset Alzheimer's disease. Activated α_2 -macroglobulin enhances the clearance of soluble α/β -amyloid via low-density lipoprotein receptor-related protein in cortical neurons, but has no effect on secreted or full-length amyloid precursor protein levels.²

α_2 -Macroglobulin accounts for approximately half of the anti-thrombin activity in plasma.³ Prostate Specific Antigen, a glycoprotein of the glandular kallikrein family, exists in free and α_2 -macroglobulin-bound forms. The ratios of free to inhibitor-bound forms may prove valuable in the diagnosis of prostate cancer.⁴

Molecular mass:⁵⁻⁷ 725 kDa.

The molecule is a tetramer with four identical subunits with molecular weights of 179 kDa.⁸ Upon binding to a protease, the 179 kDa subunit is cleaved into two 85 kDa fragments as determined by SDS-PAGE under reducing conditions.⁵⁻⁷

Carbohydrate content:⁹

Hexose (galactose:mannose, 1:1)	3.6%
Sialic Acid	1.8%
Acetylhexosamine	2.9%
Fucose	0.1%
Total carbohydrate	8.4%

Isoelectric point (pI):¹⁰ 5.0-5.2.

Protease inhibition:^{11,12}

Proteases inhibited or trapped by α_2 -macroglobulin	
acrosin	arvin
bromelain	calpain
cathepsins B, D, G, H, and L	chymosin
chymotrypsin	clostripain
leukocyte and vertebrate collagenase	ficin
leukocyte and pancreatic elastase	papain
plasma kallikrein	medullasin
plasmin	thermolysin
lysosomal proteases	trypsin
subtilisins A and B	
serine and metalloproteinases from <i>Crotalis atrox</i>	

Proteases not inhibited or trapped by α_2 -macroglobulin	
tissue kallekrein	urokinase
enteropeptidase	factor XIIa
complement C1s	rennin
<i>Clostridial</i> collagenase	

This product is prepared from human plasma by a modification of a published procedure.⁵ All plasma was tested for and found to be negative for HB_SAg and the antibody to HIV. The product is supplied as a powder lyophilized from a solution containing 100 mg/ml protein and 0.02 M Tris, 0.13 M glycine, pH 8.0, and 0.08 M trehalose.

Purity: minimum 98% (SDS-PAGE)

Activity: This product is a preparation of the intact protein with proteolytic inhibitory activity. One mg of protein will inhibit a minimum of 10 μg of trypsin with an activity of 10,000 BAEE units/mg protein.

Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

Preparation Instructions

α_2 -Macroglobulin is soluble in water (10 mg-protein/ml), yielding a clear, colorless solution.

Storage/Stability

The lyophilized powder is stable for at least 2 years when stored at $-20\text{ }^\circ\text{C}$.

Upon reconstitution, store in aliquots at $-20\text{ }^\circ\text{C}$ and avoid freeze/thaw cycles. Frozen solutions have been found to maintain full activity for at least one year. Refrigerated solutions have been found to maintain activity for at least three days. α_2 -Macroglobulin is denatured under acidic conditions (below pH 4) with dissociation into two halves.¹¹ Mild reduction by 1 mM DTT causes reversible denaturation into four inactive, native subunits.¹¹

References

1. Poller, W., *et al.*, *Hum. Genet.*, **88**, 313-319 (1992).
2. Allen, P.D., *et al.*, in *Plasma Protein. Analytical and preparative techniques*, Blackwell Science (Oxford, UK: 1977), pp. 190-194.
3. Rimon, A., *J. Biol. Chem.*, **241**, 5102 (1966).
4. Ambruster, D.A., *Clin. Chem.*, **39**, 181 (1993).
5. Swenson, R., and Howard, J., *J. Biol. Chem.*, **254**, 4452 (1979).
6. Hall, P., and Roberts, R., *Biochem. J.*, **173**, 27 (1978).
7. Virca, G., *et al.*, *Anal. Biochem.*, **89**, 274 (1978).
8. Sottrup-Jensen, L., *et al.*, *J. Biol. Chem.*, **259**, 8318 (1984).
9. Shultz, N., *Biochem. Z.*, **329**, 490 (1958).
10. Barrett, A.J., *et al.*, *Biochem. J.*, **181**, 401 (1979).
11. Barrett, A.J., *Meth. Enzymol.*, **80**, 737 (1981).
12. *Handbook of Enzyme Inhibitors*, 2nd ed., Zollner, H., VCH Verlagsgesellschaft mbH (Weinheim, Federal Republic of Germany: 1993), p. 827.
13. Qiu, Z., *et al.*, *J. Neurochem.*, **73**, 1393-1398 (1999).

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