α₂-Macroglobulin
from human plasma

Product Number M 6159
Storage Temperature –20 °C

Product Description
α₂-Macroglobulin inhibits all classes of endoproteases. The protease cleaves the α₂-macroglobulin at a “bait” sequence changing the conformation of the α₂-macroglobulin. A thioester bond is hydrolyzed that mediates the covalent binding of α₂-macroglobulin to the protease.¹

α₂-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/α₂-macroglobulin balance plays an important role in mediating inflammation-associated tissue destruction. Serum levels of α₂-macroglobulin and protease/α₂-macroglobulin complexes are increased in patients with sepsis, emphysema, periodontitis, rheumatoid arthritis, and other inflammatory diseases. It is hypothesized that the oxidant inactivation of α₂-macroglobulin contributes to tissue destruction in inflammation. α₂-Macroglobulin has been implicated as a genetic risk factor for late-onset Alzheimer’s disease. Activated α₂-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

α₂-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 α₂-macroglobulin-bound forms. The ratios of free to inhibitor-bound forms may prove valuable in the diagnosis of prostate cancer.⁴

Molecular mass⁵–⁷ 725 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.⁹

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 α₂-macroglobulin
acrosin calpain
bromelain chymotrypsin
cathepsins B, D, G, H, and L clostripain
leukocyte and vertebrate collagenase ficin
leukocyte and pancreatic elastase medullasin
plasma kallikrein papain
plasmin thermolysin
lysosomal proteases trypsin
subtilisins A and B
serine and metalloproteinases from Crotalis atrox

Proteases not inhibited or trapped by α₂-macroglobulin
tissue kallikrein urokinase
enteropeptidase factor XIIa
complement C1s rennin
Clostridial 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 HBsAg 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
α₂-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 °C.

Upon reconstitution, store in aliquots at –20 °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. α₂-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

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