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| **Name:** | **C1s-C1INH Complex** |
| **Catalog Number:** | **C1040** |
| **Sizes Available:** | 100 µg/vial |
| **Concentration:** | 0.5 mg/mL (see Certificate of Analysis for actual concentration) |
| **Form:** | Frozen liquid |
| **Purity:** | >90 % by SDS PAGE |
| **Buffer:** | 10 mM sodium phosphate, 145 mM NaCl, 5 mM EDTA, pH 7.3 |
| **Extinction Coeff.** | $A_{280\ nm}$ = 0.725 at 1.0 mg/mL for pure C1s-C1INH Complex |
| **Molecular Weight:** | 196,000 Da (1 chain) |
| **Preservative:** | None, 0.22 µm filtered. |
| **Storage:** | -70°C or below. Avoid freeze/thaw. |
| **Source:** | Normal human serum (shown by certified tests to be negative for HBsAg, HTLV-I/II, STS, and for antibodies to HCV, HIV-1 and HIV-II). |
| **Precautions:** | Use normal precautions for handling human blood products. |
| **Origin:** | Manufactured in the USA. |

**General Description**

The product C1s-C1INH Complex (CompTech #C1040) is made by interacting purified protease inhibitor C1-INH (CompTech # A140) with purified C1s enzyme (CompTech #A104) followed by purification. The protease inhibitor C1-INH prevents the spontaneous activation of complement and limits consumption of C2 and C4 by rapidly inactivating C1r, C1s and MASP2. It is the only plasma serine protease inhibitor (Serpin) capable of interacting with and inhibiting activated C1. C1-INH interacts with the catalytic sites of both C1r and C1s. The interaction with activated C1r and C1s is covalent resulting in complexes which are stable to SDS. C1s and C1r enzymes, however, are irreversibly inactivated by binding to C1-INH. C1s-C1INH (CompTech #C1040) is a very stable complex that remains intact even when subjected to freeze/thaw cycles with almost no loss of the complex form.

**Physical Characteristics & Structure**

The C1s enzyme-C1INH complex is composed of two disulfide linked chains from C1s enzyme (A chain 58,000 Da and B chain 28,000 Da) and one covalently linked chain from C1-INH (75,000 Da). SDS-PAGE analysis of the C1s-C1INH complex shows a single band of about 161,000 Da under non-reducing conditions. Under reducing conditions, the C1s-C1INH complex exhibits two bands: A 58,000 Da band corresponding to the A chain of C1s enzyme and a second 103,000 Da band resulting from C1INH (75,000 Da) covalently bound to the B chain (28,000 Da) of C1s enzyme.

**Regulation**

Activated C1s is controlled by C1-INH. C1s enzyme and C1-INH form a covalent complex that is resistant to separation on SDS gels. During complement activation C1 complex is rapidly activated by binding to immune complexes. The resulting activated C1s and C1r are rapidly inactivated by interaction with C1-INH (Ziccardi, R.J. (1982)). Binding to immune complexes is fast (10-20 sec) and activation of the bound C1 complex takes several minutes, but C1-INH has also been shown to be fast and no active C1r or C1s remain 4 min after addition of immune complexes to plasma (Ross, G.D. (1986); Ziccardi, R.J. (1981)).

The binding of C1-INH to activated C1 releases both C1r and C1s from the complex leaving C1q bound to the immune complex. The released complexes contain four molecules: C1-INH-C1r-C1s-C1-INH. The reaction of C1 esterase inhibitor with activated C1 is very fast with the estimated half-life of

C1r and C1s being approximately 15 seconds in serum. In fact, at serum concentrations of C1- INH little or no additional C4 or C2 activation occurs 3 min after immune complexes are added because all the C1r and C1s molecules have been inactivated and removed from the C1q which remains bound to the immune complex (Ross, G.D. (1986); Morley, B.J. and Walport, M.J. (2000); Rother, K., et al. (1998); Ziccardi, R.J. (1982a and 1982b); Morgan, B.P. (1990)). The interaction of purified C1s enzyme and C1-INH is slower.

**Function**

See General Description and Regulation above.

**Applications**

C1s-C1INH complex can be used in studies designed for developing and identifying inhibitors for C1s activation thus leading to the possible development of therapeutics for inhibiting complement activation via the classical pathway.

**Genetics**

The EMBL/Genbank cDNA accession number for C1s is J04080. The gene for C1s is located on chromosome 12p13. The EMBL/Genbank cDNA accession numbers for C1-INH are M13656 and X54486 (human) and Y10386 (mouse). The gene for C1-INH is located on chromosome 11p11.2-13.

**Deficiencies**

C1s deficient patients are prone to systemic lupus erythematosus (SLE) and recurrent pyogenic infections (Rother, K., et al. (1998)). They lack classical pathway function. The genetic disorder hereditary angioedema (HAE) is caused by a partial deficiency of C1-INH. Patients with HAE have low functional C1-INH levels in blood and have recurrent episodes of systemic or localized edema.

**Diseases**

See section titled Deficiencies above.

**Precautions/Toxicity/Hazards**

This protein is purified from human serum and therefore precautions appropriate for handling any blood-derived product must be used even though the source was shown by certified tests to be negative for HBsAg, HTLV-I/II, STS, and for antibodies to HCV, HIV-1 and HIV-II.

**References**

Ziccardi, RJ. (1982) A new role for C-1-inhibitor in homeostasis: control of activation of the first component of human complement. J. Immunol. 128:2505-2508.

Ross, G.D. (1986) Immunobiology of the Complement System. (ISBN 0-12-5976402) Academic Press, Orlando.

Ziccardi, R.J. (1981) Activation of the early components of the classical complement pathway under physiologic conditions. J. Immunol. 126:1769-1773.

Morley, B.J. and Walport, M.J. (2000) The Complement Facts Book. (ISBN 0127333606) Academic Press, London.

Rother, K., Till, G.O., and Hänsch, G.M. (1998) The Complement System. (ISBN 3-540- 61894-5) Springer-Verlag, Heidelberg.

Ziccardi, R.J. (1982a) Spontaneous activation of the first component of human complement (C1) by an intramolecular autocatalytic mechanism. J. Immunol. 128:2500- 2504.

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Morgan, B.P. (1990) Complement Clinical Aspects and Relevance to Disease. (ISBN 0- 12-506955-3) Academic Press, London.