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# Chondroitinase AC

Chondroitinase AC cleaves chondroitin sulfates A and C, chondroitin and hyaluronic acid.

## **Non-clinical applications:**

- Research reagent (glycobiology, preparation of oligosaccharide libraries from chondroitin sulfates).
- Degradation of hyaluronic acid.

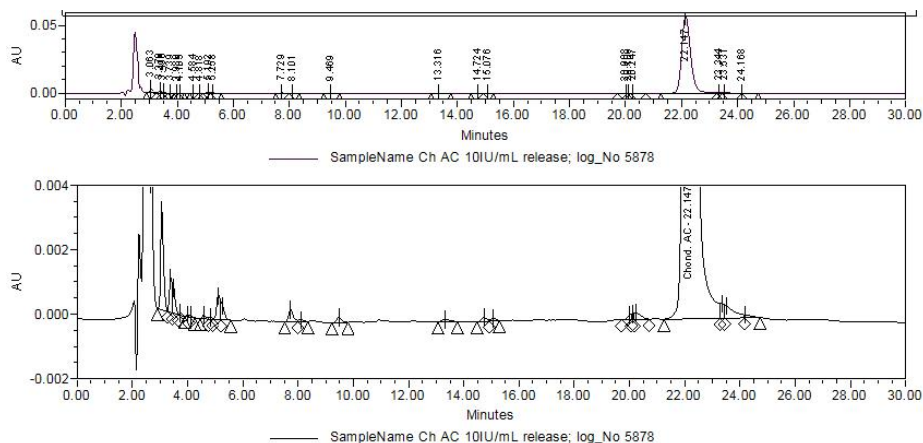
## **Potential clinical applications:**

- Anti cancer agent. The growth, development and spread of cancerous tumors is a multi-faceted process involving several mechanisms, including metastasis, tumor growth and angiogenesis. An anti-cancer agent that affects several of these processes should offer the potential for greater efficacy in treating this disease.

Chondroitin sulfates play a role in oncogenic growth factor (GF) mediated tumor cell proliferation, and formation of endothelial-cell related new blood vessels (angiogenesis) which provide for the expansion and growth of tumors. Chondroitin sulfates A and C are also a part of the CD44 complex on tumor cell membranes, which is a key component involved in tumor cell metastasis. Chondroitinase AC, and to a lesser extent, Chondroitinase B, can remove the chondroitin sulfates from tumor cells and may be able to decrease their ability to grow, form new blood vessels, and metastasize.

## Chondroitinase AC Data Sheet

<b>Synonyms</b>	Chondroitin sulfate lyase; chondroitin sulfate eliminase
<b>Source</b>	<i>Flavobacterium heparinum</i> (recombinant)
<b>EC Number</b>	4.2.2.5
<b>CAS Number</b>	9047-57-8
<b>Catalyzed Reaction</b>	The enzyme cleaves, via an elimination mechanism, sulfated and non-sulfated polysaccharide chains containing 1-4 linkages between hexosamines and glucuronic acid residues. The reaction yields oligosaccharide products (mainly disaccharides) containing unsaturated uronic acids which can be detected by UV spectroscopy at 232 nm. The enzyme is active on chondroitin sulfates A and C, chondroitin and hyaluronic acid, but is not active on dermatan sulfate (chondroitin sulfate B).
<b>Substrate Specificity</b>	Chondroitin sulfates A and C, chondroitin, hyaluronic acid. (The specific activity with chondroitin sulfate A is approx. 1.5 times higher than the specific activity with chondroitin sulfate C).
<b>Properties</b>	<ul style="list-style-type: none"> <li>• Molecular weight: 79,557 Da</li> <li>• Isoelectric point: 9.0 – 9.1</li> <li>• pH optimum for activity: 4.5 – 6 with chondroitin sulfate A 6 – 7 with chondroitin sulfate C</li> <li>• pH range for activity: 3.5 – 9 with chondroitin sulfate A 4.5 – 9 with chondroitin sulfate C</li> <li>• Optimal temperature range: 20 °C – 37 °C</li> <li>• Crystal structure has been determined and published (see references)</li> </ul>
<b>Purity</b>	≥90 % by reversed phase HPLC analysis.



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**Specific Activity**

≥200 IU/mg (substrate: chondroitin sulfate A)

One international unit (IU) is defined as the amount of enzyme that will liberate 1.0 μmole unsaturated oligosaccharides from chondroitin sulfates A and C and hyaluronic acid per minute at 30 °C and pH 8.0.

**Stability**

- PN 50-013 (0.5 IU/vial): Expiration is 18 months from date of manufacture at -70 °C in aqueous buffers containing Sodium Phosphate and Sucrose 5%.
- PN 50-017 (bulk): Expiration is 18 months from date of manufacture at -70 °C in aqueous buffers containing Sodium Phosphate and Sucrose 5%.

**Applications**

- As research reagent (glycosaminoglycan degradation).
- For the preparation of di- and oligo- saccharides of chondroitin sulfates and the preparation of oligosaccharide libraries.
- Degradation of hyaluronic acid.

**Availability**

A proprietary expression system for *F. heparinum* and the fermentation and isolation processes developed by IBEX Pharmaceuticals allow the production of large quantities of high purity product.

**References**

- Review: "Enzymatic Degradation of Glycosaminoglycans". S. Ernst et al. in *Critical Reviews in Biochemistry and Molecular Biology* (1995), 30(5): 387-444.
- "Isolation and Expression in *Escherichia coli* of *csIA* and *csIB*, Genes Coding for the Chondroitin Sulfate-Degrading Enzymes Chondroitinase AC and Chondroitinase B, Respectively, from *Flavobacterium heparinum*". A.L. Tkalec, D. Fink, F. Blain, G. Zhang-Sun, M. Laliberté, D.C. Bennett, K. Gu, J.J.F. Zimmermann and H. Su, in *Applied and Environmental Microbiology* (2000) 66(1): 29-35.
- "Purification, Characterization and Specificity of Chondroitin Lyases and Glycuronidase from *Flavobacterium heparinum*". K. Gu, R.J. Linhardt, M. Laliberté, K. Gu and J. Zimmermann, in *Biochem. J.* (1995) 312: 569-577.
- "A comparative Study Between a Chondroitinase B and a Chondroitinase AC from *Flavobacterium heparinum*". M.Y.M. Michelacci and D.C.P. Dietrich, in *Biochemical Journal* (1975) 151: 121-129.
- "Crystal Structure of Chondroitin AC Lyase, a Representative of a Family of Glycosaminoglycan Degrading Enzymes". J. Féthière, B. Eggimann and M. Cygler, in *J. Mol. Biol.* (1999) 288: 635-647.

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