NUI Galway
OÉ Gaillimh

Enzymatic degradation of Hyaluronic acid

Vinh Mai

School of Mathematics, Statistics and Applied Mathematics

20-01-2017

Outline

Outline

Outline

History

Karl Meyer (1899-1990). Photo courtesy of the National Library of Medicine.

History

Karl Meyer (1899-1990). Photo courtesy of the National Library of Medicine.

- 1934,

History

Karl Meyer (1899-1990). Photo courtesy of the National Library of Medicine.

- 1934,
- his assistant, John Palmer.

History

Karl Meyer (1899-1990). Photo courtesy of the National Library of Medicine.

- 1934,
- his assistant, John Palmer.
- high molecular weight polysaccharide.

History

Karl Meyer (1899-1990). Photo courtesy of the National Library of Medicine.

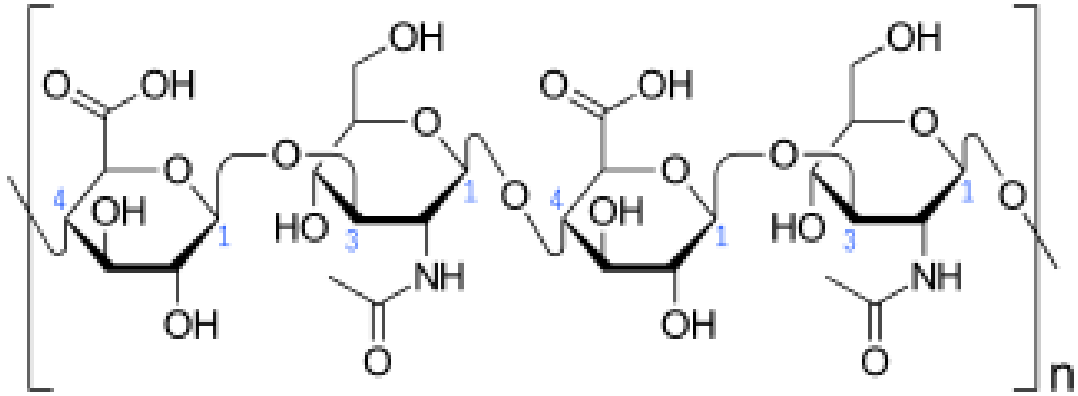
- 1934,
- his assistant, John Palmer.
- high molecular weight polysaccharide.
- the vitreous of bovine eyes.

History

Karl Meyer (1899-1990). Photo courtesy of the National Library of Medicine.

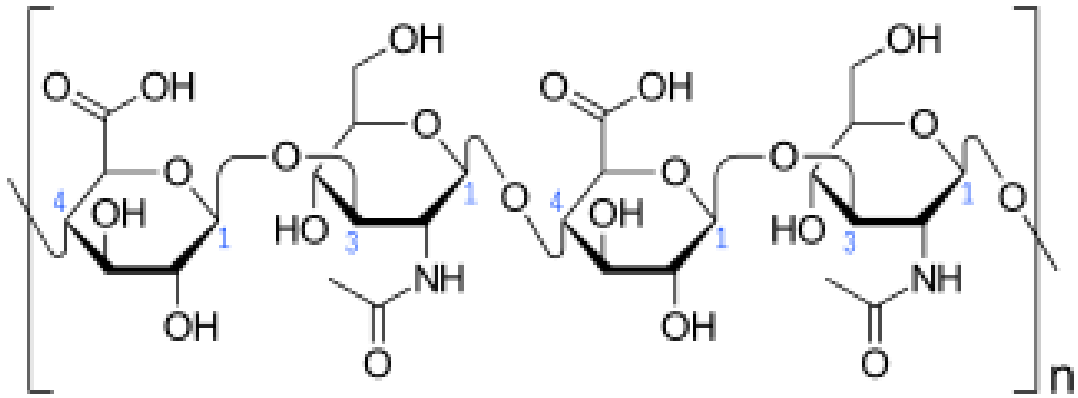
- 1934,
- his assistant, John Palmer.
- high molecular weight polysaccharide.
- the vitreous of bovine eyes.
- hyaluronic acid, also hyaluronan.

Chemical structure of Hyaluronic acid



Chemical structure of hyaluronan.

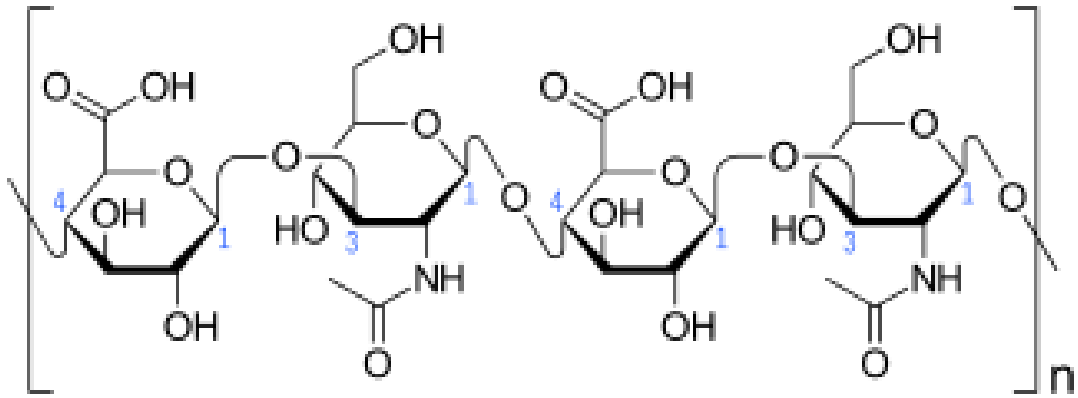
Chemical structure of Hyaluronic acid



Chemical structure of hyaluronan.

- disaccharide unit.

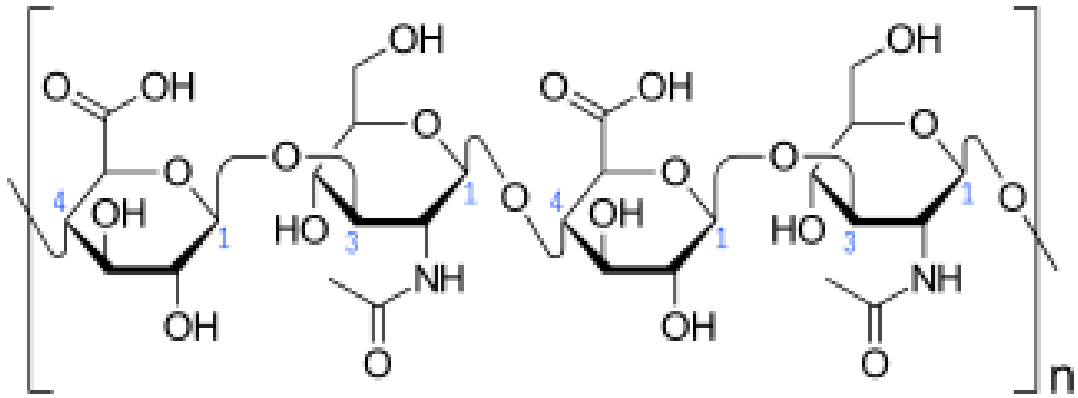
Chemical structure of Hyaluronic acid



Chemical structure of hyaluronan.

- disaccharide unit.
- β-1,4-glycosidic bond.

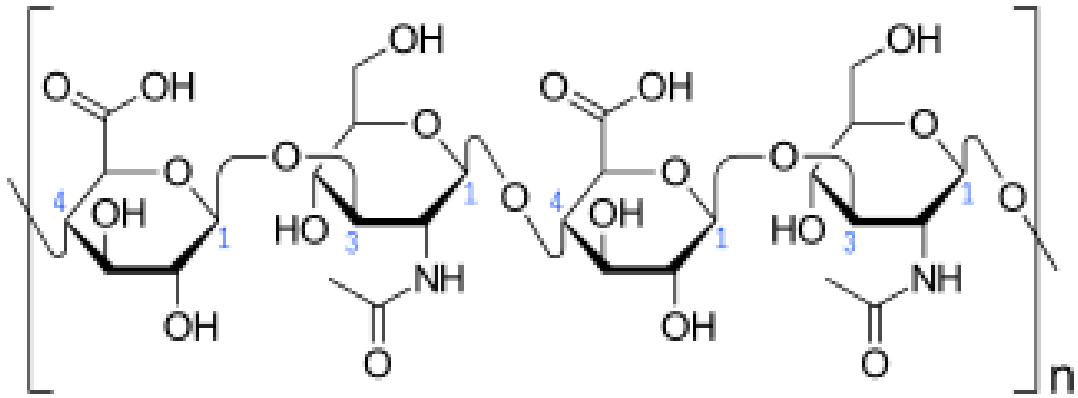
Chemical structure of Hyaluronic acid



Chemical structure of hyaluronan.

- disaccharide unit.
- β-1,4-glycosidic bond.
  - D-Glucuronic acid,

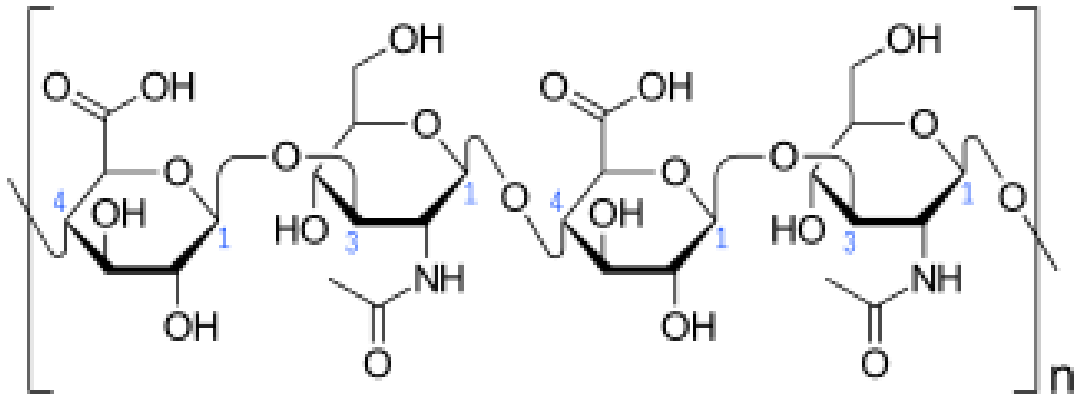
Chemical structure of Hyaluronic acid



Chemical structure of hyaluronan.

- disaccharide unit.
- β-1,4-glycosidic bond.
  - D-Glucuronic acid,
  - N-Acetylglucosamine

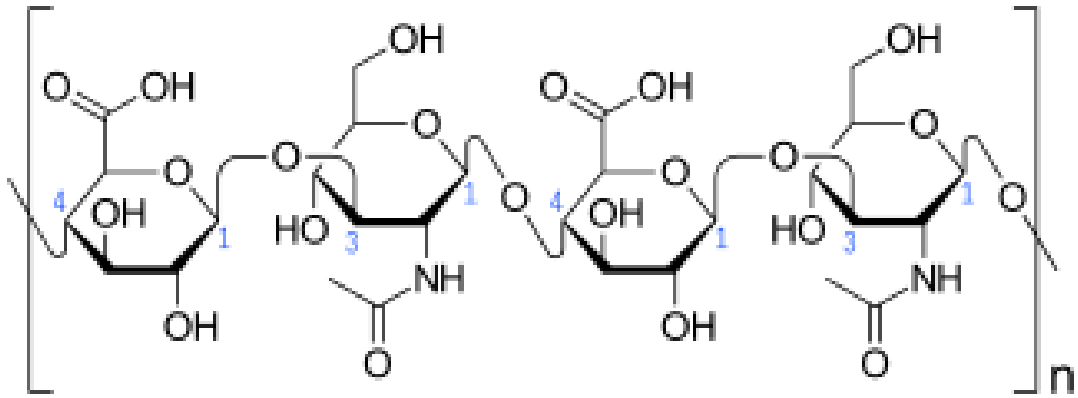
Chemical structure of Hyaluronic acid



Chemical structure of hyaluronan.

- disaccharide unit.
- β-1,4-glycosidic bond.
  - D-Glucuronic acid,
  - N-Acetylglucosamine
  - β-1,3-glycosidic bond.

Chemical structure of Hyaluronic acid



Chemical structure of hyaluronan.

- disaccharide unit.
- β-1,4-glycosidic bond.
  - D-Glucuronic acid,
  - N-Acetylglucosamine
  - β-1,3-glycosidic bond.
- the number of repeat disaccharide units in a complete hyaluronan chain: 10000 or more.

Picture from https://en.wikipedia.org

In human bodies

Picture from http://www.naturalhealingtools.com

Table 2. Sizes of HA with key functions (partial list)

Size (saccharides)	Function	References
High-molecular-mass HA > 1000–5000	Suppression of angiogenesis	Feinberg and Beebe (1983)
	Immune suppression	McBride and Bard (1979), Delmage et al. (1986)
	Inhibition of phagocytosis	Forrester and Balazs (1980)
	Suppression of HA synthesis	Lueke and Prehm (1999)
HA fragments		
~1000	Induction of inflammatory chemokines	Noble et al. (1993)
	Stimulation of PAI-1	Horton et al. (2000)
	Stimulation of urokinase	Horton et al. (2000)
10–40	Induction of CD44 cleavage	Sugahara et al. (2003)
	Promotion of tumor cell migration	Sugahara et al. (2003)
8–32	Stimulation of angiogenesis	West et al. (1985), Sattar et al. (1994), Slevin et al. (1998, 2002)
	Stimulation of tumor neovascularization	Rooney et al. (1995)
~15	Suppression of smooth muscle cell proliferation	Evanko et al. (1999)
12	Endothelial cell differentiation	Takahashi et al. (2005)
	Up-regulation of PTEN in tumor cells	Ghatak et al. (2002)
10	Displacement of matrix HA on oocyte surface	Camaioni et al. (1993)
	Displacement of proteoglycans from cell surface	Solursh et al. (1980)
6	Suppression of HA cable formation	de la Motte et al. (2003)
	Induction of NO and MMPs in chondrocytes	Knudson and Knudson (2004a, b)
	Induction of HAS2 in chondrocytes	Knudson and Knudson (2004a, b)
4–6	Induction of cytokine synthesis in dendritic cells	Termeer et al. (2000, 2002), Taylor et al. (2004)
	Transcription of MMPs	Fieber et al. (2004)
4	Up-regulation of Hsp 72 expression	Xu et al. (2002)
	Suppression of apoptosis	Xu et al. (2002)
	Induction of chemotaxis	R. Savani, personal communication
	Up-regulation of heat shock factor-1	Xu et al. (2002)
	Up-regulation of Fas expression	Fujii et al. (2001)
	Suppression of proteoglycan sulfation	Solursh et al. (1980)

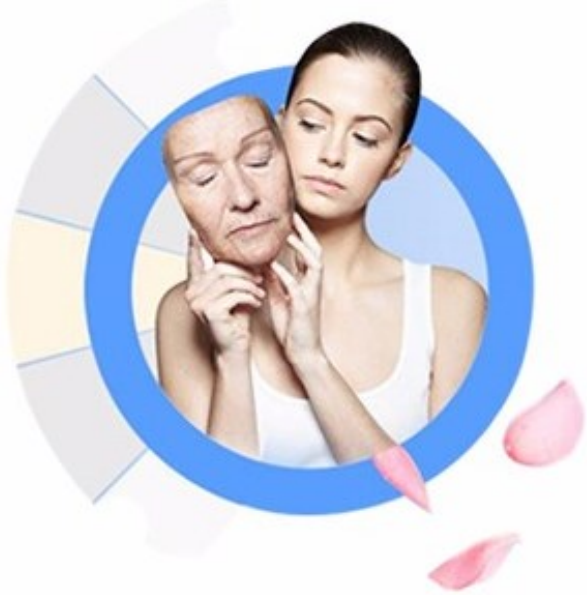
A commercial product of HA

Hyaluronic acid powder for the manufacture of eye drops

Some functions of different molecular weight HA.

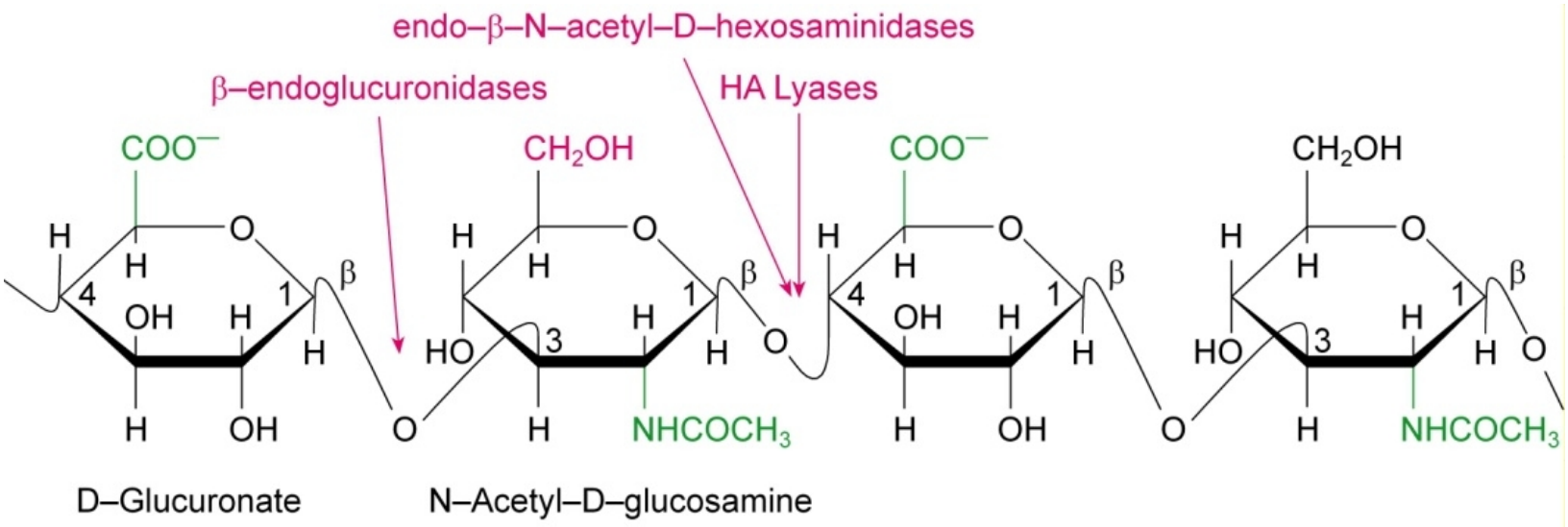
THE FUNCTION OF HA IN COSMETICS

- Protect skin and keep water in the skin
- Prepair and prevent against the injured skin
- Nourishing the skin anti-ageing
- Maintain skin good moisture and lubrication
- Thicken emulsion and stabilize emulsification

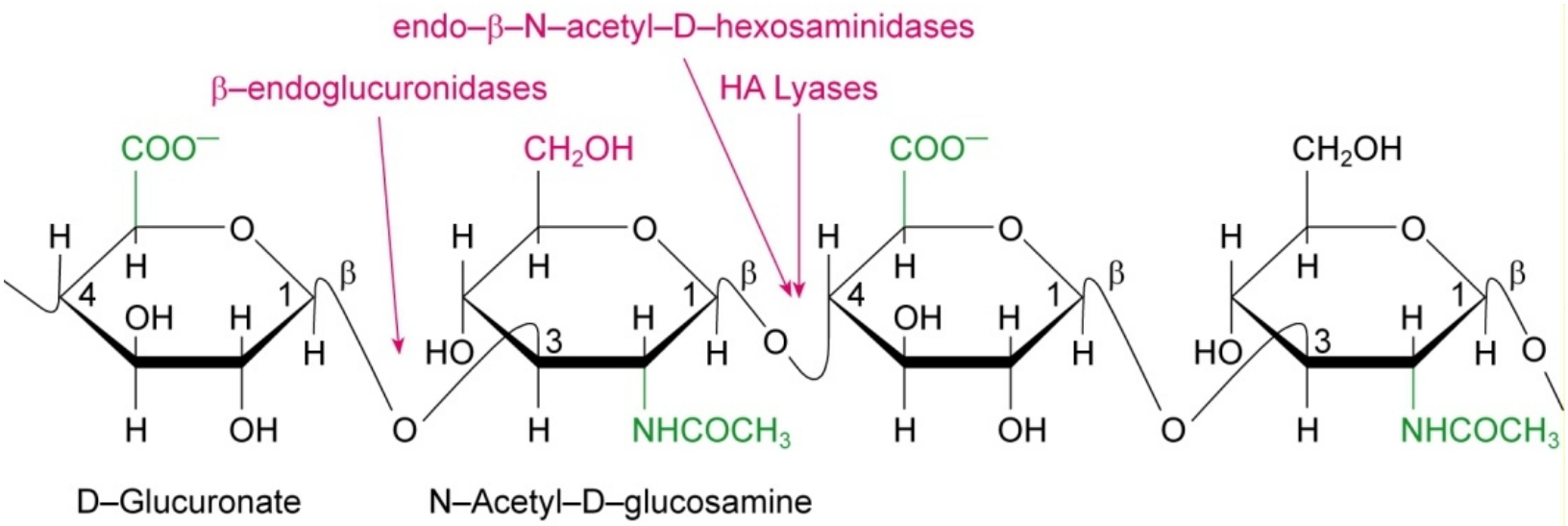


HA with different M.W	Application
0.8 million daltons	For facial cleanser and liquid agent
1~1.3 million daltons	Cream, gel, skin emulsion and skin milk
1.3~1.5 million daltons	Eye care products like eye cream

Hyaluronidases

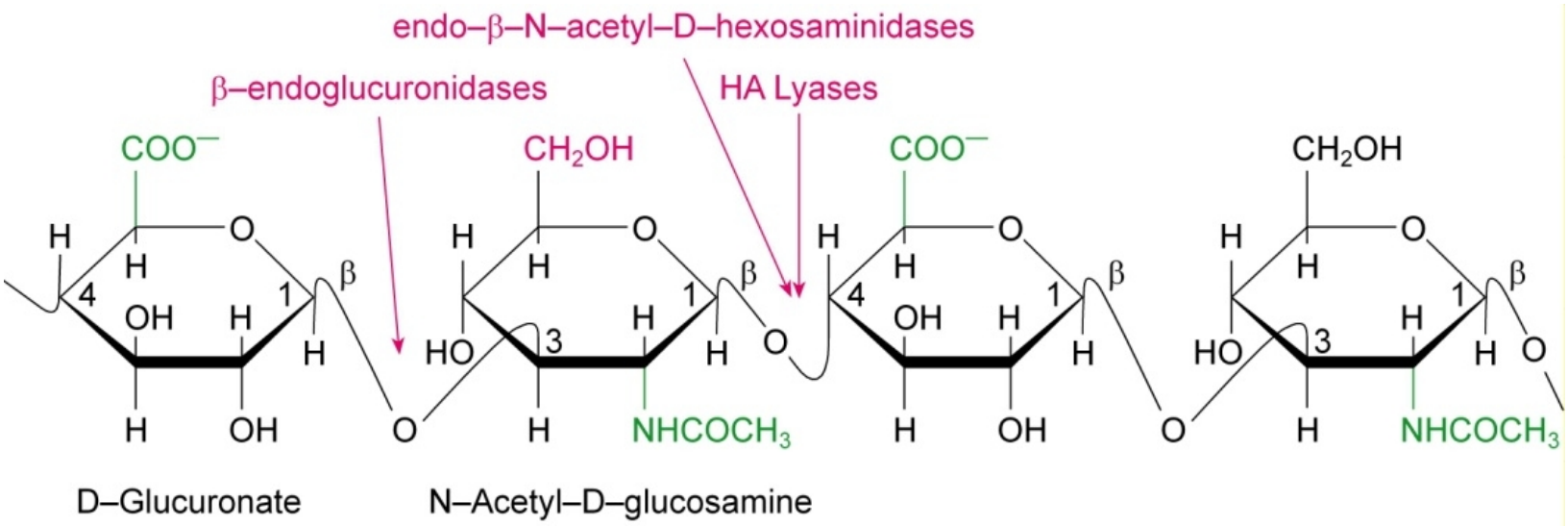


Hyaluronidases



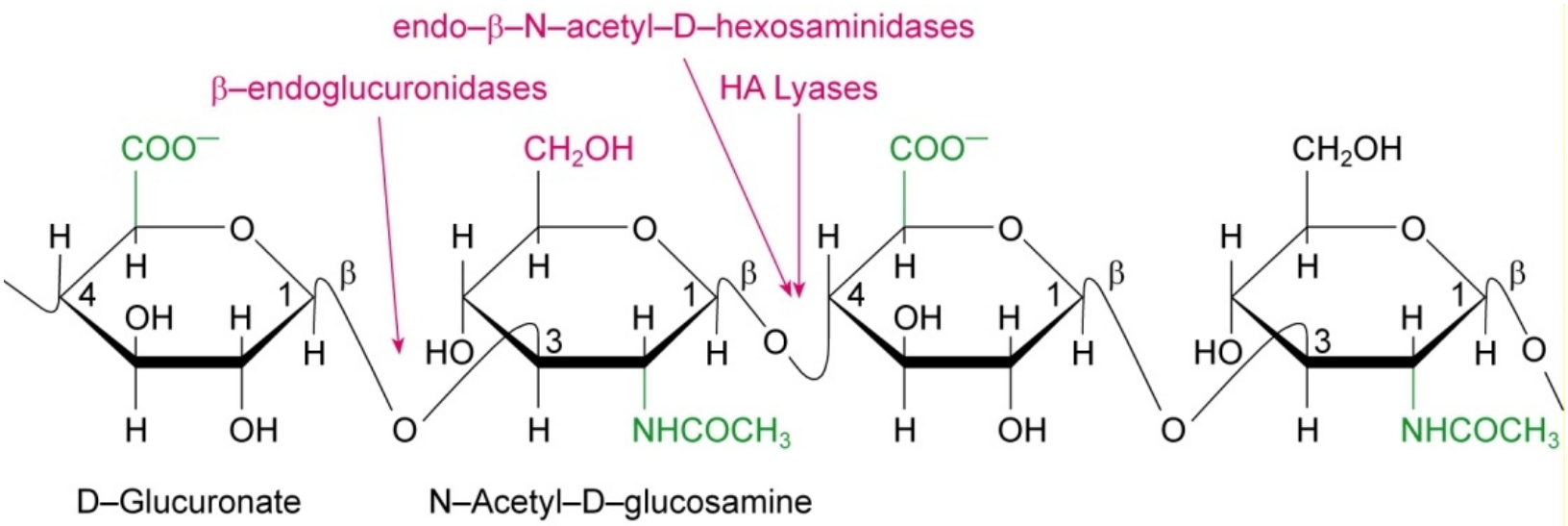
- Eukaryotic hyaluronidases

Hyaluronidases



- Eukaryotic hyaluronidases
- Invertebrate (leech) hyaluronidases

Hyaluronidases



- Eukaryotic hyaluronidases
- Invertebrate (leech) hyaluronidases
- Bacterial hyaluronidases

Picture from DOI: 10.5772/57227

Streptococcus pneumoniae Hyaluronate lyase

Streptococcus pneumoniae:

Streptococcus pneumoniae Hyaluronate lyase

Streptococcus pneumoniae:

- a major human pathogenic bacterium.

Streptococcus pneumoniae Hyaluronate lyase

Streptococcus pneumoniae:

- a major human pathogenic bacterium.
- usually in the upper respiratory tract of humans.

Streptococcus pneumoniae Hyaluronate lyase

Streptococcus pneumoniae:

- a major human pathogenic bacterium.
- usually in the upper respiratory tract of humans.

Five step process:

Streptococcus pneumoniae Hyaluronate lyase

Streptococcus pneumoniae:

- a major human pathogenic bacterium.
- usually in the upper respiratory tract of humans.

Five step process:

1. a randomly substrate binding step,

Streptococcus pneumoniae Hyaluronate lyase

Streptococcus pneumoniae:

- a major human pathogenic bacterium.
- usually in the upper respiratory tract of humans.

Five step process:

1. a randomly substrate binding step,
2. a catalytic step,

Streptococcus pneumoniae Hyaluronate lyase

Streptococcus pneumoniae:

- a major human pathogenic bacterium.
- usually in the upper respiratory tract of humans.

Five step process:

1. a randomly substrate binding step,
2. a catalytic step,
3. a hydrogen exchange with the water microenvironment step,

Streptococcus pneumoniae Hyaluronate lyase

Streptococcus pneumoniae:

- a major human pathogenic bacterium.
- usually in the upper respiratory tract of humans.

Five step process:

1. a randomly substrate binding step,
2. a catalytic step,
3. a hydrogen exchange with the water microenvironment step,
4. an irreversible product release step,

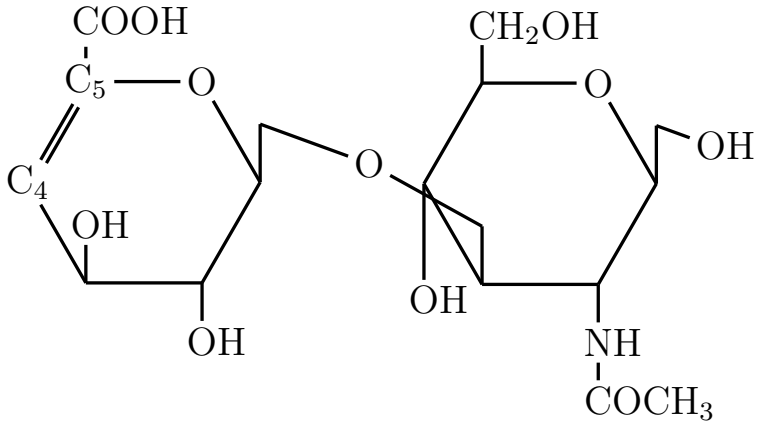
Streptococcus pneumoniae Hyaluronate lyase

Streptococcus pneumoniae:

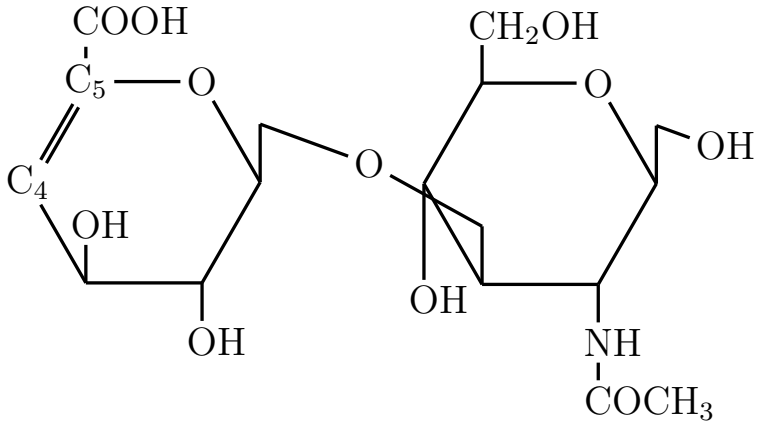
- a major human pathogenic bacterium.
- usually in the upper respiratory tract of humans.

Five step process:

1. a randomly substrate binding step,
2. a catalytic step,
3. a hydrogen exchange with the water microenvironment step,
4. an irreversible product release step,
5. a translocation of the remaining substrate step.

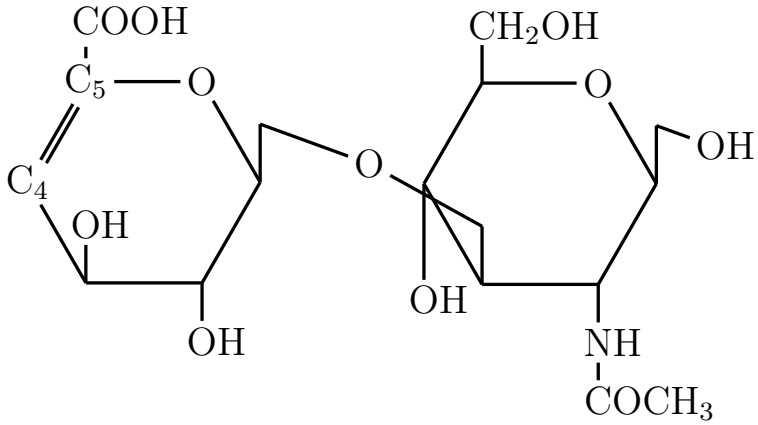


Chemical structure of an unsaturated disaccharide unit.



Chemical structure of an unsaturated disaccharide unit.

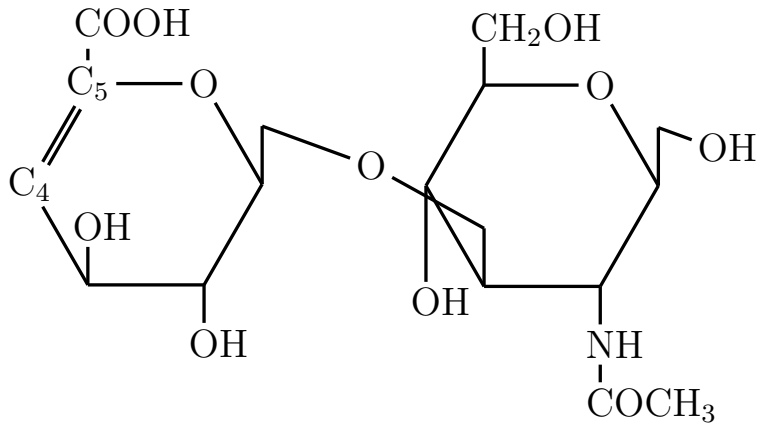
A modified three step process:



Chemical structure of an unsaturated disaccharide unit.

A modified three step process:

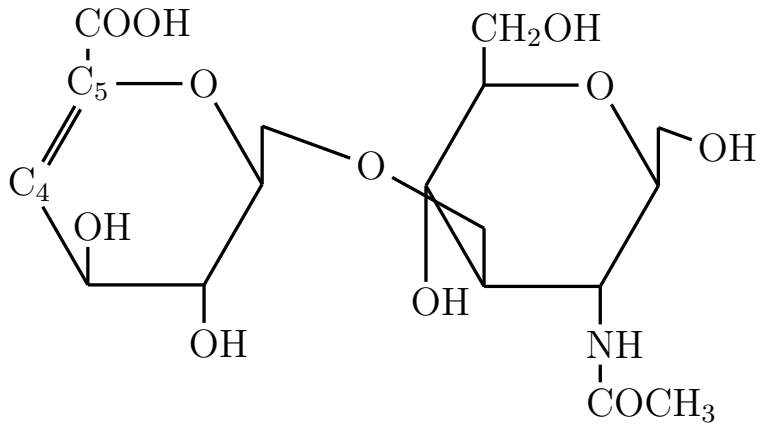
1. a randomly substrate binding step,



Chemical structure of an unsaturated disaccharide unit.

A modified three step process:

1. a randomly substrate binding step,
2. an irreversible catalytic, restoring original form and product release step,



Chemical structure of an unsaturated disaccharide unit.

A modified three step process:

1. a randomly substrate binding step,
2. an irreversible catalytic, restoring original form and product release step,
3. a translocation of the remaining substrate step.

[1] J. Necas, L. Bartosikova, P. Brauner, J. Kolar: *Hyaluronic acid (Hyaluronan): a review*. Veterinarni Medicina, 53, 2008 (8):397-411.
[2] Robert Stern, Akira A. Asari, Kazuki N. Sugahara: *Hyaluronan fragments: An information-rich system*. European Journal of Cell Biology 85 (2006) 699-715.
[3] Nermeen S. El-Safory, Ahmed E. Fazary, Chang-Kang Lee: *Hyaluronidase, a group of glycosidases: Current and foture perspectives*. Carbohydrate Polymers 81 (2010) 165-181.
[4] Mark J. Jedrzejas, Luciane V. Mello, Bert L. de Groot, Songlin Li: *Mechanism of hyaluronan degradation by Streptococcus pneumoniae hyaluronate lyase*. The Journal of Biological Chemistry, Vol 277, No. 31, Issue of August 2, pp. 28287-28297, 2002.