



**Top Quality Hyalouronic Filler**

**Age is just a number**

ZARTAUX  
**dermaFILL<sup>+</sup>**

M a d e i n S w i t z e r l a n d

## Hyaluronic acid

Hyaluronic acid (HA; also called hyaluronan and hyaluronate) is an anionic, nonsulfated glycosaminoglycan distributed widely throughout connective, epithelial, and neural tissues. It is unique among glycosaminoglycans in that it is nonsulfated, forms in the plasma membrane instead of the Golgi, and can be very large, with its molecular weight often reaching the millions.

One of the chief components of the extracellular matrix, hyaluronan contributes significantly to cell proliferation and migration, and may also be involved in the progression of some malignant tumors.

The average 70 kg (154 lb) person has roughly 15 grams of hyaluronan in the body, one-third of which is turned over (degraded and synthesized) every day. Hyaluronic acid is also a component of the group A streptococcal extracellular capsule, and is believed to play a role in virulence.



### + QualityTip:

DERMAFILL by ZARTALUX is developed by using innovative Growth Factors.

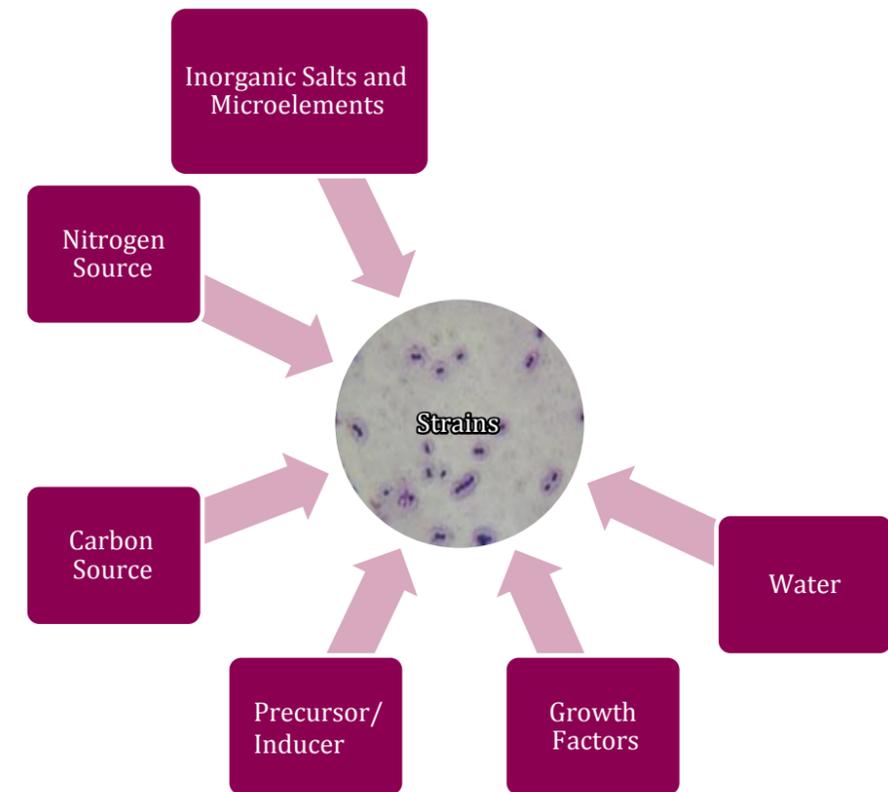
## Research

Due to its high biocompatibility and its common presence in the extracellular matrix of tissues, hyaluronan is gaining popularity as a biomaterial scaffold in tissue engineering research.

In particular, a number of research groups have found hyaluronan's properties for tissue engineering and regenerative medicine are significantly improved with crosslinking, producing a hydrogel.

This added feature allows a researcher to form a desired shape, as well as to deliver therapeutic molecules, into a host. Due to its ability to regulate angiogenesis by stimulating endothelial cells to proliferate, hyaluronan can be used to create hydrogels to study vascular morphogenesis. These hydrogels have properties similar to human soft tissue, but are also easily controlled and modified, making HA very suitable for tissue engineering studies.

For example, HA hydrogels are appealing for engineering vasculature from endothelial progenitor cells by using appropriate growth factors such as VEGF and Ang-1 to promote proliferation and vascular network formation. Vacuole and lumen formation have been observed in these gels, followed by branching and sprouting through degradation of the hydrogel and finally complex network formation. The ability to generate vascular networks using HA hydrogels leads to opportunities for in vivo and clinical applications. One in vivo study, where HA hydrogels with endothelial colony forming cells were implanted into mice three days after hydrogel formation, saw evidence that the host and engineered vessels joined within 2 weeks of implantation, indicating viability and functionality of the engineered vasculature.



## Production of Hyaluronan

Industrial manufacturing of hyaluronan is based on two main processes, while both technologies produce polydisperse high molecular weight hyaluronan (Da, polydispersity ranging from 1.2 to 2.3) for biomedical and cosmetic applications.

### 1. Extraction from animal tissues.

The first process, to be applied at industrial scale, was the extraction of hyaluronan from animal waste which is still an important technology for commercial products, but is hampered by several technical limitations. One drawback in the extraction process is the inevitable degradation of hyaluronan, caused by:

(a) The endogenous hyaluronidase activity in animal tissues, breaking down the polymer chain through enzymatic hydrolysis, and

(b) The harsh conditions of extraction. Extraction protocols have been improved over the years, but still suffer from low yields, due to the intrinsic low concentration of hyaluronan in the tissue, and from high polydispersity of polymer products due to both the natural polydispersity of hyaluronan and to the uncontrolled degradation during extraction. As in any process for the production of therapeutic compounds from animal sources, there is a potential risk of contamination with proteins and viruses, but this can be minimized by using tissues from healthy animals and extensive purification. Nevertheless, concerns on viral (particularly avian) and protein (particularly bovine) contamination increased the interest in the biotechnological production of hyaluronan.

### 2. Microbial fermentation using bacterial strains.

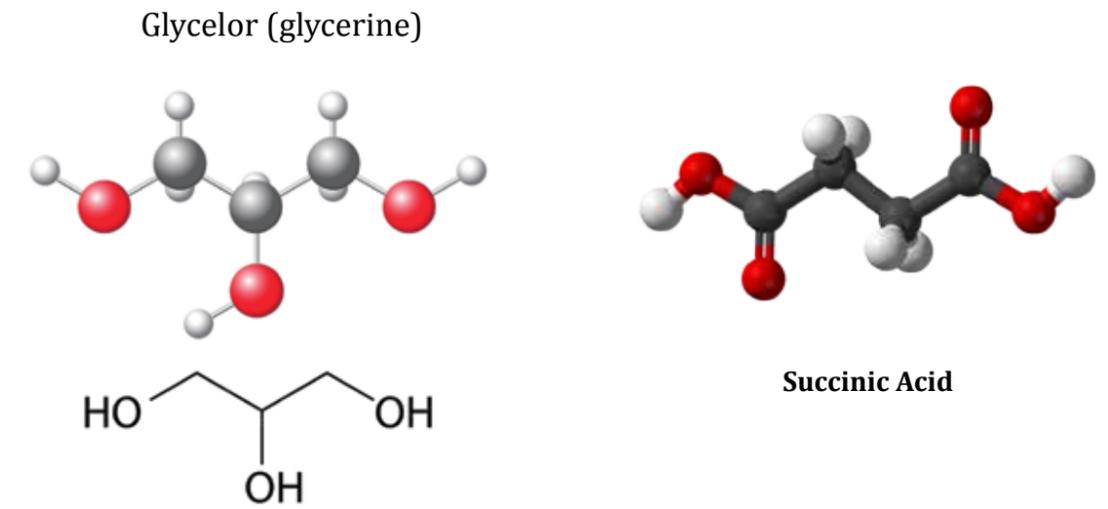
Production of hyaluronan by bacterial fermentation evolved to a mature technology in the last two decades of the 20th century. In the early developmental stages of bacterial fermentation using group A and C streptococci, optimization of culture media and cultivation conditions along with strain improvement were used to increase hyaluronan yield and quality. Hyaluronan yields reached 6-7 g L<sup>-1</sup>, which is the upper technical limit of the process caused by mass transfer limitation due to the high viscosity of the fermentation broth. Bacterial fermentation produces hyaluronan with high molecular weight and purity. The identification of the genes involved in the biosynthesis of hyaluronan and of the sugar nucleotide precursors in the 90s opened the way towards hyaluronan production using safe, nonpathogenic recombinant strains.

## Animal Extraction Method VS Bio-Fermentation

	Extraction Method	Bio-Fermentation Method
<b>State of existence</b>	Form complex with protein and other mucopolysaccharide, with complicated separation and purification	Exist freely in Fermentation liquid, prone to separation and purification
<b>Molecular weight</b>	Subject to animal tissue materials and is beyond control basically and normally $(0.1-2.5)*10^6$	It can be controlled through parameter conditions of fermentation culture and is normally $(1.0-4.0)*10^6$
<b>Quality and output</b>	Depend on the quality and quantity of animal tissues	Quality controllable, no output limit, easy for creation of large-scale industrial production
<b>Risk</b>	With risks of residual animal-derived protein, easily lead to allergy  With risks of animal-derived pathogenic virus contamination	Free of protein;  No risk of animal-derived pathogenic virus infection

## DERMAFILL By Zartaux Cross linker

When DERMAFILL by ZARTAUX degrades, it breaks down into harmless byproducts or into byproducts that are identical to substances already found in the skin.



### DERMAFILL by Zartaux PRODUCTS



**+ QualityTip:**

DERMAFILL by ZARTAUX is developed by using Bio-Fermentation of the bacteria.



**+ Ultra 1:** 22 mg/ml  
Fine Lines/Lips/Tears/  
Naso labial



**+ Ultra 2:** 24 mg/ml  
Medium Lines/Lips/  
Naso labial



**+ Ultra 3:** 26 mg/ml  
Deep Lines/ Naso  
labial



**+ Voluma:** 28 mg/ml  
Cheeks/ Body  
Volumizer

# DERMAFILL By Zartaux

HA concentration = 28mg/ml  
 pH= 6.0 – 7.5  
 Estrusion force with 27G (TSK) = 1.5 kg ca.  
 Endotoxin <0.25 EU/ml  
 BDDE residual = < 2 ppm

DermaFill by Zartaux is developed and commercialized, as Top Quality Crosslinked Hyaluronic Acid Gel, to be used in therapeutic topical skin care and in medical applications including soft tissue augmentation.

In the skincare field, Zartaux Company has already patented Dermaceutical Skin Care products.

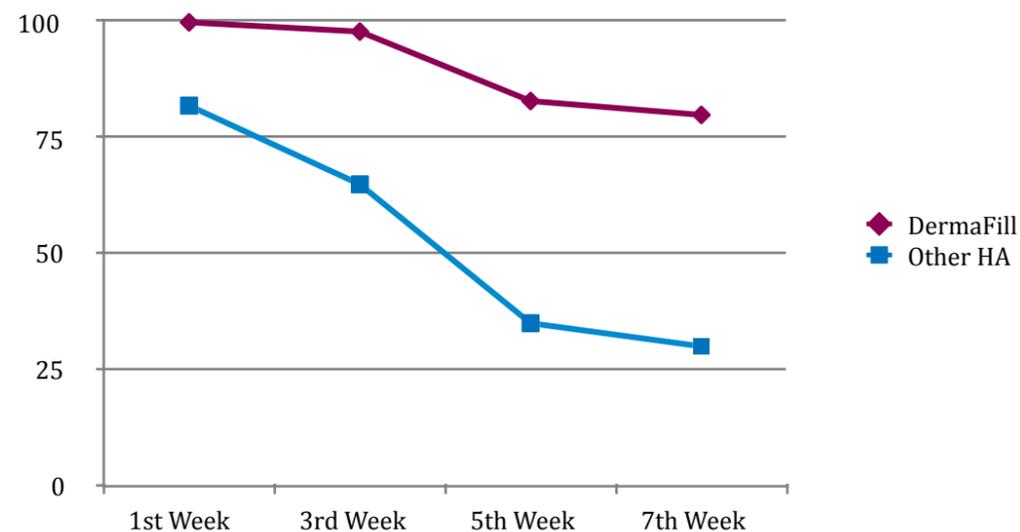
The safety and efficacy of Zartaux Dermaceutical Skin Care, makes them value-added for use in high performance demands, developed to manage dermal disorders (including dry, inflamed, burned, bruised or injured skin), improve the health and appearance of skin, protect the skin from further injury or damage from environmental stressors and address the damaging effect of ultraviolet radiation on the skin.

In the medical field, the company's novel, patented Crosslinked HA technology is designed to provide improved stability and efficacy of soft tissue implants and to provide safe, biocompatible, long-lasting depot delivery of actives.



## + QualityTip:

**DERMAFILL by ZARTAUX is resistant to enzyme degradation (hyaluronidase) as compared to regular crosslinked HA gels, measured by loss in viscosity:**



## Injection Techniques



Each technique has advantages for certain situations, and the ultimate determining factor is often surgeon preference. The angle of injection is determined by the depth of the defect. In general, more obtuse angles of insertion are used for deeper defects. Fine to moderate rhytides and other superficial defects require injection into the mid dermis with an angle of approach of 30-45 degrees. Deeper rhytides may require an entry angle of greater than 45 degrees. Fillers can be injected by one of the following 5 techniques: Serial puncture, threading, fanning, and crosshatching.

1. Serial puncture - to avoid irregularity - involves injecting a series of small boluses of the filler along the length of the defect.
2. Threading - for fine or superficial wrinkles - involves tunneling the needle beneath the defect at the appropriate depth and injecting the product as the needle is withdrawn (linear threading).
3. Serial Threading - for lip and nasolabial fold augmentation - when combined with serial puncture, the technique is called serial threading.
4. Fanning - to enhance tissue volume in areas such as the naso-labial triangle - is similar to threading, but multiple threads are injected radially by changing direction without withdrawing the needle.
5. Crosshatching - for facial contours and enhancing tissue volume - involves injection of a series of threads perpendicular to one another in a grid. Both fanning and crosshatching techniques are used to fill larger defects and for facial shaping.

The choice of needle is determined by the viscosity of the filler.



## Before & After

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# ZARTAUx dermaFILL<sup>+</sup>

M a d e i n S w i t z e r l a n d

### Bibliographical References

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Hyaluronate Sodium in the ChemIDplus database, consulté le 12 février 2009-Fraser JR, Laurent TC, Laurent UB (1997). "Hyaluronan: its nature, distribution, functions and turnover" (PDF). *J. Intern. Med.* 242 (1): 27-33. doi:10.1046/j.1365-2796.1997.00170.x. PMID 9260563.Stern, edited by Robert (2009). Stern R (2004). "Hyaluronan catabolism: a new metabolic pathway". *Eur. J. Cell Biol.* 83(7): 317-25. doi:10.1078/0171-9335-00392. PMID 15503855.Sugahara K, Schwartz NB, Dorfman A (1979). "Biosynthesis of hyaluronic acid by Streptococcus" (PDF). *J. Biol. Chem.* 254 (14): 6252-6261. PMID 376529.Wessels MR, Moses AE, Goldberg JB, DiCesare TJ (1991). "Hyaluronic acid capsule is a virulence factor for mucoid group A streptococci" (PDF). *Proc. Natl. Acad. Sci. U.S.A.* 88 (19): 8317-8321. doi:10.1073/pnas.88.19.8317. PMC 52499. PMID 1656437.Schrager HM, Rheinwald JG, Wessels MR (1996). "Hyaluronic acid capsule and the role of streptococcal entry into keratinocytes in invasive skin infection". *J. Clin. Invest.* 98(9): 1954-958. doi:10.1172/JCI118998. PMC 507637. PMID 8903312.Meyer K, Hobby GL, Chaffee E, Dawson MH (1940). "THE HYDROLYSIS OF HYALURONIC ACID BY BACTERIAL ENZYMES". *J. Exp. Med.* 71 (2): 137-46.doi:10.1084/jem.71.2.137. PMC 2135078. PMID 19870951. Coleman WP: Soft tissue augmentation. In: Ratz JL, ed. *Textbook of Dermatologic Surgery*. Philadelphia: Lippincott - Raven; 1998:565-577.Klein AW, Monheit GD, Duffy DM: Soft - tissue augmentation in the practice of dermatology. In: Lask G, Mory R, eds. *Principles and Techniques of Cutaneous Surgery*. New York: McGraw-Hill; 1996:419-436.Krauss M, Klein AW: Soft tissue augmentation. In: Kaminer MS, et al, eds. *Atlas of Cosmetic Surgery*. Philadelphia: WB Saunders; 2002:264-290.Millikan LE: The evolution of derma implants. *Cosmetic Dermatology* 2001 Dec; 14(12): 27-30.Narins RS: *Cosmetic Surgery*. New York: Marcel Dekker; 193-331.



Manufactured in Switzerland

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