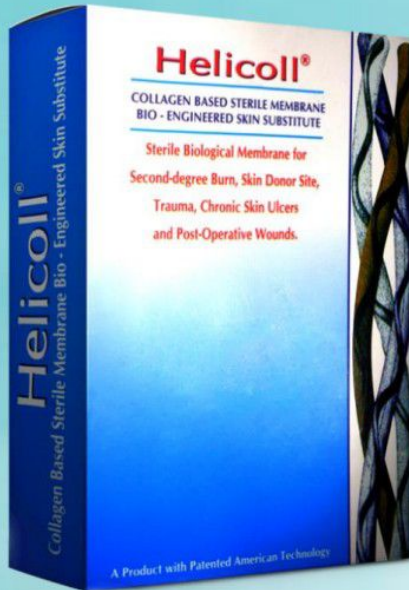


Helicoll®

Patented High Purity Type-1 Collagen Skin Substitute



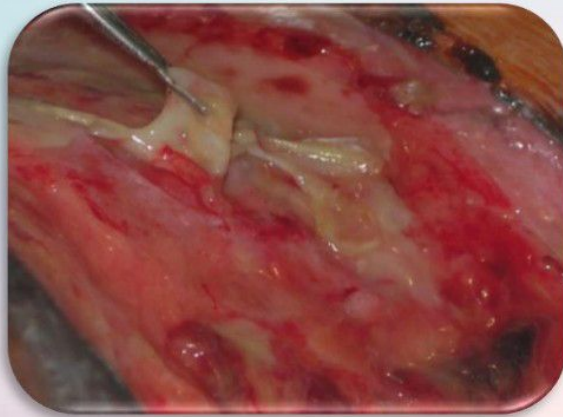
PHYSICIAN'S
1ST CHOICE



Helicoll is Indicated for:

- Venous ulcers
- Diabetic ulcers
- Pressure ulcers
- Chronic vascular ulcers
- Skin Donor Sites for Grafts
- 2nd Degree Burns
- Trauma & Surgical wounds

Adaptable solution. Remarkable results.



"Blood capillaries and granulation tissue formation are visible
at a macroscopic level within 4 to 5 days"

 **ENCOLL**
Enhancing life through collagen

4576 Enterprise Street, Fremont, CA. 94538 USA

Helicoll®

COLLAGEN BASED STERILE BIO-ENGINEERED SKIN SUBSTITUTE

Description and availability of Helicoll:

Helicoll is an approved FDA product and has been recognized and reimbursed as a high-cost skin substitute by Medicare continuously since 2017.

Helicoll is the **ONLY PRODUCT** that is patented for its specialized relatively high bio-compatibility and bio-activity. It is made up of highly purified, non-crosslinked Type-I Collagen (U.S. Patented). Additionally, it is highly bio-active due to its controlled phosphorylation for maximum wound healing benefits.

Helicoll is available in different sizes to accommodate multiple types of wounds. It has the capacity to remain clinically usable for 3 years when stored in room temperature conditions.

Indications of Helicoll:

1. Diabetic ulcers
2. Pressure ulcers
3. Venous ulcers
4. Draining wounds
5. Partial or full thickness wounds
6. Tunneled, undermined wounds
7. Surgical wounds (i.e., donor sites/grafts, post-Mohs' surgery, post-laser surgery, podiatric, wound dehiscence)
8. Trauma wounds (i.e., abrasions, lacerations, second-degree burns, skin tears)

Advantage of using Helicoll:

- ✓ **High purity Type-I Collagen:** Helicoll is a patented reconstituted bioactive collagen sheet, free of immunogenic proteins, lipids, and elastin.
- ✓ **Faster Healing:** Collagen phosphorylation attracts cells, regenerates tissue, and stimulates blood capillaries/granulation within 4 to 5 days.
- ✓ **Innovative Technology:** Better than intact tissue-based membranes like amnion, intestinal wall, urinary bladder etc. which contain > 15% elastin.
- ✓ **Easy Application:** No washing needed prior to use.
- ✓ **Pain Control:** Effectively reduces pain.
- ✓ **Various Sizes:** Choose from standard or customized dimensions.
- ✓ **Cost-Effective:** Accelerated wound healing and tissue remodeling with minimal applications.
- ✓ **Long Shelf Life:** Remains clinically usable for 3 years when stored in room temperature conditions.



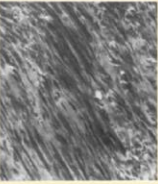
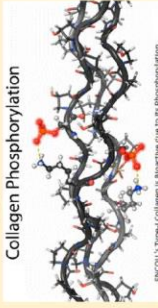
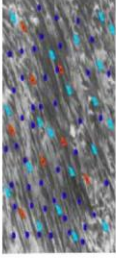
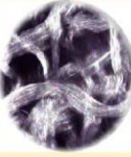
4576 Enterprise St, Fremont, CA 94538, USA || www.helicoll.com

HELICOLL® COMPARISON WITH OTHER FDA APPROVED PRIME PRODUCTS									
PRODUCT	HELICOLL®	APLIGRAF® /DERMAGRAFT®	PURAPLY® /PURAPLY® AM	XWRAP®	OASIS™/GRAFIX	INTEGRA™ /PRIMATRIX	EPIFIX™ /AMNIOFIX™	CYTAL™	
Manufacturer	ENCOLL Corp.	Organogenesis Inc.	Organogenesis Inc.	Applied Biologics	Smith & Nephew	Integra LifeSciences	MiMedX	Acell	
Matrix	Patented high purity bovine Type-I collagen	Human fibroblast - on bovine Type I collagen/polyglactin mesh	Porcine intestinal cross- linked type-III collagen	Amniotic Membrane Derived Allograft with Carcinogenic Elastin ¹	Porcine small intestinal submucosa (SIS) with 10% Carcinogenic Elastin ² / Placental membrane with 49% Carcinogenic Elastin ⁴	Collagen with or without glycosaminoglycan and a silicone layer	Dehydrated Human Amnion/Chorion Allograft with 42% Carcinogenic Elastin ¹	Porcine urinary Bladder Xenograft with 9% Carcinogenic Elastin ³	
Size/shape	5x5 cm to 60x80 cm & Custom sizes	Circular, 8 cm dia, disc / 5 cm x 7.5 cm	1.6 cm disc to 8x16 cm sizes	2x2 cm to 4x8 cm sizes	3x3.5 cm to 7x20 cm in sizes	2x2 cm to 20x25 cm in sizes	2x2 cm to 4x8 cm in sizes	3x3.5 cm to 10x15 cm in sizes	
Sterilization	Terminal sterilization	Aseptically processed	Terminal sterilization using gamma that might denature/cross-link collagen	Terminal Sterilization	Terminal sterilization	Aseptically processed	Terminal sterilization	Terminal sterilization	
Shelf life	3 years at room temperature	5 days at room temperature	Greater than 2 years	2 years & Requires Refrigeration	2 years at room temperature	1 year at room temp.	5 years at room temperature	2 years at room temperature	
Handling	Rehydrates in saline in 5 min.; easily handled, sutured & stapled	Shipped on a nutrient medium/frozen; difficult to handle, fragile	Rehydrates in saline	Rehydrates in saline	Rehydrates in saline; easily sutured & stapled	Can be sutured & stapled; easily handled	Can be sutured & stapled; easily handled	Can be sutured & stapled; easily handled	
Large presence of immunogenic Elastin/ adverse biomolecules	No	No	Yes (significant amt of Type-III Collagen)	Yes (>15% elastin presence)	Yes (>15% elastin presence)	Yes (significant amt of GAGs)	Yes (>15% elastin presence)	Yes (>15% elastin presence)	
Bioactivity expressed via neo-vascularization & granulation	Within 4 to 5 days after application (Clinically proven)	No report indicates lesser than 9 days	No such fast infiltration of blood vessels is reported	No report indicates lesser than 9 days	No report indicates lesser than 9 days	No report indicates lesser than 9 days	No report indicates lesser than 9 days	No report indicates lesser than 9 days	
Applications to Heal	1-4 applications	Up to 5 applications	variable	variable	variable	variable	variable	variable	
Control of hyper glycosylation of Diabetic Foot Ulcer Wounds to heal fast	Yes	No	No	No	No	No	No	No	
Total Advantages of the product	9 of 9	1 of 9	3 of 9	2 of 9	2 of 9	1 of 9	3 of 9	2 of 9	

Note: Intact tissue-based membrane products (like OASIS™, EPIFIX™, AMNIOFIX™, CYTAL™) naturally contain at least 15% of high immunogenic compound namely Elastin, besides other allergenic biological molecules like glycosaminoglycans and certain types of collagen other than Type-I collagen.

Ref 1. <https://pubmed.ncbi.nlm.nih.gov/16968153/>
3. <https://pubmed.ncbi.nlm.nih.gov/9852359/>

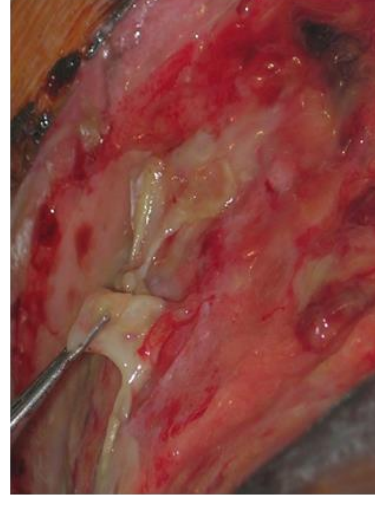
2. <https://link.springer.com/article/10.1007/s10029-020-02238-y>
4. <http://www.liebertpub.com/doi/10.1089/ten.tea.2011.0738>

219 MEDICARE-APPROVED SKIN SUBSTITUTES: PROPERTIES BY PRODUCT CATEGORY				
PRODUCT ORIGIN	PRODUCT TYPE	PRODUCT DESCRIPTION	# of Total	PRODUCT CLINICAL PROPERTIES
XENOGRAFT (ANIMAL ORIGIN)	EXTRACTED COLLAGEN SHEET	<p>Helicoll</p> <p>Patented Highly Purified, bioactive, non-immunogenic type-I collagen product. Helicoll's unique collagen scaffold with approx. 20µ Porosity and native staggered fibres.</p>   <p>Collagen Phosphorylation</p> <p><small>ENCOLL's Type-I Collagen is bioactive due to its Phosphorylation</small></p>	1	 <p>Helicoll Bioactive type-I collagen attracts cells & factors in 1 to 3 days</p> <p>Tissue regeneration in 4 to 5 days, not shown with other products</p> <ul style="list-style-type: none"> Highly regenerative, phosphorylated, clinically effective, Type-I collagen.
		<p>Primatrix, Puraply, Integra & GraftJacket</p> <p>Partially pure collagen mostly cross-linked with non-native, random distribution of fibres.</p> 	12	<ul style="list-style-type: none"> Purification not patented. Random, non-native structural configuration. Freeze-drying results in matrix with average porosity > 800µ that is not conducive for ideal cell infiltration. Gamma sterilization is not ideal as it may denature and cross-link the protein resulting in lesser bioactivity.
	INTACT TISSUE DERIVED MEMBRANE	<p>Oasis</p> <p>Porcine Intestinal Wall</p> <p>Cytal Wound Matrix</p> <p>Porcine urinary bladder matrix</p> <p>Mediskin</p> <p>Porcine dermal and epidermal layer</p> <p>Kerecis Omega3 Wound</p> <p>Fish Skin</p>	7	<ul style="list-style-type: none"> All intact tissue membrane products, by default, contain immunogenic components like Elastin (approximately > 15% w/w) and Type-III Collagen etc. In case of Kerecis, chitosan is an additional contaminant. Kerecis with Omega3 Fatty acid may result in production of free radicals that damages tissue cells resulting in lesser regeneration. Direct or indirect cross-linking done to reduce their immunogenicity may constrain bioactivity. Restricted bio-effectivity and biological regenerative capabilities in the host tissue.
ALLOGRAFT (HUMAN ORIGIN)	INTACT TISSUE DERIVED MEMBRANE	<p>Alloskin, Alloderm, Dermapure, Truskin, Miroderm, Progenamatrix</p> <p>Human Skin</p>	24	
		<p>Amnion Bio, Biovance, Epifix, Restorigin, Woundfix Biowound, Xwrap</p> <p>Amnion</p> <p>Cellesta Cord & Surgicord</p> <p>Umbilical Cord</p> <p>Grafix, NuShield, Neopatch,</p> <p>Placenta</p>	165	
		<p>Apiligrat & Dermagraft</p> <p>Cell Seeded & Others</p>	10	<ul style="list-style-type: none"> Impaired bioactivity and biocompatibility.

- ❖ Helicoll shows consistent evidence of new blood capillaries forming into the matrix at an accelerated rate



Note: capillary bleeding and incorporation of Helicoll into deeper structures



- ❖ Blood capillaries and granulation tissue formation are visible at a macroscopic level within 4 to 5 days

Helicoll[®]

Granulation Stages of Healing



Day 1



Day 5



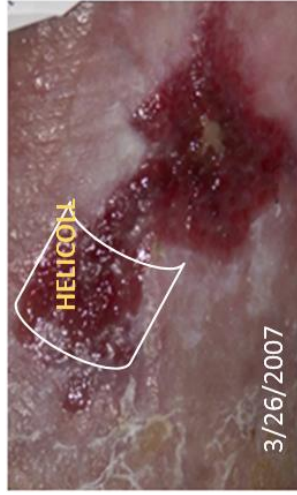
Day 7



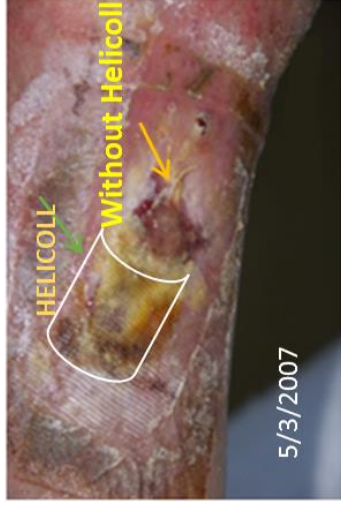
Day 10

Outstanding Regeneration in Just 10 days

Non-Healing Leg Ulcer Wound - Male Patient, age 77



Helicoll dressing on half of the Wound to assess its efficacy



Helicoll covered site was almost healed.



Significant improvement seen on the Helicoll covered portion of the wound.



Helicoll covered site was totally healed. Helicoll applied on the remaining Wound.



Significant healing observed



Complete healing of initially covered part. Good Progress on later covered wound

Helicoll Prevented Recurrence of the Wound. Evidenced through several months of Follow up.



“This dressing can be recommended for the non-healing ulcer wound treatment”. -

Mathew Kelly, MD, Plastic Surgeon, Jan Parks, RN,
St. Francis Memorial Hospital, San Francisco, CA.

Successful Usage of Helicoll on Exposed Bones



Bone-exposed wounds were successfully healed with Helicoll without the immediate need of for skin graft.

Sacral Pressure Sore



Stage 4 pressure sore



10 Days Post Helicoll application



Completely healed using Helicoll

Keloid excision and closure



Before



After

Complete Recovery in 6 weeks

Courtesy: Vinoth Philip , MD, DNB, Plastic Surgeon

No re-occurring of Keloid after healing with Helicoll

Helicoll
White paper for use in Diabetic Foot Ulcers (DFU)

Introduction:

Diabetes affects 38.4 million children and adults in the US, equivalent to 1 in 9 of the population, and costs the economy \$412.9 billion annually.^{1,2,3}

The overall perception of the delayed diabetic wound healing is neuropathy resulting in poor arterial blood supply and venous circulation.

However, high levels of blood glucose not only affect the nerves but also impedes the natural maturation of the healing/granulation tissue. This is a biochemical phenomenon called glycosylation of structural proteins.

We need to consider all the causes of Diabetic Ulcers at this point as shown below:

Understanding of the causes for Diabetic Foot Ulcers

Commonly recognized concepts of DFU

1. Nerve Damage

Damage to the nerve by increased level of glucose in blood may result in loss of sensation and the inability to feel any pain or pressure.

2. Poor Circulation

High blood glucose levels thicken the arteries and narrow its blood vessels, restricting the delivery of the blood and oxygen needed to support the body's natural healing abilities.

3. Infection

Suppressed immune system may facilitate pathogen proliferation eventually leading to an infection like non-healing diabetic ulcer.

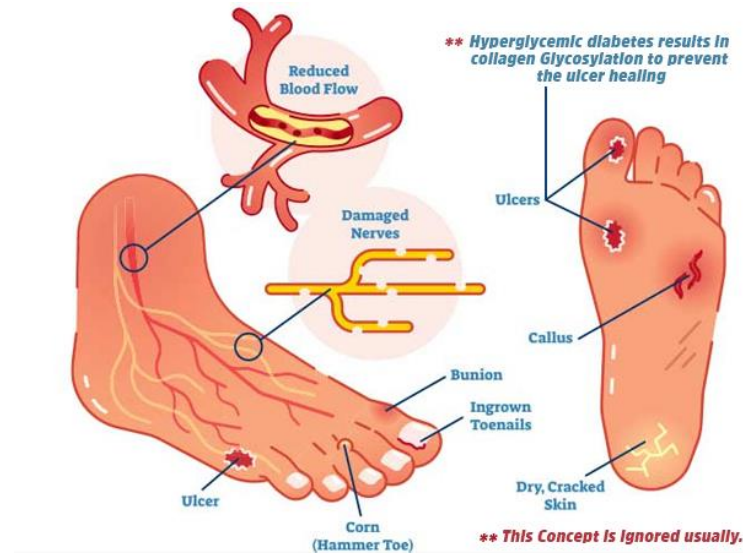
4. Immune Suppression

Diabetes may suppress the immune system that could impair the body's ability to fight-off an infection.

Unrecognized concept of DFU

5. Glycosylation of wound bed collagen

In hyperglycemic patients, Glycosylation of the newly formed wound bed collagen hinders the normal enzymatic (lysyl oxidase) maturation leading to non-healing. The hyperglycemic glucose may be absorbed by Helicoll for faster healing of the ulcer wound.



Diagrammatic representation of Hyperglycemic Diabetology

Treatment options for DFU:

Normal materials that are used to cover an ulcer:

1. Non-biological synthetic polymeric sheets and sponges
2. Cotton gauze
3. Vaseline

All such materials are able to protect wound as a wound cover and may absorb the secreted fluid (exudate). Upon usage of such non-biological scaffold materials, cells may not feel comfortable when they come in contact. Accordingly, this would un-necessarily delay the wound healing process because the exudation will continue until the cells are comfortable with the surrounding environment.

On the other hand, **Helicoll** skin substitute may provide a better result. However, all biological materials are not the same. Using an advanced biological skin substitute like **Helicoll** will not disturb the cells on the surface of the wound involved in the tissue granulation process.

All biological skin substitutes may NOT be ideal biocompatible matrices:

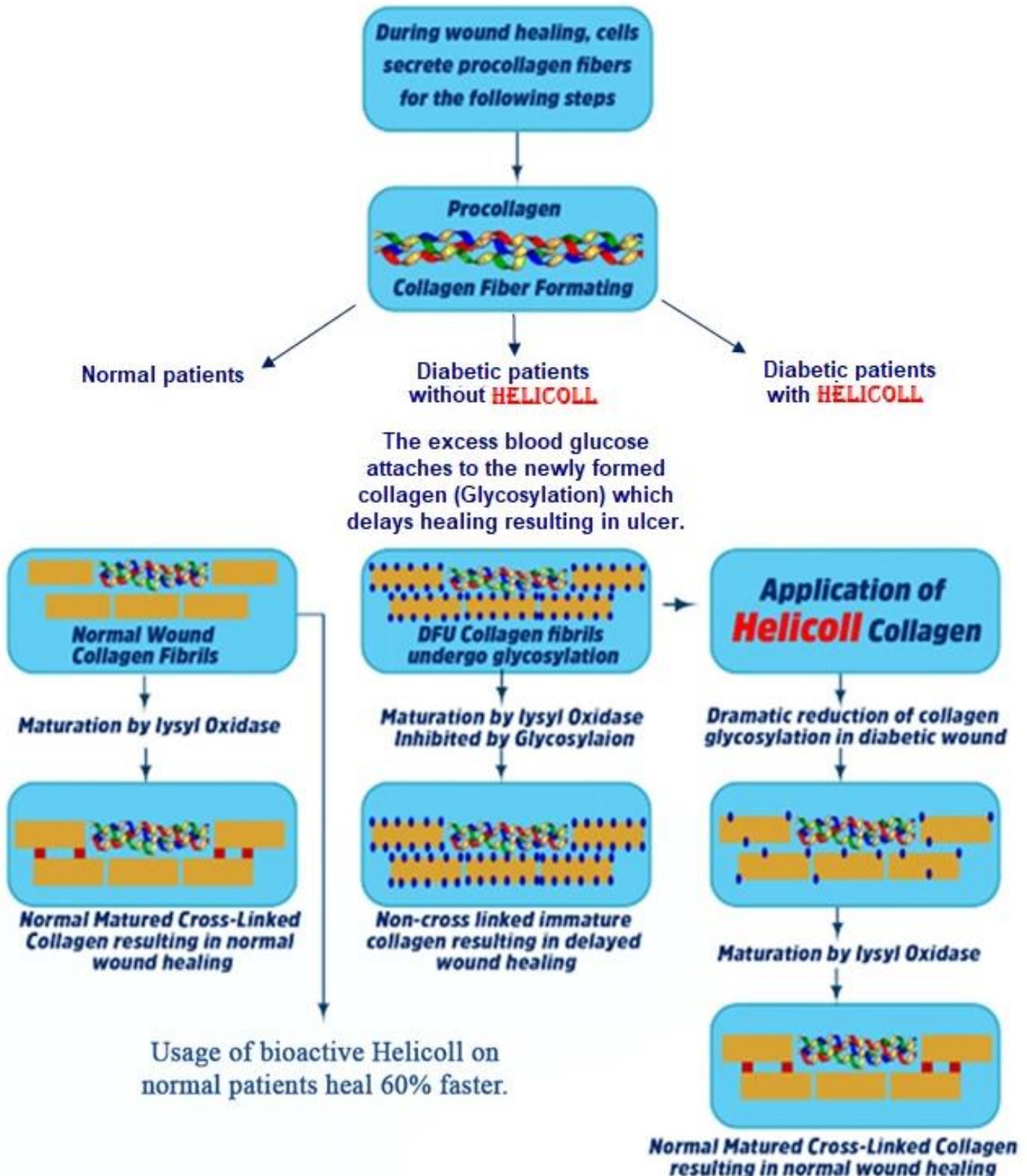
Two main categories of biological matrices:

1. **Reconstituted Collagen membranes:** This includes products made from collagen extracted from animal tissues. Only a few such products are highly biocompatible and bioactive. **Helicoll** happens to be one such unique product.
2. **Intact tissue membrane derived products:** These products are made from intact tissue membranes of amnion, pericardium, intestinal wall, urinary bladder etc. These membranes are contaminated with approximately 15% elastin, type-III collagen, lipids and other proteoglycans which are all highly immunogenic. They have to be cross-linked to minimize their immunogenicity and on the other hand loses the bioactivity and wound healing abilities if the material is not chemically modified or cross-linked, it can effectively be used in tissue regeneration and in the granulation process.

References: 1. <https://www.cdc.gov/diabetes/php/data-research/index.html>, 2. <https://pubmed.ncbi.nlm.nih.gov/37909353/>, 3. <https://www.niddk.nih.gov/health-information/health-statistics/diabetes-statistics>

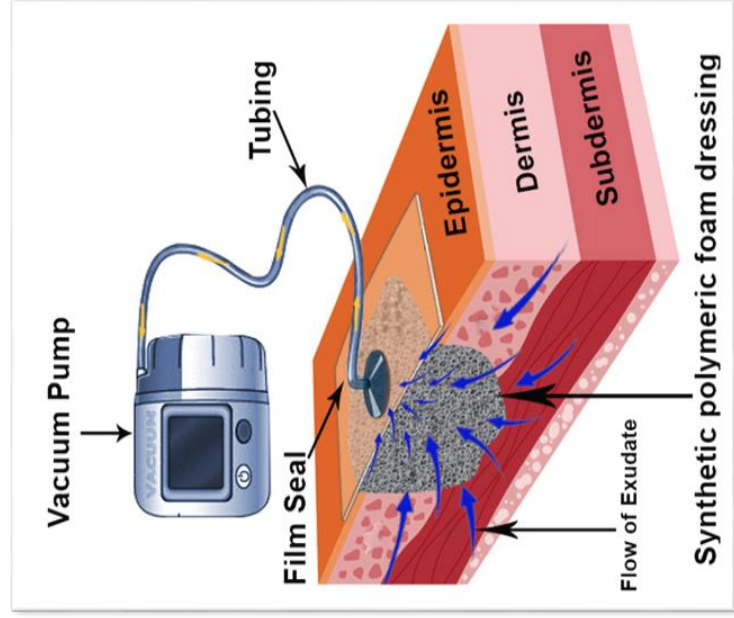
How Helicoll Nano-technology could heal a Diabetic Ulcer faster than other collagen products.

Why Helicoll works best for Diabetic Foot Ulcers (DFU)?

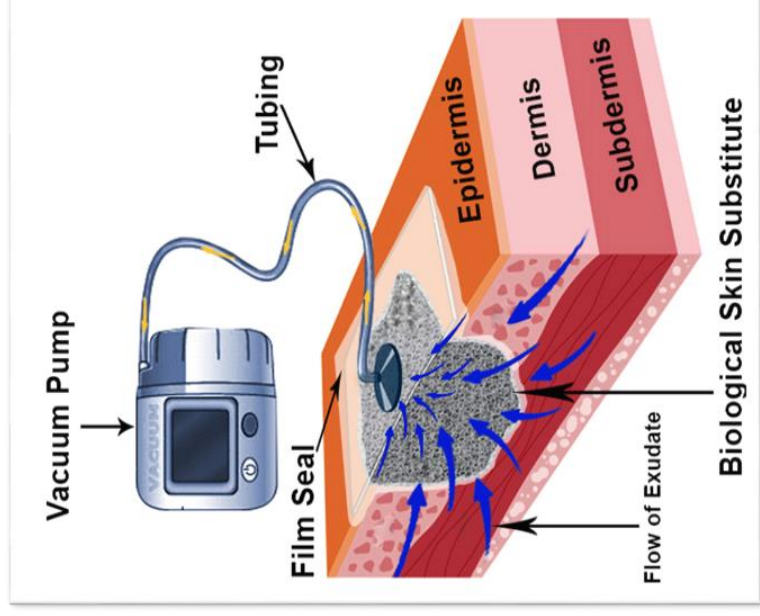


Helicoll®

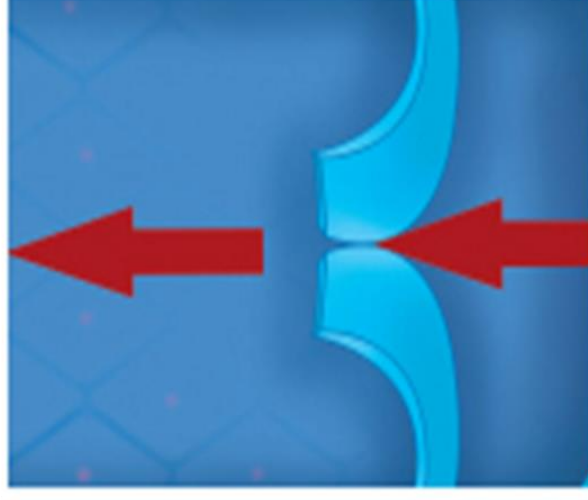
As a tissue regenerative matrix intervention
to improve NPWT (Negative Pressure Wound Therapy)



Current NPWT application process

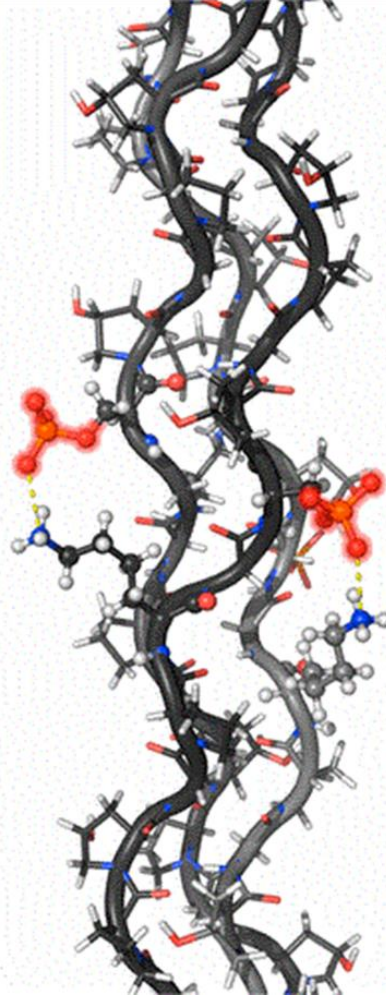


NPWT combined with Helicoll can
improve healing



Unidirectional flow of exudate
through a slit opening on the
membrane

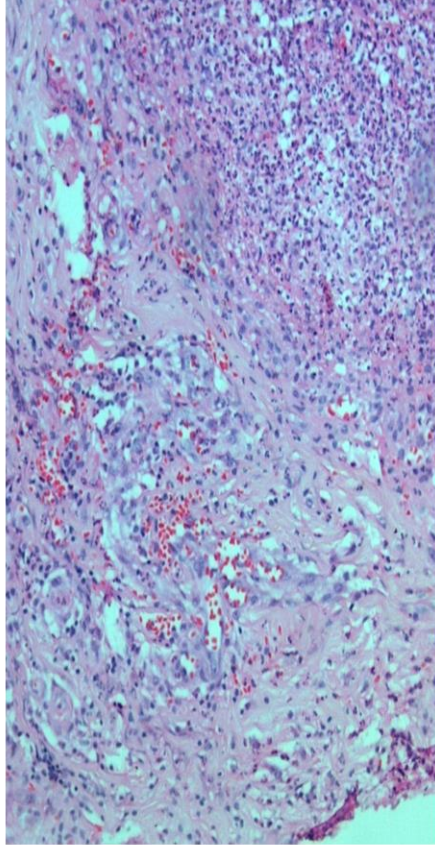
Collagen Phosphorylation



ENCOLL's Type-I Collagen is Bioactive due to its Phosphorylation

- Encoll's patented process yields high purity Type-I Collagen for maximum biocompatibility.
- Such collagen when phosphorylated results in cell signal transduction.
- Exceptional bioactivity of Helicoll collagen is derived due to its phosphorylation

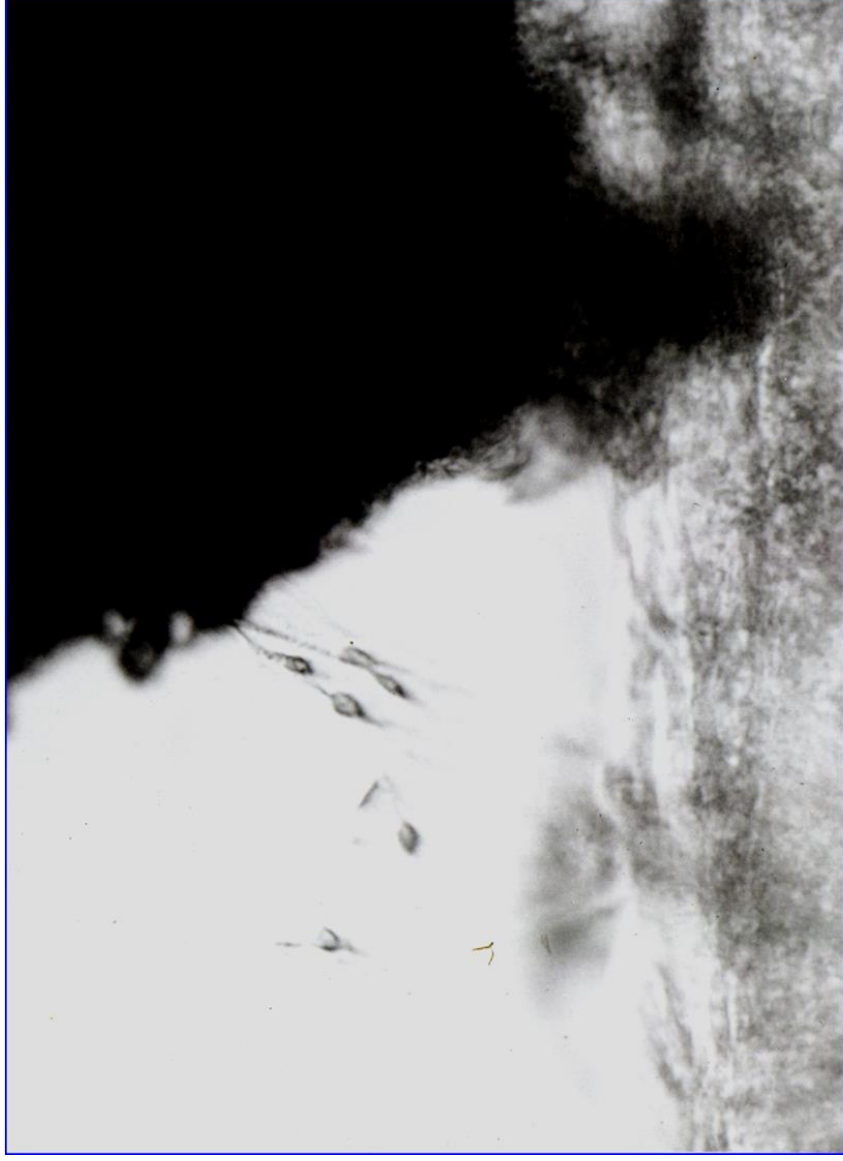
Helicoll is clinically documented to prove its faster wound healing capabilities. Helicoll encourages the formation of new blood capillaries within 4 to 5 days upon the application of the product over the wound. Helicoll also encourages the attachment of cells and growth factors for faster tissue remodeling.



H & E light microscopy after Helicoll treatment

Day 5: Neo-vascularization

After Helicoll application- acute inflammatory cells, fibroblasts and blood vessels proliferate into the collagen matrix.(50x). Absence of Lymphocytes evidences the collagen in Helicoll is not immunogenic.

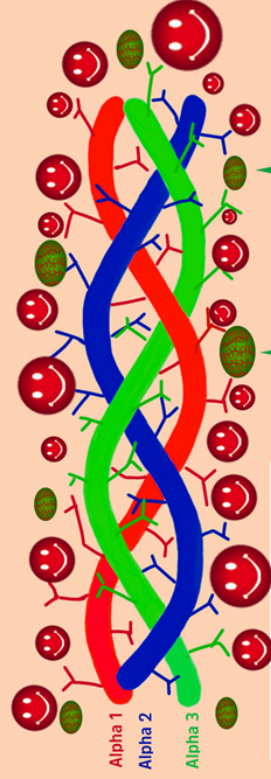


**EnColl's Patented
Charge Modified
(Phosphorylated)
Type-I Collagen
Attracts the
Neuronal Cells Under
Cell-Culture
Experiments
documented at
Stanford University,
California, USA**



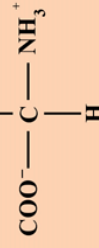
Helicoll

Ultra-pure Type I Collagen, Un-crosslinked



Amino Acid Structure

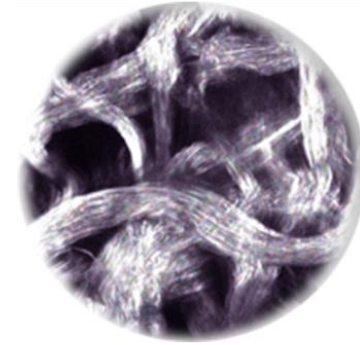
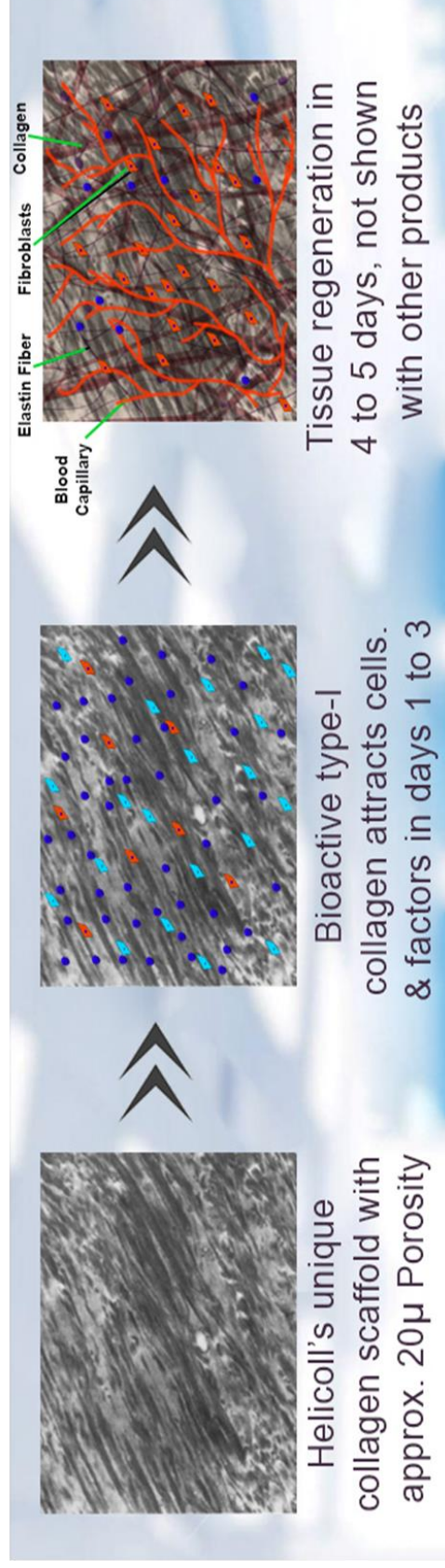
Specific reactive site
determining each
Amino Acid



Improved cell signalling
to produce molecules
for repair and regeneration

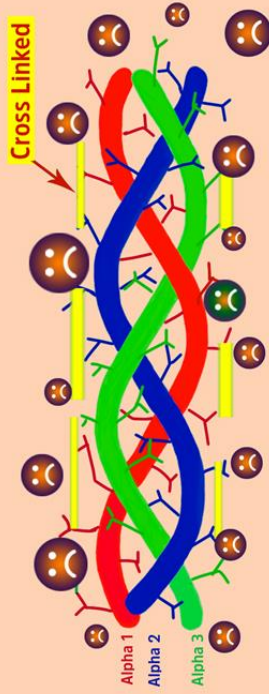
- Helicoll is a bioengineered bio-resorbable high purity Type-I collagen (> 97% pure and free of lipids, elastin and other immunogenic proteins) membrane.
- It is further bio-activated by phosphorylation results in unique cell-signaling capabilities.
- As a result, Helicoll has clinically proven to form granulation tissue and invite new blood capillaries within 4 to 5 days after application.

Structural Advantage of Helicoll Collagen Compared to Others



Other collagen preparations (ex. **Puraply**, **Primatrix** and **Integra**) as a result of lyophilization, yield random structural configuration that is non-native with avg. porosity > 800µ which is non-conducive for cell infiltration. Its bioactivity stays behind the bioactivity of sedimental preparation of **HELICOLL** type-I collagen that yields native parallel fibrils with porosity of approx. 20µ to attract more cells/regenerative factors. Additionally, **Helicoll** is EtO gas sterilized that does not denature the protein unlike gamma sterilization which is used by most other collagen preparations. Collagen when cross-linked, the natural bioactivity may be significantly minimized.

Other Products Contaminated Type I Collagen, with unwanted cross links



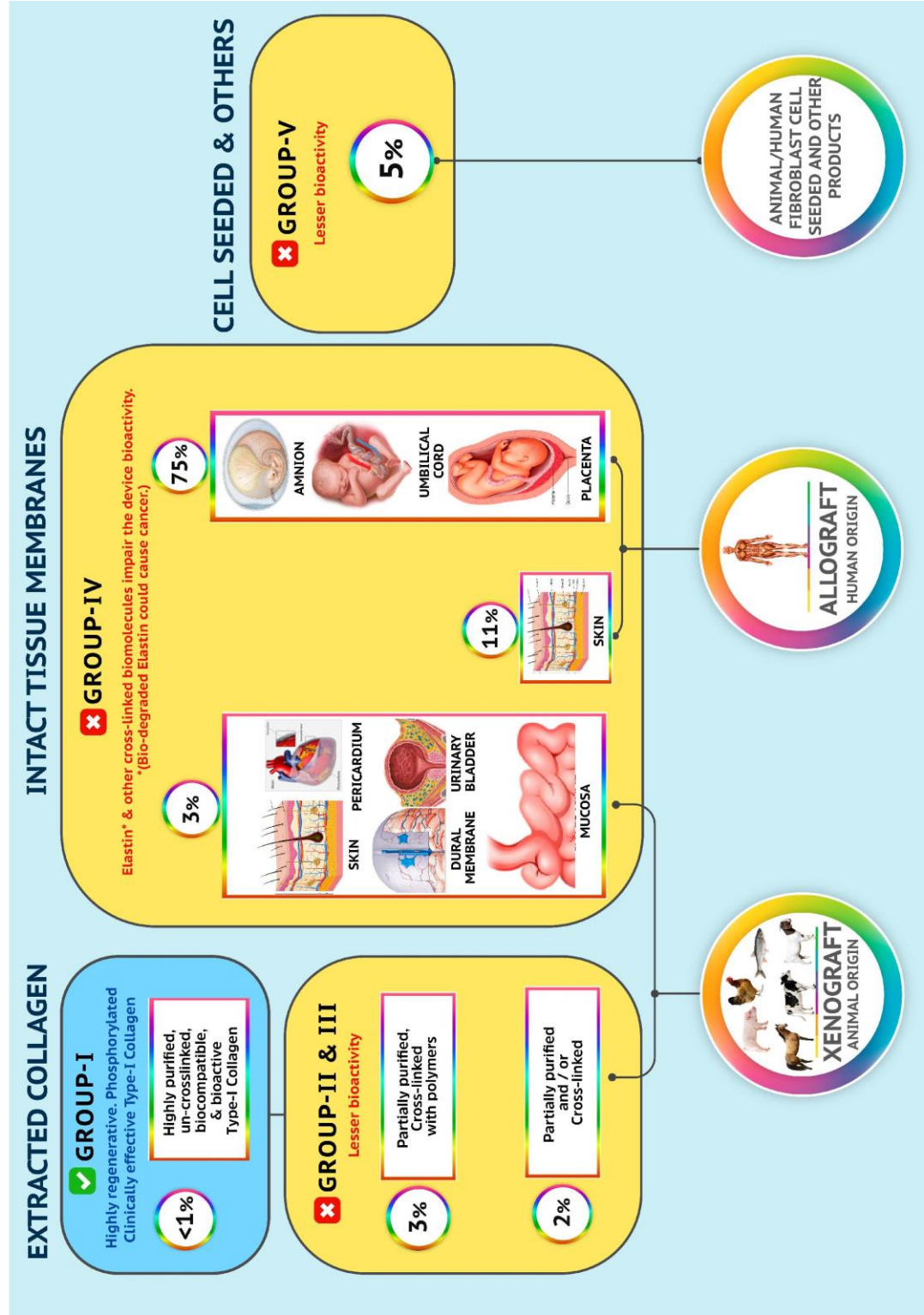
Cells are non-responsive and unhappy because of unwanted crosslinks and contaminants like:

- ▶ Type-III Collagen
- ▶ GAG's (Glycos amino glycans)
- ▶ Elastin

- Many of the available competitor skin-substitute products are derived from intact tissues (like amnion, intestinal wall, pericardium, skin etc.) of allograft or xenograft tissues.
- They incorporate all naturally immunogenic components (like Elastin, Type-III Collagen and other allergenic tissue components to the host tissue).
- Thereby, such products have to be cross-linked in order to reduce their immunogenicity.
- This process restrains the bio-effectivity of the useful Type-I collagen and its biological regenerative use in the host tissue.

MEDICARE-APPROVED SKIN-SUBSTITUTES (CURRENTLY 219)

Comparative distribution by category shown in %



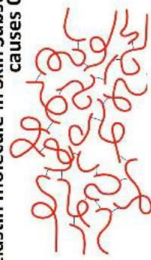
COLLAGEN PRODUCTS OF ENCOLL: UNIQUE FEATURES

Impact of Matrix Structure & Chemistry

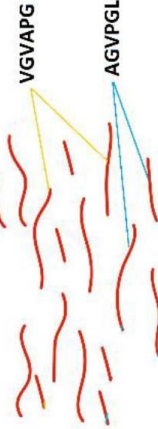
Intact Tissue Membranes

Has 15-51% Elastin which is a carcinogen

Elastin molecule in Skin Substitutes causes Cancer



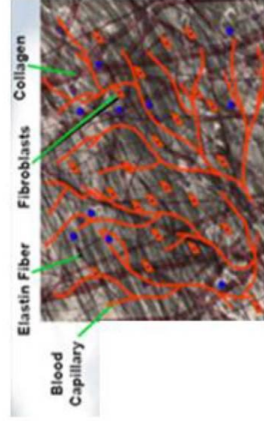
Fragmented Elastin (Elastokines/Elastomers) are CARCINOGENIC



CARCINOGENIC

Encoll Products

Parallel, organized fibres similar to that of skin



Porosity is ~ 20 microns similar to native product ideal for cell infiltration

IDEAL

Other Products

Spongy condition does not yield native structure



Porosity is ~ 400 microns not conducive for cell infiltration & tissue regeneration

LESS BIOACTIVE

White paper on Elastin Carcinogenicity

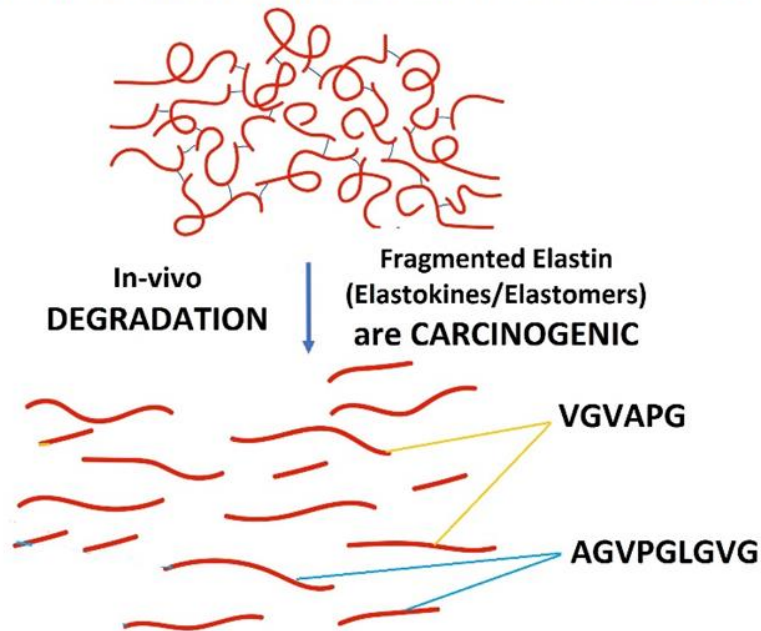
Please be aware of the alarming fact about the safety concerns of using an intact tissue membrane-based regenerative matrix. They all contain 15 to 49% elastin in them which happens to be the culprit.

Examples of such products include intact membranes of

Intact tissue	Elastin content in%	Product example
Amnion ¹	42	Amniofix, Epifix, Amnioexcel, Xwrap
Placenta ²	49	Grafix
Umbilical Cord ³	25	Cellesta Cord
Pericardium	At least 10	Architect from Equine
Urinary Bladder ⁴	9	Cytal from Porcine
Intestinal Wall ⁵	10	Oasis from porcine SIS
Skin ⁶	10	Kerecis from fish, EZ Derm from porcine, Apligraf from bovine

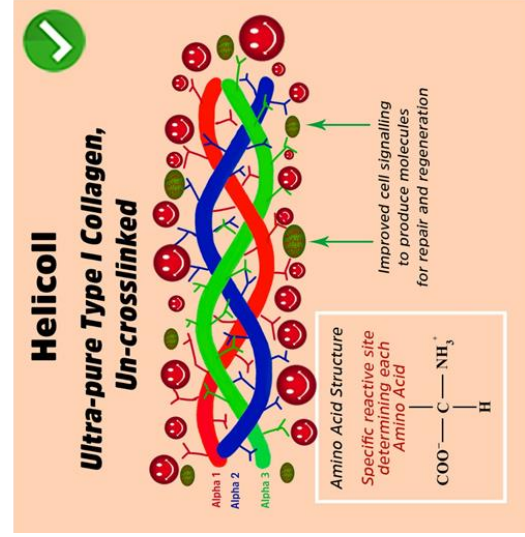
The biological degradation of Elastin resulting in Elastomer/Elastokine fragments is proven to be carcinogenic [ref. www.nature.com/articles/s41467-020-18794-x.pdf] and could cause various pathological conditions including emphysema, chronic obstructive pulmonary disease, atherosclerosis, metabolic syndrome, etc. [ref. <https://www.tandfonline.com/doi/full/10.1080/10409238.2020.1768208>].

Elastin Molecule in Skin Substitutes causes Cancer



- Ref 1. <https://pubmed.ncbi.nlm.nih.gov/16968153/>
 Ref 2. www.liebertpub.com/doi/10.1089/ten.tea.2011.0738
 Ref 3. <https://pubmed.ncbi.nlm.nih.gov/9852359/>
 Ref 4. www.scielo.br/j/ibju/a/pp3bVw7XTtLdVVMzGNFJGK/?lang=en
 Ref 5. <https://link.springer.com/article/10.1007/s10029-020-02238-y>
 Ref 6. www.ncbi.nlm.nih.gov/pmc/articles/PMC6940999/

Helicoll[®] How Helicoll differs from fish-skin products?



Helicoll is derived from patented purified type-I collagen that has never been cross-linked to retain its native bioactivity as a biomaterial.

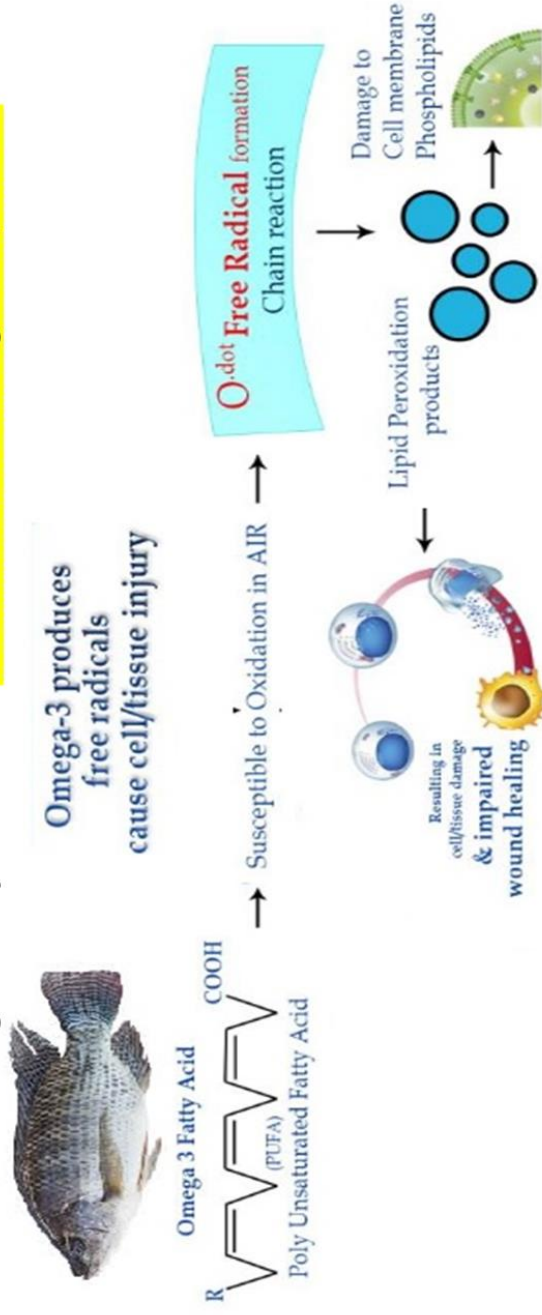
* Piscean type-I collagen is an inferior biomaterial compared to Bovine

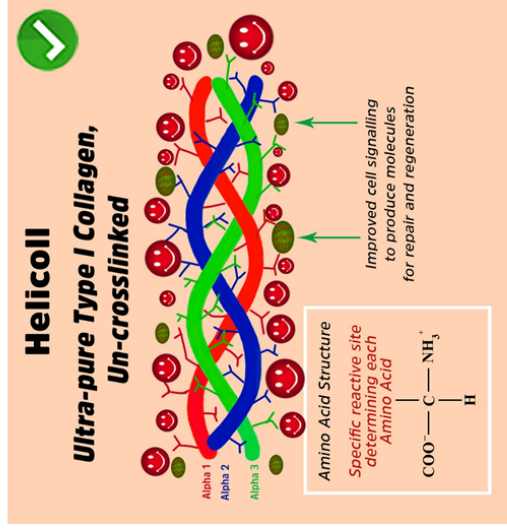
Based on public info from EXPASy Bioinformatics Resource Portal:

- ➖ Piscean collagen vs. human type-I collagen: Only 77.9% homologous - Less bioactivity.
- ➕ Bovine type-I collagen vs. human type-I collagen: 97.4% homologous High bioactivity.





* Piscean collagen also may have contaminating chitin (chitosan) possibly due to the remnants of scales in fish skin.

* Presence of Omega-3 Fatty Acid forms free radicals to damage cells/tissues





Helicoll is derived from patented purified type-I collagen that has never been cross-linked to retain its native bioactivity as a biomaterial.

ALLOGRAFT		XENOGRAFT	
Grafix	 PLACENTA	Epifix	 AMNION
		XWwrap	
		Oasis	 INTESTINAL MUCOSA
		Cytal	 URINARY BLADDER
<p>Intact tissue membrane products, by default contain immunogenic components like Elastin (approximately 15 to 49%) and Type-III Collagen etc. Elastin is recently discovered to be a potential carcinogen.</p> <p>To reduce their immunogenicity, every product is directly or indirectly crosslinked which constrains the natural bioactivity of Type-I collagen.</p> <p>Such restricted bio-effectivity of the Type-I collagen affects its natural biological regenerative capabilities in the host tissue.</p>			

Treatment of Scleroderma



Before

After

After 7 months, the wound size significantly reduced.

Treatment of Trauma Wound

- Exposed Bone and Tendon



**Wound treatment
Day - 0**



**Granulation seen
within 4-5 days.**



**6 biweekly
treatment**



**Exposed bones and
tendons are
significantly covered.
Leg is saved from
amputation.**

Treatment of Chronic Venous Ulcer



Before

After

Closure of wound from 37.5 sq. cm to complete healing within 25 weeks

Treatment of Diabetic Foot Ulcer

Post traumatic chronic ulcer
with necrotized 4th toe

31 Days Post Application



Treatment of Post Traumatic Ulcer

Post Traumatic Ulcer
Before Treatment

Completely Healed Ulcer -
Day 45



Treatment of Malignant Melanoma

Before Treatment **Day 17 and on Follow-up**
after Treatment



Treatment of Severe Burn/Pressure Ulcer



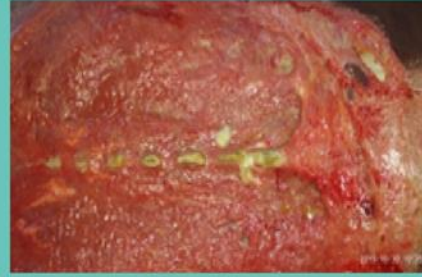
Electric Burn victim with bed sore resulting in chronic ulcer.
(Day-0)



Ulcer wound debrided & cleaned.
(Day-1)



Biological, Biocompatible Collagen product applied.
(Day-1)



Shows uplift of healthy granulation soft tissue around vertebral spinous processes. **(Day-4)**



Significant wound healing is shown here.
(Day-7)

Related Helicoll Links

➤ **For Application Procedure Animation**

<https://helicoll.com/video/Helicoll.mp4>

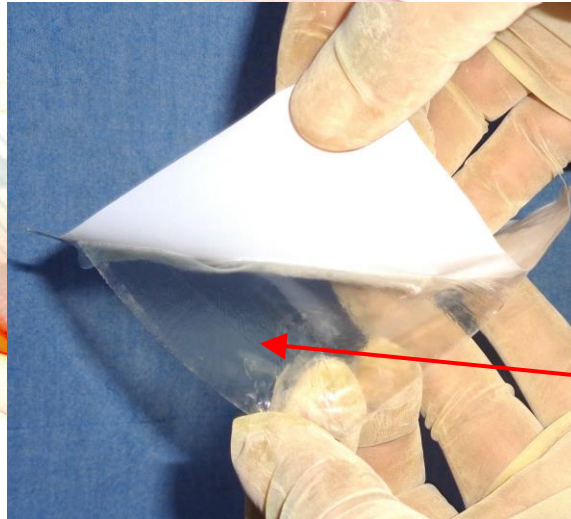
➤ **For Burn Cases with Application Procedure**

<https://www.youtube.com/watch?v=w6-oxUA1yy0>

<https://helicoll.com/video/Pediatric Burn Case.mp4>

Helicoll[®]

COLLAGEN BASED STERILE
BIO-ENGINEERED SKIN SUBSTITUTE



Helicoll Sheet

Product Profile Overview

Manufactured & Marketed by:

Encoll Corp.

4576 Enterprise Street, Fremont, CA – 94538

Website: www.Helicoll.com

Contact Information:

S. Gunasekaran, PhD (for Technology)
guna@encoll.com, +1 (510) 396-8581

Murugan G. (for Business & Sales)
murugan@encoll.com, +1 (510) 709-8663

HELICOLL PRODUCT TECHNICAL & CLINICAL FEATURES

PRODUCT OVERVIEW

Product Name	Helicoll, Biological Skin Substitute
Model/Catalog	HC0.5dia, HC1.0dia, HC0.8X1.6, HC1.2X1.6, HC1.6X1.6, HC2X2, HC2X4
Manufacturer	EnColl Corporation
Website links	www.Helicoll.com

PRODUCT DETAILS

Item Name, Size &	Cat/Item #	HCPCS Code	NDC/UDI code for Billing	Pkg Type	No. of sheets
Helicoll 0.5 in dia disc/1.27 cm dia disc (1 sq cm)		Q4164	74745-0051-01	Single Sheet	1
Helicoll 0.5 in dia disc/1.27 cm dia disc (1 sq cm)	HC0.5dia	Q4164	74745-0052-02	2 sheets per box	2
Helicoll 1.0 in dia disc/2.54 cm dia disc (5 sq cm)		Q4164	74745-0101-01	Single Sheet	1
Helicoll 1.0 in dia disc/2.54 cm dia disc (5 sq cm)	HC1.0dia	Q4164	74745-0102-02	2 sheets per box	2
Helicoll 0.8 in x 1.6 in/2 cm x 4 cm (8 sq cm)		Q4164	74745-0081-01	Single Sheet	1
Helicoll 0.8 in x 1.6 in/2 cm x 4 cm (8 sq cm)	HC0.8x1.6	Q4164	74745-0082-02	2 sheets per box	2
Helicoll 1.2 in x 1.6 in/3 cm x 4 cm (12 sq cm)		Q4164	74745-0121-01	Single Sheet	1
Helicoll 1.2 in x 1.6 in/3 cm x 4 cm (12 sq cm)	HC1.2x1.6	Q4164	74745-0122-02	2 sheets per box	2
Helicoll 1.6 in x 1.6 in/4 cm x 4 cm (16 sq cm)		Q4164	74745-0161-01	Single Sheet	1
Helicoll 1.6 in x 1.6 in/4 cm x 4 cm (16 sq cm)	HC1.6x1.6	Q4164	74745-0162-02	2 sheets per box	2
Helicoll 2in x 2in (5cm x 5cm=25 sq cm)		Q4164	74745-0221-01	Single Sheet	1
Helicoll 2in x 2in (5cm x 5cm=25 sq cm)	HC2x2	Q4164	74745-0225-05	5 sheets per box	5
Helicoll 2in x 4in (5cm x 10cm=50 sq cm)		Q4164	74745-0241-01	Single Sheet	1
Helicoll 2in x 4in (5cm x 10cm=50 sq cm)	HC2x4	Q4164	74745-0245-05	5 sheets per box	5

CONTACT INFO

Representative	Subra Guna, PhD - President
Company	EnColl Corporation
Email Address	guna@encoll.com

PRODUCT INFO

Product Description



Helicoll is a bioengineered high purity Type-I collagen (>97% pure) forming an acellular skin substitute construct that is highly bioactive, cell conducive, and supportive towards enhancing tissue generation for wound management. Helicoll is an acellular dermal replacement product and is within the definition of a bioengineered skin substitute. It provides a framework that promotes the regeneration of blood vessels and supports biologic cell migration due to the resorbable properties of Helicoll. Treatment course typically involves 1 to 4 applications.

What products are comparable to Helicoll?

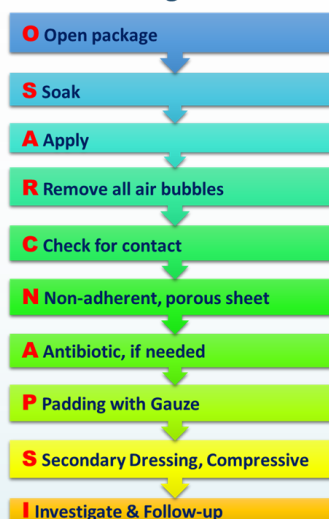
Gammagraft	Oasis wound matrix	Woundex, bioskin
Apligraf	Dermagraft	Primatrix
Theraskin	Amnioexcel biodexcel	Puraply & Puraply am
Nushield	Biovance	Amnioband, guardian
Grafix stravax prime pl	Epifix	Palingen or palingen xplus
Epicord	Affinity	Phoenix Wound Matrix

How is Helicoll better than the alternative?

Advantages of Helicoll over Alternative Products:

- **High purity type-I Collagen:** Helicoll is a patented reconstituted bioactive collagen sheet, free of immunogenic proteins, lipids, and elastin. The native structure of the collagen is not altered or cross-linked which maintains its high bioactivity.
- **Faster Healing:** Collagen phosphorylation attracts cells, regenerates tissue, and stimulates blood capillaries/granulation within 4 to 5 days through cell signal transduction.
- **Innovative Technology:** Helicoll's phosphorylated Type-I collagen is unique with high biocompatibility and bioactivity compared to other collagen products. Can be used with negative pressure wound therapy (NPWT) with slit openings for exudate release. Better than intact tissue-based membranes like an amnion, intestinal wall, urinary bladder, etc. which contain >15% elastin that is recently
- **Easy Application:** No washing is needed prior to use. The overall clinical usage of Helicoll is simple and easy as it can be cut, sutured, or stapled.
- **Pain Control:** Effectively reduces pain, as proven by clinical studies.
- **Structural advantage:** Unlike random fibrillar configuration in other collagen products, Helicoll collagen fibrils are organized in a parallel pattern similar to that of native tissue fibrillar structure. The porosity is approx. 20μ to attract more cells/regenerative factors.
- **Various Sizes:** Choose from standard or customized dimensions.
- **Cost-Effective:** Accelerated wound healing and tissue remodeling with minimal applications reduce the treatment cost by over 40%.
- **Long Shelf Life:** Remains clinically usable for 3 years when stored in room temperature conditions.

Helicoll Usage Procedure



Helicoll Product Brochure: https://helicoll.com/wp-content/uploads/2024/03/Helicoll_Brochure.pdf

Helicoll Instructions for Use: https://helicoll.com/wp-content/uploads/2024/03/Helicoll_IFU.pdf

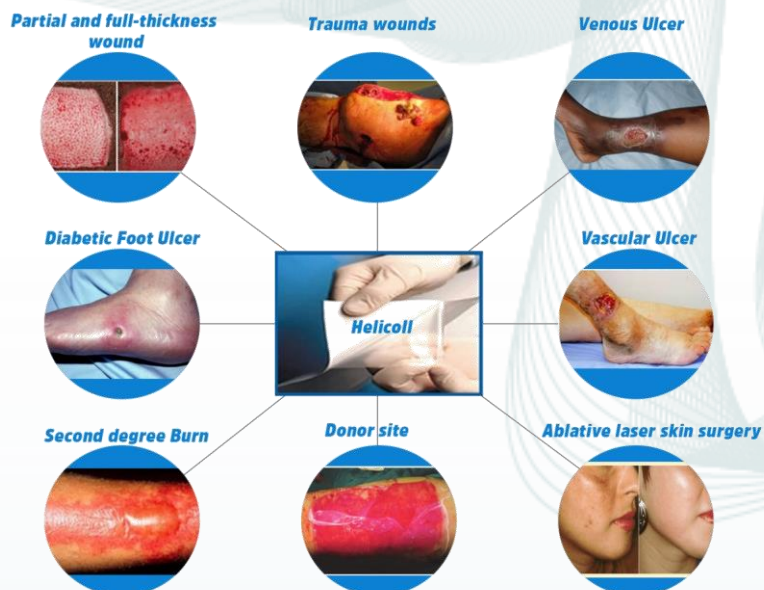
Comparative Information: https://helicoll.com/wp-content/uploads/2024/03/Helicoll_comparison_with_other_FDA_approved_prime_products_table.pdf

REGULATORY INFO

Class
FDA Product Code
FDA Registration Number
510(k) Number
Helicoll FDA Cleared Indications

Unclassified
KGN - Dressing, Wound, Collagen
3004117927
K040314
• Partial and full-thickness wounds

- Pressure, Venous, Chronic vascular and Diabetic ulcers
- Trauma wounds: Abrasions, Lacerations, Skin tears, Second-degree burns
Surgical wounds: Donor sites/grafts, Post Mohs' surgery, Post laser surgery, Podiatric, Wound dehiscence
- Excessive exudate underneath Helicoll can be drained through slit openings that also is applicable when using Negative Pressure Wound Therapy (NPWT)
- The product also can be secured in place using sutures and/or staples



FDA Contraindications

Helicoll is derived from a bovine or ovine source and should not be used in patients with known sensitivity to such material. This device is not indicated for third-degree burns.

FDA Clearance

https://helicoll.com/wp-content/uploads/2024/04/Helicoll_FDA_510k_clearance_k040314_Etc.pdf
https://helicoll.com/wp-content/uploads/2024/03/Encoll_FDA_Mfg_License_Facility_Regn.pdf

SAFETY INFO

Safety Documents

Material Safety Data Sheet for Helicoll Finished Product

https://helicoll.com/wp-content/uploads/2024/03/HELICOLL_16POINTS_MSDS.pdf

REIMBURSEMENT INFO

CPT

15271, +15272, 15273, +15274, 15275, +15276, 15277, +15278

HCPs

Reimbursement Guide

Q4164

https://helicoll.com/wp-content/uploads/2024/03/Helicoll_Billing_Guide_MEDICARE.pdf

https://helicoll.com/wp-content/uploads/2024/03/Helicoll_Billing_Guide_MEDI_CAL.pdf

https://helicoll.com/wp-content/uploads/2024/03/Sample_Medical_Necessity_Letter.docx

CLINICAL INFO

Reduces patient mortality? Yes

Our proprietary, pure Type I collagen reduces immunogenicity, promotes cell migration with increased neovascularity due to added phosphorylation of Type-I collagen.

How does Helicoll improve patient outcomes?

Helicoll has unique clinical evidence for the formation of granulation and neo-vascularization within 4 to 5 days upon application. This results in faster wound healing and tissue regeneration compared to other alternate products.

Helicoll Clinical Studies

https://helicoll.com/wp-content/uploads/2024/03/Helicoll_published_Stanford_Article.pdf

https://helicoll.com/wp-content/uploads/2024/03/Comparison_of_type-I_collagen_with_Integra_skin_substitute.pdf

https://helicoll.com/wp-content/uploads/2024/03/Shriners_Hospital_Burn_Ctr_Galveston_TX.pdf

https://helicoll.com/wp-content/uploads/2024/03/VCS_2021_Allograft_Vs_Type_I_Collagen_Abstract.pdf

https://helicoll.com/wp-content/uploads/2024/03/SAWC_Fall_2020_Collagen_Structure_Abstract.pdf

https://helicoll.com/wp-content/uploads/2024/03/SFB_2019_Collagen_Misconcept_Abstract.pdf

https://helicoll.com/wp-content/uploads/2024/03/Evaluation_of_Bovine_Derived_Collagen_of_ENCOLL_Technology.pdf

https://helicoll.com/wp-content/uploads/2024/03/Comparison_of_Helicoll_with_Scarlet_Red_Opsite_split_thickness_skin_graft.pdf

https://helicoll.com/wp-content/uploads/2024/03/Comparison_of_Helicoll_with_Scarlet_Red_Opsite_split_thickness_skin_graft.pdf

https://helicoll.com/wp-content/uploads/2024/03/Comparison_of_Helicoll_with_Scarlet_Red_Opsite_split_thickness_skin_graft.pdf

https://helicoll.com/wp-content/uploads/2024/03/Comparison_of_Helicoll_with_Scarlet_Red_Opsite_split_thickness_skin_graft.pdf

https://helicoll.com/wp-content/uploads/2024/03/Comparison_of_Helicoll_with_Scarlet_Red_Opsite_split_thickness_skin_graft.pdf

ADDITIONAL INFO

Does Helicoll require user certification, staff training or in-service?

Yes

We perform in-service training and web conferencing whichever is your preference.

Additional Notes

Please be aware of the alarming fact about the safety concerns of using an intact tissue membrane-based regenerative matrix. They all contain 15 to 49% elastin in them which happens to be the culprit.

E.g. of elastin containing products from intact tissue membranes:

Amniofix, Epifix, Amnioexcel, Xwrap: derived from amnion (42% elastin, Re

Grafix: derived from placenta (49% elastin, Ref 2)

Cellesta Cord: derived from umbilical cord (25% elastin, Ref 3)

Architect: derived from equine pericardium (at least 10% elastin)

Cytal: derived from porcine urinary bladder (9% elastin, Ref 4)

Oasis: derived from porcine SIS intestinal wall (10% elastin, Ref 5)

Kerecis: derived from fish skin (10% elastin, Ref 6)

EZ Derm: derived from porcine dermis (10% elastin, Ref 6)

Apligraf: derived from bovine skin (10% elastin, Ref 6)

The biological degradation of Elastin resulting in Elastomer/Elastokine fragments is proven to be carcinogenic [ref. www.nature.com/articles/s41467-020-18794-x.pdf] and could cause various pathological conditions including emphysema, chronic obstructive pulmonary disease, atherosclerosis, metabolic syndrome, etc.

[ref. www.tandfonline.com/doi/full/10.1080/10409238.2020.1768208].

References:

1. <https://pubmed.ncbi.nlm.nih.gov/16968153/>
2. www.liebertpub.com/doi/10.1089/ten.tea.2011.0738
3. <https://pubmed.ncbi.nlm.nih.gov/9852359/>
4. <http://www.scielo.br/j/ibju/a/pp3bVw7XTtcLdVVMzGNFJGK/?lang=en>
5. <https://link.springer.com/article/10.1007/s10029-020-02238-y>
6. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC6940999/>
https://helicoll.com/wp-content/uploads/2024/03/helicoll_unique_features.pdf
<https://helicoll.com/case-reports/>
https://helicoll.com/wp-content/uploads/2024/03/Helicoll_as_Ideal_Tissue_Regenerative_Scaffold.pdf
https://helicoll.com/wp-content/uploads/2024/03/Helicoll_in_NPWT.pdf
https://helicoll.com/wp-content/uploads/2024/03/Helicoll-Diabetic_Ulcer_Usage.pdf
<https://link.springer.com/article/10.1007/s44174-023-00106-8>

Additional Files

Helicoll[®]

COLLAGEN BASED STERILE BIO-ENGINEERED SKIN SUBSTITUTE

Manufactured & Marketed by:

 **ENCOLL**
Enhancing life through collagen

Address: 4576 Enterprise St. Fremont, CA 94538 USA
Tel: (510) 659-1466, Email: info@helicoll.com



FOOTCARE SPECIALISTS, INC., A PODIATRY GROUP

David J. Kaplan, D.P.M.
Diplomate, American Board of Foot & Ankle Surgery
Fellow, American College of Foot & Ankle Surgeons
Qualified Medical Examiner, State of California
(QME) # 902342

39 N San Mateo Dr
Suite #4
San Mateo, CA 94401
Tel: 650-343-7775 / Fax: 844-525-1516

Clinical Overview on Helicoll Skin Substitute

"I have many patients who have critical limb threatening wounds and need wound care but I have been holding off on applying skin substitutes, as many of the products contain Elastin which is an extracellular matrix protein. Previously, Elastin was deemed necessary for wound care, as it is a significant constituent of the extracellular matrix of connective tissue in the body; however, Elastin has been found to be carcinogenic as per the recent scientific publication in a reputed journal (Ref.: www.nature.com/articles/s41467-020-18794-x.pdf). This article reassures the fact that Elastin's biodegraded fragments (elastokines/elastomers) are potential carcinogens.

Having my wound care practice for many years, I can be able to well support the above concept, as I have seen several patients develop skin and bone cancers upon my usage of skin substitutes which I now know could be related to the high amounts of Elastin present in such constructs. In good conscience, I can no longer use some of the most popular products derived from amnion and placenta which contain over 40% Elastin.

Possible solution to treat my patients effectively, now I can relate to a successful product with good clinical outcome namely Helicoll, Bioengineered Skin Substitute made of Type-I Collagen without any traces of Elastin. This product provides me an alternative to heal the wounds without inducing an environment that is harmful to my patients.

Besides my private practice, I am using the Helicoll product at different Hospitals and have achieved dramatic clinical results".

Signed
David J. Kaplan, DPM, FACFAS

Helicoll Testimonial

"I'm excited to share a recent success story of one of my patients who avoided amputation of his left

As an expert in wound care, I've used various advanced skin substitutes for my patients, but the recent use of collagen type I grafts called Helicoll Collagen

My patient, a >90-year-old, had a small Achilles tendon exposed wound with mild signs of infection that turned into a disaster last Nov.

Even with his normal arterial Duplex exam, I consulted to vascular team for further evaluation which turned into significantly improved with blood perfusion to increase the chance of wound healing.

Despite repeated wound infections, multiple surgical debridements, and admission for treating MRSA infection, the patient finally started to heal after went thru total of 5x surgical debridement in OR(admission to hospital), Xcell powder, wound vac, Rehabilitation, PICC line -> About 3 months duration total.

I'm thrilled to say that the patient and his family are very happy and grateful that he does not need to lose his limb anymore.

Last photo shows how collagen grafts applied to wound bases and personally, Helicoll Collagen has been instrumental in healing many different kinds of wounds and I am quite satisfied with current result.

I will update more photos once he completely heals "



Ulcer 1 – Before Helicoll



Ulcer 1 – After Helicoll



Ulcer 2 – Before Helicoll



Ulcer 2 – After Helicoll



Ulcer 3 – Before Helicoll



Ulcer 3 – After Helicoll

Dr. Byunghee Kevin Kim, DPM, Podiatric Surgeon

Sacramento Foot & Ankle Center, Sacramento, CA & Sutter Roseville Medical Center, Roseville, CA

FREMONT DERMATOLOGY

DAVID C. GORSULOWSKY, M.D.

MATTHEW H. KANZLER, M.D.

REZA KAFI, M.D..

39210 State Street, Suite 218

Fremont, California 94538

510-790-0477 (phone)

510-790-1835 (fax)

June 17, 2010

To Whom It May Concern:

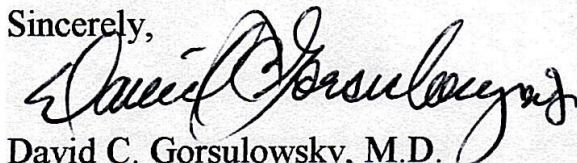
I have had the privilege of using Helicoll on numerous patients with ulcers of the skin. I have consistently found the product to be a help in wound care in these patients.

Specifically, the product has decreased healing time in these patients and afforded quicker return to normal function. In addition, pain relief has been a consistent finding.

In summary, I can recommend Helicoll without reservation for use in appropriate patient wound care.

Please contact me if I may of further assistance.

Sincerely,



David C. Gorsulowsky, M.D.

ACADEMIC AFFILIATIONS OF Dr. David Gorsulowsky:

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Colorado Infectious Disease Associates, LLP

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Fax: 303-777-0786

Email:

www.coloradoinfusion.com

September 26, 2013

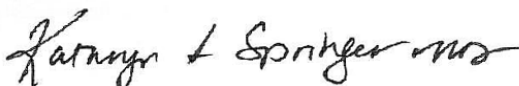
To Whom it May Concern:

I am Dr. Kathryn Springer, an Infectious Diseases physician in Denver, Colorado. I have been the director of Wound Care and of Infection Control at Select Specialty Hospital, Denver South, for 7 years. I have been involved with the care of patients with complicated wounds at Select Specialty Center and at an outpatient wound treatment center for 8 years. I was recently introduced to Helicoll™ and have been using it on many patients with severe wounds for the last 3 months. Helicoll™ is a skin substitute / dermal replacement providing collagen for all phases of wound healing. Helicoll is safe, very affordable, and is highly effective in that it rapidly granulates tissue.

My review of the literature on this product and similar products tells me that Helicoll™ has solid science behind it. It is comprised of full-molecules of phosphorylated Type-I bovine collagen. Helicoll™ is safe and I have not seen any side effects in my patients. Please see <http://mctmedical.com/helicoll-technology/> for more information. It comes in a variety of sizes and is easy to prepare and apply. It has a 3-year-shelf life, making it practical to stock.

I have used Helicoll™ on many types of wounds such as stage 4 pressure ulcers, diabetic foot ulcers, post-surgical wounds, and venous leg ulcers. I have seen granulation tissue form over bone with this product. With Helicoll™, I have seen wounds heal more quickly than with other products that aim to have similar benefits. It is also less expensive than other in-class products. For these reasons, it is currently my collagen-based treatment of choice for complicated wounds.

Sincerely,



Kathryn L. Springer, MD

ROCKY MOUNTAIN PEDIATRIC SURGERY

Saundra M. Kay, MD Steven S. Rothenberg, MD Kristin E. Shipman, MD Bethany J. Slater, MD Anna Cardinell, FNP-BC Alison Covak, PA-C
PediatricSurgeon.com RockyMountainHospitalForChildren.com

10-1-2013

Rocky Mountain Hospital for Children/Presbyterian St. Lukes Medical Center
1719 E. 19th Ave.
Denver, Co 80218

RE: Helicoll™ a type-1 uncross-linked, phosphorylated, acellular dermal matrix

I am writing to you to request that Helicoll™ officially be placed on formulary for HCA Health Care or at least be available as needed for our patients.

I am a pediatric surgeon at the Rocky Mountain Hospital for Children and I was recently introduced to Helicoll™ and have been using it on my patient in the neonatal intensive care for the last few weeks. Helicoll™ is a skin substitute / dermal replacement. It is a safe product, affordable, and is highly effective in that it provides rapid granulation and neovascularization. Helicoll™ has been directly responsible for the most rapid and effective healing of a wound I have witnessed in my career.

The science and safety behind the product is the best in-class, and Helicoll™ directly and actively heals wounds. Helicoll™ brings phosphates to the wound allowing phosphate exchange to occur, which drives balanced wound healing. This allows hemostasis, extra cellular matrix regeneration, and cell signal transduction to occur simultaneously, resulting in very rapid tissue granulation while maintaining the body's natural levels of MMPs. Helicoll™ is also incredibly safe. It has been applied on over 80,000 patients without a single side effect. This is largely due to the matrix of the product being comprised of native, uncross-linked, full-molecules of phosphorylated Type-I bovine collagen. Helicoll™ is the purest and safest product available.

Helicoll™ also healed my patient's wound rapidly.

Considering the benefits of Helicoll™ I expected it to cost much more than other in-class products, but it does not. It comes in sizes from 2 inches by 2 inches up to 8 inches by 8 inches, so I can treat most any size wound on a patient from very small to very large. Helicoll™ is also very easy to prepare and apply, and has a 3 year shelf life at room temperature making it practical to stock.

Most importantly, the results I have witnessed have been nothing short of amazing!

My patient A.W. in the NICU is a little ex-premature baby who after being critically ill, suffered a complete dehiscence of her wound. Because she had stomas on either side, it was particularly difficult

Rocky Mountain Professional Plaza 2055 High Street, Suite 370 Denver, CO 80205 Office 303.839.6001 Fax 303.839.6033



ROCKY MOUNTAIN
HOSPITAL for CHILDREN
A Service of Presbyterian/St. Luke's



to treat. The Helicoll was suggested and it has been amazing. The wound has quickly filled in with healthy tissue, allowing us to finally deal with the baby's other issues.

Please consider placing Helicoll™ on the Presbyterian St. Luke's Medical Center formulary so other patients will benefit the way my patients have benefited from this amazing product.

Sincerely,

A handwritten signature in black ink, appearing to read 'SK', with a horizontal line extending from the bottom left of the signature.

Sandra Kay, MD

Rocky Mountain Pediatric Surgery
2055 High St #370
Denver, CO 80205