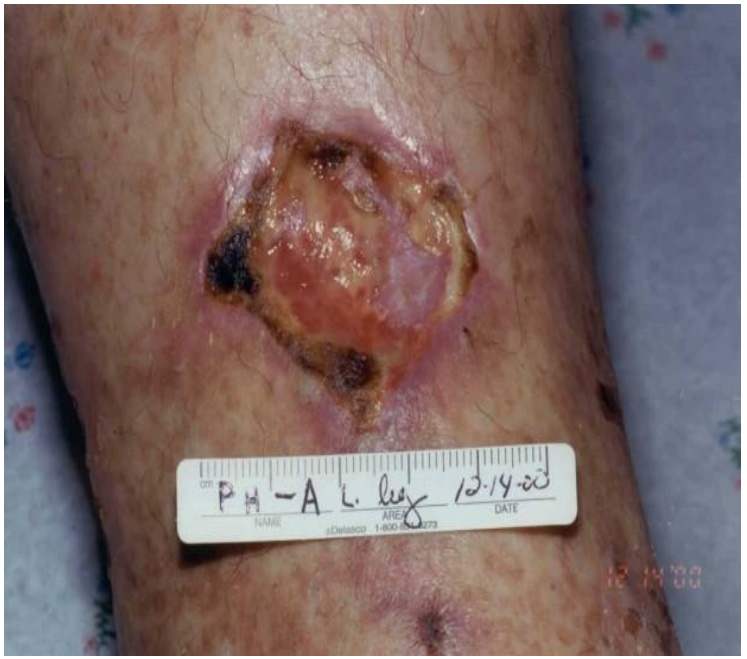
glycobiosciences

IPM™ Wound Gel Bio

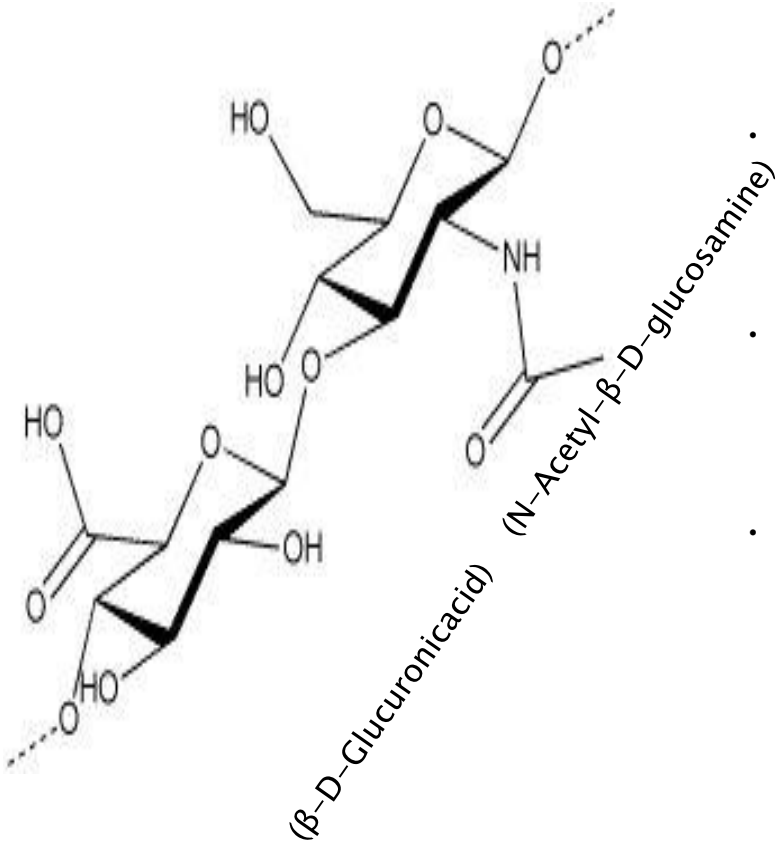
A New High Concentration (2.5%) Hyaluronic Acid (HA) Based Gel Treatment of Chronic Wounds

Part 1 of 3



Chronic wounds: widely considered to be stuck in the inflammatory phase

Hyaluronic Acid (HA)



- **Is a mucopolysaccaride (complex sugar)**
- **Part of therapeutics, food supplements, and cosmetics contain HA (eg. wrinkle creams)**
- **Vital component of extracellular matrix in all vertebrates**
- **The largest amount (50%) resides in the dermis and the epidermis of skin**
- **HA turns over approximately every 12 hours in the skin**
  - **High molecular weight HA is synthesized in the cell membrane and excreted into the extracellular matrix**
  - **Broken down by Hyaluronidase in to the low molecular weight o-HA form**

Meyer K, Palmer JW: The polysaccharide of the vitreous humor. *J. Biol. Chem.* **107**, 629-634, 1934.

J. Chen et al. / Wound Repair and Regeneration 89 (1999) 79–89

Hyaluronic Acid (HA)

Hyaluronic acid also known as sodium hylauronate is a mucopolysaccaride naturally found in healthy tissue as an integral component of the ECM. Extensive research over the past decade has demonstrated that HA is involved in tissue hydration and plays a significant bioactive role in all stages of healing.

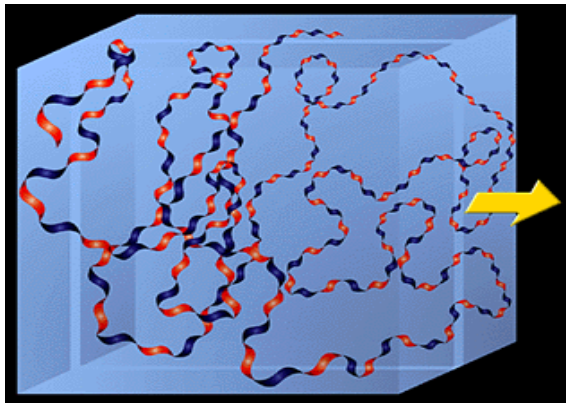
Today there are several medical and cosmetic applications of HA including its use in:

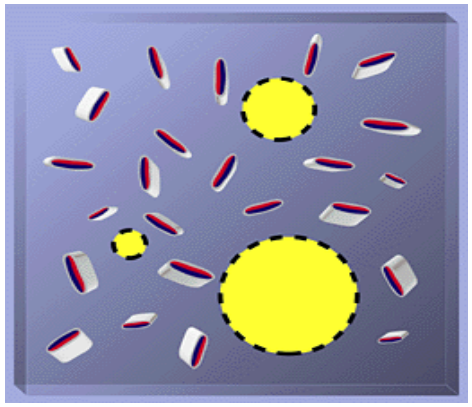
1. Ophthalmic surgery (viscosurgery),
2. Anti aging cosmetic creams and injectables as fillers to diminish wrinkles
3. For intra-articular treatment of arthritis (viscosupplementation)
4. To control postsurgical adhesions and scar formation
5. Tissue repair and hydration for burns and radiation dermititis
6. And for the treatment of chronic wounds such as DFU, VLU and pressure ulcers
7. And in oral supplements

High and Intermediate Molecular Weight HA Plays More of a Mechanical Functional Role in Skin

- HA has been called “natures moisturizer” attracting 3000 times its weight in water, expanding in volume up to 1000 times forming loose hydrated matrices (jello like)
  - Promotes tissue hydration and integrity
  - Creates a scaffolding helping facilitate cell migration and division.

- In the context of chronic wounds:
  - Moisturizing helps facilitate autolytic debridement
  - the HA forms a gel with the wound exudate.





Small molecules diffuse, where larger molecules are partially excluded

J. Chen et al. / Wound Repair and Regeneration 89 (1999) 79–89
I. Anderson The properties of hyaluronan and its role in wound healing The Nursing Times, December, 2001
J. Necas et al. Veterinarni Medicina, 53, 2008 (8): 397–411

Hyaluronan oligosaccharides promote excisional wound healing through enhanced angiogenesis

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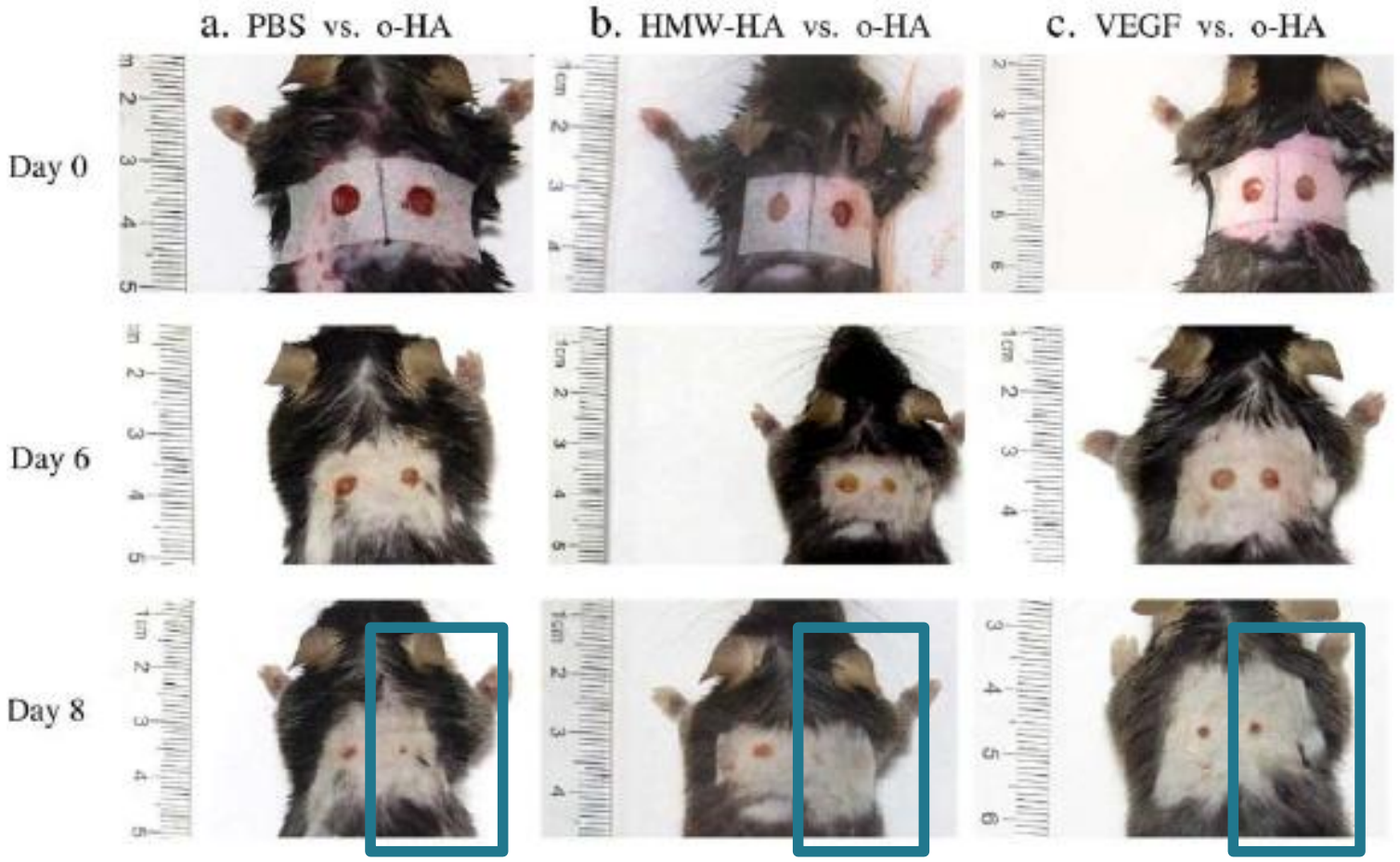


Accelerated healing of acute wounds

F.Gao et al./Matrix Biology 29 (2010) 107-116

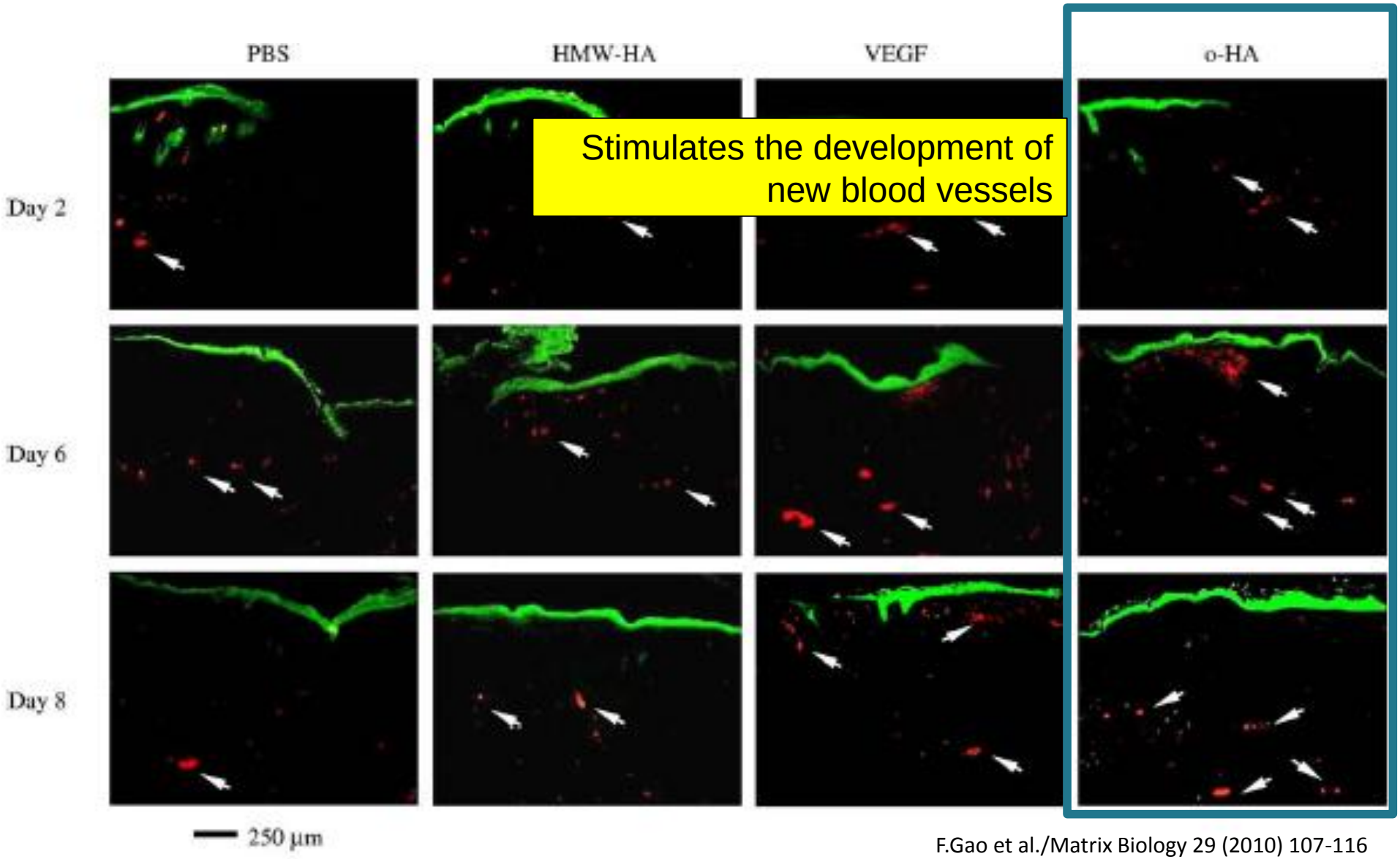
Effects of exogenous o-HA on extracellular matrix mRNA expressions in wound tissues.

	Groups	Day 2	Day 4	Day 6	Day 8
eNOS	PBS	$6.9 \pm 0.61^{\blacktriangle\blacktriangle}$	$7.25 \pm 0.54^{\blacktriangle\blacktriangle}$	6.65 ± 0.52	6.35 ± 0.69
	HMW-HA	$6.1 \pm 0.26^{\blacktriangle *}$	$6.01 \pm 0.38^{\blacktriangle\blacktriangle **}$	5.74 ± 0.48	6.29 ± 0.44
	VEGF	$6.69 \pm 0.41^{\blacktriangle\blacktriangle}$	$6.22 \pm 0.24^{\blacktriangle\blacktriangle **}$	6.79 ± 0.83	6.69 ± 0.11
	o-HA	$5.10 \pm 0.28^{**}$	$4.86 \pm 0.21^{**}$	6.10 ± 0.12	5.94 ± 0.42
E-selectin	PBS	$20.38 \pm 0.32^{\blacktriangle\blacktriangle}$	19.58 ± 1.16	20.3 ± 2.01	15.29 ± 2.22
	HMW-HA	$19.96 \pm 0.55^{\blacktriangle\blacktriangle}$	18.88 ± 0.55	20.75 ± 2.41	15.74 ± 1.42
	VEGF	$18.29 \pm 0.1^{**}$	18.26 ± 1.45	18.58 ± 1.25	15.12 ± 1.33
	o-HA	$17.71 \pm 0.68^{**}$	18.15 ± 1.59	20.37 ± 1.54	15.37 ± 2.43
Integrin-β3	PBS	$17.5 \pm 0.12^{\blacktriangle\blacktriangle}$	$14.26 \pm 0.72^{\blacktriangle}$	17.22 ± 0.78	16.69 ± 1.05
	HMW-HA	$17.19 \pm 0.22^{\blacktriangle\blacktriangle}$	$14.67 \pm 0.03^{\blacktriangle}$	16.68 ± 0.64	16.53 ± 0.83
	VEGF	$15.41 \pm 0.17^{**}$	$12.75 \pm 0.51^{*}$	16.42 ± 1.00	16.34 ± 0.98
	o-HA	$15.58 \pm 0.73^{**}$	$12.74 \pm 0.86^{*}$	16.73 ± 0.65	16.46 ± 1.00
Procollagen-1	PBS	$5.95 \pm 0.21^{\blacktriangle\blacktriangle}$	$(-0.26) \pm 0.78^{\blacktriangle}$	$(-1.87) \pm 0.19$	$(-0.83) \pm 0.48$
	HMW-HA	$4.13 \pm 0.61^{**\blacktriangle\blacktriangle}$	$(-2.96) \pm 0.91^{*}$	$(-1.58) \pm 0.55$	$(-0.35) \pm 0.10$
	VEGF	$2.89 \pm 0.34^{**}$	$(-2.94) \pm 0.71^{*}$	$(-2.59) \pm 0.55$	$(-1.58) \pm 0.79$
	o-HA	$3.18 \pm 0.26^{**}$	$(-3.67) \pm 0.59^{*}$	$(-2.99) \pm 0.42$	$(-1.72) \pm 0.86$
Procollagen-3	PBS	$(-0.74) \pm 0.13$	$(-1.11) \pm 0.28^{\blacktriangle}$	$(-3.49) \pm 0.58^{\blacktriangle\blacktriangle}$	$(-4.56) \pm 0.55$
	HMW-HA	$(-1.11) \pm 0.52$	$(-2.79) \pm 0.21^{**}$	$(-4.71) \pm 0.11^{**}$	$(-4.05) \pm 0.48$
	VEGF	$(-1.43) \pm 0.14^{*}$	$(-1.84) \pm 0.61^{*}$	$(-4.16) \pm 0.57$	$(-3.79) \pm 0.33$
	o-HA	$(-0.44) \pm 0.40$	$(-2.05) \pm 0.23^{**}$	$(-4.78) \pm 0.23^{**}$	$(-3.70) \pm 0.58$
MMP-9	PBS	$9.33 \pm 0.42^{\blacktriangle}$	$6.19 \pm 0.42^{\blacktriangle\blacktriangle}$	6.21 ± 0.85	$5.79 \pm 0.26^{\blacktriangle}$
	HMW-HA				$09 \pm 0.10^{*}$
	VEGF				$12 \pm 0.20^{**\blacktriangle}$
	o-HA				$34 \pm 0.01^{*}$
MMP-13	PBS	$7.76 \pm 0.90^{\blacktriangle\blacktriangle}$	$7.73 \pm 0.98^{\blacktriangle\blacktriangle}$	$5.84 \pm 0.11^{\blacktriangle}$	$6.07 \pm 1.15^{\blacktriangle\blacktriangle}$
	HMW-HA	$8.86 \pm 0.50^{\blacktriangle\blacktriangle}$	$9.07 \pm 0.65^{\blacktriangle\blacktriangle}$	$7.74 \pm 0.12^{**\blacktriangle}$	$11.3 \pm 0.28^{**}$
	VEGF	$9.52 \pm 0.90^{*\blacktriangle\blacktriangle}$	$9.69 \pm 0.24^{*\blacktriangle}$	$8.42 \pm 0.44^{*}$	$9.87 \pm 0.47^{**}$
	o-HA	$12.86 \pm 1.12^{**}$	$11.42 \pm 0.96^{**}$	$9.67 \pm 0.42^{*}$	$9.70 \pm 1.43^{**}$

Moderates inflammation by inhibiting the production of MMPs

Data are means ± SD. Delta Ct is evaluated from various genes between GAPDH. The One-Way ANOVA test is used to compare the mRNA expression of different groups on each time point. Compared with PBS, $^{*}P<0.05$. $^{**}P<0.01$. Compared with o-HA, $^{\blacktriangle}P<0.05$. $^{\blacktriangle\blacktriangle}P<0.01$.

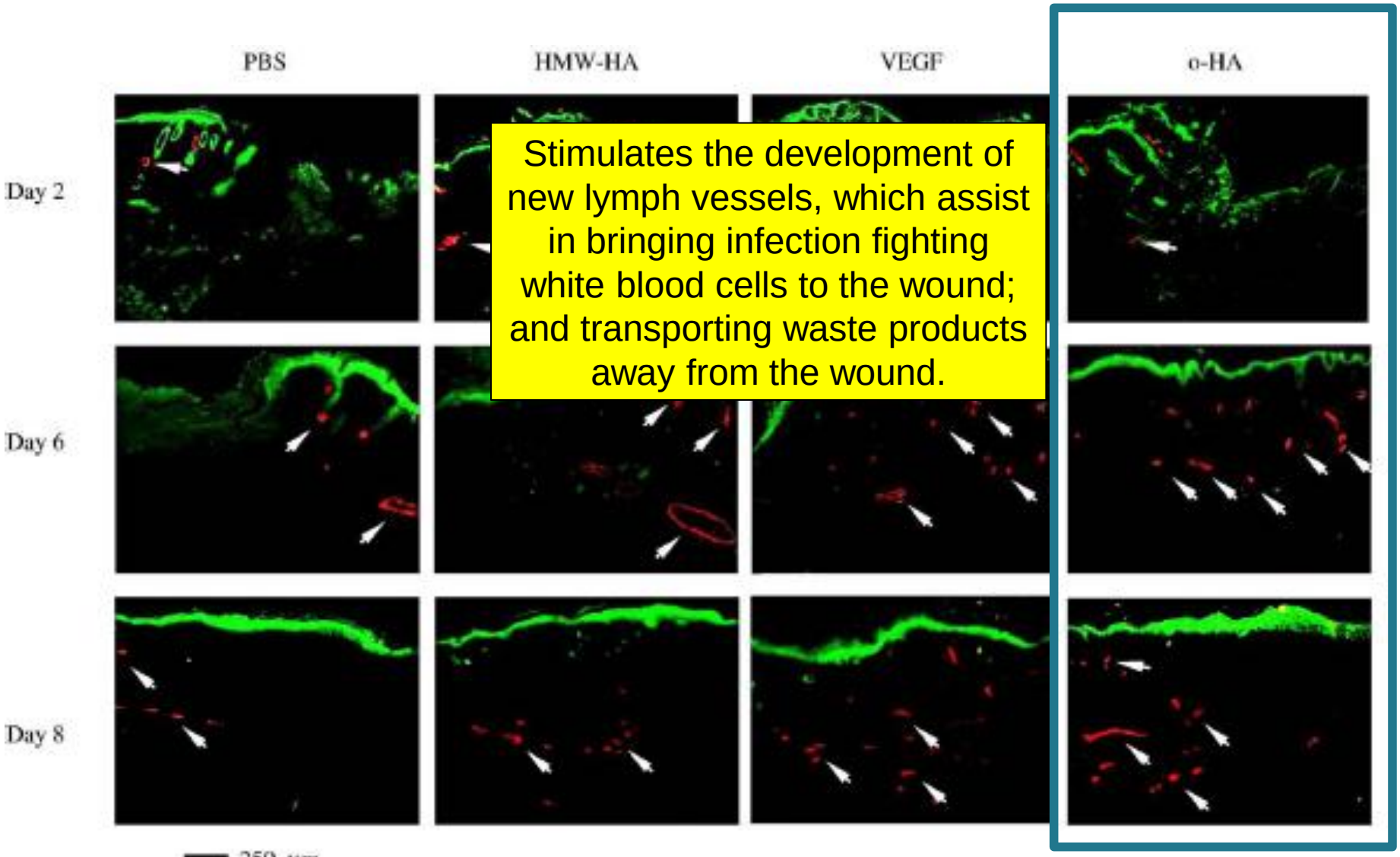
Angiogenesis



Stimulates the development of new blood vessels

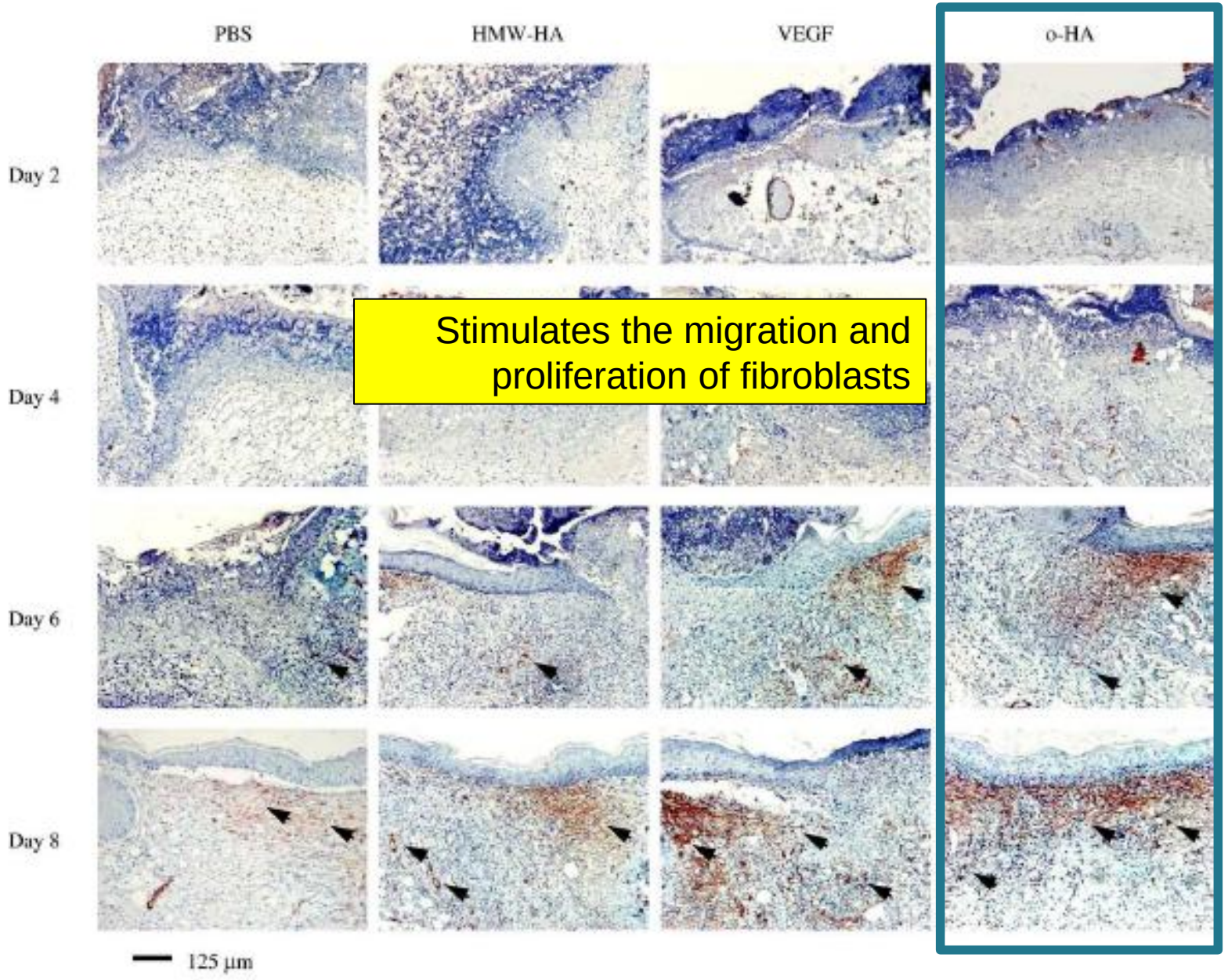
F.Gao et al./Matrix Biology 29 (2010) 107-116

Lymphangiogenesis



Stimulates the development of new lymph vessels, which assist in bringing infection fighting white blood cells to the wound; and transporting waste products away from the wound.

F.Gao et al./Matrix Biology 29 (2010) 107-116



Stimulates the migration and proliferation of fibroblasts

Fig. 6. o-HA stimulates fibroblasts proliferation in wound area of mice. α-smooth muscle actin (α-SMA) immunostaining of sections was performed to detect fibroblasts (arrowed, brown area). The groups are classified by times (days 2, 4, 6 and 8), and each treatment (o-HA, VEGF, HMW-HA and control) was the representative of three mice at each time point. The arrows indicate the positive stain of the fibroblasts. Scale bar is 125 μm and magnification is 20×.

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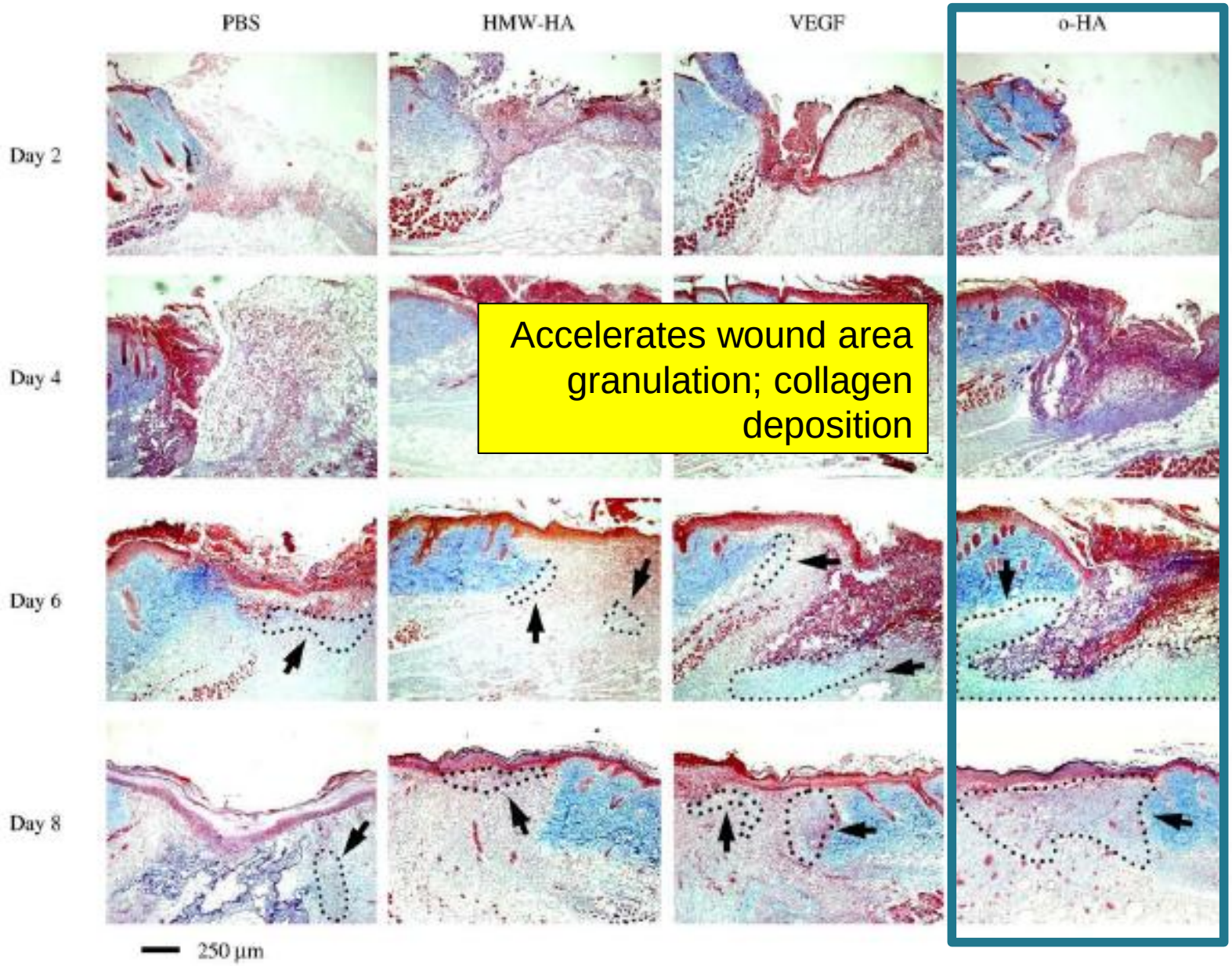

Fig. 5. o-HA accelerates wound area granulation tissue deposition. The arrows and areas within dash lines show the histological evidence of collagen deposition along wounding area. The wounds were harvested from three mice, and photomicrographs represent a typical one. All wounds were stained with Masson-Trichrome, and magnification is 10×. Bar: 250 µm.

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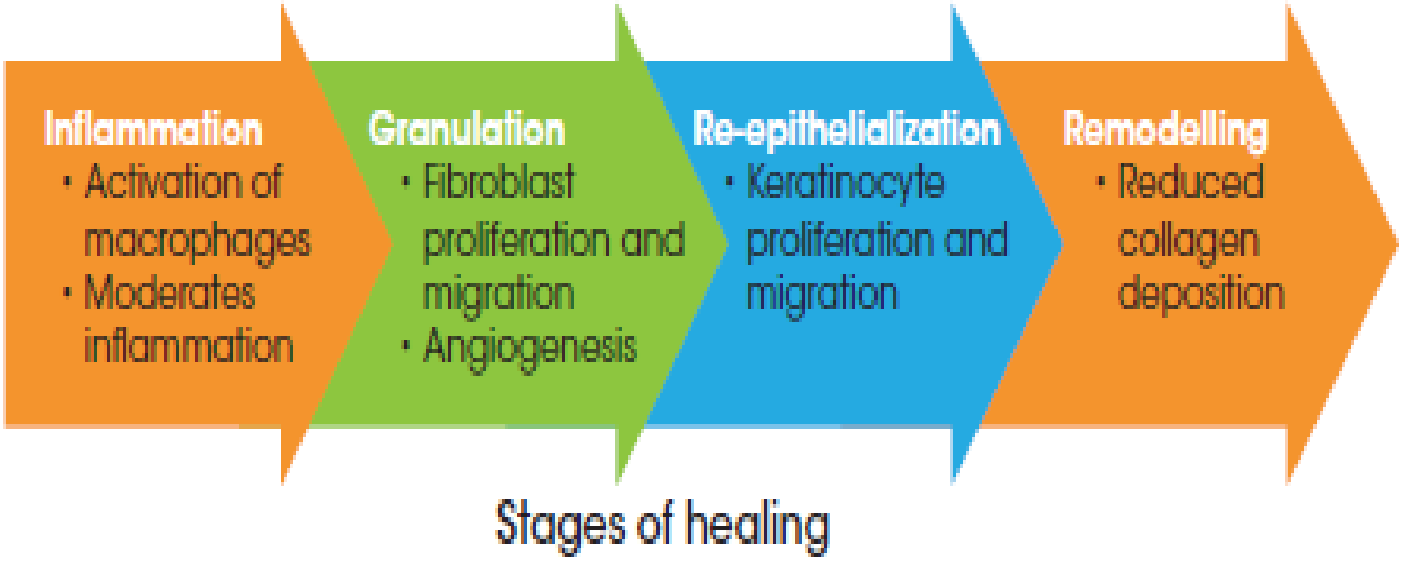
HA Biological Activity Plays a Role in All Stages of Wound Healing



- Hyaluronidase breaks down HA into the Low Molecular Weight HA (o-HA) form and facilitates most of the Biological Activity:
  - Moving wounds out of inflammation by inhibiting the production of MMPs 9 and 13
  - Stimulating vessel formation – angiogenesis and lymphangiogenesis
  - Stimulating Fibroblast and Keratinocyte activity, proliferation and migration

F. Gao et al. / Matrix Biology 29 (2010) 107–116
J. Chen et al. / Wound Repair and Regeneration 89 (1999) 79–89

Stages of healing con'd

Once inflammation begins to recede and Hyaluronidase metabolizes HA into smaller fractions that are more biologically active, the HA attracts fibroblasts to the wound site and provide a matrix to anchor granulation tissue during the proliferative phase of healing. These smaller fractions of HA also stimulate angiogenesis and epithelialization through its effect on MMP and keratinocytes respectively. During the last phase of wound healing, remodeling, HA plays a role in collagen deposition helping to restore the mechanical strength of the skin.

7 Published Controlled Clinical Trials Support HA Effectiveness

Reference	Design (n)	Indication	Outcomes
Edmonds M, Foster A. Hyalofill: a new product for chronic wound management. *The Diabetic Foot* 2000;**3**:29-30	Open randomised parallel comparative study. 30 subjects HA plus standard of care Vs. Standard of care	Diabetic Foot Ulcers Sinuses and bone exposure	Statistically significant difference seen favoring HA group vs. control in healing rate at 12 weeks: 10/15 ulcers healed in HA group vs. three/15 in control ($p < 0.05$).
Taddeucci P, Pianigiani E, Colletta V et al. An evaluation of Hyalofill-F plus compression bandaging in the treatment of chronic venous ulcers. *J Wound Care* 2004;**13**:202-204	Open parallel comparative study. HA Vs Paraffin Gauze 24 subjects: sequential assignment to treatment group	Venous leg ulcer >3 months	HA demonstrated a significant difference in surface area reduction HA: 8.1cm2 (33%) Control: 0.4cm2 (1.8%)
Ortonne JP. A controlled study of the activity of hyaluronic acid in the treatment of venous leg ulcers. *J Dermatol Treatment 1996; 7: 75–81.*	Randomized Comparative trial 50 subjects: HA vs. Dextranomer	Venous leg ulcer >3 months	Surface area (cm2) showed a statistically significant difference in reduction in favor of HA at the end of the 21-day treatment period ($p < 0.05$). HA caused a significant reduction in the incidence and severity of edema ($p < 0.001$) vs. no significant reduction in the SOC group. A significant decrease in the incidence and severity of oozing was seen in the HA group by day 14 ($p < 0.001$). A significant decrease in the incidence and severity of oozing was not seen in the SOC until day 21 ($p < 0.001$).
Mekkes JR, Nahuys M. Induction of granulation tissue formation in chronic wounds by hyaluronic acid. *Wounds 2001; 13: 159–64.*	Ten consecutive patients, Non-healing ulcer caused by venous insufficiency (n = 8) or vasculitis (n = 2) had one side of their wound treated with HA vs. IntraSite Gel in a randomized fashion.	Venous and vascular leg ulcers	Time to grafting was reduced by 29% with HA ($p = 0.004$). Total time to healing was reduced by 31% with HA ($p = 0.0003$).
Abbruzzese L et al. Effectiveness and safety of a novel gel dressing in the management of neuropathic leg ulcers in diabetic patients: a prospective double-blind randomized trial. *Int J Low Extrem Wounds 2009; 8:134–40.*	Prospective double-blind randomized trial HA Vs Inert gel; 30 diabetic subjects	Neuropathic leg ulcers	Ulcer area significantly reduced in the HA group over a 4-week period vs. control ($p < 0.05$; –58.7% vs. –23.4%, respectively). Percentage of lesional area covered by granulation at 4 weeks was significantly higher in HA group than control (62.8 14.7% vs. 28.3 10.2%, $p < 0.01$).

7 Published Controlled Clinical Trials Support HA Effectiveness

Reference	Design (n)	Indication	Outcomes
Humbert et al. Efficacy and safety of a gauze pad containing Hyaluronic acid in treatment of leg ulcers of venous or mixed origin: a double-blind, randomized, controlled trial. *Int Wound Care 2012: 1-10*	Prospective randomized multicentre double blind controlled trial HA plus standard of care Vs. Placebo Standard of care 89 subjects Patients suspected of having a local or systemic infection were excluded	Venous or mixed arterial venous origin present for >2 months	Trial terminated early: no longer ethical to keep patients on placebo At day 45, the percentage of ulcer surface reduction was significantly greater in the HA group (73 4·6%) versus neutral vehicle group (46 9·6%) (P = 0·011). The number of healed ulcers was significantly higher in the HA group at day 45 (31·1% versus 9·3% respectively) and day 60 (37·8% versus 16·3% respectively; P < 0·05). At day 30, pain intensity based on visual analogue scale was significantly lower in the HA group (12·4 mm 2·6 versus 22·8 mm 3·8; P = 0·026).
Dereure et al. Efficacy and safety of hyaluronic acid cream in treatment of leg ulcers:a double-blind RCT *Journal of Wound Care vol 21, March 2012 3:131-139*	Prospective randomized multicentre double blind controlled trial HA plus standard of care Vs. Placebo Standard of care 101 subjects Patients suspected of having a local or systemic infection were excluded	Venous or mixed arterial venous origin present for >2 months	Trial terminated early: no longer ethical to keep patients on placebo. At day 45, the percentage of ulcer surface reduction was significantly greater in the hyaluronic acid treatment group (39 6%) compared with the neutral vehicle (control) group (5 9%) (p=0.002). A similar result was obtained at day 15, day 30 and day 60. From day 0 to day 45, pain intensity (VA S) decreased by mean 9.8 3.5mm in the hyaluronic acid group, but slightly increased by 0.8 3.2mm in the control group (p=0.029). Burden of pain, as estimated by the area under the curve of daily pain (from day 0 to day 60), was significantly lower in the hyaluronic acid group (121.9 20.7mm2) than in the control group (207.4 32.9mm2; p=0.028).

HA derivatives

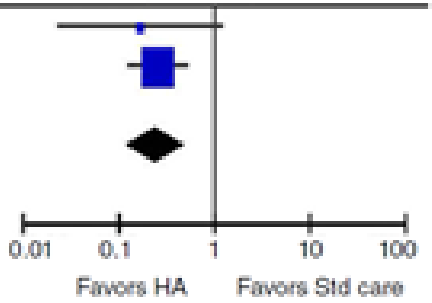
Hyaluronic acid derivatives and their healing effect on burns, epithelial surgical wounds, and chronic wounds: A systematic review and meta-analysis of randomized controlled trials

Significant results: diabetic neuropathic ulcers—number of nonhealed ulcers in each group at 12 weeks.

	HA derivative		Standard of care			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Abbruzzese 2009	1	15	6	15	11.9%	0.17 [0.02, 1.22]	
Edmonds 2000	6	28	20	24	88.1%	0.26 [0.12, 0.53]	
Total (95% CI)		43		39	100.0%	0.24 [0.12, 0.49]	
Total events	7		26				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.17$, $df = 1$ ($p = 0.68$); $I^2 = 0\%$

Test for overall effect: $Z = 4.02$ ($p < 0.0001$)

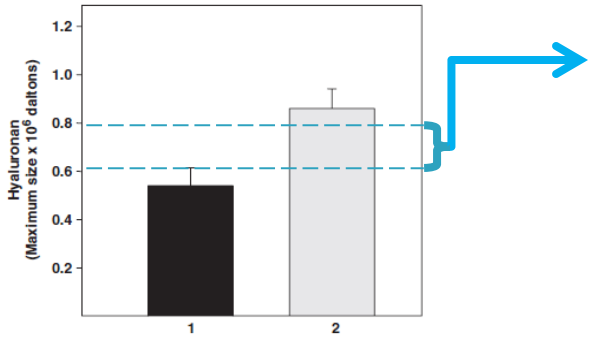


Voigt & Driver: Wound Rep Reg (2012) 20 317–331 © 2012 by the Wound Healing Society

IPM™ Wound Gel Bio features

Part 2 of 3

- 2.5% HA – 10x the concentration of other gels
- Ionic Polymer Matrix (IPM) – Hydroxyethycellulose – Provides Sustained Release Delivery



HA in IPM™ Wound Gel Bio is 600,000–750,000 Daltons – similar intermediate molecular weight as the native HA, synthesized in treated, healing chronic wounds

FDA, 510K IPM Wound Gel 2002

The maximum size of HA from pressure ulcers was compared before and after receiving standard wound care for 90 days. Maximum HA sizes increased in six of eight subjects analyzed (540,000 Da initially to 860,000 Da; $p < 0.03$ paired t-test).

T. Dechert et al. Wound Rep Reg (2006) **14** 252–258 the Wound Healing Society

Proposed Mechanism of Action:

How does IPM™ Wound Gel Bio Kick-Start Healing?

Normally Healing Acute Wounds

(10 Healthy Volunteers)

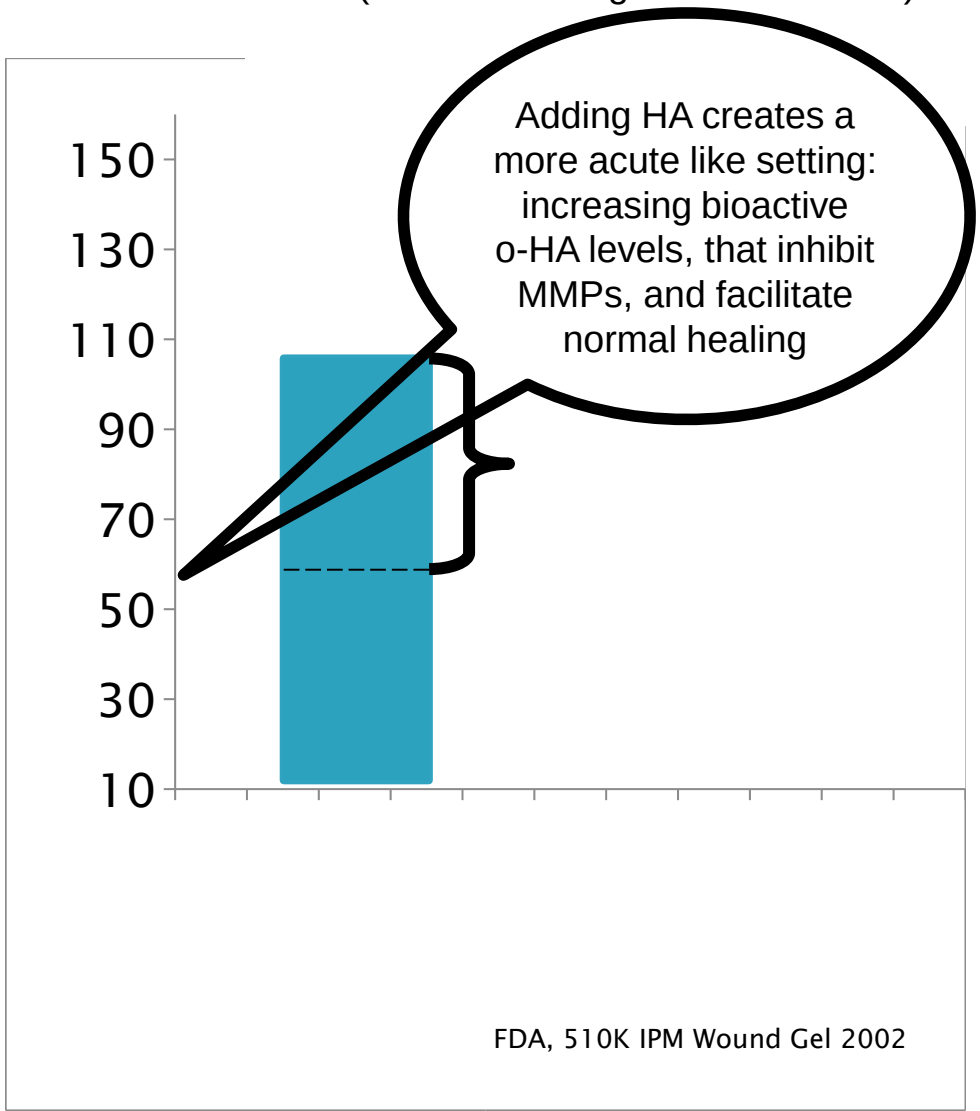
High molecular weight HA cleaved by hyaluronidase increases bioactive o-HA levels facilitating healing

In normal healing acute wounds HA levels rise. Hyaluronidse then cleaves the newly synthesized HA into smaller more biologically active fragments facilitating healing in all phases..

In contrast to normally healing wounds chronic stalled wounds exhibit lower levels of HA and high levels of Hyalurinadase. Adding exogenous HA helps to create the biochemical environment of a normally healing wound by increasing the levels of bioactive fragments of HA inhibiting MMPs and progressing a wound onto granulation and thru all the phases of healing.

Chronic Stalled Wound

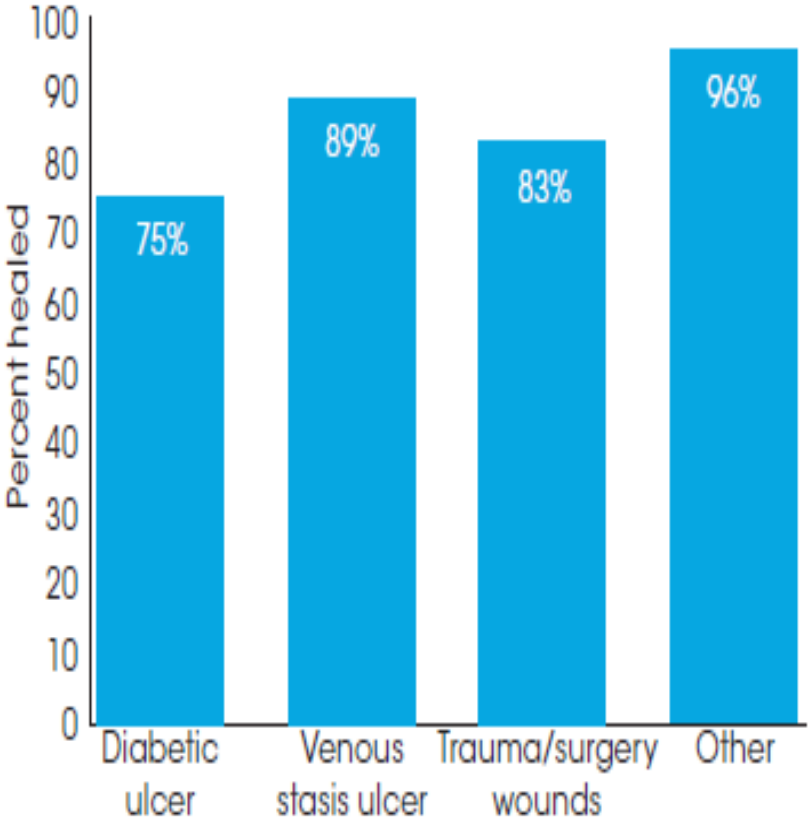
(10 Non-Healing Pressure Ulcers)



FDA, 510K IPM Wound Gel 2002

Adapted from T. Dechert et al. Wound Rep Reg (2006) **14** 252-258 the Wound Healing Society

IPM™ Wound Gel Bio: Accelerates Healing In Difficult To Treat Wounds



Included 50 ulcers of various etiology

Prior to IPM™ Wound Gel

- Average duration of ulcer: 25 weeks
- Failed standard of care and advanced therapies

After IPM™ Wound Gel:

- 88% of wounds healed
- Median time healing: 8.2 weeks
- No discontinuations due to side effects

FDA, 510K IPM Wound Gel 2002

Sub-Analysis
Once Weekly Administration

A sub analysis demonstrated comparable healing rates
for ulcers treated once weekly versus daily.
Over 80% of ulcers completed healed
with once weekly application of IPM™ Wound Gel.

Median healing time = 11.5 weeks
Average healing time = 12 weeks

FDA, 510K IPM Wound Gel 2002

Longer wear times:
Daily to Weekly Application

Effect of a once-weekly application of 2.5% sodium hyaluronate gel
for healing chronic wounds (poster presented at CAWC 2013)
Patricia Coutts RN, IIWCC ,
Laurie Goodman RN, BA, MHScN and
R. Gary Sibbald BSc, MD, M.Ed, FRCPC(Med), FRCPC (Derm), MACP, FAAD, MAPWCA

Level of evidence supporting HA effectiveness is extremely high

- IPM™ Wound Gel clinical efficacy was demonstrated with a study by Dr. Reece et al in 50 difficult to treat ulcers. The mean duration of these non healing ulcers that were proven recalcitrant to the standard of care and advanced therapies was 25 weeks.
- 88% of ulcers healed with IPM™ Wound Gel treatment. The median time to healing was 8.2 weeks.
- IPM™ Wound Gel was extremely well tolerated with no discontinuations due to adverse events.

Patients suspected of having a local or systemic infection were excluded from Dr. Ronald Reece study.
HA is not strongly antimicrobial.

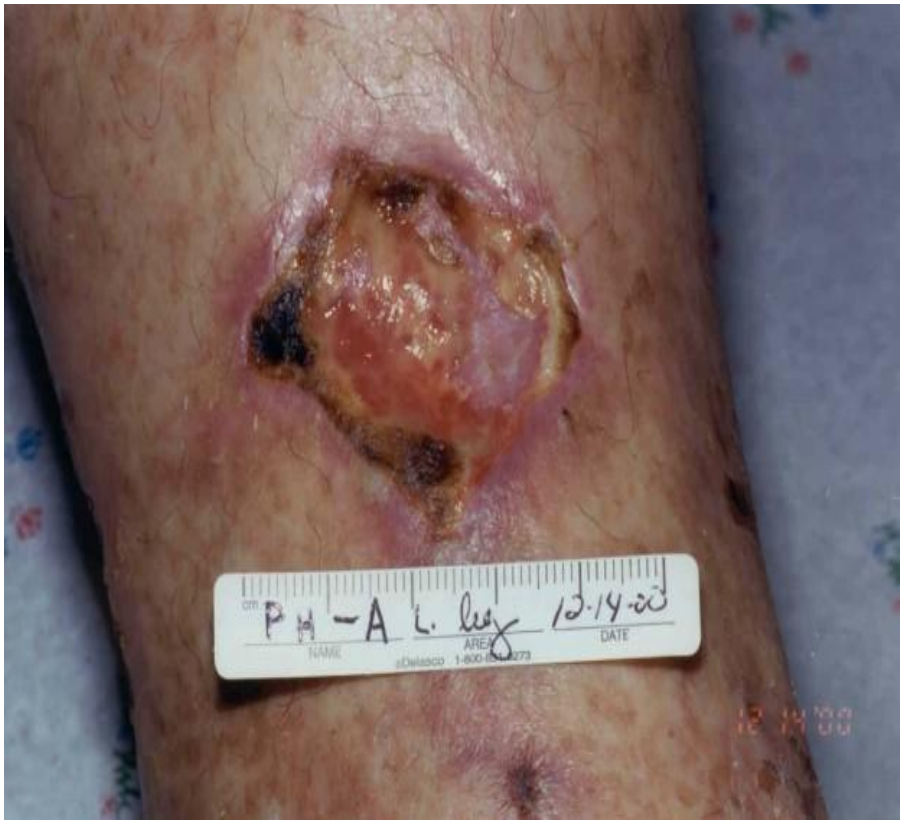
Why is HA not widely used to treat wounds?

Availability & Short Acting: <u>many applied daily</u>

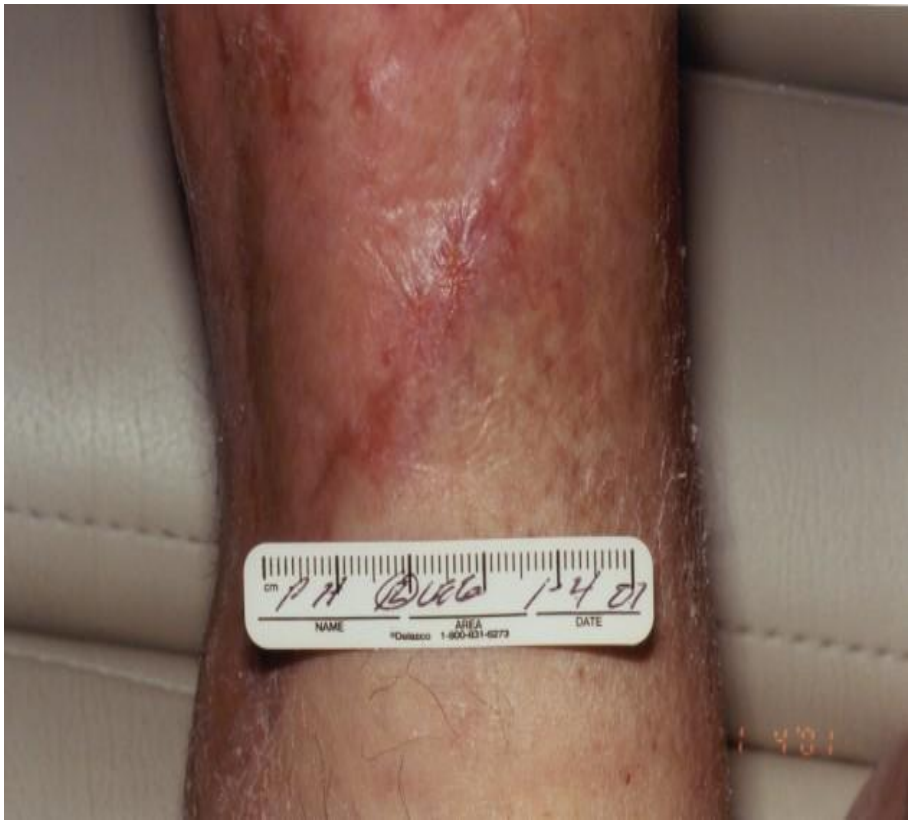
These Issues are now resolved with the introduction of IPM™ Wound Gel Bio in Canada
Up to once weekly application

Leg Ulcer

Day 0

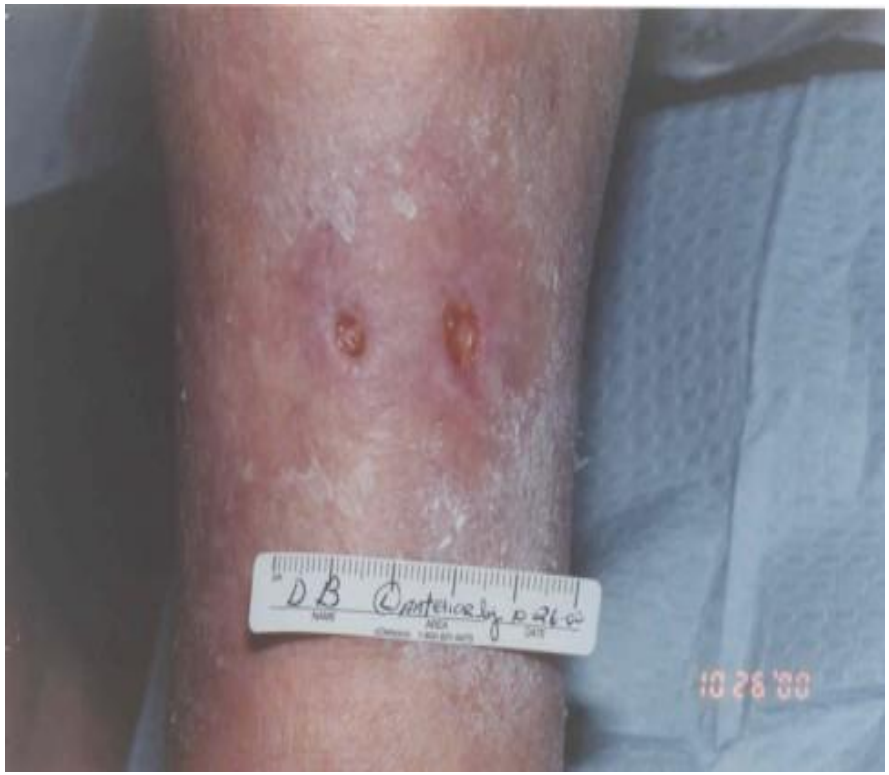


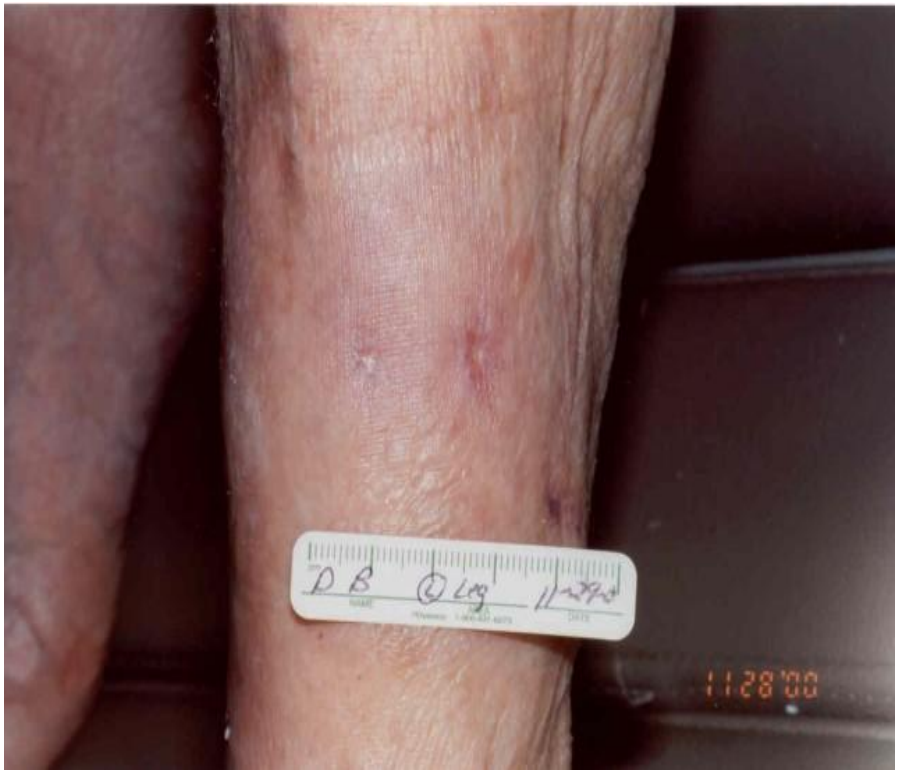
Day 33



Stasis Ulcer – 34 days

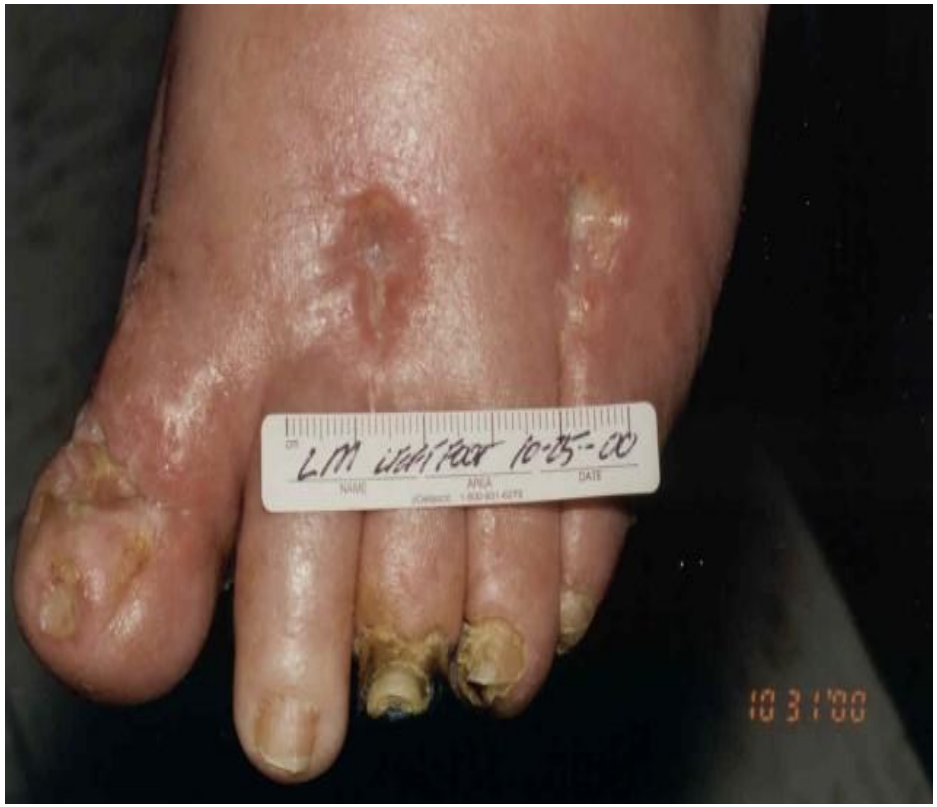
October 26, 2000 November 29, 2000



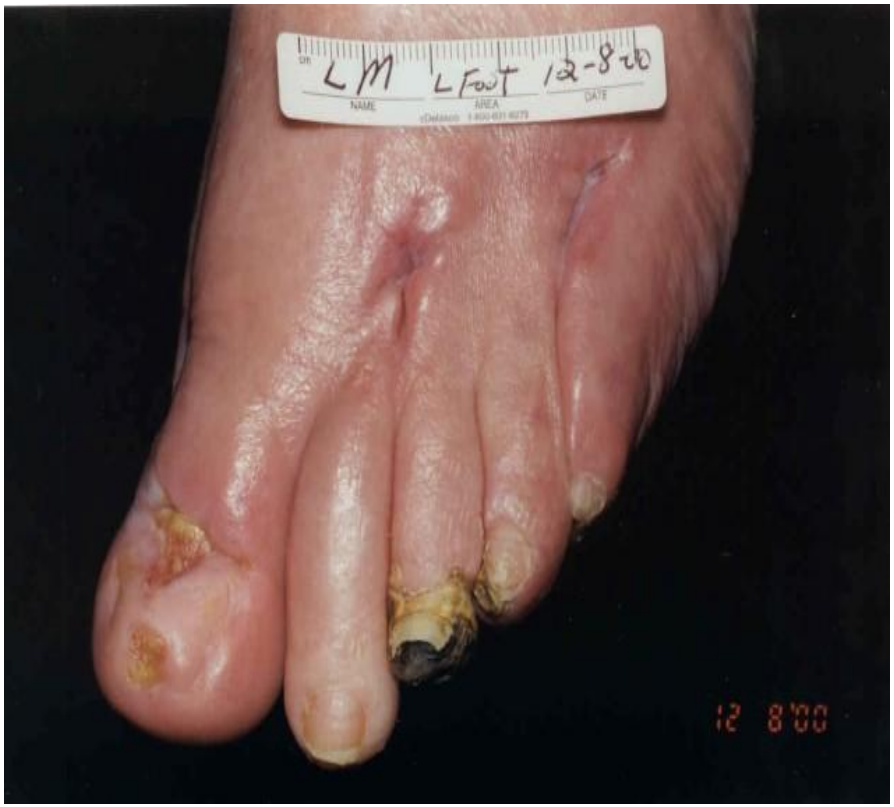


Rheumatoid Ulcer – 64 days

October 5, 2000

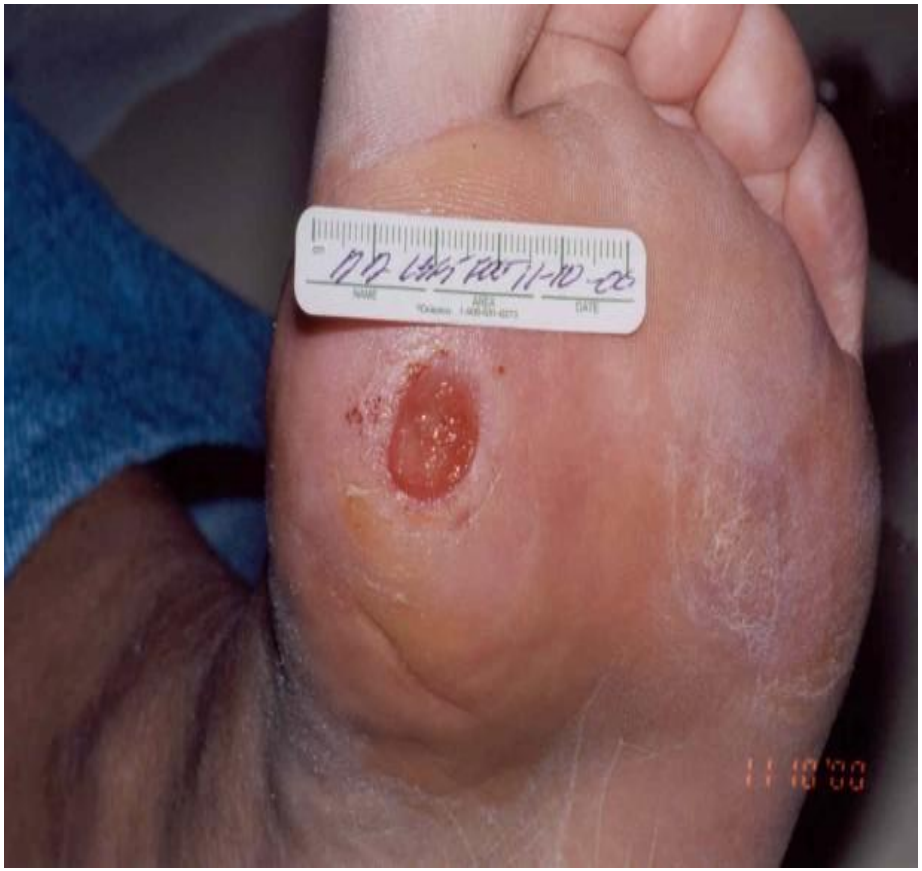


December 8, 2000

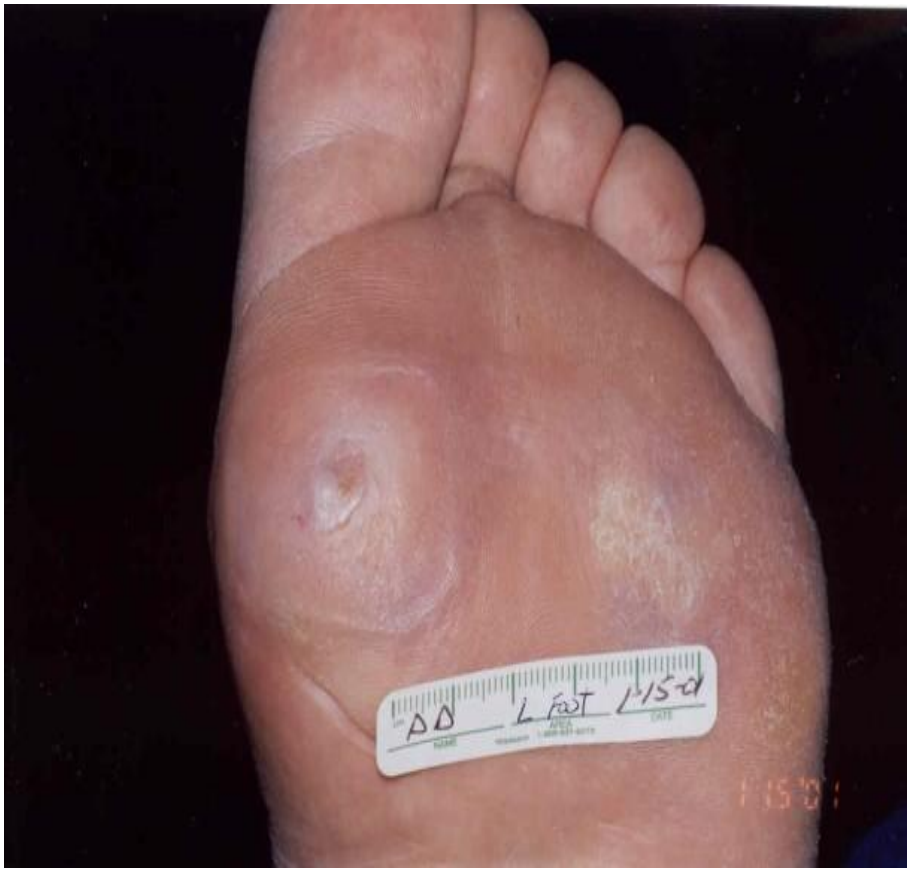


Diabetic ulcer – 66 days

November 10, 2000



January 15, 2001



78% of Patients responded that the gel made their ulcer(s) feel better

Our study corroborates the findings of several large scale randomized controlled multicentred studies that HA not only accelerates healing but also improves patient comfort by alleviating pain and soothing sore ulcers upon application.

FDA, 510K IPM Wound Gel 2002

IPM™ Wound Gel Bio

A New High Concentration Hyaluronic Acid (HA) Based Gel Treatment of Chronic Wounds

- Chronic wounds are HA depleted relative to normal healing acute wounds

- HA plays a functional role in all phases of healing
  - High molecular weight HA contributes more physical functionality, like tissue hydration, and scaffolding allowing for cell migration, and hydration
  - Low molecular weight o-HA is highly effective in moderating inflammation, stimulating angiogenesis, and granulation tissue formation

- The level of evidence supporting the application of exogenous HA as a class is strong: 6 Randomized, Prospective, Placebo Controlled trials including Diabetic and Venous ulcers:
  - Increases in healing rates: wound size decreases, and increases in total patients healed
  - Reductions in pain
- IPM™ Wound Gel demonstrated similar results in a study of 50 ulcers:
  - 88% of ulcers fully healing including venous, diabetic, pressure and other types
  - The average duration of ulcer prior to enrollment was 25 weeks
  - There were no discontinuations due to adverse events
  - Increase in patient comfort
- IPM™ Wound Gel Bio is a unique HA formulation within the class, providing a more sustained release of HA, increasing the concentration of both forms of HA, and allowing for daily to once/weekly application

•Applying IPM™ Wound Gel Bio

•**Part 3 of 3**

Practical Considerations For Using IPM™ Wound Gel Bio as a Tool for Treating Chronic Wounds

Eric Degen
PHD Biochemistry
Medical Doctor

General Treatment Guidance for Chronic Wounds and IPM™ Wound Gel Bio

- "*Treat the whole patient, not the hole in the patient*",

  Dr. Gary Sibbald

- Manage the underlying cause as the priority and then focus on the wound itself
  - IPM™ Wound Gel has demonstrated effectiveness in conjunction with off-loading in diabetic foot ulcers, and compression for venous ulcers

- Determine if the wound is healable or not
  - IPM™ Wound Gel Bio should be used in healable wounds
  - Treat non-healable maintenance wounds accordingly, not with IPM™ Wound Gel Bio

- Debridement considerations – removal of slough and necrotic tissue may decrease infection risk, and improve healing rates
  - Choose the type of debridement that best suites the situation
  - IPM™ Wound Gel Bio in addition to it's bioactivity, can help facilitate autolytic debridement as the hyaluronic acid is significantly hydrating and the water in the gel adds moisture

Practical Considerations

- Primary Treatment for Dry to moderate exudative clean wounds
  - When initiating, apply IPM™ Wound Gel Bio 3 times/week for the first two weeks
  - If the wound is healing well at that point, dressing wear times can be extended as long as healing continues at the same rate
  - IPM™ Wound Gel Bio can help facilitate autolytic debridement as the hyaluronic acid is significantly hydrating and the water in the gel adds moisture

- Highly Exudative, and Infected Wounds – Adjunctive Therapy
  - IPM™ Wound Gel Bio is not antimicrobial, and should not be used as a primary treatment of infection
  - If a biofilm is confirmed or suspected, remove it by using a wound cleanser (for example iodine, PHMB, honey) or a more aggressive debridement technique before applying IPM™ Wound Gel Bio
  - IPM™ Wound Gel Bio can be used adjunctively with antimicrobial non-stick secondary dressings (for example silver, PHMB, or iodine impregnated dressings)
  - For more guidance on managing infection consult the DIME article: Increased Bacterial Burden and Infection: The Story of Nerds and Stones by Dr. Gary Sibbald et al.

IPM™ Wound Gel Bio Use and Application

- IPM™ Wound Gel Bio is indicated and a suitable choice for a variety of chronic healable wounds
  - venous, arterial, diabetic, surgical, trauma, and burns
- Apply IPM™ Wound Gel Bio directly to the wound and cover the wound with any type of non-stick secondary dressing
  - Use a sterile applicator of your choice – wooden depressor for example
  - Apply the gel to the thickness of two loonies and fill cavities if appropriate
  - Apply the gel to skin immediately around the wound
  - Can be applied to a secondary dressing, which is then applied to the wound and gently matted with gloved hand, to make sure the gel is in the wound
- IPM™ Wound Gel Bio can be applied with dressing changes at frequency of daily to weekly
  - Higher frequency may increase efficacy and ought to be considered during treatment initiation
    - Suggest 3 times per week for the first two weeks
  - If the wound is not healing well, after 2 weeks determine why and adjust treatment plan accordingly (some common reasons: underlying cause, patient adherence, infection)
  - If the wound is healing well, consider extending dressing wear times up to once per week if appropriate

Practical Considerations – Formats and Choice

IPM™ WOUND GEL BIO IS SUPPLIED

- In a Box containing four 10g tubes

RECOMMENDATIONS:

- To prevent cross infection, a tube should be used with one patient only. As long as aseptic technique, with appropriate storage can be maintained, recapping of the tubes can be recommended. When using the 10g tubes, it may be a consideration to discard the remaining contents of the tube after application to further reduce contamination and infection risk.

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IPM™ Wound Gel Bio

Cost comparison per chronic wound treated vs. Promogran and Iodosorb

There are two wound sizes compared, 5 cm^2 and 10 cm^2

Total cost of treatment includes price of the products and nursing cost to administer them

Discounted IPM™ Wound Gel Bio Vs. Discounted Promogran & Iodosorb

Cost Comparison Assuming a 5 cm^2 Wound, Healing in 12 Weeks, used as directed, healing 30% every 4 weeks

Brand	Category	Packaging Format	Cost per unit	Cost per application 10 cm2 wound	Labelled Dressing wear time	Number of applications and Nursing costs at $50 per visit	Product cost for 12 weeks	Total Cost Nursing Plus Product
IPM™ Wound Gel Bio*	Bioactive HA Inhibits MMPs, angiogenesis, granulation	4x10g tubes	$30 per tube	$15	Higher frequency at initiation and then up to 7 days	16 applications $800	$240 assuming 3 applications for weeks 1&2, and 1/week thereafter	$1040
Promogran	Collagen MMP neutralizer	10x11 cm sheet	$15 per sheet	$15	3 days	28 applications $1400	$420	$1820
IodosorbΦ	Antibacterial Wound cleanser	4x10g tubes	$16 per tube	$16	3 times per week	36 applications $1800	$576	$2376

*Product leaflet recommends recapping as long as aseptic handling is maintained – 2 applications/tube
Φ Product leaflet recommends discarding tube after opening, therefore tubes are single application

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5 cm² wounds

Savings Relative to Promogran

Product cost savings: $420 - $240 = $180 or 43%
Nursing time savings $1400-$800 = $600 or 42%
(16 vs 28 applications)

Total savings: $1820-$1040 = $780 or 43%
OR
$780K For Every 1000 Ulcers Treated

Additional nursing time saved per application not included: Promogran needs to be cut into the shape and size of the wound. The gel is easier to apply taking less time.

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5 cm² wounds

Savings Relative to Iodosorb

Product cost savings: $576-$240 = $333 or 58%
Nursing time savings $1800-$800 =$1000 or 56%
(16 vs 36 applications)

Total savings: $2376-$1040 = $1336 or 56%
OR
$1.3M For Every 1000 Ulcers Treated

Discounted IPM™ Wound Gel Bio Vs. Discounted Promogran & Iodosorb

Cost Comparison Assuming a 10 cm^2 Wound, Healing in 12 Weeks, used as directed, healing 30% every 4 weeks

Brand	Category	Packaging Format	Cost per unit	Cost per application 10 cm2 wound	Labelled Dressing wear time	Number of applications and Nursing costs at $50 per visit	Product cost for 12 weeks	Total Cost Nursing Plus Product
IPM™ Wound Gel Bio*	Bioactive HA Inhibits MMPs, angiogenesis, granulation	4x10g tubes	$30 per tube	$20	Higher frequency at initiation and then up to 7 days	16 applications $800	$320 assuming 3 applications for weeks 1&2, and 1/week thereafter	$1120
Promogran	Collagen MMP neutralizer	10x11 cm sheet	$15 per sheet	$15	3 days	28 applications $1400	$420	$1820
IodosorbΦ	Antibacterial Wound cleanser	4x10g tubes	$16 per tube	$16	3 times per week	36 applications $1800	$576	$2376

*Product leaflet recommends recapping as long as aseptic handling is maintained – 2 applications/tube
Φ Product leaflet recommends discarding tube after opening, therefore tubes are single application

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10 cm² wounds

Savings Relative to Promogran

Product cost savings: $420 - $320 = $100 or 24%
Nursing time savings $1400-$800 = $600 or 42%
(16 vs 28 applications)

Total savings: $1820-$1120 = $700 or 38%
OR
$700K For Every 1000 Ulcers Treated

Additional nursing time saved per application not included: Promogran needs to be cut into the shape and size of the wound. The gel is easier to apply taking less time.

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10 cm² wounds

Savings Relative to Iodosorb

Product cost savings: $576-$320 = $256 or 44%
Nursing time savings $1800-$800 =$1000 or 56%
(16 vs 36 applications)

Total savings: $2376-$1120 = $1256 or 53%
OR
$1.25M For Every 1000 Ulcers Treated

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IPM™ Wound Gel Bio

Using IPM™ Wound Gel Bio is cost effective vs both Iodosorb and Promogran in both product and nursing time costs

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IPM™ Wound Gel Bio

- Effective, safe, and easy to apply
- Clients find is soothing on application
- Cost effective vs alternatives
- Less expensive as far as nursing times go resulting in significant savings