Vein Disorders Overview
Randomised, double blind, multicentre, placebo controlled study of sulodexide in the treatment of venous leg ulcers. The SUAVIS trial.

Coccheri and an Italian Collaborative Group

**SUAVIS** = **SULODEXIDE ARTERIAL VENOUS ITALIAN STUDY**
**Study design**

**DRUG**
- Sulodexide+ local therapy
  - 120 patients

**PATIENTS**
- Placebo+ local therapy
  - 110 patients

**SCHEME**
- 600 LSU: 120 days
- 500 LSU: 20 days
- 1 inj x 1
- 2 cps x 2

**OUTCOMES**
- Primary end-point: Complete ulcer healing at 2 months
- Secondary end-point: Complete ulcer healing at 3 mnts

**LOCAL THERAPY**
- Cleansing, detergents of ulcers, application of proteolytic enzymes
- Bandaging according to the local condition and patient’s compliance

**OUTCOMES**
- Leg ulcers greater than 2 cm
- Chronic venous insufficiency
- Multicenter, randomized, double-blind

**On top of compressive therapy**

_Coccheri Thromb Haemost 2002_
Results

% difference in ulcer healing

NNT = 7

NNT = 5

Placebo + local treatment

Sulodexide + local treatment

Coccheri Thromb Haemost 2002
Randomised, Double Blind, Multicentre, Placebo Controlled Study of Sulodexide in the Treatment of Venous Leg Ulcers

Sergio Coccheri¹, Gaetano Scondotto², Giancarlo Agnelli³, Daniele Aloisi², Ernesto Palazzini⁴, Villiam Zamboni⁴

for the venous arm of the SUAVIS (Sulodexide Arterial Venous Italian Study) Group

¹Department of Angiology and Blood Coagulation, University Hospital S. Orsola-Malpighi, Bologna, Italy
²AUDL Bologna City, Angiology Service and Day Hospital "Mengoli", Bologna, Italy
³Department of Internal Medicine, Division of Internal and Cardiovascular Medicine, University of Perugia, Italy
⁴Medical Department, Alfa Wassermann, Bologna, Italy
## Sellogram sulodexide in treatment of venous leg ulcer

<table>
<thead>
<tr>
<th>Features</th>
<th>Advantages (in comparison to competitors)</th>
<th>Patient Benefits</th>
<th>Doctor Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two formulation available</td>
<td>Active after parental and oral administration</td>
<td>Better recovery</td>
<td>Flexibility to use</td>
</tr>
<tr>
<td>GAG Inhibiting leukocyte-platelet activation, with antithrombotic properties by inhibiting both factor Xa and thrombin, profibrinolytic by activating tissue plasminogen activator and fibrinogen lowering activities</td>
<td>Benefits on capillary permeability by modulating endothelial function, microthrombi formation and accumulation of pericapillary fibrin and other proteins</td>
<td>Reduction of treatment cost</td>
<td>Obtain more frequent and faster ulcer healing in addition to local treatment</td>
</tr>
<tr>
<td>Highly purified glycosaminoglycan</td>
<td>Rare and non significant side effects</td>
<td>Safety intake</td>
<td>No constraints during treatment course</td>
</tr>
</tbody>
</table>
Treatment of venous leg ulcers with sulodexide

Kucharzewski M, Franek A, Koziol H

Phlebologie (2003)
Study design

**DRUG**
- Sulodexide + Unna Booth

**PATIENTS**
- 21
- 23

**SCHEME**
- 600 LSU
  - 20 days
- 500 LSU x 2
  - Until ulcer healing

**OUTCOMES**
- Primary end-point: Time to ulcer healing

Diagnosis of venous ulcers by Doppler sonography
Dress changed every 7 days until ulcer healing
All patients has previously been treated by traditional methods
Results

Surface - Time Ratio

- Unna’s boot + occlusive dressing
- Unna’s boot + occlusive dressing + sulodexide
Treatment of venous leg ulcers with sulodexide

M. Kucharzewski\textsuperscript{1}, A. Franek\textsuperscript{2}, H. Koziółek\textsuperscript{1}

\textsuperscript{1}Department of General Surgery (Head: Prof. Dr. med. A. Podwiński), Silesian Medical Academy, Bytom, \textsuperscript{2}Department of Medical Biophysics (Head: Prof. Dr. med. A. Franek), Silesian Medical Academy, Katowice, Poland
## Sellogram Treatment of venous leg ulcer with Sulodexide

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<th>Doctor Benefits</th>
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</thead>
<tbody>
<tr>
<td>Glycosaminoglycan with high affinity for antithrombin III and for heparin cofactor 2</td>
<td>Acceleration of the healing process by improving microcirculation</td>
<td>Reducing socioeconomic and medical constraints</td>
<td>Improve venous leg ulcer management in C6 class patients</td>
</tr>
<tr>
<td>Pleiotropic activity</td>
<td>Endothelium protection and prevention of morphotic blood elements aggregation</td>
<td>Faster recovery with reduction of the infectious risk</td>
<td>Reduction of the time consuming process in venous leg ulcer healing beside standard therapy</td>
</tr>
</tbody>
</table>
Double-blind, double-dummy, randomized, multi-centre clinical assessment of the efficacy, tolerability and dose-effect relationship of sulodexide in chronic venous insufficiency

Saviano M. et al.

## Study design

<table>
<thead>
<tr>
<th>DRUG</th>
<th>PATIENTS</th>
<th>SCHEME</th>
<th>OUTCOMES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulodexide</td>
<td>• 156</td>
<td>25 mg x 2</td>
<td>• Doppler examination</td>
</tr>
<tr>
<td></td>
<td>• 158</td>
<td>50 mg x 2</td>
<td>• Symptoms and signs evaluation (0-3 scale)</td>
</tr>
<tr>
<td></td>
<td>• 158</td>
<td>100 mg x 1</td>
<td>• Venous pressure evaluation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60 days</td>
<td>• Overall efficacy rated by physician</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Double blind</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Double dummy</td>
</tr>
</tbody>
</table>

*Saviano CurrMedResOpin 1993*
Results

Statistically significant differences with all dosages, regardless of measurement site (safena, tibial) and posture since the first month. The higher the dosage, the faster the results.

Orthostatic = standing upright
Clinostatic = lying down
Results

Statistically significant improvement in symptoms and signs in all monitored dose group since the first month.
Results

Statistically significant difference between the low and high dose in a number of symptoms (pain, oedema, ectasia, cramps)

Nocturnal cramps and leg oedema
Results

Global assessment

Global assessment expressed by the physician was favourable in all three dose groups.
Results

Tolerability assessed as “very good”

Physician’s global assessment of tolerability was very good no matter of the dose. Adverse events were recorded in 10% of the patients.
Double-blind, double-dummy, randomized, multi-centre clinical assessment of the efficacy, tolerability and dose-effect relationship of sulodexide in chronic venous insufficiency

M. Saviano, M.D.,
O. Maleti, M.D.,
and
L. Liguori,* M.D.

Institute of Surgical Pathology
Polyclinic of Modena, Modena,
and *Surgical Division,
“G. Pizzardi” Hospital, Bologna, Italy

Received: 17th March 1993

## Sellogram efficacy & tolerability dose effect sulodexide in CVI

<table>
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<th>Features</th>
<th>Advantages (in comparison to competitors)</th>
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<th>Doctor Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural GAG</td>
<td>Proved safety</td>
<td>Feel safe and protected</td>
<td>Suitable approach to the long term management of chronic venous insufficiency</td>
</tr>
<tr>
<td>Pleitropic GAG (enhances fibrinolysis, reduces platelets aggregation, antagonizes the plasminogen activator inhibitor and modifies plasma viscosity)</td>
<td>Improve haemorheology, hemodynamics and reduce thrombosis risk</td>
<td>Symptoms and signs relief</td>
<td>Appreciable and lasting clinical improvements of the underlying clinical conditions</td>
</tr>
<tr>
<td></td>
<td>Favorable effect in CVI through a decrease of venous blood pressure regardless of the specific etiology</td>
<td>Symptoms and signs relief</td>
<td>Adapted for different profiles in CVI treatment</td>
</tr>
<tr>
<td>Natural GAG</td>
<td>Dose-effect relationship</td>
<td></td>
<td>Maneuverability in prescription</td>
</tr>
</tbody>
</table>
Haemodynamic Effects of Sulodexide in post-thrombophlebitic syndromes

Cospite M. et al.
Acta Therapeutica (1992)
Study design

**DRUG**
- Sulodexide
- Placebo

**PATIENTS**
- 15
- 15

**SCHEME**
- 50 mg x 2
- 2 cps x 2
- 90 days

**OUTCOMES**
- Haemodynamic parameters related to venous micro- and macro-circulatory
- Double-blind

Patients suffering from post-thrombotic syndrome (PTS) for at least 1 year
Mean values of the maximal venous incremental volume (MVIV) in the two study groups, evaluated under controlled pressure condition (at 40 and 60 mmHg: MVIV - 40 and MVIV - 60)
Mean values of posterior tibial vein pressure (PTVP) in the two patient groups, after 5 min in lying (PTVPa) and standing (PTVPb) positions.
Results

Venous distensibility ($dV/dP$) and Venous tone ($dP/dV$) in the two patient groups during the study

Mean values of venous distensibility ($dV/dP$) and venous tone ($dP/dV$) in the two patient groups during the study.

* $p < 0.01$ vs P and baseline.
Results

Capillary filtration coefficient (CFC) mean values in the two patient groups during the study

- **Capillary Filtration Coefficient (CFC)**

![Graph showing CFC values over days 0, 30, and 90 for Sulodexide and Placebo groups.]

- Day 0: CFC Sulodexide = 0.007, CFC Placebo = 0.004
- Day 30: CFC Sulodexide = 0.013, CFC Placebo = 0.016
- Day 90: CFC Sulodexide = 0.01, CFC Placebo = 0.013

- *p < 0.01 vs P and Baseline
- **p < 0.001 vs P and Baseline
Percentage variation of the subjective and objective symptoms observed at the end of the study in the two patient groups
HAEMODYNAMIC EFFECTS OF SULODEXIDE* IN POST-THROMBOPHLEBITIC SYNDROMES

M. Cospite, G. Milio, F. Ferrara, V. Cospite
Department of Angiology of the University of Palermo (Italy)

E. Palazzini
Alfa Wassermann S.p.A., Medical Department, Bologna (Italy)
## Sellogram hemodynamic effects of sulodexide in PTS

<table>
<thead>
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<th>Features</th>
<th>Advantages (in comparison to competitors)</th>
<th>Patient Benefits</th>
<th>Doctor Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral formulation of glycosaminoglycans with an antithrombotic and non</td>
<td>Greatly improves micro and macro-circulatory efficiency of the limb venous system</td>
<td>Less risk of further morbidity</td>
<td>Improve post thrombotic syndrome management through an efficient effect on venous hemodynamic parameters</td>
</tr>
<tr>
<td>coagulant effect, profibrinolytic activity by inhibiting PAI and</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>reduction of plasma viscosity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral formulation of glycosaminoglycans with profibrinolytic and</td>
<td>Reduce plasma viscosity and improve dynamic interaction of endothelial cells with blood constituents improving venous distensibility and tone as well as microcirculatory flow</td>
<td>Better symptoms relief</td>
<td>Improve patient outcome</td>
</tr>
<tr>
<td>antilipemic properties</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natural GAG</td>
<td>No side effects</td>
<td>No complaints</td>
<td>Good therapy acceptance</td>
</tr>
</tbody>
</table>
Prevention of Recurrent Deep Venous Thrombosis with Sulodexide
The SanVal Registry

BM Errichi et al.
Angiology (2004)
Study design

**DRUG**
- Sulodexide + local therapy
  - 203 patients

**Patients**
- Local therapy
  - 202 patients

**Scheme**
- LMWH + oral anticoagulants until INR < 3 then only oral anticoagulants
- 6 months
- LMWH + oral anticoagulants until INR < 3 then only oral anticoagulants

**Outcomes**
- 189 patients
  - DVT recurrences at 6 months, 1 year and 2 years

- 178 patients
  - Open, registry

Eligible patients: medium and high risk according to guidelines
- D-dimer test < 200 ng/ml
- Exercise plan consisting of mild isometric exercise
- Low compression elastic stockings

Errichi Angiology 2004
Results

% subjects with recurrent DVT during follow up

Available pts

<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th>12 months</th>
<th>24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>199 control</td>
<td>5</td>
<td>6</td>
<td>7,4</td>
</tr>
<tr>
<td>198 sdx</td>
<td>12</td>
<td>17</td>
<td>17,9</td>
</tr>
<tr>
<td>182 control</td>
<td>p&lt;0.05</td>
<td>p&lt;0.05</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>198 sdx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>178 control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>189 sdx</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Results

% of subjects with increased D-dimer

Available pts

<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th>12 months</th>
<th>24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>199 control</td>
<td>198 sdx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>182 control</td>
<td>198 sdx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>178 control</td>
<td>189 sdx</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- 6 months: 4 control, 4 sulodexide
- 12 months: 3.1 control, 8.7 sulodexide
- 24 months: 2.6 control, 7.8 sulodexide

p<0.05
### Results

**Localization of DVT**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Treatment</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At inclusion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>82%</td>
<td>84%</td>
<td>ns</td>
</tr>
<tr>
<td>Distal</td>
<td>18%</td>
<td>16%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>After 24 months follow up</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent DVT</td>
<td>32</td>
<td>14</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Proximal</td>
<td>15</td>
<td>7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Distal</td>
<td>17</td>
<td>7</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
Prevention of Recurrent Deep Venous Thrombosis with Sulodexide:
The SanVal Registry

B. M. Errichi, MD,‡ M. R. Cesarone, MD,§ G. Belcaro, MD, PhD,¶ R. Marinucci, MD,‡
A. Ricci, MD,§ A. Ippolito, MD,§ R. Brandolini, MD,† G. Vinciguerra, PhD,¶
M. Dugall, MD,‡ A. Felicita, MD,‡ L. Pellegrini, MD,† G. Gizzi, MD,‡ M. Ruffini, MD,†
G. Acerbi, MD,‡ P. Bavera, MD,§ A. Di Renzo,† M. Corsi, MD,‡ M. Scoccianti, MD,‡
M. Hosoi, MD, PhD,§ and M. Lania, MD,§ Pescara, Sulmona, Milan, and Pisa, Italy
Sellogram Prevention r-DVT: San Val Registry

<table>
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<tr>
<th>Features</th>
<th>Advantages (in comparison to competitors)</th>
<th>Patient Benefits</th>
<th>Doctor Benefits</th>
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</thead>
<tbody>
<tr>
<td>GAG with Antithrombotic activity</td>
<td>Effective in reducing thrombi in subjects with thrombotic conditions</td>
<td>Sparing aggravation of the original problem</td>
<td>Additional therapeutic approach for r-DVT prevention in association with compression with stockings after discontinuation of the standard treatment</td>
</tr>
<tr>
<td></td>
<td>Reduction of D-Dimer value</td>
<td></td>
<td>Reduction of the risk of recurrences</td>
</tr>
<tr>
<td>Natural Glycosaminoglycan</td>
<td>High safety and tolerability profile</td>
<td>Easy intake</td>
<td>Long term safety and good patients’ compliance</td>
</tr>
</tbody>
</table>
The efficacy of Sulodexide in the Prevention of Postthrombotic Syndrome

Luzzi R et al.

Clin Appl Thromb Hemost (2014)
**Study design**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>PATIENTS</th>
<th>SCHEME</th>
<th>OUTCOMES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulodexide + standard</td>
<td>124</td>
<td>LMWH + oral anticoagulants until INR&lt;3 then only oral anticoagulants</td>
<td>• Occurrence of clinical significant PTS (score &gt;40)</td>
</tr>
<tr>
<td>management</td>
<td></td>
<td>250 LSU x 2</td>
<td></td>
</tr>
<tr>
<td>Aspirin + standard</td>
<td>48</td>
<td>LMWH + oral anticoagulants until INR&lt;3 then only oral anticoagulants</td>
<td>• DVT recurrence</td>
</tr>
<tr>
<td>management</td>
<td></td>
<td>100 mg x 1</td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>167</td>
<td>LMWH + oral anticoagulants until INR&lt;3 then only oral anticoagulants</td>
<td>• Open, registry, non-parallel group</td>
</tr>
<tr>
<td>management</td>
<td></td>
<td>No specific pharmacological treatment</td>
<td></td>
</tr>
</tbody>
</table>

6 months up to 5 years

Standard Management: compression, control of all thrombotic risk factors, weight, and regular exercise

Luzzi Clin Appl Thromb Hemost 2014
Results

Incidence of PTS

* p<0.05 for the comparison SDX+SM vs. SM

Luzzi Clin Appl Thromb Hemost 2014
Results

Incidence of r-DVT

- SM: 8.3%
- ASA+SM: 4.0%
- SDX+SM: 6.1%

rDVT
The Efficacy of Sulodexide in the Prevention of Postthrombotic Syndrome

Roberta Luzzi, PharmD¹, Gianni Belcaro, MD, PhD¹, Mark Dugall, MD¹, Shu Hu, MD¹, Guido Arpaia, MD¹, Andrea Ledda, MD¹, Edmondo Ippolito, MD¹, Marcello Corsi, MD¹, Andrea Ricci, MD¹, Roberto Cotellese, MD¹, Giovanni Agus, MD¹, Bruno M. Errichi, MD¹, Umberto Cornelli, MD¹, M. Rosaria Cesarone, MD¹, and Morio Hosoi, MD¹
# Sellogram Prevention of post-thrombotic syndrome

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<th>Doctor Benefits</th>
</tr>
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<tr>
<td>Highly purified mixture of glycosaminoglycans with high affinity for the endothelium</td>
<td>Anti-inflammatory activity on the vessel wall</td>
<td>Reducing impairments related to chronic incapacity or affecting working potential</td>
<td>A novel therapeutic approach for prevention of PTS in patients who had experienced DVT</td>
</tr>
<tr>
<td>Highly purified mixture of glycosaminoglycans activity on antithrombin III and heparin cofactor II</td>
<td>r-DVT prevention</td>
<td>Sparing medical, social and personal costs</td>
<td>Improve substandard management of DVT to reduce recurrences and chronically increased venous pressure</td>
</tr>
<tr>
<td>Long half life and reduced effects on global coagulation</td>
<td>No significant alterations of bleeding parameters or other tolerability events</td>
<td>Safety and easy intake</td>
<td>Insure safety and treatment compliance</td>
</tr>
</tbody>
</table>
Sulodexide suppresses inflammation in patients with chronic venous insufficiency

Urbanek T et al.
*International Angiology* (2015)
Study design

**DRUG**
- Sulodexide

**PATIENTS**
- 11

**SCHEME**
- 500 LSU x 2
- 8 weeks

**OUTCOMES**
- Phase 1: MMP-9, IL-6, MCP-1
- Phase 2: effect of patients serum on HUVEC cells proliferation and inflammatory parameters

C5 patients; excluded presence of deep or superficial thrombosis or post-thrombotic changes

All patients used class tow compression stockings continuously, before and during the study
Results

After treatment with sulodexide IL-6 and MMP-9 decreased significantly.

Sulodexide treatment reduces intravascular inflammation and is protective towards endothelial cells and extracellular matrix changes.
Sulodexide suppresses inflammation in patients with chronic venous insufficiency

T. URBANEK 1, K. ZBIGNIEW 2, B. BEGIER-KRASIŃSKA 3, E. BAUM 4, A. BRĘBOROWICZ 4

1Department of General and Vascular Surgery, Medical University of Silesia, Katowice, Poland
2Department of General and Vascular Surgery, Poznan University of Medical Sciences, Poznan, Poland
3Department of Hypertension, Poznan University of Medical Sciences, Poznan, Poland
4Department of Pathophysiology, Poznan University of Medical Sciences, Poznan, Poland
## Sellogram sulodexide suppresses inflammation in patients with CVI

<table>
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<th>Advantages (in comparison to competitors)</th>
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<th>Doctor Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly purified mixture of glycosaminoglycans with high affinity for the endothelium</td>
<td>Endothelial protection and restoration</td>
<td>Sparing complications related to recurrences</td>
<td>Novel possibility for pharmacological treatment of CVI interfering with the important steps of the process that is leading to vein incompetence and venous hypertension</td>
</tr>
<tr>
<td>Modulation of the different CVI pathways related to inflammation, oxidative stress and remodeling</td>
<td>Reduction of treatment cost</td>
<td>Slow the progression of CVI disease especially in C5 patients’ class in addition to compression stockings</td>
<td></td>
</tr>
</tbody>
</table>
Glycosaminoglycan Sulodexide Inhibition of MMP-9 Gelatinase Secretion and Activity: Possible Pharmacological Role Against Collagen Degradation in Vascular Chronic Diseases

Mannello F et al.

*Curr Vasc Pharmacol* (2013)
Study design

PATIENTS

Healthy volunteers

• 60

SCHEME

Blood samples + Sulodexide 0,24 and 0,48 LSU/ml

• 60

OUTCOMES

• Evaluation of the possible modulation of MMP activity/secretion in serum and plasma

The effect of SDX was tested in terms of inhibition potency
Results

Sulodexide reduces the MMP-9 released from blood cells and affects its activity

Dose-dependent inhibitory effect of sulodexide on serum MMP-9 forms

Addition of sulodexide to blood, serum or plasma did not cause any significant quantitative variation of MMP-2 activity
Glycosaminoglycan Sulodexide Inhibition of MMP-9 Gelatinase Secretion and Activity: Possible Pharmacological Role Against Collagen Degradation in Vascular Chronic Diseases

Ferdinando Mannello¹*, Virginia Medda¹, Daniela Ligi¹ and Joseph D. Raffetto²,³

¹Department of Biomolecular Sciences, Section of Clinical Biochemistry, Unit of Cell Biology, University “Carlo Bo,” Urbino, Italy; ²Vascular Surgery Division, VA Boston Healthcare System, West Roxbury, MA, USA; ³Harvard Medical School, Brigham and Women’s Hospital, Boston, MA, USA
### Sellogram inhibition of MMP-9 secretion and activity

<table>
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<th>Doctor Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly purified mixture of glycosaminoglycans with affinity for the endothelium</td>
<td>Decrease of MMP-9 activity</td>
<td>Sparing further morbidity</td>
<td>Faster healing of leg ulcers</td>
</tr>
<tr>
<td></td>
<td>Endothelium protection and pleitropic effects</td>
<td>Better symptoms and signs improvement</td>
<td>Prevention of disease progression</td>
</tr>
<tr>
<td></td>
<td>Dose dependent inhibition of leukocytes release of MMP-9</td>
<td></td>
<td>Different dosages available, customization</td>
</tr>
</tbody>
</table>