



Original

Efficacy of sulodexide for the control of symptoms of chronic venous insufficiency

Eficacia de la sulodexida para el control de los síntomas de la insuficiencia venosa crónica

Enrique M. San Norberto, Verónica Portillo, José Antonio Brizuela, Álvaro Revilla, María Isabel Rivera, Sergio Fernández-Bello

Department of Angiology and Vascular Surgery. Hospital Clínico Universitario de Valladolid. Valladolid, Spain

Abstract

Introduction: chronic venous insufficiency is a highly prevalent condition, affecting approximately 50% of the population. Sulodexide is the only pharmacologic treatment funded in Spain by the National Health System for the treatment of CEAP classes C3 to C6.

Material and method: this was a prospective cohort study including patients treated with sulodexide for chronic venous insufficiency (CEAP classes C3-C6). Effectiveness was assessed using a symptom and quality-of-life survey (CIVIQ-20), which includes 9 items on psychological impact, 5 on pain, 3 on physical impact, and 3 on social impact, administered before and after 3 months of treatment.

Results: a total of 280 patients were included. Most were women (64.3%), with a mean (SD) age of 56.9 (11.6) years (range, 27-71 years). CEAP classes were C3 in 60.7%, C4 in 25.0%, C5 in 10.7%, and C6 in 3.6%. The most common comorbidities were obesity (35.7%), hypertension (32.1%), and dyslipidemia (25.0%). After 3 months of treatment, patients reported improvement in symptoms of heaviness (100% vs 39%; $p < 0.001$), pain (96% vs 71%; $p = 0.017$), cramps (61% vs 36%; $p = 0.07$), paresthesia (68% vs 32%; $p = 0.005$), erythema (75% vs 39%; $p = 0.015$), burning sensation (46% vs 14%; $p = 0.026$), and induration (64% vs 36%; $p = 0.043$). The overall CIVIQ-20 score did not show significant differences before and after treatment (54.4 SD, 10.4 vs 51.8 SD, 16.8; $p = 0.36$); however, item-level analysis showed significant differences in pain impact (11.8 SD, 3.4 vs 9.5 SD, 3.7; $p < 0.001$) and physical impact (9.1 SD, 3.5 vs 8.0 SD, 3.3; $p = 0.001$).

Conclusions: treatment with sulodexide for 3 months is effective in controlling symptoms and improving quality of life, particularly regarding pain and physical impact, in patients with chronic venous insufficiency (CEAP classes C3-C6).

Keywords:

Venous insufficiency.
Sulodexide. Quality
of life.

Received: 08/10/2025 • Accepted: 09/14/2025

Conflicts of interest: the authors declare no conflicts of interest.

Artificial intelligence: the authors declare that they did not use artificial intelligence (AI) or any AI-based tools in the writing of this article.

San Norberto EM, Portillo V, Brizuela JA, Revilla Á, Rivera MI, Fernández-Bello S. Efficacy of sulodexide for the control of symptoms of chronic venous insufficiency. *Angiología* 2026;78(3):106-113

DOI: 10.20960/angiologia.00814

Correspondence:

Enrique M. San Norberto García. Department of Angiology and Vascular Surgery. Hospital Clínico Universitario de Valladolid. Avda. Ramón y Cajal, 3. 47003 Valladolid, Spain
e-mail: esannorberto@hotmail.com

Resumen

Introducción: la insuficiencia venosa crónica (IVC) es una enfermedad muy prevalente: aparece en el 50 % aproximadamente de la población. La sulodexida es el único antitrombótico heparinoide financiado en España por el Sistema Nacional de Salud para el tratamiento de grados CEAP C3 a CEAP C6.

Material y método: estudio prospectivo de cohortes en pacientes tratados con sulodexida como tratamiento farmacológico de la IVC en grados CEAP C3 a CEAP C6. Para conocer su efectividad, se realizó una encuesta sobre la aparición de síntomas y calidad de vida (encuesta CIVIQ-20: 9 preguntas sobre repercusiones psicológicas, 5 sobre la repercusión del dolor, 3 sobre la repercusión física y 3 sobre la repercusión social) antes y después de 3 meses de tratamiento.

Resultados: se incluyeron 280 pacientes en el estudio. La mayoría se trataba de mujeres (64,3 %), con una edad media de $56,9 \pm 11,6$ años (rango 27-71). Los grados de la clasificación CEAP fueron: C3, 60,7 %; C4, 25,0 %; C5, 10,7 %, y C6, 3,6 %. Las comorbilidades más frecuentes en la población estudiada fueron obesidad (35,7 %), hipertensión arterial (32,1 %) y dislipemia (25,0 %). Después de 3 meses de tratamiento los pacientes mejoraron los síntomas de pesadez (100 % frente al 39 %, $p = 0,000$), dolor (96 % frente al 71 %, $p = 0,017$), calambres (61 % frente al 36 %, $p = 0,070$), parestesias (68 % frente al 32 %, $p = 0,005$), eritema (75 % frente al 39 %, $p = 0,015$), quemazón (46 % frente al 14 %, $p = 0,026$) e induración (64 % frente al 36 %, $p = 0,043$). La diferencia global en la escala CIVIQ-20 no demostró diferencias antes y después del tratamiento ($54,4 \pm 10,4$ frente al $51,8 \pm 16,8$, $p = 0,360$). No obstante, al analizar los ítems se observaron diferencias en cuanto a la repercusión del dolor ($11,8 \pm 3,4$ frente al $9,5 \pm 3,7$, $p = 0,000$) y la repercusión física ($9,1 \pm 3,5$ frente al $8,0 \pm 3,3$, $p = 0,001$).

Conclusiones: el tratamiento con sulodexida durante 3 meses es eficaz en cuanto al control de los síntomas y mejoría de la calidad de vida en pacientes con IVC grados CEAP C3-C6.

Palabras clave:
Insuficiencia venosa.
Sulodexida. Calidad
de vida.

INTRODUCTION

Chronic venous insufficiency (CVI) is a common condition in the adult population. In Spain, where data are similar to those of other countries, it has an overall prevalence of 48.5 %; in women, 58.5 % between 40 and 49 years of age, and in men, 32.2 % between 70 and 79 years of age. Its incidence increases with age, as does the likelihood of presenting in more advanced stages (1).

Lower limb CVI is a disease caused by altered blood flow, leading to the development of venous hypertension. Increased venous pressure and impaired venous return may be affected by different mechanisms, such as structural and/or functional alterations of the venous wall, incompetence of superficial, perforator, or deep venous valves, or the presence of flow obstruction. Therefore, it can be interpreted according to the hemodynamic behavior of venous hypertension and the presence of alterations in venous flow.

Among the possible treatments, which are recommended to be combined, are hygienic-dietary measures, compression therapy, pharmacological treatment, and surgery. Regarding medical treatment, two options are available: venoactive drugs (VADs)

or antithrombotic agents, such as sulodexide, which is the focus of our study. Sulodexide is indicated at a dosage of 30 mg twice daily (Aterina®, Alfaisigma). There are no studies relating the duration of treatment to its efficacy profile in symptom control, only those showing that higher daily doses lead to symptom improvement (2). Although not all its mechanisms of action are known, it appears to act on both macro- and microcirculation, the venous wall, and the valves, reducing the inflammatory response and modifying the mechanisms that trigger venous hypertension. Anti-inflammatory, antioxidant, and venous endothelial cell-protective effects have been attributed to it (2,3).

Sulodexide is a heparinoid antithrombotic classified within the ATC (Anatomical Therapeutic Chemical Classification) under heparin group B01AB11 by the World Health Organization. It is a purified glycosaminoglycan containing a mixture of 80 % heparan sulfate and 20 % dermatan sulfate. In Spain, several venotonic agents are commercially available. Sulodexide is only reimbursed by the National Health System for CEAP C3-C6 stages of CVI (4). Different clinical practice guidelines assign varying degrees of efficacy to venotonic agents for symptom control in CVI;

however, it is not fully established whether treatment with sulodexide for 3 months is completely effective in controlling symptoms and improving quality of life in patients with advanced CVI.

MATERIALS AND METHODS

Study design

We conducted a prospective observational cohort study in patients diagnosed with CVI stages CEAP C3 to CEAP C6 and seen in consultation during 2024, aimed at assessing the outcomes of treatment with sulodexide during the months with the highest symptom incidence (summer). Data were collected through a telephone survey assessing symptoms and quality of life using the CIVIQ-20 (Chronic Venous Insufficiency Questionnaire: 9 questions on psychological impact, 5 on pain impact, 3 on physical impact, and 3 on social impact) before and after 3 months of treatment (5).

The primary endpoints were to determine the efficacy of sulodexide in symptom control and improvement, as well as to analyze its impact on quality of life. In addition to the primary endpoints, the study also explored the relationship between clinical characteristics (age, sex, BMI, comorbidities, etc.) and CVI.

We conducted an observational study with no intervention on the patients. Clinical data routinely obtained during consultations were used without including parameters beyond standard clinical practice or requesting additional tests. The variables studied were collected from patients' electronic medical records and through telephone surveys.

The variables analyzed were obtained from health records without adding personal data. To avoid patient identification, a pseudonymization process was performed in full compliance with current regulations (Organic Law 3/2018 of December 5 on Data Protection and Guarantee of Digital Rights). Each health record No. was assigned a random number unrelated to the original. Additionally, voluntary participation in the telephone survey was considered implicit consent to participate in the study, and written informed consent was deemed unnecessary, while ensuring full protection of personal data. Finally, this study was conducted following approval by the Ethics Commit-

tee for Research with Medicines (CEIm) of Valladolid (Spain) (PI-24-663) and fully complied with the ethical principles outlined in the Declaration of Helsinki.

Study population and variables analyzed

A total of 280 patients evaluated in outpatient consultations of the Department of Angiology and Vascular Surgery, Hospital Clínico Universitario de Valladolid (Spain) during 2024 were included, meeting the inclusion criteria (patients older than 18 years with CVI treated with sulodexide during the 3 summer months of 2024) and none of the exclusion criteria (patients < 18 years, pregnant women, patients with contraindications to sulodexide, and those unwilling to participate). All patients were advised to use compression therapy and adopt lifestyle changes according to the Clinical Practice Guidelines for Chronic Venous Disease of the Spanish Chapter of Phlebology and Lymphology (6).

Demographic data included age, sex, comorbidities (hypertension, diabetes *mellitus*, dyslipidemia, ischemic heart disease, arrhythmia, BMI > 30 or obesity, and smoking), and CVI stage according to the CEAP classification. Symptoms recorded were heaviness, pain, cramps, paresthesia, erythema, burning sensation, and induration. The quality-of-life questionnaire used was the CVI-specific CIVIQ-20. Both symptoms and the CIVIQ questionnaire were recorded before and after 3 months of treatment.

Statistical analysis

After data collection, analysis was performed using SPSS version 27. For continuous variables, mean and SD were calculated. For qualitative variables, univariate analysis was performed using the chi-square test and Fisher's exact test, and for quantitative variables, Student's t-test was used. Multivariate analysis was performed using logistic regression, along with a bootstrap resampling study as a validation technique. Statistical significance was established at $p < 0.05$.

The incidence rate of the variable "pain" in the studied sample was 96 %. Assuming an alpha risk of 0.05 and a statistical power of 0.80 with a two-sided test,

the required sample size to detect a 10 % improvement would be 410 patients. However, when recalculating with half of the hypothetical sample (205 patients), a reduction greater than 25 % was observed, resulting in a final sample size of 280 patients. The GRANMO statistical program was used for this sample size calculation.

RESULTS

The mean age of the 280 patients included was 56.9 ± 11.6 years (range, 27–71 years), with a predominance of female patients (64.3 %). Table I illustrates the baseline characteristics of the population and summarizes the percentage of each CEAP stage. According to the CEAP classification, most patients were in stage C3 (60.7 %), followed by C4 (25.0 %), C5 (10.7 %), and C6 (3.6 %). The most frequent comorbidities were obesity (35.7 %), hypertension (32.1 %), and dyslipidemia (25.0 %).

After 3 months into therapy, a significant improvement was observed in most of the evaluated symptoms. The prevalence of heaviness decreased from 100 % to 39 % ($p = 0.000$); pain from 96 % to 71 % ($p = 0.017$); cramps from 61 % to 36 % ($p = 0.037$); paresthesia from 68 % to 32 % ($p = 0.005$); erythema from 75 % to 39 % ($p = 0.015$); burning sensation from 46 % to 14 % ($p = 0.026$); and induration from 64 % to 36 % ($p = 0.043$), as shown in table II and figure 1.

The overall score on the CIVIQ-20 scale did not show significant differences before and after treatment (54.4 ± 10.4 vs 51.8 ± 16.8 , $p = 0.360$). However, when analyzing specific items, improvements were observed in the pain domain (11.8 ± 3.4 vs 9.5 ± 3.7 , $p = 0.000$) and in the physical domain (9.1 ± 3.5 vs 8.0 ± 3.3 , $p = 0.001$), but not in the psychological domain (29.2 ± 5.0 vs 27.5 ± 13.1 , $p = 0.519$) or the social domain (5.8 ± 2.6 vs 5.0 ± 2.4 , $p = 0.142$). These results are presented in table III and figure 2.

Considering the most prevalent clinical variable in patients with CVI (pain), a univariate analysis was performed with other risk factors, including demographic variables and comorbidities, and improvement was observed after 3 months of follow-up (Table IV). After multivariate analysis, improvement was found to be dependent only on treatment with sulodexide ($p = 0.001$).

Table I. Demographic characteristics and comorbidities of patients included in the study

Variable	<i>n</i> = 280
Age (years)	56.9 ± 11.6 (range 27–71)
Male	35.7 %
Female	64.3 %
Comorbidities	
Hypertension	89 (32.1 %)
Diabetes mellitus	31 (10.7 %)
Dyslipidemia	71 (25.0 %)
Heart disease	29 (7.1 %)
Arrhythmia	0 (0 %)
Obesity	101 (35.7 %)
Grade I	53 (18.9 %)
Grade II	37 (13.2 %)
Grade III	11 (3.9 %)
Smoking	5 (1.7 %)
CEAP classification	
C3	163 (58.2 %)
C4	78 (27.9 %)
C5	30 (10.7 %)
C6	9 (3.2 %)

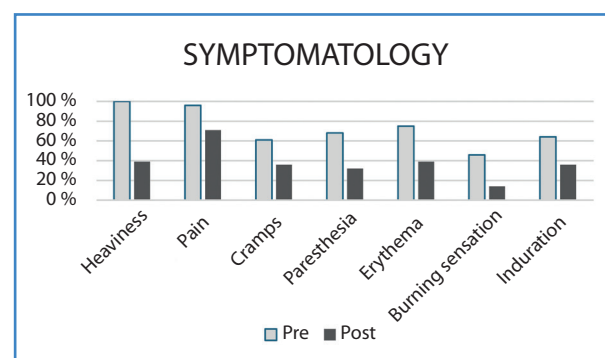


Figure 1. Graphical representation of symptom progression before and after treatment.

Table II. Progression of symptoms before and after treatment

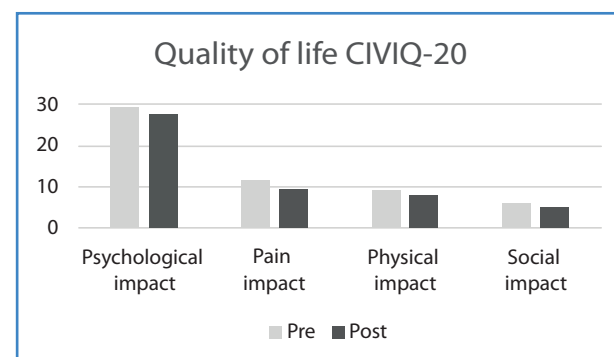
Symptom	Pre (%)	Post (%)	<i>p</i>
Heaviness	100 %	39 %	0.000
Pain	96 %	71 %	0.017
Cramps	61 %	36 %	0.037
Paresthesia	68 %	32 %	0.005
Erythema	75 %	39 %	0.015
Burning sensation	46 %	14 %	0.026
Induration	64 %	36 %	0.043

Table III. Progression of quality of life according to CIVIQ-20 questionnaire scores before and after treatment

CIVIQ domain	Pre	Post	<i>p</i>
Psychological impact (9 items / 5-point scale: 9-45)	29.2 ± 5.0	27.5 ± 13.1	0.519
Pain impact (5 items / 5-point scale: 5-25)	11.8 ± 3.4	9.5 ± 3.7	0.000
Physical impact (3 items / 5-point scale: 3-15)	9.1 ± 3.5	8.0 ± 3.3	0.001
Social impact (3 items / 5-point scale: 3-15)	5.8 ± 2.6	5.0 ± 2.4	0.142

Table IV. Results of univariate analysis on the association between demographic and comorbidity factors and improvement in the most prevalent variable (pain)

Variable	<i>p</i>
Age > 75 years	0.047
Male sex	0.123
Hypertension	0.098
Diabetes mellitus	0.203
Dyslipidemia	0.120
Heart disease	0.099
Arrhythmia	0.304
Obesity	0.042
Smoking	0.301
Treatment with sulodexide	0.012

**Figure 2.** Graphical representation of quality-of-life progression according to the CIVIQ-20 scale before and after treatment.

DISCUSSION

In this prospective cohort study, it was observed that after treatment with sulodexide during the 3 months of highest symptom incidence (i.e., summer), CVI symptoms significantly improved in the evaluated

patients. The CIVIQ-20 questionnaire also detected a significant improvement in the pain and physical domains. This suggests that sulodexide may have a positive effect on specific aspects of daily life. The observed symptomatic improvement has a relevant impact on patient functionality and well-being.

CVI is a highly prevalent disease with a wide range of clinical signs. Family history and a series of genetic factors have been implicated in the development of CVI, as well as environmental factors such as a sedentary lifestyle and obesity. Different venotonic agents have been proposed to improve venous tone, capillary permeability, or reduce leukocyte infiltration of the venous wall. Thus, α -benzopyrones, γ -benzopyrones, saponin plant extracts, and other natural compounds have been indicated (7,8). Specifically, sulodexide has been attributed beneficial effects in CVI, as well as in peripheral arterial disease, post-thrombotic syndrome, venous thromboembolism, and even diabetic microangiopathy (9).

In 2020, a systematic review and meta-analysis based on data from 1,901 patients with CVI showed that sulodexide reduced the intensity of pain, cramps, heaviness, and edema (2). Sulodexide has also been shown to decrease serum levels of cytokines such as MMP-2 and MMP-9 (10), other proinflammatory molecules such as IL-6, MDCP-1, and s-ICAM-1, and even to regulate the generation of free radicals (11). The risk of adverse effects was estimated at 3 % (95 % CI, 1-4 %), mainly dizziness, diarrhea, upper abdominal pain, rash, or agranulocytosis.

A systematic literature review and a meta-analysis on the results of CVI treatment with sulodexide (12) identified a total of 11 observational studies including 1,267 patients evaluating pain and the sensation of swelling, heaviness, cramps, and paresthesia. Estimates showed that sulodexide significantly reduced pain by 1.60 points (95 % CI, 2.47 to 0.72) on a 4-point Likert scale ($I^2 = 86$ %, $p < 0.01$) and the sensation of swelling by 1.64 points (95 % CI, 1.90–1.38). Sulodexide was also effective in significantly reducing heaviness by 1.56 points (95 % CI, –1.87 to –1.25) and paresthesia by 1.54 points (95 % CI, –2.21 to –0.83) on Likert scales, with zero and high heterogeneity ($I^2 = 82$ %), respectively (13). These results are consistent with those of our study, in which pain decreased by 61 % after

3 months of treatment, and induration and paresthesia decreased by 28 % and 36 %, respectively.

Regarding the use of quality-of-life scales to assess the effects of sulodexide, only 2 studies have been published. Bogachev et al., in 2017 (3), used the VCSS (Venous Clinical Severity Score) in their study published in Russian, and another observational study conducted in Tunisia used the CIVIQ-20. The latter evaluated the efficacy profile of sulodexide twice daily for 3 months on health-related quality of life parameters using CIVIQ-20 in 450 patients with CVI (all CEAP clinical classes) (14). At the end of treatment, a mean improvement of 44 % was observed in the pain and functional domains of CIVIQ-20 compared to baseline ($p < 0.0001$). However, the lack of significant improvement in the overall CIVIQ-20 score has also been described by some authors, who suggest that changes in global perception may require longer follow-up or even complementary interventions (15).

Among the strengths of the study are its prospective design and the collection of quality-of-life data using a questionnaire specifically validated for patients with CVI (CIVIQ-20). This is complemented by data collection before and after treatment, allowing objective assessment of patient progression. Limitations to be considered include its single-center design and the focus only on the period of highest symptom intensity, which may overestimate the treatment effect. No control group was included, and uncontrolled variables such as patients' socioeconomic or educational level, which may influence the results, were not considered. Additionally, the CIVIQ-20 quality-of-life questionnaire is not fully valid in patients with CEAP C5 or C6, as relevant items for these patients may differ. All of this may introduce selection bias and limit external validity.

There are no randomized studies on the role of sulodexide in the prevention or progression of CVI, although there are studies for the treatment of patients with or without venous ulcers (14,16,17). Only the study published by Luzzie et al. in 2014 (16), involving 339 patients treated with anticoagulation for deep vein thrombosis of the extremities, suggested a possible role in prevention. They compared three treatment groups in addition to anticoagulation: compression and risk factor reduction, sulodexide, or aspirin. The incidence of post-thrombotic syndrome after 5 years of treatment was lower in the sulodexide

vs the standard treatment group (12.2 % vs 19.5 %, $p < .05$) and the aspirin group (12.2 % vs 23.5 %, $p < 0.05$). This opens a field for further research on the effects of sulodexide in patients with CVI (17-19).

CONCLUSIONS

The results obtained suggest that treatment of CVI with sulodexide during the 3 months of highest symptom incidence, that is, the summer months, is effective in symptom control, as well as in improving certain aspects of quality of life in patients with CEAP C3 to CEAP C6 stages. However, additional studies are required to confirm these findings and to assess their overall impact, as well as to compare its effectiveness with other venotonic agents.

REFERENCES

- Escudero JR, Fernández F, Bellmunt S. Prevalencia y características clínicas de la enfermedad venosa crónica en pacientes atendidos en Atención Primaria en España: resultados del estudio internacional Vein Consult Program. *Cir Esp* 2014;92:539-46. DOI: 10.1016/j.ciresp.2013.09.013
- Bignamini AA, Matuska J. Sulodexide for the symptoms and signs of chronic venous disease: a systematic review and meta-analysis. *Adv Ther* 2020;37:1013-33. DOI: 10.1007/S12325-020-01232-1
- Bogachev VI, Golovanova OV, Malysheva IN. Efficacy of sulodexide in treatment of chronic venous insufficiency. Results of the ACCORD trial. *Angiol Sosud Khir* 2017;23:83-8.
- Ministerio de Sanidad, Consumo y Bienestar Social. Informe de posicionamiento terapéutico de sulodexida en insuficiencia venosa crónica, úlcera venosa y claudicación intermitente. Agencia española de medicamentos y productos sanitarios. Ministerio de Sanidad, Consumo y Bienestar Social. Available at: <https://www.aemps.gob.es/medicamentosUsoHumano/informesPublicos/docs/IPT-sulodexida-Aterina-Dovida-IVC-CI.pdf>
- Launois R, Mansilha A, Jantet G. International psychometric validation of the Chronic Venous Disease quality of life Questionnaire (CIVIQ-20). *Eur J Vasc Endovasc Surg* 2010;40:783-9. DOI: 10.106/j.ejvs.2010.03.034.
- Miquel Abac C, Rial Horcajo R, Ballesteros Ortega MD, García Madrid C. Guía de práctica clínica en enfermedad venosa crónica. Bilbao: Capítulo Español de Flebología y Linfología; 2015.
- De Maeseneer MG, Kakkos SK, Aherne T, et al. European Society for Vascular Surgery (ESVS) 2022 clinical practice guidelines on the management of chronic venous disease of the lower limbs. *Eur J Vasc Endovasc Surg* 2022;63:184-267. DOI: 10.1016/j.ejvs.2021.12.024
- Gloviczki P, Lawrence PF, Wasan SM, et al. The 2023 Society for Vascular Surgery, American Venous Forum, and American Vein and Lymphatic Society clinical guidelines for the management of varicose veins of the lower extremities. Part II. Endorsed by the Society of Interventional Radiology and the Society for Vascular Medicine. *J Vasc Surg Venous Lymphat Disord* 2024;12:101670. DOI: 10.1016/j.jvsv.2023.08.011
- Raffetto JD, Khalil RA. Mechanisms of lower extremity vein dysfunction in chronic venous disease and implications in management of varicose veins. *Vessel Plus* 2021;5. DOI:10.20517/2574-1209.2021.16
- Zielinski A, Jasinska-Suminska K, Breborowicz A, et al. Changes of the serum properties and its effect on the endothelial cells restoration in patients with chronic venous disease treated with sulodexide. *J Vasc Surg Venous Lymphat Disord* 2024;12:101941. DOI: 10.1016/j.jvsv.2024.101941
- Bontor K, Gabryel B. Sulodexide protects endothelial cells against 4-hydroxynonenal-induced oxidative stress and glutathione-dependent redox imbalance by modulation of sestrin2/nuclear factor erythroid 2-related factor 2 pathway. *J Physiol Pharmacol* 2024;75:373-87. DOI: 10.26402/jpp.2024.4.03
- Pompilio G, Nicolaides A, Kakkos SK, et al. Systematic literature review and network meta-analysis of sulodexide and other drugs in chronic venous disease. *Phlebology* 2021;36:695e709. DOI: 10.1177/02683555211015020
- Gloviczki ML, Kakkos SK, Urbanek T, et al. The role of venoactive compounds in the treatment of chronic venous disease. *J Vasc Surg Venous Lymphat Disord* 2025;13:102258. DOI: 10.1016/j.jvsv.2025.102258
- Elleuch N, Zidi H, Bellamine Z, et al. CVD study investigators. Sulodexide in patients with chronic venous disease of the lower limbs: clinical efficacy and impact on quality of life. *Adv Ther* 2016;33:1536-49. DOI: 10.1007/s12325-016-0359-9
- Ulloa JH, Lurie F, Santiago FR, et al. Systematic literature review and expert meeting report on health-related quality of life in chronic venous disease. *Int Angiol* 2023;43:465-76. DOI: 10.23736/S0392-9590.23.05108-8
- Saviano M, Maleti O, Liguori L. Double-blind, double dummy, randomized multi-centre clinical assessment of the efficacy and dose-effect relationship of sulodexide in chronic venous insufficiency. *Curr Med Res Opin* 1993;13:96-108. DOI: 10.1185/03007999309111538
- Wu B, Lu J, Yuang M, et al. Sulodexide for treating venous leg ulcers. *Cochrane Database Syst Rev* 2016;2016:CD010694. DOI: 10.1002/14651858.CD010694.pub2
- Luzzi R, Belcaro G, Dugall M, et al. The efficacy of sulodexide in the prevention of postthrombotic syndrome. *Clin Appl Thromb Hemost* 2014;20:594-9. DOI: 10.1177/1076029614533143
- Carroll BJ, Piazza G, Goldhaber SZ. Sulodexide in venous disease. *J Thromb Haemost* 2019;17:31-8. DOI: 10.1111/jth.14324

