# Effects of Sulodexide on damaged endothelial Glycocalyx in pAtients with Diabetes Mellitus type II; Reversing damage (SUGAR).

No registrations found.

| | |
|---|---|
| **Ethical review** | Positive opinion |
| **Status** | Recruitment stopped |
| **Health condition type** | - |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON24257

**Source**
Nationaal Trial Register

**Brief title**
SUGAR

**Health condition**

In patients with diabetes mellitus type II with and without microalbuminuria.

### Sponsors and support

**Primary sponsor:** AlfaWasserman, Italy

### Intervention

### Outcome measures

**Primary outcome**

Main study parameter/endpoint:

The difference in systemic glycocalyx volume after sulodexide and after placebo treatment.

**Secondary outcome**

Secondary study parameters/endpoints (if applicable)
The difference in systemic glycocalyx volume after sulodexide and after placebo treatment in local sublingual glycocalyx volume, vascular permeability and endothelial function in all patients.

The percentage change from baseline to end of the study in microalbuminuria in patients with DM type II who have microalbuminuria.

# Study description

**Background summary**

Introduction and rationale:

The glycocalyx, a gel-like layer covering the endothelium (0.5-1.0 µm thick) has emerged as a primary defence layer against atherogenic stimuli. Thus, the glycocalyx shields vascular endothelial cells from direct exposure to flowing blood by forming a highly hydrated mesh of membrane-associated proteoglycans, glycosaminoglycans, glycoproteins and glycolipids on top of the endothelial lining (1;2). In support of the protective effects of the glycocalyx, experimental models have confirmed that the glycocalyx indeed exerts a wide array of anti-atherogenic effects (3;4). Accordingly, damage to the glycocalyx has been shown to be a hallmark during the development of atherosclerosis, characterized by increased vascular permeability and adhesiveness (5-9).

Recently, we have developed techniques which allow reliable estimation of glycocalyx volume in humans. Using these techniques, we were able to show that during hyperglycemic-normoinsulinemic clamping glycocalyx volume was firmly reduced (1.8 to 0.7 liters) with subsequent coagulation activation and endothelial dysfunction (10). In subsequent experiments in diabetic patients, glycocalyx volume was found to be reduced by approximately 50% in uncomplicated diabetic patients, surmounting to more than 75% reduction in patients characterized by proteinuria.

Combined, these findings have led to the hypothesis that reversal of glycocalyx damage may provide an attractive therapeutic target to lower the pro-atherogenic state. Unfortunately, to date no drugs are available, which have the capacity to specifically improve glycocalyx perturbation. In this respect, experimental data have suggested that supplementation of glycocalyx constituents may have the capacity to restore glycocalyx damage to some extent (11;12). In this respect, our attention has been drawn to sulodexide, comprising a mixture of

glycosaminoglycans as well as heparan and dermatan sulphates. These substances are all abundantly present within the glycocalyx layer. Interestingly, sulodexide has been shown to decrease microalbuminuria in both type I and type II diabetic patients (13;14), the mechanism of which remains to be elucidated.

We hypothesize that sulodexide has the capacity to reverse glycocalyx damage in diabetic patients, which will result in decrease in systemic vascular permeability, restoration of endothelial function and attenuation of the pro-atherogenic state.

**Study objective**

Primary Objective:

Aim of the study is to investigate whether sulodexide treatment reverses damage of the systemic glycocalyx in patients with DM type II. The effect of sulodexide will be addressed in this prospective cross-over study measuring systemic and local glycocalyx volume, vascular permeability as well as endothelial function in patients with DM type II who have microalbuminuria and in patients with DM type II who do not have microalbuminuria.

Secondary Objective(s):

The second objective of the present study is to measure the effect of sulodexide on biochemical parameters, including micro-albuminuria and HBA1c, in patients with DM type II with and without microalbuminuria.

**Study design**

N/A

**Intervention**

Patients with DM type II and healthy volunteers will visit the hospital on 4 occasions: screening-inclusion visit, end of study period I, end of washout visit and end of study period II. At the end of each study period, we will evaluate glycocalyx volume and vascular permeability using dextran-40 and albumine-I125 for estimation of perm- versus charge selectivity. In addition, we will evaluate vascular function as well as routine laboratory parameters, including micro-albuminuria and safety parameters.

# Contacts

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# Eligibility criteria

## Inclusion criteria

Inclusion criteria are:

1. Male;

2. Age between 18 and 65 years.

## Exclusion criteria

Exclusion criteria are:

1. Smoking;

2. Immunosuppressive drugs;

3. Serious previous illnesses;

4. Coagulation disorders;

5. Primary dyslipidemias;

6. BMI > 30 kg/m2;

7. Hypertension (systolic >140 mm Hg or diastolic >90 mm Hg).

# Study design

## Design

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|---|---|
| Study type: | Interventional |
| Intervention model: | Crossover |
| Allocation: | Randomized controlled trial |
| Masking: | Single blinded (masking used) |
| Control: | Placebo |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-11-2006 |
| Enrollment: | 26 |
| Type: | Actual |

# Ethics review

Positive opinion

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|---|---|
| Date: | 25-09-2006 |
| Application type: | First submission |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| NTR-new | NL769 |
| NTR-old | NTR780 |
| Other | : 1 |
| ISRCTN | ISRCTN82695186 |

# Study results

**Summary results**
N/A