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

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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...

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|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving gestopt |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON24257

**Bron**
Nationaal Trial Register

**Verkorte titel**
SUGAR

**Aandoening**

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

### Ondersteuning

**Primaire sponsor:** AlfaWasserman, Italy

### Onderzoeksproduct en/of interventie

### Uitkomstmaten

**Primaire uitkomstmaten**

Main study parameter/endpoint:<br>
The difference in systemic glycocalyx volume after sulodexide and after placebo treatment.

# Toelichting onderzoek

### Achtergrond van het onderzoek

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.

### Doel van het onderzoek

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.

### Onderzoeksopzet

N/A

### Onderzoeksproduct en/of interventie

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.

## Contactpersonen

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### Wetenschappelijk

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## Deelname eisen

### Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Inclusion criteria are:

1. Male;

2. Age between 18 and 65 years.

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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).

# Onderzoeksopzet

## Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Cross-over |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Enkelblind |
| Controle: | Placebo |

## Deelname

Nederland

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|---|---|
| Status: | Werving gestopt |
| (Verwachte) startdatum: | 01-11-2006 |
| Aantal proefpersonen: | 26 |
| Type: | Werkelijke startdatum |

# Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 25-09-2006 |
| Soort: | Eerste indiening |

# Registraties

## Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

## Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

## In overige registers

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

# Resultaten

**Samenvatting resultaten**
N/A