

# **ARTEROSIL & THE ENDOTHELIAL GLYCOCALYX OVERVIEW OF RESEARCH STUDIES TO DATE**

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- **Carotid Plaque Regression**
- **Glycocalyx Regeneration**
- **Leukocyte Adhesion**
- **Arterial Elasticity**
- **Hypertension**

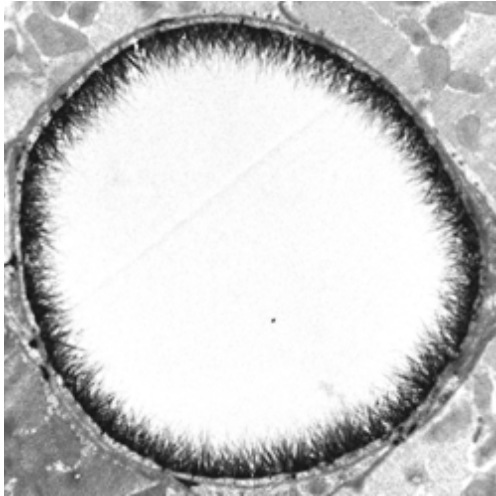
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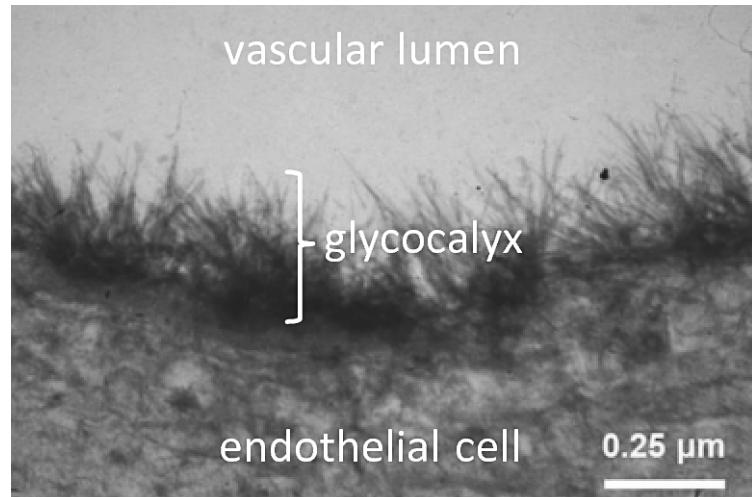
## The Endothelial Glycocalyx

The glycocalyx is a micro-thin gel covering the endothelial surface of every artery, vein and capillary. It protects the endothelium and regulates the following functions:

- Transduces blood shear to induce nitric oxide (NO) production
- Houses extra-cellular superoxide dismutase
- Acts as a selectively permeable barrier for molecules and cells such as LDL and leukocytes
- Inhibits platelet aggregation
- Harbors coagulation regulatory factors
- Prevents leukocyte adhesion



van den Berg, et al. *Circ Res* 2003 &  
*Endothelial Biomedicine* ed., W.C. Aird, 2007



Wiesinger A, Peters W, Chappell D, Kentrup D, Reuter S, Pavenstädt H, et al.  
(2013) Nanomechanics of the Endothelial Glycocalyx in Experimental Sepsis.  
*PLoS ONE* 8(11): e80905

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## The Studies: Overview

Numerous cellular, animal and human studies have been conducted to evaluate the biological activities, mechanism of action, and the health benefits of Arterosil, a patent-pending dietary supplement.

### 1. MRI Carotid Plaque Regression Study

Hospitals in Beijing—Human Proof-of-Concept Pilot

Burke Study Finding: Arterosil caused a significant reduction of lipid-rich necrotic core (LRNC) of carotid atherosclerotic plaque

### 2. Plaque Reduction Retrospective Case Study

Private Practice—True North Center for Functional Medicine

Finding: Arterosil caused a significant reduction of atherosclerotic plaque.

### 3. Glycocalyx Regeneration Study

Chinese Academy of Sciences—Cellular Study

Finding: Arterosil repairs and regenerates glucose-impaired endothelial glycocalyx

### 4. Leukocyte Adhesion Study

Maastricht University—Animal Study

Finding: Arterosil prevents the increase of leukocyte adhesion caused by enzymatic removal of the endothelial glycocalyx

### 5. Arterial Elasticity Study

Baylor Heart Institute Campus—Human Study

Finding: Arterosil improved endothelial function—arterial elasticity increased by an average of 89.6%

### 6. Hypertension Study

The Hypertension Research Institute—Human Study

Finding: Arterosil significantly lowered diastolic blood pressure

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# MRI Carotid Plaque Regression Study

Beijing Hospitals—Human Proof-of-Concept Pilot

**Preliminary Findings to Date**

**47% and 64% reduction of lipid-rich necrotic core (LRNC) of carotid atherosclerotic plaque in 60 days.**

**Maximal wall thickness (MWT) reduction was also observed.**

## Overview

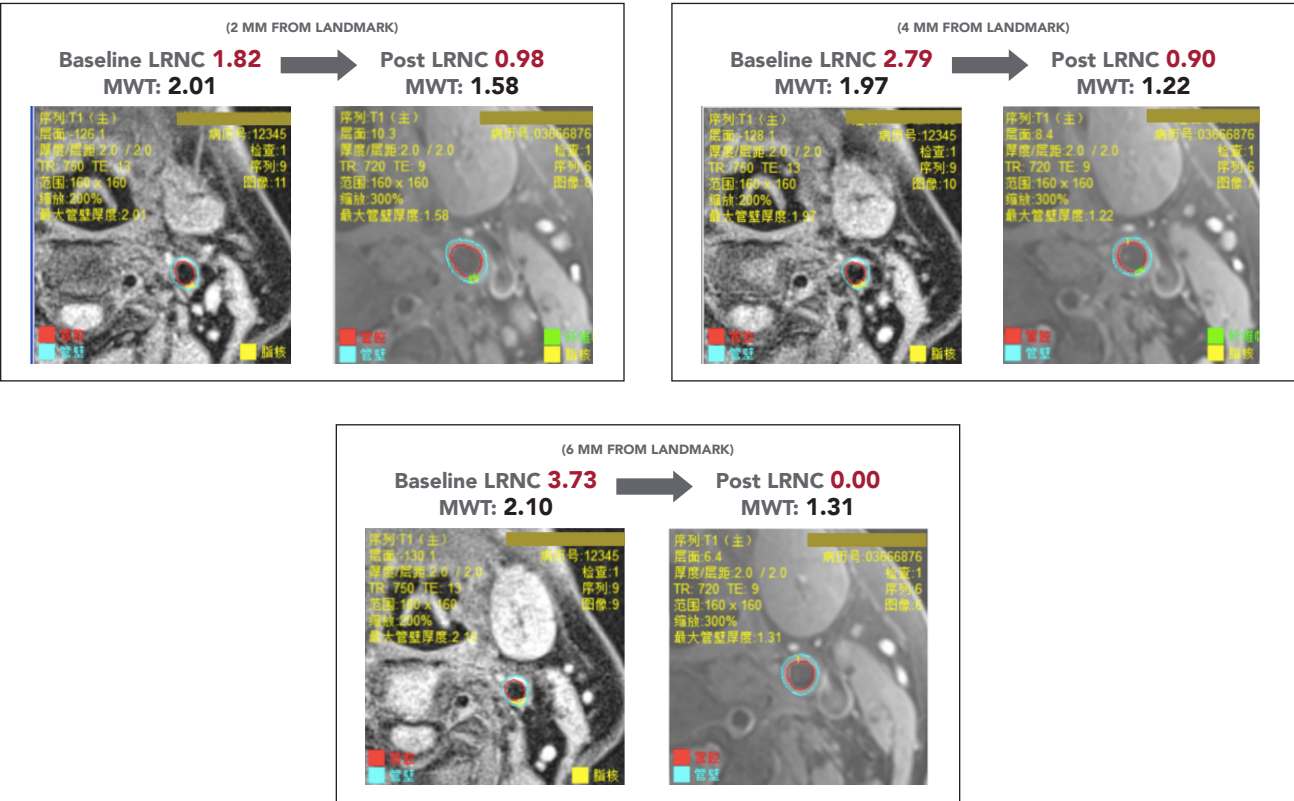
This proof-of-concept pilot study employs MRI PlaqueView®, an FDA-approved technology for advanced plaque characterization and quantification, to analyze the composition and morphology of atherosclerotic plaque including the lipid rich necrotic core (LRNC) of carotid plaque.

Following baseline MRI PlaqueView scans, two (2) Arterosil capsules were administered per day for 60 days. Post MRI scans were taken at 65 to 70 days, and data was analyzed using MRI PlaqueView. Based on the encouraging results of this pilot, a larger study is currently under design.

## Lipid Rich Necrotic Core (LRNC) Volume—Baseline, Post, and % Regression

Gender	Age	Baseline	Post	% Regression
Female	65	12.6%	4.5%	-64.3%
Male	65	7.7%	4.1%	-46.8%

## Sample Slice-by-Slice Baseline & Post Comparisons of LRNC and MWT at Varying Distances from Landmark



# Plaque Reduction Retrospective Case Study

Kristine Burke, MD—True Health Center for Functional Medicine

## Finding

Ten patients showed a reduction of atherosclerotic plaque averaging 52.2% following consumption of Arterosil over a period of 4 to 11 months.

## Overview

This retrospective study involved 10 male and female subjects ranging in age from 46 to 73. All had been treated over many years for difficult-to-reverse carotid atherosclerotic plaque. Over a 12-month period, Arterosil treatment was introduced, with patient usage varying from 4 to 11 months, consuming 1 capsule twice a day. Plaque was measured at the beginning and conclusion of the treatment period, using the carotid intima-media thickness test (CIMT). This non-invasive ultrasound technology measures the thickness of the intima and media, the inner two layers of the carotid artery.

Results varied, with seven patients showing a reduction of atherosclerotic plaque and three showing an increase. The average reduction of plaque across the whole group was 52%. A notable finding was that the patient group showed at the outset a mixture of calcified (echogenic) plaque and heterogeneous (echogenic plus echolucent) plaque, while at the conclusion of the study only heterogeneous plaque appeared.

## Total Plaque Burden (mm)

Subject ID	Age	Sex	Visit 1	Visit 2
1	73	Male	7.37	6.384
2	63	Male	0	1.899
3	50	Male	8.911	3.826
4	71	Male	10.464	2.516
5	71	Female	4.821	1.307
6	62	Male	12.52	4.442
7	64	Male	1.406	2.491
8	72	Female	11.33	5.13
9	46	Male	0	3.49
10	52	Female	2.49	0
Mean			5.331	2.928
% Change				-52.20%

# Glycocalyx Regeneration Study

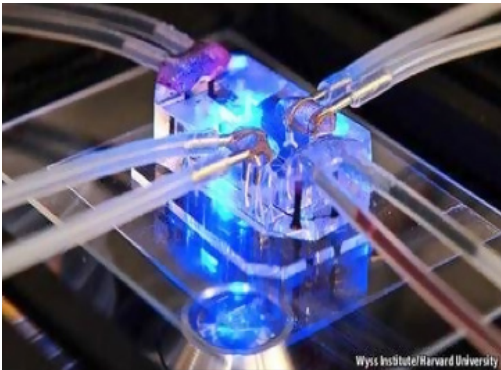
Chinese Academy of Sciences—Cellular Study

**Finding**  
**Arterosil repairs and regenerates glucose damaged endothelial glycocalyx.**

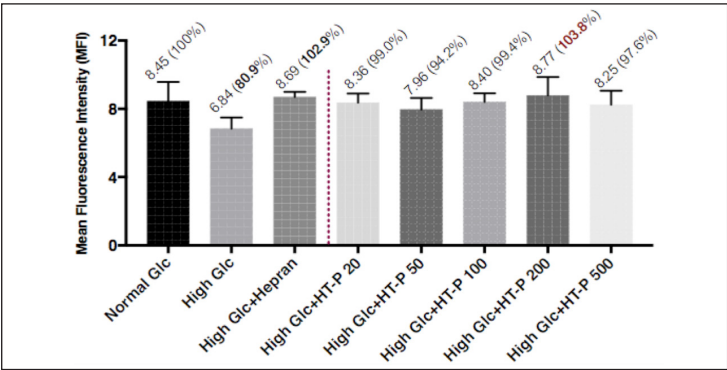
## Overview

A multi-layer microfluidic chip model was created to mimic the human endothelium with the endothelial glycocalyx under relevant physiological and pathological conditions. The model, with living human endothelial cells and living human endothelial glycocalyx, adequately simulates response of the endothelium with glycocalyx to various mechanical, biochemical, and biophysical stimuli. The “lab-on-a-chip” allows for rapid screening of glycocalyx regenerating compounds (GRCs) and evaluation of the endothelial glycocalyx under different physiological and pathological conditions in vitro.

Using a conjugated fluorescent probe, the study established that Arterosil prevents and repairs damage of the endothelial glycocalyx caused by excessive glucose in vitro.



Microfluid chip model of glycocalyx



# Leukocyte Adhesion Study

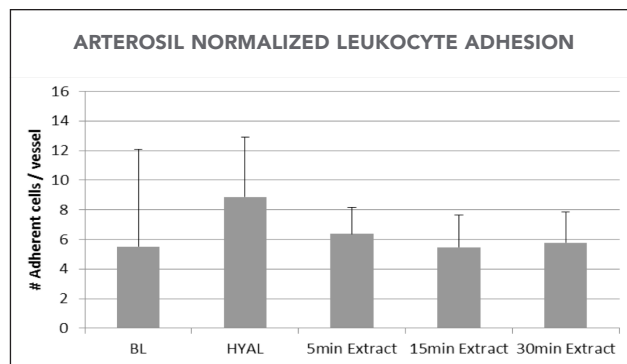
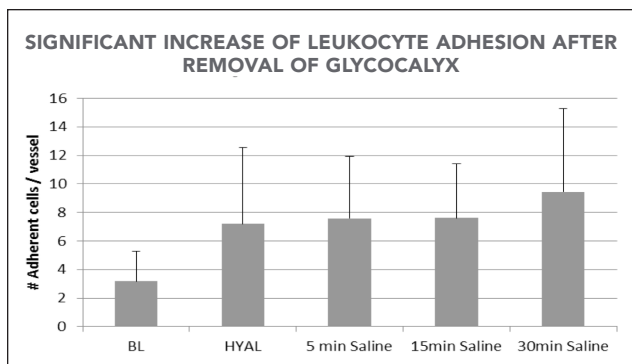
Maastricht University—Animal Study

**Finding**  
**Arterosil prevents the increase of leukocyte adhesion and inhibits endothelium-mediated inflammation.**

## Overview

The experiment was conducted by examining cremaster venules of male mice in vivo. The endothelial glycocalyx was removed using hyaluronidase enzyme. Numbers of patrolling leukocytes and adhering leucocytes were measured using intravital microscope.

The data showed a significant increase in leukocyte adhesion, with a simultaneous loss of patrolling leukocytes, after enzymatic removal of the glycocalyx. Arterosil normalized leukocyte adhesion and leukocyte patrolling activity.



## Arterial Elasticity Study

*Baylor Heart Institute Campus—Human Study*

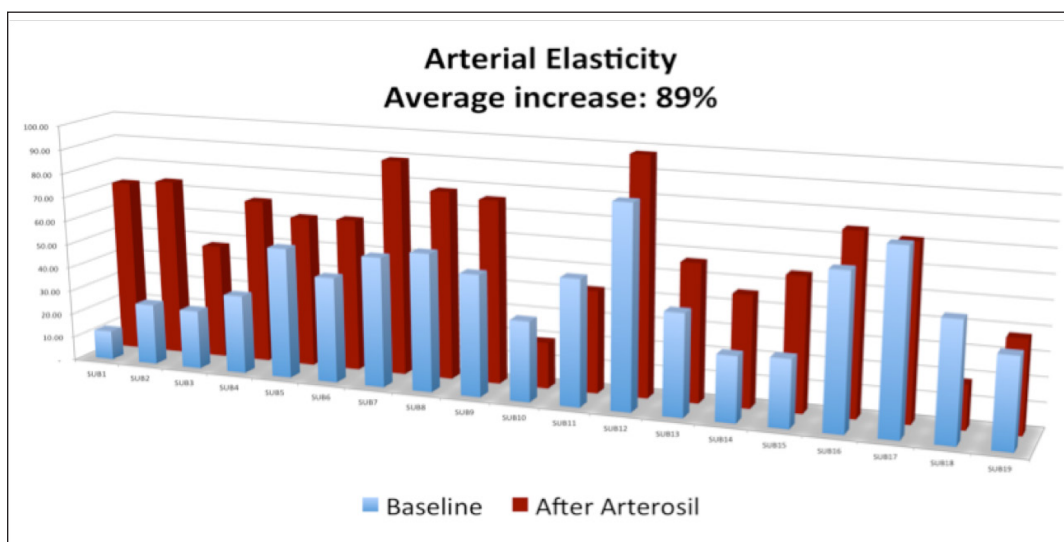
### Finding

**Arterosil improved endothelial function as demonstrated by an average of 89.6% increase in arterial elasticity.**

### Overview

Nineteen healthy human subjects were randomly recruited (11 females age 22 to 64 and 8 males age 30 to 60). Their vascular health condition was evaluated by an FDA-approved pulse wave analyzer. Their baseline reading was taken at approximately 2 hours (+/- 30 minutes) post consumption of a breakfast of their choice. Immediately after the baseline reading, one capsule of ArterosilHP was swallowed. A post-dose reading was taken every 30 minutes for 3 hours, for a total of 7 readings (baseline, 30 min, 60 min, 90 min, 120 min, 150 min & 180 min +/- 5 minutes).

Arterosil increased arterial elasticity by an average of 89.6% 2 hours post consumption, an indication of significant improvement of endothelial function.



# Hypertension Study

The Hypertension Research Institute at St. Thomas West Hospital—Human Study

**Finding**  
Arterosil significantly reduced diastolic blood pressure throughout the study.

## Overview

Ten uncontrolled hypertensive subjects were selected and placed on ArterosilHP (1 BID) for 3 months. They were measured for clinic blood pressure before (time zero), and 1, 2, and 3 months after taking Arterosil.

Diastolic blood pressure was significantly reduced after 1, 2, and 3 months of Arterosil therapy while systolic blood pressure also showed a downward trend.

Blood Pressure	Time Zero		1 Month		2 Months		3 Months	
	Mean	STDEV	Mean	STDEV	Mean	STDEV	Mean	STDEV
Systolic	151.5	10.5	151.0	12.3	142.6	12.6	147.5	16.1
Diastolic	93.2	2.3	85.1a	6.6	83.1b	7.5	82.3c	6.6

ap-Value = 0.003 (1 month vs time zero)  
bp-Value = 0.005 (2 months vs time zero)  
cp-Value = 0.0004 (3 months vs time zero)

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## Further Studies

Calroy is committed to an ongoing program of clinically relevant research. More studies have been designed and are being conducted to further our understanding of health benefits associated with endothelial glycocalyx restoration by Arterosil.

### The following studies are pending initiation:

#### **Hypertension Clinical Trial**

*The Hypertension Research Institute at St. Thomas West Hospital—Human Study*

This randomized, double-blinded, placebo-controlled clinical trial will expand on our initial study with Dr. Mark Houston at the Hypertension Institute.

#### **Atherosclerotic Plaque**

*Drexel University—Animal Study*

For this study we will use ApoE KO mice, which develop atherosclerosis rapidly on a high fat diet. We will have 2 groups of 10 mice, one on a control high fat diet with a placebo and the other on a test high fat diet with Arterosil for a total of 12 weeks. At the end of the study, plaque area in the aorta outside of the heart will be quantified as well as inflammation markers and liver fat. Blood lipid profile will also be monitored throughout the 12 weeks.

### The following studies are in design:

#### **Atherosclerotic Plaque w/o Statins**

*National Clinical Study Institute for Drugs at the Beijing University of Traditional Chinese Medicine—Human Study*

#### **Atherosclerotic Plaque w/ Statins**

*Multi-center USA—Human Study*

#### **Diabetic Neuropathy Pain**

*Multi-center USA—Human Study*

#### **Erectile Function**

*Multi-center USA—Human Study*

If you would like to know more about our research program, or are interested in participating in future studies, please contact us: [info@calroy.com](mailto:info@calroy.com)

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