ARTEROSIL & THE ENDOTHELIAL GLYCOCALYX
OVERVIEW OF RESEARCH STUDIES TO DATE

• 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 selective permeability barrier for molecules and cells such as LDL and leukocyte
- Inhibits platelet aggregation
- Harbors coagulation regulatory factors
- Prevents leukocyte adhesion

The Studies: Overview

Numerous cellular, animal and human studies have been conducted to evaluate the biological activities, mode of mechanisms, and therapeutic benefits of Arterosil, a patent-pending nutraceutical.

1. MRI Carotid Plaque Regression Study
   Hospitals in Beijing—Human Proof-of-Concept Pilot
   Finding: Arterosil caused a significant reduction of lipid-rich necrotic core (LRNC) of carotid atherosclerotic plaque

2. Glycocalyx Regeneration Study
   Chinese Academy of Sciences—Cellular Study
   Finding: Arterosil repairs and regenerates glucose-damaged endothelial glycocalyx

3. Leukocyte Adhesion Study
   Maastricht University—Animal Study
   Finding: Arterosil prevents the increase of leukocyte adhesion caused by enzymatic removal of the endothelial glycocalyx

4. Arterial Elasticity Study
   Baylor Heart Institute Campus—Human Study
   Finding: Arterosil improved endothelial function—arterial elasticity increased by an average of 89.6%

5. Hypertension Study
   The Hypertension Research Institute—Human Study
   Finding: Arterosil significantly lowered diastolic blood pressure

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, two (2) Arterosil capsules were administered per day for 60 days. Post MRI scans were taken at 65 to 70 days, and data 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

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>Baseline</th>
<th>Post</th>
<th>% Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>65</td>
<td>12.6%</td>
<td>4.5%</td>
<td>-64.3%</td>
</tr>
<tr>
<td>Male</td>
<td>65</td>
<td>7.7%</td>
<td>4.1%</td>
<td>-46.8%</td>
</tr>
</tbody>
</table>

Sample Slice-by-Slice Baseline & Post Comparisons of LRNC and MWT at Varying Distances from Landmark
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 to mimic the human endothelium with the endothelial glycocalyx under relevant physiological and pathological conditions was created. 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.

Leukocyte Adhesion Study
Maastricht University—Animal Study

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

Overview
Experiment 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 of 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.

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Time Zero</th>
<th>1 Month</th>
<th>2 Months</th>
<th>3 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>STDEV</td>
<td>Mean</td>
<td>STDEV</td>
</tr>
<tr>
<td>Systolic</td>
<td>151.5</td>
<td>10.5</td>
<td>151.0</td>
<td>12.3</td>
</tr>
<tr>
<td>Diastolic</td>
<td>93.2</td>
<td>2.3</td>
<td>85.1a</td>
<td>6.6</td>
</tr>
</tbody>
</table>

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)
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:

Randomized Hypertension Study
The Hypertension Research Institute at St. Thomas West Hospital—Human Study
This will be a carefully designed study expanding 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
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