Beyond LDL-Cholesterol: Vascular Endothelium as a Target for Optimal Cardiovascular Health

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Pleiotropic Cardiovascular Benefits of LCn-3PUFAs


Cerebro and Cardiovascular Disease: Mortality
(International data 1993; Sri Lanka 1995)

French Paradox vs Sri Lankan Paradox

- Only 10% of the Sri Lankan population is hypercholesterolaemic (>6.5 mmol/L); as compared to USA (39%) and Japan (11%)
- Average energy intake from fat - 25%; quality vs quantity?

Cardiovascular Disease Risk Factors

Diet and Cardiovascular Disease

“The paradigm that dietary fats act exclusively via effects on serum lipids and lipoproteins has been challenged”

AHA statement on Dietary Fats and Cardiovascular Health (2001)

- Better understanding of the disease process
- Evidence from epidemiological studies and dietary intervention trials

The diet (rich in n-3 PUFA) of the Eskimos, French Paradox as well as the Mediterranean diet played major role in the advancement of this knowledge

Cardiovascular diseases

• Infection/truma
• Catecholamines
**Sri Lanka: Average Dietary Intakes**

<table>
<thead>
<tr>
<th>Component</th>
<th>% of Total Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates</td>
<td>52</td>
</tr>
<tr>
<td>Fat</td>
<td>25</td>
</tr>
<tr>
<td>Protein</td>
<td>12</td>
</tr>
</tbody>
</table>

**Dietary Fat Composition (%):**

- Saturated: 10-15%
- Polyunsaturated: 1-2%
- Monounsaturated: 2-5%
- Sat./Poly: 9/0

**Total energy: 2000-3000 Kcal/day**

**Dietary cholesterol: High carbohydrate diet**

- ↑↑ ↑↑ blood glucose (postprandial period)
- ↑↑ ↑↑ insulin level
- ↑↑ ↑↑ plasma triglycerides

**Endothelial dysfunction**

- ↑↑ ↑↑ total cholesterol
- ↑↑ ↑↑ HDL
- ↑↑ ↑↑ LDL

**Vascular disease**

- ↑↑ ↑↑ triglycerides
- ↑↑ ↑↑ cholesterol
- ↑↑ ↑↑ low density lipoproteins

**Adverse Dietary Matrix Interactions and Vascular Endothelium**

- Excess carbohydrates (highly digestible) vs. High saturated fat intake

**Strategies for correction?**

- **Dietary**
- **Lifestyle**

**Experimental Protocol**

- **Animal model:** Normotensive WKY rat
- **Base diet:** AIN-93 diet formulation (corn starch)
- **Test Diets:**
  - Base diet + 5% w/w coconut oil (CO diet)
  - CO diet + 1% (sunflower oil)
  - CO diet + 1% L-arginine
  - CO diet where corn starch was replaced with Hi-Maize™ (a low digestible starch)
- **Control diet:** Standard laboratory chow
- **Pre-feeding:** 3 months pre-feeding prior to LAD coronary artery ligation
- **VEB, VT, VF, mortality quantified and AS (arrhythmia score) calculated**
In Vivo Coronary Artery Ligation Model

Pro-arrhythmic Actions of Dietary Coconut Oil:
Ventricular Tachycardia (VT) and Ventricular Fibrillation (VF)

15 min. ischaemic episode

*** P<0.0001

VT
VF

0
20
40
60
80
100
120

WKY Control (AIN-93) (N=9)
WKY Control (AIN-93 / CO) (N=23)
NIL

Pro-arrhythmic Actions of Dietary Coconut Oil:
% Mortality

15 min. ischaemic episode

% Mortality

Nil

Adverse Dietary Matrix Interactions:
Strategies for Correction

15 13 (2/15) 3.9 ± 0.4* 67 100 34.8 ± 13.9* 27.1 ± 6.4 504 ± 83 CO+SSO(1%) 15 60(9/15) 5.9 ± 0.4 87 93 100.4 ± 13.1 37.5 ± 15.1 606 ± 161 CO 14.2 ± 10.9** 0 ± 0**

VF (sec)

12 9

N

8 (1/12) 0 (0/9)

%Mortality

2.7 ± 0.4** 1.8 ± 0.5**

Diet Induced Abnormalities in Vascular Function
(changes in vascular relaxation)
Cardiovascular Benefits of Grape and Tea Polyphenols

- Oxidative stress / LDL oxidation
- Atherosclerosis
- Vascular relaxation / flow
- Platelet aggregation
- Myocardial ischemia / reperfusion
- Inflammation
- Cellular signalling / gene expression

Look After your Endothelium!