Cost Versus Benefit of Plant Extracts (Pycnogenol®) in Diabetes Risk Reduction
Pycnogenol

- Standardized extract from bark of French maritime pine (Pinus maritima)
- Primarily comprises of
  - Phenolic compounds (catechin, epicatechin, and taxifolin)
  - Flavonoids (procyanidins and proanthocyanidins)
- Mediates a number of beneficial effects in the cardiovascular system
  - Hypertension, diabetes, dyslipidemia
  - Improvement of endothelial function and NO production
Bioflavonoids (Pycnogenol®) in Reduction of Hypertension During Treatment of Diabetics to Minimize use of Pharmaceutical Drugs

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Mel and Enid Zuckerman College of Public Health, and College of Medicine, Tucson
Sugar utilization in type 2 diabetes

body cell

glucose transporter

is impaired
American Diabetes Association Statistics

There are 23.6 million people in the USA 8% of the population, who have diabetes

The total prevalence of diabetes increased 13.5% from 2005-2007.

Only 24% of diabetes is undiagnosed, down from 30% in 2005 and from 50% 10 years ago.

www.diabetes.org
Heart Disease Risk in Diabetes

Heart disease and stroke
Heart disease and stroke account for about 65% of deaths in people with diabetes. Adults with diabetes have heart disease death rates 2 to 4 times higher than adults without diabetes. The risk for stroke is 2 to 4 times higher.

High blood pressure
About 73% of adults with diabetes have blood pressure $\geq 130/80$ mmHg or use prescription medications for hypertension.

Cholesterol
Improved control of LDL cholesterol can reduce cardiovascular complications by 20% to 50%.

www.diabetes.org
Diabetes Study at
the University of Arizona Tucson

- 48 type II diabetes patients (40-75 years)
  double-blind, placebo controlled, 12 weeks treatment

- They are on medication: sulfonylurea, metformin, glitazones
  but fasting blood is still high: >140 mg/dL (120 is healthy)

- Patients are medicated with ACE-inhibitors
  But patients remain borderline hypertensive
  (average baseline systolic blood pressure 137 mmHg)

Constituents

Procyanidins: linked catechin subunits

Composition defined in:
United States Pharmacopoeia (28)
Pycnogenol® inhibits α-glucosidase

Pycnogenol® slows sugar absorption and prolongs satiety

Pycnogenol® lowers blood glucose

Blood glucose after meals

Patient’s baseline values

3 weeks
50 mg a day

225 mg/dL
-10.5%

209 mg/dL
-7.8%

185 mg/dL
-2.1%

181 mg/dL

3 weeks
100 mg a day

156 mg/dL
-5.3%

147 mg/dL
-4.7%

140 mg/dL
-3.3%

3 weeks
200 mg a day

136 mg/dL

Fasting blood glucose in the morning

Liu et al., Diabetes Care 27: 839, 2004
Pycnogenol® lowers fasting blood glucose

Pycnogenol® lowers blood glucose

Pycnogenol® releases artery constriction

In diabetes, endothelin-1 causes constriction

Pycnogenol inhibits endothelin-1 and increases NO, causing relaxation

Pycnogenol® releases artery constriction

Plasma Endothelin-1 pg/ml

Pycnogenol® lowers blood pressure in diabetic patients

At trial end, 58.3% of patients had a healthy blood pressure (<130 mmHg)

50% of these patients required less medication
Pycnogenol® lowers LDL cholesterol


**Pycnogenol® lowers LDL cholesterol**

- Serum LDL (mg/dL):
  - Start: 4
  - 1 month: 2
  - 2 months: 0
  - 3 months: -2

**Placebo**
- Start: 104.0
- 3 months: 107.0

**Pycnogenol**
- Start: 106.4
- 3 months: 93.7
  - Reduction: -12%
Pycnogenol® improves kidney function

Complications with chronic high blood sugar

Hyperglycemia (blood glucose levels too high)

- Ulcer (diabetic foot)
- Neuropathy (nerve damage)
- Retinopathy (eye damage)
- Macrovascular disease (arteriosclerosis)
- Nephropathy (kidney damage)
**Comparison of risk-factor reduction with cardiovascular risk-reducing drugs versus Pycnogenol**

<table>
<thead>
<tr>
<th>Improvement in:</th>
<th>Pycnogenol</th>
<th>Ramipril (10-5 mg daily)</th>
<th>Pravastatin (10-20 mg daily)</th>
<th>Nifedipine (10 mg daily)</th>
<th>Aspirin (500 mg daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP</td>
<td>5% Decrease 200 mg daily</td>
<td>50% Dose reduction</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mean total cholesterol</td>
<td>7.9% 120 mg daily</td>
<td>-</td>
<td>11.5%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td>19.2% 120 mg daily</td>
<td>-</td>
<td>18.0%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Serum endothelin-1</td>
<td>20% 100 mg daily</td>
<td>-</td>
<td>-</td>
<td>50% dose reduction</td>
<td>-</td>
</tr>
<tr>
<td>Platelet Reactivity</td>
<td>12.7% 125 mg daily</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.75%</td>
</tr>
</tbody>
</table>
## Cost comparison of cardiovascular risk-reducing drugs with Pycnogenol

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg)</th>
<th>Cost per Pill</th>
<th>Yearly Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pycnogenol</td>
<td>100</td>
<td>$0.61</td>
<td>$223</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>$0.39</td>
<td>$142</td>
</tr>
<tr>
<td>Ramipril</td>
<td>10</td>
<td>$1.67</td>
<td>$608</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>40</td>
<td>$1.67</td>
<td>$608</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>20</td>
<td>$2.50</td>
<td>$913</td>
</tr>
<tr>
<td>Aspirin</td>
<td>325</td>
<td>$0.01</td>
<td>$4.85</td>
</tr>
</tbody>
</table>
## Side effects for diabetes treatments

<table>
<thead>
<tr>
<th></th>
<th>Pycnogenol</th>
<th>Metformin</th>
<th>Glipizide</th>
<th>Repaglinide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Side effect</td>
<td>Minimal</td>
<td>Common</td>
<td>Minimal</td>
<td>Minimal</td>
</tr>
<tr>
<td>Side effect</td>
<td>Dizziness,</td>
<td>Abdominal</td>
<td>Hypoglycemia</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>description</td>
<td>nausea</td>
<td>pain, diarrhea</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Cost-effectiveness of pycnogenol and traditional treatments for type II diabetes

<table>
<thead>
<tr>
<th></th>
<th>Pycnogenol (125 mg/day)</th>
<th>Metformin (2,000 mg/day)</th>
<th>Glipizide (20 mg/day)</th>
<th>Repaglinide (2 mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Improvement in:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>0.80</td>
<td>1.4</td>
<td>1.82</td>
<td>1.1</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>23.7</td>
<td>52</td>
<td>74</td>
<td>36.1</td>
</tr>
<tr>
<td>LDL level (%)</td>
<td>11.94</td>
<td>15</td>
<td>No effect</td>
<td>9.51</td>
</tr>
</tbody>
</table>
Cost-effectiveness of pycnogenol and traditional treatments for type II diabetes

<table>
<thead>
<tr>
<th>Cost for each increment of improvement</th>
<th>Pycnogenol (125 mg/day)</th>
<th>Metformin (2,000 mg/day)</th>
<th>Glipizide (20 mg/day)</th>
<th>Repaglinide (2 mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (cost for a reduction of 1 percentage point)</td>
<td>$181</td>
<td>$415</td>
<td>$184</td>
<td>$844</td>
</tr>
<tr>
<td>Fasting glucose (cost per mg/dL reduction)</td>
<td>$10</td>
<td>$11</td>
<td>$5</td>
<td>$26</td>
</tr>
<tr>
<td>LDL level (cost for each percent reduction)</td>
<td>$19</td>
<td>$39</td>
<td>N/A</td>
<td>$98</td>
</tr>
<tr>
<td>Total yearly cost</td>
<td>$226</td>
<td>$582</td>
<td>$336</td>
<td>$929</td>
</tr>
</tbody>
</table>
The total economic cost of diabetes in 2007 for the USA was 147 billion dollars, excluding the losses in quality of life. Per capita annual cost of health care for people with diabetes was $11,744. Globally, direct health care costs of diabetes range from 2.5% to 15% of annual health care budgets. The significant costs of poorly controlled diabetes clearly place a strain on individuals and communities.
Pycnogenol shows promise as a supplement to traditional diabetes treatments and is competitively cost-effective as compared to the pharmaceutical regimen.
The cost and prevalence of diabetes continues to increase, which makes a cost-effective supplement like Pycnogenol very promising as a mediator of this cost and should be considered as a supplement for type II diabetics after considering the potential benefits.
Due to the relative cost-effectiveness of Pycnogenol, supplementation should be beneficial for patients at risk for CVD who are maxed out on the traditional treatment but still exhibit uncontrolled risk factors.

While CVD remains the leading cause of death in the USA, innovative and effective therapies are necessary, and Pycnogenol offers a potential cost-effective treatment that may help reduce the prevalence of CVD.