The antitumor effect of Samento, pentacyclic chemotype of *Uncaria tomentosa*, is probably due to its anti-inflammatory activity

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Samoto: pentacyclic chemotype (TOA free) of *Uncaria tomentosa*. The same botanical species that appears in other forms (composition of different secondary metabolites) due to different growing conditions

- **Pentacyclic oxindole alkaloids (POA)**
  Inhibits NF-κB, and the production of TNF-α, inhibits proliferation of human lymphoblasts and promotes phagocytosis

- **Tetracyclic oxindole alkaloids (TOA)**
  Antagonistic effects on POA, decreasing its effect

Bacher et al., 2005; Heitzman et al., 2005; García Prado et al., 2007; Pilarski et al., 2007
Objective

Evaluate the anti-inflammatory and anti-tumour effects of Samento (pentacyclic chemotype of Uncaria tomentosa)
## Results

### Effect of the extracts on cell viability *in vitro.*

<table>
<thead>
<tr>
<th></th>
<th>RAW 267.4</th>
<th>LSEC</th>
<th>4T1</th>
<th>HeLa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Macrophages</td>
<td>Mouse liver endothelial cells</td>
<td>Mouse mammary carcinoma</td>
<td>Human endocervix carcinoma</td>
</tr>
<tr>
<td></td>
<td>GI&lt;sub&gt;50&lt;/sub&gt;</td>
<td>TGI</td>
<td>LC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>GI&lt;sub&gt;50&lt;/sub&gt;</td>
</tr>
<tr>
<td>Samento</td>
<td>97.9</td>
<td>&gt;100</td>
<td>&gt;100</td>
<td>49.98</td>
</tr>
<tr>
<td>Fraction A</td>
<td>58.1</td>
<td>&gt;100</td>
<td>&gt;100</td>
<td></td>
</tr>
<tr>
<td>Fraction B</td>
<td>62.3</td>
<td>&gt;100</td>
<td>&gt;100</td>
<td></td>
</tr>
</tbody>
</table>

Cell viability was measured by the Sulphorhodamine B chromogenic assay after a 48 h incubation in the presence of Samento, Fraction A, and Fraction B.

GI<sub>50</sub> – 50% growth inhibition  
TGI – 100% growth inhibition  
LC<sub>50</sub> – 50% citotoxicity

Column chromatography RP18  
A - ~ Alkaloids  
B - ~ Tanins, sugars
Macrophages were treated with Samoto, Fraction A and Fraction B for 2 h, then challenged with LPS (2 ug/ml). After 48 h, supernatant was extracted and then assayed for NO.
Results

Inhibition by Samoto and their fractions of IL-6 response to LPS in RAW 267.4 macrophages.

Macrophages were treated with Samoto, Fraction A, and Fraction B on 2 h, then challenged with LPS (2 ug/ml). After 48 h, supernatant was extracted and then assayed for IL-6.
Results

Inhibition by Samento and their fractions of TNF-α response to LPS in RAW 267.4 macrophages.

Macrophages were treated with Samento, Fraction A, and Fraction B on 2 h, then challenged with LPS (2 ug/ml). After 48 h, supernatant was extracted and then assayed for TNF-α.
HeLa cells, transfected with the NF-κB luciferase reporter system, were treated for 1 h, then stimulated with hu TNF-α for a further 4 h. NF-κB activity was assessed using luciferin as substrate.
Results

**Inhibition by Samento of the NO and IL-6 to LPS in mice**

BALB/c mice were pretreated with Samento i.p. on 2 h, then challenged with LPS. After 1 h, blood was extracted and the serum assayed for NO and IL-6.
Results

Inhibition by Samento of the TNF-α to LPS in mice

BALB/c mice were pretreated with Samento i.p. on 2 h, then challenged with LPS. After 1 h, blood was extracted and the serum assayed for TNF-α.
Results

Effect of Samento on growth of 4T1 primary mammary tumours in Balb/c mice.

BALB/c mice were inoculated s.c. with $5 \times 10^5$ 4T1 R+G+ tumor cells to initiate a primary tumor and injected i.p. 5 times a week up to day 35 with 0,8 mg/kg y 4 mg/kg Samoto.
Results

Effect of Samento on 4T1 metastasis in Balb/c mice.

BALB/c mice were inoculated s.c. with $5 \times 10^5$ 4T1 R+G+ tumor cells to initiate a primary tumor and injected i.p. 5 times a week up to day 35 with 0,8 mg/kg y 4 mg/kg Samento. Lung metastases were counted on day 35.
The GI50 of Samento for the 4T1 cells (81 µg/ml) cannot explain the inhibitory effect of Samento on tumour growth in the mice (16 µg/animal).

Samento shows an inhibitory effect on several inflammatory mediators (here and in the literature).

The antitumor effect of Samento, pentacyclic chemotype of *Uncaria tomentosa*, is probably due to its anti-inflammatory activity.

Further evaluation of the fractions of Samento should elucidate the role of the POA’s and TOA’s in this activity.