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

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Samento

Samento: 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.*

	RAW 267.4			LSEC			4T1			HeLa		
	Macrophages			Mouse liver endothelial cells			Mouse mammary carcinoma			Human endocervix carcinoma		
(µg/ml)	**GI_{50}**	**TGI**	**LC_{50}**	**GI_{50}**	**TGI**	**LC_{50}**	**GI_{50}**	**TGI**	**LC_{50}**	**GI_{50}**	**TGI**	**LC_{50}**
Samento	97.9	>100	>100	49.98	>100	>100	81	>100	>100	97.4	>100	>100
Fraction A	58.1	>100	>100				47.2	>100	>100	9.2	90.6	>100
Fraction B	62.3	>100	>100				87.1	>100	>100	35.8	>100	>100

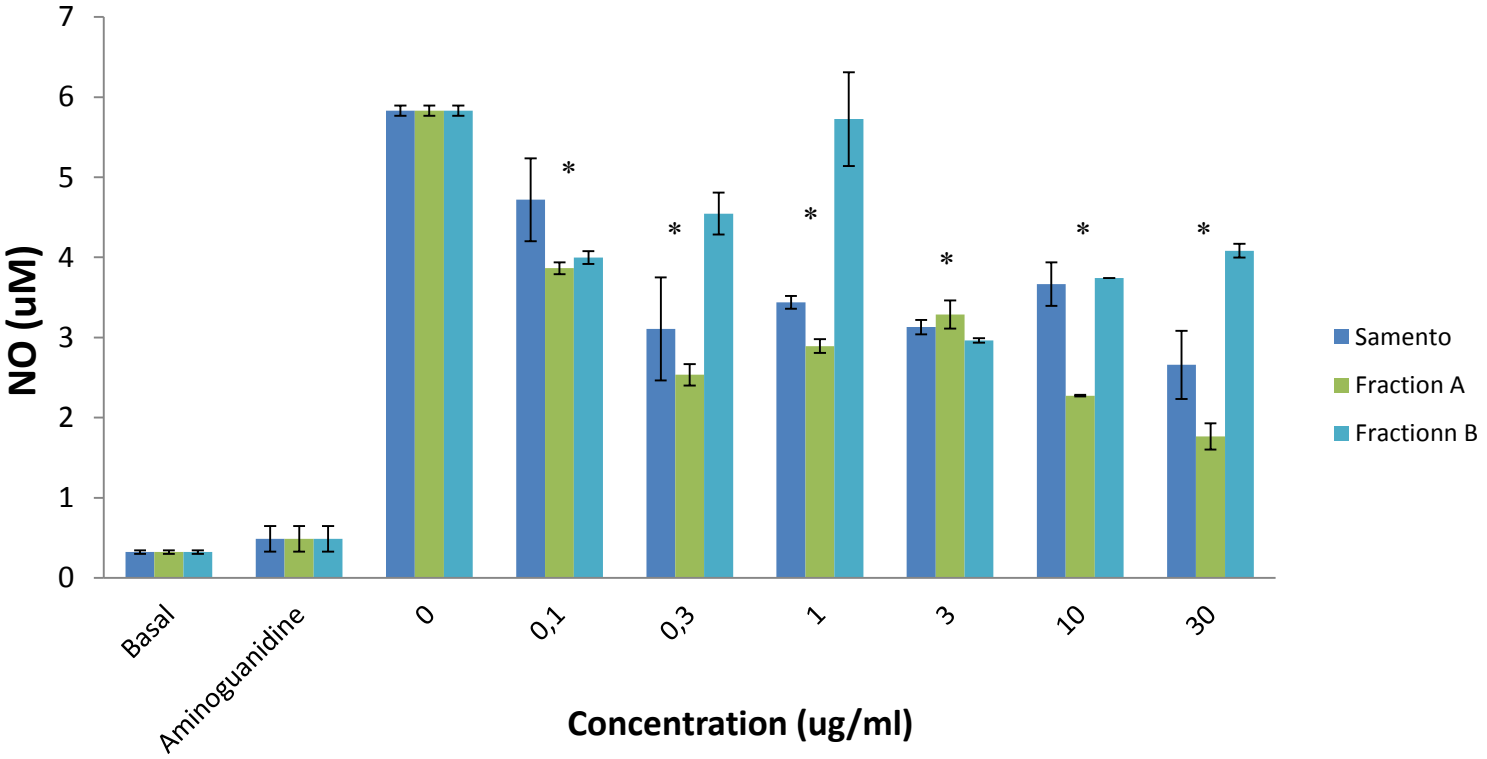
Cell viability was measured by the Sulphorhodamine B chromogenic assay after a 48 h incubation in the presence of Samento, Fraction A and Fraction B.

Column chromatography RP18
A - ~ Alkaloids
B - ~Tanins, sugars

GI_{50} – 50% growth inhibition
TGI – 100 % growth inhibition
LC_{50} – 50 % citotoxicity

Results

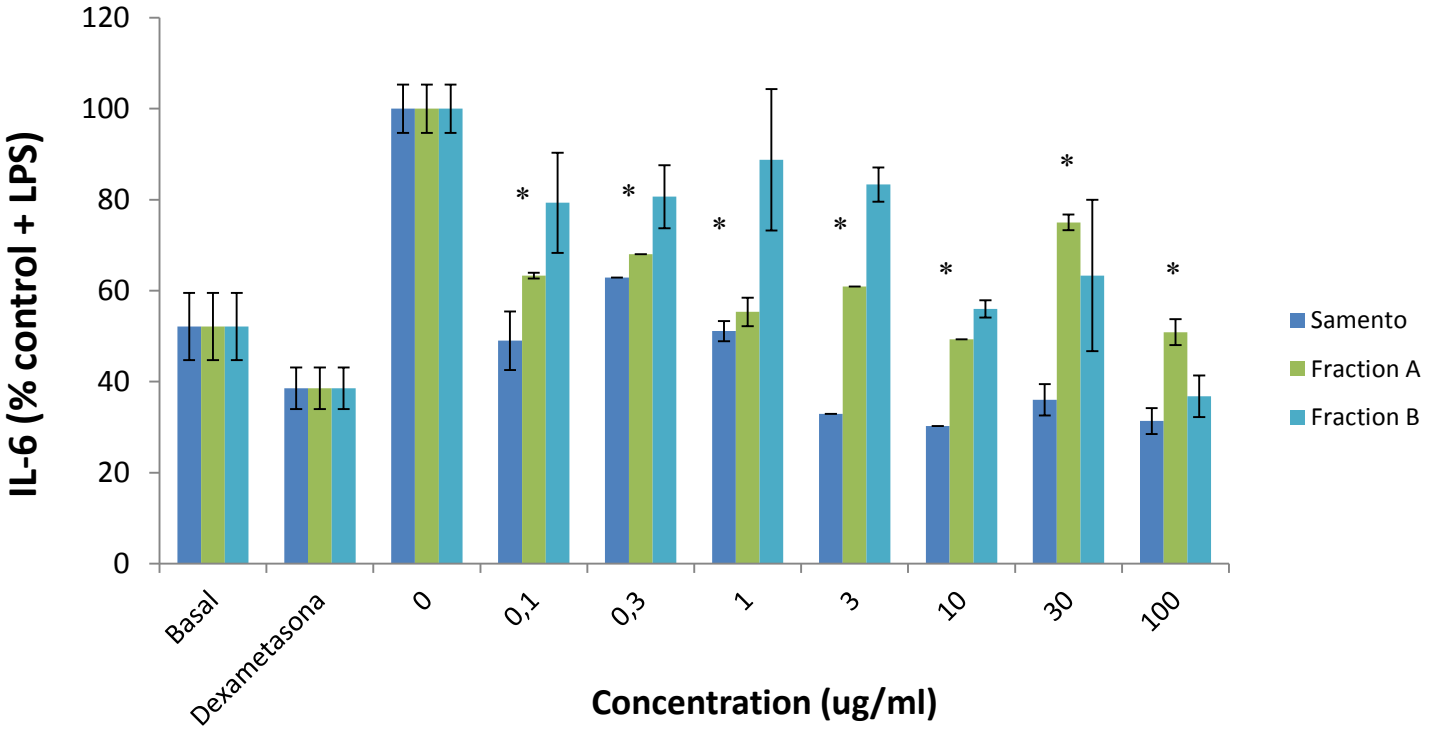
Inhibition by Samento and their fraction of the Nitric Oxide response to LPS in RAW 267.4 macrophages.



Macrophages were treated with Samento, 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

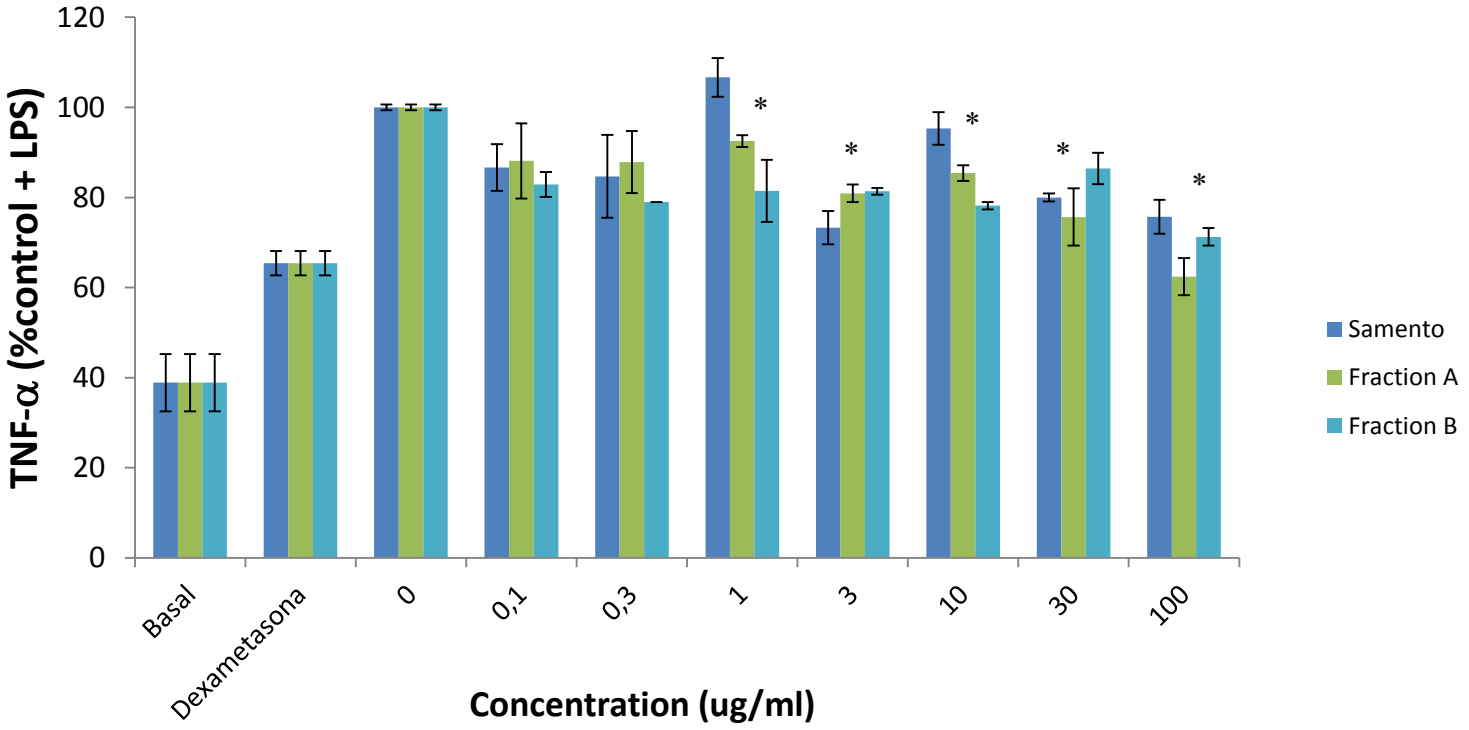
Inhibition by Samento and their fractions of IL-6 response to LPS in RAW 267.4 macrophages.



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 IL-6.

Results

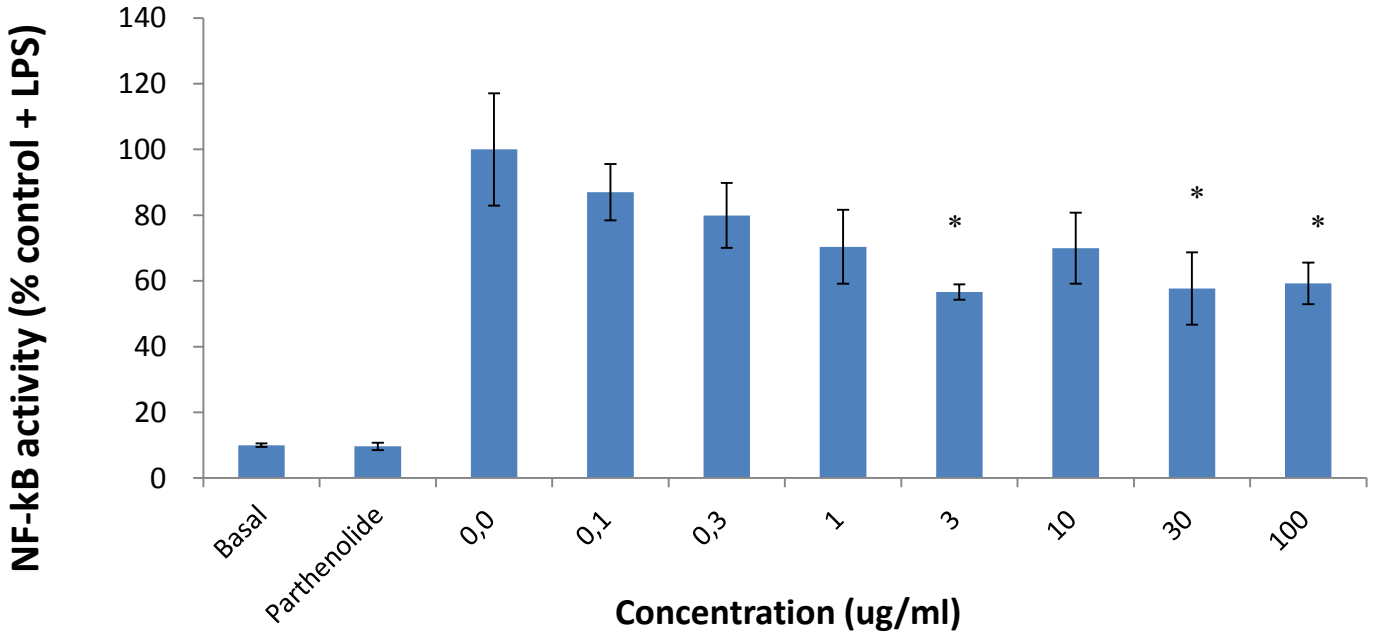
Inhibition by Samento and their fractions of TNF- α response to LPS in RAW 267.4 macrophages.



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.

Results

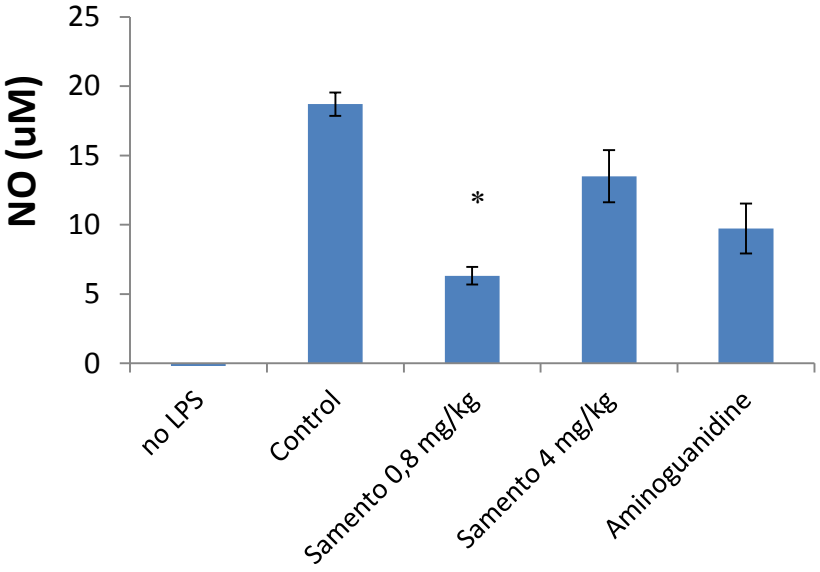
Effect of Samento on NF-κB activity.

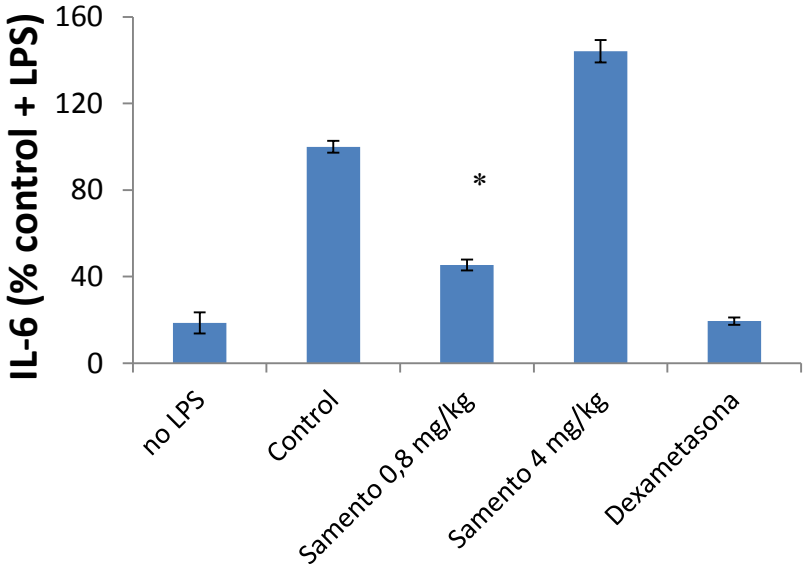


HeLa cells, transfected with the NF-κB luciferase reporter system, were treated for 1 h, then stimulated with hu TNF-α for a further 4 h. NF-κB activity was assessed using luciferin as substrate

Results

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

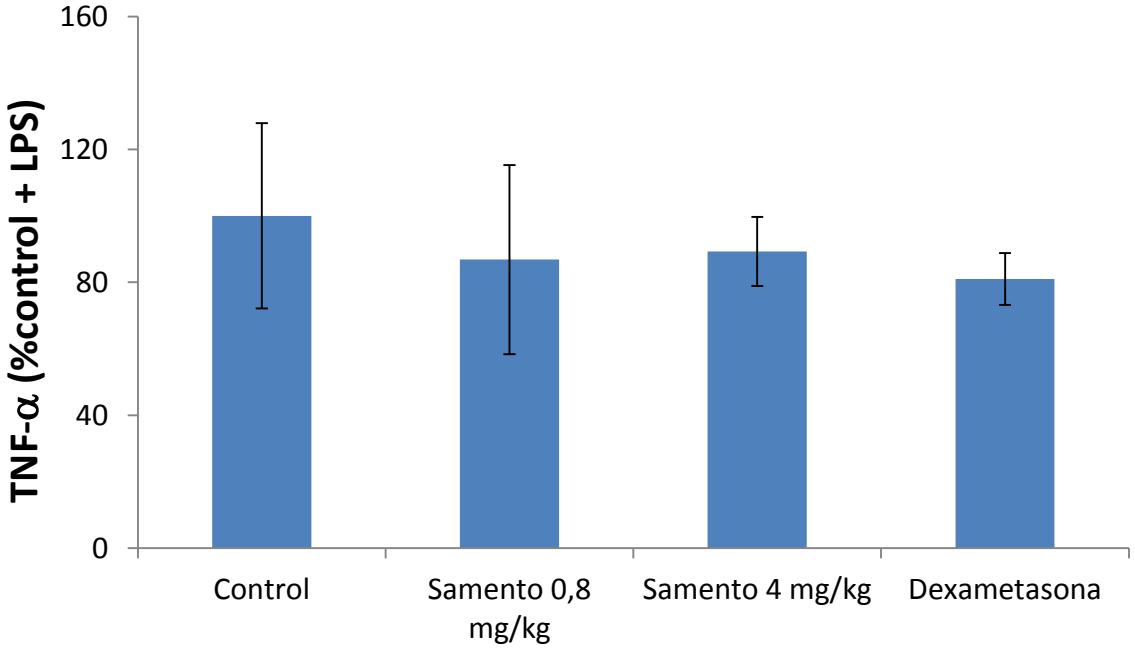




BALB/c mice were pretreated with Samento i.p. on 2 h, then challenged with LPS. After 1 h, blood was extracted and the serum assayed for NO and IL-6

Results

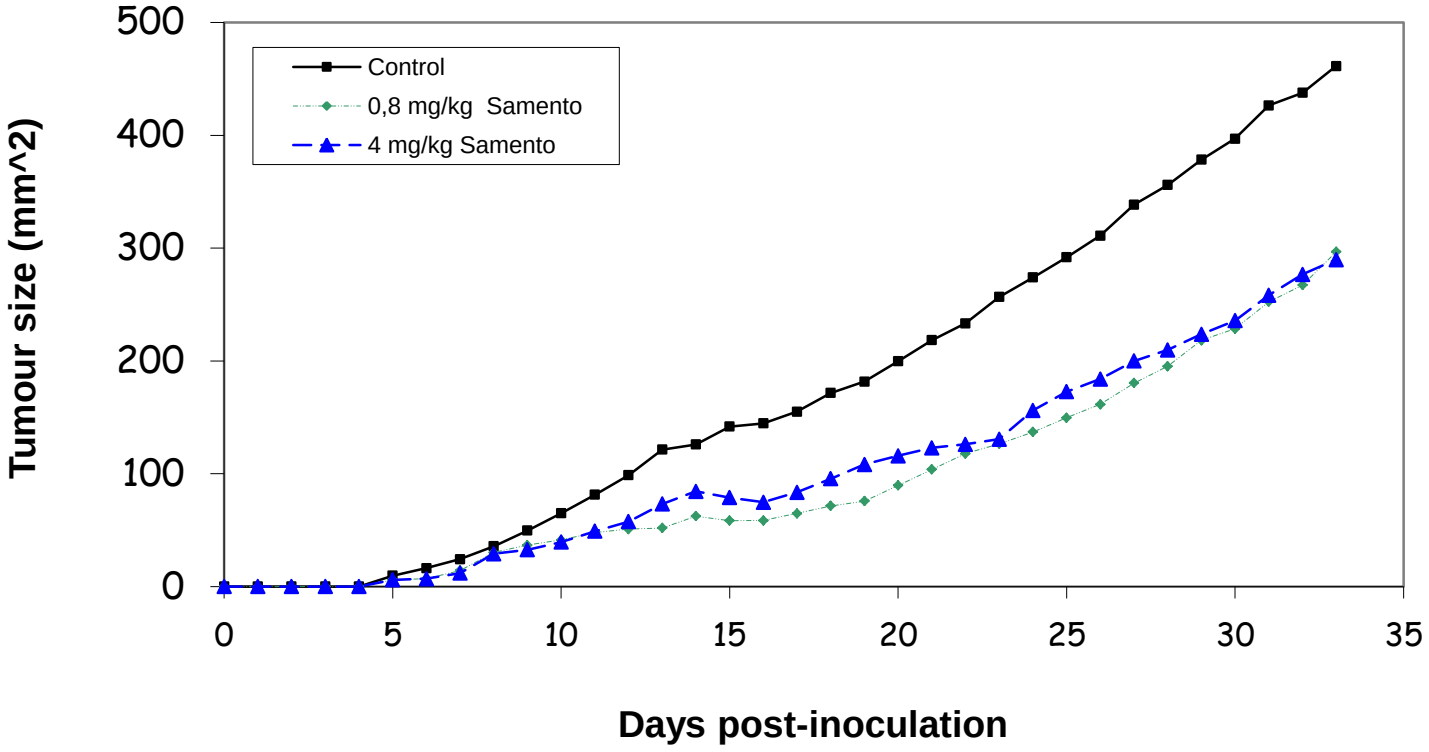
Inhibition by Samento of the TNF-α to LPS in mice



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

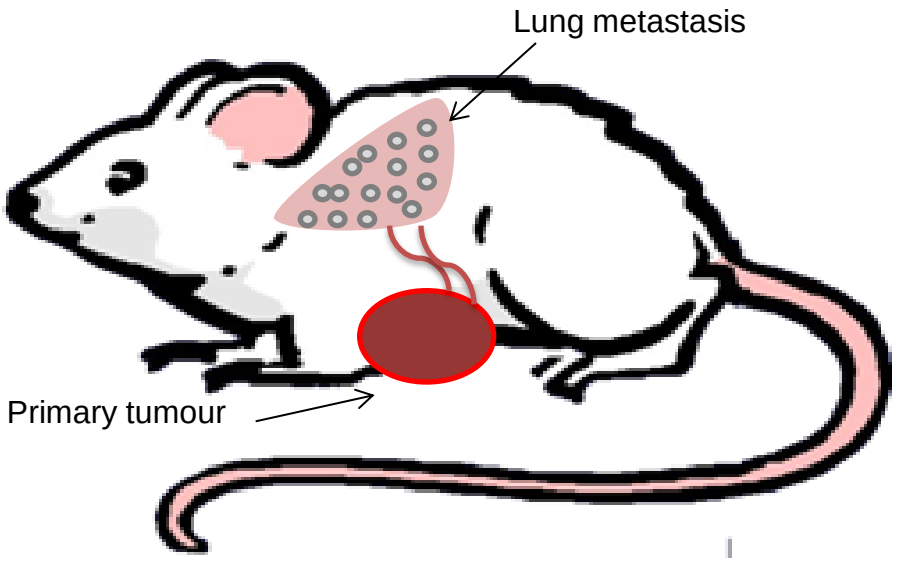
Effect of Samento on growth of 4T1 primary mammary tumours in Balb/c mice.



BALB/c mice were inoculated s.c. with 5 x 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.

Results

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



Control	Samento 0,8 mg/kg	Samento 4 mg/kg
4/7	0/7	0/7

BALB/c mice were inoculated s.c. with 5 x 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.

Conclusions / working hypothesis

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.