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CATALYSIS FOR A SUSTAINABLE WORLD

The antiparasite activity of bioactive isoflavans from *Tabebuia chrysantha* timber by-products

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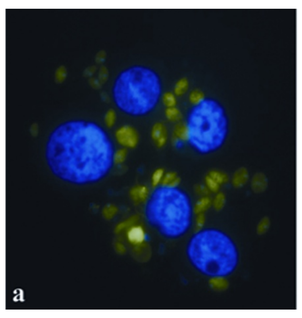
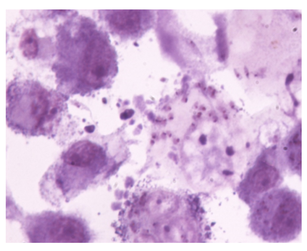
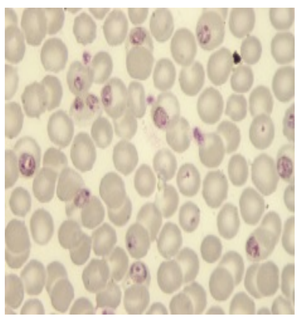
INTRODUCTION



Leishmania amastigotes



T. cruzi amastigotes



P. falciparum Intraerhytrocytes stages

Parasitic diseases, including malaria, leishmaniasis, and Chagas disease, represent one of the most significant morbidity and mortality burdens worldwide, and many of them affect the most impoverished populations of the world but very few therapeutic options are available. Timber by-products are an interesting and emerging source of secondary metabolites. *Tabebuia chrysantha* (Jacq.) G. Nicholson 1887, is a tree of the Family Bignoniaceae, commonly known by the name of "guayacan Amarillo" (yellow guayacan). It is native to the dry forests of the American intertropical zone. Through bio-guided in vitro assays, high activities in the ethanolic extract (SQB-11) and metabolites from *T. chrysantha* sawdust were detected against *Leishmania braziliensis, Trypanosoma cruzi* and *Plasmodium falciparum.*

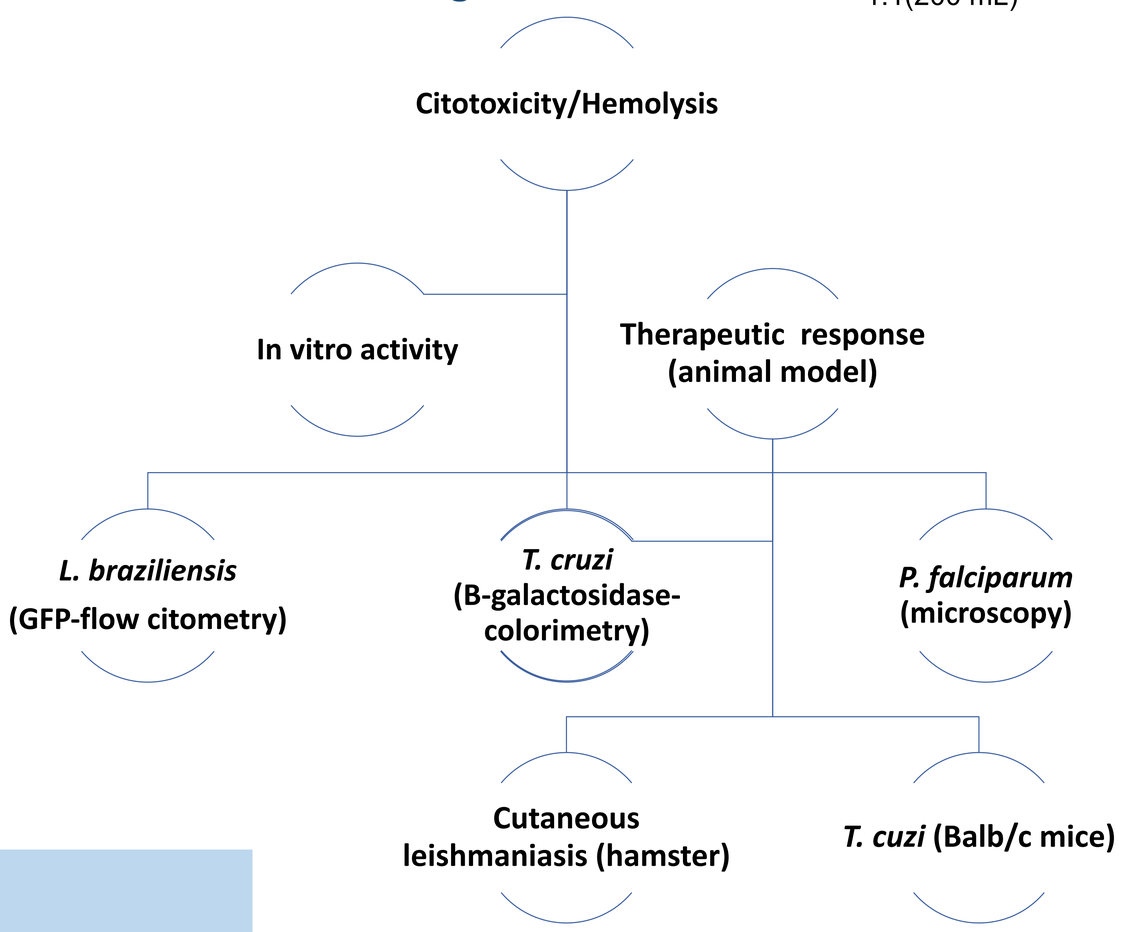
EXPERIMENTAL STRATEGY

Obtention extracts/fractions/metabolites

Extract: exclusion chromatography (Sephadex LH-20 and 100% methanol.

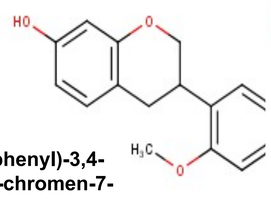
Fractions: column chromatography (silica gel 60 and mixture of petroleum ether : ethyl acetate 4:1(250 mL), 3:1(400 mL), 2:1(300 mL), 1:1(200 mL)

Biological activities



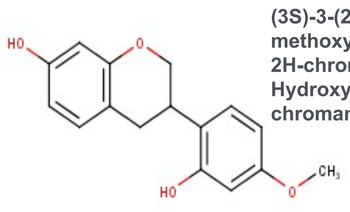
RESULTS

Structure of active metabolites isolated from *T. chrysantha* sawdust.



(3R)-3-(2,4-dimethoxyphenyl)-3,4-dihydro-2H-chromen-7-ol)

Sativan



Vestitol

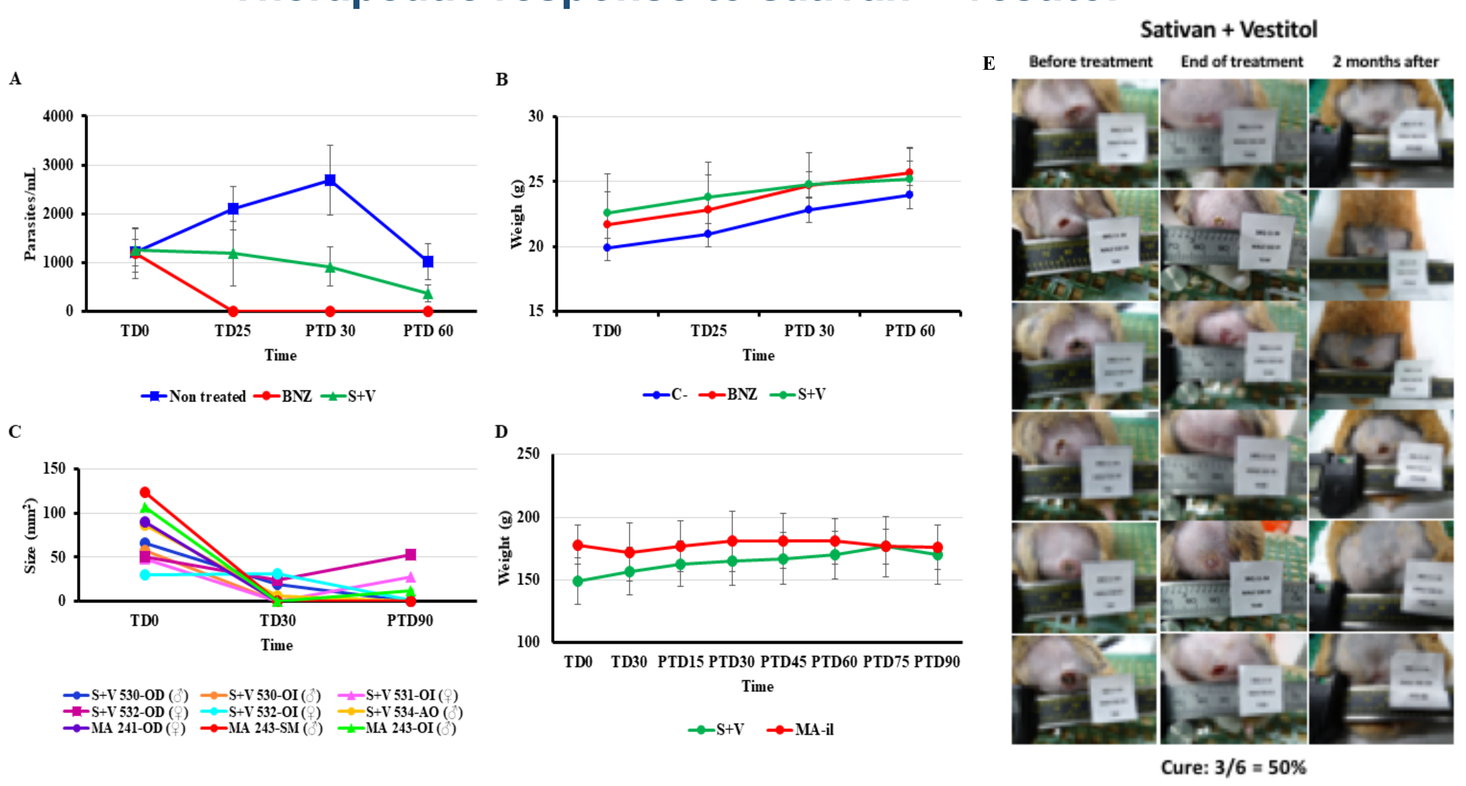
(3S)-3-(2-hydroxy-4-methoxyphenyl)-3,4-dihydro-2H-chromen-7-ol. (3S)-3-(2-Hydroxy-4-methoxyphenyl)-7-chromanol

In vitro activity of *T. chrysantha* fractions and pure compounds

Sample	Code	Cytotoxicity LC_{50} (µg/mL) [a]	Antiparasite activity					
		U-937 cells	*L. braziliensis*		*T. cruzi*		*P. faciparum*	
			EC_{50} (µg/mL) [b]	SI [c]	EC_{50} (µg/mL)	SI	EC_{50} (µg/mL)	SI [d]
Crude Extract	SQB-11	60.8 ± 5.2	17.7 ± 1.4	3.4	21.3 ± 1.9	2.9	14.4 ± 0.4	14
Fractions	SQB-11 S3	13.2 ± 1.7	7.9 ± 0.3	1.7	58.9 ± 8.3	0.2	84.7 ± 19.6	0.16
	SQB-11 S4	13.2 ± 0.8	11.1±	1.20	5.1 ± 0	0.1	85.8 ± 20.4	0.2
	SQB-11 S5	7.7 ± 0.3	6.7 ± 1.7	1.15	47.7 ± 12.4	0.2	78.2 ± 19.6	0.1
	SQB-11 S6	7.9 ± 0.3	3.3 ± 0.3	2.38	32.8 ± 5.8	0.2	20.0 ± 0.5	0.4
	SQB-11 S8	128.9 + 28.2	23.3 ± 4.2	<2.57	36.7 ± 4.2	3.8	20.0 ± 0.6	7.1
Sativan	S4-S4	7.3 ± 0.7	5.5 ± 0.5	1.3	6.6 ± 0.8	1.7	20.6 ± 1.0	>20. 7
Vestitol	S4-S6	10.0 ± 2.4	5.3 ± 0.4	1.9	7.1±0.5	1.4	37.4 ± 2.8	5.3
AMB[e]		36.6 ± 3.0	0.3 ± 0.1	122.0	NA[f]	NA	NA	NA
BNZ[g]		>200.0	NA	NA	15.8 ± 2.6	>12.7	NA	NA
DOX[h]		1.0 ± 0.2	NA	NA	NA	NA	NA	NA
CQ[i]		155.2 ± 5.2	NA	NA	NA	NA	3.4 ± 0.4	58.8

Data represent the mean value ± standard deviation. Bold values are active compounds (EC50 < 25 µg/mL). a: LC_{50}: Lethal concentration on U-937 cells; b: EC_{50}: Effective concentration on intracellular amastigotes of *L. braziliensis or T. cruzi;* c: SI: Selectivity index for *L. braziliensis* and *T. cruzi* calculated by LC_{50} in U937 cells ÷ EC_{50}; d:SI: Selectivity index for *P. falciarum* calculated by LC_{50} in huRBC ÷ EC_{50}; e: amphotericin B; f:Not applicable; g: Benznidazole; h: Doxorubicin; i: Chloroquine.

Therapeutic response to sativan + vestitol



Upper panel: Evolution of parasitemia (A) and weight (B) in Balb/c mice infected by *T. cruzi* and treated with intraperitoneal Vestitol + Sativan vs BNZ (100 mg/d/25 Lower panel: Evolution of lesion (C) and weight (D) in golden hamsters infected by *L. braziliensis* and treated topically with Vestitol+Sativan (60 µL/d/60d) vs intralesional meglumine (200 mg/3x week/4 weeks). E: appareace of lesion before and after treatment with a mixture of sativan and vestitol in hamsters with cutaneous leishmaniasis

CONCLUSIONS

***T. chrysantha* sawdust has metabolites with activity against *L. braziliensis* and *T. cruzi* but not against *P. falciparum.* These results highlight the pharmacological potential of waste from the wood industry, which has tons of useful chemicals for the development of new anti-parasite drugs.**

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