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CATALYSIS FOR A SUSTAINABLE WORLD

# The triterpene hederagenin glucoside saponins and chromane hydrazone 2-(2,3-dihydro-4h-1-benzopyran-4-ylidene) hydrazide as active ingredients of topical formulation to treat cutaneous leishmaniasis

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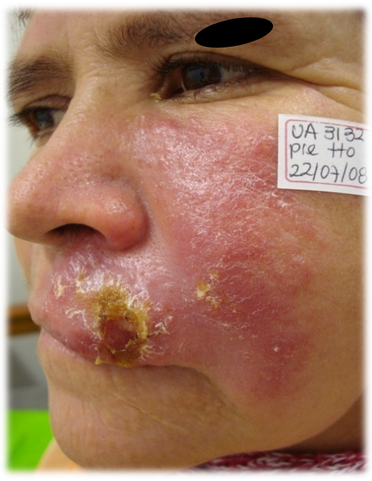
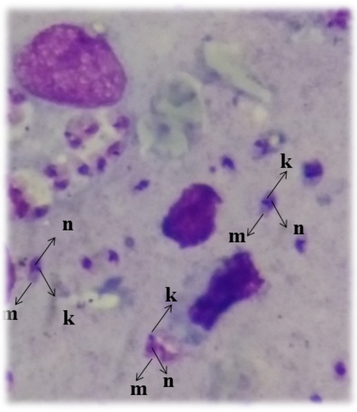
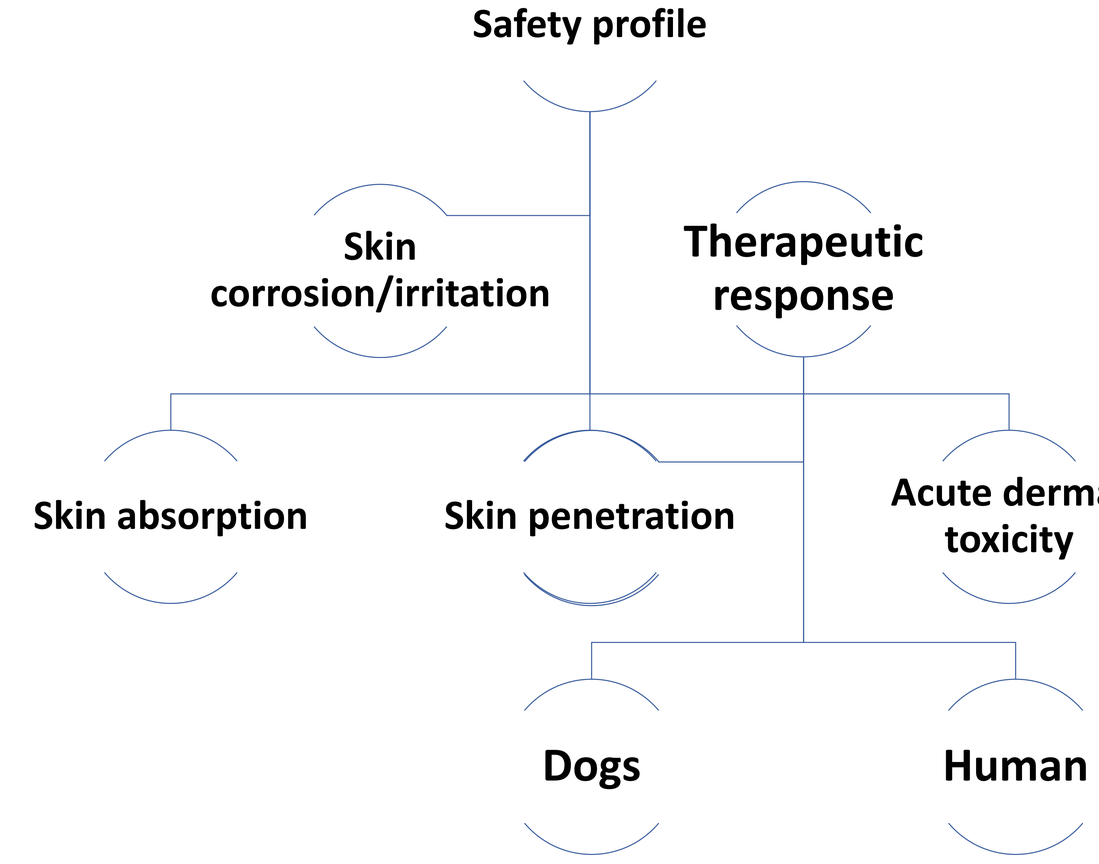
## INTRODUCTION





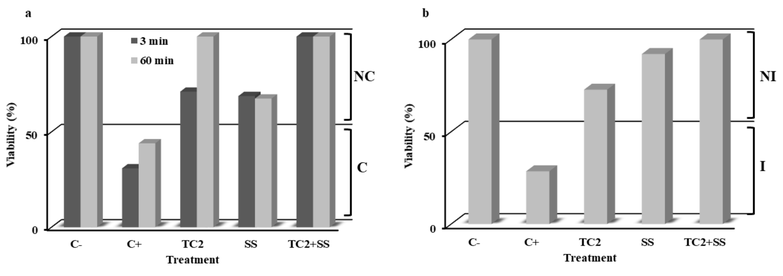

Cutaneous leishmaniasis (CL) is an endemic infection worldwide. Due to variable response to therapy and frequency of relapses, a more effective, safe, and inexpensive treatment is needed. Previously it was reported that the hederagenin glucoside saponins (SS) and chromane hydrazone (TC2) combined in a 1:1 ratio has high potential in antileishmanial therapy since both compounds may alter the survival of *Leishmania* and the ability to infect adjacent macrophage. In this work, we developed an ointment formulation containing 2% TC2 and 2% SS (w/w) and determined the skin permeation and the absorption but also the acute dermal toxicity by in vitro and in vivo assays.

## EXPERIMENTAL STRATEGY

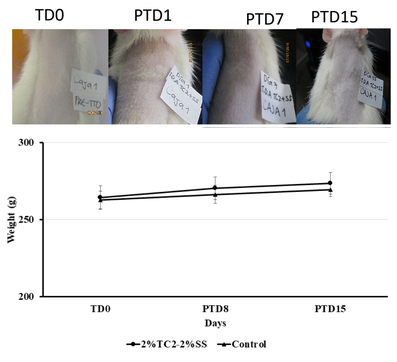

## RESULTS

### In vitro skin corrosion and irritation test



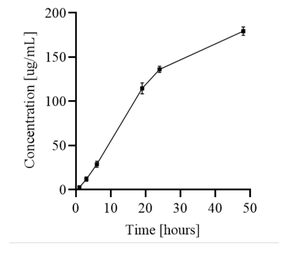

The bars represent the mean±SD of the percentage of cell viability after 3 min and 60 min of exposure for corrosion (a) and 42 min of exposure for irritation (b). TC2: 2% solution; SS: 2%

### Dermal toxicity in Wistar rats

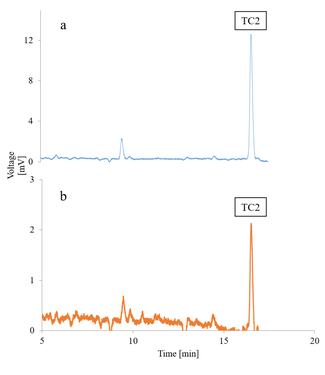



No bodyweight alterations nor signs of dermal toxicity were observed

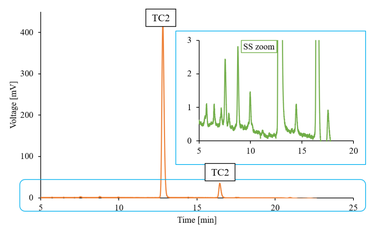
### Kinetic of TC2 and SS



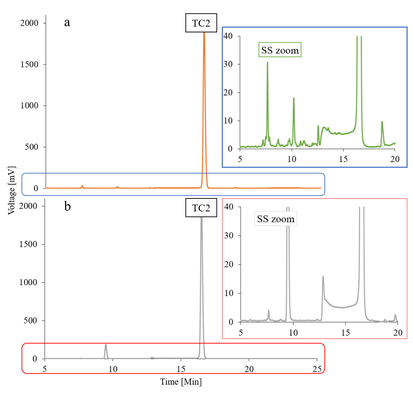

Kinetic of TC2 permeation. The figure shoes the permeability profile of TC2 for 48 h in acceptor solution and pig ear skin membrane.



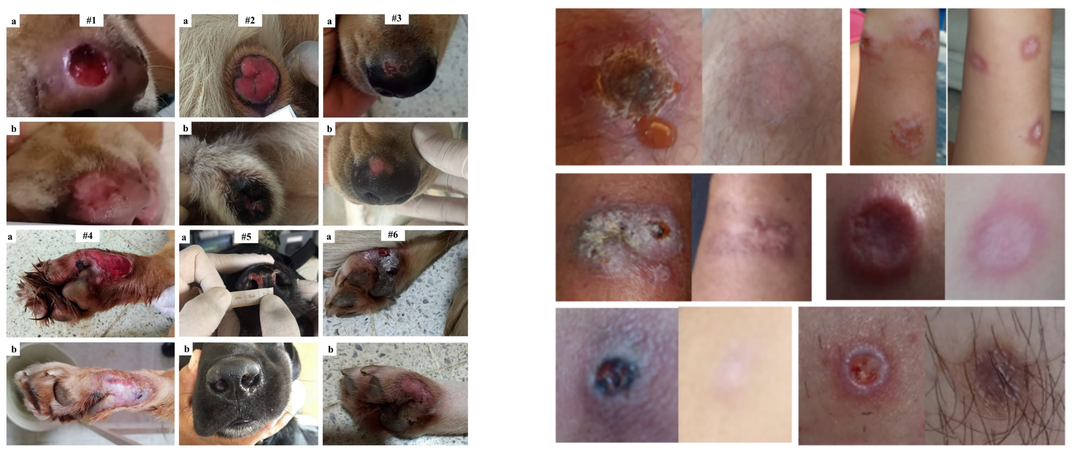

Chromatographic profile of TC2 detected in mice *stratum corneum*. The figure shows the amount of TC2 after (a) 6 hours and (b) 24 hours of ointment application.




Chromatographic profile of 2% TC2 and 2% SS mixture that diffused through pig ear skin after 48 hours. The figure shows the chromatographic profile of TC2 and SS recovered from the acceptor compartment at 48 hours. Some zooms were made to the profiles to observe the SS signals




### Therapeutic response canine and human patients



Clinical appearance of canine (A) and human (B) CL before and after treatment with 2% TC2 and 2% SS ointment. The fgure shows representative cases. Patients were treated 3x/day/75 days. Lesions were not occluded during treatment application.

## CONCLUSIONS

The combination of hederagenin glucoside saponins obtained from *Sapindus saponaria* fruit (SS) with a chroman derived hydrazone TC2 is able to healing canine cutaneous leishmaniasis. - The ointment containing a mixture of 2% SS and 2% TC2 allows the adequate epithelialization of the damaged skin without adverse effects in dogs with cutaneous leishmaniasis.- The ointment containing a mixture of 2% SS and 2% TC2 is safe in rats after dermal application. The formulation containing 2% SS and 2% TC2 constitutes an alternative for the topical treatment of canine cutaneous leishmaniasis. - Topical therapy can be a safer new first-line treatment of canine cutaneous leishmaniasis.These results support the use of topical therapy as a safer and new first-line local treatment of CL that could be further validated by controlled clinical trials.

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