

### Photoinactivation of *Leishmania amazonensis* by natural anthraquinones

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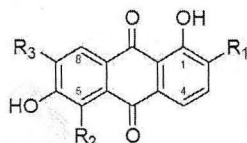
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Cutaneous leishmaniasis is a clinical form of a parasitic disease characterized by developing skin lesions with raised borders, eventually ulcerated, and limited to a specific area.<sup>1</sup> The potential toxicity as well as the increased resistance of standard treatments have led to development of alternative medication. Antimicrobial photodynamic therapy appears as an alternative treatment for localized infections caused by microorganisms.<sup>2</sup>

Our research group has succeeded in the isolation of several anthraquinones (AQs) obtained from *H. lycioides* with good photosensitizing properties.<sup>3</sup> The aim of this work was to study the photoinactivation of *Leishmania amazonensis* by using soranjidiol (sor) and derivatives structures: 5-chlorosoranjidiol (5-clsor), bisoranjidiol (bis), 7-chlorobisoranjidiol (7-clbis) y lycionine (lyc) (Fig. 1).



| AQs      | R <sub>1</sub>     | R <sub>2</sub> | R <sub>3</sub> |
|----------|--------------------|----------------|----------------|
| sor      | CH <sub>3</sub>    | H              | H              |
| 5-clsor  | CH <sub>3</sub>    | Cl             | H              |
| bis*     | CH <sub>3</sub>    | sor            | H              |
| 7-clbis* | CH <sub>3</sub>    | sor            | Cl             |
| lyc*     | CH <sub>2</sub> OH | sor            | H              |

Fig. 1 Soranjidiol derivatives. \*bianthraquinones formed by two monomers linked in position 5-5'.

AQs were tested at 2.5  $\mu$ M and photoactivated with blue LED ( $\lambda = 410 \pm 10$  nm and irradiance=50 mW/cm<sup>2</sup>). The exposure times corresponded to radiant exposures of 9, 18, 27 and 36 J/cm<sup>2</sup>. Metacyclic promastigote form of transfected *L. amazonensis* expressing luciferase enzyme (La-LUC) was used to quantify metabolic activity.<sup>4</sup>

Results showed that sor, 5-clsor and bis produce a decrease above 90% in La-LUC metabolic activity with a radiant exposure of 27 J/cm<sup>2</sup>, while 7-clbis and lyc exhibited no photoinactivation. Additionally, 5-clsor was tested by using other wavelengths (LEDs emitting at  $\lambda = 450 \pm 20$  nm and  $\lambda = 520 \pm 20$  nm) keeping the same irradiance. This AQ displayed the same reduction in La-LUC metabolic activity when it was photoactivated with the three wavelengths but using a radiant exposure of 36 J/cm<sup>2</sup>.

In conclusion, bis, sor and 5-clsor are natural anthraquinones that exhibited photodynamic inactivation on *Leishmania amazonensis*, making them potentially attractive for application in cutaneous leishmaniasis treatment.

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