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SHORT COMMUNICATION



## Anti-inflammatory and antiproliferative activities of *Ixora brevifolia* Benth. (Rubiaceae)

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### ABSTRACT

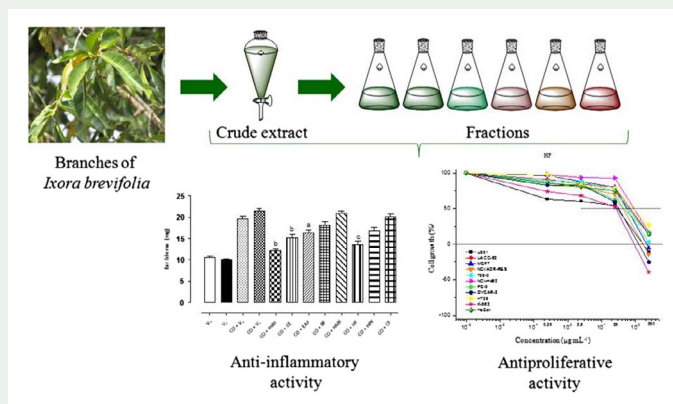
The crude extract and fractions from the branches of *Ixora brevifolia*, a tree found in the Brazilian Cerrado, were tested for anti-inflammatory and *in vitro* antiproliferative effects. The crude extract and *n*-hexane fraction exhibited significant inhibition of ear oedema in mice, while *n*-hexane-precipitated and chloroform fractions strongly inhibited the myeloperoxidase activity in ear tissue. The *n*-hexane and *n*-hexane-precipitated fractions showed strong growth inhibition for glioma cell line and the hydromethanolic fraction inhibited the growth of leukaemia cell line.

### ARTICLE HISTORY

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### KEYWORDS

*Ixora brevifolia*; Rubiaceae;  
antiproliferative activity;  
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## 1. Introduction

*Ixora* is a genus of ca. 400 species; several are used in traditional medicine for treatment of diarrhoea, fever, headaches, ulcers and cancer (Nair & Panikkar 1990; Chen, Zhang et al.

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2016). Previous phytochemical and biological studies of species from *Ixora* genus and their isolated compounds showed the presence of phenols, terpenoids and peptides (Lee et al. 2010; Chen, Zhan, et al. 2016; Ikram et al. 2016) and a variety of activities are related to traditional uses (Chen, Zhang et al. 2016).

*Ixora brevifolia* Benth. is a tree found in Brazilian Cerrado and popularly known as 'ixora-arborea'. One of our previous studies, carried out with the branches of this species, described the isolation and identification of a new cyclopeptide alkaloid, named ixorine, along with five known compounds, frangulanine, cinnamtannin B-1, syringaresinol, daucosterol and mannitol. The study also reported the activity of two cyclopeptide alkaloids mixture against *Leishmania amazonensis* (Medina et al. 2016).

The present work describes the anti-inflammatory and antiproliferative potential of methanol crude extract and fractions from the branches of *Ixora brevifolia*.

## 2. Results and discussion

To evaluate the anti-inflammatory activity, croton oil was used to induce the local inflammatory process, characterised by an oedema formation and increased activity of myeloperoxidase (MPO) in the injured tissue. The results of anti-inflammatory activity assays are expressed as percentage of inhibition of ear oedema (weight) and MPO activity (absorbance) (Figures S1 and S2, Table S1).

The crude extract (**CE**) showed moderate inhibition of ear oedema (49.4%,  $p < 0.001$ ) and the *n*-hexane fraction (**HF**) caused a high inhibition (68.8%,  $p < 0.001$ ). In addition, the **HF**, *n*-hexane precipitated (**HPF**, obtained from **HF**) and chloroform (**CF**) fractions were effective in inhibiting the MPO activity (57.9%,  $p < 0.001$ ; 81.5%,  $p < 0.001$  and 76.4%,  $p < 0.001$ , respectively). MPO is a heme-enzyme used as a marker of migration of polymorphonuclear cells related to inflammation response. An inhibition of its activity could indicate that the main anti-inflammatory mechanism of these fractions is related to the inhibition of migration of polymorphonuclear cells.

The *in vitro* antiproliferative activity of the crude extract and fractions was evaluated using 10 different human cancer cell lines and a non-tumoural cell line. The results are expressed as the concentration that produced 50% of cell growth inhibition ( $GI_{50}$ ,  $\mu\text{g mL}^{-1}$ ) for each cell line (Table S2).

The **CE** exhibited antiproliferative activity against all tumour cell lines and presented marked inhibitory effect on the growth of glioma (U251,  $GI_{50} = 26.8 \mu\text{g mL}^{-1}$ ) and leukaemia (K562,  $GI_{50} = 28.0 \mu\text{g mL}^{-1}$ ) cell lines. The **HF** and **HPF** fractions showed significant selectivity and potent antiproliferative activity for the glioma cell line (U251,  $GI_{50} = 4.1$  and  $1.5 \mu\text{g mL}^{-1}$ , respectively). The **HPF** fraction also inhibited the growth of ovary (OVCAR-3,  $GI_{50} = 10.1 \mu\text{g mL}^{-1}$ ) and leukaemia (K562,  $GI_{50} = 19.6 \mu\text{g mL}^{-1}$ ) cell lines. The **CF** fraction exhibited antiproliferative activity against all tumour cell lines, with  $GI_{50}$  values in the range 25.5–81.8  $\mu\text{g mL}^{-1}$ . The hydromethanolic (**HMF**) and butanolic (**BF**) fractions presented selectivity against leukaemia cell line with high and moderate growth inhibition (K562,  $GI_{50} = 4.6$  and  $25.2 \mu\text{g mL}^{-1}$ , respectively).

Finally, previous phytochemical work described the isolation of some bioactive compounds: lignan syringaresinol and cyclopeptide alkaloids ixorine and frangulanine from **CF**; and daucosterol from **HF** and **HF** (Medina et al. 2016) (Figure S11). The cyclopeptide alkaloids ixorine and frangulanine have never been described as antiproliferative or anti-inflammatory

agents. However, the peptides isolated from *I. coccinea*, ixora peptide I and ixora peptide II, exhibited selective potential against Hep3B liver cancer cell line and significant anti-inflammatory effects on neutrophils, respectively (Lee et al. 2010). Syringaresinol possesses strong cytotoxic activity against hepatocarcinoma cell line HepG2, high anti-inflammatory activity as indicated by inhibited LPS-induced NO generation and presents strong scavenging activity against DPPH (El-Desouky & Gamal-Eldeen 2009). Daucosterol has been described as inhibiting the growth of human colon cancer cell line HCT-116 (Wang et al. 2016), and to present anti-inflammatory activity in lipopolysaccharide-stimulated RAW 264.7 murine macrophages (Choi et al. 2012). Therefore, the presence of these metabolites could explain the positive results presented by **CF**, **HF** and **HPF** in anti-inflammatory and *in vitro* antiproliferative assays.

### 3. Conclusion

This is the first evaluation of biological activities of the plant *I. brevifolia*. Our study demonstrates the antiproliferative and anti-inflammatory properties of this species, and the results corroborate the pharmacological properties observed for other members of the *Ixora* genus, which could be attributed to the similar compounds or the same active metabolites being present in this species.

### Supplementary material

Experimental details, Tables S1 and S2 and other data are available online.

### Disclosure statement

No potential conflict of interest was reported by the authors.

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