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Chemical constituents, anti-inflammatory and antioxidant activities of bark extracts from *Prunus tucumanensis* Lillo

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SHORT COMMUNICATION

Chemical constituents, anti-inflammatory and antioxidant activities of bark extracts from *Prunus tucumanensis* Lillo

Sandra M. Bach^a, Marina E. Perotti^a, Ana P. Merep^a, Guillermo E. Marcial^a, Alfredo Grau^b, Rodgoun Attarian^c, Yossef Av-Gay^c, Horacio Bach^{c*} and César A.N. Catalán^a

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The anti-inflammatory, antioxidant, antimicrobial and cytotoxic activities of the hexane (HE), chloroform (CE) and methanol (ME) extracts obtained from the bark of *Prunus tucumanensis* Lillo were investigated. Both ME and CE extracts displayed a significant *in vitro* anti-inflammatory activity similar to dexamethasone and to a commercial formulation (*Pygeum*) used for the treatment of benign prostatic hyperplasia (BPH). ME exhibited powerful antioxidant (67.6% relative to BHT) and free radical scavenging ($RC_{50} = 5$ ppm) activities, antimicrobial activities against *Staphylococcus aureus* and *Mycobacterium smegmatis* and did not show any cytotoxic effect on human-derived macrophage cells. Chemical analyses showed that (2R,3R)-3,5,7,3',5'-pentahydroxyflavan, β -sitosterol and β -sitosterol-3-O- β -D-glucopyranoside (daucosterol) are relevant components of ME.

Keywords: *Prunus tucumanensis*; anti-inflammatory activity; antioxidant activity; cytotoxicity; benign prostatic hyperplasia

1. Introduction

In a survey on bioactivities of native trees, we found that an alcoholic extract from the bark of *Prunus tucumanensis* Lillo displayed significant anti-inflammatory activity. *Prunus tucumanensis* (Rosaceae family) is a middle-sized tree that grows in North-Western Argentina and Southern Bolivia (Santos Biloni, 1997). Interestingly, *P. tucumanensis* is a relative of the African plum tree *P. africana* (Hook F.) Kalkman (= *Pygeum africanum*) whose bark extracts (*Pygeum*) have been intensively exploited for the treatment of benign prostatic hyperplasia (BPH) (Ishani, MacDonald, Nelson, Rutka, & Wilt, 2000). The aim of this study was to evaluate the anti-inflammatory, antimicrobial, antioxidant and cytotoxic activities of bark extracts from *P. tucumanensis* as well as to determine their phytochemical profile.

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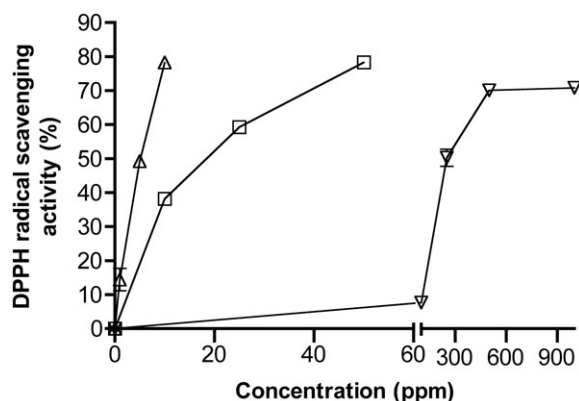


Figure 1. FRS activity of the chloroform (CE) (∇) and methanol (ME) (Δ) extracts from *P. tucumanensis* on 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical. BHT (□) was used as a control. The means \pm SD of three independent experiments are shown.

2. Results and discussion

2.1. Chemical composition of bark extracts and antioxidant properties

Chemical analysis identified, in the methanol extract (ME), the anti-allergic compound (2 R,3 R)-3,5,7,3,5'-pentahydroxyflavan (Samaraweera, Sotheeswaran, Uvais, & Sultanbawa, 1983), which is reported here for the first time in a member of the Rosaceae family. Chemical profile of the chloroform and hexane extracts (CE and HE, respectively) are listed in Table S1. The total phenolic content (TPC) amount in the CE and ME was 163.2 ± 1.9 and 0.18 ± 0.01 mg GAE per gvm, respectively. Analysis of the free radical scavenging (FRS) activity shows that the highest level was observed in ME ($RC_{50} = 5$ ppm), which was even higher than that of the synthetic radical scavenging agent BHT ($RC_{50} = 17$ ppm, control) (Figure 1). In turn, an antioxidant activity of 67.6% and 34.5% relative to BHT were measured for ME and CE, respectively, in a β -carotene/linoleic acid system.

2.2. Anti-inflammatory, cytotoxic and antimicrobial activities

The secretion of the pro- and anti-inflammatory IL-6 cytokine was measured in the supernatant of the cultures. Results show that 546 pg mL^{-1} of IL-6 was measured when an inflammatory process was induced in macrophages by lipopolysaccharides (LPS) (Figure 2), whereas 185 and 162 pg mL^{-1} were measured when cells were treated with either CE or ME, respectively. These values were comparable to untreated macrophages (156 pg mL^{-1}). The anti-inflammatory activities of CE and ME were significant and similar to dexamethasone (98 pg mL^{-1}) used as a control. We conclude that both CE and ME showed anti-inflammatory activities similar to the *Pygeum* extract (148 pg mL^{-1}) and dexamethasone (Figure 2).

Polyphenols have been recognised as potent inhibitors of lipo-oxygenase and cyclooxygenase, and histamine release inhibition (Hong, Smith, Ho, August, & Yang, 2001; Le, Li, Qian, M.M. Kim, & S.K. Kim, 2009). Moreover, β -sitosterol has been shown to exhibit anti-inflammatory, antineoplastic and immunomodulating activities (Patrick & Lamprecht, 1999). These facts linked to the very high TPC of ME suggest that 3,5,7,3',5'-pentahydroxyflavan and other polyphenolic compounds together with sitosterol play a role in the anti-inflammatory effect of the ME of *P. tucumanensis*.

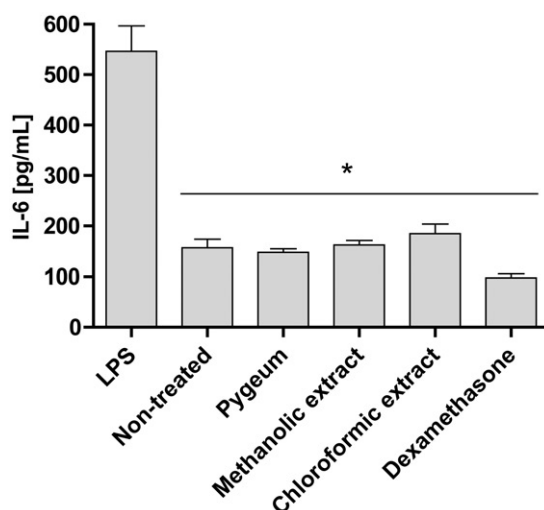


Figure 2. Anti-inflammatory activity of HE and ME. An inflammatory process was elicited by exposing macrophages to LPS. Extracts were exposed to macrophages prior to the addition of LPS. The anti-inflammatory process was evaluated by measuring the secretion of IL-6 into the supernatant. The means \pm SD of three independent experiments are shown. * $p < 0.0001$.

Cytotoxic analyses of the extracts on human macrophages show that a similar distribution of the population was observed in the ME (1298 events) and non-treated cells (1316 events). In contrast, CE and HE (both showing 591 events) produced a significant change in both granularity and cellular volume of the treated macrophages and were comparable to H_2O_2 used as a positive control (504 events) (Figure S1). These results suggest that ME does not possess cytotoxic effect on macrophages.

Results show that only the ME was active against *Staphylococcus aureus* representing a decrease of 50% when compared to vancomycin activity, whereas *Mycobacterium smegmatis* shows a 30% of the activity of rifampicin (45 mm) (Table S3). Taking together, the ME could be developed for the treatment of infections.

3. Conclusions

The results presented here indicate that the bark of *P. tucumanensis* is a mixture of compounds with powerful anti-inflammatory and antioxidant properties deserving to be evaluated as a phytotherapeutic for the treatment of BPH.

Supplementary material

The experimental details used in this study are available on line, alongside Tables S1–S3 and Figure S1.

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