



In vitro and *in vivo* assessment of meadowsweet (*Filipendula ulmaria*) as anti-inflammatory agent



Jelena Katanić^{a,*}, Tatjana Boroja^a, Vladimir Mihailović^a, Stefanie Nikles^b, San-Po Pan^b, Gvozden Rosić^c, Dragica Selaković^c, Jovana Joksimović^c, Slobodanka Mitrović^d, Rudolf Bauer^b

^a Department of Chemistry, Faculty of Science, University of Kragujevac, Radoja Domanovića 12, 34000 Kragujevac, Serbia

^b Institute of Pharmaceutical Sciences, Department of Pharmacognosy, University of Graz, Universitaetsplatz 4, 8010 Graz, Austria

^c Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Svetozara Markovića 69, 34000 Kragujevac, Serbia

^d Department of Pathology, Faculty of Medical Sciences, University of Kragujevac, Svetozara Markovića 69, 34000 Kragujevac, Serbia

ARTICLE INFO

Chemical compounds studied in this article:

hyperoside (PubChem CID: 5281643)
 rutoside (PubChem CID: 5280805)
 apigenin (PubChem CID: 5280443)
 spiraeoside (PubChem CID: 5320844)
 quercetin (PubChem CID: 5280343)
 isoquercitrin (PubChem CID: 5280804)
 indomethacin (PubChem CID: 3715)
 NS-398 (PubChem CID: 4553)
 dexamethasone (PubChem CID: 5743)
 λ-carrageenan (PubChem CID: 91972149)

Keywords:

Filipendula ulmaria

Inflammation

Cyclooxygenase

Hot plate test

Carrageenan-induced edema

ABSTRACT

Ethnopharmacological relevance: Meadowsweet (*Filipendula ulmaria* (L.) Maxim, Rosaceae) has been traditionally used in most European countries for the treatment of inflammatory diseases due to its antipyretic, analgesic, astringent, and anti-rheumatic properties. However, there is little scientific evidence on *F. ulmaria* anti-inflammatory effects regarding its impact on cyclooxygenases enzymatic activity and *in vivo* assessment of anti-inflammatory potential. This study aims to reveal the anti-inflammatory activity of methanolic extracts from the aerial parts (FUA) and roots (FUR) of *F. ulmaria*, both in *in vitro* and *in vivo* conditions.

Materials and methods: The characteristic phenolic compounds in *F. ulmaria* extracts were monitored via high performance thin layer chromatography (HPTLC). The *in vitro* anti-inflammatory activity of *F. ulmaria* extracts was evaluated using cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) enzyme assays, and an assay for determining COX-2 gene expression. The *in vivo* anti-inflammatory effect of *F. ulmaria* extracts was determined in two doses (100 and 200 mg/kg b.w.) with hot plate test and carrageenan-induced paw edema test in rats. Inflammation was also evaluated by histopathological and immunohistochemical analysis.

Results: FUA extract showed the presence of rutoside, spiraeoside, and isoquercitrin. Both *F. ulmaria* extracts at a concentration of 50 µg/mL were able to inhibit COX-1 and -2 enzyme activities, whereby FUA extract (62.84% and 46.43% inhibition, respectively) was double as effective as the root extract (32.11% and 20.20%, respectively). Extracts hardly inhibited the level of COX-2 gene expression in THP-1 cells at a concentration of 25 µg/mL (10.19% inhibition by FUA and 8.54% by FUR). In the hot plate test, both extracts in two doses (100 and 200 mg/kg b.w.), exhibited an increase in latency time when compared with the control group ($p < 0.05$). In the carrageenan-induced acute inflammation test, FUA at doses of 100 and 200 mg/kg b.w., and FUR at 200 mg/kg, were able to significantly reduce the mean maximal swelling of rat paw until 6 h of treatment. Indomethacin, FUA, and FUR extracts significantly decreased inflammation score and this effect was more pronounced after 24 h, compared to the control group ($p < 0.05$).

Conclusions: The observed results of *in vitro* and, for the first time, *in vivo* anti-inflammatory activity of meadowsweet extracts, provide support of the traditional use of this plant in the treatment of different inflammatory conditions. Further investigation of the anti-inflammatory compounds could reveal the mechanism of anti-inflammatory action of these extracts.

1. Introduction

Filipendula ulmaria (L.) Maxim. (syn. *Spiraea ulmaria* L.), also known as meadowsweet or queen of the meadow, belongs to the

Rosaceae family and is found widely in damp meadows trough Europe and Asia (Barros et al., 2011). *F. ulmaria* is used in traditional European medicine for treatment of various ailments due to its antipyretic, diuretic, analgesic, and anti-inflammatory properties

Abbreviations: FUA, *F. ulmaria* aerial part extract; FUR, *F. ulmaria* root extract; COX-1, cyclooxygenase-1; COX-2, cyclooxygenase-2; LOX, lipoxygenase; NSAIDs, nonsteroidal anti-inflammatory drugs; HPTLC, high performance thin layer chromatography; HPLC, high performance liquid chromatography; IL, interleukin; dex, dexamethasone; NFκB, nuclear factor kappa B; TNF-α, tumor necrosis factor alpha; PAF, platelet-activating factor; PPAR α and γ, peroxisome proliferator-activated receptors

* Corresponding author.

E-mail address: jkatanic@kg.ac.rs (J. Katanić).

<http://dx.doi.org/10.1016/j.jep.2016.10.015>

Received 28 June 2016; Received in revised form 30 September 2016; Accepted 5 October 2016

Available online 06 October 2016

0378-8741/© 2016 Elsevier Ireland Ltd. All rights reserved.

