

Epilobium parviflorum, hemorrhagic risk with anticoagulants

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Case Report

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Abstract

Plants have a crucial importance in our ecosystem. They contain complex mixtures of compounds that can interact with various therapeutics. Among them, the small-flowered willowherb (*Epilobium parviflorum*) has seen its use expand in recent years, particularly for prostate diseases.

The aim of this work is to demonstrate the risk of interaction between the use of *E. parviflorum* and medications, especially anticoagulants, illustrated by the case of our patient suffering from dilated cardiomyopathy, treated with acenocoumarol 4 mg, a vitamin K antagonist (VKA), for over a year.

The recent intake of small-flowered willow herb tea, rich in tannins and flavonoids, increased the patient's INR (International Normalized Ratio), indicating an increased risk of haemorrhage. A therapeutic education session was then held, with management of interactions and monitoring of the patient until stabilisation.

The intake of *E. parviflorum* or any other plant with anticoagulants requires rigorous pharmacological therapeutic monitoring to anticipate the risk of bleeding and improve the quality of life of patients.

Introduction

Plants are essential for the survival of humans and ecosystems. They contain complex mixtures of compounds capable of modifying biological, biochemical and metabolic activities and interacting with various therapeutics.

In recent years, there has been growing interest in certain plants because of their potential pharmacological and therapeutic properties, and willow herb is one of them [1–3].

small-flowered willow herb (*Epilobium parviflorum*) is a herbaceous plant belonging to the Onagraceae family, which includes over 200 species worldwide [4, 5].

The main species are: *Epilobium angustifolium*, *Epilobium parviflorum*, *Epilobium hirsutum* et *Epilobium palustre* [6].

1. Folk use

The most commonly used part of small-flowered willowherb is the flowers, which traditional medicine recommends for the treatment of fever, rheumatic pains and headaches, without any proven scientific evidence, but also for skin and mucous membrane infections, respiratory infections and the treatment of benign prostatic hyperplasia [5, 6].

2. Chemical composition

The aerial parts of *Epilobium* spp are rich in secondary metabolites, mainly polyphenols such as flavonoids, phenolic acids and tannins, as well as lipophilic compounds such as steroids [1].

the small-flowered species are rich in flavonoids, mainly myricetin and quercetin, and in tannins, mainly oenothien B, giving them anti-inflammatory, analgesic, antioxidant, antibacterial and antiproliferative properties [4, 6, 7, 8].

The complex constituents of *Epilobium* spp makes it dangerous in combination with medication.

3. Clinical case

The growing interest in certain species of fireweed for its potential efficacy in treating benign prostatic hyperplasia has led to an increase in its consumption, often without consideration of its potential risks [8].

To illustrate this risk, let's take the example of our patient, a 69-year-old man who presented for the first time to the laboratory of the hospital Didouche Mourad, Constantine, Algeria, for a haemostasis test.

The result showed a low PT and an INR of 5.6.

The patient's history revealed that he was diabetic, in addition to having dilated cardiomyopathy for which he had been treated with acenocoumarol 4 mg, a vitamin K antagonist(VKA) for over a year at a dose of 3/4 tablet (Cp) – 1/2 Cp in alternation.

The last INR value recorded one month previously was within the therapeutic range [2–3].

As the patient's treatment remained unchanged, the questioning focused on his diet, which showed that he had no notion of the need for a diet adapted to his anticoagulant treatment. In addition, he had been taking a cup of fireweed-tea every evening for more than a week.

The high tannin and flavonoid content of *E. parviflorum* may explain the increase in INR and the risk of haemorrhage. In fact, tannins' ability to complex proteins gives them an inhibitory effect on multiple enzyme systems [9]. Flavonoids, such as myricetin and quercetin, also have an antiplatelet aggregation effect [9] in addition to an inhibitory effect on CYP450 isoenzymes 2C9 and 3A4, which significantly increases the activity of anticoagulants [11–15].

A therapeutic education session was then required, and led to the following recommendations:

- Skip the day's anticoagulant intake and check the INR the next day,
- Explanation of the effects of acenocoumarol, the need for regular monitoring and the many interactions with drugs, food and plants,
- And finally, the need to stop taking herbal tea, which increased the effect of the VKA.

The patient was cooperative and receptive to the information, but he wanted to continue taking the herbal tea because since he started taking it, his prostate problems had disappeared, specifically his polyuria, incontinence, urinary retention and pelvic pain, which gave him a better quality of sleep.

We then advised limiting the daily amounts consumed and instituting withdrawal periods with close monitoring of INRs in order to manage the interaction and find the appropriate dosage.

The patient resumed his treatment at 1/2 Cp the following day, as he was unable to perform an INR.

Subsequent INR tests were carried out on D5 and D9 after resumption, and the results were between 2 and 3.

Our patient finally stopped taking herbal tea after a month and a half, which led us to increase the dosage (3/4 tablet).

Conclusion

Various traditional medicinal plants offer an alternative treatment for BPH, particularly in the early stages of its development or as a preventive approach, including small-flowered fireweed.

Often regarded as 'alternative medicine', herbal products are rarely mentioned by patients when they are interviewed, but their use can expose them to drug interactions and sometimes serious adverse effects [2, 3]; Our patient is a case in point of the interaction between *E. parviflorum* and anti-vitamin K anticoagulants, requiring rigorous pharmacological therapeutic monitoring in order to anticipate the hemorrhage risk and improve patients' quality of life.

Abbreviations

BPH: Benign prostatic hyperplasia

Cp: tablet

D: Day

INR: International Normalized Ratio

PT: prothrombin time

SPP: species

VKA : vitamin K antagonist

Declarations

- statement on ethics approval and consent: Not applicable
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References

1. Joseph E. Pizzorno, ND. Michael T. Murray, ND. Textbook of Natural. 5th Edition. (2020) 581-583
2. Revue prescrire, Se soigner avec des plantes n'est pas forcément sans risque. Septembre 2023.
3. Beghriche I, Belhachem A, Hamidene I, Fendri AH. Origanum vulgare and hemorrhagic risk, about a case. Annales de cardiologie et d'angiologie 74 (2025) 101856.
4. Sebastian Granica, Jakub P. Piwowarski, Monika E. C zerwińska, Anna K. Kiss. Phytochemistry, pharmacology and traditional uses of different Epilobium species (Onagraceae):Areview.
5. Tomáš Bajer, David Šilha, Karel Ventura, Petra Bajerová. Composition and antimicrobial activity of the essential oil, distilled aromatic water and herbal infusion from Epilobium parviflorum Schreb. Industrial Crops and Products, Volume 100, June 2017, Pages 95-105
6. Radosław Kujawski* *et al.* Effect of Willow herb (Epilobium angustifolium L.) extract on gene expression of selected P450 cytochromes in rat liver – preliminary study. Herba Polonica Vol. 55 No 4 2009 ISSN: 0018-0599
7. Barbara Hevesi Tóth*, Balázs Blazics, Ágnes Kéry. Polyphenol composition and antioxidant capacity of Epilobium species. Journal of Pharmaceutical and Biomedical Analysis 49 (2009) 26–31.
8. Olta Allkanjari, Annabella Vitalone. What do we know about phytotherapy of benign prostatic hyperplasia? Life Sciences Volume 126, 1 April 2015, Pages 42-56
9. dictionnaire de l'académie nationale de pharmacie 2018.
<https://dictionnaire.acadpharm.org/w/Tanin>
10. Jing Wang , Yingying Hu , Qingqing Li , Ya-nan Liu, Jingjing Lin , Ren-ai Xu. Effects of myricetin and quercetin on ticagrelor metabolism and the underlying mechanism. Chemico-Biological Interactions. Volume 392, 1 April 2024, 110924
11. N. He, T. Edeki The inhibitory effects of herbal components on CYP2C9 and CYP3A4 catalytic activities in human liver microsomes Am J Ther, 11 (2004), pp. 206-212
12. Sudhir N. Umathe, Pankaj V. Dixit, Vijendra kumar, Kuldeep U. Bansod, Manish M. Wanjari Quercetin pretreatment increases the bioavailability of pioglitazone in rats: Involvement of CYP3A inhibition. biochemical pharmacology 75 (2008)1670–1676
13. M.M. Cotreau, L.L. von Moltke, M.C. Beinfeld, D.J. Greenblatt Methodologies to study the induction of rat hepatic and intestinal cytochrome P450 3A at the mRNA, protein, and catalytic activity level J Pharmacol Toxicol Methods, 43 (2000), pp. 41-54)

14. D. Lou, S.S. Bao, Y.H. Li, Q.M. Lin, S.F. Yang, J.Y. He Inhibitory mechanisms of myricetin on human and rat liver cytochrome P450 enzymes Eur. J. Drug Metab. Pharm., 44 (5) (2019), pp. 611-618
15. Zhize Ye , Hailun Xia , Jinyu Hu , Ya-nan Liu , Anzhou Wang , Jian-ping Cai , Guo-xin Hu, Ren-ai Xu. CYP3A4 and CYP2C19 genetic polymorphisms and myricetin interaction on tofacitinib metabolism Author links open overlay panel.

Figures

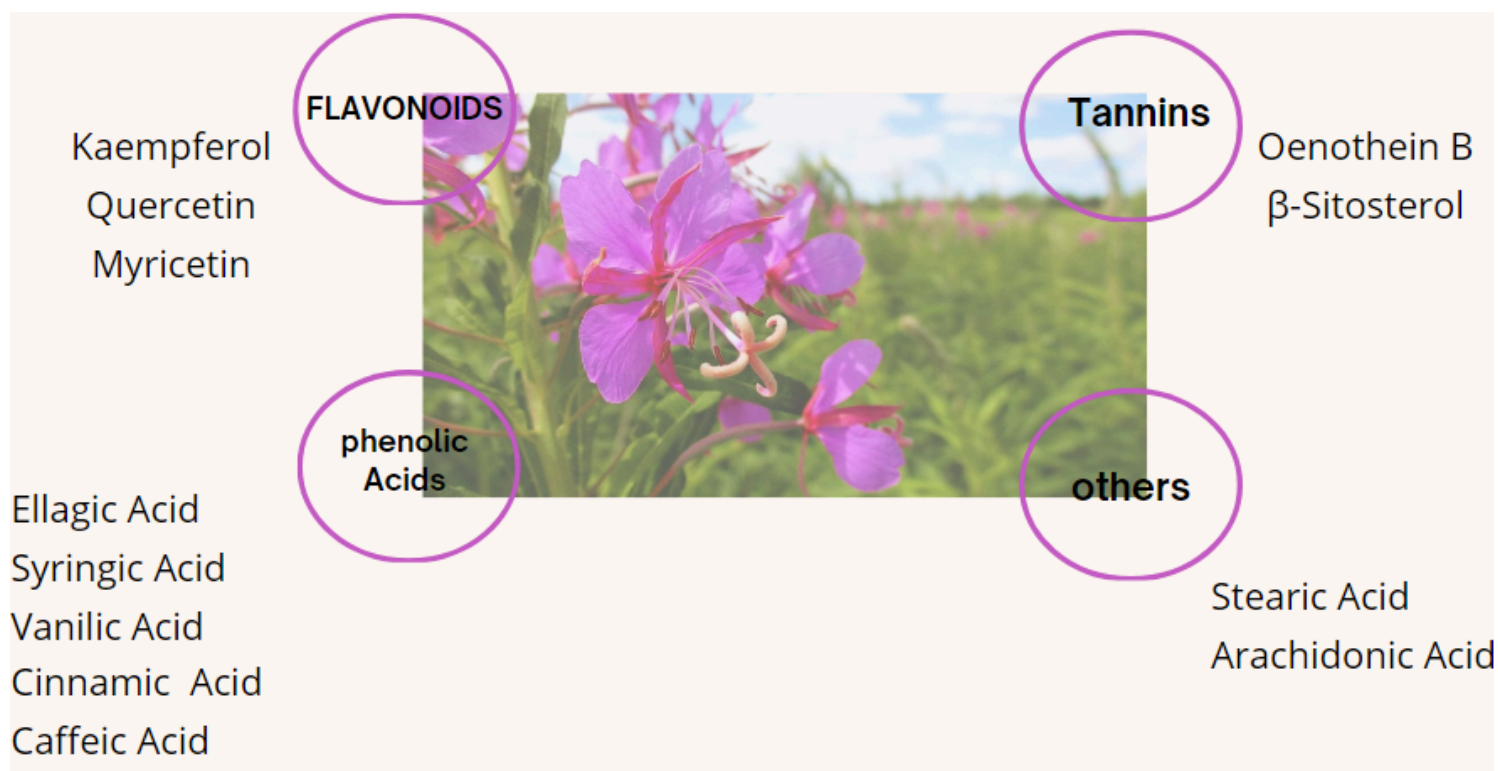


Figure 1

Main secondary metabolites of the small-flowered willowherb

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