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Podophyllotoxin content analysis of *Linum album* Kotschy ex Boiss subjected to short-term potassium deficiency stress

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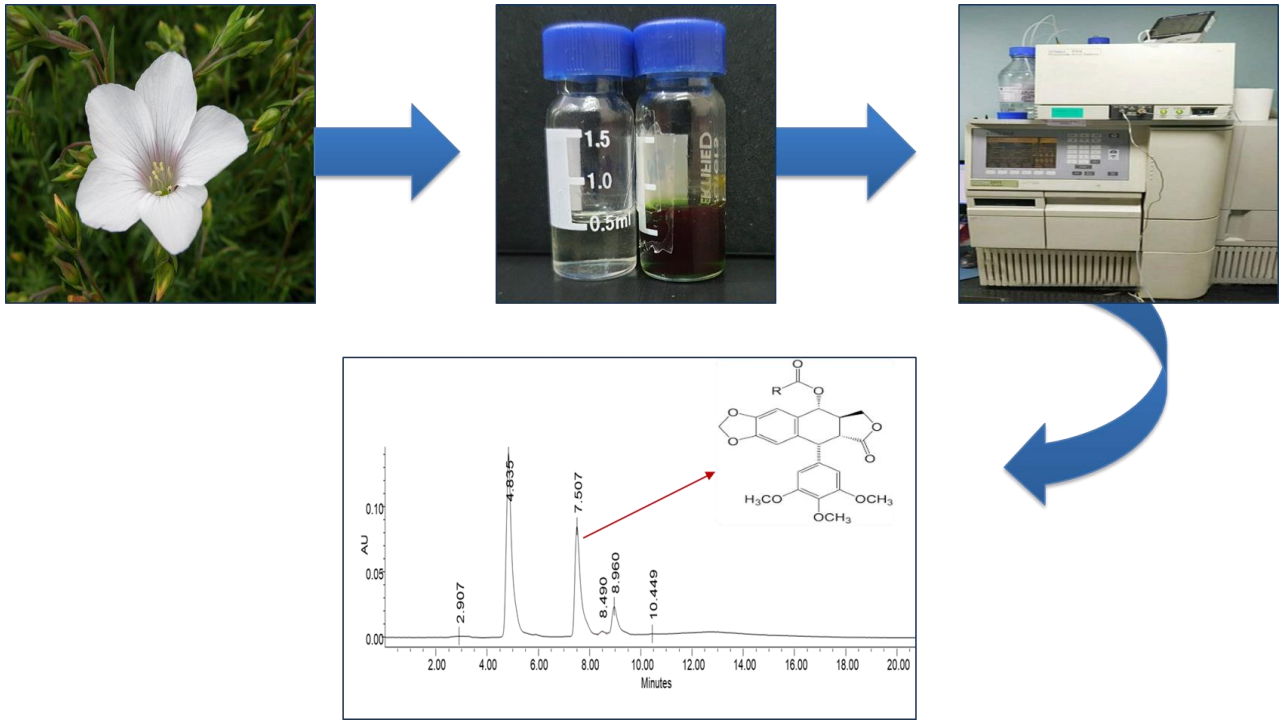
Graphical Abstract



Abstract:

Podophyllotoxin (PTOX), one of the most important natural medicinal compounds, has anticancer properties. Its effective medicinal derivatives, such as etoposide and teniposide, have been approved by the FDA for cancer treatment. This compound is found as a specialized metabolite in the *Linum album* Kotschy ex Boiss., belonging to the Linaceae family. PTOX is the major aryltetralin lignans resulting from the shikimic acid/phenylpropanoid pathway and accumulates in the shoot and roots of *L. album*. PTOX play a necessary role in plant defense systems, protecting against abiotic and biotic stresses and helping their adaptation to adverse environmental conditions. Therefore, the content of specialized metabolites increases under stress. In this study, the content of PTOX under stressful conditions (potassium deficiency stress at two-time points of 12 and 48 hours) was examined using HPLC in a completely randomized design with three replications. The results of HPLC showed that the content of PTOX first decreased in 12 hours, while after 48 hours of treatment compared with the control plants, it showed a significant increase with the value of 135.8 in the shoot. In the root, the results were consistent with the results of the aerial parts, and the amount increased significantly after 48 hours. In general, the results show that *L. album* as a suitable natural source for PTOX has great potential to generate Large-scale products for commercial and pharmaceutical purposes.

Keywords: *Linum album*, Podophyllotoxin, Anticancer, Potassium deficiency

Introduction

Podophyllotoxin (PTOX) was first isolated from *Podophyllum sp.*

PTOX, one of the most important compounds, has anti-cancer properties.

It is a precursor of drugs such as etoposide, etopofs and teniposide.

Two main mechanisms of action of PTOX derivatives:

A. inhibit tubulin polymerization and cause G2/M arrest in tumor cells.

B. can inhibit topoisomerase II degradation, leading to DNA damage and eventually cell death.

Other medicinal uses:

Antiviral

Antirheumatic

Purgative

Antimalarial

Antifungal

In addition to medicinal properties, PTOX and other lignans have broad applications in the food and textile industry.

- *Linum album* Kotschy ex Boiss., belonging to the Linaceae family, is a well-known natural rich source of podophyllotoxin and other lignans.
- *L. album*, an endemic species of Iran, grows in arid and semiarid regions. Thus, this is often exposed to multiple stresses in its natural habitat, such as potassium deficiency.

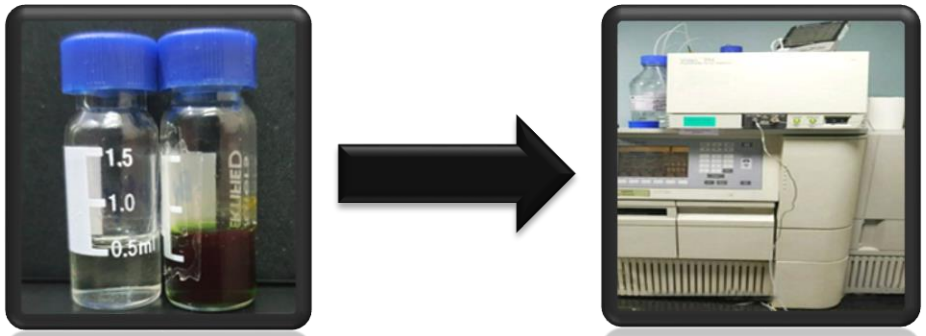
- unfavorable environmental conditions, in many cases, stimulate to generate the specialized metabolites. Nowadays, severe climate change increases the frequency of unfavorable conditions leading to multiple stresses.
- The plants have adapted to favorable physiological, biochemical, and molecular properties.
- In many studies, abiotic stress increase the content of lignans in plants.
- In *L. album*, PTOX and its derivative, particularly 6-methoxypodophyllotoxin (6-MPTOX), are the major aryltetralin lignans resulting from the shikimic acid/phenylpropanoid pathway.
- Therefore, the present work evaluated the content of podophyllotoxin under potassium deficiency stress.

Materials and Methods

- The seeds were planted in pots in a greenhouse at Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, Tehran.
- They were then irrigated with Hoagland's nutrient solution.
- Seedlings were treated with Hoagland's nutrient solution and Hoagland's nutrient solution without potassium at 12 and 48h.
- The shoot and root samples harvesting were instantly frozen in liquid nitrogen and stored at -80◦C

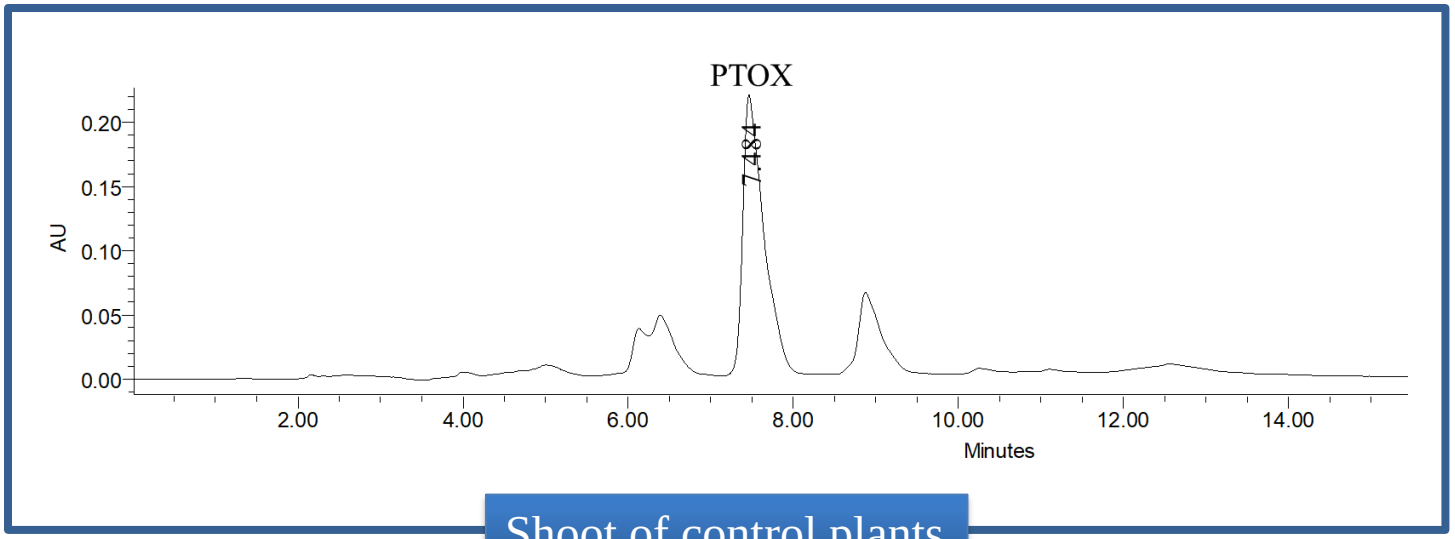
Materials and Methods

- The fresh samples were prepared using a pestle and mortar in liquid nitrogen, followed by extraction in methanol and sonicated.
- Dichloromethane and water were added and centrifuged.
- The dichloromethane fractions were then collected, dried, and dissolved in 1.0 ml of HPLC grade methanol for HPLC analysis.
- The presence of podophyllotoxin was identified on the basis of retention time and comparison of UV spectra with the authentic podophyllotoxin.



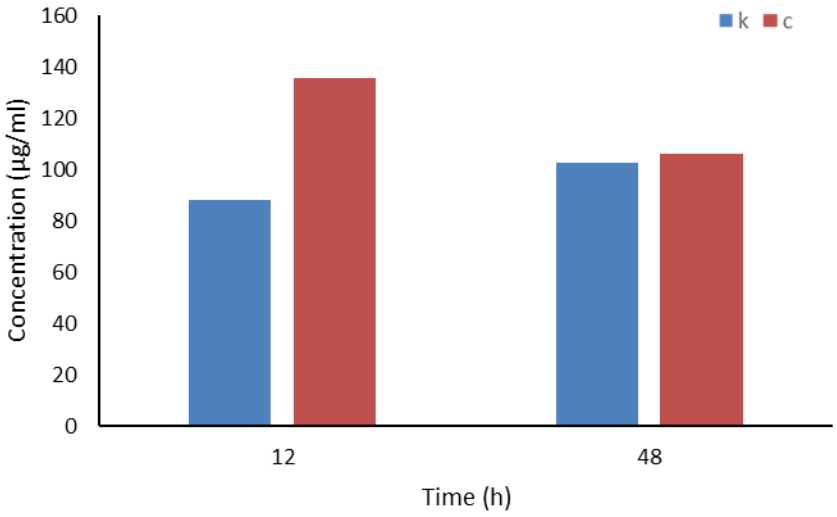
Results and discussion

The results of HPLC showed that the content of PTOX first decreased in 12 hours, while after 48 hours of treatment compared with the control plants, it showed a significant increase with the value of 135.8 in the shoot. In the root, the results were consistent with the results of the aerial parts, and the amount increased significantly after 48 hours.

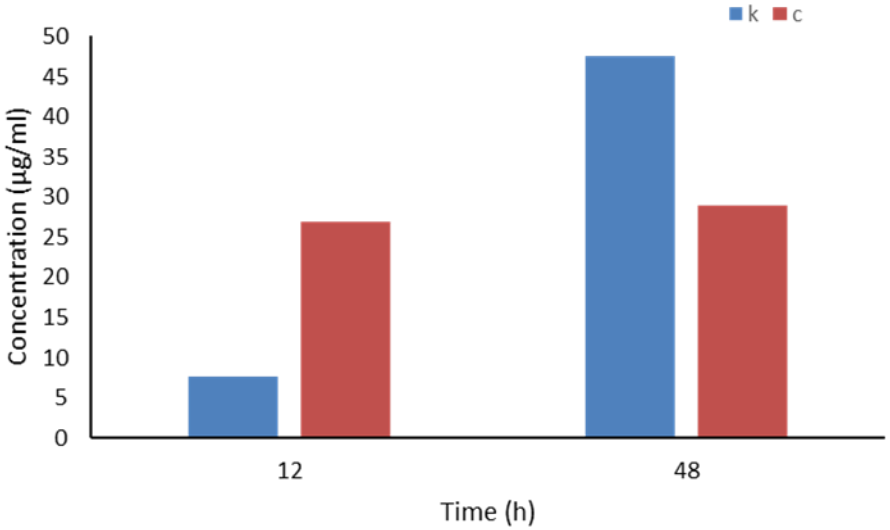


Shoot of control plants

Results and discussion



Shoot



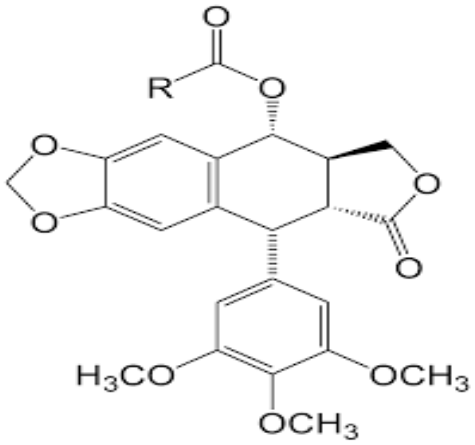
Root

In pervious study, treatment of abiotic and biotic elicitors, including chitosan, methyl jasmonate, salicylic acid, yeast extract, and Ag^+ has mostly established lignan content enhanced in *Linum spp*. in vitro.

a study carried out on different accessions of *L. album* under drought stress presented the different patterns based on physiological and biochemical responses. Therefore lignan content enhanced of *L. album* may be different in some cases due to species or genotype differences, type of culture, and stress intensity.

Conclusions

The potassium deficiency increased the amount of PTOX content in both of shoot and root tissues, which shows that the plant increases its lignan compounds in facing with stress. Accordingly *L. album* as a suitable natural source for PTOX has great potential to generate Large-scale products for commercial and pharmaceutical purposes.



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