

HPLC Quantification of Hydroxycinnamic and Organic Acids of Canadian Goldenrod (*Solidago canadensis* L.)

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ABSTRACT

Background: Canadian goldenrod (*Solidago canadensis* L.) is a medicinal plant widely used in traditional medicine across the world for several hundred years. According to literature data, *S. canadensis* contains various groups of biologically active substances, including tannins, flavonoids, etc. The aim of the study was to identify and quantify hydroxycinnamic and organic acids in aerial parts of Canadian goldenrod, as these groups of substances demonstrate a broad spectrum of therapeutic activities. **Materials and Methods:** Ethanolic extracts of *S. canadensis*, gathered in Central Russia, were analyzed using High-performance liquid chromatography (HPLC). Hydroxycinnamic acids (HCA) determination was carried out by HPLC method with UV detection at 330 nm using HCA Reference standards (RS). Organic acids (OA) determination was performed in the same manner, utilizing UV detection at 210 nm and corresponding OA RS. **Results:** It was established that *S. canadensis* HCA composition is represented by cichoric, caffeic, chlorogenic, quinic and ferulic acids. The total HCA content in was $1.16 \text{ g} \pm 10.7 \text{ mg} / 100 \text{ g}$. Main OA, found in *S. canadensis*, are ascorbic, citric, tartaric, succinic, gallic, malic, oxalic and fumaric acids, with the total OA content of $426.5 \text{ mg} \pm 6.4 \text{ mg} / 100 \text{ g}$. **Conclusion:** The described HPLC method was successfully used for analysis of *S. canadensis* aerial parts ethanolic extracts. The method can be utilized for HCA and OA identification and quantification in both herbal raw material and herbal medicinal products containing Canadian goldenrod.

Key words: Hydroxycinnamic acids, Organic acids, *Solidago canadensis*, Canadian goldenrod, HPLC.

INTRODUCTION

Traditional medicine widely utilizes various herbal raw materials which are often used as a substitute of conventional drug products or as their supplement. Canadian goldenrod (*Solidago canadensis* L.) is well known in European traditional medicine for more than 700 years due to its pronounced anti-inflammatory properties.¹ Goldenrod is also known to be used in ethnomedicine of people inhabiting Russia (Caucasus, Siberia), Moldavia and Belarus.²⁻³ Currently, the importance of *S. canadensis* as a source of biologically active substances is officially recognized: corresponding monographs are included in the European and the British pharmacopoeias.⁴⁻⁵

Canadian goldenrod contains various groups of biologically active substances: flavonoids, tannins, saponins, essential oils.²⁻³ Many organic substances exhibit antioxidant activity, which is a natural factor of body protection. It is known that phenolic acids, tannins, flavonoids, quinones and organic acids¹ display antioxidant activity.⁶⁻⁸

Hydroxycinnamic acids are the most common polyphenolic acids present in higher plants in the form of derivatives of glycosides or esters of cichoric, ferulic,

coumarinic, caffeic acids with tartaric and quinic acids, as well as complexes with proteins, lignin and cellulose. In vitro tests of HCAs, namely chicoric,⁹ caffeic, quinic,¹⁰ ferulic¹¹ and chlorogenic, have confirmed their antioxidant and antiradical properties.¹² Moreover, ferulic acid demonstrates its therapeutic effects in a number of pathological conditions, including diabetes mellitus, cardiovascular and neurodegenerative disorders and even cancer.¹¹

Organic acids include fumaric, malic, citric, tartaric, ascorbic, succinic, acetic, oxalic and others acids which show a wide spectrum of biological activity: anti-inflammatory, immunomodulating, and antioxidant activity.^{12,13}

For example, succinic acid represents a good support for organism during hypoxia, as it plays an important role in citric acid cycle. A good antioxidant by itself, succinic acid effectively inhibits free-radical lipid peroxidation, activates superoxide dismutase, binds free radical and protects cellular membrane and apparatus. In addition, it also decreases histamine production, which, in turn, neutralizes inflammation and allergic reactions. It was found that succinic

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acid and its salts act as adaptogens that help organism to defend itself against negative effects of the environment.¹⁴

Ascorbic acid also involved in oxidation-reduction processes in living organisms and is an effective antioxidant.¹⁵

Oxalic acid is usually considered an inert product of metabolism; it was thought that only plant could metabolize oxalic acid. However, recent studies showed that oxalate level in animals are too high for it to be just an end product. It is suggested that there could be an oxalate oxidase pathway which utilizes oxalate to product hydrogen peroxide. Hydrogen peroxide, in turn, is used to stimulate oxidative burst.¹⁶

Literature data shows that citric acid demonstrates antibacterial properties against microorganisms present in dental plaque.¹⁷

Gallic acid and its salts, just as tartaric and citric acids, demonstrate antioxidant properties and is able form chelate complexes with metal ions.¹⁸⁻¹⁹

Together with citric acid, malic and fumaric acids are a part of tricarboxylic acid cycle which supplies cells with energy.²⁰

Chlorogenic acid is an important biologically active dietary polyphenol that shows wide spectrum of biological activities: antibacterial, hepatoprotective, cardioprotective, antiinflammatory and antiviral. It was also found that this acid can modulate lipid and glucose exchange in metabolic disorders and, therefore, can possibly act as a therapeutic agent in cardiovascular diseases, diabetes mellitus, obesity and liver steatosis.²¹

Among therapeutic properties of cichoric acid, antiviral and anticancer activity should be mentioned. It was also suggested that cichoric acid and its analogues possess an anti-HIV activity due to its role in HIV integrase inhibition.²²

Caffeic acid and quinic acid derivatives show demonstrate antioxidant properties.²³⁻²⁴

Some of the abovementioned properties may play pivotal role in the treatment of inflammatory periodontal diseases. Gum diseases not only may lead to tooth loss – they also can cause coronary heart disease and negatively affect adult population mortality rate,²⁵ so, periodontal disease remains an important public health problem.²⁶ It is recognized that antioxidant activity expressed by different chemical substances is able to suppress periodontitis development.²⁷ Therefore, herbal drug preparations containing Canadian goldenrod are important candidates for development of anti-inflammatory periodontal medicines.

Quantification of hydroxycinnamic and organic acids in raw plant material is one of the first steps in its standardization and development of novel herbal drug products that can be used to treat various diseases. Therefore, the aim of the study was to assess the content of HCA and OC in the dried aerial parts of *S. canadensis*.

MATERIALS AND METHODS

Chemicals

Reference standards (RS) of HCA ($\geq 98.0\%$, HPLC) (cichoric, caffeic, chlorogenic, quinic, chicoric and ferulic acids) and OA (ascorbic, citric, tartaric, succinic, gallic, malic, oxalic and fumaric acids) were purchased from Sigma-Aldrich Company Ltd (St. Louis, USA). High purity water was prepared using Millipore Milli-Q (Merck, Germany) water purification system. All other chemicals and reagents, such as potassium dihydrogen phosphate and phosphoric acid, were of analytical grade purity and were obtained from Merck (Darmstadt, Germany).

Plant material collection

The object of the study was whole aerial parts of the Canadian goldenrod collected in the Tver Region (56°50'41.4"N 35°51'10.1"E), Russia and identified at the Department of Pharmaceutical Natural Science of the Institute of Pharmacy of Sechenov First Moscow State Medical

University (Sechenov University) and voucher specimen was stored at the department. Obtained material was air-dried under shade for 30 days.

Determination of HCA

HCA determination was carried out by HPLC method with UV detection at 330 nm using RS of HCA. HCA concentration was determined by means of external calibration (HCA standards by Sigma-Aldrich), using obtained peak areas. To prepare the HCA RS solutions with a concentration of 0.001 mg/ml, 25 mg of substance was placed in a 50 ml volumetric flask, dissolved in 25 ml of 70% ethyl alcohol and brought to volume with ethanol. Gathered aerial parts of Canadian goldenrod (about 2.0 g) were grounded in a mortar to a mushy state. Extraction was performed by 70% ethyl alcohol in a boiling water bath under reflux for 1 h. Extracts analysis was performed using GILSON-305 liquid chromatography system (GILSON, France), which consisted of degasser, pump 5SC, thermostated autosampler (sample temperature – 15°C), diode-array detector and thermostated chromatographic column (250 × 4.6 mm, 5 μm, Kromasil C₁₈). A phosphate buffer with pH 2.2 was used as the mobile phase (27.2 g of potassium dihydrogen phosphate are placed in a 1-liter volumetric flask, dissolved in 500 ml of purified water, brought to the volume with the same solvent and orthophosphoric acid is added to pH 2.2.). Chromatography parameters: flow rate – 1 mL/min, column temperature – 25°C, injection volume – 20 μl. Chromatograms were processed using Multichrom software (Ampersend, Moscow, Multichrom Ltd, Russia).

Determination of OA

OA determination was carried out by HPLC method with UV detection at 210 nm using RS of OA. OA concentration was defined with the aid of external calibration (OA standard by Sigma-Aldrich), based on peak areas. To prepare the OA RS solutions with a concentration of 0.001 mg/ml, 25 mg of substance were placed in a 50 ml volumetric flask, dissolved in 25 ml of 70% ethyl alcohol and brought to volume with ethanol. Gathered aerial parts of Canadian goldenrod (about 2.0 g) were grounded in a mortar to a mushy state. Extraction was performed by 70% ethyl alcohol in a boiling water bath under reflux for 1 h. Extracts analysis was performed using GILSON-305 liquid chromatography system (GILSON, France) which consisted of degasser, 5 SC pump, thermostated autosampler (samples temperature – 15°C), diode-array detector and thermostated chromatographic column (250 × 4.6 mm, 5 μm, Kromasil C₁₈). A phosphate buffer with pH 2.2 was used as the mobile phase (prepared in the same manner as for determination of HCA.). Chromatography parameters: flow rate – 1 mL/min, column temperature – 25°C, injection volume – 20 μl. Chromatograms were processed using Multichrom software (Ampersend, Moscow, Multichrom Ltd, Russia).

RESULTS AND DISCUSSION

Hydroxycinnamic acids

The total HCA content in *S. canadensis* was found to be 1.16 g ± 10.7 mg / 100 g. The HPLC-chromatogram of *S. canadensis* extract (cichoric, caffeic, chlorogenic, quinic and ferulic acids) is shown in Figure 1. The results of HCA determination are shown in Table 1.

Organic acids

The total OA content in *S. canadensis* was found to be 426.5 ± 6.4 mg / 100 g. The HPLC-chromatogram of *S. canadensis* extract (ascorbic, citric, tartaric, succinic, gallic, malic, oxalic and fumaric acids) is shown in Figure 2. The results of OA determination are shown in Table 2.

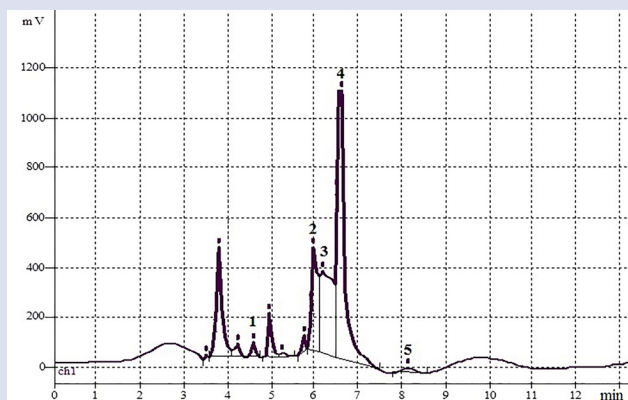


Figure 1: HPLC-UV chromatogram of *S. canadensis*: 1. Quinic acid; 2. Cichoric acid; 3. Chlorogenic acid; 4. Caffeic acid; 5. Ferulic acid.

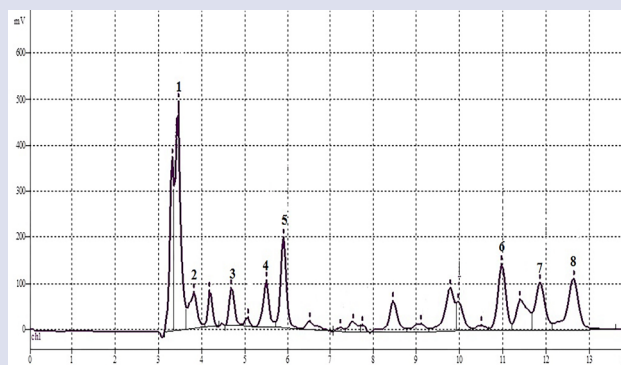


Figure 2: HPLC-UV chromatogram of *S. canadensis*: 1. Oxalic acid; 2. Tartaric acid; 3. Malic acid; 4. Ascorbic acid; 5. Gallic acid; 6. Citric acid; 7. Fumaric acid; 8. Succinic acid.

Table 1: Hydrocinnamic acids of Canadian goldenrod.

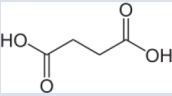
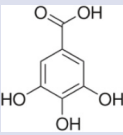
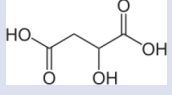
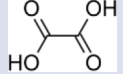
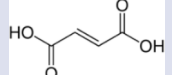
HCA	Retention time, t_R	Content, mg /100 g of dry material	IUPAC name	Structure
Cichoric	5.948	240.0±6.3	(2R,3R)-2,3-bis{[(E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy}butanedioic acid	
Chlorogenic	6.175	320.2±5.4	(1S,3R,4R,5R)-3-[[[(E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy]-1,4,5-trihydroxycyclohexanecarboxylic acid	
Caffeic	6.567	600.1±12.3	3-(3,4-Dihydroxyphenyl)-2-propenoic acid	
Quinic	4.554	80.7±4.7	(1S,3R,4S,5R)-1,3,4,5-tetrahydroxycyclohexanecarboxylic acid	
Ferulic	8.113	4.3±0.7	(E)-3-(4-hydroxy-3-methoxyphenyl)prop-2-enoic acid	

Table 2: Organic acids of Canadian goldenrod.

OA	Time retention, t_R	Content, mg /100 g of dry material	IUPAC name	Structure
Ascorbic	4.27	11.3±0.8	(5R)-[(1S)-1,2-Dihydroxyethyl]-3,4-dihydroxyfuran-2(5H)-one	
Citric	8.05	11.1±0.8	2-Hydroxypropane-1,2,3-tricarboxylic acid	
Tartaric	4.22	6.3±0.3	2,3-Dihydroxybutanedioic acid	

Continued...

Table 2: Cont'd.

OA	Time retention, t_R	Content, mg /100 g of dry material	IUPAC name	Structure
Succinic	9.17	66.7±2.5	Butandioic acid	
Gallic	7.96	96.2±3.7	3,4,5-Trihydroxybenzoic acid	
Malic	3.11	36.2±3.9	2-Hydroxybutanedioic acid	
Oxalic	17.15	200.1±5.4	Oxalic acid	
Fumaric	6.89	5.0±1.1	(2E)-But-2-enedioic acid	

CONCLUSION

In this study, using the HPLC-UV method, organic and hydroxycinnamic acids contained in the aerial parts of *S. canadensis* were detected and quantified. The data obtained can be used to assess biological activity of Canadian goldenrod herbal raw material as well as the quality of herbal medicinal products containing this herb.

ACKNOWLEDGMENT

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

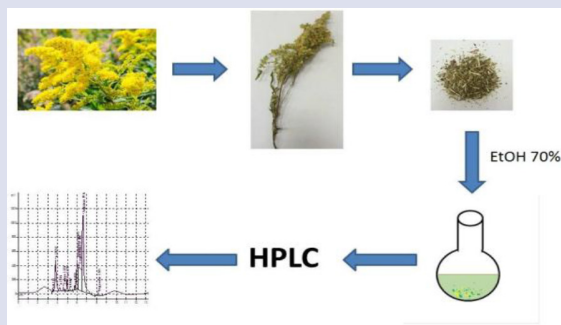
ABBREVIATIONS

HCA: Hydroxycinnamic acid; **HPLC:** High performance liquid chromatography; **OA:** Organic acid; **RS:** Reference standard; **UV:** Ultraviolet.

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GRAPHICAL ABSTRACT



SUMMARY

- An HPLC method was used to assess hydroxycinnamic and organic acids content in Canadian goldenrod aerial parts.
- The total HCA and OA content was $1.16 \pm 10.7 \text{ mg} / 100 \text{ g}$ and $426.5 \pm 6.4 \text{ mg} / 100 \text{ g}$, respectively.
- Among Canadian goldenrod OAs, oxalic acid was found to be most abundant ($200.1 \pm 5.4 \text{ mg} / 100 \text{ g}$), the least abundant being fumaric acid ($5.0 \pm 1.1 \text{ mg} / 100 \text{ g}$).
- Between HCAs, the caffeic acid content was found to be the highest ($600.1 \pm 12.3 \text{ mg} / 100 \text{ g}$), whereas ferulic acid content was the lowest ($4.3 \pm 0.7 \text{ mg} / 100 \text{ g}$).

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