

東北薬科大学

審査学位論文（博士）要旨

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学位の種類	博士（薬学）
学位記番号	甲第 140 号
学位授与の日付	平成 26 年 3 月 18 日
学位授与の要件	学位規則第 4 条 1 項該当
学位論文題名	Studies on phytochemical constituents and their biological activities from Mongolian medicinal plants, Dracocephalum and Chamaerhodos species
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**Studies on phytochemical constituents and their biological activities
from Mongolian medicinal plants, *Dracocephalum* and
Chamaerhodos species**

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Traditional Mongolian Medicine (TMM) has been revived and continues to be practiced widely, playing vital role in the health care needs of a large portion of the population of Mongolia. It includes the use of crude drugs, acupuncture, moxibustion, cupping, and massage. Most of the crude drugs used in medicine are derived from plant sources, while the others from animal and mineral sources.

In Mongolia, over 800 plant species are recognized as medicinal plants. Since ancient times, these plants are used for remedy and to prevent various infectious and non-infectious diseases, as well as improving the fertility of livestock. Some of typical medicinal plants are easily accessible within the country, and are widely used by Mongolian nomads as not only preventing and treating illnesses, but also a tonic to improve the health, because they cannot obtain modern drugs easily in nomadic life. Even though city dwellers have access to modern medication use of traditional medicine is quite popular, as they have a few side effects.

TMM is being used for since several generations, and the traditional knowledge is extremely valuable. Hence a policy of state of Mongolia, making National herbal pharmacopoeia is needed and discussed. Thus it is the demand of the hour to conduct study of TMM using scientific approaches, so that traditional knowledge can be backed up by scientific data. In case of the medicinal plants, vegetation surveys and ecological researches have been done more than phytochemical study.

On the other hand, studies of Mongolian medicinal plants are still at a nascent stage and even phytochemical constituents and the basic biological activities have not yet been investigated sufficiently. So, there is a real need for scientific studies and knowledge about TMM to provide scientific rationality. The knowledge of the basic scientific data of phytochemical constituents will contribute to the pharmacopoeia, which specifies effective and safe use of each medicinal plant for patients.

Mongolian extreme climate damages skin and induces many other skin problems

during the whole year, and increase especially in winter. Hence much attention has been paid to skin inflammation and its related diseases including allergies, severe rashes, dryness, and aging of skin by Mongolians. There are a lot of medicinal plants which have been handed down through the history, for skin care and protection from inflammation and its related diseases. A major focus of this study was identification of active components and action mechanisms of the plants in skin-care.

At first 51 extractions of Mongolian medicinal plants were tested for their hyaluronidase inhibitory and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activities. Then, out of these extracts, 2 genus and 4 species were picked up, which showed significant activity and are commonly used as herbal medicine in TMM.

Dracocephalum L. is one of the important members of Lamiaceae family for TMM. The genus consists of 17 species distributed in Mongolia and traditionally used for the treatment of inflammatory diseases, rheumatism, and external injury. Especially, *D. foetidum* has been widely used as traditional medicine among Mongolian nomads. In this research, two *Dracocephalum* plants, *D. ruyschiana* and *D. foetidum* were revealed to have hyaluronidase inhibitory activity, which is known to be related with anti-inflammatory mechanism. The phytochemical constituents were isolated from the two plants by chromatography and chemical structures were determined by using instrumental analyses.

Ten new and 19 known compounds were identified from *D. ruyschiana*, and 13 new and 13 known compounds were identified from *D. foetidum*. Plants were found to contain polyphenolic compounds such as phenylpropanoids and flavonoids. Rosmarinic acid was obtained as one of the main constituents of *D. foetidum*, but it was not found in *D. ruyschiana*, even when these are from same genus. The structure determination process is presented in **Chapter 2** and **3**.

Chapter 2 presents isolation and structure elucidation of five new flavone tetraglycosides, five new benzyl alcohol glycosides, and 19 known compounds from *D. ruyschiana*.

In **Chapter 3**, three new limonene glycosides, a new caffeic acid trimer, four new rosmarinic acid derivatives, five new acacetin acyl glycosides, as well as 13 known compounds from *D. foetidum* were characterized.

Chamaerhodos plants, *C. erecta* and *C. altaica* were revealed having potent

antioxidant activity by screening of 23 Mongolian medicinal plants, and the plants are known to be used for skin-care, traditionally. Phytochemical investigations of *C. erecta* and *C. altaica* were followed the same processes as *Dracocephalum* plants and identified 4,5-dihydroxybenzaldehyde-3-*O*- β -D-glucopyranoside from *C. erecta* and quercetin-3-*O*- β -D-glucuronopyranosyl-4'-*O*- β -D-glucopyranoside from *C. altaica* as new compounds with 37 known compounds. A number of hydrolyzable tannins were isolated as typical constituents of *Chamaerhodos* plants. These results are explained in **Chapter 4**.

To elucidate skin-care effects and biological activities of the obtained 91 compounds (**1 - 91**), four basic tests hyaluronidase inhibitory, DPPH radical scavenging, Advanced glycation endproducts (AGEs) inhibitory, and tyrosinase inhibitory activities were evaluated. The tests were related with anti-inflammatory, antioxidant, antipigmentation activities, and their results are discussed in **Chapter 5**.

Highlight of the four assays is detailed in here. Rosmarinic acid derivative (**34**), and acacetin glycosides (**43** and **46**) showed stronger hyaluronidase inhibitory activity than positive control disodium cromoglicate. Some of flavone glycosides, catechin, and some of hydrolyzable tannins showed moderate activity. Hyaluronidase inhibitory activity is expected to be involved anti-inflammatory and anti-allergic reactions, and this activity can be used as primary screen of anti-allergic effects.

Antioxidant activities of rosmarinic acid and hydrolyzable tannins were more than the positive control trolox, while some flavonoid glycosides and rosmarinic acid derivatives were similar to that of trolox.

A series of flavonols and their glycosides, catechins, and hydrolyzable tannins showed AGEs inhibitory activities. It is thought that the prevention of AGEs formation is promoted by antioxidant compounds, and almost of these active compounds also had DPPH radical scavenging activity. Antioxidant activity of natural products protects cells against the damaging effects of free radicals and is expected to be useful for the prevention and treatment of many diseases including skin inflammations, allergies, and aging – related diseases.

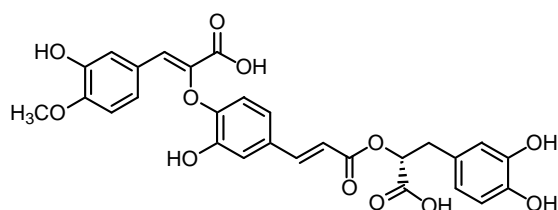
Although tyrosinase inhibitory effects of all compounds of *D. foetidum* were examined, they did not show any significant activity.

Dracocephalum and *Chamaerhodos* plants which contain rosmarinic acid and its

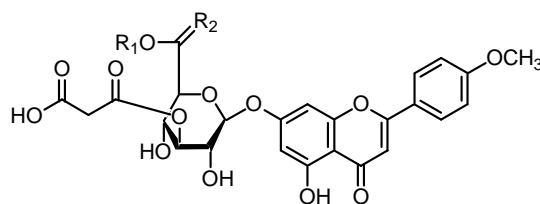
derivatives, some flavonoid glycosides, and hydrolyzable tannins as potent hyaluronidase inhibitors and antioxidants may be useful in cosmetic for anti-inflammation, anti-allergies, and antioxidation.

It is rational that nomadic Mongolians used *Dracocephalum* and *Chamaerhodos* plants for their ailments because the present study showed that constituents from those have beneficial biological effects. These four medicinal plants have been important parts for TMM. The scientific data are expected to be useful and important information for the crude drugs which are being used by Mongolian people and generate data for the Mongolian National herbal pharmacopoeia.

Basic studies like above would increase understanding of the value of medicinal plants in Mongolia and increase the evidence for the efficacious use of herbs in health care.



34



43 $R_1 = \text{malonyl}$, $R_2 = \text{H}_2$

46 $R_1 = \text{H}$, $R_2 = \text{O}$

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