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Large Leaf Gentian as a Promising Source of Biologically Active Substances

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Abstract

The article describes large leaf gentian (*Gentiana macrophylla* Pall.) as a source of biologically active substances. The authors analyze local and foreign literature sources on the traditional use of large leaf gentian, its phytochemical composition, and pharmacological properties. The results of the study show, that *Gentiana macrophylla* Pall. contains a large number of chemical constituents demonstrating wide range of pharmacological activities which allows authors to conclude, that it is a promising new herbal raw material. However, further studies including standardization and quality control methods development should be performed prior to its inclusion in the State Pharmacopoeia of the Russian Federation as an officinal herbal raw material and its introduction into official medical practice.

Keywords: *Gentiana macrophylla* Pall., medicinal plant, phytochemical composition, pharmacological activity, ethnoscience.

INTRODUCTION

An evergrowing demand for new sources of biologically active substances (BAS) is supported by strong interest in herbal drug products. The scientific and methodological approaches to search for new herbal sources of BAS were developed in order to facilitate development of the pharmacopoeial monographs for the State Pharmacopoeia of the Russian Federation and expand herbal drugs product range [1, 2].

Because gentianaceae family is rather large and only underground parts (roots) of yellow gentian are included in the leading world pharmacopoeias it is necessary to review another species of the gentianaceae family. The study of literature sources, including books, dissertations, scientific articles, and electronic resources, containing information about the family have revealed, that most of them are devoted to the gentian genus. One of the genus' species – the large leaf gentian (*Gentiana macrophylla* Pall.) – is of a particular interest.

METHODS

There are several groups of criteria that can be used to make conclusion about prospects of studying certain herbal raw material (HRM) [2, 3]:

- Officinal status of the HRM in more than three countries;
- An amount of knowledge about medicinal plant (MP) and HRM in the national and international medical practice;
- Pharmacotherapeutic criteria;
- Resource criteria;
- Economic criteria.

Based on these groups of criteria, the following algorithm for preliminary assessment and selection of medicinal plants and HRM which represent foremost interest for their introduction into medical practice was proposed in previous studies [1, 2, 3, 4]:

- Confimation of successful usage of MP and HRM in domestic and/or foreign traditional medicine;
- Confirmation of safety and efficacy of MP and HRM in the Russian Federation and/or worldwide;
- Determination of the disease/condition relevance in which MP and HRM can be used;
- Determination of disease (condition) prevalence;
- Evaluation of possible usage of MP and HRM for prolonged treatment;
- Evaluation of possibility for replacement of synthetic drug products by MP and HRM;
- Evaluation of possibility for introduction of medicinal plant into local climate zone and environmental conditions.

Using this algorithm several promising medicinal plant families were selected, from which we chose the gentian family, because 90 out of about 360 species of this family grow in the Russian Federation [5].

RESULTS

Different species of the gentianaceae family are widely used in traditional medicine of different countries all over the world, mainly in Tibet and China. Roots, rhizomes, flowers, and whole herb are usually used to prepare infusions, decoctions, powders and other dosage forms [6,7,8,9].

Members of the family usually contain glucosides (gentiopicrin), glycosides (gentisin, gentiamarin), alkaloids (gentianin), flavonoids, xanthones, iridoids and other chemical constituents [9,13,19,20]. The European Pharmacopoeia, [10], Belarus Republic Pharmacopoeia [11], British Pharmacopoeia [12], Spanish Pharmacopoeia [13], French Pharmacopoeia [14], Japanese pharmacopoeia [15] and several other pharmacopoeias include monographs on only one type of HRW – yellow gentian (*Gentiana lutea* L.) roots.

G. macrophylla Pall. (GM) belongs to the gentian genus of the gentianaceae family. Its traditional chinese name is *qinjiao*; in Russia it is called "Cossack herb" [9,16].

In the Russian Federation GM can be found in Altai Territory, adjacent regions of the Western Siberia, all over Middle and Eastern Siberia, in the southern parts of the Amur Region and Khabarovsk Territory, in the Primorye Territory, and in Republic of Tuva. Besides Russia, it grows in Mongolia, Western and Northern China [8,9].

The herb can be introduced in European Russia, South Siberia, and in Northwest China, since these regions have climate conditions necessary for its growth.

Traditional Tibetan Medicine includes large leaf gentian in formulations for treatment of respiratory tract diseases, gastrointestinal tract diseases, neurasthenia, and in hemostatic compositions [18]. In Traditional Chinese Medicine it is used as a choleretic, analgesic, wound healing, anti-inflammatory, hepatoprotective remedy, and as a treatment for rheumatism. Traditional Mongolian Medicine describes *G. macrophylla* as antipyretic and analgesic herb. In the Russian Federation GM is traditionally used to treat burns and cold-related injuries, to improve digestion, and as a hemostatic, wound healing, and immunomodulating remedy [5,8, 9, 19, 20, 21, 22].

GM is a pharmacopoeial plant of the Pharmacopoeia of the People's Republic of China [17]. Currently, only roots of large leaf gentian are described in the monograph, therefore it is challenging to call this source of HRM perspective. This governs the need for evaluation of large leaf gentian aerial parts as a source of biologically active substances.

DISCUSSION

Aerial parts of large leaf gentian contain flavonoids, their content depends on the vegetative stage and is between 4.9 and 10.6 mg [23, 24]. Some of the identified flavonoids are homoorientin, saponaretin, homoorientin 4'-O-glucoside [25]. The plant contains alkaloids: gentianin, gentianidin, gentianamine, and gentianal [6]. It was confirmed, that GM contains the same alkaloids as yellow gentian does [23, 26].

Three unidentified xanthones were obtained from GM, their content being 0.70 ± 0.02 % in aerial parts, and 0.5 ± 0.03 % - in roots [27].

Gentiopicroside - an iridoid compound – has also been identified in large leaf gentian. The sum of iridoids depends on the GM growth region and is between 0.99% and 1.12% [27, 28]. *G. macrophylla* also contains several seco-iridoids, which possess anti-inflammatory, analgesic, and anti-fungal activity: sweroside, swertamarine, loganic acid [22, 29, 30, 31].

According to the published data, aerial parts of GM also contain macrophylosides A, B, C, and D, kurarinone, kushenol I, β-sitosterol, lupeol, sigmasterol, sitostenone, campesterol, squalene, daucosterol, β-sitosterol-3-O-gentiobioside, α- and β-amyrin, oleanolic acid, isovitexin, stigmastan-3 5-diene, methyl-2-hydroxy-3-(1-β-D-glucopyranosyl)oxybenzoate, gentiobiose, methylmontanate, and the following acids – 2-methoxyanofinic, montanic, and roburic [9, 26, 32, 33, 34].

Pharmacological properties of the large leaf gentian are quite diverse. For example, earlier studies show, that flavonoids of GM demonstrate antioxidant, hemostatic, and angioprotective action, stimulate gastric juice secretion [9, 23, 32]. Gentianine has antihelminthic and sedative properties. Similar sedative effect is demonstrated by gentianidine. Japanese scientists have developed a drug formulation, based on gentianine and nicotinic acid, with sedative, hypotensive, and antipyretic properties [6,32]. It was confirmed, that prolonged use of these alkaloids is safe [6].

It was shown experimentally, that GM iridoids increase gastric juice secretion and lower its pH. Therefore, development of drug formulations based on aerial parts of large leaf gentian for treatment of atrophic gastritis accompanied by low stomach acid looks promising. Therapeutic activity of GM iridoids is comparable to that of prednisone as was demonstrated in an *in vivo* study on male Sprague-Dawley rats [22,35,36].

The same rats, along with ICR mice, were used to confirm anti-inflammatory and analgesic activity of GM [29]. Other study shows, that roots and aerial parts of *G. macrophylla* demonstrate hypolipidemic and cardioprotectiv activity in NZB/WF1 mice [37].

GM is widely used in China, alone or in formulations prescribed to be used in fever, inflammations, to treat wounds, rheumatoid arthritis, gastrointestinal tract disorders [9].

CONCLUSION

The results of previous active studies of GM in Russia and China allow us to conclude, that aerial parts of large leaf gentian is a prospective source of biologically active substances demonstrating wide range of pharmacological activity. However, there are still lots of gaps in the knowledge about this particular species of the gentian genus, that should be filled before it's future inclusion into the State Pharmacopoeia of the Russian Federation.

CONFLICT OF INTEREST

None declared.

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