Scutellaria Baicalensis Georgi: A Rising Paradigm Of Herbal Remedies

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Scutellaria Baicalensis Georgi: A Rising Paradigm Of Herbal Remedies

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Abstract

There is a growing interest in the use of natural products like herbs, spices and plant extracts in the human food and animal feed industries. *Scutellaria baicalensis* Georgi from the Labiatae family is one of the fifty fundamental herbs of traditional Chinese medicine is thus used to treat a number of health disorders for over two thousand years. It is also called baical or Chinese scutellaria or skullcap. The genus of scutellaria includes approximately 300 species. The New York university medical center reports that baicalin can enhance the activity of antibiotics against antibiotic resistant staph bacteria. Other highly preliminary evidence suggests that skullcap have anti diabetic, anti inflammatory, antiviral, antitumor, antioxidative and hepatoprotective properties, anti anxiety, and anti hypertensive effects. The present paper is an overview on scientifically established and published phytopharmacological properties of the plant.

Introduction

Baical is obtained from dried root of *Scutellaria baicalensis* Georgi is officially listed in the Chinese Pharmacopoeia. It is a perennial herb that has long been used in official and traditional medicine mainly in Russia, Japan, Korea and Mongolia. The principal active compounds determining skullcap’s pharmacological properties are found in its roots and short rhizomes. The high level of physiological and therapeutic activities of skullcap root extracts is due to the presence of almost 70 flavonoids chalcones, flavanones, flavonones, flavonols, and anthocyanidines. Flavones (wogonin, baicalein, and baicalin) and their glycosides (mainly glucuronides) are the most abundant. The total content of flavonoids in the roots of wild-grown skullcap varies from 15 to 20% of the dry weight (12–17% is baicalin, a flavone glucuronide, and 3–4% is wogonide), with glycosides predominating. At harvest, the dry weight of roots is 10–15 g per plant.1

Review

Analytical and pharmacological profile of *Scutellaria baicalensis* Georgi

Identification and quantification of eight flavones

A method of analysis of eight flavones using high-performance liquid chromatography (HPLC)-diode array detection mass spectrometry in root and aerial tissues of the medicinal plant *Scutellaria baicalensis* was developed by Christopher RH et al (2005).2 The identity of the analytes was confirmed using retention time UV–visible and mass spectral comparisons to commercial standards. Both UV–visible and mass spectral patterns were characterized for glycosylated flavones. Two additional flavone glycosides were tentatively identified as chrysin-7-glucuronide and wogonoside but not quantified. Greenhouse and in vitro-grown tissues were analyzed with flavone concentrations ranges of 0.14–150 and 0.030–1.7 µg/mg for greenhouse root and shoot tissue respectively and 0.0068–6.4 and 0.082–1.5 µg/mg for in vitro-grown roots and shoots, respectively.

Isolation and purification of baicalein, wogonin and oroxylin A from the medicinal plant *Scutellaria baicalensis* by high-speed counter-current chromatography

A high-speed counter-current chromatography (HSCCC) method was developed by Li H B et al (2005)3 for the preparative separation and purification of three bioactive flavonoids, namely, baicalein, wogonin and oroxylin A, from *Scutellaria baicalensis* Georgi. Preparative HSCCC with a two-phase solvent system composed of n-hexane–ethyl acetate–n-butanol–water (1:1:8:10, v/v/v/v) was successfully performed by increasing the flow-rate of the mobile phase stepwise from 1.0 to 2.0 ml min−1 after 4 h. The components purified and collected were analyzed by HPLC. The method yielded 144.8 mg of baicalein at 95.7% purity, 50.2 mg of wogonin at 98.5% purity, and 12.4 mg of oroxylin A at 93.2% purity from 500 mg of the crude extract in a one-step separation. The recoveries of baicalein, wogonin and oroxylin A were 92.7%, 91.6% and 92.5%, respectively. Separation and purification of baicalein and wogonoside from the Chinese medicinal plant *Scutellaria baicalensis* Georgi by high-speed counter-current chromatography

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1. Li H B et al. (2005)
2. Christopher RH et al. (2005)
3. Li H B et al. (2005)
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A preparative high-speed counter-current chromatography (HSCCC) method for isolation and purification of baicalin and wogonoside from the Chinese medicinal plant Scutellaria baicalensis Georgi (Huang-qin in Chinese) was successfully established by Sujuan W U et al (2005)4 using ethyl acetate–methanol–1% acetic acid water (5:0.5:5, v/v) as the two-phase solvent system. The upper phase of ethyl acetate–methanol–1% acetic acid water (5:0.5:5, v/v) was used as the stationary phase of HSCCC. Baicalin (58.1 mg) and wogonoside (17.0 mg) with the purity of 99.2 and 99.0%, respectively, were separated successfully in one-step separation from 120 mg of crude sample from S. baicalensis Georgi. The structures of baicalin and wogonoside were identified by 1H NMR and 13C NMR.

Cytoxic activities of flavonoids from two Scutellaria plants in Chinese medicine

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Sonoda M et al (2004)5 investigated effects of 17 flavonoids, isolated from two flavonoid-rich Scutellaria species (Scutellaria baicalensis Georgi and Scutellaria rivularis Wall) used in traditional Chinese medicine, on HL-60 cells were assessed by WST-8. Ten of the flavonoids inhibited the proliferation of HL-60, as shown by IC50 values used as indexes of the inhibition. 2′,3′,5,7-tetrahydroxy flavone (IC50=9.5 µM), apigenin (15.0 µM), viscidulin III (17.4 µM), wogonin (17.4 µM) and luteolin (18.4 µM) were more effective than baicalein (23.0 µM) which reportedly decreases the proliferation of some cancer cell lines. Others were less effective, and oroxylin A stimulated the proliferation. Scutellaria rivularis, used for the treatment of tumors in the clinic, contained flavonoids that were more inhibitive than those in Scutellaria baicalensis. These results are demonstrative of some reasons for the use of Scutellaria rivularis as a crude antitumor drug.

Mode of action of the anti-influenza virus activity of flavonoid, 5, 7, 4′-trihydroxy-8-methoxyflavone, from the roots of Scutellaria baicalensis

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Nagai T et al (1995)6 reported that when mouse-adapted influenza virus A/PR/8/34 (A/PR8) (10 PFU/cell) was adsorbed to madin-darby canine kidney (MDCK) cells at 4°C for 1 h and incubated at 37°C, release of the virus from the cells was detected in the medium from 4 h after incubation and reached to plateau at 8 h. However, 5, 7, 4′-trihydroxy-8-methoxyflavone (F36) from the roots of Scutellaria baicalensis significantly reduced this single-cycle replication of A/PR8 from 4 h to 12 h after incubation by dose-dependent manner and the dose which decrease the virus titer one tenth was 11 µM. F36 (50 µM) did not inhibit the adsorption of A/PR8 to MDCK cells, but reduced release of the virus in the medium, when it was added at 0 or 2 h after the incubation. The cell-associated virus determined by sialidase activity was also reduced by F36 treatment at 0 or 2 h. F36 also inhibited the fusion of A/PR8 with liposomes containing bovine brain mixed gangliosides at pH 5.0. However, F36 little affected on the elongation activity of the viral RNA-dependent RNA polymerase in vitro. These results suggest that F36 reduces the replication of A/PR8 by inhibiting the fusion of the virus with endosome/lysosome membrane which occurs at early stage of virus infection cycle. Whereas, when F36 was added to the MDCK cells infected with A/PR8 at 3 or 4 h after incubation, release of the virus in the medium was reduced but the cell-associated virus was increased in comparison with control. Scanning and transmission immunoelectron microscopic studies revealed that F36 inhibited the budding of progeny A/PR8 from the MDCK cell surface and microvilli, when it was added at 3 h after incubation. The accumulation of the A/PR8 antigen was observed on the cell surface by immunofluorescence and transmission immunoelectron microscopies by the addition of F36. These results suggest that F36 also shows anti-influenza virus activity against A/PR8 by inhibiting the budding of the progeny virus from the cell surface, when it was added at budding stage of virus infection cycle.

Application of HSCCC to the preparative separation and purification of baicalin from the Chinese medicinal plant Scutellaria baicalensis

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Lu H T et al (2003)7 reported that baicalin was separated and purified for the first time from the traditional Chinese medicinal plant Scutellaria baicalensis Georgi by HSCCC. Crude baicalin was obtained by extraction with methanol–water (70:30, v/v) from S. baicalensis Georgi. The separation was performed in two steps with a two-phase solvent...
system composed of n-butanol–water (1:1, v/v), in which the lower phase was used as the mobile phase at a flow-rate of 1.0 ml min−1 in the head-to-tail elution mode. A total of 37.0 mg of baicain at 96.5% purity was yielded from 200 mg of the crude baicain (containing 21.6% baicain) with 86.0% recovery as determined by HPLC analysis.

Antiviral activity of plant flavonoid, 5,7,4′-tri-hydroxy-8-methoxyflavone, from the roots of Scutellaria baicalensis against influenza A (H3N2) and B viruses

Nagai T et al (1995)8 investigated effects of isoscutellarein-8-methylether (5,7,4′-tri-hydroxy-8-methoxyflavone, F36) from the roots of Scutellaria baicalensis on the single-cycle replication of mouse-adapted influenza viruses A/Guizhou/54/89 (H3N2 subtype) and B/Ibaraki/2/85 in Madin-Darby canine kidney (MDCK) cells. The agent suppressed replication of these viruses from 6 to 12 h after incubation in a dose-dependent manner by 50% at 20 µM and 90% at 40 µM, respectively. F36 (50 µM) reduced the release of B/Ibaraki virus in the medium by 90-93% when it was added to the MDCK cells at 0 to 4 h after incubation. The cell-associated virus determined by sialidase activity was also reduced by the treatment at 0 to 4 h. F36 (120 µM) inhibited the low pH-dependent membrane fusion of both the viruses with the liposome containing mixed gangliosides from bovine brain. However, the agent caused the hemagglutination and RNA-dependent RNA polymerase activities of these viruses in vitro. These results suggest that F36 inhibits the replication of A/Guizhou and B/Ibaraki viruses at least partly by inhibiting the fusion of viral envelopes with the endosome/lysosome membrane which occurs at the early stage of the virus infection cycle. F36 (0.5 mg/kg) showed no antiviral activity against A/Guizhou and B/Ibaraki viruses in mice when administered intranasally 5 min prior to virus inoculation, whereas it significantly inhibited their proliferation in the mouse lung when administered intranasally 7 times (total 3.5 mg/kg) from 18 h before to 54 h after viruses infection. Cloning and expression of UDP-glucose: flavonoid 7-O-glycosyltransferase from hairy root cultures of Scutellaria baicalensis

Hirotani M et al (1999)9 reported that a cDNA encoding UDP-glucose: baicalein 7-O-glycosyltransferase (UBGT) was isolated from a cDNA library from hairy root cultures of Scutellaria baicalensis Georgi probed with a partial-length cDNA clone of a UDP-glucose: flavonoid 3-O-glycosyltransferase (UGFT) from grape (Vitis vinifera L.). The heterologous probe contained a glucosyltransferase consensus amino acid sequence which was also present in the Scutellaria cDNA clones. The complete nucleotide sequence of the 1688-bp cDNA insert was determined and the deduced amino acid sequences are presented. The nucleotide sequence analysis of UBGTA revealed an open reading frame encoding a polypeptide of 476 amino acids with a calculated molecular mass of 532094 Da. The reaction product for baicalein and UDP-glucose catalyzed by recombinant UBGTA in Escherichia coli was identified as authentic baicalein 7-O-glucoside using high-performance liquid chromatography and proton nuclear magnetic resonance spectroscopy. The enzyme activities of recombinant UBGTA expressed in E. coli were also detected towards flavonoids such as baicalein, wogonin, apigenin, scutellarein, 7,4′-dihydroxyflavone and kaempferol, and phenolic compounds. The accumulation of UBGTA mRNA in hairy roots was in response to wounding or salicylic acid treatments.

Free radical scavenging and antioxidant activities of flavonoids extracted from the radix of Scutellaria baicalensis Georgi

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Free radical scavenging and antioxidant activities of baicalein, baicalin, wogonin and wogonoside, the four major flavonoids in the radix of Scutellaria baicalensis Georgi were examined in different systems by Gao Z et al (1999)10. Electron spinning resonance results showed that baicalein and baicalin scavenged hydroxyl radical, DPPH radical and alkyl radical in a dose-dependent manner, while wogonin and wogonoside showed subtle or no effect on these radicals. Ten µmol/l of baicalein and baicalin effectively inhibited lipid peroxidation of rat brain cortex mitochondria induced by Fe2+-ascorbic acid, AAPH or NADPH, while wogonin and wogonoside showed significant effects only on NADPH-induced lipid peroxidation. In a study on cultured human neuroblastoma SH-SY5Y cells system, it was found that 10 µmol/l of baicalein and baicalin significantly protected cells against H2O2-induced injury. Baicalein was the most effective antioxidant among the four tested compounds in every system due to its o-tri-hydroxyl structure in the A ring. Compared with a well-known flavonoid, quercetin, the antioxidant activity of baicalein was lower in DPPH or AAPH system, but a little higher in those systems which might associate with iron ion. These results suggest that flavonoids in the radix of Scutellaria baicalensis with o-di-hydroxyl group in A the ring, such as baicalein and baicalin, could be good free radical
scavengers and might be used to cure head injury associated with free radical assault.
Synergistic effect of Scutellaria baicalensis and grape seed proanthocyanidins on scavenging reactive oxygen species in vitro.
Using an in vitro model to produce the reactive oxygen species (ROS) generation (H2O2/FeSO4 for hydroxyl radicals, xanthine/xanthine oxidase for superoxide). Shao ZH et al (2004)11 observed that Scutellaria baicalensis and grape seed proanthocyanidins acted synergistically to scavenge ROS. They suggested that a combination of these two herbs can potentially enhance their antioxidant efficacy allowing lower dosages of each drug to be used. This has the advantage of avoiding possible side effects that may arise when higher doses of a single herb are used in an attempt to achieve a maximum degree of antioxidant activity.
Scutellaria baicalensis enhances the anti-diabetic activity of metformin in streptozotocin-induced diabetic wistar rats
Viduranga Y et al (2008)12 investigated the effect of combining the antidiabetic drug metformin in streptozotocin (STZ)-induced diabetic rats with an ethanolic extract of Scutellaria baicalensis a plant whose root is known for its radical scavenging activity. Three groups of STZ-induced diabetic rats were given the following treatments for 30 days: (1) metformin 500 mg/kg (2) S. baicalensis 400 mg/kg (3) metformin 500 mg/kg + S. baicalensis extract 400 mg/kg. In addition, vehicle-treated diabetic and nondiabetic controls were used in the experiment. The rats treated with S. baicalensis and metformin + S. baicalensis had elevated hepatic activities of the antioxidant enzymes-superoxide dismutase, catalase and glutathione peroxidase compared to the vehicle- and metformin-treated diabetic groups (p < 0.05). Plasma and hepatic lipid peroxide concentrations in the herb-treated and herb + metformin-treated groups were also significantly reduced (p < 0.05). In addition, the combined treatment caused significant elevations of plasma and pancreatic insulin levels and reductions of plasma and hepatic triglycerides and cholesterol levels. The study thus showed that S. baicalensis enhanced the antidiabetic effect of metformin in STZ-induced diabetic rats by improving the antioxidant status. It also increased pancreatic insulin content as well as improved the lipid profile in these rats.
Anticancer activity of Scutellaria baicalensis and its potential mechanism
Fei Ye et al (2002)13 were determined its ability to inhibit human cancer cells in vitro because of the inhibition of prostaglandin E2 (PGE2) production that is derived from arachidonic acid through cyclooxygenase-2 (COX-2) pathway.
Baicalein protects rat cardiomyocytes from hypoxia/reoxygenation damage via a prooxidant mechanism
Anthony Y.H. et al (2005)14 investigated alternative protective mechanisms of baicalein in a cardiomyocyte model. Neonatal rat cardiomyocytes pretreated with the test compound were subjected to hypoxia/reoxygenation. The extent of cellular damage was accessed by the amount of released lactate dehydrogenase pretreatment with baicalein up to 10 µm reduced lactate dehydrogenase release significantly (P
Benzodiazepine binding site-interactive flavones from Scutellaria baicalensis root
A benzodiazepine binding assay directed separation led to the identification of 3 flavones baicalein, oroxylin A and skullcapflavone II from the water extract of Scutellaria baicalensis root. According to Liao JF et al (1998)15 these three flavones interacted with the benzodiazepine binding site of GABAA receptors with a Ki value of 13.1, 14.6 and 0.36 µm/L respectively. Scutellaria baicalensis decreases ritonavir-induced nausea
Protease inhibitors, particularly ritonavir causes significant gastrointestinal disturbances such as nausea even at low doses. This ritonavir-induced nausea could be related to its oxidative stress in the gut. Rats respond to nausea-producing emetic stimuli by increasing consumption of non-nutritive substances like kaolin or clay, a phenomenon known as pica. Aung H et al(2005) 16 used this rat pica model to evaluate the effects of Scutellaria baicalensis a commonly used oriental herbal medicine on ritonavir-induced nausea.
Discrimination among three species of medicinal Scutellaria plants skullcap using RAPD markers
An analysis of random amplified polymorphic DNA (RAPD) was performed using nine accessions of three species of medicinal plants in the genus Scutellaria (S. galericulata, S. lateriflora and S. baicalensis) in an effort to distinguish between members of these three species. Dried aerial parts of the two species S. galericulata and S. lateriflora are difficult to distinguish morphologically. Ten arbitrary primers produced 92 fragments and eight of the primers yielded 23 species-specific fragments among the three species. Six fragments were specific for S. galericulata, seven for S. lateriflora and ten for S. baicalensis. Hosokawa K et al (2000)17 were used primers A02 and A06 in the polymerase chain reaction, RAPD fragments that were specific for each of the three species were generated simultaneously. Primer A02 produced five species-specific fragments: one was specific for S.
galericulata, two for S. lateriflora and two for S. baicalensis. Primer A06 produced three species-specific fragments: one for S. galericulata, one for S. lateriflora and one for S. baicalensis. The RAPD markers that were generated with these two primers should rapidly identify members of the three species of Scutellaria. The consistency of the identifications made with these species-specific RAPD markers was demonstrated by the observation that each respective marker was generated from three accessions of each species, all with different origins. Furthermore, cluster analysis using the 92 RAPD fragments produced a dendrogram of genetic relatedness that was in good agreement with the taxonomic designations of the three species. Thus, the RAPD markers should be useful for the future identification of members of the three species of medicinal Scutellaria plants.

Conclusion(s)

Scutellaria baicalensis Georgi (Labiatae) is Chinese herb used in both traditional as well as modern system of medicine to treat number of physiological conditions. It is important source of various types of compounds with diverse chemical constituents and pharmacological activity. Further research in view of fulfilling the need of quality control aspects, standardization of various constituents and explore its maximum potential in the field of medicinal and pharmaceutical sciences for novel and fruitful applications.

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