

Coptis chinensis - An amazing medicinal plant from China

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Introduction

Because of its declining habitat in the wild, Golden Seal (*Hydrastis canadensis*) is a herb that should only be purchased from cultivated rather than wildcrafted sources (Oliver, 2017). Even then, however, it is a challenging plant to grow, and securing sufficient volumes from the annual harvest, can be difficult. Therefore, continuing to place high-demand pressure on this herb is not considered ideal. Given that the alkaloid constituent berberine is widely regarded as having numerous pharmacological actions, and seems to account for a significant part of Golden Seal's antimicrobial actions, other medicinal plants rich in this phytochemical, are of interest. Other berberine-containing herbs are of course Oregon Grape (*Mahonia aquifolium*) and Barberry (*Berberis vulgaris*), but a very interesting one from China, is Coptis (*Coptis chinensis*), which generally contains much higher levels of berberine than Golden Seal.

Huang Lian

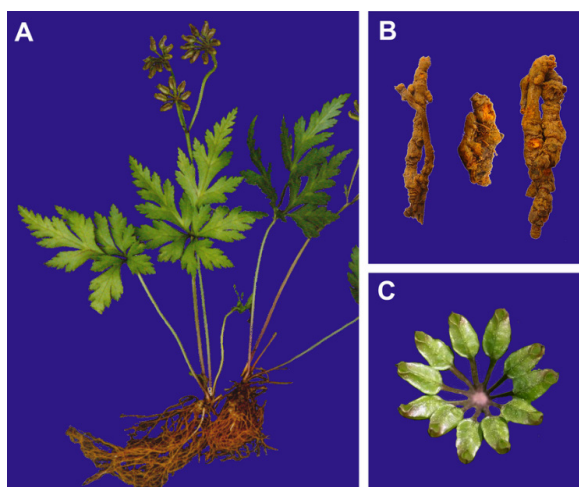
More than 380 papers have been published in peer reviewed journals on this medicinal plant, and Coptis (known as Huang lian in Mandarin), is one of the many Chinese herbs that stands out for its established medicinal properties. The name huang lian literally translates to "yellow thread", because of the intense golden colour (due to berberine content) of its rhizomes.

There are a number of Coptis species in use, but the most commonly used, with the greatest amount of research and traditional use, is *Coptis chinensis* (Coptis). It is a low growing plant indigenous to the mountainous regions of China. Originally a woodland understory plant, Coptis has now been cultivated in China for hundreds of years, and cultivated sources are preferred when they are environmentally sustainable (Qin, 2010).

One of the fifty fundamental herbs of Traditional Chinese Medicine, the rhizomes of Coptis have been used to treat digestive, respiratory, and infectious disorders for more than 2,000 years (Ho et al 2014). It's TCM properties are cold and bitter, with anti-inflammatory and antibacterial actions (A Barefoot Doctor's Manual, 1977).

Principle constituents include isoquinoline alkaloids such as berberine (3-8%), palmatine, jatrorrhizine, coptisine and columbamine; lignans, phenylpropanoids, flavonoids, phenolic acids and sterols (Friedemann et al, 2015).

One of these main constituents, berberine, has been intensively studied, and has many actions attributed to it, as alluded to earlier. Practitioners should note, however, the finding that berberine does not cross the gastrointestinal tract membrane readily; its actions are most focussed therefore, in the gastrointestinal tract itself, or on other bodily surfaces within which it comes into contact (Kamath et al, 2009).



Coptis chinensis A: whole plant. B: Dried rhizome. C: Carpels. (Creativecommons.org, n.d.)

Gastrointestinal (GIT) system

Irritable and Inflammatory Bowel conditions

Coptis is traditionally used to address syndromes involving abdominal pain and diarrhoea. Berberine can reduce inflammation in the intestines, significantly reduce smooth muscle contraction and intestinal motility (thus reducing cramping), and delay intestinal transit time (Habtermariam, 2016).

Potential benefits in Inflammatory Bowel Disease, and on gut microbiota, have also been reported (Cui et al, 2018).

Gastroenteritis and Antimicrobial activity

Coptis has been used extensively in Chinese medicine to treat gastroenteritis and dysentery. Modern studies focus on berberine, determining it to be safe and effective in treating common gastrointestinal infections, including *Escherichia coli* (the common cause of 'traveller's diarrhoea'), *Salmonella typhimurium* (food poisoning), and *Shigella dysenteriae* (Wu et al, 2005; Shi et al, 2018).

Berberine's efficacy may be due to a combination of direct antimicrobial activity, inhibition of microbial attachment to mucous membranes and epithelial surfaces, and an ability to block actions of toxins produced by pathogenic bacteria (Sack & Froelich, 1981; Habtermariam, 2016).

Coptis may inhibit bacterial biofilm formation, demonstrated with regards to *Klebsiella pneumoniae* (Magesh et al., 2013) and *Salmonella* (Shi et al, 2018). However, it may also kill *bifidobacteria* in the process, and berberine itself, like most other phytoconstituents, can be prone to cellular efflux by resistant bacteria (Budeyri Gokgoz, et al., 2017). Practitioners should consider appropriate approaches regarding antimicrobial GIT issues with all herbs to balance this aspect.

Berberine extracts have also shown promise treating *Mycoplasma* species (Arjoon et al., 2012) as well as urethritis and cervicitis due to *Chlamydia spp.* (Li et al., 2008).

Coptis extracts also strongly inhibit *Candida spp.* growth and biofilm (da Silva et al., 2016). Antibiofilm and P-glycoprotein inhibitory effects by berberine and other alkaloids, may contribute to the synergistic effects shown with several antibiotics against resistant bacteria (Zhou et al., 2016; Morita et al., 2016).

Antiparasitic

Coptis extracts were found to be highly inhibitory against *Blastocystis spp.* in a number of *in vitro* trials (Su et al., 2007), while berberine has demonstrated activity against *Entamoeba histolytica*, *Giardia lamblia*, and *Trichomonas vaginalis* (Kaneda et al., 1990). Berberine hydrochloride at 10mg/kg/day for 10 days in children achieved a 90% reduction in *Giardia*-positive stools (Gupte, 1975).

Endocrine system

Much research has been undertaken into the influences of Coptis as well as berberine on diabetes and metabolic syndrome in recent years, including the ability to regulate glucose and cholesterol levels, and have anti-obesity and anti-diabetic effects (Hi 2018; Zhang 2019). Systemic reviews have noted that Coptis demonstrated anti-obesity results including weight reduction, lowered lipids, reduced lipid synthesis, and inhibited adipogenesis, while regulating gut microflora to promote weight reduction (Liu et al., 2017; Wu et al., 2014).

A meta-analysis concluded that Coptis alkaloids significantly lowered total and LDL cholesterol and triglycerides, while raising HDL cholesterol (Dong et al, 2013) apparently in part at least, through bile flow promotion via gene expression (Cao et al, 2012).

Coptis also demonstrates beneficial effects for blood glucose control in the treatment of type 2 diabetic patients, potential protection against diabetic kidney disease, and co-administration with conventional oral hypoglycaemic drugs improved glycaemic control (Dong et al, 2013; Prabhakar & Doble, 2017; Zhang 2019).

Coptis may have strong benefits for women with Polycystic Ovarian Syndrome (PCOS). Berberine has shown promise due to its ability to regulate insulin and glucose, inhibit excessive testosterone production, and, as above, benefit the gut microbiota, and reduce acne (Yarnell & Abascal, 2006; Wang et al., 2014).

In a clinical trial, researchers compared berberine to metformin for women with PCOS. After three months, both berberine and metformin groups exhibited improvements in insulin, body weight, and testosterone levels (Wei et al, 2012). In another clinical study, both berberine and metformin increased pregnancy rate and reduced the incidence of severe ovarian hyperstimulation syndrome for women with PCOS undergoing fertility treatment. Berberine treatment was associated with greater decreases in BMI, lipid parameters, total FSH requirement, and an increase in live birth rate with fewer GI adverse events than metformin (An et al., 2014).

Other uses

Antiviral

In parallel to traditional uses, preclinical trials have shown Coptis alkaloids effective against viruses, including herpes simplex and human cytomegalovirus (Hayashi et al, 2007; Song et al., 2014).

Antioxidant with skin protective applications

Coptis, as well as its major alkaloids, demonstrates potent protective activity against oxidative damage, as demonstrated in multiple pharmacological investigations (Pang et al., 2015). It elevates antioxidant enzymes such as SOD and glutathione peroxidase, while reducing ROS. Studies demonstrate effects topically and internally, suggesting a protective effect against UVB light as well as supporting liver and erythrocyte function (Xu et al, 2013).

These actions may contribute to protective effects against radiation and UV-induced skin damage (Wang et al., 2015; Wang et al 2013).

Suppression of inflammation as a result of *Propionibacterium* acne, has also recently been reported (Lee et al., 2018).

Anticancer

Many studies have evaluated the anti-cancer potential of berberine. In summary, it has inhibitory effects on colorectal cancer, lung cancer, ovarian cancer, prostate cancer, liver cancer, and cervical cancer cell lines *in vitro* through multiple mechanisms (Wang et al., 2015; Liu et al, 2019).

Conclusion

Coptis is a well-researched and highly regarded medicinal plant with a long history of traditional use in China, and as

cultivated sources of its rhizomes are available from sustainable sources, it should be regarded as a potentially very useful addition to our dispensaries.

While it adds to our treatment options for gastrointestinal tract infections, reducing pressure on the vulnerable Golden Seal resources, it also has a different spectrum of therapeutic actions, including for endocrine conditions such as acne, diabetes, metabolic syndrome and PCOS.

The concept of pathogenic involvement in endocrine dysfunction is further developing (Hechtman, 2018), and practitioners are outlining their experiences identifying the effects of pathogens as underlying causes in systemic situations. *Coptis* has fascinating potential for this paradigm, as revealed in the above literature.

References

- An, Y., Sun, Z., Zhang, Y., Liu, B., Guan, Y., & Lu, M. (2014). The use of berberine for women with polycystic ovary syndrome undergoing IVF treatment. *Clinical Endocrinology*, 80, 425-431. doi:10.1111/cen.12294
- Arjoon, A. V., Saylor, C. V., & May, M. (2012). In vitro efficacy of antimicrobial extracts against the atypical ruminant pathogen mycoplasma mycoides subsp. Capri. *BMC Complementary and Alternative Medicine* 12: 69. doi: 10.1186/1472-6882-12-169
- A Barefoot Doctors Manual: The American Translation of the Official Chinese Paramedical Manual. (1977). Philadelphia PA: Running Press
- Budeyri Gokgoz, N., Avci, F. G., Yoneten, K. K., Alaybeyoglu, B., Ozkirimli, E., Sayar, N. A., & Sariyar Akbulut, B. (2017). Response of *Escherichia coli* to prolonged berberine exposure. *Microbial Drug Resistance*, 23(5). doi: 10.1089/mdr.2016.0063
- Cao, Y., Bei, W., Hu, Y., Cao, L., Huang, L., Wang, L.,...& Guo, J. (2012). Hypocholesterolemia of rhizoma coptidis alkaloids is related to the bile acid by up-regulated CYP7A1 in hyperlipidemic rats. *Phytomedicine*, 19(8-9), 686-692. doi: https://doi.org/10.1016/j.phymed.2012.03.011
- Cui, H., Cai, Y., Wang, L., Jia, B., Li, J., Zhao, S., ...& Zhuang, P. (2018). Berberine regulates treg/th17 balance to treat ulcerative colitis through modulating the gut microbiota in the colon. *Frontiers in Pharmacology*, 9, 571. doi:10.3389/fphar.2018.00571
- da Silva, A. R., de Andrade Neto, J. B., da Silva, C. R., Campos, R., Costa Silva, R. A., Freitas, D. D., & Nobre Júnior, H. V. (2016). Berberine antifungal activity in fluconazole-resistant pathogenic yeasts: action mechanism evaluated by flow cytometry and biofilm growth inhibition in candida spp. *Antimicrobial agents and chemotherapy*, 60(6), 3551-3557. doi:10.1128/AAC.01846-15
- Dong, H., Zhao, Y., Zhao, L., & Lu, F. (2013). The effects of berberine on blood lipids: a systemic review and meta-analysis of randomized controlled trials. *Planta Medica*, 79(6), 437-446. doi: 10.1055/s-0032-1328321
- Friedemann, T., Schumacher, U., Tao, Y., Leung, A., & Schröder, S. (2015). Neuroprotective activity of coptisine from *Coptis chinensis* (franch). *Evidence-based Complementary and Alternative Medicine*, 827308. doi: 10.1155/2015/827308.
- Gupte S. (1975). Use of berberine in treatment of giardiasis. *American Journal of Diseases of Children*, 129(7), 866. doi:10.1001/archpedi.1975.02120440082020
- Habtemariam, S. (2016). Berberine and inflammatory bowel disease: A concise review. *Pharmacological Research*, 113, 592-599. doi: https://doi.org/10.1016/j.phrs.2016.09.041
- Hayashi, K., Minoda, K., Nagaoka, Y., Hayashi, T., & Uesato, S. (2007). Antiviral activity of berberine and related compounds against human cytomegalovirus. *Bioorganic & Medicinal Chemistry Letters* 17(6), 1562-1564. doi: https://doi.org/10.1016/j.bmcl.2006.12.085
- Hechtman, L. (2018). *Endometriosis: The interplay between the immune and reproductive systems*. Honouring the Herbs New Zealand Association of Medical Herbalists Conference. Auckland, 20 May 2018.
- Ho, C. E., Goh, Y. L., & Zhang, C. (2014). From prejudice to evidence: the case of rhizoma coptidis in Singapore. *Evidence-Based Complementary and Alternative Medicine*, 871720. doi: https://doi.org/10.1155/2014/871720.
- Hu X, Zhang Y, Xue Y, Zhang Z, Wang J, (2018). Berberine is a potential therapeutic agent for metabolic syndrome via brown adipose tissue activation and metabolism regulation. *Am J Trans Res* 10(11):3322-3329.
- Kamath, S., Skeels, M., & Pai, A. (2009). Significant differences in alkaloid content of *Coptis chinensis* (huanglian), from its related American species. *Chinese Medicine* 4(1). doi: https://doi.org/10.1186/1749-8546-4-17
- Kaneda, Y., Tanaka, T. & Saw, T. (1990). Effects of berberine, a plant alkaloid, on the growth of anaerobic protozoa in axenic culture. *Tokai Journal of Experimental and Clinical Medicine*, 15(6), 417-423
- Lee, J. W., Kang, Y. J., Choi, H. K., & Yoon, Y. G. (2018). Fractionated *Coptis chinensis* extract and its bioactive component suppress propionibacterium acnes-stimulated inflammation in human keratinocytes. *Journal of Microbiology and Biotechnology*, 28(6), 839-848. doi: 10.4014/jmb.1712.12051
- Li, J., Lin, Y., Wu, Y., & Wang, P. (2008). Clinical observation of berberine in treatment of non- gonococcal urethritis and cervicitis due to chlamydia trachomatis. *Chinese Archives of traditional Chinese Medicine*. Retrieved from http://en.cnki.com.cn/Article_en/CJFDTOTAL-ZYHS200808075.htm
- Liu, D., Meng, X., Wu, D., Qiu, Z., & Luo, H. (2019). A natural isoquinoline alkaloid with antitumor activity: studies of the biological activities of berberine. *Frontiers in Pharmacology*, 10, 9. doi:10.3389/fphar.2019.00009
- Liu, Y., Sun, M., Yao, H., Liu, Y., & Gao, R. (2017). Herbal medicine for the treatment of obesity: an overview of scientific evidence from 2007 to 2017. *Evidence-Based Complementary and Alternative Medicine*, 8943059.

- doi:10.1155/2017/8943059
- Magesh, H., Kumar, A., Alam, A., Priyam, Sekar, U., Sumantran, V. N., & Vaidyanathan, R. (2013). Identification of natural compounds which inhibit biofilm formation in clinical isolates of *Klebsiella pneumoniae*. *Indian Journal of Experimental Biology*, 51, 764-72.
- Morita, Y., Nakashima, K., Nishino, K., Kotani, K., Tomida, J., Inoue, M., & Kawamura, Y. (2016). Berberine is a novel type efflux inhibitor which attenuates the mexxy-mediated aminoglycoside resistance in *Pseudomonas aeruginosa*. *Frontiers in Microbiology*, 7, 1223. doi:10.3389/fmicb.2016.01223
- Oliver, L. 2017. *Hydrastis canadensis*. *The IUCN Red List of Threatened Species*. doi: 10.2305/IUCN.UK.2017-2.RLTS.T44340011A44340071.en.
- Pang, B., Yu, X., Zhou, Q., Zhao, T., Wang, H., Gu, C., & Tong, X. (2015). Effect of rhizoma coptidis (huang lian) on treating diabetes mellitus. *Evidence-based Complementary and Alternative Medicine*, 921416. 10.1155/2015/921416.
- Prabhakar, P. K., & Doble, M. (2011). Mechanism of action of natural products used in the treatment of diabetes mellitus. *Chinese Journal of Integrative Medicine*, 17(8), 563-74. doi: 10.1007/s11655-011-0810-3
- Qin, Y. (2010). Finding a sustainable way for *Coptis chinensis* cultivation in china. *World Journal of Agricultural Sciences*, 6(4), 457-459. Retrieved from <http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.415.3675&rep=rep1&type=pdf>
- Sack, R. B., & Froelich, J. L. (1981). Berberine inhibits intestinal secretory response of *Vibrio cholerae* and *Escherichia coli* enterotoxins. *Infection and Immunity*, 35(2), 471-475. Retrieved from <https://iai.asm.org/content/iai/35/2/471.full.pdf>
- Shi, C., Li, M., Muhammad, I., Ma, X., Chang, Y., Li, R., & Liu, F. (2018). Combination of berberine and ciprofloxacin reduces multi-resistant salmonella strain biofilm formation by depressing mRNA expressions of luxS, rpoE, and ompR. *Journal of veterinary science*, 19(6), 808-816. doi:10.4142/jvs.2018.19.6.808
- Song, S., Qiu, M., Chu, Y., Chen, D., Wang, X., Su, A., & Wu, Z. (2014). Downregulation of cellular c-Jun N-terminal protein kinase and NF- κ B activation by berberine may result in inhibition of herpes simplex virus replication. *Antimicrobial agents and chemotherapy*, 58(9), 5068-5078. doi:10.1128/AAC.02427-14
- Su, S., Chen, G., Zhang, R., Xie, Q., & Liao, H. (2007). The trichomonocidal effect of nine chinese herbs on the *Blastocystis hominis*. *Lishizhen Medicine and Materia Medica Research*. Retrieved from http://en.cnki.com.cn/Article_en/CJFDTOTAL-SZGY200703056.htm
- Wang, H., Mu, W., Shang, H., Lin, J., & Lei, X. (2014). The antihyperglycemic effects of rhizoma coptidis and mechanism of actions: a review of systematic reviews and pharmacological research. *BioMed Research International*, 798093. doi:10.1155/2014/798093
- Wang, N., Tan, H., Li, L., Yuen, M., & Feng, Y. (2015). Berberine and coptidis rhizoma as potential anticancer agents: Recent updates and future perspectives. *Journal of Ethnopharmacology*, 176, 35-48. doi: 10.1016/j.jep.2015.10.028
- Wang, X. J., Lin, S., Kang, H. F., Dai, Z. J., Bai, M. H., Ma, X. L., & Wang, B. F. (2013). The effect of rhizoma coptidis and *Coptis chinensis* aqueous extract on radiation-induced skin injury in a rat model. *BMC Complementary and Alternative Medicine*, 13, 105. doi:10.1186/1472-6882-13-105
- Wei, W., Zhao, H., Wang, A., Sui, M., Liang, K., Deng, H., & Guan, Y. (2012). A clinical study on the short-term effect of berberine in comparison to metformin on the metabolic characteristics of women with polycystic ovary syndrome. *European Journal of Endocrinology*, 166(1), 99-105. Retrieved Apr 11, 2019, from <https://ej.e.bioscientifica.com/view/journals/eje/166/1/99.xml>
- Wu, H., He, K., Wang, Y., Xue, D., Ning, N., Zou, Z.,...& Pang, J. (2014). The antihypercholesterolemic effect of jatrorrhizine isolated from rhizoma coptidis. *Phytomedicine*, 21(11), 1373-81. doi: 10.1016/j.phymed.2014.05.002
- Wu, L. T., Tsou, M. F., Chuang, J. Y., Kuo, H. M., & Chung, J. G. (2005). Berberine inhibits arylamine n-acetyltransferase activity and gene expression in salmonella typhi. *Current Microbiology*, 51(4), 255-261. doi: 10.1007/s00284-005-4569-7
- Yarnell, E., & Abascal, K. (2006). Herbal medicine for acne vulgaris. *Alternative and Complementary Therapies*, 12(6), 303-309. doi:10.1089/act.2006.12.303
- Xu, Y., Luiiu, C. F., Wang, Y. W., Yang, B., Li, X. L., Qiao, L., & Lin, N. (2013). Water decoction of coptidis rhizoma prevents oxidative damage in erythrocytes of mice. *Indian Journal of Pharmaceutical Sciences*, 75(3), 270-276. doi:10.4103/0250-474X.117408
- Zhang X, Guan T, Yang B, Chi Z, Wan Q, Gu HF. (2019). Protective effect of berberine on high glucose and hypoxia-induced apoptosis via the modulation of HIF-1 α in renal tubular epithelial cells. *Am J Trans Res*; 11(2):669-682.
- Zhou, X. Y., Ye, X. G., He, L. T., Zhang, S. R., Wang, R. L., Zhou, J., & He, Z. S. (2016). *In vitro* characterization and inhibition of the interaction between ciprofloxacin and berberine against multidrug-resistant *Klebsiella pneumoniae*. *The Journal of Antibiotics*, 69(10), 741-746. doi:10.1038/ja.2016.15

Editors Note: There are several species of *Coptis*, and as is the case with so many herbs now some are indeed endangered in the wild, hence *Coptis chinensis* being cultivated for several hundred years. This is why companies such as Phytomed source their *Coptis chinensis* from cultivated suppliers rather than wildcrafted plant material. NZAMH members are encouraged to source *Coptis chinensis* from cultivated sources to reduce the risk of extinction.