ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info

ISSN
0976-9595
Review Article

PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE OF *CYNANCHUM AURICULATUM* ROYLE EX WIGHT - A REVIEW

Gowher Guna

Department of Botany, Islamia College of Science and Commerce, Srinagar, Jammu and Kashmir, India
**Corresponding author: gunagowher@gmail.com*

ABSTRACT

The aim of this review is to correlate active principles of *Cynanchum auriculatum* (CA) to their pharmacological activity and thus explore the potential of *Cynanchum auriculatum* (CA) as a source of therapeutic agents. *Cynanchum auriculatum* (CA) has been used for centuries to treat a variety of ailments. Extracts of *Cynanchum auriculatum* (CA) are found in a variety of herbal preparations, as well as homeopathic remedies. In recent years, immense phytochemical and pharmacological screening of *Cynanchum* has shown tremendous activity against various diseases. Extensive and exhaustive literature survey was done to record pharmacological activity of the plant. The plant has shown biological activity as an Antioxidant, Antitumerogenic, Neuroprotective, Appetite suppressant, Antidepressant, Hepatoprotective, Anti-ageing, Gastroprotective, Anti-injurious, Imunosuppressive agent. The present review highlights botanical description, distribution, chemical constituents, and the pharmacological effects of CA.

Keywords: *Cynanchum auriculatum*, Pharmacology, Plant profile, Chemical constituents.

1. INTRODUCTION

With increase in wealth of developed nations, people have become more conscious about health. A lot of money is being spent on food and medicine. For sustainable health benefits and disease treatment with less side effects, people have shifted to the use of natural herbs and remedies. Food and medicine are perceived to be closely linked as both stems from the same origin with different uses and applications. *Cynanchum* has been traditionally used in various communities for various ailments such as sore throat, rashes, boils, and skin infections. The aim of this review is to summarize the currently available scientific information with regard to its therapeutic effects, so as to provide a comprehensive overview of this herb.

2. PLANT PROFILE

Cynanchum auriculatum Royle ex Wight, Contr. Bot. India. 58. 1834.

Cynanchum saccatum W. T. Wang ex Tsiang & P. T. Li; *Diploglossum auriculatum* (Royle ex Wight) Meisner; *Endotropis auriculata* (Royle ex Wight) Decaisne; *Vincetoxicum auriculatum* (Royle ex Wight) Kuntze.

Family: Apocynaceae, Common name: Baishouwu, English name: Heart Leaf Swallow Wort.

Morphological Features: Stems twining, puberulent along 1 side to uniformly puberulent, sometimes glabrescent. Leaves opposite; petiole 2.4-3.5(-8.5) cm, axillary stipulelike leaves sometimes present; leaf blade ovate, 4.5-11(-16) × 2.6-7(-11.5) cm, papery, puberulent, densely so on veins abaxially, base cordate with rounded sinus, apex acuminate; basal veins 5, lateral veins 2 or 3 pairs. Inflorescences racemelike, many flowered, to 23 cm; peduncle 4.5-15 cm. Pedicel 0.9-2.8 cm, puberulent. Sepals lanceolate, 2.2-5.2 × 0.8-2 mm, puberulent; basal glands 5. Corolla white, pale yellow, pink, or purple, rotate; tube short; lobes lanceolate to lanceolate-oblong, 5.5-8(-10) × 2-3 mm,

coarsely pubescent to pilose inside. Corona very deeply 5-lobed, white; lobes much longer than gynostegium, elliptic, to ca. 4.5 mm, fleshy, obtuse, with narrowly triangular adaxial appendages. Stigma head conical. Follicles oblong-lanceolate, ca. 8 × 1 cm. Seeds ovate, truncate, ca. 6 × 3 mm; coma ca. 2.5 cm.

Flowering Period: Jun-Aug, Fruiting: Aug-Dec. Geographical Distribution: Bushland on mountain slopes; 2800-3600 m. China, Bhutan, India, Kashmir, Nepal, Pakistan.

3. CHEMICAL CONSTITUENTS

Cynandione A, *p*-hydroxyacetophenone, and 2', 4'-dihydroxyacetophenone were obtained from roots [1]. Ethanol extract of *Cynanchum auriculatum* revealed the presence of sarcosin-3-O-β-cymaropyranoside (1), cynotophylloside B (2), clemaphenol A (3), deacetyl-metaplexigenin (4), methyl-2,6-dideoxy-3-O-methyl-β-D-arabino-hexopyranosyl- (1 -> 4) -6-deoxy-3-O-methyl-α-L-ribo-hexopyranoside (5), trans-p-hydroxy cinnamic methyl ester (6), cyclo(D-Pro-D-Leu) (7), 3α-hydroxy-5α ,6α-epoxy-7-megastigmen9-one (8) and ferulic acid methyl ester (9) on the basis of spectral analysis [2]. Three new steroidal glycosides, cyanoauriculosides F, G and H (1-3), were isolated from the roots along with two known steroidal derivatives. On the basis of spectroscopic analysis and chemical methods, their structures were identified as 20-O-acetyl-8,14-seco-penupogenin-8-one 3-O-α-L-cymaropyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4) -α-L-diginopyranosyl-(1→4)-β-D-cymaropyranoside (1), 2',3'-Z-gagaminine 3-O-α-L-cymaropyranosyl-(1→4)-β-D-cymaro-pyranosyl-(1→4)-α-L-diginopyra-nosyl-(1→4)-β-D-cymaropyranoside (2), 17-O-acetyl-kidjoranin 3-O-α-L-cymaropyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-α-L-cymaro-pyranosyl-(1→4) -β-D-digitoxopyranosyl-(1→4)-β-D-digitoxopyrano-side (3), gagaminine 3-O-α-L-cymaropyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-α-L-digino-pyranosyl-(1→4)-β-D-cymaropyranoside (4) and wilfoside D1N (5) [3]. Seven compounds were obtained from plant and identified as: taraxasterol acetate (I), cynanchone A (II), succinic acid (III), betulinic acid (IV), kidjoranin (V), wilfoside CIN (VI), wilfoside KIN (VII)[4]. Root tuber showed presence of caudatin (1), metaplexigenin (2), cynauricuoside A (3), succinic acid (4), azelaic acid (5), wilforibiose (6), sucrose (7), 1-O-hexadecanolenin (8), beta-amyrin acetate (9), cynanchone A (10), acetylquinol (11), beta-sitosterol (12), daucosterol (13) [5].

4. THERAPEUTICS AND PHARMACOLOGY

4.1. Antioxidant activity

C-21 steroidal glycosides TCSGs can protect human normal liver cell line, L02 cells against H_2O_2-induced oxidative toxicity and inflammatory injury by increasing the expression of Nrf2 and HO-1, mediated by the NF-κB signaling pathway [6]. Polysaccharide fraction (CAP2-1) from *Cynanchum auriculatum* Royle ex Wight provided a significant protective effect against hydrogen peroxide-induced oxidative stress in HepG2 cells by a compositive oxidation defense mechanism. CAP2-1 could reduce oxidative stress by significantly enhancing the contents of antioxidant enzyme SOD and non-enzymatic antioxidant GSH in oxidative damaged cells, in addition to scavenging ROS directly and improving cell viability and membrane integrity, consequently achieving the intracellular antioxidant activity [7]. Thermal stability, resistant starch content as well as antioxidant activity of *C. auriculatum* starch was greatly enhanced by grafting with quercetin thereby indicating the potential of quercetin-g-starch in the development of a novel resistant starch with antioxidant activity [8]. Free radical damage is prevented by extracts from *Cynanchum auriculatum* [9].

4.2. Antitumerogenic activity

Caudatin significantly inhibited HUVEC human umbilical vein endothelial cell proliferation, blocked the HUVECs migration, invasion and capillary-like tube formation by disturbing the vascular endothelial growth factor (VEGF)-VEGFR2-protein kinase B (AKT)/focal adhesion kinase (FAK) signal axis. Caudatin treatment abolished the glioma cell growth by suppression of the in vivo angiogenesis, which involved FAK and AKT dephosphorylation and inhibition of VEGF expression [10].C-21 steroidal glycosides possessing antitumor activity were concentrated in the chloroform and ethyl acetate fractions, and the total contents of different fractions in the root tuber were significantly higher than those of corresponding ones in the root bark [11].Caudatin - an antitumerogenic agent was found in the plasma and livers of hepatocellular carcinoma (HCC) model rats [12]. Caudatin 3-O-β-D-cymaro-pyranosyl-(1→4)-β-D-oleandropyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside (CGII) inhibits cell growth of human gastric cancer (SGC-7901) cells by inducing G1 phase cell cycle arrest and

caspase-dependent apoptosis cascades [13]. C21-steroidal glycoside (CG) is able to inhibit the growth of human cancer cells (SGC-7901 cells) and induce cancer cell apoptosis through caspase-3-dependent pathways. SGC-7901 cells exposed to CG (10.8 and 21.6 μM) exhibited typical morphological apoptosis characteristics, such as nuclear-chromatin condensation and apoptotic body formation. Treatment with CG at a concentration of 21.6 μM for 24 h significantly increased the expression of caspase-3 and the activity of caspase-3 was increased ~3-fold in SGC-7901 cells [14]. *Cynanchum auriculatum* (CGB) at 30, 60, 120 mg/L concentration-dependently decreased rat glioma C6 cell viability ($P<0.001$). CGB at 60 and 120 mg/L induced C6 cell apoptosis and cell cycle arrest. The fraction of G0/G1 cells was increased ($P<0.05$) and that of S phase cells was decreased ($P<0.01$) [15].Caudatin-2,6-dideoxy-3-O-methy-β-D-cymaropyranoside and caudatin inhibited human tumor cell line SMMC-7721 with IC(50) values of 13.49 and 24.95 μM, respectively. Caudatin-2,6-dideoxy-3-O-methy-β-D-cymaropyranoside and caudatin significantly inhibited the growth of transplantable H(22) tumors in mice [16].Caudatin-2,6-dideoxy-3-O-methy-β-D-cymaropyranoside (CDMC), inhibited the growth of human hepatoma cell line- SMMC7721 cells in a time- and dose-dependent manner and resulted in cell cycle arrest in G(0)/G(1) phase. CDMC induced SMMC7721 cell apoptosis rather than necrosis through caspase 3 activation, and a caspase 3 inhibitor, Ac-DEVD-CHO, could attenuate the apoptosis induced by CDMC [17].Wilfoside C3N- a C21 steroidal glycoside inhibited the proliferation of ECA109 cells moderately in a dose and time-dependent manner and induced apoptosis in the ECA109 cell line through a mitochondrial pathway by triggered cytochrome c release from the mitochondria, with caspase-2 functioning upstream of caspase-9 rather than association with Fas and caspase-8 [18]. Three C21 steroidal saponins could inhibit the proliferation of human lung cancer A549 cells in dose-dependent manner and the mechanism may be related to its arresting the cell cycle [19]. Pregnane glycosides, kidjoranin 3- O- alpha-diginopyranosyl-(1-->4)- beta-cymaropyranoside (1) and kidjoranin 3-O-beta-digitoxopyranoside (2), together with one known compound caudatin 3 -O-beta-cymaropyranoside (3), inhibited growth of human tumor cell lines SMMC-7721, HeLa and MCF7. They displayed marked cytotoxic activities against cells SMMC-7721 and HeLa with IC (50) values ranging from 8.6 microM to 58.5 microM, yet no activity against the cell line MCF7 was detected [20]. MCF-7 Cells exposed to C21-steroidal glycoside auriculoside A displayed typical morphological apoptosis characteristics such as cytoplasm contraction and nuclear-chromatin condensation. MCF-7 cell cycle was arrested at the G0/G1 phase [21]. Ethanol extract from the root tuber exhibited cytotoxic activity on human tumor cell lines K562, SHG44, HCT-8, A549, PC3, in vitro and inhibition in mouse implanted sarcoma S180, in vivo [22].

4.3. Neuroprotective activity

Twenty-three C_{21} steroidal glycosides isolates produced significant activities against H_2O_2-induced cell damage ($P < 0.001$) to PC 12 cells. Cynsaccatols I, N, O and S caused obvious inhibition of damaged PC12 cell apoptosis at their dosages of 1 μM [23]. Cynandione A, an acetophenone from the roots of *Cynanchum auriculatum* dose-dependently attenuated glutamate-induced cytotoxicity, caused down-regulation of high mobility group box 1 (HMGB1) and dihydro-pyrimidinase-like 2 (DPYSL2) in PC12 cells and markedly improved neurological deficit and reduction in cerebral infarction size thereby mitigating ischemic injuries [24].

4.4. Appetite suppressant activity

Out of the 15 pregnane glycosides tested, wilfoside K1N showed considerable Appetite suppressant and body weight loss effect, in an in vivo test with rats [25].

4.5. Antidepressant activity

Total glycosides of C. auriculatum (TGC) and its $CHCl_3$/MeOH (10:1) fractions (TGC-D and TGC-E) decreased the immobility time in tail suspension test, forced swimming test and also decreased the crossing distances in locomotor activity test. TGC, TGC-D and TGC-E (10 mg/L) inhibited serotonin reuptake by 7.4, 4.5, and 71.1% in rat brain synaptosomes, and IC50 value of TGC-E was 5.2 mg/L [26].

4.6. Hepatoprotective activity

The elevation of serum GPT, GOT, HA, PCIll, MDA and HyP and the content of liver homogenates induced by CCl_4 treatment were attenuated remarkably by *Cynanchum auriculatum* treatment. It also increased the level of SOD of liver homogenates, and makes the fibrotic liver better [27].

4.7. Anti-ageing activity

C21 steroidal glycoside (CSG) antagonize free radical injury, increase the SOD activity and decrease the MDA content of serum, heart, liver and brain in D-gal aging mice, and increase the telomerase activity in serum and heart tissues but not in liver and brain tissue [28].

4.8. Gastroprotective activity

Oral administrations of ethanol extract and chloroform fraction of *c* at the doses of 300 and 69 mg/kg, respectively, significantly inhibited ethanol- and indomethacin-induced gastric lesions [29].

4.9. Anti-injurious activity

Extracts from *Cynanchum auriculatum* have shown anti injurious activity against toxicity caused by ozone [30].

4.10. Imunosuppressive activity

C21 steroid ester glycosides have been shown to have immune-modulatory effect [31].

5. CONCLUSION

The present review has shown that *Cynanchum auriculatum* (CA) contains many active ingredients which have therapeutic effects against various ailments. Clinical observations on traditional remedies have shown the efficacy of *Cynanchum auriculatum* (CA) as safer, cheaper, and much effective alternative to other costly drugs for various ailments. It is expected that further investigations will lead to a better understanding of the mechanism of its action against various ailments.

6. REFERENCES

1. Uchikura T, Tanaka H, Sugiwaki H, Yoshimura, M, et al. *Molecules*, 2018; **23(3)**:256.
2. He JB, Jia J, Gou HP, Zhang XM, Miao XS, He F, Tao J. *Zhong Yao Cai*, 2015; **38(11)**:2318-20.
3. Lu Y, Teng HL, Yang GZ, Mei ZN. *Molecules*, 2011. 23:**16(2)**:1901-1909.
4. Yin M, Chen Y, Wang M, Dong YF, et al. *Zhong Yao Cai*, 2007; **30(10)**:1245-1247.
5. Zhang JF, Li YB, Li CL, Jiang JQ. *Zhongguo Zhong Yao Za Zhi,* 2006; **31(10)**:814-816.
6. Wu Z, Wang Y, Meng X, Wang X, et al. *Int J Mol Med*, 2018; **42(6)**:3157-3170
7. Chai Z, Huang W, Zhao X, Wu H, et al. *Int J Biol Macromol*, 2018; **119**:1068-1076.
8. Liu J, Wang X, Yong H, Kan J, et al. *Int J Biol Macromol*, 2018; **114**:130-136.
9. Guo ZZ, Lu YC and Liu XQ. *Zhong Xi Yi Jie He Za Zhi*, 1988; **8(5)**:282-284.
10. Wang X, Fu X, Zhao S, Fu X, et al. *Mol Med Rep*, 2017; **16(6)**:8937-8943.
11. Wang XJ, Li ZL, Lv XH, Zuo QY, et al. *J Sep Sci*, 2017; **40(15)**:3054-3063.
12. Peng Y, Ding Y. *Molecules*, 2015; **20(3**):4225-37.
13. Wang YQ, Zhang SJ, Lu H, Yang B, et al. *Evid Based Complement Alternat Med*, 2013; **2013**:180839.
14. Ye LF, Wang YQ, Yang B, Zhang RS. *Oncol Lett*, 2013; **5(4)**:1407-1411.
15. Wang YQ, Yang B, Zhang RS, Wei EQ. *Zhejiang Da Xue Xue Bao Yi Xue Ban*, 2011; **40(4)**:402-407.
16. Peng YR, Li YB, Liu XD, Zhang JF et al. *Phytomedicine*, 2008; **15(11)**:1016-1020.
17. Peng YR, Ding YF, Wei YJ, Shu B, et al. *Phytother Res*, 2011; **25(5)**:631-637.
18. Liu K, Chen F, Zhang H. *Anticancer Drugs*, 2010; **21(6)**:625-631.
19. Yao N, Gu X and Li Y. *Zhongguo Zhong Yao Za Zhi*, 2009; **34(11)**:1418-1421.
20. Li Y, Zhang J, Gu X, Peng Y et al. *Planta Med*, 2008; **74(5)**:551-554.
21. Zhang R, Liu Y, Wang Y, Ye Y et al. *Chem Biodivers*, 2007; **4(5)**:887-892.
22. Shan L, Zhang WD, Zhang C, Liu RH, et al. *Phytother Res*, 2005; **19(3)**:259-261.
23. Qian X, Li B, Li P, Wang D, et al. *Phytochemistry*, 2017; **140**:1-15.
24. Yue R, Yuan X, Liu X, Zhang J, et al. *J Neurochem*, 2012; **121**(3):451-464.
25. Liu S, Chen Z, Wu J, Wang L, et al. *Phytochemistry*, 2013; **93**:144-153.
26. Ji CX, Li XY, Jia SB, Liu LL, et al. *Pharm Biol*, 2012; **50(9)**:1067-1072.
27. Lv W, Zhang A, Xu S, Zhang H. *Zhongguo Zhong Yao Za Zhi*, 2009; **34(19)**:2508-2511.
28. Zhang SX, Li X, Yin JL, Chen LL, et al. *Zhongguo Zhong Yao Za Zhi*, 2007; **32(23)**:2511-2514.
29. Shan L, Liu RH, Shen YH, Zhang WD, et al. *J Ethnopharmacol*, 2006; **107(3):**389-394.
30. Wang S, Liu X, Lu Y, Guo Z, et al. *Zhongguo Zhong Yao Za Zhi*, 1990; **15(7):**431-448.
31. Gu LG. *Hong Yao Tong Bao*, 1986; **11(11):**50-22.