CHAPTER 16

Uncaria rhynchophila or Cat's Claw Herb as a Natural Treatment for Hypertension

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SUMMARY

Cat's Claw Herb, or *Uncaria rhynchophila*, is a traditional medicinal plant. It has drawn interest due to its possible application in the management of hypertension, a disorder marked by elevated blood pressure. Because cat's claw herb contains active chemicals like flavonoids and alkaloids that may help relax blood vessels and lower blood pressure, it is thought to have antihypertensive qualities. More research is required to completely understand its processes and develop standardized dosages for safe and effective usage in the control of hypertension, even if some studies suggest that it is useful in decreasing blood pressure.

INTRODUCTION

Hypertension is a leading cause of cardiovascular diseases and mortality. Hypertension is prevalent in over 1.2 billion people worldwide and significantly resulting in drastic outcomes (De-Giuseppe et al., 2019). Pressure overload in people with hypertensive disorders can result in pathological modifications such as left ventricular enlargement and myocardial fibrosis, which continue towards gradual cardiac remodeling and finally culminate in heart failure (Slivnick et al., 2019). The main contributory factor of heart failure in people with high blood pressure is myocardial fibrosis. Therefore, the medical management of hypertensive cardiovascular disease needs to concentrate on avoiding myocardial fibrosis (Petersen et al., 2020). In the regions of Asia, Africa, and Latin America, *Uncaria* (*U.*) *rhynchophylla*, commonly referred to as "Gou-Teng" or "cat's claw herb", has been employed in traditional medicine as a natural treatment for hypertension (Liu et al., 2016). There are thirty-four varieties of the genus *Uncaria*, which belongs to the *Rubiaceae* family, with three distinct genera across Africa and the island of Madagascar, two kinds in the tropical region of America, and twenty-nine types in the Asian continent and Australia (Liang et al., 2020). The other species of this herb identified in China include *U. hirsuta*, *U. lancifolia*, *U. scandens*, *U. macrophylla*, *U. homomalla*, *U. sessilifructus*, *U. laevigata*, *U. yunnanensis*, *U. lanosa*, and *U. sinensis* (Tian et al., 2020).

This herb works by lowering blood pressure, inverting the development of cardiac hypertrophy, and lessening the magnitude and rate of heart contractions. It is well-recognized that several chemical components in *U. rhynchophylla* such as rhynchophylline have antihypertensive properties and can prevent cardiac ischemia-reperfusion damage (Qin et al., 2019). Due to diverse physiological targets, numerous metabolic processes, and lack of adverse effects of this herb, it has been used as a reliable and potent medication for the treatment of hypertension. The most significant associated risk factor for heart and chronic kidney conditions as well as hypertension is an intricate, multifaceted disorder that is strongly correlated with genetic, biological, environmental, and biochemical components (Feng et al., 2019).

Uncaria Ramulus Cum Uncis, which is included in traditional Chinese Pharmacopoeia, is a traditional Chinese medicine employed to treat migraine, colds, convulsions, high

How to Cite: Asra A, R Altaf, S Saeed, W Majeed, S Shahzad, M Iftikhar, A Liaqat, A Habib & I Fatima, 2023. *Uncaria rhynchophila* or cat's claw herb as a natural treatment for hypertension. In: Complementary and Alternative Medicine: One Health Perspective (Sindhu ZuD, B Aslam, U Uslu & M Mohsin, eds): FahumSci, Lahore, Pakistan, pp. xx-xx. ISBN: 978-627-7745-01-1. https://doi.org/10.61748/CAM.2023/016

blood pressure, and gestational eclampsia. It is formed by using the dry stem along with a segment that consists of five curled hook-shaped forms of the plants with medicinal properties consisting of *U. rhynchophylIa* and *U. sinensis*.

CHEMICAL COMPONENTS OF *U. RHYNCHOPHYLIA*

Several metabolites, alkaloid components, triterpene constituents, and flavonoids have been successfully discovered over the past few years as the outcome of extensive studies on the chemical components of the species of *Uncaria*. Monoterpenoid indole alkaloids, such as hirsutanine elements, units of rhynchophyllioniums, and uncarialins have been discovered and recognized as distinctive components of this herb. These constituents have shown a variety of pharmacological effects such as anti-depressant, anti-malignant, and anti-hypertensive effects (Zhou & Zhou 2012). *U. rhynchophylla* grows natively in tropical areas and contains phenolic substances (the hyperin, caffeic acid, procyanidin B2, epicatechin, chlorogenic acid, rutin, hyperoside), pentacyclic class of triterpene esters, and indole alkaloids (rhynchophylline and isorhynchophylline).

Plant-derived phenols are natural chemical compounds that are abundantly present in plants all over the world. Over eight thousand phenolic compounds are identified for their physiological and pharmacological effects and also have been continuously investigated. It ought to be mentioned that only a small number of phenolics have undergone extensive experimental research. Phenolic substances have anti-inflammatory, antioxidant, and anti-hypertensive properties (Ożarowski et al., 2021).

By tracing the antioxidant potential in *Uncaria rhynchophylla* leaves through different processes, it was discovered that flavonoids and polyphenols are mostly responsible for the antioxidant properties of this herb. Five bioactive molecules, chlorogenic acid, epicatechin, rutin, hyperoside, and vincoside lactam, have been found in the leafy portion of the plants by using the method of Photodiode-Array Detection (PDA) in High Performace Liquid Chromatography by following the principle of gradient elution mode using acetonitrile 1% phosphoric-acid (Huang et al., 2019). The ethyl acetate fraction of *Uncaria rhynchophylla* is reported to contain a high phenolic content (373.7 gallic acid equivalent). The *Uncaria rhynchophylla* extract showed remarkable activity against mutagens (above 90%) and has strong scavenging activity due to 2,2-diphenyl 1-picrylhydrazyl and 2,2′-azino-bis or 3-ethylbenzothiazoline 6-sulfonic-acid (Lim et al., 2022).

Alkaloids in *Uncaria* are medicinally effective. Rhynchophylline makes up 28–50% of Uncaria's entire alkaloid content, whereas isorhynchophylline accounts for 15%. The biological agents such as rhynchophylline and isorhynchophylline in the *Uncaria* extract lower blood pressure. Depending on the elemental concentration, the mixture of *Uncaria* showed varying lowering blood pressure potential in decreasing order as isorhynchophylline, rhynchophylline, total alkaloid, and non-alkaloid fraction (Tian et al., 2020).

The primary biologically active elements of *U. rhynchophylla* are indole alkaloids, and these compounds are essential for enhancing anti-inflammatory effects and lowering hypertensive conditions. By hindering nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), the extracellular signal-regulated kinases (ERK), and p38 Mitogen-activated protein kinases (MAPKs) activation, alkaloids were able to alleviate its anti-inflammatory effects. The anti-inflammatory properties of *U. rhynchophylla* make it possible to prevent and cure pre-eclampsia caused by inflammation (Wu et al., 2019).

ANTIHYPERTENSIVE EFFECTS OF *U. RHYNCHO-PHYLLA*

Effect on cardiac output

The hypotensive effects of the whole alkaloid content of *U. rhynchophylla* extract have been reported due to its tendency to lower cardiac output, which comes through bradycardia rather than by suppressing cardiac contractility. Both constituents rhynchophylline and isorhynchophylline have been reported to achieve these antihypertensive effects by acting in three ways like by suppressing the vasomotor unit, through sympathetic system neurons, and by hindering the functioning of L-type Ca^{2+} channels (Gai et al., 2020). Rhynchophylline has no discernible impact on renal blood flow.

In spontaneously hypertensive rats, rhynchophylline has been shown to improve endothelial dysfunction by activating the Src-PI3K/Akt-eNOS signaling pathway. To cure

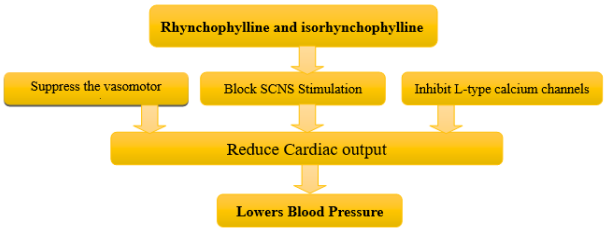

Fig 1. Effect of rhynchophylline and isorhynchophylline on blood pressure.

cardiovascular illnesses, isorhynchophylline can halt the cell cycle and is effective against Angiotensin II-induced amplification in rat's smooth muscle cells of the vascular system

as depicted in Fig 1., (Liang et al., 2020). Alkaloid components, triterpenoids, flavonoids, and phenylpropanoids are some of the bioactive constituents of *U. rhynchophylla* which have shown remarkable pharmacological activity against hypertension (Yang et al., 2022).

Effect of *U. rhynchophylla* on hypertensive heart failure

Studies have shown that cardiac fibroblast growth, extracellular protein accumulation, and collagen deposition are the major factors of myocardial fibrosis (Petersen et al., 2020). Angiotensin II (Ang II) is particularly crucial in the stimulation of the Renin angiotensin aldosterone system, which is the primary reason for myocardial fibrosis. By activating the angiotensin type 1 receptor, Ang II can enhance the production of extracellular matrix proteins, which results in myocardial fibrosis. Hence, it tends to expedite the hypertensive cardiovascular failure system (Beak et al., 2019). The RhoA/ROCK signaling pathway is involved in myocardial hypertrophy, vascular smooth muscle hyperplasia, and myocardial fibrosis. According to research studies, in heart tissues, *U. rhynchophylla* bioactive constituents are reported to decrease the number of RhoA, ROCK1, TGF-1, collagen I, and collagen III which are the by-products of activation of angiotensin II as well as the conversion of fibroblasts components into myofibroblasts caused by Ang II (Xie et al., 2022).

Effect of *U. rhynchophylla* on neurotransmitter imbalance in the hypothalamus

In rats who were experiencing the development of spontaneous hypertension, isorhynchophylline has significantly reduced the imbalance of transmitters in neurons inhabiting the hypothalamus and prevented the overstimulation of the sympathetic and renin-angiotensin system [Fig 2., (Li et al., 2020)].

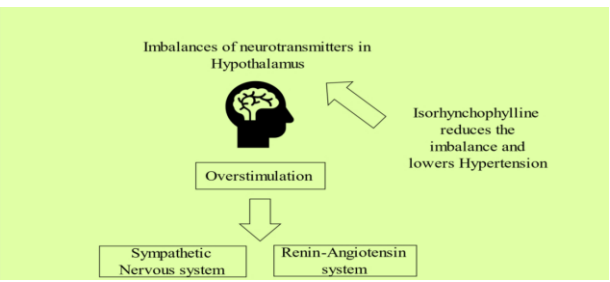

Fig 2. Effect of *Uncaria rhynchophylla* on neurotransmitter imbalance.

CONCLUSION

Hypertension is posing a threat to the health of individuals around the globe. Traditional medicinal herbs offer the most effective treatment strategies with low side effects for the management of hypertension. Uncaria rhynchophylla plays a vital role in curing hypertension. Its two main constituents rhynchophylline and isorhynchophylline lowers blood pressure by decreasing cardiac output, inhibiting RAAS and Rho/ROCK signaling pathway-induced hypertensive heart failure and regulating the balance of neurotransmitters in the hypothalamus.

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