Cultivation practices of *Picrorhiza kurroa*: Current perspective & future opportunities

Manya Tyagi[1], Prof. Ashwani Mathur[1]

[1]Jaypee Institute of Information Technology, Sector-62, Noida

Abstract

Globalization leads to the dynamic change in the lifestyle which has driven a boom in hepatic diseases worldwide. As per the data reported by World Health Organization in 2023, around 4% of the annual deaths (approximately 2 million annually) were reported due to liver related diseases, with cirrhosis in which the major cause being caused by hepatocellular cancer whereas the smaller number being caused by acute hepatitis. Although many existing medicines alleviate disease symptoms, they are associated with side effects, necessitating alternative therapies, including plant-derived bioactive phytocompounds. *Picrorhiza kurroa*, is a medicinal plant well known for its hepatoprotective nature. Picrorhiza kurroa is classified within the family of *Scrophulariaceae*, this plant is mainly present in the subcontinent area of South Asia which includes the Himalayan regions of India, Bhutan, China, Pakistan & Nepal. *Picrorhiza kurroa* also referred as "Kutki" in local language, is enriched in many bioactive compounds such as Picroside I, Picroside II, Kutkoside and others, which are iridoid glycosides in nature and they cumulatively known as Picroliv or Kutkin. These bioactive compounds exhibit strong immunomodulatory and liverprotective effects. Existing studies highlight key advances in the production of Picroside through different cultivation strategies, including micropropagation, cell suspension culture, and meristem culture. However, techniques such as hydroponic cultivation are rarely reported.

Recent advances in *Picrorhiza kurroa* cultivation have opened avenues for formulating herbal therapeutics with anti-inflammatory, antimetastatic, antiangiogenic, antimicrobial, chemoprotective, and antioxidant properties. This study will pave the way in highlighting the key advancements of modern cultivation practices.

Keywords: - Hepatoprotective, *Picrorhiza kurroa*, Picroside, hydroponics, chemoprotective, immunomodulatory.

INTRODUCTION: -

India had always been a demography with enrich vegetations and environmental conditions supporting cultivation of the medicinal plants. Being the originator of *Charak samita* and with ancient sculpture such as *Ayurveda*, India is one of the leading cultivator or medicinal plants of immense therapeutic importance.

Among various diseases, World health Organization had reported the increasing mortality rate attributed to hepatic diseases, which is affecting the population of different age group and race. Medicinal plants emerge as a safe alternative for alleviating disease symptoms and diseases (Table 1) lists some of the therapeutically important hepatoprotective plants and their bioactive compounds.

Table 1. Some commonly reported medicinal plants known for their hepatoprotective nature.

S.No.	Medicinal plant	Bioactive compound	Mechanism	References
1.	*Silybum marianum* (Milk thistle)	silymarin complex (silybin / silibinin)	Stabilizes hepatocyte membrane; free radical scavenging; anti-oxidant; also increase protein synthesis	[1]; [2]
2.	*Ocimum sanctum* (Tulsi /Holy basil)	epicatechin, eugenol, ursolic acid and catechin	anti-oxidant, reduces hepatic inflammation	[3]; [4]
3.	*Curcuma longa* (Turmeric/Haldi)	Curcumin	ROS Scavenging, antiinflammatory, anti-fibrotic; prevents lipid peroxidation	[5]; [6]
4.	*Picrorhiza kurroa* (Kutki)	Picroside I, Picroside II	Anti-oxidant, anti-inflammatory, preserves hepatic enzymes	[7]; [8]

5.	*Glycyrrhiza glabra* (Licorice)	Glycyrrhizin, Glycyrrhetinic acid	reduces oxidative stress and reduced hepatocellular damage in chronic hepatitis B& C	[8]; [9]
6.	*Boerhaavia diffusa*	Boeravinones, Rotenoids, Phenolic compounds	protects against druginduced hepatotoxicity	[10]
7.	*Andrographis paniculata*	Andrographolide (diterpenoid lactone)	Inhibits inflammatory cytokines, enhances detoxifying enzymes.	[11]

Table 2. *Picrorhiza kurroa*: Bioactive compounds of therapeutic importance

Bioactive Compounds	**Reference**
Picroside I	**[12]**
Picroside II	**[12]**
Picroside III	**[12]**
Picroside IV	**[13]**
Kutkoside	**[12]**
Verminoside	**[13]**

Picrorhiza kurroa is a medicinal herb that is commonly found in the northwestern Himalayan region, in the Indian subcontinent [14]. This medicinal plant belongs to the family of *Scrophulariaceae* and is found at very high altitudes, which range from 3000m to 4500m [15] . “Kutki” and “Kutka” are other names of P*icrorhiza kurroa* in India. The ancient Indian *Ayurveda* also documented plant use for its hepatoprotective properties [16]. It does show properties like anti-oxidant [17], anti-inflammatory [18], anti-asthmatic [19], anti-microbial [20], antidiabetic [21]. The recent studies have shown that under both in-vivo and in-vitro conditions; its bioactive phytocompound, namely Picroside II can reduce metastasis and angiogenesis of cancer cell [22]. The current burden of hepatic disease requires the high demand of this plant, which is evident from

the diverse metabolite pool and bioactivities shown by plant extract (Fig. 1). The emerging cultivation strategies may be pivotal for scaling up the plant cultivation and production of bioactive compounds of *Picrorhiza kurroa.* Many bioactive compounds from *Picrorhiza kurroa* has been reported for their bioactivities such as Picroside (I, II, III, IV), Kutkoside, Verminoside (Table 2).

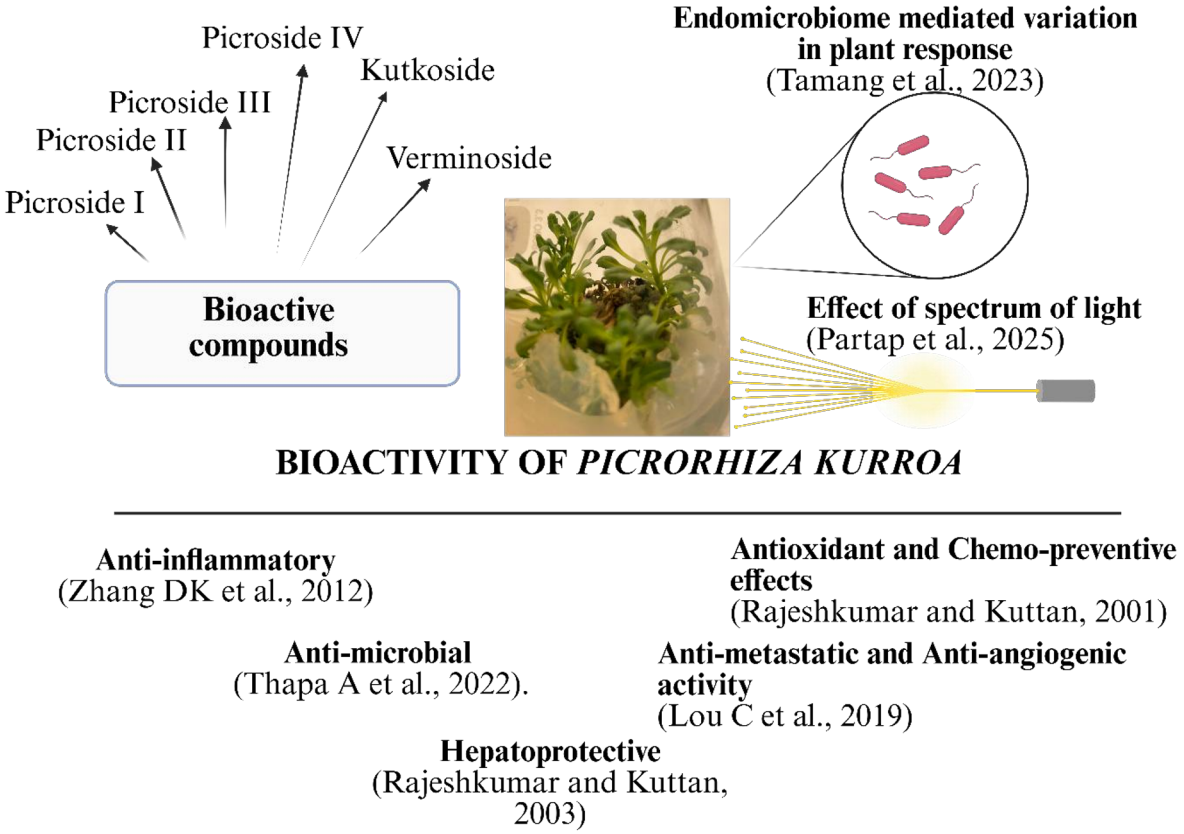

Fig 1.: *Picrorhiza kurroa*: phytocompound diversity and associated bioactivity

Hepatoprotective mechanism

*Picrorhiza kurro*a is a well-documented plant rich in bioactive phytocompounds for alleviating symptoms of hepatic disorder and conferring hepatoprotective properties. Picroliv (a standard mixture of Picroside I and Kutkoside) demonstrated hepatoprotective effects against oxidative damage and chemically induced carcinogenesis [23]. It helps in the reduction of lipid peroxidation and the restoration of glutathione levels [23] . Recent studies show that Picroliv effectively reduced tumor formation in chemically generated sarcoma and papilloma models [24].

Anti- inflammatory response

The anti-inflammatory response is reported to trigger the expression of key pathways associated with the expression of pro-inflammatory cytokines such as IL-1β and TNF-α. Picroliv treatment significantly reduces the expression of pro-inflammatory cytokines such as IL-1β and TNF-α. It also suppressed the activation of NF-κB by reducing p65 expression. Additionally, Picroliv diminished myeloperoxidase (MPO) activity, indicating reduced neutrophil infiltration, while enhancing superoxide dismutase (SOD) levels, thereby strengthening antioxidant defense mechanisms [18].

Anti-metastatic and Anti-angiogenic activity

Picrorhiza kurroa have bioactive phytocompound Picroside II which suppresses MMP-9 activity and also suppress the tumor migration and invasion and angiogenesis in in-vitro and in-vivo model [22].

Anti-microbial properties

It has been found that both ethanolic extract and the isolated picroside-I shows strong antimicrobial activity against *Yersinia enterocolitica* in which cell lysis under SEM has been observed [20].

Antioxidant and Chemo-preventive effects

Picroliv from the *Picrorhiza kurroa* helps in the reduction of tumor incidence and restores antioxidant enzymes which leads to the high survival chances in carcinogen- treated mice [24].

Recent advancements in cultivation strategies of *Picrorhiza kurroa* and bioactive compounds

There are different techniques, attracting scientific inclination towards propagation of medicinal plant *Picrorhiza kurroa* with their own sets of efficacy and limitations (Table 3). Most studies on the cultivation strategies of *Picrorhiza kurroa* primarily rely on efficient micropropagation using phytohormones or on elicitor-mediated improvement in shoot regeneration [25] reported a correlation between shoot regeneration and gene expression profile of Picroside biosynthetic pathways [25] **.** Furthermore, ex-situ cultivation of *Picrorhiza kurroa* has shown the presence of Picroside-I and Picroside-II in both roots/rhizomes and leaves, with levels varying with plant age [26]. In another significant study, the effect of spectral light treatment on the Picroside yield of different morphologies has been reported, indicating the possible association between morphological state and abiotic culture conditions [27]. The detailed understanding of the pathway

precursors is also useful in determining the flux of nutrient components of intermediates towards secondary metabolite biosynthesis. A similar assessment has been reported in the study by [28]. Along with abiotic factors, the associated microflora (biotic factors) has scarcely been explored for their effect on plant growth and metabolite yield. One of the studies has shown the relevance of the diverse Endo microbiome of *Picrorhiza kurroa* in modulating plant growth and Picroside yield. In the study, results showed a more diverse microbial composition in plants propagated in in-situ conditions than in ex-situ conditions, and this was associated with variations in responses [29]. The hydroponic cultivation studies for Picrorhiza kurroa is less explored [30]**.** Studies evaluating the endomicrobiome were important for developing a microflora-rich, efficient agricultural practice to preserve the endangered plant germplasm and for developing cultivation strategies. The studies are relevant for analyzing the roles of abiotic and biotic factors, morphological forms, and in-situ or ex-situ cultivation environments in affecting plant growth and metabolite yield. One of the significant studies shown an association between metabolic pathways and endophytic communities were established. Providing an insight to the relevance of dynamic endomicrobiome with plant mediated secondary metabolite pathways [29]. The studies also pave the way for developing a robust, scalable strategy for the mass propagation of *Picrorhiza kurroa* and for studying its impact.

Table 3: - Comparative assessment of different cultivation techniques for cultivation of *Picrorhiza kurroa.*

Techniques	Key parameter	Efficacy	Scalability	Cost	Limitations
Micropropagation	Harnessing the totipotency of meristematic cells	High	Moderate	High	Highly aseptic conditions required' Selective media with high purity elicitors increases the cost.

Cell suspension culture	Friable cells converted to suspension culture; Every cell is a microbioreactor responsible for large scale production of phytocompounds;	Moderate	High	Moderate	Disposal challenges, SIP (Sterilization in Place)
Hydroponics	In-situ and ex-situ cultivation; Lowcost media with maintained osmolarity and electrical conductivity	High	High	Low	Limited report on hydroponic cultivation of medicinal plants including
	(CV); early acclimatization of plant to environmental conditions				*Picrorhiza kurroa*

Conclusion and Future Prospects

In the raising demand of liver diseases and the limitation of the presence of synthetic drugs with least side effects this Himalayan plant, *Picrorhiza kurroa* offers a promising as well as a safer therapeutic alternative. It is a potent hepatoprotective herb because of its scientifically validated bioactive compounds mainly Picroside I, Picroside II, Kutkoside and others. Recent breakthrough in both in-situ cultivation as well as ex-situ cultivation significantly advanced our understanding of picroside biosynthesis and yield optimization. A high value, endangered plant inhabiting the higher altitude, the traditional practices to cultivate it are often limiting the germplasm preservation, necessitating the development of alternative cultivation strategies, such as hydroponics. Furthermore, the integration of biotechnology, molecular insights and controlled cultivation strategies open strong avenues for development of sustainable cultivation approach for *Picrorhiza kurroa*.

Collectively, these advancements position *Picrorhiza kurroa* not only as a traditional remedy but as a scientifically backed, future-ready phytotherapeutic resource with substantial clinical and commercial potential.

Reference

[1] N. Vargas-Mendoza, Hepatoprotective effect of silymarin, World J. Hepatol. **6**, 144 (2014).

[2] G. Jiang, C. Sun, X. Wang, J. Mei, C. Li, H. Zhan, Y. Liao, Y. Zhu, and J. Mao, Hepatoprotective mechanism of *Silybum marianum* on nonalcoholic fatty liver disease based on network pharmacology and experimental verification, Bioengineered **13**, 5216 (2022).

[3] F. O. Kamel, S. Karim, D. A. O. Bafail, H. M. Aldawsari, S. Kotta, and U. K. Ilyas, Hepatoprotective effects of bioactive compounds from traditional herb Tulsi (Ocimum sanctum Linn) against galactosamine-induced hepatotoxicity in rats, Front. Pharmacol. **14**, (2023).

[4] P. Pattanayak, P. Behera, D. Das, and S. Panda, Ocimum sanctum Linn. A reservoir plant for therapeutic applications: An overview, Pharmacogn. Rev. **4**, 95 (2010).

[5] M. H. Farzaei, M. Zobeiri, F. Parvizi, F. F. El-Senduny, I. Marmouzi, E. Coy-Barrera, R. Naseri, S. M. Nabavi, R. Rahimi, and M. Abdollahi, Curcumin in Liver Diseases: A Systematic Review of the Cellular Mechanisms of Oxidative Stress and Clinical Perspective, Nutrients **10**, 855 (2018).

[6] W. Bao, K. Li, S. Rong, P. Yao, L. Hao, C. Ying, X. Zhang, A. Nussler, and L. Liu, Curcumin alleviates ethanol-induced hepatocytes oxidative damage involving heme oxygenase-1 induction, J. Ethnopharmacol. **128**, 549 (2010).

[7] T. M. Almeleebia, A. Alsayari, and S. Wahab, Pharmacological and Clinical Efficacy of Picrorhiza kurroa and Its Secondary Metabolites: A Comprehensive Review, Molecules **27**, 8316 (2022).

[8] S. K. Bhardwaj and T. Satapathy, A Systematic Review on Hepatoprotective Medicinal Plants, Their Bioactive Compounds, and Pharmaceutical Formulations, Journal of Drug Delivery and Therapeutics **15**, 193 (2025).

[9] C. Fiore, M. Eisenhut, R. Krausse, E. Ragazzi, D. Pellati, D. Armanini, and J. Bielenberg, Antiviral effects of *Glycyrrhiza* species, Phytotherapy Research **22**, 141 (2008).

[10] K. Y. Thajudeen, A. Alsayari, S. N. M. Najib Ullah, S. Salam, M. Elayadeth-Meethal, and I. Uoorakkottil, Validation, Optimization and Hepatoprotective Effects of Boeravinone B and Caffeic Acid Compounds from Boerhavia diffusa Linn, Separations **9**, 177 (2022).

[11] S. Kumar, K. K. Ratha, S. Jaiswal, M. M. Rao, and R. Acharya, Exploring the potential of andrographis paniculata and its bioactive compounds in the management of liver diseases: A comprehensive food chemistry perspective, Food Chemistry Advances **4**, 100674 (2024).

[12] K. Weinges, P. Kloss, and W. Henkels, Naturstoffe aus Arzneipflanzen, XVII. Picrosid-II, ein neues 6-Vanilloyl-catalpol aus *Picrorhiza kurrooa* Royle und Benth, Justus Liebigs Ann. Chem. **759**, 173 (1972).

[13] J. X. Li, P. Li, Y. Tezuka, T. Namba, and S. Kadota, Three phenylethanoid glycosides and an iridoid glycoside from Picrorhiza scrophulariiflora, Phytochemistry **48**, 537 (1998).

[14] T. Sharma, N. K. Sharma, P. Kumar, G. Panzade, T. Rana, M. K. Swarnkar, A. K. Singh, D. Singh, R. Shankar, and S. Kumar, The first draft genome of Picrorhiza kurrooa, an endangered medicinal herb from Himalayas, Sci. Rep. **11**, 14944 (2021).

[15] H. Sood and R. S. Chauhan, Biosynthesis and accumulation of a medicinal compound, Picroside-I, in cultures of Picrorhiza kurroa Royle ex Benth, Plant Cell, Tissue and Organ Culture (PCTOC) **100**, 113 (2010).

[16] D. Soni and A. Grover, “Picrosides” from Picrorhiza kurroa as potential anti-carcinogenic agents, Biomedicine & Pharmacotherapy **109**, 1680 (2019).

[17] V. Rajkumar, G. Guha, and R. Ashok Kumar, Antioxidant and anti-neoplastic activities of Picrorhiza kurroa extracts, Food and Chemical Toxicology **49**, 363 (2011).

[18] D.-K. Zhang, J.-J. Yu, Y.-M. Li, L.-N. Wei, Y. Yu, Y.-H. Feng, and X. Wang, A Picrorhiza kurroa derivative, picroliv, attenuates the development of dextran-sulfate-sodium-induced colitis in mice., Mediators Inflamm. **2012**, 751629 (2012).

[19] W. Dorsch, H. Stuppner, H. Wagner, M. Gropp, S. Demoulin, and J. Ring, Antiasthmatic Effects of <i>Picrorhiza kurroa</i>: Androsin Prevents Allergen- and PAFinduced Bronchial Obstruction in Guinea Pigs, Int. Arch. Allergy Immunol. **95**, 128 (1991).

[20] A. Thapa et al., Biological Activity of Picrorhiza kurroa: A Source of Potential Antimicrobial Compounds against Yersinia enterocolitica, Int. J. Mol. Sci. **23**, 14090 (2022).

[21] K. L. Joy and R. Kuttan, Anti-diabetic activity of Picrorrhiza kurroa extract, J. Ethnopharmacol. **67**, 143 (1999).

[22] C. Lou, Z. Zhu, X. Xu, R. Zhu, Y. Sheng, and H. Zhao, Picroside II, an iridoid glycoside from Picrorhiza kurroa, suppresses tumor migration, invasion, and angiogenesis in vitro and in vivo, Biomedicine & Pharmacotherapy **120**, 109494 (2019).

[23] N. V. Rajeshkumar and R. Kuttan, Modulation of carcinogenic response and antioxidant enzymes of rats administered with 1,2-dimethylhydrazine by Picroliv, Cancer Lett. **191**, 137 (2003).

[24] N. V. Rajeshkumar and R. Kuttan, Protective effect of Picroliv, the active constituent of *Picrorhiza kurroa* , against chemical carcinogenesis in mice, Teratog. Carcinog. Mutagen. **21**, 303 (2001).

[25] S. K. Shishodia, A. Chauhan, H. Sood, G. Mudgal, and G. Abdi, Direct shoot regeneration and gene expression profiling for optimized picroside-I biosynthesis in Picrorhiza Kurroa, Sci. Rep. **15**, 34325 (2025).

[26] P. K. Chandra and B. Rakesh, Productivity and picroside contents of Picrorhiza kurroa Royle ex Benth. cultivated at multi-locations in Uttarakhand, India, Journal of Medicinal Plants Research **18**, 14 (2024).

[27] M. Partap, A. Kumar, P. Kumar, D. Kumar, and A. R. Warghat, Spectral light treatment and exogenous feeding of precursors enhanced the picrosides content in dedifferentiated cell culture of Picrorhiza kurroa, Biocatal. Agric. Biotechnol. **64**, 103501 (2025).

[28] M. Partap, J. Chhimwal, P. Kumar, D. Kumar, Y. Padwad, and A. R. Warghat, Growth dynamics and differential accumulation of picrosides and its precursor metabolites in

callus cell lines of Picrorhiza kurroa with distinct anti-steatotic potential, Process Biochemistry **120**, 85 (2022).

[29] A. Tamang, M. Swarnkar, P. Kumar, D. Kumar, S. S. Pandey, and V. Hallan, Endomicrobiome of *in vitro* and natural plants deciphering the endophytes-associated secondary metabolite biosynthesis in *Picrorhiza kurrooa* , a Himalayan medicinal herb, Microbiol. Spectr. **11**, (2023).

[30] Kanika, Ashrita, S. S. Pandey, P. Kumar, D. Kumar, and A. R. Warghat, Insight into hydroponic nutrient solution mediated morpho-physiological, iridoid glycosides accumulation and gene expression modulations in Picrorhiza kurroa Royle ex Benth, Plant Biotechnol. Rep. **19**, 741 (2025).