Picrorhiza (family Scrophulariaceae), commonly known as ‘kuki’ is a small perennial herb found in the Himalayan regions of China, Pakistan, India, Bhutan and Nepal at an altitude of 3000-5200 m. Different plant parts and its extract have traditionally been used as a remedy of various ailments such as fever, asthma, jaundice, anemia, abdominal pain, dysentery, cold, stomach problems. Picrorhiza has been investigated for its chemical composition and biological activities by various researchers. The major chemical constituents found in this plant were iridoid glycosides, cucurbitacins (triterpenoids) glycosides, phenylethanoid glycosides and phenolics. The Picrorhiza has various pharmacological properties, including hepto-protective, antimicrobial, ant-mutagenic, cardio-protective, anti-malarial, anti-diabetic, anti-cancer, anti-inflammatory, anti-ulcer, and neuroprotective and antioxidant activities. A thorough bibliographic investigation was carried out by analyzing worldwide scientific databases including Pub Med, Science Direct, Google Scholar and Wiley online as well as offline sources. The Present review is aimed to provide an updated overview of traditional uses, chemical constituents and biological activities of Picrorhiza to explore its therapeutic potentials and to provide bases for future research.

**Keywords:** Picrorhiza, Traditional uses, Phytochemistry, Biological activity, Chemical constituents

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**ABSTRACT**

Picrorhiza (family Scrophulariaceae), commonly known as ‘kuki’ is a small perennial herb found in the Himalayan regions of China, Pakistan, India, Bhutan and Nepal at an altitude of 3000-5200 m. Different plant parts and its extract have traditionally been used as a remedy of various ailments such as fever, asthma, jaundice, anemia, abdominal pain, dysentery, cold, stomach problems. Picrorhiza has been investigated for its chemical composition and biological activities by various researchers. The major chemical constituents found in this plant were iridoid glycosides, cucurbitacins (triterpenoids) glycosides, phenylethanoid glycosides and phenolics. The Picrorhiza has various pharmacological properties, including hepto-protective, antimicrobial, ant-mutagenic, cardio-protective, anti-malarial, anti-diabetic, anti-cancer, anti-inflammatory, anti-ulcer, and neuroprotective and antioxidant activities. A thorough bibliographic investigation was carried out by analyzing worldwide scientific databases including Pub Med, Science Direct, Google Scholar and Wiley online as well as offline sources. The Present review is aimed to provide an updated overview of traditional uses, chemical constituents and biological activities of Picrorhiza to explore its therapeutic potentials and to provide bases for future research.

**INTRODUCTION**

Natural products have been commonly used as an herbal drug for the treatment of various diseases and disorders from ancient times [1-3]. Natural products are substances or chemical compounds produced by living organisms, usually plants, that have many pharmacological activities [4-7]. Plants produce the vast and diverse array of structurally different organic compounds or secondary metabolites. Biosynthesis of the secondary metabolites is strongly affected by different abiotic and biotic factors. The stress conditions affects secondary metabolites or active ingredients that the plants produce, which are usually the basis for their medicinal activity [8-9]. Secondary metabolites have a wide spectrum of uses ranging from flavoring agents to medicinal values [10]. Thus, natural products (secondary metabolites) have been utilized in both traditional and modern medicine for treating various diseases [11-16]. The majority of rural population mainly depends upon the medicinal plants as a source of remedies [17-20].

The Genus Picrorhiza is well known for its medicinal values belonging to the family Scrophulariaceae having two important endangered medicinal plant species, *Picrorhiza kurroa* Royle ex Benth and *Picrorhiza scrophulariiflora* Pennell, native of India, Nepal, China, Tibet and Pakistan. *P. kurroa* (Vernacular name-kutki) is predominant in the western Himalayas of Northern India, while *P. scrophulariiflora* is mainly occure in the Himalayan regions of Sikkim, Nepal and Tibet. In India genus Picrorhiza is distributed in alpine region of Kashmir to Sikkim Himalayas [21, 22].

In Ayurvedic medicine system, Picrorhiza is generally used for treatment of disorder of the liver, upper portion of the respiratory tract; to reduce fever, chronic diarrhea, dyspepsia, and scorpion sting [23]. There have been many reports to show a wide spectrum of biological activities having therapeutic importance of its extract and constituents [24-27]. Different formulations of *Picrorhiza Kurroa* extract and constituents are available viz-Kutki root powder, Picrorhiza kurroa standardized extract containing 7-14% kutkin, Liver support and Arogya vardhani, etc. Picroliv, a standardized mixture of iridoid glycoside, prepared from alcoholic extract of Picrorhiza kurroa root and rhizome has shown strong hepatoprotective activity against the liver damage caused by various hepatotoxins, it has also been investigated as anti-anaphylactic and anti-allergic [28, 29]. *Picrorhiza Kurroa* root and rhizome contain kutkin as active constituent. Other identified active constituents are apocynamine, androecine and cucurbitacin glycoside [30, 31]. The constituents of *Picrorhiza kurroa* are reported to show a number of pharmacological activities such as hepatoprotective, anti-allergic, immunomodulatory properties, free radical scavenging, gastric ulcer, anti-allergic and many more [32-35]. *P. scrophulariiflora* is used for antioxidant and antiradical activities, anti diabetic, anti healing, antiasthmatic, cardio protective, anticancer and antilucre activity [36-40].

This study presents the current update on phytochemistry, medicinal uses, biological activities and toxicities of *P. kurroa* to reveal their pharmacological potentials and lacking that offer scope for future research.

**About the genus picrorhiza**

The *Picrorhiza* is small genera belonging to the family Scrophulariaceae, having two species namely *P. kurroa* Royle ex Benth and *P. scrophulariiflora* Pennell. The name Picrorhiza is derived from the Greek word ‘pico’and ‘rhiza’, which means bitter root and it is used in native medicine. The specific name derived from Kuru, the Punjabi name of the plant, which means bitter as well [41]. *P. kurroa* is a vulnerable, perennial medicinal herb prevalent in alpine region. The plant grows in Himalayan region in moist rock crevices as well as in organic soils. It grows typically on clifffy and sloppy mountains. It is chiefly abundant in Himalayan province i.e. from Garhwal to Bhutan, north Burma west China and southeast Tibet. The species is found in large quantities in high altitudes ranged between 3000 to 5000 m [42]. The roots of *P. kurroa* are inflexible, almost 6-10 inches long, creeping and bitter in taste. The leaves are oval-shaped, 2-4 inches long, with a sharp apex or serrated. The flowers are pale purple or white in colour, occurring on a long spike. Furthermore, the fruit is about ½inch long and oval shaped. *P. scrophulariiflora* is a species located in the moist eastern Himalayas having short stamens and a bilabiate corolla, upper lip of which is longer and the lower lip consists of three shorter lobes while *P. Kurroa* has long stamens with a short corolla and five sub-equallobes [43].
Iridoid glycosides

Medically important iridoid glycosides have been isolated and characterized from Picrorhiza species. P. kurroa; Kutkin is a main herbal preparation of P. kurroa; Kutkin is a mixture of picrose I and kuttoside [46-48].

Cucurbitacins

These are triterpenoid compounds containing a cucurbitane skeleton characterized as 9β-methyl-19nor lanosta-5,23-diene. Cucurbitacins possess a wide range of biological activities and the present in the form of β-glycosides in plants. A large number of cucurbitacin glycosides have been isolated from Picrorhiza species, mainly from P. kurroa [49, 50].

Table 1: Chemical constituents isolated from Picrorhiza species and bioactivities

| Glycoside | Compound / Name | Plant part / solvent of extraction | Bio-activities & Reference |
|-----------|-----------------|----------------------------------|---------------------------|
| **Iridoid Glycoside; Picrorhiza I:** | [(2R,3S,5S,6S)-3,4,5-trihydroxy-6-[[1S,2S,4S,5S,6R,10S]-5-hydroxy-2-(hydroxymethyl)-3,9-dioxatricyclo[4.4.0.02,4]dec-7-en-10-yl]oxy-3,9-dihydroxyoxan-2-yl]methyl(E)-3-phenylprop-2-enoate, (1) | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Hepato-protective Activity, Collagenase Inhibitory Activities, Anticancer Activity, Antiarthritis Activity, Antidiabetic Activity, Collagenase Inhibitory Activities, Antimicrobial Activity | [44, 45, 54, 55, 56] |
| **Iridoid Glycoside; Picrorhiza II:** | [(1S,2R,3R,4S,5R,6S)-6-hydroxy-6-methoxyphenylprop-2-enoate, (3)] | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Collagenase Inhibitory Activities, Anticancer Activity | [57, 58] |
| **Iridoid Glycoside; Picrorhiza III:** | [(1S,2S,4S,5S,6R,10S)-2-(hydroxymethyl)-10-[[1S,2S,4S,5S,6R,10S]-3,4,5-trihydroxy-6-hydroxy-6-methoxyphenylprop-2-enoate, (2)] | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Collagenase Inhibitory Activities, Anticancer Activity | [59] |
| **Iridoid Glycoside; Picrorhiza I:** | [(2R,3S,5S,6S)-3,4,5-trihydroxy-6-[[1S,2S,4S,5S,6R,10S]-5-hydroxy-2-(hydroxymethyl)-3,9-dioxatricyclo[4.4.0.02,4]dec-7-en-10-yl]oxy-3,9-dihydroxyoxan-2-yl]methyl(E)-3-phenylprop-2-enoate, (4) | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Collagenase Inhibitory Activities, Anticancer Activity | [60] |
| **Iridoid Glycoside; Picrorhiza I:** | [(2R,3S,5S,6S)-3,4,5-trihydroxy-6-[[1S,2S,4S,5S,6R,10S]-5-hydroxy-2-(hydroxymethyl)-3,9-dioxatricyclo[4.4.0.02,4]dec-7-en-10-yl]oxy-3,9-dihydroxyoxan-2-yl]methyl(E)-3-phenylprop-2-enoate, (5) | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Collagenase Inhibitory Activities, Anticancer Activity | [61] |
| **Iridoid Glycoside; Picrorhiza I:** | [(2R,3S,5S,6S)-3,4,5-trihydroxy-6-[[1S,2S,4S,5S,6R,10S]-5-hydroxy-2-(hydroxymethyl)-3,9-dioxatricyclo[4.4.0.02,4]dec-7-en-10-yl]oxy-3,9-dihydroxyoxan-2-yl]methyl(E)-3-phenylprop-2-enoate, (6) | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Collagenase Inhibitory Activities, Anticancer Activity | [62] |
| **Iridoid Glycoside; Picrorhiza I:** | [(2R,3S,5S,6S)-3,4,5-trihydroxy-6-[[1S,2S,4S,5S,6R,10S]-5-hydroxy-2-(hydroxymethyl)-3,9-dioxatricyclo[4.4.0.02,4]dec-7-en-10-yl]oxy-3,9-dihydroxyoxan-2-yl]methyl(E)-3-phenylprop-2-enoate, (7) | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Collagenase Inhibitory Activities, Anticancer Activity | [63] |
| **Iridoid Glycoside; Picrorhiza I:** | [(2R,3S,5S,6S)-3,4,5-trihydroxy-6-[[1S,2S,4S,5S,6R,10S]-5-hydroxy-2-(hydroxymethyl)-3,9-dioxatricyclo[4.4.0.02,4]dec-7-en-10-yl]oxy-3,9-dihydroxyoxan-2-yl]methyl(E)-3-phenylprop-2-enoate, (8) | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Collagenase Inhibitory Activities, Anticancer Activity | [64] |
| **Iridoid Glycoside; Picrorhiza I:** | [(2R,3S,5S,6S)-3,4,5-trihydroxy-6-[[1S,2S,4S,5S,6R,10S]-5-hydroxy-2-(hydroxymethyl)-3,9-dioxatricyclo[4.4.0.02,4]dec-7-en-10-yl]oxy-3,9-dihydroxyoxan-2-yl]methyl(E)-3-phenylprop-2-enoate, (9) | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Collagenase Inhibitory Activities, Anticancer Activity | [65] |
| **Iridoid Glycoside; Picrorhiza I:** | [(2R,3S,5S,6S)-3,4,5-trihydroxy-6-[[1S,2S,4S,5S,6R,10S]-5-hydroxy-2-(hydroxymethyl)-3,9-dioxatricyclo[4.4.0.02,4]dec-7-en-10-yl]oxy-3,9-dihydroxyoxan-2-yl]methyl(E)-3-phenylprop-2-enoate, (10) | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Collagenase Inhibitory Activities, Anticancer Activity | [66] |
| **Iridoid Glycoside; Picrorhiza I:** | [(2R,3S,5S,6S)-3,4,5-trihydroxy-6-[[1S,2S,4S,5S,6R,10S]-5-hydroxy-2-(hydroxymethyl)-3,9-dioxatricyclo[4.4.0.02,4]dec-7-en-10-yl]oxy-3,9-dihydroxyoxan-2-yl]methyl(E)-3-phenylprop-2-enoate, (11) | Rhizomes of P. K/ Methanol, Ethanol: water (1:1) | Collagenase Inhibitory Activities, Anticancer Activity | [67] |
| Glycoside                          | Plant part/solvent of extraction | Bio-activities                                      | Reference |
|----------------------------------|---------------------------------|-----------------------------------------------------|-----------|
| Iridoid Glycoside: Picurosides:  |                                 |                                                     | [64]      |
| [1R,4S,5R,6S,7R,8S,9S]-4,5-dihydroxy-9-[2S,3R,4S,5S,6R]-3,4,5-trihydroxy-6-(hydroxymethyl)octan-2-yl]oxy-2,10-dioxatricyclo[5.3.1.0]undecan-6-yl]-4-hydroxy-3-methoxybenzoate, (12) | Rhizomes of P. K/ EtOAc |                    |           |
| Iridoid Glycoside: Acubins:      |                                 |                                                     | [58]      |
| [2S,3R,5S,6R]-2-[1S,4R,6S,7S,8S,9S,10S]-5-hydroxy-7-(hydroxymethyl)-1,4a,5,7,9-pentahydroxy-11,14a,15-tri-(hydroxymethyl)octane-3,4,5-triol, (13) | Rhizomes of P. S/ Methanol |                    |           |
| Iridoid Glycoside: Picrorhizoeasides-A, (14) |                                 |                                                     |           |
| Iridoid Glycoside: Picrorhizoeaside-B, (15) |                                 |                                                     |           |
| Iridoid Glycoside: Picrorhizoeaside-C, (16) |                                 |                                                     |           |
| Iridoid Glycoside: Picrorhizoeaside-D, (17) |                                 |                                                     |           |
| Iridoid Glycoside: Picrorhizoeaside-E, (18) |                                 |                                                     |           |
| Iridoid Glycoside: Picrorhizoeaside-F, (19) |                                 |                                                     |           |
| Iridoid Glycoside: Picrorhizoeaside-G, (20) |                                 |                                                     |           |
| Phenylethanoid Glycosides: Kurroaside-A, (21) |                                 |                                                     |           |
| Phenylethanoid Glycosides: Kurroaside-B, (22) |                                 |                                                     |           |
| Phenylethanoid Glycosides: Kurroaside-C, (23) |                                 |                                                     |           |
| Phenylethanoid Glycosides: Calcetarioside-A, (24) |                                 |                                                     |           |
| Phenylethanoid Glycosides: Calcetarioside-B, (25) |                                 |                                                     |           |
| Phenylethanoid Glycosides: Plantamajoside, (26) |                                 |                                                     |           |
| Phenylethanoid Glycosides: Isopelanomajoside, (27) |                                 |                                                     |           |
| Phenylethanoid Glycosides: Scirosides-D |                                 |                                                     |           |
| (25-Hydroxy-4-methoxyphenyl)ethyl-3-0-β-D-glucopyranosyl-β-D-glucopyranosyl-4-[β(2E)-3-[4-Hydroxy-3-methoxyphenyl]prop-2-enolate] (28) | Rhizomes of P. and collagenase |                    |           |
| Phenylethanoid Glycosides: Scirosides-D |                                 |                                                     |           |
| (25-Hydroxy-4-methoxyphenyl)ethyl-3-0-β-D- |                                 |                                                     |           |
| Glucopyranosyl-β-D-glucopyranoside-6-[1(2E)-3-[4-Hydroxy-3-methoxyphenyl]prop-2-enolate] (29) | Rhizomes of P. and collagenase |                    |           |
| Phenylethanoid Glycosides: Scirosides-A |                                 |                                                     |           |
| 6-[[2E]-3-[3-hydroxy-4-methoxyphenyl]-2-propenoate]-2-(3-hydroxy-4-methoxyphenyl)ethyl-1-0-β-D-glucopyranosyl-1(1→2)-0-β-D-glucopyranosyl (30) |                   |                    |           |
| Phenylethanoid Glycosides: Scirosides-B, |                                 |                                                     |           |
| 6-[[2E]-3-[3-hydroxy-4-methoxyphenyl]-2-propenoate]-2-(3-hydroxy-4-methoxyphenyl)ethyl-1-0-β-D-glucopyranosyl-1(1→2)-0-β-D-glucopyranosyl (31) |                   |                    |           |
| Phenylethanoid Glycosides: Scirosides-C, |                                 |                                                     |           |
| 6-[[2E]-3-[3-hydroxy-4-methoxyphenyl]-2-propenoate]-2-(3-hydroxy-4-methoxyphenyl)ethyl-1-0-β-D-glucopyranosyl-1(1→2)-0-β-D-glucopyranosyl (32) |                   |                    |           |
| Phenylethanoid Glycosides: Hemiophoreside-A, |                                 |                                                     |           |
| 2-(3-Hydroxy-4-methoxyphenyl)ethyl-3-0-β-D-Glucopyranosyl-β-D- |                                 |                                                     |           |
| glucopyranoside-4-[β(2E)-3-[4-Hydroxy-3-methoxyphenyl]β-prop-2-enolate] (33) | Stems of P. S/Methanol |                    | [67]      |
| Phenylethanoid Glycosides: Chionoside, (34) |                                 |                                                     |           |
| Glycosyranoside:                   |                                 |                                                     |           |
| 6-O(E) Cinnamoyl-β-D-glucopyranoside, (35) |                                 |                                                     |           |
| Glycosyranoside:                   |                                 |                                                     |           |
| Methyl 6-O(E) feruloyl-β-D-glucopyranoside, (36) |                                 |                                                     |           |
| Glycosyranoside:                   |                                 |                                                     |           |
| 6-O(E) Cinnamoyl-β-D-glucopyranoside, (37) |                                 |                                                     |           |
| Quinino Glycoside: Herbitol III, (38) |                                 |                                                     |           |
| Quinino Glycoside: Scrophulodeside, (39) |                                 |                                                     |           |
| 4-hydroxyacetophenone, (40)        |                                 |                                                     |           |
| 4-hydroxy, 3 methoxy acetophenone, (41) |                                 |                                                     |           |
| Caprylic vanillic acid;            |                                 |                                                     |           |
| 3-methoxy-4-decanoyl benzoic acid, (42) |                                 |                                                     |           |
| Lauryl picraldehyde; 3-methoxy-4-dodecanoylphenyl-n-pent7, 9-dien-11-al (43) | K/methanol |                    | [68]      |
| Myristyl picraldehyde; 3-methoxy-4-tetradecanoyl-phenyl n-pent-7, 9-diene-11-al (44) | K/methanol |                    |           |
| α-glucovanillin; vanillin-α-D-glucopyranoside, (45) |                                 |                                                     |           |
| Picraldehyde 3-0-D-glucopyranoside; |                                 |                                                     |           |
| Picraldehyde 4-O-α-D-glucopyranosyl (6′→1′)-O-α-D-glucopyranoside (46) |                                 |                                                     |           |
| Picorretol-glucoside, (47)         |                                 |                                                     |           |
| 3-methoxy-4-hydroxyphenyl-n-butanyl-α-0-D-glucopyranosyl-6α-1β)-α-O-D-glucopyranosyl-6β-1α)-α-0-D-glucopyranosyl-6α-1β)-α-O-D-glucopyranosyl-4α-3′-methoxy-4′-hydroxyphenyl-n-pent7, 9′-dien-11′-oate |                                 | Antidiabetic |           |
| Glycoside | Compound/Name | Plant part/solvent of extraction | Bio-activities | Reference |
|----------|---------------|---------------------------------|---------------|-----------|
| Iridoid Glycoside; Abeloside A (48) | Stems of P. K/r-butanol | Anti-Vpr activity | [69, 104] |
| Iridoid Glycoside; Abeloside B (49) | | | |
| Iridoid Glycoside; Sylvestroside IV dimethyl acetal (50) | | | |
| Iridoid Glycoside; Sylvestroside (51) | | | |
| Iridoid Glycoside; Sylvestroside (52) | | | |
| Iridoid Glycoside; 8-Epi-Loganic acid (53) | | | |
| Bis-Iridoid Glycoside; Saungmaya glycoside A (54) | | | |
| Bis-Iridoid Glycoside; Saungmaya glycoside B (55) | | | |
| Bis-Iridoid Glycoside; Saungmaya glycoside C (56) | | | |
| Bis-Iridoid Glycoside; Saungmaya glycoside D (57) | | | |
| Cucurbitacin glycosides | | | |
| 2-0-glycoside of cucurbitacin B: (25-acetoxy-2-beta-gluco-syloxy-16,20-dihydroxy-9-methyl-19-norlanosta-5,23-diene-3,11,22-trione) (58) | Roots of P. K/EtOAc | | [65] |
| 2-0-glycoside of cucurbitacin B: (25-acetoxy-2-beta-gluco-syloxy-16,20-dihydroxy-9-methyl-19-norlanosta-5,23-diene-3,11,22-trione) (59) | | | |
| 2-beta-gluco-syloxy-3,16,20,25-tetrahydroxy-9-methyl-19-norlanost-5-enene-2,11,22-trione (60) | | | |
| 2-beta-gluco-syloxy-3,16,20,25-tetrahydroxy-9-methyl-19-norlanost-5-enene-2,1122-trione (61) | | | |
| the 2-0-glycoside of cucurbitacin O (25-acetoxy-2-beta-gluco-syloxy-3,16,20-trihydroxy-9-methyl-19-norlanosta-5, 23-diene-11,22-dione) (62) | | | |
| 2-0-glycoside of deacetylcucurbitacin B (2-beta-gluco-syloxy-16,20-dihydroxy-9-methyl-19-norlanosta-5,24-diene-3,11,22-trione) (63) | | | |
| Arvenin III | | | |
| 2-beta-gluco-syloxy-3,16,20,25-tetrahydroxy-9-methyl-19-norlanosta-5,23-diene-1,2,2,2,2,4-dione and 2-beta-gluco-syloxy-16,20,22-trihydroxy-9-methyl-19-norlanost-5-enene-2,11,22-trione (66) | Roots of P. K/Butanol | | [70] |
| 2-beta-gluco-syloxy-3,16,20,25-tetrahydroxy-9-methyl-19-norlanosta-5,23-diene-1,2,2,2,2,4-dione (67) | | | |
| 2-beta-gluco-syloxy-3,16,20,22-trihydroxy-9-methyl-19-norlanosta-5,24-diene-3,11,1-dione (68) | | | |
| 25-(acetyl)oxy-2-(beta-D-glucopyranosyloxy)-3,16,21-dihydroxy-9-methyl-19-norlanosta-5,23-diene-22-one (69) | Roots of P. K/EtOAc | | [63] |
| 25-(acetyl)oxy-2-(beta-D-glucopyranosyloxy)-3,16,20-trihydroxy-9-methyl-19-norlanosta-5,23-diene-2,11-dione (70) | | | |
| 25-(acetyl)oxy-2-(beta-D-glucopyranosyloxy)-3,16,20-trihydroxy-9-methyl-19-norlanosta-5,23-diene-2,11,1-dione (71) | | | |
| 25-(acetyl)oxy-2-(beta-D-glucopyranosyloxy)-3,16,20-trihydroxy-9-methyl-19-norlanosta-5,23-diene-2,11,1-dione (72) | | | |
| 2-beta-gluco-syloxy-3,16,20,25-tetrahydroxy-9-methyl-19-norlanosta-5,24-diene-3,11,1-dione (73) | | | |
| (2beta,9beta,10alpha,16alpha,20alpha,24-epoxy)-2-(beta-D-glucopyranosyloxy)-16,25-dihydroxy-9-methyl-19-norlanosta-5-enene-3,11,1-dione (74) | Roots of P. K/methanol | | [64] |
| 2-beta-gluco-syloxy-3,16,20,25-tetrahydroxy-9-methyl-19-norlanosta-5-enene-3,11,1-dione (75) | | | |
| Cucurbitane-type triterpene glycosides; Kurroasoid D (80) | Roots of P. K/methanol | Collagenase inhibitory activities | [67] |
| Nortriterpene glycosides; 25-acetonoxy-2-beta-D-xyloxy-3,16,20,22-trihydroxy-9-methyl-19-norlanosta-5-enene-22-one, (81) | Roots of P. K/methanol | Anti-tumorous activities and collagenase inhibitory activities | [67] |
| Phenolics | | | |
| Vanillic acid: 4-hydroxy-3-methoxybenzoic acid (82) | Rhizomes of P. K/methanol, P. S with ethanol | | [49] |
| Ferulic acid: (E)-3-(4-hydroxy-3-methoxyphenyl) prop-2-enio acid (83) | Rhizomes of P. K/95% ethanol | | [72, 73] |
| Isoferulic acid: (E)-3-(3-hydroxy-4-methoxyphenyl) prop-2-enio acid (84) | Rhizomes of P. K/95% ethanol | | [72, 73] |
| Apocynin: 1-(4-Hydroxy-3-methoxyphenyl)ethan-1-one | Rhizomes of P. K/95% ethanol | | [74] |
### Glycoside

| Compound/ Name | Plant part/solvent of extraction | Bio-activities | Reference |
|----------------|----------------------------------|----------------|-----------|
| Picatin | K/methanol | Anti-inflammatory | [61] |
| 1-[4-[[2S,3R,4S,5S,6R]3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxypyphenyl]ethane (86) | K/methanol | --- | |
| Androisn | Rhizomes of P. | anti-arithmetic properties | [61, 58] |

### Bio-activities

- Anti-inflammatory
- Anti-arithmetic properties

### Reference

[61, 58]

### Notes

- **Compounds:**
  - R1, R2, R3, R4, R5 represent various substituents.
  - Substituents include Cin (cinnamoyl), Van (vanillyl), Fer (feruloyl), Cou (coumaroyl), IFer (isoferuloyl), Caf (caffeoyl), Glc (glucopyranosyl), Gal (galactopyranosyl).
  - Substituents with additional groups include OMe (methoxy), CHO (carbonyl), COOH (carboxyl), CH(OMe) (methoxymethyl), CHO (formyl), OH (hydroxyl).

### Structures

- The structures are depicted in the image, showing the compounds and their substituents in detail.

- The structures illustrate the different bio-activities and the corresponding plant parts/solvents of extraction.

### Additional Information

- The references [61, 58] provide further details on the bio-activities and the compounds' structures.

- The compounds are shown in various configurations, including平面 configurations and molecular models.

- The image includes structural formulas and 3D models of the compounds, which are crucial for understanding their properties and interactions.
Glycoside/Compound

| Glycoside/Compound | Plant part/solvent of extraction | Bio-activities | Reference |
|--------------------|---------------------------------|---------------|-----------|

R=$\beta$-D-Glc
R=OH

(80)

(58) R=O, R=O, R=OAc
(59) R=O, R=O, R=OAc
(60) R=OH, R=OH, R=OAc
(61) R=OH, R=OH, R=OAc
(62) R=OH, R=H, R=OH
(63) R=OH, R=O, R=OAc

(66)

R=$\beta$-D-Glc

(74-79)

Biological activates

The wide range of biological activities of extracts and isolated chemical constituents of P. kurroa include anti microbial [75], hepatoprotective [76], antioxidant activity [77], anticancer [78], anti arthritic [80], anti diabetic [87], anti-mutagenic, cardioprotective, anti-malarial, anti-inflammatory, anti-ulcer, anti-asthmatic activity [79], immunomodulatory activity, hypo lipemic activity and nephro-protective activity.

Antimicrobial activity

An antimicrobial activity was observed in the ethanol and methanol extracts of Picrorhiza kurroa rhizome against selected bacterial strains. Ethanol extract of Picrorhiza kurroa rhizome showed high antibacterial activity against E. coli, B. cereus, S. aureus, K. pneumoniae, S. typhi and, S. pyogenes. The methanol rhizome extracts showed high antibacterial activity against S. aureus and P. aeruginosa, whereas acetone and hexane extract showed intermediate activity against E. coli, S. aureus, B. cereus, K. pneumoniae, S. typhi, P. aeruginosa and S. pyogenes by P. Vinoth Kumar et al.,[81] Usman et al., evaluated the antimicrobial potential of Picrorhiza. They conducted an in vitro study on different bacterial stars such as gram-positive bacteria-Staphylococcus aureus and Bacillus subtilis and gram-negative bacteria-Escherichia coli and Pseudomonas aeruginosa and Aspergillus niger, Malassezia furfur and Candida albicans fungal strains. It was observed that ethanolic extract of this plant showed efficient action against all the used strains of microbes, which suggests its use an anti-microbial [82]. Antimicrobial activity of methanol extract of Picrorhiza kurroa was also investigated by Sharma et al.,[83] observed that it was more potent actions against bacterial strain (E. coli, B. subtilis, S. aureus) than antibacterial drug ciprofloxacin and aqueous extract was found to be more effective against fungal strain (A. niger, C. albicans) than Fluconazole which is a standard antifungal drug.

Hepatoprotective activity

Picroliv, possess hepatoprotective activity. Alcohol-fed rats reduced the viability of isolated hepatocytes, reduced the levels of alcohol-metabolizing enzymes (acetaldehyde dehydrogenase, aldehyde dehydrogenase) in rnt hypatocytes and also produced cholestasis, as indicated by the reduction in bile volume, bile salts and bile acids. After treatment with Picroliv all these altered parameter were restored. A hydroalkoholic extract of P. kurroa has been shown to be effective against
P. Kurroa alcoholic extract have also show hepatoprotective activity. Plant is a potent immune stimulant of both hormonal immunity and cell-mediated and shows choleretic activity in dogs. Picrorhiza kurroa is also beneficial in the management of bronchial asthma. The crude extract, and the isolated bioactive of the roots have shown to protect the liver from various types of drug-induced injury [85]. Hepatoprotective activity of Picrorhiza kurroa was investigated by Shetty et al., on male Wistar rat models. The administration of hydroalcoholic extract for 4 w at the dosage of 200 mg/kg and 400 mg/kg showed potent hepatoprotective actions by restoring all the changes in the liver induced in the liver [86].

Anti-inflammatory activity

Anti-inflammatory activity of extract of Picrorhiza kurroa was evaluated by Kumar et al., on rat models, suggested that this plant is a potent source of anti-inflammatory drug [87]. Apocynin possess anti-inflammatory properties. The rhizome of Picrorhiza scrophulariiflora is used to treat inflammatory diseases as a traditional medication and its ethanol extract improves accelerated atherosclerosis through inhibition of redox-sensitive inflammation in rabbits [89].

Antioxidant activity

Kalaivani et al., conducted an in vitro study to evaluate the antioxidant and free radical scavenging potential of Picrorhiza kurroa. It was observed that ethanol extract of this plant showed significant antioxidant properties due to the presence of flavonoid and phenolic compounds [91]. The butanol extract of P. kurroa leaves were evaluated for antioxidant activity against two assays, 2,2-diphenyl-1-picrylhydrazyl radical and 2,2′-azino-bis([3-ethylbenzothiazoline-6-sulphonic acid]) assay. Compounds, luteolin-5-O-glucopyranoside and picein were also shown the antioxidant activity by kant et al. [92]

Antidiabetic activity

Antidiabetic activity of Picrorhiza extract was found to lower blood glucose in laboratory animals. Chronic administration of the extract significantly reduced blood sugar in alloxan-induced diabetic rats for 10 d. The extract was also to find to reduce the increased blood urea nitrogen and serum lipid peroxides in alloxan-induced diabetic animals and to inhibit the bodyweight reduction and leukopenia induced by alloxan administration [93]. Kumar et al., evaluated the antihyperglycemic effects and improved renal and hepatic functions in the hydroalcoholic extract of P. kurroa rhizome. It is observed that extract possesses increased insulin-stimulated glucose uptake potential [94]. Husain et al., conducted an in vivo study on rat models to investigate the antidiabetic potential of Picrorhiza kurroa. The models were administered with streptozotocin for 4 w at the dosage of 20 and 40 mg/kg p.o showed inhibitory effects against 20% and 40% DMBA by decreasing sarcoma and papilloma. This study suggested that picroliv is a potent anti-cancer agent [97].

Anti-mutagenic

As per the reported study conducted by Zaberi et al., hydroalcoholic extract of Picrorhiza kurroa is associated with anti-mutagenic actions. It was found that hydroalcoholic extract exhibited inhibitory actions against Salmonella typhimurium MTCC 1251 and MTCC 1252 strains by direct-acting mutagen of sodium azide [98].

Antiviral activity

The n-butanol extract of Picrorhiza kurroa stems was assayed for anti-Vpr activity using TREX-HeLa-Vpr cells. Among the isolates, sylvestroside IV dimethyl acetal, saungmaygoside D and siverside were the most potent inhibitors with effective doses of 5 and 10 μM, respectively, without showing any notable cytotoxicities [99].

Anti-collagenase activity

A methanol extract of Picrorhiza kurroa rhizomes along with picroside-I II, III, and IV 6-erukylolatapol, phenylethanoid glycosides, triterpene glycosides, cucurbitacin B 2-β-D-glucopyranoside and 25-acetoxy-2-β-D-glucopyranosylxylosioxy-3,16,20-trihydroxy-9-methyl-19-norlanosta-5-en-22-one, and an acetonophene glycoside, picein, exhibited collagenase inhibitory activity by 10–30 μM, with no cytotoxicity being observed at the effective concentrations [67].

RESULTS AND DISCUSSION

Genus Picrorhiza (family Scrophulariaceae) has great importance in Ayurvedic system of medicines. Picrorhiza species accumulate cucurbitacin glucosides, triterpenoid glucosides, phenylethanoid glucosides, and phenolics. Its two species P. kurroa and P. scrophulariiflora have so much similarity due to the presence of similar active constituents like picroside-I, picroside-II, kutkoside while P. scrophulariiflora contains some additional phenylethanoid glycoside and plantamajoside, which are absent in the species P. kurroa. So, the P. scrophulariiflora is closely related to P. kurroa and used as a substitute or adulterants. Thus, reviewing the genus Picrorhiza it is clear that the lot of work has been done on species P. kurroa in comparison to other species P. scrophulariiflora. However, more research is needed to know about the chemical constituents of P. scrophulariiflora and its biological activities.

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All the work has been carried out by me.

CONFLICTS OF INTERESTS

Declared none

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