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Short Communication

Hepatoprotective effect of *Picrorrhiza kurroa* on antioxidant defense system in antitubercular drugs-induced hepatotoxicity in rats

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The hepatoprotective effect of the ethanol extract of *Picrorrhiza kurroa* rhizomes and roots (PK) on liver mitochondrial antioxidant defense system in isoniazid and rifampicin-induced hepatitis in rats was investigated. In liver mitochondria of antitubercular drugs administered rats, a significant elevation in the level of lipid peroxidation with concomitant decline in the level of reduced glutathione and in the activities of antioxidant enzymes was observed. Co-administration of PK (50 mg/kg/day for 45 days) significantly prevented these antitubercular drugs-induced alterations and maintained the rats at near normal status.

Key words: *Picrorrhiza kurroa*, hepatoprotective activity.

INTRODUCTION

The rhizomes and roots of *Picrorrhiza kurroa* Royle ex Benth. (Scrophulariacae), Indian name, 'Kutki', were collected from the hilly areas of Sikkim and authenticated by Captain Srinivasamurthi Drug Research Institute for Ayurveda, Arumbakkam, Chennai, India.

In Indian ayurvedic medicine, the oral administration of extract of dried rhizomes and roots is claimed as a cure for human viral hepatitis (Kapahi et al., 1993; Anandan and Devaki, 1998). In traditional medicine, the plant has also been used to cure heart ailments, abdominal pain, stomach disorders, anaemia, jaundice, and for promoting bile secretion (Anand, 1990; Anandan and Devaki, 1999).

MATERIALS AND METHODS

Crude ethanol extract of dried rhizomes and roots of *P. kurroa* (PK) (yield: 8.2%) was obtained. Hepatoprotective activity of PK on hepatic mitochondrial defense system against antitubercular drugs-induced toxicity was in investigated in male albino rats.

Male Wistar strain albino rats, weighing 120 - 150 g were selected for the study. The animals were housed individually in polypropylene cages under hygienic and standard environmental conditions (28 ± 2ºC, humidity 60 - 70%, 12 h light/dark cycle). The animals were allowed a standard diet [M/s Sai Feeds, Bangalore, India] and water *ad libitum.* The experiment was carried out as per the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), New Delhi, India.

RESULTS AND DISCUSSION

Administration of antitubercular drugs [isoniazid and rifampicin, 200 mg each/ kg body weight/ day for 45 days], caused a significant elevation in the level of lipid peroxidation (Table 1) with concomitant decline in the level of reduced glutathione [GSH] and in the activities of glutathione-dependent antioxidant enzymes (glutathione peroxidase [GPX] and glutathione-S-transferase [GST]) and antiperoxidative enzymes (catalase [CAT] and superoxide dismutase [SOD]) (Table 2) in liver mitochondria of experimental groups of rats as compared to that of normal control animals. Oral co-administration of PK [50 mg/kg/day for 45 days] significantly these antitubercular drugs-induced adverse effects and maintained the rats at near normal status.

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Table 1. Protective activity of the ethanol extract of *Picrorrhiza kurroa* [PK] on liver mitochondrial lipid peroxidation [basal and in the presence of promoters like ascorbate, FeSO4 and *t*-butyl hydroperoxide] in antitubercular drugs-induced hepatitis in rats.

Group	Group I normal control	Group II PK-administered (A)	Group III antitubercular drugs-administered (B)	Group IV (A+B)
Basal	0.98 ± 0.06	0.83 ± 0.04	2.34 ± 0.11*	1.18 ± 0.05*
Ascorbate	2.78 ± 0.14	2.47 ± 0.10	4.63 ± 0.29*	2.91 ± 0.18*
FeSO4	4.15 ± 0.31	3.88 ± 0.25	6.89 ± 0.47*	4.36 ± 0.28*
t-butyl hydroperoxide	5.61 ± 0.42	5.49 ± 0.47	8.94 ± 0.67*	5.98 ± 0.54*

Values are expressed as mean ± S.D.; n = 6; *P < 0.001; Group III vs. Group I; Group IV vs. Group III; Student's *t*-test.
(A): PK, 50 mg/ kg body weight/day for 45 days.
(B): Antitubercular drugs (isoniazid and rifampicin), [isoniazid and rifampicin, 200 mg each/ kg body weight/ day for 45 days]. Lipid peroxidation in nmol malondialdehyde/mg protein.

Table 2. Protective activity of the ethanol extract of *Picrorrhiza kurroa* [PK] on liver mitochondrial defense system [reduced glutathione (GSH), glutathione peroxidase (GPX), glutathione-S-transferase (GST), catalase (CAT) and superoxide dismutase (SOD)] in antitubercular drugs-induced hepatitis in rats.

Group	Group I normal control	Group II PK-administered (A)	Group III antitubercular drugs-administered (B)	Group IV (A+B)
GSH	4.08 ± 0.34	4.36 ± 0.39	2.18 ± 0.12*	3.94±0.27*
CAT	7.11 ± 0.55	6.94 ± 0.46	3.49 ± 0.24*	6.43 ± 0.41*
SOD	3.73 ± 0.19	3.85 ± 0.21	1.68 ± 0.09*	3.38 ± 0.18*
GPx	3.05 ± 0.17	3.27 ± 0.21	1.86 ± 0.11*	2.77 ± 0.15*
GST	1412 ± 118	1374 ± 105	612 ± 58.4*	1211 ± 98.3*

Values expressed: GSH, nmol g^{-1}; CAT, nmol H2O2 decomposed min^{-1} mg^{-1} protein; SOD, one unit of the SOD activity is the amount of protein required to give 50% inhibition of epinephrine autoxidation; GPx, nmol GSH oxidized min^{-1} mg^{-1} protein; GST, µmol 1-chloro-2,4-dinitrobenzene conjugate formed min^{-1} mg^{-1} protein.

The hepatoprotective effect of PK is probably due to the increase of the activities of the antioxidant enzymes, or to a counteraction of the free radicals by the presence of the electrophilic constituent's picroside I, picroside II and kutkoside (Kumar et al., 2001; Ramesh et al., 1992), or to an activated conjugation of antitubercular drugs with GSH in liver.

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