WWW.IJAPC.COM

IJAPC

e ISSN 2350 0204

VOLUME 12 ISSUE 1 2020

GREENTREE GROUP PUBLISHERS (GGP)

Int J Ayu Pharm Chem

REVIEW ARTICLE

www.ijapc.com

e-ISSN 2350-0204

Role of *Katuka* (*Picrorrhiza* kurroa Royle ex Benth.) in Obesity w.s.r to Ayurvedic and Modern aspect: A Review

Surekha Khandekar[1]*, Tabassum Pansare[2], Abhijeet Pachpor[3] and Sharadkumar Maurya[4]

[1-2]Dravyaguna Department, Government Ayurvedic College, Osmanabad, Maharashtra, India

[3]Dept. of Dravyaguna Vigyan Dr. V.J.D.G.A.M, Patur, Maharashtra, India

[4]Dept. of Sharirkriya, Govt. Ayurved College, Osmanabad, Maharashtra, India

ABSTRACT

The global epidemic Obesity is affecting 300 million people world-wide and 22 million people in India. According to *Ayurveda Kaphavatavikruti*, hypo functioning of *Jathragni*, *Medodhwagni* and *Am*- production lead to excess enhancement of vitiated *medovriddhi*. The patho-physiological changes in *medovridhhi* have shown similarity with those of obesity. *Katuka* (*Picrorrhiza kurroa* Royle ex Benth.) on account of its attributes like *tikta rasa*, *sheeta Virya*, *katu Vipaka* and *laghu*, *ruksha guna* perform the function of *Lekhan* (Scraping), *Deepan* (restoration of *Agni*), *Pachan* (Digetion), *Bhedan* (purgative), *vatkapha*nashan (alleviates *vata* and *kapha* in the body) and *Hridya* (cardio-protective), *Pramehaghna* (Anti-diabetic) and *Yakrutrogaghna* (Hepato-protective) *karma* (action). *Katuka* possesses choleretic (*Pittavirechak*) and cholegogue (*Virechak*- purgative) action. Moreover, *Katuka* is useful in Obesity associated with comorbidities like Cardiac disorder, Hyperlipidemia, Diabetes and Liver disorder. This paper presents its role in obesity on the basis of *ayurvedic* and modern parameters.

KEYWORDS

Obesity, Katuka, Picrorrhiza, Hyperlipidemia

Greentree Group Publishers

Received 24/09/19 Accepted 11/12/19 Published 10/01/2020

INTRODUCTION

Obesity is known as corpulence or fatness. It is characterized by unessential increase of body fat caused by the intake of more calories than the body can use. The overload calories are then stored as fat or adipose tissue. Obesity is a globalepidemic[1]. This global epidemic has affected 300 million people world-wide and 22 million people in India. In Northern India, obesity is most prevailing in Urban population (Male=5.5%, Female=12.6%) [2]. Statins are the drugs extensively used for the treatment of obesity. Anti-obesity drugs have many side effects like gastrointestinal symptoms, nuisance, myalgia and giddiness[3]**.** In *Charaksamhita sutrasthan* 4th chapter deals with 50 different groups of 10 herbs with common action. The third *Mahakashaya* of this group is *Lekhaniya Mahakashaya* i.e. group of plants acting as scraping agents. *Katuka* (*Picrorrhiza kurroa* Royle ex Benth.) is included in *LekhaniyaMahakashaya*[4]. This plant occurs in alpine Himalayas, from Kashmir to Sikkim up to 3000 m to 4500 m altitudes. It is a small perennial herb[5]. *Katuka* has *Bhedan* (Purgative), *Hridya* (Cardioprotective), *Prameghna* (Anti-diabetic), *Lekhan* (Scraping), and *Yakrutrogaghna* (Hepato-protective), *Deepan* (restoration of *Agni*) properties[6]. It has also shown the Cardioprotective, Hepatoprotective, Hypolipidemic, Anti-obesity, Purgative, Anti-oxidant, Anti-inflammatory, Anti-diabetic action. This review highlights pharmacokinetics of *katuka* in obesity with special reference to *ayurvedic* and modern aspect.

AYURVEDIC ASPECT

Thorough review of *Katuka* was taken from various *nighantu*. The study of phytochemistry and anti-obesity mechanism of *katuka* from various related work done published in research papers and articles was also studied**.**

Obesity (*Medorog*)

Atisthaulya (Obesity) is described as unnecessary deposition of *meda* (fat) due to hypo-functioning of *Medodhatu* leading to flaccidity of hips, abdomen, and breast. *Atisthaulya* is one of the *Santarpanotha* vikaras (utilization of excessive calories) in *Ayurveda*[7].

Information about *Katuka*

Synonyms[8]

Matsyasakala - The part used rhizome, has fishy scales.

Chakrangi - Is circular on section.

Krishnbheda - Blackish on breaking.

Katvi- Unpalatable.

Tikta- Bitter in taste.

Matsyapitta, *Sakuladani*- Like fish bile.

Rohini, *k\Katurohini*, *Asokarohini*- Regenerative.

Amaghni- It removes ama (Immature ahara rasa/waste substances associated with ama).

Arishta- Safeguards against disease.

Raspanchaka

Rasa: Tikta

Virya: Shita

Vipaka: Katu

Guna: Laghu, Ruksha

Karma

Bhedan (Purgative), *Lekhan* (Scraping), *Deepan* (restoration of *Agni*), *Pachan* (removes toxins), *Hridya* (Cardioprotective), *Prameghna* (Anti-diabetic), *Lekhan* (Scraping), *Deepan* (restoration of Agni), *Pachan* (removes toxins), *Yakrutrogaghna* (useful in hepatic disorders) *karma* (Actions)[9].

MODERN ASPECT

Obesity-Obesity is a medical condition in which excess body fat get accumulated to an extent that it may have a negative effect on health[10].

Hyperlipidemia-

The term Hyperlipidemia is used to describe high levels of fat in the blood, such as cholesterol and triglycerides.

Taxonomical classification[11]

Kingdom -Plantae

Division – Dicotiledonae

Class- Asteride

Order- Scrophulariales

Family- Scrophulariaceae

Genus – Picrorrhiza

Species- Picrorrhiza kurroa

Phytoconstituents

Picrorhizin, kutkin-glycosides, D-manittol, Bainilik, Kutkiol, Kutakaki-sterol, Picrohizetin, Kutkoside, Picroside, Apocynin[12].

PHARMACOLOGICAL ACTIONS

Anti-obesity

Diabetes often exists with Obesity. The antihyperglycemic activity of *Picrorrhiza kurroa* (Katuka) in STZ (Streptozotocin) induced diabetic rats was proved. To estimate the result of *Picrorrhiza kurroa* (Katuka) on high fat diet (HFD) induced obesity in rats, models which imitate several features of human obesity was taken. Rats were provided with HFD libitum for 15 days, rats with significant weight gain compared to normal pellet diet (NPD) group. *Picrorrhiza kurroa* treatment was started on 16th days forwards till 30th day. Control group rats were given NPD for 30 days. Body weight was noted on day 1 followed by weekly basis. Fasting blood samples were collected on 15th and 30th day and total cholesterol, LDL-C, HDL-C and triglycerides level were estimated[13]. Rats feed with HFD (High fat diet) gain significant weight compared to NPD (normal pellet diet)-feed rats after 15 days. The rise in body weight was continued upto

30th day in rats maintained on HFD. Unlike *Picrorrhiza kurroa* treatment significantly inhibited weight gain compared to vehicle treated HFD rats. *Katuka* (*Picrorrhiza kurroa)* extensively reduced ($p<0.05$) total cholesterol, LDL-C, triglycerides while HDL-C was significant increase compared to vehicle treated HFD rats.

Antioxidant activity

Antioxidant agents work like radical scavengers. They prevent the human body from a variety of diseases. It is reported that activities of liver enzymes are reduced among the liver cirrhosis patients subsequent the treatment with the *Picrorrhiza Kurroa* plant extract[14]. The antioxidant effectiveness of plant extracts were reported employing radical scavenging assays, ferric reducing antioxidant property and thiobarbituric acid assay for analyzing inhibition of lipid peroxidation[15, 16]. The rhizome ethanol extract of *Picrorrhiza kurroa* at the dose of 20 mg/ kg body weight, healed speedily the stomach wall of indomethacin induced gastric ulcerated rats by an in vivo free radical scavenging action used diverse antioxidant testing methods to corroborate the antioxidant efficacy of the leaf fractions of *Picrorrhiza kurroa*. The extract showed DPPH radical scavenging and metal chelating activities with IC50 of 75.16±3.2 and 55.5±4.8 ìg/mL and exhibited potent reducing power with antioxidant activities. Antioxidant and radical scavenging activity of *Picrorrhiza kurroa* (*Katuka*) extract indicate its active role toward different oxidative stress related diseases, as a food supplement and source of natural antioxidants[17, 18] .

Hypolipidemic activity

A Hypolipidemic effect of the water extract of *Picrorrhiza kurroa* was observed in a high fat diet feeding hyperlipiemia mouse at doses of 50, 100 and 200 mg/kg, orally, once a day for 12 weeks. Liver weight, serum aspartate transferase (AST), alanine transferase (ALT), low density lipoprotein (LDL), triglyceride (TG) and total cholesterol levels were significantly reduced by the treatment. On the contrary, serum HDL level seems not affected by *Picrorrhiza Kurroa* (*Katuka*) water extract [19].

Anti-inflammatory-

Anti-inflammatory activities Inflammation is a restricted defensive response of tissue to irritation or infection, characterized by redness, swelling, pain and at times loss of function. Apocynin, an active phyto-constituent of root extracts has been revealed to possess anti-inflammatory properties. The inhibition of oedema at the rate of 29.8% shows that (*Picrorrhiza kurroa*) is an active anti inflammatory drug[20]. The application of *Katuka*

(*Picrorrhiza kurroa*) rhizome extract significantly inhibited joint inflammation. It also demonstrates potent anti-inflammatory activity against chemically induced inflammation and may be considered as a high-quality naturally occurring analgesic[21].

Antidiabetic activity

DM (Diabetes mellitus) is a common group of metabolic disorders that show the phenotype of hyperglycemia. It is distinguished by high blood glucose level caused due to insulin deficiency and often associated with insulin resistance *Picrorrhiza kurroa* root extract treatment influenced significant ($p<0.001$) reduction in fasting blood glucose level in streptozotocin -nicotinamide induced type-2 diabetic rats, illustrating antidiabetic activity[22] .

Hepatoprotective activity

Kutkin (Picrosides and kutkosides) has hepato-protective activity. A cell of the main parenchymal tissue of the liver is a hepatocyte and make up 70-85% of the liver's mass. Hepatocytes death results in hepatic injury when there is an elevation in the level of normal serum transaminase enzymes. *Picrorrhiza kurroa* has noteworthy hepato-protective action against carbon tetrachloride intoxicated rats and Amanita poisoning[23-25].The herbal extract supplies advanced neutraceutical activity for superior hepato-protection by improving intestinal absorption [26].

Cardioprotective effect

Normal rat pre-treated with *Picrorrhiza kurroa* (200 mg/kg) alone did not show noteworthy change; however, application of isoproterenol leads to hemodynamic and left ventricular dysfunction, lipid peroxidation and oxidative stress. Such type of cardiac dysfunction was considerably prohibited by the plant's root extract. Pre-treatment with root extract significantly checked the isoproterenol-induced oxidative stress by renovating various enzymes like myocardial superoxide dismutase, catalase and glutathione in lipid peroxidation, which prevent the outflow of myocytecreatinekinase MB and lactate dehydrogenase enzymes. The outcome suggests that the root extract possesses effective cardioprotective properties that may be attributed to its future use[27].

Anticancer activity

Malfunctioning in the mechanism of apoptosis may lead to infinite growth and cell division. The dichloromethane fraction of *Katuka* (*Picrorrhiza kurroa*) showed efficient anticancer activity and may be recommended to explore for cancer therapy[28].

Analgesic activity

Analgesic activity of the plant was assessed by the treatment with alcoholic root extract. The analgesic activity was assessed by employing the Hot plate and Acetic acid induced-writhing technique in Albino mice of either sex. The 500 mg/kg extract dose of *Picrorrhiza Kurroa* had shown comparable effect in comparison to the standard drug Pentazocin when kept for ½ hr[29].

Antimicrobial activity

Antifungal activity of root extract of *Picrorrhiza kurroa* was examined against Candida tropicalis, C. albicans, Penecillium marneffi and Trichophyton rubrum. Alcoholic solvents of the root extract at 10% were efficient in the inhibition of these clinical fungal isolates [30]. Moreover, acetone and methanol extracts of dried stolons of *Picrorrhiza kurroa* exhibited broad range of antimicrobial activity against majority of the pathogenic microbes such as Gloeocerco sporasorghi, Erwinia chrysanthemi, Rhizocto niasolani, Fusarium oxysporum and Sporisorium scitamineum[31]. Also, 0.1% stock solution of chloroform, methanol and water extract was found to demonstrate antimicrobial activity[32].

Immunomodulatory activity

An immunomodulatory agent is a sort of drug that may work as an immunostimulator or an immunosuppressant based on its effect on the immune system. The immunostimulatory activity of biopolymeric fraction RLJ-NE-205 from *Picrorrhiza Kurroa has been reported* [33]. Biopolymeric fraction induced both the humoral and cellular parts of the immune system. Ethanolic extract of *Picrorrhiza kurroa* leaves was able to stimulate humoral as well as cellmediated components of the immune system and also phagocytosis in investigational animals[34, 35]. Two powerful anticomplementary polymeric fractions were isolated that plays an important role in the antigen non-specific defence defence. The analysis supports the assumption that therapeutical preparations made from *Picrorrhiza kurroa* roots may influence on immune mechanisms. It was further noted that the alcoholic extract of the root is more potent than aqueous extract in producing delayed type hypersensitivity response [36, 37].

Digestive activity

Picrorrhiza kurroa (*Katuka*) is used in India for the people with constipation due to insufficient digestive secretions[38].

DISCUSSION

According to Ayurveda Katuka has properties like *Lekhan* (Scraping), *Deepan* (restoration of *Agni*), *Pachan* (removes toxins), *Bhedan* (Purgative), *Hridya*

(Cardioprotective), *Prameghna* (Anti-diabetic), *Yakrutrogaghna* (Hepato-protective) *Karma* (Actions) which play major role in obesity.

Tikta Rasa-

Mainly *tikta* rasa has catabolic and absorbing effect on *meda* and it reduces the excess of *kleda* (Fat) in the body. It also decreases the *Medodhatu* (excess of fat from the body).*Tikta rasa* has *srotoshodhan* property (channel cleaning). It absorbs the fluid and slimy material on account of *vayu* and thus vacating space (*saushirya)* due to *Aakash mahabhoota*. *Acharya Charaka* in *sutrasthan* 26 has explained the properties of *tikta rasa* like *deepen* (restoration of *Agni*), *pachan* (appetiser), *lekhan* (scraping), *and kledamedaupashoshan* (It reduces the excess of fat, lipid from the body) [4].

Katu Vipaka

It has predominance of *Agni*, *vayu* and *aakash mahabhootas*. It is responsible for *medodhatukshay* (reduction in excessive *Medodhatu*).

Laghu, Ruksha Guna

Due to its *laghu*, *ruksha guna* it pacifies increased *kapha*. These *gunas* help to reduce *Kapha* and *meda* which are the main responsible factors of Hyperlipidemia and thus potentiates their action by way of synergism. *Laghu Guna* produces *Laghutva* (decreases weight or bulk) and *Ruksha guna* produces *Rukshtva* (Dryness) in the body.

Deepan, Pachan, Lekhan, Bhedan Karma

The *Katuka* has *tikta* rasa which stimulates the *jadhargni* and decreases the excess of *meda* by *deepan* property (restoration of *Agni*). Due to *katu Vipak, it* digests the excess of *Aama* and *kleda* by *pachan* property (Digetion). It reduces the excess of meda *dhatu* by *Lekhan* property (Scraping). *Katuka* also shows bhedan (purgative) property due to its *TiktaRasa*[4].

***Medoghna* (Anti-obesity Action)**

In medorog, unnecessary deposition of *meda* (fat) due to hypo-functioning of *Medodhatu* occurs. By the virtue of *Deepan-Pachan Karma, Katuka* increases *Agni* at all levels and it reduces *Ama* and corrects *Medo dhatvagnimandya*. Because of its *Lekhan* action, it reduces *meda* (Fat). *Katuka* is one of the most important drugs mentioned in *Lekhaniya Mahakashaya*, which has choleretic *(Pittavirechak)* and cholegogue-*Virechak* (purgative) action. *Katuka* possesses Choleretic action i.e. it increases bile production. It has cholegogue action which promotes flow of bile from gall bladder into the intestines. The bile salts are essential for absorption of fats and lipids from gut, thus the excretion of bile in feces leads to decrease absorption of fats, lipids in the gut hence concentration of lipids in serum is decreased.

***Hridya* (Cardioprotective) action**

Improper diet & sedentary lifestyle leads to thickening of arteries resulting in obstruction (*Margavarod/Srotorodha*) in the normal pathway of *vayu*. *Vata* especially *vyanvayu* associated with *aam* (Contributing formation of athermanous plaque and thrombus) is concerned with the pathogenesis of *Hridroga* (Cardiac disorders). *Katuka* establishes normalcy of *Agni* (metabolism) and *rasa dhatwagni* (Tissue metabolism) and digests *Aam*. It eliminates morbid *doshas* through *bhedan* (piercing) and *Rechan* (purgative) action. Due to its *Lekhan* action and predominance of *Vayu and Aakash mahabhootas*, it successfully removes the obstruction (*Sanga*/*Srotorodhan*) in the *srotos* (channels of transportation of nutrients). Thus *Picrorrhiza kurroa* (*Katuka*) plays an important role in the management of cardiac disorders.

***Pramehaghna* (Anti-diabetic action)**

Prameh is *Tridoshaj* (involves all the three *doshas*) diseases. But initially it starts with derangement of *kapha dosha* due to prolonged and excess use of *kapha* provoking *aahar* (diet) and *vihar*(life style) leading to vitiation of *kapha* (*Bahudravakapha*) which has basic resemblance with characteristic of *meda*. Both *Kapha* and *meda* interact with each other. Vitiated *kapha* further interact with *mansa and* produces *pramehapidika* and association of vitiated *Kapha* with *kleda* converts *kleda* into *mutra* (urine) resulting frequent urination. *Tikta rasa*, *katu vipak*, *ruksha* and *laghu guna* alleviate *kapha* which is the predominant *dosha* in the pathogenesis of *Prameh* (Diabetes mallitus). *Katuka* helps to correct *Medodhatawagnimandya* (tissue metabolism) due to its *deepan* and *pachan* activities. *Tikta rasa* and *ruksha guna* of *Katuka* help to absorb *kleda* and clears the channels. Thus *Katuka* possesses significant place in the treatment of *Prameh*.

***Yakrutrogaghna* (Useful in hepatic disorders)**

Katuka is a very common plant used in *Ayurveda* mainly for liver disorders and gallstones. It stimulates liver and relieves its inflammation due to its *deepan* (corrects metabolism) and *Aampachan* (removes toxins from liver) *karma* (action). It is also useful in gall stones on account of its *bhedan* (piercing) and *rechan* (purgative) action. Moreover it is pitta*sravi* (cholorectic) and *Pittavirechak* (chologouge).

The research work reveals that its anti-obesity, cardioprotective, anti-diabetic and hepatoprotective actions are pharmacologically evaluated for its efficacy.

CONCLUSION

Katuka (*Picrorrhiza kurroa*) has the *deepan* (restoration of *Agni*), *pachan* (Digetion), *lekhan* (Scraping) and *Bhedan* (purgative) properties. *Picrorrhiza kurroa* possesses *tikta rasa*, *sheeta virya*, *katu vipak*, *laghu* and *ruksha guna.* It has predominance of *vayu* and *aakash mahabhootas*. Due to all these virtues, it reduces the excess of *kleda*, *meda* from the body (lipid, fat reduces). In addition to this it has choleretic *(Pittavirechak)* and cholegogue-*Virechak* (purgative) action which results in excretion of bile in feces leading to decrease in absorption of fats, lipids in the gut which results in the reduction in the concentration of lipids in serum. This explains its effectiveness in obesity. Moreover, *Katuka* is beneficial in Obesity when it is connected with co-morbidities like Diabetes, Liver disease, Cardiac disorders due to its *Pramehaghna* (Anti-diabetic), *Yakrutvikarghna* (hepato-protective) and Hridya (Cardio-protective) action. The research work has revealed its Anti-obesity, Hypolipidemic, Cardioprotective, Anti-diabetic action, Hepatoprotective, Anti-cancer, Anti-oxidant, Anti-inflammatory and Immunomodulatory actions. Better randomized, double blinded, placebo-controlled clinical trials on *Katuka* are required which will attract the end users by effective benefits. This data will be surely useful for further scientific research.

REFERENCES

1. Dan Longo, et.al. Harrison's principles of internal medicine. 16th ed. P. 422429.
2. Doon, Nicholas A editor. Davidson's, principles and practice of medicine, Sir Stanley. 20th ed. P. 111-117.
3. http://en.m.wikipedia.org.>wiki>Anti.
4. Pandit Kashinath Pandeya and Dr. Gorakshanath Chaturvedi. Charak Samhita (Hindi translation) Chaukhamba Bharati Acadamy; Varanasi, Reprinted 2013. P.65-72.
5. Vikaspedia.in>package-of –practices.
6. Dravyaguna-Vijnana. (2006). Vegetable Drugs, Vol.II, by Prof. P.V. Sharma, Chaukhambha Bharati Academy, Varanasi.
7. Acharya Vidyadhar Shukla and Prof Ravidutta Tripathi editor Charaksamhita of Agnivesha, elaborated by charak and Drudhabal with Vaidyamanorama Hindi commentary. Chaukhamba Sanskrit Pratishthan, p. 317, 430, 300.
8. Bhavamisra Bhavprakasa Nighantu. Edited by Pandey G S. Chaukhambha Bharati Academy, Varanasi, 2004; 152/70.
9. Dravyaguna-Vijnana, Vol.II, Vegetable Drugs, by Prof. P.V. Sharma, Chaukhambha Bharati Academy, Varanasi, Reprint: 2006.
10. http:// en.m.wikipedia.org>wiki
11. Chettri, N., Sharma, E. and Lama, S.D. Non-timber forest produces utilization, distribution and status in a trekking corridor of Sikkim, India, (2005); 8:89-101.
12. Sharma, S.K. and Kumar, N. Antimicrobial Screening of Picrorrhiza kurroa Royle Ex Benth Rhizome. Int J Current Pharm Rev Res, (2012); 3:60-65.
13. Srinivasan K, Viswanad B, Asrat L, Kaul CL, Ramarao p. Combination high fat diet fed and low dose streptozotocin treated rat: Amodel for type 2 diabetes and pharmacological screening , Pharmacol Res, 2005; 52:313-320.
14. Kalaivani, T. and Mathew, L. Free radical scavenging activity from leaves of Acacia nilotica (L.) Wild. Ex Delile, an Indian medicinal tree. Food Chem Toxicol (2010); 48:298305.
15. Rajkumar, V., Guha, G. and Kumar, R.A. Antioxidant and anti-neoplastic activities of Picrorrhiza kurroa extracts. Food Chem Toxicol (2011); 49:363–369.
16. Ray, A., Chaudhuri, S.R., Majumdar, B. and Bandyopadhyay, S.K. Antioxidant activity of ethanol extract of rhizome of Picrorrhiza kurroa on indomethacin induced gastric ulcer during healing. Indian J Clin Biochem (2002); 17:44-51.
17. Kant, K., Wwalia, M., Agnihotri, V.K., Pathania, V. and Singh, B. Evaluation of antioxidant activity of Picrorrhiza kurroa (leaves) extracts. Indian J Pharm Sci. (2013); 75:324329.

18. Krupashree, K., Kumar, K.H., Rachitha, P., Jayashree, G.V. and Khanum, F. Chemical composition, antioxidant and macromolecule damage protective effects of Picrorrhiza kurroa Royle ex Benth. S Afr J Bot, (2014); 94:249–254.

19. Lee HS, Yoo CB, Ku SK (2006): Hypolipemic effect of water extracts of Picrorrhiza kurroa in high fat diet treated mouse. Fitoterapia, 2006; 77(7-8): 579-84.

20. Kantibiswas, T., Marjit, B. and Maity, L.N. Effect of Picrorrhiza kurroaBenth. in acute inflammation. AncSci Life, (1996); 17:11-14.

21. Kumar, R., Gupta, Y.K., Singh, S. and Arunraja, S. Picrorrhiza kurroa Inhibits Experimental Arthritis through Inhibition of Pro-inflammatory Cytokines, Angiogenesis and MMPs. PhytotherRes, (2016); 30:112–119.

22. Husain, G.M., Singh, P.N. and Kumar, V. Antidiabetic activity of standardized extract of Picrorrhiza kurroa in rat model of NIDDM. Drug Discov Ther, (2009); 3:88-92.

23. Navarro, V.J. and Senior, J.R. Drug related hepatotoxicity. N Engl J Med, (2006); 354:731739.

24. Kaur, S., Vetriselvan, S., Hemah, C., Gayathiri, S., Yaashini, A., Singh, I. and Shankar, J. Hepatoprotective activity of aqueous extract of Picrorrhiza kurroa in carbon tetrachloride (ccl4) induced hepatotoxicity in albino wistar rats. Int J Pharm Ther,(2012); 3: 207-214.

25. Dwivedi, Y., Rastogi, R., Garg, N.K. and Dhawan, B. Effects of picroliv, the active principle of Picrorrhiza kurroa, on biochemical changes in rat liver poisoned by Amanita phalloides. Chung Kuo Yao Li Hsueh Pao, (1992); 13:197–200.

26. Jia, D., Barwal, I., Thakur, S. and Subhash, C.Y. Methodology to nanoencapsulate hepatoprotective components from Picrorrhiza kurroa as food supplement. Food Biosci, (2015); 9:28-35.

27. Nandave, M., Ojha, S.K., Kumari, S., Nag, T.C., Mehra, R., Narang, R. and Arya, D.S. Cardioprotective effect of root extract of Picrorrhiza kurroa (Royle Ex Benth) against isoproterenol-induced cardiotoxicity in rats. Ind J Exp Biol, (2013); 51:694-701.

28. Mallick, M.N., Singh, M., Parveen, R., Khan, W., Ahmad, S., Najm, M.Z. and Husain, S.A. HPTLC Analysis of Bioactivity Guided Anticancer Enriched Fraction of Hydroalcoholic Extract of Picrorrhiza kurroa. Bio Med Res Int. (2015). (http://dx.doi.org/10.1155/2015/513875).

29. Rupali, S., Raha, S.B. and Santosh, S. Evaluation of analgesic activity of roots of Picrorrhiza kurroa. J Drug Deliv Ther, (2013); 3:99-104.

30. Shubha, K.S., Sumana, K. and Lakshmidevi, L. Antifungal Activity of Solanum xantocarpumSch and Wend and Picrorrhiza kurroaRoyle ex Benth against Some Clinical Dermatophytes. Int J Curr Microbiol App Sci, (2016); 5:236-244.

31. Laxmi, V. and Preeti, C. Antimicrobial activity of dried stolon extracts of Picrorrhiza kurroaRoyle ex. Benth.- An endemic and endangered Himalayan herb. ENVIS B Himalayan Ecol, (2015); 23: 127-132.

32. Sharma, S.K. and Kumar, N. Antimicrobial Screening of Picrorrhiza kurroaRoyle Ex Benth Rhizome. Int J Current Pharm Rev Res, (2012); 3:60-65.

33. Gupta, A., Khajuria, A., Singh, J., Bedi, K.L., Satti, N.K., Dutt, P., Suri, K.A., Suri, O.P. and Qazi, G.N. Immunomodulatory activity of biopolymeric fraction RLJ-NE205 from Picrorrhiza kurroa. Int Immunopharmacol, (2006); 6: 1543–1549.

34. Sharma, M.L., Raob, C.S. and Duda, P.L. Immunostimulatory activity of Picrorrhiza kurroa leaf extract. J Ethnopharmaco, (1994); l 41:185- 192.

35. Simons, J.M., Hart, B.A., Ip Vai Ching, T.R., Van Dijk, H. and Labadie, R.P. Metabolic activation of natural phenols into selective oxidative burst agonists by activated human neutrophils. Free Radical Bio and Med, (1990); 8:251-258.

36. Hussain, A., Shadma, W., Maksood, A. and Ansari, S.H. Protective effects of Picrorrhiza kurroa on cyclophosphamide induced immunosuppression in mice. Pharmacognosy Res, (2013); 5:30–35.

37. Picrorrhiza root Pharmacology (http://www.mdidea.com/products/new/new04806.html). Accessed on 20 September, 2011.

38. JameelMohd, Ansari Javed Akhtar et.al hepatoprotective evidence of higher altitude Medicinal plant Picrorrhiza kurroa Royle ex benth: “threatened with extinction” Journal of Herbal Medicine and Toxicology 6 (2) 1 – 5 (2012) ISSN 0973-4643 p.1-5