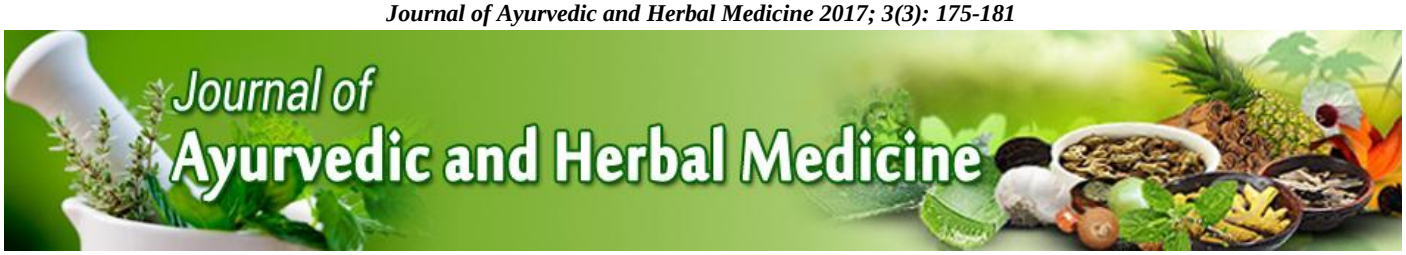


Review Article

ISSN: 2454-5023
J. Ayu. Herb. Med.
2017; 3(3): 175-181

www.ayurvedjournal.com
Received: 18-07-2017
Accepted: 04-09-2017

***Corresponding author:**
Om Prakash
Goel Institute of Pharmacy and Sciences, Faizabad Road, Lucknow, Uttar Pradesh - 226 016, India
*Email:*opverma2007[at]gmail.com

Gentiana lutea Linn. (Yellow Gentian): A comprehensive review

Om Prakash[1], Ruchi Singh[1], Saroj Kumar[1], Shweta Srivastava[1], Akash Ved[1]
1 *Goel Institute of Pharmacy and Sciences, Faizabad Road, Lucknow, Uttar Pradesh - 226016, India*

ABSTRACT

Gentiana lutea Lin. commonly known as yellow gentian, bitter root and bitterwort belonging to family Gentianaceae is a common traditional medicine freely available in hilly areas in Japan, Europe and adjoining continents, its medicinal properties are also mentioned in Ayurveda. The plant is reported to posse's antioxidant, antifungal, anti-inflammatory, stomachic, appetizer and immunomodulatory properties etc.*Gentiana lutea* is an important source of bitter phytoconstituents such as amarogentin, gentiopicrinor gentiopicroside, gentiolutelin and its dimethyl acetal, gentioluteol, gentanine, amaroswerin, gentioside including a new iridoid named gentiolutelin. Traditionally the plant is used as stomachic tonic, bitter tonic, dyspepsia, gastric inefficiency in infants, digestive tonic, catarrhal diarrhoea, anaemia, malarial disease etc. The present review is an effort to generate an interest among the mosses regarding its immense potential in preventing and treating several diseases.

Keywords:*Gentiana lutea* Lin., Yellow Gentian, Bitter Root, Gentianaceae, Phytochemistry, Pharmacological activities.

INTRODUCTION

Gentiana lutea belonging to Gentianaceae family which comprises more than 400 species spread in the mountain areas of central and Southern Europe, Americas, Australia and New Zealand, Alps, Jura, Massif Central, Pyrenees as well asadjoining continent up to the altitude of 2500 m[1, 2]. Yellow gentian is also widely cultivated in China, France and Germany[3]. Very early, it also started in Romania[4, 5] and later in Italy, Finland, and the Balkans[6, 7]. The plant is commonly known by other names in Ayurvedic: Traayamaana, Traayanti, Anujaa, Balbhra, Girisaanja, Girijaa; Chinese: Qin Jiao; German: Großer Enzian, (Berg)-Fieberwurzel, Hochwurzel; English: Bitter wort, Common gentian, Great yellow gentian, Yellow gentian; French: Gentiane jaune, Grande gentiane; Ital.: genziana maggiore. The freshly sliced sections of roots and rhizomes appear white in colour and do not have any odour. However, air dried drugs are dark or yellow coloured that have a strong, disagreeable odour and the taste is slightly sweet at first, but afterward very bitter[8]. The root is long and thick, generally approximately a foot long and an inch in diameter, but sometimes even a yard or extended and 2 inches in diameter and The stem rises 3 or 4 feet long or more, with a pair of wide lanceolate to elliptic leaves contrary to one another, at every joint[9, 10]. The large flowers are in whorls in the axils of the uppermost few pairs of leaves, forming big orange-yellow clusters[11]. The yellow flowers have elongated stalks and carry 3 to 10 flowering cymes in the axils of cup-shaped bracts. The fruit is a spiked cone-shaped capsule, up to 6cm long with numerous seeds. Flowering time is June to August. Strong plants produce seeds in abundance, and stock is easily raised from them[12, 13].For the flourishing cultivation of *G. lutea*, a heavy, loamy soil is extremely suitable, the deeper the better, as the stout roots sink a long way down into the soil. Plenty of moisture is also desirable and a position where there is shelter from cold winds and exposure to sunshine[14, 15].The roots are abundant in medicinal properties before the plants have flowered. A big clump of *G. lutea* is worthy of a prominent position in any large flower garden, quite apart from its medicinal value[16, 17].

***Taxonomical Classification*[18]**

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Gentianales
Family: Gentianaceae
Genus: Gentiana
Species: *Gentiana lutea*

Parts Used

The underground components are used consisting of the rhizome (rootstock) and roots.

Synonyms

About 180 species of Gentians, distributed widely throughout the world. The most frequently found native Gentians are *Gentiana crinita, Gentaian kurroo, Gentaina campestris* Lin., *Gentiana pneumonanthe* Lin., *Gentiana catesbaei, Gentiana verna, Gentiana nivalis, Gentiana acaulis, Gentiana cruciata, Gentiana quinqueflora, Gentiana amarelle* Lin. *Gentiana alba, Gentiana acaulis, Gentiana bavarica* etc[19].

Growth and Distribution

For the favourable growth of gentian is normally required rich, the loamy somewhat acidic soil in grassy alpine and sub-alpine continents. The long and fully grown fleshly roots of 2 to 5 year aged plants are dug up carefully and collected preferably in autumn. *G. lutea* is native to the hilly zones in Central and Southern Europe from Spain to Greece and spread up to the North-West regions of Turkey[20]. It is also spread on hill regions of China, Vosges Mountains, Yugoslavia (now known as Serbia and Crotia) and Jura[21].

MORPHOLOGY

Size and form

Gentiana lutea is an herbaceous perennial plant, rising to 1–2 m (3.3–6.6 ft) tall, with wide lanceolate to elliptic leaves 10–30 cm (3.9–11.8 in) long and 4–12 cm (1.6–4.7 in) broad. The flowers are yellow, with the corolla distributed nearly to the base into 5–7 narrow petals.

Roots

Dried, fragmented underground parts of *Gentiana lutea* L. are identified by thin, branched, the disagreeable odour with a strong and the taste is slightly sweet at first, but afterward persistent very bitter. Tap root system occurs as single or branched sub-cylindrical pieces of various lengths and usually 10-40 mm thick but hardly up to 80 mm thick at the crown (fig. 1). The quantity of the bitter constituents depends on the season as well as the age of the roots and the altitude[22].

Figure 1: Roots and leaves of *Gentiana lutea* L.

Leaves

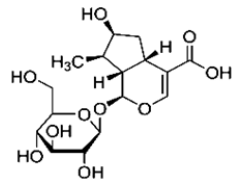
Gentian is a perennial herb that raises up to 180 cm morphologically *Gentiana lutea* leaves is characterized by green in colour, characteristic odour with bitter in taste.The size of leaves ranges from 10-30 cm long and 4-12 cm broad with broad lanceolate to elliptic leaves.

Flower

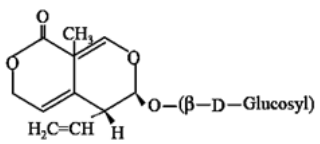
Gentiana lutea L. has brightly yellow trumpet-shaped flowers, which are designed in terminal and axillary clusters.*Gentiana lutea* L. var. aurantiaca is characterized by its orange flowers due to presence of red anthocyanin and yellow carotenoids[23]. The last flowers are frequently pentamerous, i.e. with 5-7 corolla lobes (petals) and 5 sepals without folds between lobes. This is one of the few species in Gentiana that has rotated, very deeply divided corollas and no secretory disk at the base of the ovary.

PHYTOCHEMISTRY

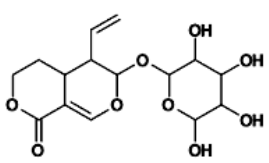
The dried gentian root contains gentisein, gentisin, iso-gentisin, gentinin and gentiamarin, bitter glycosides, together with gentianic acid (gentisin), the later being physiologically inactive[24]. The major constituents of *Gentiana lutea* are bitter iridoids commonly known as loganic acid (fig. a), secoiridoids[25], xanthones, gentiopicrin (fig. b) (2–8%, sometimes up to almost 10%), sweroside (fig. c) (0.05–0.08%), swertiamarin (fig. d), amarogentin (fig. e) (0.03–0.08%, bitter index: 58 x 106), amaroswerin are bitterest of whole compounds in this substance[26-28]. Secoiridoids glycoside contains, gentiopicroside (fig. b) (also known as gentiopicrin and gentiamarin)[29]. Gentiopicrin is crystalline pale yellow bitter glycosides occurs in fresh root, and may be isolated from it by treating with boiling alcohol. Gentinin crystalline glycoside is not a pure chemical substance, but a mixture of gentiopicrin and a colouring substance gentisin (gentianine) or gentlanic acid. Other constituents include two xanthone glycosides (fig. f) in which aglycone moiety is known as gentiosides (up to 0.1%) such as gentisin (gentianin) and isogentisin[30-32]. Trace amount of an alkaloids, phytosterols, triterpenes and essential oil are also reported in roots of Yellow gentian[33, 34]. Up to 1% xanthones: gentisine or gentianin (fig. g), isogentisine (fig. h), methylgentisine, 1-hydroxy-3, 7-dimethoxyxanthone, 1,3,7-trimethoxyxanthone, dihydroxy-1,3-dimethoxy-2,7-xanthone and gentisine-1- O-primveroside and gentioside-7-O-primveroside. Xanthones are also responsible for the yellow colour of the root[35-37]. *Gentiana lutea* contains bitter trisaccharides, gentianose which on hydrolysis yields two molecules of glucose and one molecule of fructose. The saccharine constituents of *Gentiana lutea* are dextrose, laevulose, sucrose and gentianose, a crystalline, fermentable sugar [38]. The root and rhizome also contain small quantities of free amino acids. The plant *Gentiana lutea* also contains pectin, tannin, triterpines (known as β- amyrin, lupeol) and traces of essential oils (0.1 – 0.2%) responsible for characteristic flavour. It is free from starch and yields 3 to 4 % ash[39].



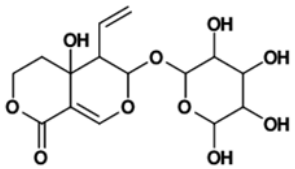
a: Loganic acid



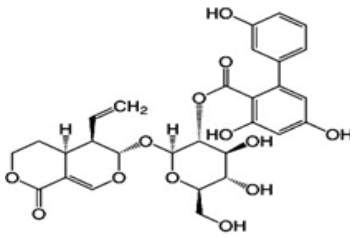
b: Gentiopicroside or Gentiopicrin



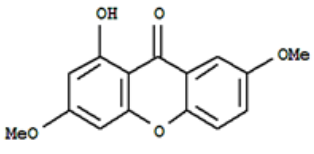
c: Sweroside



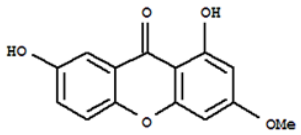
d: Swertiamarin



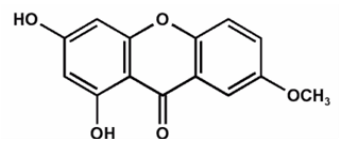
e: Amarogentin



f: Xanthone



g: Gentisin or Gentianin



h: Isogentisin

Figure 2: Chemical Structure of Phytoconstituents from *Gentiana lutea* Lin.

TRADITIONAL/ETHNOBOTANICAL USES

Gentiana lutea L.is widely used as folk medicine, for the mitigation, prevention, and treatment various ailments. Traditionally Gentian herb has been used in European and Eastern herbal medicine throughout the 3,000 years widely used as a bitter tonic, cholagogues, emmenagogue, febrifuge, refrigerant, stomachic bitter, stimulant, anorexia, laxative, excites appetite, indigestion, increases circulation and body temperature[40]. The extracts are applied in a variety of foods, beautifiers, and some anti-smoking products. The plant has been used externally to heal wounds, and internally to treat a sore throat, arthritic inflammation, and jaundice[41]. *Gentiana lutea* is the classic bitter digestive due to the presence of amarogentin (it can be tested at concentration 1:50,000 times). The bitter value of gentiopicroside is 12000 times more than amarogentin, so they are recognized as natural bitter standard. Yellow gentian stimulates the taste receptors on the tongue, causing an increase in the production of saliva and gastric secretion. The herb also used as a stimulant on gallbladder and liver, encouraging them to function more efficiently. The plant is also a remedy for diarrhoea, with relaxation of mucous membranes, chronic malarial poisoning, and dyspepsia, with mental and physical depression, general debility and exhaustion. In homeopathy, tincture of the root of *Gentiana lutea* is prescribed in anorexia, biliousness, dyspepsia, colic, diarrhoea, disorders of the stomach, fever, rawness in the throat and rheumatic pain [42].

PHARMACOLOGY

Although a lot of pharmacological investigations have been carried out based on the phytoconstituents present in it but a lot more can still be explored and utilized in a therapeutic manner. A summary of the finding of some of these studies is listed below.

Neuritogenic activity

Numerous natural products have been proven to prevent neurodegenerative disorders by potentiating the action of nerve growth factor. Among them, secoiridoids have recently brought attention for their potential use as neuritogenic compounds. A source of these compounds is the root of *Gentiana lutea* L. used in food products to improve digestion. This study was focussed on evaluating the neuritogenic action of methanolic extracts of cultivated, wild and commercial roots of *G. lutea* utilizing rat pheochromocytoma (PC-12) cells. Neuritogenic activity was assessed by xCELLigence real-time cell analysis system, neurite prominence image examination, and immunofluorescence staining. Extracts at 12.5 and 25 µg/ml with or without NGF revealed a marked stimulation of neuritogenesis, without cytotoxic activity, and their neuritogenic action was synergistic to NGF activity. These results represent the first evidence of the neuritogenic effects of *G. lutea* and of its significance use as a functional food ingredient[43].

Anti-inflammatory and wound healing

Gentiana lutea Linn (Gentianaceae) commonly recognized as Yellow gentian is widely used in the traditional system of medicine as an anti-inflammatory and wound healing agent. Investigations were carried out the effectiveness of alcohol and petrol ether extracts of rhizomes of *Gentiana lutea* at 500 and 1000 mg/kg doses per oral in the carrageenan-induced rat paw edema, xylol-induced mouse ear edema and cotton pellet-induced chronic inflammatory models. Both extracts exhibited notable dose-dependent anti-inflammatory activities in all of these models. Both extracts exhibited potent wound healing activity at 300 and 500 mg/kg, per oral, in excision, resutured incision and dead space wound models[44].

Choleretic Activity

The crude ethanolic extract prepared from roots of *G. lutea* ssp. *symphyandra* on the bile generation and liver in rats were studied. Bile flows of rats were administered by a single per *i.p.* dose of CCl_4 24 h preceding to tests was estimated following the cannulation of bile duct under urethane anaesthesia. After an equilibration interval of 1 h, the lyophilized extract was applied intraduodenally (500 mg/kg per *i.p.*), whereas control animals got physiological saline only. To monitor the outcome of multiple-dose therapy, rats received the same dose of *G. lutea.* ssp. *symphyandra* extract for 3 days (2 days before CCl_4 treatment) and their bile flows were estimated after the cannulation. In whole groups, bile samples were collected for 3 h at 15 min intervals. After the completion of bile flow experiment, rat livers were removed and put in neutral formaldehyde solution (10%) for the histological examination. It was observed that, multiple dose therapy of rats with the plant extract overcome the reduced bile flow due to CCl4, while single dose treatment was useless on the impaired bile flow. These data revealed that the extract prepared from *Gentiana lutea* ssp. *symphyandra* roots have a significant hepatoprotective activity[45].

Antioxidant activity

Gentiana lutea root is a remedial herb, traditionally used as a bitter tonic in GIT ailments for better digestive system. The active constituents of *G. lutea* were observed to be secoiridoid bitter compounds as well as several other active compounds causing the pharmacological effects. The purpose of current study was to assess the effects of an extract of Yellow Gentian on lipid oxidation throughout storage of an emulsion. *G. lutea* extracts exhibited remarkable antioxidant activity estimated by DPPH scavenging assay and Trolox equivalent antioxidant capacity (TEAC) assays. An amount of 0.5% w/w *G. lutea* lyophilise was capable to inhibit lipid oxidation throughout storage ($p < 0.05$). A mixture of *G. lutea* with 0.1% (w/w) BSA showed a good synergic impact and beneficial antioxidant activity in the emulsion. Quantitative analysis of HPLC confirmed that *G. lutea* contained secoiridoid-glycosides (gentiopiocroside and sweroside) and post column analysis revealed radical scavenging activity of *G. lutea* extract towards the ABTS radical. The results from this study highlight the potential of *G. lutea* as a food ingredient in the design of better food commodities[46]. Investigators was also observed that *Gentiana lutea* extracts also exhibits the inhibitory action on the enzyme myeloperoxidase, as well as the antioxidant activity of these extracts and their relationship with the total polyphenol amount. Extracts were

prepared using methanol (100%), aqueous and ethanol-water solutions (96, 75, 50 and 25% v/v) as solvents for extraction. Moreover, isovitexin, amarogentin and gentiopicroside, pharmacologically active constituents of *G. lutea* were examined as potential inhibitors of myeloperoxidase. Antioxidant activity of extracts was concluded using the 2, 2-diphenyl-1-picrylhydrazyl (DPPH) scavenging test and also using cyclic voltammetry[47, 48].

Antimicrobial Activity

The methanolic extracts of *Gentiana lutea* L., flowers and leaves are usually with the isolated mangiferin, isogentisin and gentiopicrin, were used to review the antimicrobial activity of the plant. A kind of Gram-positive and Gram-negative bacteria as well as the yeast Candida albicans has been included in this investigation. Both extracts and isolated compounds showed antimicrobial activity with MIC values ranging from 0.12 - 0.31 mg/ml. Our study showed that the synergistic activity of the pure compounds may be responsible for the significant antimicrobial effect of the extracts. Quantification of the secondary metabolites was examined by using HPLC[49].

Anti-tubercular activity

The anti-tubercular activity of four ethanol extract A, B, C and D prepared from leaves, flowers and roots of *G. lutea*, as well as of the isolated compound isogentisin was evaluated against *Mycobacterium bovis*. Extract D, obtained from flowers, and showed strong inhibition with the minimum inhibitory concentration of 1000 mug/ml. As the extract D consisted of the considerable proportion of isogentisin that compound was isolated and was subjected to anti-tubercular testing under identical experimental conditions[50].

Radio-protective activity/ sensitizing actions

Radio-protective or sensitizing actions of *Gentiana lutea* aqueous-ethanol extract and mangiferin on radiation-induced effects on different types of cells were examined. The study focused on the decreasing survival of normal human immunocompetent cells, the survival of the malignant cells *in vitro*, and the survival of *ex vivo* irradiated cells before and after consumption of the extract by healthy volunteers. The *in vitro* experiments showed that mangiferin could inhibit cytotoxic action of ionizing irradiation (doses of 6 and 8 Gy) only on normal resting Human Peripheral Blood Mononuclear Cells (PBMC), not stimulated for proliferation. Orally consumed *G. lutea* extract showed the potential to reduce the cytotoxic effect of x-ray irradiation on normal human immunocompetent cells PBMC of some healthy people, without changing the susceptibility of malignant cells to be destroyed by irradiation[51].

CNS Stimulan

A methanolic extact of *Gentiana lutea* ssp. *symphyandra* roots has been investigated for its potential impacts on the central nervous system of mice. At doses of 250 and 500 mg/kg per *i.p*., the methanol extract of Gentiana roots induced a significant improvement in the swimming endurance test and showed weak analgesic activity, but no lethality in mice implying remarkable activity on the central nervous system. However, there was no indication of sedation or muscular fatigue at the doses exercised. HPLC analysis exhibit that three secoiridoid compounds, gentiopicroside, swertiamarine and sweroside were reported and may have been responsible for the CNS effects of the methanol extract of *Gentiana lutea* ssp*. symphyandra* roots[52].

Anti-atherosclerotic effects

Investigators were found that anti-atherosclerotic propertiesof *Gentiana lutea*, is due to its component isovitexin. In this study, we sought to investigate the protective mechanism of *Gentiana lutea* aqueous root extract and isovitexin on endothelial inflammation, smooth muscle cell migation, and on the onset and progression of atherosclerosis in streptozotocin (STZ)-induced diabetic rats. It was approved that both Yellow gentian extract and isovitexin, block leukocyte adhesion and augmentation of reactive oxygen species in human umbilical vein endothelial cells and rat aortic smooth muscle cells, following TNF-alpha and platelet originated growth factor-BB (PDGF-BB) challenges respectively. Both the extract and isovitexin blocked TNF-α induced expression of ICAM-1 and VCAM-1 in HUVECs. PDGF-BB influenced migration of RASMCs and phospholipase C-γ activation, were also abrogated by *Gentiana lutea* extract and isovitexin. Fura-2 based ratiometric investigations demonstrated that both the extract and isovitexin, inhibit PDGF-BB mediated intracellular calcium rise in RASMCs. Supplementation of conventional nutrition with 2% *Gentiana lutea* root powder for STZ rats diminished entire cholesterol in the blood. Oil Red O staining demonstrated lowered lipid build up in the aortic wall of diabetic animals upon treatment with same plant. Medial thickness and deposition of collagen in the aortic portion of diabetic rats were also reduced upon supplementation. Immunohistochemistry confirmed diminished expression of vascular cell adhesion molecule-1 (VCAM-1), inducible nitric oxide synthase (iNOS), and vascular endothelial cadherin (VE-cadherin) in aortic segments of diabetic rats following *Gentiana lutea* treatment. Therefore, *Gentiana lutea* root extract/powder and isovitexin exhibit significant anti-atherosclerotic activities[53].

Synergistic effect

Gentiana lutea Linn., is herb known for its therapeutic characteristics, with a long tradition of use for the therapy of a variety of disorders including the use as a remedy for digestion, also in food commodities and as bitter beverages. The objective of the current investigation is to estimate, the genotoxicity of gentian alone, and its antigenotoxicity against methyl methanesulfonate. The water infusion of the radical component of gentian was evaluated in-vivo using the Drosophila wing spot test. While the antigenotoxic study, two types of treatment with gentian and methyl methanesulfonate were conducted chronic co-treatment, as well as post-treatment by gentian after the acute appearance with methyl methanesulfonate. Water infusion of gentian alone did not exhibit genotoxicity. The results of co- and post-treatment analyses with gentian show that gentian enhanced the frequency of mutant clones over the values obtained with methyl methanesulfonate alone, instead of reducing the genotoxicity of methyl methanesulfonate, for 22.64% and 27.13% respectively. This result suggests a synergism of gentian with methyl methanesulfonate, and that water infusion of gentian used in traditional medicine may have selective effects about genotoxicity indicating careful use[54].

Atherosclerosis

Gentiana lutea plants are commonly practiced in traditional Serbian medicine for their useful GIT and anti-inflammatory characteristics. The objective of the investigation was to conclude that aqueous root extracts of *Gentiana lutea* comprises gentiopicroside, gentisin, bellidifolin-8-O-glucoside, demethylbellidifolin-8-O-glucoside, isovitexin, swertiamarin and amarogentin inhibits multiplication of aortic smooth muscle cells in response to PDGF-BB. Cell proliferation and cell cycle investigation were performed based on alamar blue assay and propidium iodide labeling frequently. In primitive cultures of rat aortic smooth muscle cells (RASMCs), PDGF-BB (20 ng/ml) influenced a two-fold increase in cell propagation which was significantly blocked by the root extract (1 mg/ml). The root extract also prevented the S-phase entrance of synchronized cells in response to PDGF. Moreover, PDGF-BB induced the extract also blocked ERK1/2 activation and consequent increase in cellular nitric oxide levels. These impacts of extract were due to blockade of PDGF-BB-induced expression of iNOS, cyclin D1 and proliferating cell nuclear antigen (PCNA). Docking analysis of the extract ingredients on MEK1, the upstream ERK1/2 activating kinase using AutoDock4, showed a possible

junction of isovitexin to the inhibitor binding site of MEK1. Analyses conducted with purified isovitexin demonstrated that it successfully blocks PDGF-induced ERK1/2 activation and proliferation of RASMCs in cell culture. Therefore, *Gentiana lutea* can produce the novel medicinal agent for prevention and treatment of atherosclerosis[55].

Gastroprotective effects

Gentianae Radix, the dried root and rhizoma of *Gentiana lutea* L. (Gentianaceae), are traditionally used a remedy for liver and stomach inflammation, eye troubles, etc. Current study revealed that, the gastroprotective effects of the methanol extract of Gentian root were evaluated using different gastric lesion models. In pylorus-ligated rats, administration of methanol extract in the duodenum suppressed gastric juice secretion and total acid output in a dose-dependent manner. As per oral or duodenum administration of methanol extract exhibits significant action against acute gastric ulcer induced by aspirin plus pylorus ligation, water-immersion restraint stress-induced ulcers, and gastric mucosal injury induced by ethanol. Furthermore, four secoiridoid glycosides, amarogentin, gentiopicroside, amaroswerin, and swertiamarin, were obtained from Gentian root or Swertia herb, and their protective effects against stress-induced ulcers and ethanol-induced gastric mucosal injury were evaluated[56].

Blood coagulation

The dry extract of *Gentiana Lutea* were investigate the pharmacological influence of obtained extract on the coagulating properties of blood revealed that after its per oral instillation into experimental animals the time of the formation of active thromboplastin reliably increases, while the time of thrombin and fibrinous cluster formation is slightly decreases in comparison with those indices in the animals, that did not receive phyto-preparation, at the same time morphological appearance of the peripheral blood remains unchanged. Dry extract of terrestrial parts of *Gentiana Lutea* prepared in accordance to the technology recommended by us, together with widely known pharmacological effects, is characterized with new activity - influence on haemostasis. Obtained preliminary data concerning influence of the extract on coagulation of the blood request further deep studies of its mechanism. Revealed new activity of the terrestrial parts of *Gentiana Lutea* and the studies of the mechanism of its activity will serve in future as a basis for the recommendation of its use in new nosology. Terrestrial parts of *Gentiana lutea* L. are proposed as an alternative of the underground parts of the plant. Alongside with that, it is expedient to continue the studies devoted to the development of the haemostatic remedies of plant origin with systemic and local action (sponges, films, skin glues) from terrestrial parts of *Gentiana lutea*[57].

INTERACTIONS

According to laboratory confirmation, gentisin and isogentisin from *Gentiana lutea* may potently inhibit monoamine oxidase types A and B. Gentian may interact with antidepressant herbs and supplements, antifungal herbs, monoamine oxidase inhibiting herbs and supplements[58]. Three monoamine oxidase inhibitors isolated from *Gentiana lutea* have shown competitive MAO inhibition more effectively against MAO-B than against MAO-A[59]. Gentian may raise blood sugar levels. Caution is advised with some gentian preparations that may contain sugar and may interfere with blood sugar control. *Gentiana lutea* extract may protect against conceptive toxicity when administered concurrently with ketoconazole related agents[60].

PESTS AND DISEASES

Under high humidity conditions, nursery plants can be infected by *Alternaria alternata, Fusarium oxisporum, Aspergillus flavus, Penicillium* spp., the roots can be damaged by *Botrytis cinerea*. Regarding pests, only snails in rainy years and mice that gnaw the roots were recorded [61-62].

CONCLUSION

In recent years, traditional and pharmacological utilization of natural products, mainly of plant source obtained much consideration as they are well tested for their safety and efficacy for human use. They obviously deserve scrutiny on modern scientific lines such as phytochemical investigations, biological evaluation in experimental animal models, drug interactions, and investigation of the molecular mechanism of actions of isolated active principles. The active constituent and the bioactivities associated with these ingredients as presented in this short but concise review are strongly deemed to be valuable for those researchers who are previously running or planning to begin evaluating a particular biological aspect of this precious natural remedy. Thorough screening of literature available on *Gentiana lutea* explained the evidence that it is a natural remedy among the many ethnic groups, Vaidya, Hakims and Ayurvedic practitioners for remedy of kind of ailments. In this regards, further studies need to be carried out to explore *Gentiana lutea* for its potential in preventing and treating diseases. The current study is an effort to compile all basic information on its taxonomical, phytochemical as well as pharmacological profile published till now in different textbooks and journals.

Acknowledgement

Authors are thankful to Dr. N. P. Yadav, Scientist, Department of Phytopharmacognosy, Central Institute of Medicinal & Aromatic Plants, Lucknow for providing library and internet facility for free access of journals. Authors are also thankful Er. Mahesh Goel, Managing Director, Goel Institute of Pharmacy & Sciences, Lucknow, Uttar Pradesh, India for providing the library facilities to compilation of current review.

Source of support – Nil.

Conflict of interest – None declared.

REFERENCES

1. Kohlein F. In: Kohlein F, editor. Gentians, London: Christopher Helm, 1991; p. 9-27.
2. Nastasijevic B, Milosevic M, Janjic G, Stanic V, Vasic V. *Gentiana lutea* Extracts and their Constituents as Inhibitors of Synaptosomal Ecto-NTPDase*, Gentiana lutea* Extracts and their Constituents as Inhibitors of Synaptosomal Ecto-NTPDase. International J Pharmacol. 2016;12:272-89.
3. Franz C, Fritz D. Cultivation aspects of *Gentiana lutea* L. Acta hort l978;73:307-14.
4. Camelia SS. Peculiarities for Agricultural Techonolgy of *Gentiana Lutea,* Scientific Papers Series Management. Econom Engineer AgriRural Develop 2015;15:449-54**.**
5. Heltmann H. Introducerea in Cultura a Speciei *Gentian alutea* L. in Romania. Rev Medical1970;16:389.
6. Catorci A, Piermarteri K, Tardella FM. Pedo-climatic and land use preferences of *Gentiana lutea* subsp. lutea in central Italy. Plant Ecol Evol 2014;147:176-86.
7. Bezzi A, Aiello N. The cultivation of yelow gentian (*Gentiana lutea* L.) on the pre-Alps and Apenninic Mountains: results and applications. Acta hort 1993;331:19-5.
8. Khare CP. Indian Medicinal Plants: An Illustrated Dictionary, Springer Science, Business, MediaVerlag Berlin, Heidelberg, 2007; p. 290-91.
9. Radanovic, Marković TL, Janković T. Morphological and chemical parameters of importance for cultivation of *Gentiana lutea* L. in mountain region of Serbia,1st International Scientific Conference on Medicinal, Aromatic and Spice Plants, 2007; p. 28-32.
10. Aiello N, Bontempo R, Vender C. Use of morphological features and amarogentin content for characterization of wild yellow gentian (*Gentiana lutea* L.) populations in north-east Italy. Acta Bot Gallica 2013;160:33-41.

11. Fritz D, Bezzi A, Marocke R. Cultivation of *Gentiana lutea* L. in marginal arable areas (e.g. hilly upland regions). Results of the AGRIMED working group (1986–1988) *Gentiana lutea*. In: Marshall G, Svoboda K, Editors. The Production and Impact of Special Minor Crops in the Rural Community. Proceedings of a Workshop in the CEC Programme. Belgium, 1993; p. 129-39.
12. Hatakeyama Y, Honma N, Henmi S. Studies on the cultivation of *Gentiana lutea* L. Eisei Shikenjo Hokoku 1969;87:52-8
13. Franz C, Fritz D. Cultivation of *Gentiana lutea* and main substances of some ecotypes. Planta Med 1975;28:289-300.
14. Ho T, Liu SA. Worldwide Monograph of Gentiana. Science Press, Beijing, China, 2001.
15. Radanović D, Marković T, Mladenović SA. Production of Yellow Gentian (*Gentiana lutea* L.) Nursery Plants Suitable for Transplanting and Cultivation under Dry Farming Conditions in Mountain Region of Serbia. Ratarstvo i povrtarstvo2013;50:13-21.
16. Alessandro B, Nicola A. The cultivation of Yellow gentian (*Gentiana lutea* L.) on the pre-alps and Appenninic Mountains: results and applications (1). Acta hort (ISHS) 1993;331:19-6.
17. Richard VT, Bayne J. A Pharmacopoeia including the outlines of *Materia Medica* and therapeutics for the use of practitioners and students of veterinary medicine. In: James Bayne, editors. 5th ed. Philadelphia: P. Blakiston Son & Co., 1895; p. 126.
18. http://www.wikidoc.org/index.php/*Gentiana_lutea*.
19. https://en.wikipedia.org/wiki/Gentiana.
20. Aiello N, Bontempo R, Vender C. Use of morphological features and amarogentin content for characterization of wild yellow gentian (*Gentiana lutea* L.) populations in north-east Italy. Acta Botanica Gallica 2013;160:33-41.
21. Radanović D, Marković T, Aiello N, Fusani P. Cultivation trials on *Gentiana lutea* L. in Southern and South Eastern Europe. J Appl Res Medi Aromat Plants. 2014;1:113-22.
22. González LÓ, Mayo S, Rodríguez GÁ, Guzmán C, da Silva PH, Casquero PA. Evolution with age of main bitter compounds in the roots of cultivated *Gentiana lutea* subsp. aurantiaca. Planta Med 2016;81(S 01):S1-S381.
23. Berman J, Sheng Y, Gómez LG, Tania V, Xiuzhen N, Gemma F,*et al*. Red Anthocyanins and Yellow Carotenoids Form the Color of Orange-Flower Gentian (*Gentiana lutea* L. var. aurantiaca). Plos One 2016;11(9):1-20.
24. Atkinson JE,Gupta P,Lewis JR. Some phenolic constituents of *Gentiana lutea.* Tetrahedron 1969;25:1507-11.
25. Wu S, Zhao Y, Sun W, Thorimbert S, Dechoux L, Sollogoub M, *et al*. Research Progress of Natural Product Gentiopicroside- A Secoiridoid Compound. Mini Rev Med Chem 2017;17:62-7.
26. Verotta L. Isolation and HPLC determination of the active principles *of Rosmarinus officinalis* and *Gentiana lutea*. Fitoterapia 1985;56:25-29.
27. Hostettmann K, Bellmann G, Tabacchi R, Jacot GA. Phytochemistry of the *Gentiana* genus III. Flavonic and xanthonic compounds in the leaves of *Gentiana lutea*. Helv Chim Acta 1973;56:3050-4.
28. Aberham A, Pieri V, Croom Jr, Ellmerer E, Stuppner H. Analysis of iridoids, secoiridoids and xanthones in *Centaurium erythraea*, *Frasera caroliniensis* and *Gentiana lutea* using LC–MS and RP-HPLC. J Pharm Biomed Anal. 2011;54:517-25.
29. Ando H, Hirai Y, Fujii M, Hori Y, Fukumura M, Niiho Y,*et al*. The chemical constituents of fresh gentian root. J Nat Med. 2007;61:269-79.
30. Menković NR, Živković JČ, Šavikin KP, Janković TR, Zdunić GM, Pljevljakušić DS. Optimization of ultrasound-assisted extraction of isogentisin from *Gentiana lutea* L. roots by response surface methodology. Planta Med 2016; 81(S 01):S1-S381.
31. Aberham A, Schwaiger S, Stuppner H, Ganzera M. Quantitative analysis of iridoids, secoiridoids, xanthones and xanthone glycosides in *Gentiana lutea* L. roots by RP-HPLC and LC-MS. J Pharm Biomed Anal. 2007;5:45(3):437-42.
32. Aberham A, Pieri V, Croom EM, Ellmerer E, Stuppner H. Analysis of iridoids, secoiridoids and xanthones in *Centaurium erythraea*, *Frasera caroliniensis* and *Gentiana lutea* using LC-MS and RP-HPLC. J Pharm Biomed Anal. 2011;54:517-25.
33. Citová I, Ganzera M, Stuppner H, Solich P. Determination of gentisin, isogentisin, and amarogentin in *Gentiana lutea* L. by capillary electrophoresis. J Sep Sci. 2008; 31:195-200.
34. Leung AY. Encyclopedia of Common Natural Ingredients Used in Food, Drugs, and Cosmetics, Wiley, 1980.
35. Hayashi T, Yamagishi T. Two xanthone glycosides from *Gentiana lutea*. Phytochemistry 1988;27:3696-99.
36. Hostettmann K, Bellmann G, Tabacchi R, Jacot-Guillarmond A. Phytochemistry of the *Gentiana* genus III. Flavonic and xanthonic compounds in the leaves of *Gentiana lutea*. Helv Chim Acta 1973;56:3050-54.
37. Pan Y, Zhao YL, Zhang J, Li WY, Wang YZ. Phytochemistry and Pharmacological Activities of the Genus Gentiana (Gentianaceae). Chem Biodivers 2016;13:107-50.
38. Rossetti, V, Lombard A, Sancin P, Buffa M, Menghini A. Composition of *Gentiana lutea* L., dried roots harvested at different altitudes. Plant Med Phytother 1984;18:15-23.
39. Biren NS. Textbook of Pharmacognosy and Phytochemistry, Elsevier India-Botanical chemistry, 2009; p. 273-4.
40. Lloyd Brothers. Dose book of Specific Medicines. Lloyd Brothers, Cincinnati, 1907; p. 139.
41. Ellingwood F. American Materia Medica, Therapeutics, and Pharmacognosy. Ellingwood's Therapeutist. Chicago, 1919; p. 267.
42. Khare CP. Indian Herbal Remedies: Rational Western Therapy, Ayurvedic and Other Traditional Usage, Botany. Springer Science & Business Media, 2011; p. 231-2.
43. Ahmed MM, Giovanni C, Miris D, Kaya E, Maggi F, Sagratini G,*et al*. Evaluation of neuritogenic activity of cultivated, wild and commercial roots of *Gentiana lutea* L. J Funct Foods. 2015;19:164-73.
44. Mathew A, Taranalli AD, Torgal SS. Evaluation of Anti-inflammatory and Wound Healing Activity of *Gentiana lutea* Rhizome Extracts in Animals. Pharma Biology 2008;42:8-12.
45. Oztürk N, Herekman-Demir T, Oztürk Y, Bozan B, Başer KH. Choleretic activity of *Gentiana lutea* ssp. symphyandra in rats. Phytomed 1998;5:283-8.
46. Nurul AMA, Segovia F,Xavier MF,Gil E, Almajano MP. Screening of Antioxidant Activity of *Gentian Lutea* Root and Its Application in Oil-in-Water Emulsions. Antioxidants (Basel) 2014;3:455-71.
47. Nastasijević B, Lazarević-Pašti T, Dimitrijević-Branković S, Pašti I, Vujačić A, Joksić G, *et al*. Inhibition of myeloperoxidase and antioxidative activity of *Gentiana lutea* extracts. J Pharm Biomed Anal. 2012; 66:191-6.
48. Kusar A, Zupancic A, Sentjurc M, Baricevic D. Free radical scavenging activities of yellow gentian (*Gentiana lutea* L.) measured by electron spin resonance. Hum Exp Toxicol 2006;25:599-604.
49. Katarina Šavikin, Nebojša Menkovic´, Gordana Zdunic´, Tatjana Stevic´, Dragoja Radanovic´, Teodora Jankovic. Antimicrobial Activity of *Gentiana lutea* L. extracts. J Biosci. 2009;64:339-2.
50. Menkovik N, Savikin K, Cebedzik R. Investigation of the activity of *Gentiana lutea* extracts against *Mycobacterium bovis*. Pharm Pharmacol Lett1999;9:74-75.
51. Menkovic N, Juranic Z, Stanojkovic T, Raonic-Stevanovic T, Savikin K, Zdunić G, *et al*. Radioprotective activity of *Gentiana lutea* extract and mangiferin. Phytother Res 2010;24:1693-6.
52. Öztürk N, Başer KHC, Süleyman A, Öztürk Y, Çaliş A. Effects of *Gentiana lutea* ssp. symphyandra on the Central Nervous System in Mice. Phytother Res 2002;16:627-31.
53. Kesavan R, Chandel S, Upadhyay S, Bendre R, Ganugula R, Potunuru UR,*et al*. *Gentiana lutea* exerts anti-atherosclerotic effects by preventing endothelial inflammation and smooth muscle cell migration. Nutr Metab Cardiovasc Dis 2016;26:293-301.
54. Patenković A, Stamenković-Radak M, Nikolić D, Marković T, Anđelković M. Synergistic effect of *Gentiana lutea* L. on methyl methanesulfonate genotoxicity in the Drosophila wing spot test. J Ethnopharmacol. 2013;27:632-6.
55. Kesavan R, Uma RP, Nastasijevic B, Avaneesh T, Gordana J, Dixit M. Inhibition of Vascular Smooth Muscle Cell Proliferation by *Gentiana lutea* Root Extracts. Plos One 2013;8:1-13.
56. Yujiro N, Takashi Y, Yoshijiro N, Toshinori Y, Hidehiro A, Yasuaki H, *et al*. Gastroprotective effects of bitter principles isolated from Gentian root and Swertia herb on experimentally-induced gastric lesions in rats. J Nat Med. 2006;60:82-88.
57. Bakuridze AD, Nikolaev SM, Tsagarenshvili NT, Kurdiani NG, Mikaia GA. Influence of *Gentiana lutea* L extract on blood coagulation. Georgian Med News 2009;172:89-1.
58. Citová I, Ganzera M, Stuppner H, Solich P. Determination of gentisin, isogentisin, and amarogentin in *Gentiana lutea* L. by capillary electrophoresis. J Sep Sci. 2008; 31:195-200.
59. Haraguchi H, Tanaka Y, Kabbash A, Fujioka T, Ishizu T, Yagi A. Monoamine oxidase inhibitors from *Gentiana lutea*. Phytoch 2004; 65:2255-60.
60. Amin A. Ketoconazole-induced testicular damage in rats reduced by *Gentiana extract*. Exp Toxicol Pathol 2008;59:377-4.

61. Kostic M, Rajkovic S, Drazic, Stankovic S. Bioagents of yellow gentian (*Gentiana lutea* L.). J Sci Agri Res. 2006; 67.
62. Millaku F, Gashi B, Abdullai K, Aliu S, Osmani M. Elez Krasniqi1, Effects of cold-stratification, gibberellic acid and potassium nitrate on seed germination of yellow gentian (*Gentiana lutea* L.). Afri J Biotechnol. 2012;11:13173-78.

HOW TO CITE THIS ARTICLE
Prakash O, Singh R, Kumar S, Srivastava S, Ved A. *Gentianalutea*Lin. (Yellow Gentian): A Comprehensive Review.J Ayu Herb Med 2017;3(3):175-181.