IJBPAS, September, 2016, 5(9): 2231-2238

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

NUPHAR LUTEUM – A REVIEW

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Received 5th June 2016; Revised 26th July; Accepted 4th August 2016; Available online 1st Sept. 2016

ABSTRACT

Nuphar luteum (Yellow Water-lily, Brandy-Bottle) synonym *Nuphar lutea* is an aquatic plant of the family Nymphaeaceae, native to temperate regions of Europe, northwest Africa, and Western Asia. It has been used in dysentery, gonorrhoea and leucorrhoea. The leaves and roots have been used as a poultice for boils and inflamed skin. Medicinal herb contains multitude of chemical compounds like alkaloids, anthraquinone glycosides, terpenoids, saponins, flavonoids, tannins and phenolic compounds, proteins, amino acids, carbohydrates, starch and vitamin C. Plant possesses anti-leishmanial activity, antineoplastic, anti-inflammatory, antifungal, and antibacterial activities. This review illustrates its major constituents, pharmacological actions substantiating the claims made about this plant in the traditional system of medicine.

Keywords: Alkaloids, Anti-leishmanial, *Nuphar luteum*, Pharmacological.

INTRODUCTION

Genus *Nuphar*

Nuphar is genus of aquatic plants in the family Nymphaeaceae, with a temperate to subarctic Northern Hemisphere distribution. There are seven known species of this genus such as *Nuphar advena* (Aiton) W.T.Aiton commonly known as Spatterdock, *Nuphar japonica* DC, *Nuphar luteum(* L.) Sm. Known as Yellow water-lily, *Nuphar polysepala* Engelm known as great yellow pond-lily, *Nuphar pumila* (Timm) DC. Commonly known as Least

water-lily, *Nuphar sagittifolia*(Walter) Pursh commonly named as Arrow-leaved water-lily and *Nuphar variegata* Engelm. ex Durand (the variegated pond-lily). The number of species in the genus is still under review [1,2]. *Nuphar lutea* (Yellow Water-lily, Brandy-Bottle) is an aquatic plant of the family Nymphaeaceae, native to temperate regions of Europe, northwest Africa, and Western Asia [3,4].

***Nuphar luteum* plant**

ETHNOPHARMACOLOGY

The root is astringent, demulcent and anodyne. It has been used in dysentery, gonorrhoea and leucorrhoea. The leaves and roots have been used as a poultice for boils and inflamed skin, while an infusion has been used as a gargle for oral and pharyngeal ulcers. It was an important medicinal plant for Aboriginal peoples. Thompson peoples mixed dry powdered leaves with grease to make an ointment for infections, bites and swellings. Tsimshian peoples boiled the heart of the rootstock and ate it for bleeding lungs and as a contraceptive. Other groups used the root to treat tuberculosis. An infusion of dried, grated plant was taken for heart trouble [5].

TOXICOLOGICAL REPORTS

The use of natural plants as emergency food in Finland and northern Europe has been described by Airaksinen MM et al. The chemical contents of the commonly used "pettu" (pine bark), lichen (Cetraria islandica, Cladonia sp.) and water plants (*Calla palustris*, *Menyathes trifoliata*, Nymphea sp. and *Nuphar luteum*) are described and their toxicity after traditional pretreatments were studied in mice and rats. As 50% w/w mixture in normal food none of them were tolerated by mice. However, rats tolerated 25% of "pettu" and ash-treated *C. islandica* in 3-month tests rather well, although the body weight did not increase as much as in controls. At the end of experiment in the lichen group, the rats had proteinuria, and on autopsy some tubular changes were found probably due to high concentrations of lead in the lichen and kidneys. All the rhizomes studied contain toxic compounds, but they, particularly *calla*, would be nutritionally valuable. Boiling poorly eliminated their toxicity, but after baking at 180-200^{o}C the most toxic *Nuphar* and *Calla* were well tolerated as 25% mixture during a 6-week test [6].

PHYTOCHEMICAL REPORTS

The preliminary phytochemical screening of petroleum ether, chloroform and methanol extracts of rhizomes of *Nuphar luteum* showed the presence of different chemical constituents. The phytochemical screening of petroleum ether extract showed the presence of anthraquinone and cardiac glycosides whereas chloroform extract along with anthraquinone and cardiac glycosides showed presence of alkaloids, terpenoids and carbohydrates. Maximum diversity of chemical constituents were present in methanol extract that includes alkaloids, anthraquinone glycosides, terpenoids, saponins, flavonoids, tannins and phenolic compounds, proteins, amino acids, carbohydrates, starch and vitamin C [7]. The dry rhizomes of *Nuphar luteum* have yeilded three sulphur containing alkaloids : thiobinupharidine, neothiobinupharidine and nuphaleine ($C_{30}H_{42}O_4N_2S$)[8]. From the rhizomes of *Nuphar luteum* a new C_{15} alkaloid, nuphacristine, has been isolated. The structure and stereochemistry of nuphacristine have been established on the basis of spectral analysis and chemical transformations [9]. Four new alkaloids were isolated from the rhizomes of *Nuphar lutea*. Their structures were established as syn-6-hydroxythiobinupharidine sulphoxide, syn-6'-hydroxythiobinupharidine sulphoxide, syn-6,6'-dihydroxy thiobinupharidine sulphoxide and anti-thiobinupharidine sulphoxide[10].

PHARMACOLOGICAL REPORTS

Anti-leishmanial activity

The extracts prepared from 522 plants collected from various parts of the North America by Jain S et al. were screened *in vitro* against blood stage trypamastigote forms of *T. brucei*. Active extracts were further screened at concentrations ranging from 10 to 0.4 µg/mL. Active extracts were also investigated for toxicity in Differentiated THP1 cells at 10 µg/mL concentration. The results were computed for dose-response analysis and determination of IC50/IC90 values. A significant number (150) of extracts showed >90 % inhibition of growth of trypomastigote blood forms of *T. brucei* in primary screening at 20 µg/mL concentration. The active extracts were further investigated for dose-response inhibition of *T. brucei* growth. The antitrypansomal activity of 125 plant extracts was confirmed with IC50 < 10 µg/mL. None of these active extracts showed toxicity against differentiated THP1 cells. Eight plants extracts namely, *Alnus rubra*, *Hoita macrostachya*, *Sabal minor*, *Syzygium aqueum*, *Hamamelis virginiana*, *Coccoloba*

pubescens, *Rhus integrifolia* and *Nuphar luteum* were identified as highly potent antitrypanosomal extracts with IC50 values <1 μg/mL [11].

Anti-cancer activity

Ozer J et al. screened thirty-four methanolic plant extracts for inhibition of the constitutive nuclear factor κB (NFκB) activity by a NFκB-luciferase reporter gene assay. Strong inhibition of NFκB activity was found in extracts of leaf and rhizome from *Nuphar lutea* L. synonym *Nuphar luteum*. The inhibitory action was narrowed down to a mixture of thionupharidines and/or thionuphlutidines that were identified in chromatography fractions by one- and two-dimensional NMR analysis. Dimeric sesquiterpene thioalkaloids were identified as the major components of the mixture. The *Nuphar* alkaloids mixture (NUP) showed a dose dependent inhibition of NFκB activity in a luciferase reporter gene assay as well as reduction of nuclear NFκB subunits expression as tested by western blots and immunohistochemistry. Decreased DNA binding was demonstrated in electro mobility shift assays. NUP inhibited both inducible and constitutive NFκB activation and affected the canonical and alternative pathways. Suppression of NFκB was not cell type specific. Induction of apoptosis by the alkaloid mixture was demonstrated by time-dependent and dose-dependent cleavage of procaspase-9 and paRp. Synergistic cytotoxicity of the active mixture with cisplatin and etoposide was demonstrated. Overall, our results show that NUP inhibits the NFκB pathway and acts as a sensitizer to conventional chemotherapy, enabling the search for its specific target and application against cancer and inflammation [12].

Yildirim AB *et al*., investigated antibacterial and antitumor activities of 51 different extracts prepared with 3 types of solvents (water, ethanol and methanol) of 16 different plant species *Ajuga reptans* (*A. reptans*) L., *Phlomis pungens* (*P. pungens*) Willd., *Marrubium astracanicum* (*M. astracanicum*) Jacq., *Nepeta nuda* (*N. nuda*) L., *Stachys annua* (*S. annua*) L., *Genista lydia* (*G. lydia*) Boiss., *Nuphar lutea* (*N. lutea*) L., *Nymphaea alba* (*N. alba*) L., *Vinca minor* (*V. minor*) L., *Stellaria media* (*S. media*) L., *Capsella bursa-pastoris* (*C. bursa-pastoris*) L., *Galium spurium* (*G. spurium*) L., *Onosma heterophyllum* (*O. heterophyllum*) Griseb., *Reseda luteola* (*R. luteola*) L., *Viburnum lantana* (*V. lantana*) L. and *Mercurialis annua* (*M. annua*) L.) grown in Turkey was conducted. Antibacterial activity was evaluated with 10 bacteria including *Streptococcus pyogenes* (*S. pyogenes*), *Staphylococcus aureus* (*S. aureus*), *Staphylococcus epidermidis* (*S.*

epidermidis), *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*), *Salmonella typhimurium* (*S. typhimurium*), *Serratia marcescens* (*S. marcescens*), *Proteus vulgaris* (*P. vulgaris*), *Enterobacter cloacae* (*E. cloacea*), and *Klebsiella pneumoniae* (*K. pneumoniae*) by using disc diffusion method. Antitumor activity was evaluated with *Agrobacterium tumefaciens* (*A. tumefaciens*)-induced potato disc tumor assay. Best antibacterial activity was obtained with ethanolic extract of *P. pungens* against *S. pyogenes*. Ethanolic and methanolic extract of *N. alba* and ethanolic extract of *G. lydia* also showed strong antibacterial activities. Results indicated that alcoholic extracts especially ethanolic extracts exhibited strong antibacterial activity against both gram-positive and gram-negative bacteria. Best antitumor activity was obtained with methanolic extracts of *N. alba* and *V. lantana* (100% tumor inhibition). Ethanolic extract of *N. alba*, alcoholic extracts of *N. lutea*, *A. reptans* and *V. minor* flowers, methanolic extracts of *G. lydia* and *O. heterophyllum* and ethanolic extract of *V. lantana* and aqueous extract of *V. minor* leaves exhibited strong tumor inhibitions [13].

Antimicrobial activity

Boyko NN et al. presents data on screening of antimicrobial properties of extracts from the raw materials (18 plants) containing alkaloids. The microbiological method of studying antimicrobial properties of extracts, agar well diffusion method, has been applied; special mathematic method of comparison of antimicrobial properties of extracts vector theory has been applied. The most active extracts have been selected; they have antimicrobial activity of medium strength from *Phellodendron amurense* bark; *Macleaya cordata* herb; *Nuphar lutea* root; *Corydalis marshal* tubers; Belladonna herb; *Solanum dulcamara* herb and fruits. A potential to use in practice of the extracts obtained from *Echinops sphaerocephalus* seeds and *Cynoglossum* herb as antimicrobial medicinal products has been shown. Low levels of antimicrobial activity have been demonstrated by the extract obtained from *Peganum harmala* herb. Data show significant antimicrobial properties of numerous kinds of raw materials that contain alkaloids and high possibility of their use in complex phytochemical medicinal products, but with certain restrictions and thorough side effect examination [14].

Antineoplastic, Anti-inflammatory, Antifungal, and Antibacterial activity

Kurashov EA et al. carried out study on the assessment of the spectrum of biological activities (antineoplastic, anti-

inflammatory, antifungal, and antibacterial) with PASS (Prediction of Activity Spectra for Substances) for the major components of three macrophytes widespread in the Holarctic species of freshwater, emergent macrophyte with floating leaves, *Nuphar luteum* (L.) Sm., and two species of submergent macrophyte groups, *Ceratophyllum demersum* L. and *Potamogeton obtusifolius* (Mert. et Koch), for the discovery of their ecological and pharmacological potential. The predicted probability of anti-inflammatory or antineoplastic activities above 0.8 was observed for twenty compounds. The same compounds were also characterized by high probability of antifungal and antibacterial activity. Six metabolites, namely, hexanal, pentadecanal, tetradecanoic acid, dibutyl phthalate, hexadecanoic acid, and manool, were a part of the major components of all three studied plants, indicating their high ecological significance and a certain universalism in their use by various species of water plants for the implementation of ecological and biochemical functions. This report underlines the role of identified compounds not only as important components in regulation of biochemical and metabolic pathways and processes in aquatic ecological systems, but also as potential pharmacological agents in the fight against different diseases [15].

CONCLUSION

Nuphar luteum is an potential aquatic plant with multitude of chemical compounds like alkaloids, anthraquinone glycosides, terpenoids, saponins, flavanoids, tannins and phenolic compounds, proteins, amino acids, carbohydrates, starch and vitamin C. Further plant exihibits anti-cancer, anti-leishmanial activity, anti-inflammatory and antimicrobial activity. The present review summarizes the comphrehensive information concerning traditional uses, toxicology, phytochemistry and pharmacological activities which will serve as a guideline for the researchers in future work related to phytochemistry or pharmacological activity.

ACKNOWLEDGEMENTS

The authors acknowledge I.K Gujral Punjab Technical University Jalandhar-Kapurthala, Punjab, India for providing facilities to do literature survey and research.

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