IJRAR.ORG E-ISSN: 2348-1269, P-ISSN: 2349-5138

INTERNATIONAL JOURNAL OF RESEARCH AND ANALYTICAL REVIEWS (IJRAR) | IJRAR.ORG

An International Open Access, Peer-reviewed, Refereed Journal

A REVIEW ON THERAPEUTIC AND BIOLOGICAL DIVERSITY OF *OPHIORRHIZA* SPECIES

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I. ABSTRACT

The current study reports on a *Ophiorrhiza* genus with their various species and its respective chemical constituents according to their potency. This *Ophiorrhiza* genus belongs to rubiaceae family. Ophio' means snake, 'rhiza' means root. Traditionally, *Ophiorrhiza* species have been called "snake roots" due to their healing properties for snake bites. These species having characteristics of alkaloids, secoiridoidmonoterpenes, sesquiterpenes, steroids, quinines and phenylpropanoids and also it possesses many biological activities such as anticancer, antiviral, antiulcer, antivenom, antimicrobial. *Ophiorrhiza* species is an alternative source of camptothecin. This camptothecin helps to synthesize some of the major anticancer agents such as irinotecan and topotecan. The current review focus on chemical constituents, traditional uses as well as biological activities of *ophiorrhiza* species and its future prospects.

Index Terms: *Ophiorrhiza* species, Camptothecin, Biological activity

II. INTRODUCTION

Ophiorrhiza belongs to family of rubiaceae. *Ophiorrhiza* species can be distinguished by its fivepetal flower with slightly unequal opposite leaves, succulent stems, humorous capsular seed of small rhomboid shape and laterally compressed fruits. Most of the *ophiorrhiza* species are abiding herbs (perennial herbs) which has capability of growing from relatively 10cm to 1m in height. Due to the presence of camptothecin they possess cytotoxic activity. Presently *Ophiorrhiza* genus comprises of 321 species, 5 varieties and 1 subspecies. *Ophiorrhiza* are mainly found in western ghats region in specific, 46 species and 5 varieties are mainly allocated in the north eastern states and western ghats of India, whereas 16 species and 3 varieties can be found in the state of Kerala, India.[2]

Ophiorrhiza species generally possess chemical constituents such as camptothecin, pumiloside, luteolin, Harman, bracteatine, blumeanine, tetrahydro alastonine, strictosidinic acid and lyalosidic acid in varying concentration. Camptothecin is an inhibitor of topoisomerase enzyme which was originally derived from

camptotheca acuminata in 1958.Camptothecin helps to synthesize many anticancer drugs such as Topotecan, Irinotecan and Belotecan. It had been temporarily withdrawn from the market because of its low aqueous solubility and toxicity. *Ophiorrhiza* species are usually referred to as snake roots because they have curative properties against snake bite. Roots of *ophiorrhiza mungos* and *ophiorrhiza japonica* also are typically used for snake bite, tumors and toxic wounds. *Ophiorrhiza* species are associated with antiviral, antibacterial, anthelmintic, antivenom properties. They are economic and possess minimum side effects when compared to synthetic drugs.[2] By combining large-scale plant production through irradiation and elicitation, both biotic and abiotic chemicals can be reported, leading to the high synthesis of camptothecin.. Today's technological advancements in apparatus and equipment allow for the quick identification of newly identified bioactive chemicals with inhibitory effects on cancer cells. In order to find additional bioactive compounds, considerable research and investigations should be carried out. The therapeutic benefits of the chemicals found in this species, highlight the usage of naturally occurring medicines in the medical industry that are thought to be more cost-effective and well-tolerated.[2]

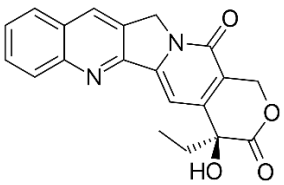

Fig 1: chemical structure of Camptothecin

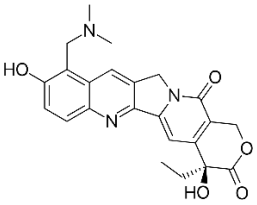

Fig 2: chemical structure of Topotecan

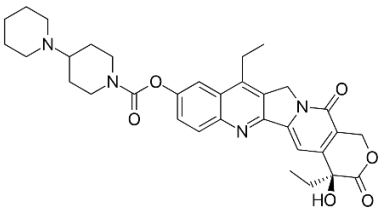

Fig 3: chemical structure of Irinotecan

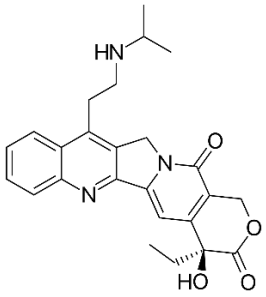

Fig 4: chemical structure of Belotecan

III. CHEMICAL CONSTITUENTS:

The genus of *ophiorrhiza* contains various species and each species are having their own chemical constituents according to their potencies. Based on the presence of chemical constituents with respective *ophiorrhiza* species are enlisted below in Table 1.[2]

table 1

SL. NO.	***Ophiorrhiza* species**	**Chemical constituents reported**
1	*Ophiorrhiza accuminata L.*	Palicoside, lyalosidic acid, palicoside methyl ester, harman
2	*Ophiorrhiza discolor R. Br. ex G. Don*	Tetrahydroalstonine

3	*Ophiorrhiza filistipula Miq*	7-Methoxy camptothecin, camptothecin, normalindine, strictosidinic acid
4	*Ophiorrhiza japonica Blume*	Harman, 6-hydroxy harman, lyaloside, lyalosidic acid, 10 hydroxylyalosidic acid, ophiorine A and B, ophiorine A and B methyl ester, pumiloside, deoxypumiloside, strictosamide, camptothecin, hydroxycamptothecin, friedelin.
5	*Ophiorrhiza kuroiwae Makino*	Camptothecin, 9-methoxycamptothecin, harman, lyalosidic acid, ophiorine A and B.
6	*Ophiorrhiza major Ridl.*	Bracteatine, ophiorrhizine
7	*Ophiorrhiza pumila Champ. Ex Benth.*	Camptothecin, strictosidine, 9-methoxycamptothecin, 10-hydroxy camptothecin, strictosamide, 3-(S)-pumiloside, 3-(S)-deoxypumiloside, 3-(R)-deoxypumiloside, chaboside, strictosidinic acid, lucidin3-O-β-purimeveroside, 3-hydroxy,2-hydroxymethylanthraquinone, 1-hydroxy2-hydroxymethyl-3-hethoxyanthraquinone, 3-O-caffeoylquinic acid, 9-β-glucosyloxy camptothecin, pentaacetate,1,3-dihydroxy-2-hydroxymethyl-anthraquinone, 2-methylanthraquinone, 2-hydroxy-3-methyl-anthraquinone, 2-hydroxy-3-hydroxy- methyl anthraquinone, 1-hydroxy-2-hydroxymethyl-anthraquinone, 1,3-dihydroxy-2-methoxymethyl anthraquinone, 1-hydroxy-2-methyl-anthraquinine, 1-hydroxy-2-hydroxy-methyl-3-methoxy anthraquinone, 3-hydroxyantraquinone-2-carbaldehyde, 2-n-butoxymethyl-1,3-dihydroxy anthraquinone, tetraacetylsweroside, inamoside, 3-O-caffeoylquinic acid, penta-O-acetyl loganin, β-sitosterol, 3-O-β-D-glucosyl- β-sitosterol, cholesterol, phaeophytin a, phaeophytin b
8	*Ophiorrhiza hayatana Ohwi*	Ophiohayatone A, B, C and D, 1 methyl-9Hcarboline 3-carboxylic acid, norharman, 6-hydroxyharmane, pumiloside, strictosamide, lyalosidic acid, lyalosidic acid, 9H-β-carboline-1-carboxylic acid, 1-methoxycarbonyl- β-carboline, 1-methyl-9-carboline-3-carboxylic acid, maxonine, lyaloside, desoxycordifolinic acid, vincoside, 2-hydroxymethyl-3-methoxyanthraquinone, methyl-p-hydroxycinnamate, methyl paraben, vanillin, ophiorridin-C, p-hydroxybenzaldehyde,

		ophiorridin-A, nonadecylferulate, ophiorridin-B, scopoletin, umbelliferone, 132 -hydroxy-(132 -R)-phaeophytin-a, aristophyll-c, methyl (10S)-hydroxypheophorbide-a, 132 -hydroxy-(132 -S)-phaeophytin-a, ursolic acid, adenine, nicotinamide.
9	*Ophiorrhiza mungos L*	Camptothecin, hydroxyl camptothecin, 10-methoxy camptothecin, 9-methoxy camptothecin, luteolin-7-O-Glucoside, 5α-ergosterol-8(14) - ene-3β-ol, 5α-ergosterol-7-ene- 3β-ol.
10	*Ophiorrhiza liukiuensis Hayata*	Pumiloside, deoxypumiloside, strictosamide, demethylsecologanol, 3'''-O-Glucosylsenburiside II, sweroside, epi-vogeloside, loganic acid, loganin, swertiaside-A, scopoletin, hyperin, (6S,9R)- reoside, (6R,7E,9R)-9-hydroxy megastima-4,7-dien-3-one-9-O-β-D-glucoside, chlorogenic acid, ursolic acid, β- sitosterol, daucosterol, 2-methyl-1,3,7-trihydroxyanthraquinone, 1-hydroxy-3- methyl-anthraquinone, 2-methyl-1-3-6-trihydroxyanthraquinone, harman, norharman,ophiorrhizine-A, ophiorrhizine-B, strictosamide, lyalosidic acid, ophiorrhizinone E,soranjidiol-1-methyl ether, ophiorrhizinone-C, ophiorrhizinone-Bb, 1,3-dihydroxy-2-hydroxy ethylanthqaquinone, ophiorrhizinone-D, 1-hydroxy-2-methyl-anthraquinine, 1,3-dihydroxy-2,8-dimethoxy-7-methyl- anthraquinone, 2,8-dihydroxy-1,3-dimethoxy-7-methyl-anthraquinone, 8- hydroxy-3-methoxy-7-methyl-1,2-methylenedioxy- anthraquinone, ophiorrhizinone-A, ophiorrhisin-A, ophiorrhizol A, inamoside, 3-O-caffeoylquinic methyl ester, sodium chlorogenate, quinic acid 3,4-di-O-caffeate, quinic acid 3,5-di-O-caffeate, ursolic acid.
11	*Ophiorrhiza blumeana Korth.*	Bracteatine, blueanine, ophiorrhizine, ophiorrhizine12- carboxylate
12	*Ophiorrhiza communis Ridl.*	Isomalindine, isomalidine-16- carboxylate
13	*Ophiorrhiza tomentosa Jack ex Roxb.*	Strictosidinic acid
14	*Ophiorrhiza ferruginea Valeton*	Isomalindine, malindine, dihydrocycloakagerine, 3,14-dihydrodecussine, tetrahydrocycloakagerine, dihydrocyclol-

		akagerine
15	*Ophiorrhiza rosacea Ridl.*	Harman-2-oxide, harman, lyalosidic acid, tetrahydroalstonine, strictosidinic acid, valesiaschotamine, isovalesiaschotamine,
16	*Ophiorrhiza kunstleri King*	19-Methyl 3-14-didehydro normalindine, palicoside
17	*Ophiorrhiza bracteata Korth.*	Bracteatine, ophiorrhizine

IV. TRADITIONAL USES

The genus *ophiorrhiza* exhibits numerous therapeutic qualities and uses in both conventional and modern medicine. [2] The extract of root barks of *ophiorrhiza* species has laxative and sedative properties and practiced in treating gastropathy, leprosy, amenorrhea.[2] In Bangladesh, *ophiorrhiza harrisiana* leaves are made into tea and used for treating body pain and chest pain. Facial blemishes are cured by using leaves and roots of *ophiorrhiza subcapitata*. *Ophiorrhiza filistipula* has been used in Nepal for treatment of scalp infection in children.[4] *Ophiorrhiza rugosa var prosata (D.Don)* and *mondal* are used for treating skin infections like boils, body pain, chest pain, dysentery, diarrhoea, carache.[2] *Ophiorrhiza mungos L* is used in development of photo protective cosmetic products by analyzing its sun protection factor (SPF) and antioxidant property.[8] Habitually these plants were used to treat pain, cancer, bacterial and viral infection and inflammation. It also plays an important role in recovery of snake bite, ulcer, wounds, vesicular stomatitis. They are also used as cough suppressants, pain relievers and antioxidants. [2]

V. EXTRACTION TECHNIQUE

With the aid of the High-Performance Thin Layer Chromatography densitometry technique, camptothecin was isolated from various *ophiorrhiza* species, and the yield for each species was determined. Shade dried and powdered plant material of *ophiorrhiza* species were extracted by using methanol in soxhlet apparatus. After extraction, extract was completely removed by using rotary evaporator and subjected to HPTLC and yield was found and recorded. Various species of *Ophiorrhiza* yields were compared and it was found that *ophiorrhiza mungos* has high amount of camptothecin present in it.[2]

Solvent used: Ethyl acetate, Chloroform, Methanol.

Various *Ophiorrhiza* species with their respective yield is provided below in the figure 5, figure 6, figure 7, figure 8, figure 9, figure 10, figure 11.

figure5: *ophiorrhiza eriantha* (0.06±0.02)

figure6: *ophiorrhiza hirsutula* (17.14±4.42)

figure7: *ophiorrhiza mungos* (396.54±0.81)

figure8: *ophiorrhiza pectinata* (2.84±0.02)

figure9: *ophiorrhiza rugosa var decumbens* (18.55±0.02)

figure10: *ophiorrhiza trichocarpon* (0.97±0.02)

figure11: *ophiorrhiza mungos var angustifolia* (373.19±0.04)

VI. BIOLOGICAL ACTIVITY

There have been numerous reports of biological activity with *Ophiorrhiza* species. Fresh methanol extract of *ophiorrhiza marginata* and *kunstleri* stems and leaves possesses anti-nematode properties. Ethanol extracts of *ophiorrhiza mungos* roots, stems, and leaves demonstrated antiviral activity, particularly against the herpes virus, and the root extract acts as an antidote to neutralise Russells viper venom in vitro and in vivo. Antioxidant and cytotoxic activity of various parts of *ophiorrhiza mungos* and *ophiorrhiza prostrata* were investigated, and high cytotoxic activity was later confirmed. In addition, *ophiorrhiza mungos var. angustifolia* hexane extract inhibits pathogens, bacteria, and fungi. Different *ophiorrhiza mungos* and *ophiorrhiza prostrata* sections were examined for antioxidant and cytotoxic action, and considerable cytotoxic activity was later confirmed. Additionally, the *ophiorrhiza mungos var. angustifolia's* hexane extract inhibits pathogens, bacteria, and fungi.

4.1 Anticancer activity

Ophiorrhiza plants contain camptothecin, a potent alkaloid with anticancer properties. It works as a DNA topoisomerase-I enzyme inhibitor by capturing the reaction intermediate throughout the breaking and rejoining process. The division of cancer cells is hampered as a result. Additionally, it binds to tubulin and prevents the development of microtubules in dividing cells, so preventing the DNA topoisomerase enzyme from functioning. [2]

4.2 Antiviral activity

Flavonoids have the ability to inhibit virus activity. Catechin can inhibit the activity of respiratory syncytial virus (RSV) and herpes simplex virus (HSV) but not their intracellular replication. Quercetin has the ability to inhibit the majority of virus activity. They also inhibit the DNA-gyrase enzyme to some extent. Coumarins, too, have antiviral properties. They work by attracting macrophages to the infection. Harmane has the ability to insert DNA viruses. It inhibits the activity of the Leishmanial protein kinase C. [2]

4.3 Antimicrobial activity

The microbial membrane is destroyed by flavonoids when they combine with the soluble proteins and cell walls of extracellular bacteria. This is as a result of the membrane's lipophilic makeup. Comparatively to gramme negative bacteria, coumarins and terpenoids are more active against gramme positive bacteria such *Bacillus subtilis* and *Staphylococcus aureus*. The microbial membrane is destroyed by flavonoids when they combine with the soluble proteins and cell walls of extracellular bacteria. This is as a result of the membrane's lipophilic makeup. When compared to gramme negative bacteria like *Bacillus subtilis* and *Staphylococcus aureus*, coumarins and terpenoids have more action. [2]

V. DISCUSSION AND CONCLUSION

Ophiorrhiza species belong to rubiaceae family which shows many therapeutic and biological activities such as anticancer, antivenom, antimicrobial etc. *Ophiorrhiza* species contain camptothecin, strictosidinic acid, lyalosidic acid etc. *Ophiorrhiza* species yield were compared and it was found that *ophiorrhiza mungos* has high amount of camptothecin present in it. Hence other new *ophiorrhiza* species like *ophiorrhiza recurvipetala*, *ophiorrhiza sahyadriensis* etc may have the content of camptothecin and exhibit anticancer activity. As a result , even though they may not be considered medications , substances obtained to *ophiorrhiza* are crucial in the treatment of diseases particularly for the creation of prospective anticancer medicines, the medicines can be used as lead compounds. This may help researchers better understand diseases and develop treatments that are more effective using novel methods of action, improving patient compliance and reducing the need for side effects associated with synthetic anticancer drugs, as well as encouraging the development of upcoming and innovative antitumor drugs. Despite the fact that only a small number of *ophiorrhiza* species have been studied, they exhibit a great deal of diversity.

VI. FUTURE PROSPECTS

On the anatomy, cytology, palynology, and embryology of the genus *Ophiorrhiza*, little research has been done. According to UNESCO, Kerala's western ghats are a protected area for *ophiorrhiza* species. In-vitro multiple shoots were found to produce camptothecin at a rate that was comparable to that of wild plants of *ophiorrhiza* species. Numerous techniques, including medium optimization, cell line selection, cell immobilization, elicitation, genetic transformation, organ or hairy root culture, integrated bioreactor engineering, and metabolic engineering, were also developed to increase the productivity of camptothecin. [2]

VII. ACKNOWLEDGEMENT

“Milestones in life are achieved not by individual efforts but by blessings and guidance of elders, near and dear ones”

It is proud and privileged honor for us to express my heartfelt thanks and gratefulness to all the persons who backed me directly or indirectly throughout the modeling of this review article work at this magnitude.

First and foremost, I place my heartfelt gratitude to my respected chairman, Sri S N V L Narasimha Raju Garu whose guidance, motivation as well as his constructive suggestions, constant support and timely help have made the materialization of my review article.

I wholeheartedly thank Dr Padmaa M Paarakh, M Pharm, Ph.D., Principal, The Oxford College of Pharmacy, for her help and support.

I am very much indebted to Dr. Jyoti Shrivastava, M. Pharm, Ph. D, HOD, Department of Pharmaceutical chemistry for her valuable support and advice.

I am grateful to Mrs. Vishnupriya, Assistant professor, Department of Pharmaceutical Chemistry for her valuable support.

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