



Study on Antimicrobial, Anti-inflammatory, Antitumor Activity of Some medicinal Orchids – A Review

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ABSTRACT

Plants have been used for medical purposes since the beginning of human history and are the basis of modern medicine. Most chemotherapeutic drugs for cancer treatment are molecules identified and isolated from plants or their synthetic derivatives. Our hypothesis was that whole plant extracts selected according to ethnobotanical sources of historical use might contain multiple molecules with antitumor activities that could be very effective in killing human cancer cells. This study examined the effects of three whole plant extracts (ethanol extraction) on human tumor cells. The extracts were from *Urtica membranacea* (Urticaceae), *Artemisia monosperma* (Asteraceae), and *Origanum dayi post* (Labiatae). All three plant extracts exhibited dose- and time-dependent killing capabilities in various human derived tumor cell lines and primary cultures established from patients' biopsies. The killing activity was specific toward tumor cells, as the plant extracts had no effect on primary cultures of healthy human cells. Cell death caused by the whole plant extracts is via apoptosis. Plant extract 5 (*Urtica membranacea*) showed particularly strong anticancer capabilities since it inhibited actual tumor progression in a breast adenocarcinoma mouse model. Our results suggest that whole plant extracts are promising anticancer reagents

Key words

Antimicrobial, Anti-inflammatory, Antitumor, and Antioxidative activity

1. INTRODUCTION

In recent times, medicinal plants occupy an important position for being the paramount sources of drug discovery, irrespective of its categorized groups-herb, shrub or tree. Plants have been indispensable in treating diverse forms of diseases including cancer. According to World Health

Organisation, 80% of the people living in the rural areas depend on medicinal plants as primary health care system. These practices are solely based on the knowledge of traditional use of medicinal plants. Natural products are formulated to generate different types of effective drugs to enhance anticancer activities. Proper understanding of the complex synergistic interaction of various constituents of anticancer herbs, would help in formulating the design to attack the cancerous cells without harming the normal cells of the body. Orchids have been widely used in traditional Chinese medicine and some them have been subjected for phytochemical and pharmacological studies. India is one of the richest habitats of orchid. India comprise of about 2500 species in 167 genera. In India, some orchids like *Eulophia campestris*, *Orchis latifolia*, *Vanda roxburgii* have drawn the attention of scientific community because of their medicinal properties [3, 4]. Medicinal orchids mainly belong to genera: *Calanthe*, *Coelogyne*, *Cymbidium*, *Cypripedium*, *Dendrobium*, *Ephemerantha*, *Eria*, *Galeola*, *Gastrodia*, *Gymnadenia*, *Habenaria*, *Ludisia*, *Luisia*, *Nevilia* and *Thunia* [2, 5]. Certain constituent of orchids such as alkaloids, flavonoids etc. suggest medicinal properties. The present review deals with the phytochemistry and medicinal uses of orchids.

Antimicrobial Activity

A number of members of orchid family are used as potent inhibitor against gram positive and gram negative bacteria and also proved to be a potent antimicrobial agent. *Gastrodia* nin, a protein isolated from orchid *Gastrodia elata* have shown invitro activity against plant pathogenic fungi [2]. *Gastrodianin* is homologous to mannose binding proteins of other orchids some of which also displayed invitro antifungal activity [22]. The methanolic extract from different parts of orchids has shown antimicrobial activity. The methanolic extract derived from the leaves of *Spiranthes mauritianum* have shown inhibitory effect against gram positive bacteria and also showed anti-inflammatory activity [23]. The methylene chloride extract from the leaves and stem bark of *Galeola foliata* have shown a broad spectrum antibacterial activity against gram positive and gram negative bacteria, however the extract was found to be inactive against moulds [24]. Vanillin, the major flavoring component of vanilla is a membrane active compound which results in dissipation of ion gradients and the inhibition of respiration [25]. Vanillin has shown antimicrobial activity against *Escherichia coli*, *Lactobacillus plantarum* and *Listeria innocua* [25]. Antimicrobial activity of vanillin and vanillic isolated from *Vanilla planifolia* have been studied against several strains of *Listeria monocytogenes*, *Listeria innocua*, *Listeria grayi* and *Listeria seeligeri* and it was found that mixture of vanillin and vanillic acid exhibited additive inhibitory effects particularly at low pH [26]. The herb extract from *Bletilla striata* have shown to possess antioxidant and antimicrobial capacity

[27]. The ethanolic extract of seedlings of *Cypripedium macranthos* var. *rebutense* was found to contain antifungal compounds *lusianthrin* and *chrysin*. *Lusianthrin* maintains the perilous symbiotic association for germination was found to be more potent antifungal compound than *chrysin* which helps to protect adult plants [28]. The methanolic extract from the leaves of *Acanthephippium bicolor* Lindley was found to have antimicrobial activity against *Staphylococcus aureus*, *Streptococcus foecalis*, *Bacillus cereus*, *Proteus vulgaris*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Shigella dysenteriae*, *Escherichia coli*, *Microsporium audouinii*, *Microsporium fulvum*, *Candida albicans* and *Trichophyton rubrum*[29]. The gram positive bacteria are found to be more sensitive than gram negative bacteria and fungi [29]

Anti-inflammatory Activity

Several members of orchid family were found to have anti-inflammatory activity. Marked anti-inflammatory activity in carrageenan induced oedema in rats and mice is shown by *Vanda roxburghii*. The anti arthritic activity was found to be superior to that of phenyl butazone [30]. Heptacosane and octacosanol isolated from *Vanda roxburghii* root was found to have anti-inflammatory activity [31]. The anti-inflammatory activity is due to long chain alkanes and alkanols (ranging C-27 to C-32) which are ubiquitous in plants [31]. The ethanolic extract from the leaves of *Anoectochilus formosanus* have showed delayed onset of anti-inflammatory activity starting from 4 hours post carrageenan administration. *Anoectochilus formosanus* have also produced histological changes. Improvement in inflammatory infiltration of lymphocytes and kupffer cells around the central vein was achieved by the use of this orchid [32]. Several compounds with anti-inflammatory activity were isolated from *Dendrobium moniliforme* [33, 34]. 7-hydroxy-5,6-dimethoxy-1,4-phenanthrenequinone isolated from *Dendrobium moniliforme* have shown inhibitory effect on VHR dual specificity protein tyrosine phosphatase activity[34], whereas *Dendroside A, C* and *vanilloside* from the same source have shown stimulatory effect on proliferation of B cells and inhibitory effect on proliferation of T cells [35]

Antitumor Activity

Several species of orchids have been studied and a number of compounds with antitumor activity have been isolated. *Dendrobium nobile* has been a good source of compounds with anti-tumor activity. *Denbinobin* and 4, 7-Dihydroxy-2-methoxy-9, 10-dihydrophenanthrene from *Dendrobium nobile* showed cytotoxicity against human lung carcinoma, human ovary adenocarcinoma and human promyelocytic leukemia cell lines [39]. *Dendroside A* and *dendronobiloside A* obtained from the stem of *Dendrobium nobile* showed stimulatory effect on

proliferation of murine T and B lymphocytes [40]. Erianin obtained from the stem of *Dendrobium chrysanthum* was found to be a potent inhibitor of proliferation of HL-60 cells and the inhibition might be due to erianin induced apoptosis and altered expression of bcl-2 and bax genes in HL-60 cells [41]. In another study erianin leads to extensive tumor necrosis, growth delay and rapid vascular shutdown in hepatoma Bel7402 and melanoma A375 [42]. Dendrochrysanene isolated from stems of *Dendrobium chrysanthum* was found to suppress the mRNA level of TNF-alpha, IL8, IL10 and iNOS in murine peritoneal macrophages [43]. Fimbriatone isolated from *Dendrobium fimbriatum* was found to be a potent inhibitor of BGC cell line [44]. A number of compounds such as 7,8-dihydro-4-hydroxy-12,13-methylenedioxy-11-methoxydibenz[bf]oxepin, 7,8-dihydro-4-hydroxy-12,13-methylenedioxy-11-methoxydibenz[bf]oxepin, 7,8-Dihydro-5-hydroxy-12,13-methylenedioxy-11-methoxydibenz[bf]oxepin, cumulating, densiflorol A and plicatol B isolated from *Bulbophyllum kwangtungense* have shown anti tumor activities against HeLa and K562 human tumor cell lines [18]. The methanolic extract obtained from *Anoectochilus Formosanus* has shown to induce apoptosis of MCF-7 cells [45]. However, the water extract from the same source was found to have a potent tumor inhibitor which might be due to its potent immunostimulating effect [46]. It has shown an inhibitory effect in BALB/c mice after subcutaneous transplantation of CT-26 murine colon cancer cells by stimulating proliferation of lymphoid tissues and activating the phagocytosis of peritoneal macrophages against *Staphylococcus aureus* [46]. The tuber of *Cremastra appendiculata* yields cirrohopetalanthrin and 2,7,2',7',2''-pentahydroxy-4,4',4''7''-tetramethoxy-1,8,1',1''-triphenanthrene which were found to have moderate cytotoxicity against human colon cancer, human stomach cancer, human hepatoma, human breast cancer, human lung adenocarcinoma and human ovarian cancer cell lines [17,47]. The homoisoflavanone 5,7-dihydroxy-3-(3-hydroxy-4-methoxybenzyl)-6-methoxychroman isolated from *Cremastra appendiculata* was found to be a potent inhibitor of angiogenesis [17]. Lonchophylloids A and Lonchophylloids B obtained from the stems of *Ephemerantha lonchophylla* were found to sensitize those cells which have expressed the multidrug resistance phenotype to the toxicity of the anticancer drug doxorubicin [48]. Denbinobin isolated from the same source displayed anticancerous effects in K562 cells by increasing polymerization of tubulin and degranulation of Bcr-Abl signaling [49]. Methanolic extract of *Gastrodia elata* prevents serum deprived apoptosis through activation of serine/threonine kinase-dependent pathway and suppression of JNK activity [50], whereas the ethanolic extract from the rhizomes has shown potent anti tumor activity *in vitro* in a dose dependent manner [51]. (2S)-5, 2',6'-trihydroxy-6-lavandulyl-4''-(γ,γ -dimethylallyl)-2'',2'''-dimethylpyrano-[5'',6'',7,8]-flavanone, a dihydroflavanoid

isolated from *Spiranthes australis* (R. Brown) Lindl inhibits human cancer cells growth including A498, A549, BEL-7402,SGC-7901,MCF-7, HT-29 and K562 cell lines [52]. A phenanthrene derivative 3,7-dihydroxy-2,4,6-trimethoxyphenanthrene from *Bulbophyllum odoratissimum* was found to have cytotoxicity against the human cancer cell lines such as human leukemia cell lines K562 and HL-60, human hepatoma BEL-7402, human lung adenocarcinoma A549 and human stomach cancer cell lines SGC-7901[53]

Antioxidative Property

Several compounds from orchid family were found to have strong antioxidative property. Ephemeranthon, a dihydrostilbene obtained from the leaf ethanolic extract of *Ephemerantha lonchophylla* was found to have strong antioxidative property for invitro inhibition of human low density lipoprotein[54]. Another dihydrostilbene isoamoenylin obtained from the roots of *Dendrobium amoenum* var. *denneanum* showed moderate antioxidative property [55]. Cismelilotoside, dihydromelilotoside and trans-melilotoside obtained from stems of *Dendrobium aurantiacum* were found to be potent antioxidants [16]. Antioxidative compounds like alkyl ferulates and quercetin were also isolated from *Dendrobium monoliforme* and *Dendrobium tosaense* [15]. The ethanolic extract of *Dendrobium nobile* was found to exhibit antioxidative property equivalent or higher to ascorbic acid [56]. Kinsenoside from *Anoectochilus Formosanus* was reported to have antioxidative property [57]. The aqueous leaf extract from *Anoectochilus Formosanus* shows inhibitory effect on proteolytic cleavage of poly(ADP-ribose) polymerase during apoptosis [58]. Several phenolic compounds such as kaempferol-3-O- β -glucopyranoside (59), kaempferol-7- β -D -glucopyranoside (60), isorhamnetin-3- β -D-rutinoside (61), 8-droxybenzylquercetin (62), 5-hydroxy-3',4',7-trimethoxyflavonol-3- β -D-rutinoside (63), and quercetin-7-O- β -D-[6"-O-(trans-feruloyl)]-glucopyranoside were isolated from *Anoectochilus roxburghii* (Wall.) Lindl that possess scavenging activity of DPPH radicals (64). Hydroxybenzyl alcohol, hydroxybenzaldehyde, vanillin and vanillyl alcohol obtained from leaf methanolic extract *Gastrodia elata* were reported to possess antioxidative property [65]. Several phenanthrenes isolated from 60% ethanolic extract of air dried plant of *Pholidota yunnanensis* were found to show the DPPH free radical scavenging activity [66]

2. CONCLUSION

Orchids are generally known for its beautiful flowers and very less known for its medicinal uses. However, a number of compounds have been isolated from the different parts of the plant which possess medicinal properties. Compounds with antimicrobial, antitumor, anti-inflammatory, antioxidative, antidiabetic, neuroprotective, antiallergic properties have been isolated and tested on

animal models but clinical trials with orchid plant parts have not been a regular practice. Emphasis on the clinical trials will provide a new gateway for treatment of diseases with herbal medicines. The orchid components still requires proper study with full experimental trials which will lead to its acceptance as medical recommendations.

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