



Anticancer Activities of Selected Members in Family Orchidaceae

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Abstract: Orchidaceae is one of the largest families among angiosperm monocots and the members commonly known as orchids. They are cultivated worldwide for their beautiful flowers with variety of colours, shapes and sizes. Many plants are medicinally important and extensively using in drugs for treating various human diseases. Likewise, most of the species contain antibacterial, antiinflammatory, antimicrobial, antioxidative and antitumour compounds. Recently there are a number of investigations going on revealing the anticancerous properties and antitumour compounds of different orchids, as a solution to treat various types of cancers in human beings.

Keywords: Orchids, secondary metabolites, cancer, anticancerous, cytotoxicity

All living organisms are made up of many microscopic cells, irrespective of their size. Some are unicellular and others are multicellular forms. The growth and development of these organisms mainly relies upon the controlled division and multiplication of these cells. Cancer occurs when the cellular reproduction process become out of control. Nowadays cancer is one of the major threats facing by human population which will ultimately leads to death. Any cell in any part of the body may become cancerous by several environmental and genetic factors.

The cancer burden continues to grow globally, exerting tremendous physical, emotional and financial strain on individuals, families, communities and health systems. Various treatment options such as surgery,

chemotherapy, hormone therapy, biological therapy etc. developed by modern medical systems are highly expensive. Moreover, all these treatments had its own difficulties and side effects in the patients. In this scenario, the herbal medicines play an important role to replace with the expensive and side effects creating allopathic medicines.

Medicinal plants continue to play a central role in the healthcare system of large proportions of the world's population. Human beings are using medicinal plants to treat many diseases today. Recognition and development of the medicinal and economic benefits of plants are on the increase in both developing and industrialized nations. The plant or plant parts are using for its scent, flavour or therapeutic properties (Jain et al., 2016). Many

herbs have been evaluated in clinical studies and are currently being investigated phytochemically to understand their antitumour actions against various cancers (Harpreet et al., 2011).

The family Orchidaceae includes about 1000 genera and more than 25,000 species. They are cultivated and protected worldwide for their attractive flowers. The information regarding their medicinal properties especially the anticancerous secondary metabolites are not much known. Orchids are traditionally used in folk medicine for the cure of various infectious diseases and tumours (Hu et al., 2008). Based on recent investigations, many of the orchids contain antibacterial, antiinflammatory, antimicrobial, antioxidative and antitumour compounds. Extract investigation of different species confirms the presence of anticancer compounds. Moreover, the isolates from various plant parts exhibit cytotoxic activity against leukemia and melanoma as well as against brain, breast, cervical, gastric, liver and lung cancer cells (Sliwinski et al., 2022).

1. Anticancer plants in Orchidaceae

Several orchid species contain a large number of potential anticancerous secondary metabolites (Pant et al., 2021). Alkaloids, terpenes, stilbenoids, bibenzyls, phenanthrenes, flavonoids and polysaccharides isolated from Orchidaceae indicate their potential medical usefulness. Gigantol and batatasin III are the main bibenzyls occurring in orchids with cytotoxic activity (Chen et al., 2008). Most of the orchids are cytotoxic and kill human cancer cell lines which possess antiallergic, antimicrobial, antiinflammatory and antioxidant properties (Toth et al., 2017). Beyond this,

antitumour properties are reported for monomeric phenanthrenes, biphenanthrenes and triphenanthrenes which include in orchids (Teoh et al., 2016). Bibenzyl derivatives of phenanthrenes are effective antitumour chemicals and using in the preparation of anticancer drugs (Wang et al., 2014). The secondary metabolite present in some genera, denbinobin, triggers apoptosis of numerous human cancer cell lines (Chen et al., 2013). Interestingly, some bioactive compounds of orchids are produced by symbiotic microbes within them which carry excessive cytotoxic effects (Favre-Godal et al., 2020). The main genera which are possessing potential anticancerous and antitumour properties include *Dendrobium*, *Vanda*, *Bulbophyllum*, *Vanilla*, *Spathoglottis*, *Eulophia*, *Nervilia*, *Malaxis*, *Luisia* and *Habenaria*.

1.1. *Dendrobium Sw.*

The genus *Dendrobium* includes about 1,500 species of epiphytic orchids. Many are cultivated as ornamentals and some are important in the floral industry. They are native to tropical and subtropical Asia, many Pacific islands and Australia. Species are sympodial herbs with cylindrical roots usually arising from the base of a pseudobulb. The pseudobulbs are hard, cylindrical, cone shaped and more or less covered with the bases of the leaves.

Anticancer activities: The extracts of several species of *Dendrobium* have cytotoxic effects and are inhibitors of the growth of cervical cancer and glioblastoma brain tumour cells (Paudel et al., 2020). The extracts in different solvents consists a number of bioactive constituents having medicinal values. Major macromolecules include lectins, chalcone

synthase, sucrose synthase, cytokinin oxidase and polysaccharides. The polysaccharides mainly display immunomodulatory and hepatoprotective activities; while the alkaloids exhibit antioxidant, anticancer and neuroprotective activities (Ng et al., 2012).

D. longicornu carries extremely beautiful flowers and native to warm-temperate, subtropical and tropical regions of Asia and Australia. The whole plant of *D. longicornu* contains bibenzyl and phenanthrene as well as minimal amounts of monoaromatics, steroid and flavonoid derivatives in turn causes antiproliferative activity (Paudel et al., 2017). Protocorm is a special organ induced from seed culture that belongs to the somatic embryo and undergoes growth and differentiation into plants. They are highly proliferated tissues which accumulate high content of secondary metabolites (Cui et al., 2015). Anticancer effect of the protocorm extract from *D. longicornu* toward human cervical cancer (HeLa) and brain tumour (U251) cell lines determined using MTT colourimetric assay (Paudel et al., 2019). The ethanolic extract of *D. chrysanthum* and *D. venustum* perturbs cell cycle progression and results in a delay in the growth of cells; moreover, it exerts anticancer activity (Prasad et al., 2017; Phibonchaiyanan et al., 2018). *D. crepidatum* is significantly cytotoxic against both cervical cancer (HeLa) and glioblastoma brain tumour (U251) cell lines (Paudel et al., 2018). The medicinally active compounds like stilbenoids and phenolic derivatives in the extract have high cytotoxic effects. Similarly, the extract of *D. transparens* shows high cytotoxic effect towards the HeLa and U251 cell lines (Joshi et

al., 2020). The stem extract of wild pineapple orchid, *D. densiflorum*, inhibits the growth of 50% cervical cancer cells (HeLa) and glioblastoma cells (U251). Chloroform extract of *D. lasianthera* stem demonstrates cytotoxicity against T47D cancer cells that can be considered as a potential anticancer natural product (Pant et al., 2022). *D. nobile* is a good source of anticancer compounds in which denbinobin and 4, 7-Dihydroxy-2-methoxy-9, 10-dihydrophenanthrene show cytotoxicity against human lung carcinoma, ovary adenocarcinoma and promyelocytic leukemia cell lines (Lee et al., 1995).

1.2. *Vanda Jones ex R.Br.*

The genus *Vanda* includes about 50 species of colourful orchids distributed from East Asia to Australia. Most species are epiphytic and have long sturdy stems that bear closely spaced strap like leaves. Some species have cylindrical leaves in a form known as terete. The long lasting fragrant flowers usually are flat and have a short spur on the lip. The plants grow well in warm temperatures with high humidity and require a well draining potting medium.

Anticancer activities: The methanolic leaf extract of *V. spathulata* has anticancer action in breast cancer MCF-7 cells via producing cell toxicity and apoptosis (Jeline Rani et al., 2022). *V. bensonii* is a promising source of bioactive molecules with anticancer potential, which can be developed further as pharmaceutical products to optimize the future pharmacotherapy of lung cancer (Jimoh et al., 2022). Four phytochemicals including phloretic acid methyl ester, cymbinodin-A, ephemeranthequinone B and protocatechuic acid in whole plant

methanolic extract demonstrates varying bioactivities to inhibit growth and metastasis of NCI-H460 cells. The whole plant methanol extracts of wild orchid, *V. cristata*, show significant cytotoxic activity against cervical cancer and brain tumour cell lines (Joshi et al., 2020).

1.3. *Bulbophyllum* Thouars

Bulbophyllum, one of the largest genera of orchids, composed of more than 2,000 species of flowering plants. The genus is found in warm climates throughout Africa, Asia and the Americas. Some species are of horticultural interest due to their unusual flowers. Several species are endangered and are threatened by habitat loss. *Bulbophyllum* species have creeping rhizomes and rounded pseudobulbs. Most species have a single leaf per pseudobulb, and the leaves are often succulent and usually are folded along the midrib. The genus displays a wide diversity of growth forms, ranging from small epiphytes to large cane like. Many of the orchids have small flowers with coloured sepals that are often larger than the petals. Some species are pollinated by flies and give off an offensive odour.

Anticancer activities: *B. kwangtungense* shows antitumour activity against cervical cancer (HeLa) and leukemia (K562) cell lines (Wu et al., 2006). Beyond, *B. odoratissimum* is cytotoxic against leukemia cell lines (K562, HL-60), hepatoma (BEL-7402), lung adenocarcinoma (A549) and stomach cancer (SGC-7901) cell lines (Xu et al., 2009). Extracts of *B. sterile* bulbs and roots cause apoptosis in human colon cancer (HCT116) cell lines by arresting the G2/M phase of the cell cycle (Biswas et al., 2016).

1.4. *Vanilla* Plum. ex Mill.

Vanilla is tropical climbing orchids with the flavouring agent vanillin, extracted from the pods. *Vanilla* plants have a long, fleshy climbing stem that attaches to trees by aerial rootlets. Moreover, the roots also penetrate the soil for nutrient absorption. Numerous flowers open a few at a time and last a single day during the blooming season, which lasts about two months.

Anticancer activities: *Vanilla* leaf extract has a dose dependent antiproliferative effect in human beings. The extract might contain the lead molecule which may be developed as chemotherapeutic agent for treating skin cancer of squamous cell carcinoma type (Vijaybabu et al., 2019). Essential oil of *Vanilla* has ability to inhibit the growth of cancerous cells due to anticarcinogenic and antioxidant properties by killing free radicals in the body and inhibiting the growth of cancerous cells. The bioactive compound, 3-hydroxy-4-methoxybenzaldehyde, present in *Vanilla* plays great role in anticancer activity and inhibits migration of human lung cancer cells which are induced by the hepatocyte growth factor (Hanif et al., 2020).

1.5. *Spathoglottis* Blume

The genus *Spathoglottis* consisting of 49 species with evergreen plant body which are terrestrial orchid plants with pseudobulbs just below the soil and large narrow leaves above the surface. The flowering stem arising from the pseudobulb bears medium sized colourful flowers. Because of their attractive flowers they are extensively cultivated in outdoor gardens.

Anticancer activities: Even though there are

many species under this genus, only one species is reported to contain anticancer agents. Chloroform extracts of leaf and whole plant, *S. plicata* have moderate potency to develop as anticancer agents, especially on breast cancer (Holle et al., 2015).

1.6. *Eulophia* R.Br.

Eulophia covers more than 200 species which spread throughout tropical Americas, Asia and South Africa. They are characterized by being terrestrial, rarely epiphytic and are tall having globose corms, short stalks and long plicate leaves. The basal inflorescence can attain a length of 5 meters with a raceme of several medium sized flowers. The flowers are with upwardly arched lateral sepals, deeply concave basal lip and longitudinal crests on its blade. There is a long foot on the column carrying two pollina with a stipe.

Anticancer activities: The ethanolic extract of *E. macrobulbon* roots and its components show notable cytotoxic effects on the human cervical adenocarcinoma cell line HeLa, the human colorectal adenocarcinoma cell line CaCo-2 and the human breast adenocarcinoma cell line MCF-7 (Schuster et al., 2017).

1.7. *Nervilia* Comm. ex Gaudich.

The genus includes terrestrial orchids, commonly known as shield orchid which has about 80 species. The plant body is perennial, sympodial and deciduous with one or two flowers born on an erect fleshy leafless stalk.

Anticancer activities: *N. fordii* is a species using in Chinese folk medicine. Both petroleum ether and ethyl acetate extracts of the species

show anticancerous properties and can prolong the life of cancer induced mice. The exact phytochemicals which are responsible for anticancerous properties is not known yet (Prakash et al., 2013).

1.8. *Malaxis* Sol. ex Sw.

The genus is commonly known as 'Adder's Mouth' and consisting of terrestrial and semi epiphytic orchids with a variety of vegetative growth. It shows worldwide distribution except in Africa.

Anticancer activities: Cytotoxicity of methanol extract of the whole plant of *M. rheedii* toward MCF-7 suppresses the cell proliferation and it shows good cytotoxicity than HeLa cell line (Haridas et al., 2016).

1.9. *Luisia* Gaudich.

The genus is commonly known as 'Velvet Orchids'. Some members are epiphytic and others show lithophytic nature. The plant body has thick flattened roots and long fibrous leafy stem branching near the base. The leaves are narrow, thick and leathery. Inflorescences are very short racemes having a number of flowers.

Anticancer activities: The ethyl acetate and methanol extracts of shade dried leaves of *L. zeylanica* show cytotoxicity against HeLa and MCF-7 cell lines. The viability of these cell lines decreases considerably with increasing concentrations of extracts. Nowadays, the phytochemicals present in the leaves are using to develop anticancer drugs (Khasim et al., 2019).

1.10. *Habenaria* Willd.

Habenaria is a large terrestrial genus with more than 800 species having colourful flowers. They are commonly known as 'Ghost

Orchids'. The species have small to large underground root tubers with erect stem of 20 to 80 cm. Some members have two flat leaves and others are with many leaves. The small or large flowers in the inflorescence are green, yellow or white in colour.

Anticancer activities: *H. digitata* is a species with a wide range of cytotoxic properties due to the presence of phytochemical compounds present like flavonoids and phenolic compounds having potential antitumour properties (Alshehri et al., 2022).

2. Outlook

Medicinal plants have important roles in curing various diseases of human beings. In different parts of the world, a wide variety of

herbs are using as folk medicines. Cancer treatment aiming at reducing the risks of using allopathic methodologies in patients and replacing them by medicinal plants is very interesting in the present scenario. Recent studies reveal that there are many plants which contain cytotoxic secondary metabolites and their extracts can be used to kill or control the cancer cells. Especially, the Orchidaceae members are rich in anticancerous metabolites according to modern research. But we are not much aware of many orchids and investigations carried out only in very few members. In future, Orchids will become as a very good source of antitumour compounds and in turn can produce plant derived anticancer drugs to treat various types of human cancers.

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