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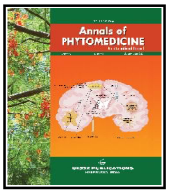

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Medicinal orchids: Traditional uses and recent advances

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Abstract

Orchids are one of the world's largest, most diverse, and intriguing blooming plants belonging to the Orchidaceae family, which has around 30,000-35,000 species worldwide. Orchid being an exotic and high value crop, its cultivation is now in vogue at the commercial level as it exhibits a fascinating range of colour patterns, high keeping quality and had a reputed medicinal efficacy. The ecological factors greatly influenced the medicinal plants. This may lead to altering the level of bioactive compounds in the plant metabolic system. Pharmacological research has revealed that several phytoconstituents in some orchid species exhibit biological health-promoting activities such as; antibacterial, antifungal, antioxidant, anti-inflammatory, anticancer, and neuroprotective properties. Although, orchids are grown for decorative purposes and have a wide range of traditional uses, recent biotechnology breakthroughs in orchids have significantly contributed to the production of exotic varieties with improved aesthetic and therapeutic values. In this review, we put an extensive effort into compiling the available medicinal orchid species featured across the globe and their applications in the pharmaceutical field. In addition, the recent advancements made for the improvement of orchid production are also covered precisely.

1. Introduction

As the people of world recently encountered with the pandemic like COVID-19, now people have become very careful in adopting new foods and always seek for the food that may enhance their immune system much stronger (Rizwana *et al.,* 2021). Hence, the use of medicinal plants becomes more popular than earlier and establishing a new era in the treatment of various chronic diseases including diabetes, hypertension and obesity, *etc.* New formulations using plant extracts have proven to be the most widely accepted therapies today (Kumaraswamy *et al.,* 2022). Among these, orchids are one of the most important herbs known for its aesthetic qualities. Nowadays, they are often used as decorative item in many rituals. People from many different cultures have utilized orchids as medicinal plants for a very long time. It is a member of the largest and most evolved flowering plant family, Orchidaceae, which contains between 25,000 and 35,000 species and 750 and 850 genera, accounting for 6.83% of all flowering plants (Singh *et al.,* 2001; De *et al.,* 2019). Except for cold Antarctica and scorching deserts, they are found almost everywhere on the planet, although the tropical and subtropical areas have the most diversity. Because of their perplexingly intricate blossoms of great beauty, orchids are unquestionably the decorative elite. They are an essential element of cut flower trade, however, it is claimed within numerous scriptures that it has been used as a remedy for a variety of diseases (Hossain, 2011). The following Orchidaceae genera are notable for their pharmacological properties, *viz., Anoectochilus, Coelogyne, Cymbidium, Calanthe, Nevilia, Dendrobium, Cypripedium, Ephemerantha, Ludisia, Gastrodia, Eria, Gymnadenia, Habenaria, Galeola, Luisia,* and *Thunia* (Szlachetko, 2001). Anthocyanins, orcinol, bibenzyl derivatives, hircinol, cypripedium, jibantine, nidemin, loroglossin and phenanthrenes are among the main secondary metabolites recovered from these therapeutic orchids. However, stilbenoids and phenantropyrans are thought to be the most gifted metabolites of medicinal world (Ye *et al.,* 2002). By using quantitative phytochemical screening, Hossain *et al.* (2020) discovered the presence of various bioactive phytochemicals, such as steroids, phlobatannins, phenols, cardiac glycosides, phytosterols, terpenoids, saponins, tannins, alkaloids, quinines, coumarins, xanthoproteics, glycosides, proteins, flavonoids, *etc.*, in medicinally notable epiphytic orchids. Orchids' history most likely began with its usage for therapeutic purposes. Numerous orchid species have been discovered and to be continued utilized for their medicinal benefits in various nations. Orchids are the most diverse group of angiosperms, with about 28,000 species and 736 genera (Hossain, 2009). Although, orchids may be found in natural areas all throughout the world, their numbers are declining owing to high population demand (Kim *et al.,* 2020). Orchid species are declining due to habitat damage and uncontrolled collecting (Pant, 2013; Fonge *et al.,* 2019). According to Papenfus *et al.* (2016) and Gantait and Kundu (2017), the cultivation of medicinal orchids is threatened by deforestation, which causes habitat loss and the threat of extinction. The traditional technique of propagating every plant has several different flaws, including sluggish growth, susceptibility to pests, poor germination and nutritional inadequacies. Furthermore, the conventional technique of secondary metabolite

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extraction has various flaws, including a long extraction time and a higher extraction cost; by-products created might pollute the environment (Chinsamy *et al.,* 2014). As a result, biotechnology breakthroughs are critical for plantlet propagation and secondary metabolite extraction. This article details the breakthroughs of medicinally important derived metabolites found in orchids. Some of the orchid species along with their secondary metabolites are mentioned in Table 1.

Table 1: Key orchid species with secondary metabolites and their medicinal uses

Name of species	Secondary metabolite	Medicinal uses	References
Dendrobium nobile Lindl.	Denbinobin (Phenanthrene)	Antitumor activity	Mohanty *et al.,* 2012
D. densiflorum Lindl.	Scoparone	Antiplatelet aggregation	Pradhan *et al.,* 2013
D. chrysanthum Wall. ex Lindl.	Dendrochrysanene	Antipyretic	Mohanty *et al.,* 2013
Anoectochilus roxburghii	Rutinoside	Antioxidative activity	Jin *et al.,* 2017
D. fimbriatum Hook.	Fimbriatone	Antitumor activity	Paul *et al.,* 2017
Cymbidium goeringii Reichenbach fil.	Cymbidine	Diuretic and hypotensive activities	Park *et al.,* 2018
Vanda tessellate [(Roxb.) Hook. ex G. Don]	Octacosanol	Antiinflammatory	Manokari *et al.,* 2021

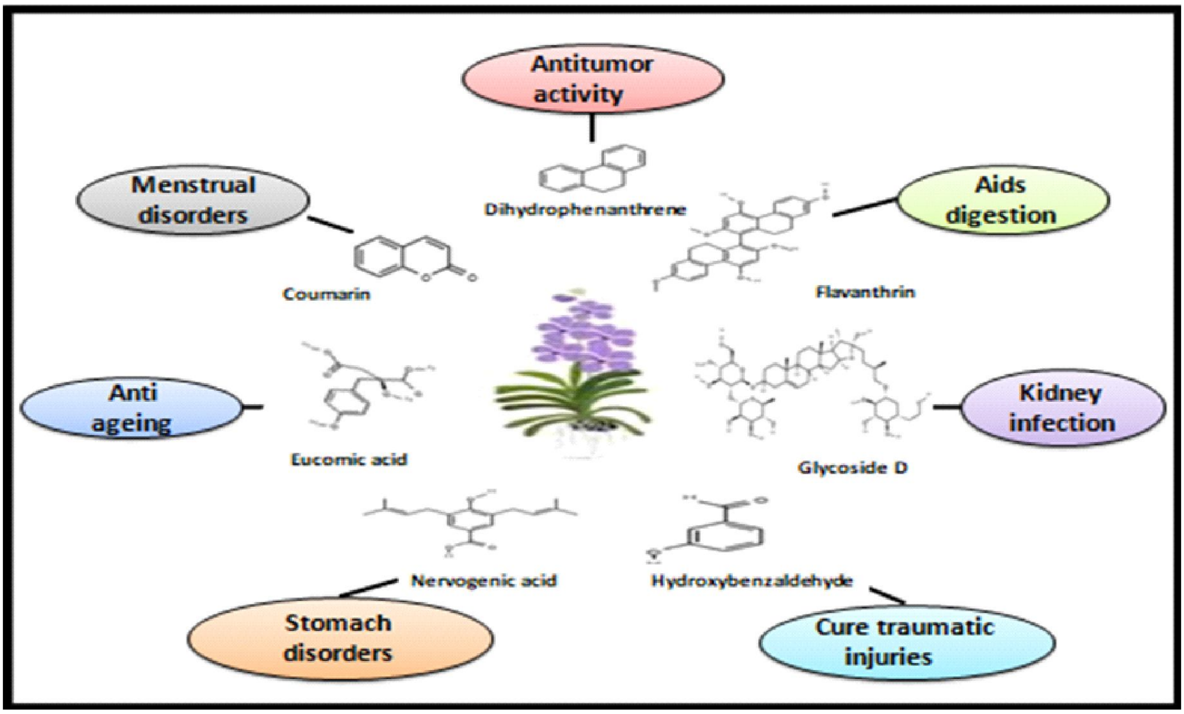

Figure 1: Medicinal uses of secondary metabolites found in orchids (Structure source: PubChem; Diagram prepared by Diksha Choudhary).

2. Traditional uses of orchids

Orchids are said to have originated on Earth 120 million years ago. However, extant written documents date only back to the fourth millennium B.C. Since 2800 B.C., orchids are being utilized as a resource of ayurvedic treatments in China (Kimura, 1936; Luning, 1974). Some species of orchids have also been utilized by Indians for their medicinal and aphrodisiac powers since the Vedic period (2000 B.C.-600 B.C.) (Kaushik, 1983). The orchid is referred to as 'Vanda' in Indian Vedic literature. Orchids have long been used as a natural remedy in regions of Europe, Australia, America, and Africa. Orchids are widely used in ayurvedic or traditional medicine in many regions of the world, which has sparked intense interest in studying their pharmacological characteristics and bioactive ingredients.

One of the older, more conventional medical systems is the Siddha system of medicine, which is mostly used in Tamil-speaking regions of India. In contrast to Ayurveda, the Siddha system of medicine does not give orchids much credit for remedies. But, Tamil Nadu's tribal population employs orchids to treat ailments. The history of the Unani medical system, which started in Greece and was brought to India by Arabs and Persians in the eleventh century, also mentions the use of orchids as medicinal plants. It was used to make salep, a plant extract that was intended to treat a variety of illnesses by grinding up different plant components. Salam Badshah (like an emperor), Salam Panja (palm-like), Salam Mishri (translucent and spherical), Salam lahsunia (garlic kind), and others are prominent. These names were chosen based on how the salep-making tubers looked (Pal *et al.,* 2020). The first mentions of the use of medicinal herbs in India are in Sanskrit literature. The "Sushruta Samhita" written by Acharya Sushruta in 600 B.C. is known as a more comprehensive and authoritative treatment of "Ayurveda" that includes descriptions of 1120 illnesses, 700 therapeutic plants, and 121 formulations. Interestingly, all of the ancient Sanskrit literature mentions orchids as medicinal plants.

Indian people were more familiar with a substantial number of orchid species than any other nation on the earth (Kirtikar and Basu, 1918). In Ayurveda, *Flickingeria macraei* is referred to as "jeevanti" and is used as an astringent for the bowels, an aphrodisiac, and in the treatment of asthma and bronchitis. Jewanti (*Dendrobium alpestre*), salem (*Orchis latifolia* and *Eulophia latifolia*), shwethuli, and rasna (*Acampe papillosa* and *Vanda tessellate*; Manokari *et al.,* 2021) are additional orchids utilized in Ayurveda for their unique medicinal value. The subsurface tuber of *Orchis latifolia* is used to make the cough medication munjatak, in accordance with the Susruta Samhita (Khasim and Rao, 1999). Indian tribes employ a variety of plant species, including orchids, to treat a wide range of illnesses. 16 varieties of orchids are used by the Dongaria Kondha tribes of the Niyamgiri highlands in southwest Odisha, India, to heal 33 different ailments. In Andhra Pradesh, Pragada and Rao (2012) conducted a survey of 53 indigenous communities and found that *Geodorum densiflorum* is utilised to treat ephemeral fever. Nagaland, a state in the northeastern Himalayas, is home to 396 species of orchids that belong to 92 genera. There are 15 different types of orchids that are used by local doctors to cure a range of ailments, including rheumatism, cholera, neurological disorders, and TB. They are also utilised as antibacterial agents and antivenoms for snake bites and insect stings (Deb *et al.,* 2009).

Table 2: Traditional medicinal uses of orchids

Species	Trivial name	Useful part (s)	Therapeutic uses	References
Cymbidium aloifolium (L.)	Boat orchid	Root, leaf, whole plant	The plant is said to be emetic and purgative. Root powder is used to reduce paralysis.	Hossain, 2009
Acampe carinata (Griff.)	Pantl. Rasna (Sanskrit);	Root,	The paste made out of its root is used to cure acute rheumatism, neuralgia and sciatica, it is also beneficial in uterine diseases, secondary syphilis, scorpion and snake bites	Jalal *et al.,* 2008
Acampe papillosa (Lindl.) Lindl.	Rasna (Sanskrit)	Roots	Crushed roots are taken as tonic and are believed to be beneficial in curing uterine diseases and secondary syphilis.	Roy *et al.,* 2007
Acampe carinata (Griff.)	Kano-kato	Leaf	Leaf mixed with garlic and made into paste was found useful in stomach disorders and chest pain caused by hyperacidity.	Dash *et al.,* 2008
Aerides multiflorum	Draupadi puspa	Whole plant	Antibacterial action against *Salmonella aureus* and *Klebsiella pneumonia*.	Singh and Duggal, 2009
Bulbophyllum lilacinum	Gota parchallow (Rakhain)	Pseudobulbs	It helps keep the body fresh by removing fatigue and restlessness.	Hossain, 2009
Coelogyne cristata	–	Pseudobulb	The gum of the bulb is applied to the sores.	Bhattacharjee, 2006
Corymborkis veratrifolia	_	Leaf	The juice extracted from fresh leaves is given as an emetic especially to children for reducing fever.	Bhattacharjee, 2006
Dendrobium macraei	Jivanti, Yasasvini	Entire plant	It is given as a stimulant for general debility.	Singh and Duggal, 2009
Dendrobium macrostachyum	Radam	Tender shoot tip	Juice from tender tips is used as eardrops to cure earache	Roy *et al.,* 2007
Dendrobium normale	Blue orchid	Entire plant	The entire plant is well used for its tonic and aphrodisiac properties.	Jalal *et al.,* 2008
Gastrodia elatablume	Tian-Ma (Chinese)	Tuber	Tubers are used and served as tonic to cure nervous disorders and common cold.	Bulpitt *et al.,* 2007
Geodorum densiflorum	Kukurmuria, Donthulagadda	Root, tuber	Paste from fresh root is used to regularize menstrual cycle in women (ingested on a clear stomach)	Roy *et al.,* 2007
Rhynchostylis retusa	Blume Banda Seeta pushpa	Leaves, entire plant	Its leaves are known in curing the disease rheumatic.	Ghanaksh and Kaushik, 2007
Tropidia curculigoides	_	Root	Root decoction of this plant helps treating diarrhea. Extract (boiled) of entire plant is helpful in curing malaria.	Hossain, 2009

3. Major threats to orchids

Orchids are believed as the soul of herbal medicine. Unfortunately, many orchid species involving *Habenaria intermedia*, *Eulophia dabia*, *Satyrium nepalense*, *Malaxis mucifera*, *Dactylorhiza hatageria*, and others, have become rare and endangered. But one species, *Paphiopedilum vietnamense*, has already been disappeared. The reasons behind are habitat destruction, unethical use, loss of pollinators, genetic drift, anthropogenic pressures, illegal trade, deforestation, over-exploitation of conventional systems, *etc*. So, the time has come to protect this potentially valuable reservoir of medication for long-term human utilization.

4. Recent advances in orchid production and improvement

With rising need for improved quality orchid and increase in its production, the development of novel, appealing varieties with distinct colors and forms, as well as complete tolerance to diverse stressors, is critical. In general, plant breeders are expected to do all whatever is possible to pace up the breeding progression in order to develop new varieties of many well-known decorative flowers as roses, chrysanthemums, and orchids as well. It is important to mentioning that either this is achieved by molecular breeding or traditional breeding, foundation will always be genetics (Li *et al.,* 2021).

4.1 Cross breeding

Natural as well as artificial breeding has the outcome of merging the finest qualities of both the parents into the hybrid progeny. *P.intermedia* is among one of the oldest known natural hybrids, a cross involving *P. rosea* and *P. aphrodite* published in 1853, where as Dominy in 1856 documented the first artificial orchid hybrid *Calanthe*, which was result of a cross among *C. furcata* and *C. masuca* (De *et al.,* 2019). There are several hurdles to the hybridization process, including post-fertilization embryo abortion and parent incompatibility, resulting in the collapse of remote hybridization. To design an effective germination system, profound research of germination mechanisms and developmental traits of outlying hybrid seeds is very important. After hybrid seeds are produced, a proper cultivation method is required to maintain or expand the populace. Because seeds of orchid are very difficult to replicate in the ordinary environment, among the most essential breeding procedures *in vitro* propagation is followed for orchids. Numerous orchid species have been studied *in vitro*, together with those of the genus *Phalaenopsis, Cymbidium, Oncidium, Dendrobium, Calanthe alliance* and *Dactylorhiza* (Kanchanapoom *et al.,*2014; Bae *et al.,* 2015; Bezerra *et al.,* 2019; Gao *et al.,* 2020).

4.2 Mutation breeding

It includes both man-made and natural mutations and is ideal for the breeding of ornamental plants since numerous species may be reproduced with no difficulty, allowing for the development of induced and spontaneous mutants (Yamaguchi, 2018). It also provides several advantages, which include an elevated mutation rate, trait separation, effective enhancement of particular characteristics, and a shorter breeding phase (Toker *et al.,* 2007) as time passed, mutational breeding had been employed to create orchids having distinct phenotypic features, increased medicinal component content, and improved resistance and adaptation (De *et al.,* 2019). A popular mutant breeding technique employed for this is polyploidization. Many orchid species, including *Dendrobium* (Li and An, 2009; Zhang *et al.,* 2011), *Cymbidium*, *Phalaenopsis* and *Oncidium* (Cui *et al.,* 2010a), have successfully undergone polyploid breeding (Cui *et al.,* 2010b; Cheng, 2011). Colchicine was used to create tetraploid plants with bigger roots, rhizomes and leaves, as well as a reduced growth rate and a deep shoot colour (Yin *et al.*, 2010). Jin *et al.* (2012) used donor sodium nitroprusside nitric oxide (NO) on the protocorm of *D. huoshanensis* hybrid to increase the amount of alkaloid in medicinal *Dendrobium* generated by micropropagation. Chen *et al.* (2018) used an artificially simulated UV-B radiation to irradiate *D.catenatum* seedlings, resulting in the rise in amount of overall flavonoids, alkaloids, polysaccharides and several additional significant specialized chemicals found in plant.

4.3 Polyploidy breeding

Tetraploids of *A. formosanus* Hayata are much efficient and more reliable in establishing of polyploidy as they produced significantly higher contents of bioactive compounds, including total flavonoid and possess a higher activity of phenolic glycoside biosynthesis that could accumulate a higher content of gastrodin than the diploids (Letchamo, 1996; Zahedi *et al.,* 2014; Chung *et al.,* 2017a).

4.4 Selection breeding

In comparison to cross breeding, it employs the inherent variety of already existing kinds as the source of selection in the present breeding programme (Osadchuk, 2020). Three crucial genetic characteristics must be considered while doing selection breeding: genetic correlations among phenotypes, heritability, and relations among varieties and the related atmosphere (Falconer and Mackay, 1996; Boudry, 2009). *In vitro* propagation, selection and hybridization were used to create the novel *Phalaenopsis* cultivar 'SM 333'(Park *et al.,* 2015). Bezerra *et al.* (2019) created a variety named 'Jinhui' novel *Oncidium* using somaclonal mutations, chosen strain selection, genetic identification, multi-point testing and tissue culture. Yuan *et al.* (2020) evaluated three medicinal components such as total alkaloid, total flavonoid and polysaccharide level in *D. officinale* at different cultivation modes and noticed that these were highest in the wild cultivation mode and the lowest were in the greenhouse mode. Among them, the average content of polysaccharides was as high as 650.56 mg/g of dry weight and the total flavonoid content was up to 5.07 mg/g of dry weight. Further employment of these selected wild relatives in selection breeding may help us to achieve fortified varieties.

4.5 Molecular marker-assisted breeding

Molecular markers are used to investigate genetic linkage with genes encoding for nutraceuticals, including bioactive molecules. The molecular marker-assisted breeding offers rapid, defined, and free of the impact of environmental conditions (Jiang, 2015).SSR transcriptome sequencing of *Paphiopedilum concolor* roots has offered important insight into the development and growth mechanism of the root, as well as molecular marker-assisted research and specialized metabolism-related genes (Li *et al.,* 2015). Single Sequence Repeat was employed to discover the genetics in *Phalaenopsis* relevant to floral colour, flower form, and resistance, offering an essential reference for *Phalaenopsis* genetic engineering and the Orchidaceae breeding in general (Chung *et al.,* 2017b).

4.6 Transgenic technology

Transgenic approaches provide a higher potential for producing new traits than standard breeding procedures. Introducing new qualities, like disease resistance and new colours into orchids by cross-breeding or mutational breeding is generally challenging, however, transgenic technology makes it comparatively simple (Mii and Chin, 2010; Nirmala *et al.,* 2006). It transmits the preferred selective genes into the desired plant and increases or suppresses the expression of desirable genes (Zhu *et al.,* 2018). Transgenic technologies can also enhance aesthetic attributes by altering the plant DNA (Kishi-Kaboshi *et al.,* 2018). Successful orchid transformations facilitated by particle bombardment were initially reported in *Dendrobium* (Nan and Kuehnle, 1995; Kuehnle and Sugii, 1992) and *Vanda* (Chia *et al.,* 1990). At the moment, effective transformation systems for a few vital commercial varieties of orchids have been established, including *Vanda* (Shrestha *et al.,* 2007), *Phalaenopsis* (Tong *et al.,*2020; Hsieh *et al.,* 1997), *Dendrobium* (Chen *et al.,* 2018; Xian *et al.,* 2017), *Cattleya* (Li and Chan, 2018; Zhang *et al.,* 2010), *Cymbidium* (Chin *et al.,* 2007). An anthocyanin synthesis gene was electrophoretically inserted into the remains of *Doritis pulcherrima* and acquired a transitory appearance in flowers, which resulted in a change in the colour of the flower petals (Griesbach and Hammond, 1993). Particle bombardment technique was used to transfer a plasmid containing GUS and NPTII marker genes to *Cymbidium* orchids, resulting in transgenic kanamycin resistant plants (Yang *et al.,* 1999). Wang *et al.* (2011) identified two C-class AGAMOUS-like genes which were designated as CeMADS1 and CeMADS2 from *Cymbidium ensifolium* through the identification of C-class MADS-box genes. They revealed that different spatial and temporal expression patterns of these two genes indicate functional diversification during gynostemium development, and CeMADS1 may play a crucial role in the development of reproductive organs.

4.7 Plant tissue culture

In the past few years, plant tissue culture techniques have been employed to regenerate orchids. A few species of orchids have been multiplied either by direct shoot regeneration (Singh *et al.,* 2014) or through the creation of protocorm-like bodies (PLBs) from the culture of vegetative explants (Chug *et al.,* 2009; Sarmah *et al.,* 2017). For multiplication, explants such apical meristems, nodes, pseudonodes, shoots, leaves, leaf tips, rhizomes, *etc*., have been exploited. It results in heterozygous plant population when orchids are propagated from seeds, however, this issue can be resolved by micropropagating orchids from different vegetative sections. A variety of media such as Murashige and Skoog (Murashige *et al.,* 1962; Kundson *et al.,* 1946; Gamborg *et al.,* 1968) have been used for proliferation through tissue culture techniques. Auxins and cytokinins, two growth regulators, are added to the medium to promote the germination and development of many orchid plants. For shoot proliferation and PLB production, various cytokinins are utilised, including BAP (6-benzylaminopurine), Kinetin, 2-iP (2-isopentyladenine), and TDZ (Thidiazuron), either alone or in conjunction with auxin 2,4-D (2,4-dichlorophenoxy acetic acid), NAA (1-naphthalene acetic acid) and IAA (Lal and Singh, 2020)

In *Oncidium flexuosum*, TDZ was found to be successful in the immediate creation of PLB from leaf explants under darkness, but plants with fully formed shoots and roots only grew after being transferred from PLBs to under light and growth regulator-free medium. According to Mayer *et al.* (2010) and Roy *et al.* (2012), *Cymbidium giganteum* pseudostem segments from seedlings were more likely to produce PLBs at low concentrations (0.909 µM) of TDZ than at high concentrations, which resulted in enhanced PLB multiplication but decreased plantlet and root growth. In *Dendrobium longicornu*, shoot production from the nodal explants was shown in media containing 15 µM BAP and 5 µM NAA, whereas PLBs were produced in media containing BAP combined with 2,4-D (Dohling *et al.,* 2012).

4.8 Artificial seed production

A particularly effective method for creating orchid cultivars with appealing flower shape, colour, and scent is hybridization. By using the artificial seed production (a plant tissue culture technology), it is undoubtedly feasible to multiply large numbers of hybrid orchids. It is regarded as an efficient and widely utilised technique for plant species displaying reproductive barriers (Cardoso *et al.,* 2020; Ara *et al.,* 2000; Singh *et al.,* 2018; Mathur *et al.,* 1989). Artificial seeds can be used to circumvent the challenges associated with growing orchids from seeds. Artificial seeds make it simple to move propagules around and distribute them. Several orchid species, *viz., Cymbidium devonianum* (Das *et al.,* 2011), *Cymbidium eburneum*, *Cymbidium hookerianum* (Gogoi *et al.,* 2018), *Geodorum densiflorum* (Datta *et al.,* 1999), *Paphiopedilum wardii* (Zeng *et al.,* 2012), *Dendrobium wardianum* (Sharma *et al.,*1992), *Ansellia Africana* (Bhattacharya *et al.,* 2018), *etc*., have been successfully mass propagated with the help of artificial seed. Several studies have reported on its use in the conservation of valuable, uncommon, and endangered orchids. *Vanda coerulia* plantlets were created by encapsulating PLBs that were six months old and had been grown from leaf explants. The encapsulated PLBs were then kept at 4°C for 100 day (Sarmah *et al.,* 2010). *Cymbidium aliofolium* artificial seeds were made by encapsulating protocorms with 4% (w/v) sodium alginate and 0.2 mol/l calcium chloride solution. These artificial seeds had 100% germination and could be kept at 4°C for 28 days (Pradhan *et al.,* 2014). *Cymbidium devonianum* PLB storage time is increased by lowering the temperature and reducing the nutrient strength in the encapsulated matrix (Das *et al.,* 2011). Including sucrose and mannitol (7.5 and 12%) into the encapsulating matrix in *Dendrobium nobile* demonstrated storage of encapsulated PLBs upto 60 days (Mohanty *et al.,* 2013).

5. Conclusion

Orchids have traditionally been farmed for cut flowers and are artificially reproduced. The orchid business has thrived by leaps and bounds in the last decade, both internationally as well as domestically. Nearly 80% of herbal medications meet the needs of a large population around the world, and orchids hold a great amount of bioactive phytochemicals, making them a prospective source of medication. Genetically modified plant species are not widely used because of concerns about changes to their natural genetic makeup. Additionally, it encourages the use of natural products. Traditional breeding practices has made momentous contributions to introducing and developing unique plant features in orchid varieties, and significantly increasing plant commercialization worldwide, with enormous economic gains. The use of biotechnological tools and studies on the genes that control secondary metabolite synthesis and its mechanisms, however, are still in the early stages. This involves in-depth research on the orchids genetics and genetic variability of the relevant qualities, methods for creating new variability, efficient selection techniques, high-performance, low-cost and reliable methods for the trait refinement. It is necessary to find novel orchidaceous formulations that support conventional wisdom in the context of practical phytotherapy.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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