Phytochemical, Pharmaceutical and Biochemical Activities of Selected Climber Plants: A Review

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Authors' contributions

This work was carried out in collaboration between all authors. Authors MMM and ABAA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors ADEN and DR managed the analyses of the study. Author FMMTM managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Climber plants have attracted global attention for their hidden therapeutic potential and are generally rooted on the ground, but leaves often in full sun and blanketing canopies of trees. Climbers rely on some support from other plants and have active and passive climbing mechanisms with great diversity. Tropical forests are the harbors of enormous different fauna and flora species than any other ecosystem on earth and Malaysia is a biodiversity hotspot in Asia with a good amount of tropical forest cover. On the other hand, Iran is an important source of Herbal plants due to the weather and geographical situation. In this review six species of Malaysian and Iranian plants (Hedera helix, Rosa canina, Vitis vinifera, Aristolochia tagala, Gynura procumbens and Antigonon leptopus) are selected and botanical description, geographical distribution, chemical constituent and medicinal properties of each species is discussed. Despite the rich ethno-medicine knowledge

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1. INTRODUCTION

Climber plants are an important source of novel drugs for many diseases but to attain that numerous challenges are encountered including the procurement of climber plant material, the selection and implementation of appropriate high-throughput screening bioassays and the scale up bioactive compounds [1]. In tropics trees, aquatic plants, legumes, palm, farns, shrubs, herbs, epiphytes, and climbers compose the vast majority of the plant species diversity [2]. Climbers are also called as lianas and are generally rooted on the ground, but leaves often in full sun and blanketing canopies of trees. Climbers rely on some support from other plants, due to their axes have reduced to provide higher hydraulic conductivity in their stems and invest resources in growth in length while tree allocate resources to supportive tissues [3]. Lianas have active and passive climbing mechanisms with great diversity; wind around, leaning on, anchoring or adhering to other plants [4] to attain great statue [5].

Climbers are integral part of every woody ecosystem and play variety of roles such as ecosystem functioning and dynamics [6,7], floristic, structural, functional diversity [8,9,10], create microclimate for the under growers [11], food for animals, provide habitat for arboreal animals [12], Carbon budgeting [7,13], last but not at least medicinal usages against numerous diseases [14,15,16]. However, they possess numerous advantages, they have their fair share of adverse effects as well, i.e. woody climbers could negatively impact on natural regeneration of forest trees, seedlings, saplings [17,7], they add considerable amount of weight and shading the canopy of the trees, they considered as structural parasites too [18], affect the soil properties [19] and competition among other plants for water, nutrients, sunlight and space [11,20].

World Health Organization (WHO) reported that 80% of the emerging world population relies on plant based traditional treatments [21,22]. Medicinal plants have been defined several ways, but simpler and more comprehensive definition proposed by WHO (2003), “A medicinal plant organ, contains substances that can be used for therapeutic purposes, or which are precursors for chemo-pharmaceutical semi-synthesis”. These chemicals include a vast variety of primary and secondary metabolites, such as alkaloids, Anthraquinones, flavonoids, phenolic compounds, saponins, tannins, terpenoids and many more [23,24,25].

From earliest days mankind has used plants in attempt to cure diseases and relieve physical sufferings. Hence, knowing the sources and an effective plan to practice them is helpful in profiling the potentials. Iran is a source of Herbal plants due to the weather and geographical situation. Traditional medicinal plants refer to old time in Iran. There are 8000 species of plants available in Iran that about 2300 species of them are among herbal medicine and only about 450 of them are used by people [26]. The variety of soil made it a suitable place for the growth of various plants and different kind of species.

Tropical forests are belongs to the different fauna and flora species than any other Ecosystem on earth [26,27,28] and Malaysia is a biodiversity hotspot in Asia with a good amount of tropical forest cover [29,30,31,32,33]. Apart from that, Malaysia is regarded as one of the twelve mega biodiversity hotspots in the world and woody climbers from 30% of all woody plants in the Malaysian rain forest, but unfortunately they have been undervalued due to various reasons [16,34,35,36,37,38].

Malaysian folk medicine is a derivative of the Unani medicinal system, but not limited to this and influenced by Ayurvedic, Homeopathy, Siddha, Indonesian, Chinese, Japanese and Orang Asli (aborigines) practices as well [39] where plants play a central part. This glorious medication contains of single or multiple medicinal plants may be prepared in many forms such as powders, pills, granules, capsules, oils,

Keywords: Hedera helix; Rosa canina; Vitis vinifera; Aristolochia tagala; Gynura procumbens and Antigonon leptopus; phytochemical; pharmacological; saponin; quercetin; anthocyanins; anticancer; grape; Ivy.
plasters, poultices and paste [39,40]. These different medications are famous and accessible in South East Asia [41]. Overall, 40%, almost 70% in rural areas of the Malaysian population prevail and accept the Malay traditional medicines [22]. Over 40% of medicines now prescribed in the world contains chemicals derived from plants. Burkhill [42] produced an outstanding book on Malaysian medicinal plants and it had been a strong base for further studies which still counting on. From The taxonomical data of the medicinal plants has been carried out in several parts of Malaysia [43]. It has been reported by several authors that more than 1000 medicinal plants distributed throughout Malaysia which is 10% of the all flowering plants present in Malaysia [44,45,46] and a comprehensive report on all of them is still a long way to travel [36,42,45,47,48]. About 90% of the medicinal plants are collected in the wild without human involvement and very few countries are seriously considering the maintaining the cultivation [49]. Some medicinal plants are facing rapid extinction threats due to the habitat disturbance via forest fire, logging, or encroachment by human [50,51]. Lee [52] reports that, agro-forestry system is the best option to plant medicinal plants and it could be considered for the conservation purposes too and medicinal plant used, and knowledge that leads to discovery of new medicines can be promoted.

2. MALAYSIAN CLIMBER PLANTS

2.1 Aristolochia tagala Cham

Genus Aristolochia L. is the largest of the Family: Aristolochiaceae, widely distributed in tropical and subtropical countries [53,54] where some of them cultivated as ornamental plants but most of them are medicinal plants [55]. Aristolochia species has been reported as an important medicinal plant by Greek physician/pharmacologist-botanist Dioscorides in the first Century [56]. Since Aristolochia species have a long history, these woody climbers utilized for a considerable amount of research on its ethnobotanical and pharmacological aspects. Numerous researchers are working on this species and the turn of the millennium has triggered the acceleration of them in various angles (Fig. 1). Some of the studied plants from this genus as follows: A. indica, A. serpentaria, A. elegans, A. cucurbitifolia, A. pubescens, A. debilis, A. anguicida, A. cymbifera, A. chamissonis, A. trilobata, A. fimbriata, A. paucinervis, A. bracteolate, A. clematidis etc [56,57,58]. However, Aristolochia species have been widely reported in its traditional medical use, it was later discovered the presence of naturally occurring carcinogenic compounds Aristolochic Acids I & II (AA) and it is the causal agent for the so-called AA Nephropathy (AAN) or Chinese Herb Nephropathy (CHN) [59]. It has been a concern since first reported from Belgium during the 1990s, but it didn’t hamper the use of Aristolochia species as popular herbal medicine [56,60]. Most of this Genus showed good antioxidant properties too. On the other hand more than 200 terpenoids have been successfully isolated from Genus Aristolochia by different research groups in China, Taiwan, Brazil, India and Germany [61].

Aristolochia tagala Cham. (syn: Aristolochia acuminata Lam.) (Aristolochiaceae) is commonly known as Indian birthwort or Dutchman's pipe or Oval leaf in English while in Bahasa Melayu, it’s called as Akar Ketola Hutan or Akar petola hutan. Whole plant and as well as different parts of this plant has been used in treating cancer, fever, gastrointestinal/bowel complaints, snake and scorpion bites, fit, malaria, toothache, to promote menstrual bleeding, all kinds of pains, food poisoning and many more diseases in different part of the world [62]. Different extraction methods displayed presence of steroids, flavonoids, phenolic compounds and terpenoids in A. tagala [62,63] reported that A. tagala displays most affective free radical scavenging activity via different solvent extraction methods [63]. Kaempferol is also available in this herbal that is responsible for the anti-inflammatory effect similar to the Cyclooxygenase and Lipoxygenase inhibitors as reported by Butt and coworkers [64].

Presence of scanty endosperm is the major issue which reduces the viability of the A. tagala seeds where propagation is solely depending upon. Furthermore, this herb has been assigned Vulnerable/Rare (VU/R) status in the Red List of South Indian medicinal plants due to deforestation and indiscriminate harvesting. Therefore, the alternative propagation method is a pre-requisite of such a highly valuable and widely used medicinal plant [65]. Shoot organogenesis from callus cultures is a successful method among medicinal plants. Micro propagation of A. tagala using leaf explants was produced highest successful and rapid shoot proliferation [57,66].
2.2 Botanical Description

A. tagala is a perennial, tropical, slender, aggressive climber with simple leaves oval to oblong shaped, tip abruptly pointed, heart shaped and alternatively arranged. Bisexual flowers are produced in axillary cymes with three perianths that unite into a slender tube. The base of the tube is globular, within which is a stumpy column bearing many stamens. This globular base narrows into a curved, cylindrical tube, before ending in a funnel-shaped mouth with a prominent reddish brown to purple, tongue-shaped lip. The mouth opening is pale yellow with a reddish brown to purple rim. The ovary is inferior and fruits are globular capsule. At maturity, it splits into six parts, looking like an inverted parachute. As the fruit sways in the breeze, the numerous, flat and winged seeds are dispersed. The pollinator of A. tagala is a Dipterean Chironomid fly [53]. Chromosomal number is 2n=12.

2.3 Geographical Distribution

A. tagala is distributed throughout Asia, some part of Africa, Central and Southern America. The plant is available in India, Sri Lanka, Bangladesh, China, Thailand, Malaysia, Australia, Indonesia, Philippines, Papua New Guinea, Vietnam Ghana, Nigeria and Solomon Islands. This species plays an important role to the biodiversity richness of Southern and Northeast India. They distributed in the plains, lower hills around 900 m elevation from the sea level and the Western Ghats [53,67]. Queensland province of Australia is grown with this species and lower watershed areas of the Philippines are also reported with these plants. A. tagala is one of the five Aristolochiaceae species found in Peninsular Malaysia with a wide range of distribution where the rest four of them have a very narrow range [57].

2.4 Chemical Constituent

Whole plant, leaves, roots, fruits and bark of A. tagala have been extensively used not only in Malaysia but also around the globe for various disease treatments [56]. The root and rhizomes contain isoaristolochic acid, Allantonin, alkaloid Aristolodin, Sesquiterpene hydrocarbon, Ishwarane Aristolochine, alcohol Ishwararol and essential oil containing carboxyl compounds [57,62]. Heinrich and coworkers [56] report about the lack of phytochemical data of A. tagala’s AA content and requires more attention in order to counter the AAN.

2.5 Medicinal Properties

Traditionally Malays used A. tagala leaves by applying the pounded leaves. The leaves are made into a poultice and applied to swollen...
abdomen or limbs in Indonesia. Used for snake bite and treating malaria in the Philippines. Leaves also used for swollen limbs, abdomen and bilious disorders. Leaves in medicated oil used as an external application for prevention of snake bites. Pounded roots also utilized for snake and scorpion bites in rural areas [68]. In India it has a very wide range of medical use when compared to the other part of the world. The whole plant is used for anti-implantation and bowel complaints in India whereas in Nepal-Eastward Himalayan to control menstrual bleeding. In Andhra Pradesh (India), it is constantly used to increase breast milk production and as a carminative agent. Throughout India fruit and root are used to treat for malaria, toothaches, rheumatism, treating snakebites and dyspepsia, stomachaches, fevers and fits [56]. It is used for dysentery, hypertension, beriberi and swollen feet in China. Different parts of A. tagala used as antimicrobial, antiprofibrative, cytotoxic, analgesic, antioxidant, antifertility, insecticidal and nephrotoxic agent. Different extraction methods have been employed in order to utilize the chemical constituents of this plant such as ethanol, methanol, petroleum ether, acetone and water [57].

3. Gynura procumbens (Lour.) MERR.

It belongs to Family Asteraceae, one of the most interesting plants from health perspectives, widely used in South East Asia for medicinal purposes in traditional treatment methods [69]. Genus Gynura consists of 44 species and is found from tropical Africa to Asia and Australasia with one species in tropical Australia [70]. Some of the other species of Gynura have been used medically; G. divaricata helps to combat craving for opium and Gynura formosana has antihemorrhagic activity and is applied externally to wounds and snake bites [71]. G. procumbens is commonly known as Akar Sebiak or Sambung Nyawa in Malaysia, Paetumpung in Thailand, Mollucan Spinach or Daun Dewa in Indonesia, Bai Bing Ca in China and Green Harmony or Longevity Spinach or Cholesterol Spinach or Leaves of God in English. G. procumbens has several scientific synonyms as well; Gynura sarmentosa, DC., Cacalia procumbens Lour. and Calacia procumbens, Lour [72].

They are traditionally used in treating eruptive fevers, rash, kidney disease, migraine, constipation, hypertension, diabetes mellitus and cancer. Since this plant has been mentioned as numerous medicinal properties, the traditional cutting propagation method used for this plant couldn't meet the demand [73]. Therefore, in vitro cultivation methods could be a very good alternative for the continuous provision of seedlings for the large scale field cultivation. Keng and coworkers (2009) reports that, nodal segments derived from adult plants as explants are produced promising results [74].

3.1 Botanical Description

Fast growing, herbaceous G. procumbens is an annual evergreen shrub generally grows well in tropical conditions. The fleshy, hairy stem with purple tint is highly branched bearing alternately arranged green hairy leaves. The leaves are ovate-elliptic or lanceolate, 3.5 to 6 cm long and 0.8 to 3.5 cm wide. Flowering heads are panicled, narrow and 1 to 1.5 cm long. The bisexual tubular flowers are purple in color [72,74,75].

3.2 Geographical Distribution

The highest diversity of these plants had been reported in Southeast Asia [76]. G. procumbens is indigenous to Malaysia, Indonesia and Thailand [74] but it is widely found in the Philippines, India, China, Sri Lanka, Thailand, Singapore and Bangladesh. Interestingly, it was introduced to Bangladesh via a social worker to treat diabetic for his friend’s father and it’s widely used as a treatment for diabetic in Bangladesh as well [75]. It is also found in Western and Central African countries [77].

3.3 Chemical Constituent

Several researchers have been reported about the chemical composition of this plant. Akowuah and coworkers reported on the presence of flavonoid, saponin, tannin, sterol glycosides and terpenoid [78]. Presence of pyrrolizidine alkaloids [79,80,81], spirostanol [82] coumarins [81,82,83], anthocyanins [84], kaempferol, quercetin, rutin [85], chlorogenic acid [86], sitosterol, stigmasterol, nucleic acid [87], plant defense proteins (peroxidase, thaumatin-like proteins and miraculin) [88] are also reported in literature.

3.4 Medicinal Properties

G. procumbens leaves and stems are used as food in Southeast Asian countries, since it possesses useful protein [89]. According to Malaysian folk medicine, this plant has been
used as a remedy for diabetes and hyperlipidemia [90]. In Thai folk medicine, the aerial parts of this plant are used as a topical therapy for treating inflammation, rheumatism and viral diseases of the skin. In Indonesia, the aerial and some other parts are used to treat fevers, skin rashes and as a remedy for ringworm infection. Notably, in Malaysia, Singapore, and Indonesia, the plant has been used as remedies for eruptive fever, rash, kidney disease, migraine, constipation, hypertension, diabetes mellitus, and cancer [91]. Apart from those, this plant has been used in treating cancer, inflammation, cholesterol, diabetes mellitus, kidney issues, hypertension and many more diseases [92]. The leaves and leaf extracts also possesses anti-herpes simplex virus, antibiotic, anti-hyperglycemic and anti-hyperlipidaemic, anti-inflammatory, anti-carcinogenic, blood hypertension reduction capabilities, anti-proliferative on human mesangial cell, anti-oxidative and anti-ulcerogenic properties [69,75,92,93]. There are some studies on rats to elucidate the potentials of G. procumbens in treating some of the diseases such as, sperm quality [94], acute toxicity and wound healing potential [95], blood pressure [96,97,98,99] and anti-therapeutic effects [100].

G. procumbens leaf extract using different organic solvents (hexane, methanol, chloroform, acetonitrile, distilled water and ethanol) has shownsome positive effects on free radical scavenging and iron chelating which may use as preliminary information and develop further to be commercially useful in food industry or health products as medicinal food [89]. In another study by Zhang and Tan [101] reported the ethanolic extract of G. procumbens has shown antihyperglycaemic and antihyperlipidaemic activities, but the whole process and the mechanisms related are not well studied. On the other hand, aqueous extract of this plant leaves possess significant hypoglycaemic effects [102]. Nisa and coworkers [103] showed that G. procumbens leaf extracts have cytotoxic activity and anticancer activity in rat liver. Whole plant except the root is used to study the blood pressure control measure in rats by vasodilatation via inhibition of calcium channels produced positive results [96]. Some recent findings are exhibiting chemopreventive properties for tumor inhibition on several types of cancer by both in vitro and in vivo administration of G. procumbens. This plant enhances breast cancer cell death and could be developed as a co-chemotherapeutic agent for reducing side effects in treating breast cancer [104]. Another study by Wang et al. [105] reports the apoptosis and suppresses proliferation via inhibition of nuclear translocation in treating tumors. The traditional use of this plant against bacterial and fungal infections has been supported by the findings of Rahman and Al Asad, [106]. The ethanol extract of G. procumbens showed virucidal and antireplicative actions against herpes simplex virus HSV-1 and HSV-2 [100].


A. leptopus Hook. & Arn. is commonly known as Mexican Creeper, cadena de amor, flores kadena, bride’s tears, chain-of-love, confederate vine, coral vine, bee bush or San Miguelito Vine in English while it’s called as Air Mata Pengantin, Bunga Berteh, Bunga Bonet in Bahasa Malaya. This plant is from Family Polygonaceae (buckwheat family), native to Mexico and commonly found in tropical Asia, Africa, the Caribbean and Americas [107] (Fig. 2). Family Polygonaceae consists of around 50 genera [108]. Some members of this family are used as salads, culinary purposes and ornamental plants; A. leptopus one among them. A. leptopus has many scientific synonyms i.e. Antigonon cinerascens Martens & Galeotti, Antigonon cordatum M. Martens & Galeotti, Antigonon platypus Hook. & Arn., Corculum leptopum (Hook. & Arn.) Stuntz and Corculum leptopus (Hook. & Arn.) Stuntz.

4.1 Botanical Description

Antigonon leptopus, known as coral vine and queen’s wreath, is one of the examples. It is native to Mexico and commonly found in tropical Asia, Africa, Caribbean and the Americas. Antigonon leptopus is a fast growing perennial woody climber used to attain 5-13 m in length. Stems are laterally branched and leaves are alternate and ovate or triangular-ovate in shape. The lower surface is green, dull, with prominent venation where, upper part of leaves are shiny light green with sunken venation. Bisexual flowers are most commonly pink in color, found in axillary racemes or terminal panicles [109,110].

4.2 Chemical Constituent

Aerial parts of Antigonon leptopus are used to produce tea in many countries which is utilized as a remedy for cold and pain relief in traditional
Fig. 2. A. leptopus global distribution (Derived from Burke and DiTommaso\textsuperscript{109})

Figures and diagrams are not provided in the text. The text discusses the medicinal properties of A. leptopus, including the presence of flavonoidal glycosides, triterpenoids, flavonoids, tannins, steroids, alkaloids, and glycosides in different parts of the plant. It also mentions the use of A. leptopus in traditional and alternate medicine for various ailments, such as treating colds, throat constriction, pain relief, diabetes, hypertension, menstrual pains, nephritis, hepatitis, and colitis. Root and rhizome extracts show significant antibacterial and antifungal activity against common microorganisms. A study on rats has displayed considerable amount of anti-diabetic activity as well. Anthelmintic activity of A. leptopus is also reported by several authors.

5. IRANIAN CLIMBER PLANTS

5.1 Hedera helix L.

Hedera helix L. familiar with common names of English ivy, common ivy or European ivy is a plant and the most studied plant from the family of Araliaceae. It is a flowering, dicotyledonous, clinging and evergreen climbing plant, which in case of being close to any vertical surface such as trees, cliffs and walls, it climbs by its root-like structure and secrete glue like substance that let it attach to any surface. Otherwise, it grows as a ground cover. Hedera helix usually grows to 20-30 m (to 50 m is also reported). Its fruits are purple-black to orange-yellow color that they appear about 8-10 years after planting and have a stone like seeds and it can survive for 400-500 years.

5.2 Botanical Distribution

Hedera helix is originated from western Asia, northern Africa and Europe. It is widely distributed in northern Iran, Turkey, Ukraine and Portugal. Later this plant was introduced to other countries in the world as ornamental purpose, which can be cultivated carefree in many types of soil and weather. Hedera helix easily grows in different situations; such as well drained soils and can tolerate drought, followed that grows in full shade to part shade. It prefers loamy and rich soils, but persist the clay, sand and well drained soils. It is resistant to...
atmospheric pollutions. Birds, insects and bees have an important role in pollination and dispersing seeds [128]. *Hedera helix* propagates by seeds or by vegetating. Besides, if the spreading stems touch the soil, new roots from the nodes appear. It is better to prevent *Hedera helix* from climbing the boughs as its overgrowth dry the tree. *Hedera helix* is cultivated for the winter decoration. Besides, it is a wildlife shelter, food source and an attraction for wildlife. It is useful in covering eroded walls and surfaces, covering the fences and performs as weed suppression. The seeds and leaf of *Hedera helix* is not edible. In addition, ingestion of large amount of this plant is toxic and can leads to gastrointestinal irritation [129]. The seeds were used to treat cough and bronchitis.

### 5.3 Chemical Constituent

*Hedera helix* has a high digestibility organic matter and contains fibers, lignin, silica and crude protein. Its leaf extract contains Saponosides, Flavonoids, Bidesmoside and sterols [130]. In addition, the leaf contains α-hederin which is appetite suppression. Various Triterpenoid Saponins are available in different part of this plant [126]. The Triterpenoids Saponins; α-hederin and β-hedermins derive from the hydrolysis of Hederasaponins [130]. The fruit pulp has 32% lipid content and 5% protein content but seeds contain 5% palmitic, 20% oleic, 13% linoleic and 62% petroselenic [131]. Cyanogenic glycosides and flavonoid rutin are present in the pulp of the berries and the saponin β-hederin and saponin hederagenin 3-O-β-L-arabinopyranoside are present in the seeds [132].

### 5.4 Medicinal Properties

*Hedera helix* has potential activity against fire blight which is caused by a gram-negative bacterium, *Erwinia amylovora*. The extract made a high resistance against the bacteria, which polyphenol oxidation activity in leaves of M26 rootstock increased significantly [133]. In field experiments on the apple variety, *Hedera helix* showed efficiency the same as streptomycin against fire blight [134]. In another experiment against fire blight, spraying 3% (3 ml plant extract: 100 ml water) of *Hedera helix* extract showed the best result among different doses in inhibiting disease development [135]. In Anglo-Saxon medicine, the ivy’s juice was used to pour into ear to improve hearing. Besides, the berries were used for liver disease, lung wound, and headache and loin sickness. Its shoots used for sunburn and leaves for salving the wen [136]. *Hedera helix* is a toxic plant if it is taken intravenously. The Saponins have the potential to damage cells [137]. In case of consumption, various symptoms such as bloody diarrhea, death and contact dermatitis are reported. On the other hand, having anti-inflammatory [138] antifungal [125], antispasmodic [139] antibacterial [140] and anthelmintic [141] of *Hedera helix* made it an important plant for further studies. Nowadays saponins are known to have anti-inflammatory activity and English ivy are a source of this triterpenoid saponins. Besides, Mendeland coworkers showed that the dry extract of *Hedera helix* leaf caused a strong contractile effect on the rat stomach corpus and fundus under the *in vitro* condition. It was claimed that α-hedrin is responsible for all the effect of an ivy extract [142]. In addition, bronshidilating property is because of the presence of saponins, especially α-hedrin [143]. On the other hand, investigations show that the extracts of the leaves of *Hedera helix* have potentials in the treatment of bronchitis disease. This effect is more intense when other drugs, especially non-antibiotic, are added to the *Hedera helix* syrup [144]. The other studies show the effectiveness of *Hedera helix* and its leaf extract in the form of cough syrups for bronchial asthma in children [145].

### 5.5 Other Usage

*Hedera helix* contributes to reduce global warming and it is considered as a high quality ornamental plant due to energy-saving property of temperature integration combining with DIF. Another possibility of energy-saving greenhouse strategy performs by using temperature integration. It approaches energy-saving by a reduction in energy consumption and using the fluctuations within the certain bandwidths and keep the temperature in average for a specific period of time [146]. In the study performed by Pollet and coworkers showed that the positive DIF controls made the ivy plant having a long shoots with dark green leaf. These characters are highly appreciated in commercial production of the ivy plant with a higher market value [147]. It is claimed that urban vegetation reduces the impact of air pollution on people and the build environment by using particles sink [148]. Sternberg and coworkers showed that English ivy is effective at absorbing dust particles. It has adheres the airborne particles and effective for reducing the decay process on stone walls. They
suggest that English ivy can be used as an atmospheric pollution reduction [149].

6. Rosa canina

*Rosa canina* is known as dog rose from the family of Rosaceae. This plant is a climbing wild rose having small and sharp thorns which help the plant in climbing. *Rosa canina* is a deciduous shrub and it’s tall around 3-5 meters. The leaves are dark green and have 3-5 leaflets [150]. Similar to red rose, dog roses have pale pink, white and red flowers [151]. Cynorrhodon is the name of dog rose’s fruit or hip with the color of red-orange. After drying, cynorrhodon has a sweet taste. Since ancient times in Iran, *Rosa canina* has been a very important plant in curing diseases because of a wide range of antioxidants, minerals and vitamins it possesses.

6.1 Botanical Distribution

*Rosa canina* grows vertically around trees and can climb vertical surfaces by using the thorny stem it has. It grows in woodlands and hedges and survives in sun or full shade. Dog rose thrives in well drained, acidic soil, clay, sand and loam. Wet and moist soils are preferred. It is noted as an attraction for the wildlife and it has tolerated the strong winds and cold weather up to -10 centigrade. This plant is a self-fertile and pollinates by bees, flies self-fertilization and apomictic. *Rosa canina* is native to western Asia, Africa and Europe. *Rosa canina* is among the oldest plants in Iran. It has been used in cooking and producing jam. The flower and leaves were used for making tea and tea substitutes. Distilled water from hip rose was used as skin lotions and anti-aging solution. In addition, this plant encounter as a beautiful, amenity planting due to the nice odor and color it has. In traditional Iranian medicine, dog rose is known as a treatment for kidney inflammation, stomachache and diarrhea, gallstone and insomnia. It was mentioned that dog rose was used to treat the bite of rabid dogs, the reason *Rosa canina* is named dog rose.

6.2 Chemical Constituent

*Rosa canina* is a rich source of minerals, vitamins and biologically active compounds. It contains pectins, tannins, flavonoids, sugars, organic acids, carotenoids, fatty acids (linoleic, oleic, linolenic, palmitic, stearic and arachidonic acid [152] and vitamin C, B1, B2, E extracted from dog rose hip. Besides, other macronutrients and micronutrients; crude protein, ascorbic acid, and Na, K, P, Mn and Mg were available in dog rose extract [150]. Sometimes the vitamin C content in dog rose alleviates. This reduction is because of the temperature, light, environment oxygen level and variations in endogenous plant growth regulators [153]. Furthermore, more phenolic contents isolated from dog rose; such as sinapic, chlorogenic, catechin, gallic acid, ferrulic, procyanidin-B2, t-caffeic and p-coumaric [154]. It is also mentioned that the presence of monoterpenes and sesquiterpenes lead to the aroma of dog rose [154]. Various amounts of ascorbic acid and antioxidant activity were reported for dog rose. Different concentrations of ascorbic acid are because of different harvesting period species, altitude, ecological factors and variety [155]. Jabłońska-Ryś and coworkers reported the antioxidant activity of dog rose (127.78 mM Fe·100 g⁻¹, on average, FRAP method), ascorbic acid of 1252.37 mg·100 g⁻¹ and phenolic contents 3217.28 mg·100 g⁻¹ on average [156] Ascorbic acid in dog rose equals six times of ascorbic acid available in orange.

6.3 Medicinal Properties

*Rosa canina* (rose hip) powder (5 g per day) was found to be efficient in the reduction of osteoarthritis through in clinical trials. In addition, the patients treated with rose hip for three months showed a decrease in their cholesterol level [157]. *In vitro* studies showed that dog rose extract reduce the chemotaxis of monocytes and neutrophils in order to alleviate inflammatory effect in patients with osteoarthritis [158]. Besides, anti-nociceptive effect in osteoarthritis patients [159], anti-inflammatory and immunological effect [160], dropy [161], treatment for biliary complaints [162] and treatment for disordered kidney [163] was reported for dog rose treatments. Sadigh-Eteghad and co-workers study shows an increase in monocytes, neutrophils, gamma globins and phagocyte activity in groups of rats treated with 250-500 mg dog rose extract. In addition, vitamin C content, next to the polyphenolics content of dog rose contributed to a high antioxidant activity [164]. Vitamin C is involved in enhancing the immune system by integrating the important immune cells [165]. Furthermore, antidiabetic activity of dog rose is proved [161]. The antidiabetic activity depends on monosaccharides, polysaccharides and pectin content [153]. In a study conducted by Štajner and co-workers concluded that honey, which is
enriched with 5-10 g of *Rosa canina* fruit is a rich source of naturally occurring antioxidants such as flavonoids, vitamin C and phenolic acids [166].

### 6.4 Other Usage

The skin protects itself from UV radiation of the sun using the melanin. When the melanin accumulates abnormally in a specific part of the skin, it may cause an esthetic problem. Using the skin Lighteners can help to remove this unwanted problem. A study of Fujii and coworkers showed that dog rose extract has a high potential to help to remove the melanin patches due to the presence of quercetin in its extract. Quercetin has a high inhibitory action against melanogenesis [167]. The water extract of *Rosa canina* has an antibacterial effect against *Bacillus cereus*, *Bacillus subtilis*, *Escherichia coli* and *Candida albicans* and its acetone extract has an antibacterial effect against *E. coli* and *C. albicans* [168]. Litovet a rose hip powder produced by HybenVital for animals has antibacterial effect [169].

### 7. Vitis vinifera

*Vitis vinifera* known as grape, wine grape, purple leaf. Grape or common Grape is a plant from Vitaceae family, is one of 60 *Vitis* species. Grape is a plant that has been used since ancient time. It is a climber, growing to 10-15 meters. The leaves are lobed, long-stalked and broad (about 10 to 30 cm wide) and have a dark green color. *Vitis vinifera* is pollinated by insects and wind as it is a hermaphrodite plant and possessing both male and female organs. The edible parts of a grape plant are its oil, flowers, fruits and leaves. According to the color, the grapes are classified as green grape, red grape, black grape and yellow grape. The colors can be different due to a variety of genetic materials and cultivating environment.

#### 7.1 Botanical Distribution

*Vitis vinifera* are native to the Mediterranean region and east Europe. Some species occur in Asia, southern Germany and east to northern Iran. *Vitis vinifera* are one of the oldest fruit crop in the world and its Antiquity can reach over 5000 years old [26]. It prefers dry or moist soils and it needs the mild and warm weather to grow. Although the grape is resistant to very cold weather it needs a sunny and hot weather in spring and summer, whereas exposure to sun increases the amount of anthocyanin and soluble solids with a lower weight of the berries, juice pH and malate [170]. *Vitis vinifera* are resistant to drought, especially if it is placed in deep soil. Besides, it is resistant to wind if it grows in vertical surfaces. Strong winds can be more harmful than the cold weather where, increasing by 10 centigrade in springs, cause to start the growth of the plant. The hot and dry weather is a suitable condition for pollination. Therefore, pollination by insects is not essential. Acidic or salty soil is not suitable to cultivate grapes. The most suitable soil for grape cultivation is deep, clay and sandy soils which are well drained. Raw or dried fruit of *Vitis vinifera* is widely used in Iran. The dried fruit is raisins, sultanas and currants. Different products are because of different variety of fruits. Besides, *Vitis vinifera*'s fruit is used as wine production. Wine production used to be popular in Iran. The current usage is more on fruit production, vinegar production and fruit juice extraction. The leaves are used for wrapping the ingredients of the food and make a delicious taste and a nice aroma. In addition, the leaves are important in ceasing bleeding, wound healing and treatment of hemorrhoids and capillary fragility. A polyunsaturated oil extract from the seeds that is healthy and mostly suitable for frying. Most of the benefits of grape are because of its seeds. The graph contains natural sugar, therefore the sap is used due to its sweet flavor mostly for breakfasts.

#### 7.2 Chemical Constituent

*Vitis vinifera* is a rich source of phenolic acids, flavonoids, anthocyanin, proanthocyanin, amino acids, minerals, sterols and sugars [171]. Various chemicals in grape represented by different phytochemical compounds; such as terpenoids, alkaloids, sterols, phenolic and tannins [172]. The compounds made grape an interesting crop for researchers due to its biological activity. The seeds contain procyanidins, while the skin has a wide range of phenolics; such as procyanidins, anthocyanin, flavonoids, prodelphinidin, flavonols (quercetin and kaempferol) cinnamic acid, benzoic and stilbenes. Phenolics consist of flavan-3-ols, (+) -catechin, -epicatechin-3-O-gallate and (-) -epicatechin, which all known by procyanidin [173]. Flavan-3-ols and proanthocyanidin are best known for their high antioxidant activity. The study conducted by Hilbert and co-workers, they showed that *Vitis*...
*Vitis vinifera* has a higher total flavonol concentration than wild *Vitis* species [174,175]. Besides, they mentioned that the quercetin content is among the highest in derivatives [176]. They claimed that the grape’s stem is a rich source of polyphenols; such as flavonoids, hydroxycinnamic, hydroxybenzoic, stilbenes and phenolic acids [177]. Stilbenes are belongs to phytoalexins and its synthesis induces by abiotic and biotic stress factors, such as; UV light [178], soil lime [179], fungal infection [180], mineral nitrogen depletion [181] and water stress [182]. Leaf aqueous extract in red and white varieties of *Vitis vinifera* revealed high amount of phenolic content, its regulate the high antioxidant activity [183]. It is also mentioned that the red variant contains more phenolic content in comparison to its white type. The red/blue color of berries is due to the presence of anthocyanin. The genes responsible for the color are organized in complex clusters and they are present in any tissue of the grape plant that are known to accumulate flavonoids ex, root, seeds, flower leaves [184]. While genetic background and maturation stage are two critical factors in the formation of anthocyanin in grape berries, factors such as water availability, altitude, pathogens exposure and slope are important in grape quality [185,186,187]. The quality, flavor and aroma of the grape is due to its compounds and pathways that the compounds. These compounds and nutrients drag many attentions in pharmacology and the food industry.

### 7.3 Medicinal Properties

*Vitis vinifera* are potential in pharmacological activities due to its phytochemical content. Excessive production of reactive oxygen species, end to degenerative processes; such as cancer and cardiovascular diseases [188]. Grape extract inhibits reactive oxygen species production. Researches show that grape extract has cytotoxicity activity in human cancer cell culture [189,190]. Furthermore, grape extract exhibit anti-inflammatory [171] antibacterial [191], antimicrobial activity [192] and anti-carcinogenic [193,194] activity. Besides, grape extract prevents Alzheimer disease [195]. Reduction in glutathione level, increasing nitric acid production in the rat pouch oedema model, in vitro cytotoxicity effect of the extract and increasing superoxide dismutase activity is among the pharmacological activity of grape extract [171]. Inhibition of topoisomerase I, which is active for cell proliferation is another activity for antitumor and chemopreventive activity of grape extract [188]. Lakshmi and co-workers generated a study about the neuroprotective effect of grape extract. They exhibited that the grape extract is a neuroprotectant for patients against aluminum induced neurotoxicity [196]. Grape’s stem has an antioxidant activity comparable to seed extract and has inhibition against liver and cervical cancer [197]. *Vitis vinifera* is reported to be useful in the treatment of snakebite, dog bite and bee sting [198]. Raisin, the dried fruit of grape showed an antimicrobial activity in oral health. The phytochemical compounds in the raisin suppress the growth of oral bacteria and protect gum and dental health [199].

### 7.4 Other Usage

Grape pomace is useful in production and activities in industries other than pharmaceutical that is used in production of hydrolytic enzymes [200], livestock feeds [201], food colorants [202] and biofuels [203]. The residues and by-products are used in wine industry, grape marc (skin and seeds), attracted attention due to their phenolic content, biological activity specially its antioxidant activity [204]. The low molecular weight phenolic compound attributed to antioxidant activity. In addition, the process of winemaking, other compounds such as anthocyanin-derived pigments, hydrolysis of flavonol glycosides and tartaric esters of hydroxyxinnamic acid forms due to the action of yeast mediated enzymes [205]. Oven dried is not recommended in the wine making industry because of degrading and deforming the needed compounds. High flavonoid content cooperates with cell structure protection against UV light and its harmful effects by absorbing high radiation wavelength [183]. Furthermore, grape seed extract inhibits the growth of *Alicyclobacillus acidoterrestris* cells and spores in apple juice. The inhibition is because of high phenolic content and its target is the cell membrane of *A. acidoterrestris* [206].

### 8. CONCLUSION

Plants have a high potential in producing new and beneficiary drugs and pharmaceutical production, which is harmless and highly efficient to human. *Aristolochia tagala*, *Gynura procumbens*, *Antigonon leptopus*, *Hedera helix*, *Rosa canina* and *Vitis vinifera* are among Malaysian and Iranian plants that are very beneficial to human. Their antioxidant property, phenolic contents other micro nutrients will leads to further studies in this field. The potential of producing medicines and drugs such as
anticancer drugs and their availability and ease of growing of these plants attracted many scientists’ attention. Climber medicinal plants are multipurpose potential medicinal plant having high market potential all over the world. Hence it is utmost important to monitor the progress the biochemical and pharmaceutical literature to assess the efficacy before being recommended for the various therapies.

**SIGNIFICANT STATEMENT**

Significant of this paper is to highlight the importance of phytochemical, pharmaceutical and biochemical activity of important climber plants in Iran and Malaysia. Traditional medicine has many advantages. It is easy to accessible, also it is cheaper than modern medicine, and well known to widely acceptable to those in developing countries. These significant reports demonstrate the significant impact of these climber medicinal plants for the treatment of a variety of diseases by integrating the traditional and modern medicine could help to provide improve health of people living in this globe.

**COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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15


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