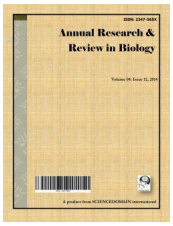

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Phytochemical, Pharmaceutical and Biochemical Activites of Selected Climber Plants: A Review

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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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behind the traditional uses of climber plants, the current scientific evidence to support these claims remains scant. More research is still needed to validate the medicinal aspects, beginning by increasing the understanding of the biological actions of the climber plants.

Keywords: Hedera helix; Rosa canina; Vitis vinifera; Aristolochia tagala; Gynura procumbens and Antigonon leptopus; phytochemical; pharmacological; saponin; quercetin; anthocyanins; anticancer; grape; Ivy.

1. INTRODUCTION

Climber plants are an important source of novel dirugs 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, ferns, 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 organs, 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 profiting 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,

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 contain chemicals derived from plants. Burkill [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 ethno botanical 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. clematitis* 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].

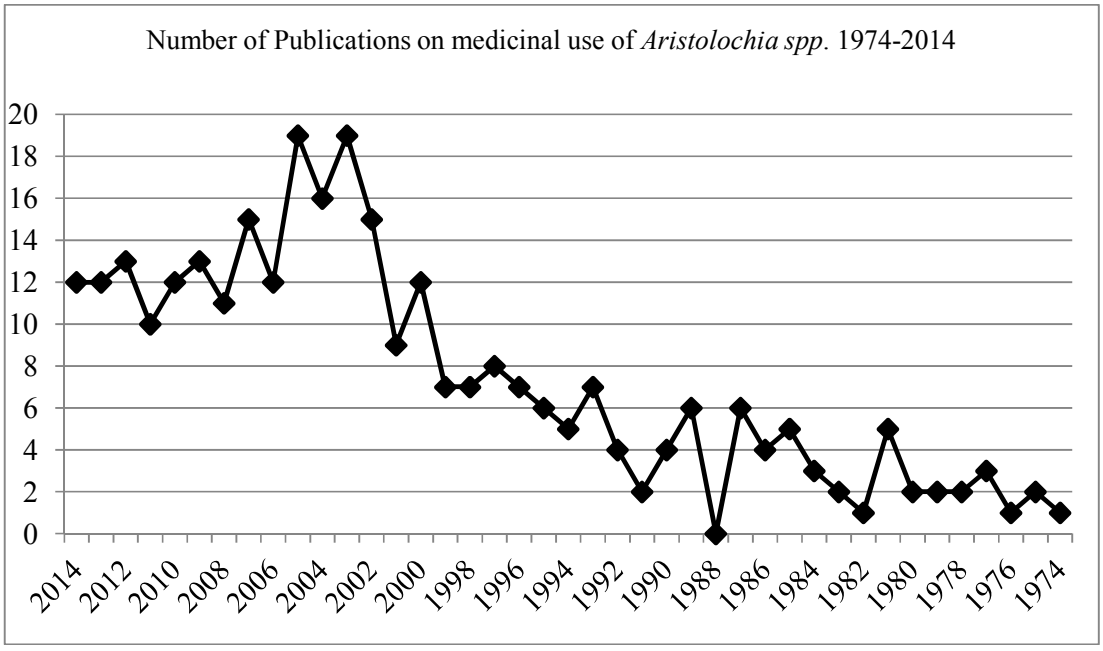

Fig. 1. Number of publications on medicinal uses of *Aristolochia* species from 1974 to 2014

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 Sothern 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 containisoaristolochic 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, antiproliferative, 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 have 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 8 cm long and 0.8 to 3.5 cm wide. Flowering heads are panicled, narrow, yellow 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 plantare 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 *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].

4. *Antigonon leptopus* HOOK. & ARN.

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 1200 populated in 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* M.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

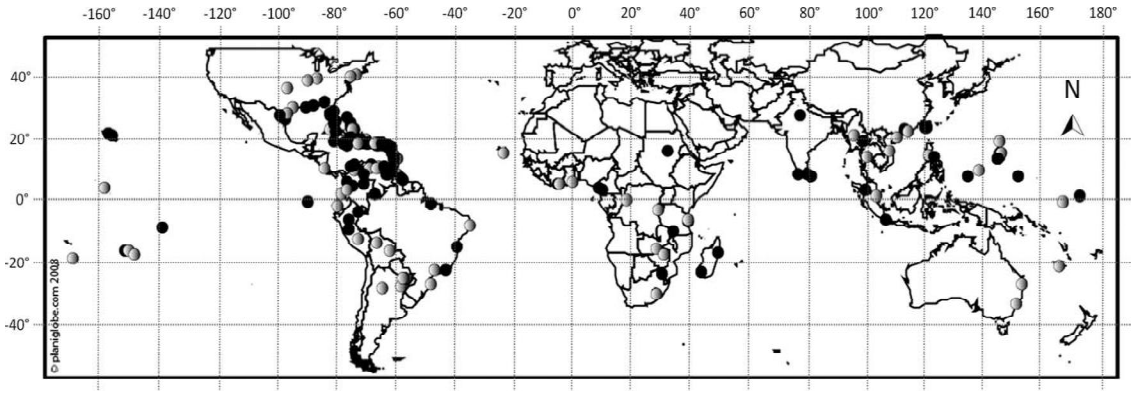

Fig. 2. *A. leptopus global distribution (Derived from* Burke and DiTommaso[109])

medicine [111]. Chemical investigations of aerial parts (leaves and flowers) of *A. leptopus* have shown the presence of lavonoidal glycosides viz quercetin-3-rhamnoside, quercetine-3-o-glucoro and several other phenolic compounds [112]. Roots and rhizomes are found to contain triterpenoids, flavonoids, tannins, steroids, alkaloids and glycosides [113,114].

4.3 Medicinal Properties

Recent understandings of traditional and alternate medicine have been created a massive awareness to investigate the medicinal plants on earth. Phenolic compounds always showed considerable health benefits such as antimicrobial, anti-oxidant, anti-inflammatory activities. Tea prepared from the aerial parts of *A. leptopus* is used as a remedy for colds, throat constriction, and pain relief in Jamaica, St. Lucia, Mexico, and Trinidad-Tobago [111,115]. Some other studies have shown the leaves of *A. leptopus* are used to reduce swelling and to treat diabetes, hypertension, and menstrual pains [116], whereas, vines are utilized in the treatment of cough and throat constrictions. It has been used in Chinese folk medicine to treat nephritis, hepatitis and colitis [117].

Gupta and coworkers [118] reported that flower extracts of this plant possess potent anti-microbial activity against *Staphylococcus aureus*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Micrococus albus* which are common human dental pathogens. Roots of *A.leptopus* have analgesic and anti-inflammatory properties as reported by Carey and coworkers [119] and the methanolic extract of vine has displayed anti-thrombin activity [120,121]. Roots and rhizome extracts displayed significant antibacterial and antifungal activity against several common microorganisms [113]. A study on rats has displayed considerable amount of anti-diabetic activity as well [122]. Anthelmintic activity of *A. leptopus* is also reported by several authors [123,124].

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 [125]. *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 isoriginated from western Asia, northern Africa and Europe. It is widely distributed in northern Iran, Turkey, Ukraine and Portugal [126]. 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 [127]. 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-hederins 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- hederin is responsible for all the effect of an ivy extract [142]. In addition, bronshidilating property is because of the presence of saponins, especially α- hederin [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 atmospheric pollutionreduction [149].

6. *Rosa canina*

Rosa canina known as dog rose from the family of Rosaceae. This plant is a climbing wild rose having small and sharp thorns which is 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 time 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 sesquiterpens 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], dropsy [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 anti-inflammatory effect on horses. It improves the flexibility of the hip and knee joints. The horses treated with Litovet had improvement in their speed running [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*

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 medicial 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.

REFERENCES

1. Hogan CM. Plant. In: Encyclopedia of Earth. Eds. Cutler J. Cleveland and Taub, DR. Washington, D.C.: Environmental Information Coalition. National Council for Science and the Environment; 2010.
2. Schnitzer SA, Dalling JW, Carson WP. The impact of lianas on tree regeneration in tropical forest canopy gaps: Evidence for an alternative pathway of gap-phase regeneration. Journal of Ecology. 2000;88(4):655-666.
3. Gillespie TW, Grijalva A, Farris CN. Diversity, composition and structure of tropical dry forests in Central America. Plant Ecology. 2000;147:37-47.
4. Jongkind CCH, Hawthorne WD. A botanical synopsis of the lianas and other forest climbers. In: Forest climbing plants of West Africa: Diversity, Ecology and Management, Bongers, F., Parren, MPE. and Traore, D. (Eds). CAB International. Oxfordshire, UK; 2005.
5. Swaine MD, Hawthorne WD, Bongers F, Aceves MT. Climbing plants in Ghanaian Forests: In: Forest climbing plants of West Africa: Diversity, Ecology and Management, Bongers, F., Parren, MPE. and Traore, D. (Eds). CAB International. Oxfordshire, UK; 2005.
6. Bongers FJJM, Schnitzer SA, Traore D. The importance of lianas and consequences for forest management in West Africa. BioTerre, Special Edition. 2002;59-70.
7. Addo-Fordjour P, Rahmadand ZB, Shahrul AMS. Impacts of forest management on community assemblage and carbon stock of lianas in a tropical lowland forest, Malaysia. Tropical Conservation Science. 2014;7(2).
8. Benavides AM, Alvaro J, Duque M, Duivenvoorden G, Vasco A, Callejas R. A first quantitative census of vascular epiphytes in rain forests of Colombian Amazonia. Biodiversity and Conservation. 2005;14:739-758.
9. Muoghalu JI, Okeesan OO. Climber species composition, abundance and relationship with trees in a Nigerian secondary forest. African Journal of Ecology. 2005;43:258-266.
10. Azam AWM, Marikarand FMMT, Muneeb MM. Transnational trading of biological materials and products from Sri Lanka. Journal of Biodiversity Management & Forestry. 2016;5:35(3):1-6.
11. Schnitzer SA, Bongers F. The ecology of lianas and their role in forests. Trends in Ecology and Evolution. 2002;17:223-230.
12. Schnitzer SA, Carson WP. Treefall gaps and the maintenance of species diversity in a tropical forest. Ecology. 2001;82:913-919.
13. Perera PAJ, Marikar FMMT. Nutrition metabolism. Bangladesh Journal of Medical Biochemistry. 2013;6(2):68-76.
14. Hashim MH, Ahmad R, Noor MZ, Ismail NH, Ahmat N, Lajis NH, Shaari K. Antioxidant and antimicrobial properties of malaysian *Uncaria longiflora* var. pteropoda. Planta Medica. 2009;75(09): PH9.
15. Eswani N, Kudus KA, Nazre M, Awang Noor AG, Ali M. Medicinal plant diversity and vegetation analysis of logged over hill forest of Tekai Tembeling forest reserve,

Jerantut, Pahang. Journal of Agricultural Science. 2010;2(3):189-210.

16. Ong HC, Zuki RM, Milow P. Traditional knowledge of medicinal plants among the malay villagers in kampung mak kemas, Terengganu, Malaysia. Ethno Med. 2011;5(3):175-185.
17. Schnitzer SA, Carson WP. Have we forgotten the forest because of the trees?. Trends in Ecology & Evolution. 2000;15(9):375-376.
18. Stevens GC. Lianas as structural parasites: The *Bursera simaruba* example. Ecology. 1987;68:77-81.
19. Nurfazliza K, Nizam MS, Nur Supardi MN. Association of liana communities with their soil properties in a lowland forest of Negeri Sembilan, peninsular Malaysia. Sains Malaysiana. 2012;41(6):679-690.
20. Carsten LD, Juola FA, Male TD, Cherry S. Host associations of lianas in a south-east Queensland rain forest. Journal of Tropical Ecology. 2002;18(1):107-120.
21. Pushpangadan P, Kumar B. Ethnobotany, CBD, WTO and the biodiversity act of India. Ethnobotany. 2005;17:2-12.
22. World Health Organization. WHO guidelines on good agricultural and collection practices (GACP) for medicinal plants. Geneva: World Health Organization; 2003.
23. Hill AF. Economic botany. A text book of useful plants and plant products. McGrow-Hill. New York; 1952.
24. Edeoga HO, Okwu DE, Mbaebie BO. Phytochemical constiuents of some nigerian medicinal plants. African Journal of Biotechnology. 2005;4(7):685-688.
25. Krishnaiah D, Bono DT, Sarbatly R. Studies on phytochemical constituents of six Malaysian medicinal plants. Journal of Medicinal Plants Research. 2009;3(2): 067-072.
26. Groombridge B, Jenkins MD. Global Biodiversity: Earth's living resources in the 21st century. Cambridge. The World Conservation Press; 2000.
27. Lugo AE. Diversity of tropical species: Questions that Elude Answers. International Union of Biological Sciences. Rio Piedras; 1988.
28. Kricher J. Tropical ecology. Princeton University Press. Princetown; 2011.
29. Myers N, Mittermeier RA, Mittermeier CG, da Fonseca G, Kent J. Biodiversity hotspots for conservation priorities. Nature: 2000;43:853-8.
30. Latiff A. Valuing the biodiversity of medicinal plant species in Malaysia. Sustainable management and utilization of medicinal plant resources in proceedings of the international conference on medicinal plants. 2005;3-16.
31. Outlook GB, Cooperation SS, Fund JB, Protocol C, Planand S, Decisions COPMOP. Global biodiversity outlook 3. In Montréal, Canada: Secretariat of the Convention on Biological Diversity. (http://gbo3. cbd. int/) Phil. Trans. R. Soc. B. 2010;9.
32. Sodhi NS, Posa MRC, Lee TM, Bickford D, Koh LP, Brook BW. The state and conservation of Southeast Asian biodiversity. Biodiversity Conservation. 2010;19:317-328.
33. Squires D. Biodiversity conservation in asia. Asia and the Pacific Policy Studies. 2014;1(1):144-159.
34. Whitmore TC, Burnham CP. Tropical rain forests of the Far East. Clarendon Press; 1975.
35. Appanah S, Gentry AH, LaFrankie JV. Liana diversity and species richness of Malaysian rain forests. Journal of Tropical Forest Science. 1993;6(2):116-123.
36. Kulip J. An ethnobotanical survey of medicinal and other useful plants of Muruts in Sabah, Malaysia. Telopea. 2003;10(1): 81-98.
37. Kammesheidt L, Berhaman A, Tay J, Abdullah G, Azwal M. Liana abundance, diversity and tree infestation in the Imbak Canyon conservation area, Sabah, Malaysia. Journal of Tropical Forest Science. 2009;21(3):265-271.
38. Ghollasimood S, Farida-Hanum I, Nazre M, Kamziah AK. Abundance and distribution of climbers in a Coastal Hill Forest in Perak, Malaysia. Journal of Agricultural Science. 2012;4(5):245-254.
39. Jamia AJ. Malay traditional medicine: An overview of scientific and technological advancement. Asia Pacific Tech Monitor. 2006;23(6):37-49.
40. Pan SY, Litscher G, Gao SH, Zhou SF, Yu ZL, Chen HQ, Ko KM. Historical perspective of traditional indigenous medical practices: The current renaissance and conservation of herbal resources.

Evidence-Based Complementary and Alternative Medicine; 2014.

41. Shein K. Traditional medicine in Asia, SEARO regional publications (No. 39), World Health Organization Regional Office for Southeast Asia, New Delhi, India; 2001.
42. Burkill IH. Economic products of malay peninsula. Crown Agent for the Colonies, London; 1935;2.
43. Sekar M, Abdullah MZB, Azlan AYHBN, Nasir SNB, Zakaria ZB, Abdullah MSB. Ten commonly available medicinal plants in Malaysia used for the treatment of Diabetes - A review. Asian Journal of Pharmaceutical and Clinical Research. 2014;7(1):1-5.
44. Faridah Hanum I, Rahim A, Lepun P, Edham I, Nazre M. Tree taxa inventory at Ayer Hitam forest base-camp. Pertanika Journal Tropical Agricultural Science. 2001;24(1):29-34.
45. Kadir AA. Conservation and economic potential of plant genetic resources in Malaysia. In Medicinal and Aromatic Plants. strategies and technologies for conservation. Proceedings of the Symposium State-of-the-Art Strategies and Technologies for Conservation of Medicinal and Aromatic Plants. Kuala Lumpur, Malaysia, 29-30 September 1997. Ministry of Science, Technology and Environment, and the Forest Research Institute, Malaysia; 1997.
46. Khatijah H, Noraini T. Anatomical atlas of Malaysian medicinal plants. Malaysia, Universiti Kebangsaan Malaysia Bangi, Selangor; 2006.
47. Chang YS, Rasadah MA. Inventory and documentation of medicinal plants in malaysia. in medicinal plants research in Asia, Volume 1: The framework and project work plans. International Plant Genetic Resources Institute- Regional Office for Asai, The Pacific and Oceania (IFGRI-APO), Serdang, Selangor, Malaysia, Botugal, Pons, A, Jayashree Kanniah, Lee Sok Young and Jeffrey T Oliver (eds). 2004;61-62.
48. Latiff A. Forestry, forest resources and forest biodiversity conservation in Peninsular Malaysia. Proceedings of the National Conference on the Management and Conservation of Forest Biodiversity in Malaysia. 2007;167-184.
49. Chapman K, Chomchalow N. Production of medicinal plants in Asia. In *III* WOCMAP Congress on Medicinal and Aromatic Plants-Volume 5: Quality, Efficacy, Safety, Processing and Trade in Medicinal 2003;679:45-59.
50. Mojiol AR, Adella A, Kodoh J, Lintangah W, Wahab R. Common medicinal plants species found at burned and unburned areas of klias peat swamp forest, beaufort, Sabah Malaysia. Journal of Sustainable Development. 2010;3(1):109-115.
51. Sabah Forestry Department. Klias Peat Swamp Forest, Sabah, Malaysia: Hydrological Process and Strategies for Water Management, Sabah Forestry Deparment. UNDP/GEF and Danida Klias Peat Swamp Forest Conservation Project. Sabah, Malaysia*;* 2005.
52. Lee HS. Introducing the cultivation of medicinal plants and wild fruits in forest rehabilitation operations on former shifting cultivation sites in Sarawak Malaysia: Issues and challenges. Southeast Asian Studies. 2004;42(1):60-73.
53. Murugan R, Shivanna KR, Rao RR. Pollination biology of *Aristolochia tagala*, a rare species of medicinal importance. Current Science. 2006;91:795-798.
54. Evans WC. A taxonomic approach to the study of medicinal plants and animal derived drugs. Eds: Pauline graham and publisher: Saunders Ltd In: Trease and Evans Pharmacognosy. Elsevier; 2009.
55. Nortier JL, Martinez MC, Schmeiser HH, Arlt VM, Bieler CA, Petein M, Depierreux MF, De Pauw L, Abramowicz D, Vereerstraeten P, Vanherweghem JL. Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). New England Journal of Medicine. 2000;342:1686-92.
56. Heinrich M, Chan J, Wanke S, Neinhuis C, Simmonds MSJ. Local uses of *Aristolochia* species and content of nephrotoxic aristolochic acid 1 and 2-A global assessment based on bibliographic sources. Journal of Ethnopharmacology. 2009;125:108-144.
57. Dey A, De JN. Pharmacology and medicobotany of *Aristolochia tagala* cham: A review. Pharma Science Monitor. 2012; 3(1):110-122.
58. Kazembe T, Munyarari E, Charumbira I. Use of traditional herbal medicines to cure

malaria. Bulletin of Environment. Pharmacology & Life Sciences. 2012;1(4): 63-85.

59. Debelle FD, Vanherweghem JL, Nortier JL. Aristolochic acid nephropathy: A worldwide problem. Kidney International. 2008;74(2): 158-169.
60. Gold LS, Slone TH. Aristolochic acid, an herbal carcinogen, sold on the Web after FDA alert. New England Journal Medicine. 2003;349:1576–1577.
61. Wu TS, Damu AG, Su CR, Kuo PC. Terpenoids of aristolochia and their biological activities. Natural Product Reports. 2004;21(5):594-624.
62. Kalaiarasi V, Johnson M, Sivaraman A, Janakiraman N, Babu A, Narayani M. Phytochemical and antibacterial studies on A*ristolochia tagala* cham. World Journal of Pharmaceutical Research. 2014;3(2): 2172-2178.
63. Thirugnanasampandan R, Mahendran G, Bai VN. Antioxidant properties of some medicinal *Aristolochiaceae* species. African Journal of Biotechnology. 2008; 7(4).
64. Butt GR, Parimi R, Sekar KBC. *In vivo* and *in vitro* pharmacological activity of *Aristolochia tagala* (syn: *Aristolochia acuminata*) root extracts. Pharmaceutical Biology. 2011;49(11):1210-1214.
65. Biswas A, Bari MA, Roy M, Bhadra SK. *In vitro* regeneration of *Aristolochia tagala* Champ. A rare medicinal plant of Chittagong hill tracts. Journal of Bio-Science. 2007;15:63-67.
66. Remya M, Narmatha Bai V, Mutharaian VN. *In vitro* regeneration of *Aristolochia tagala* and production of artificial seeds. Biologia Plantarum. 2013;57(2):210-218.
67. Tandon P, Kumaria S, Nongrum L. Conservation and management of plant genetic resources of Northeast India. Indian Journal of Traditional Knowledge. 2009;8(1):29-34.
68. Perry LM, Metzger J. Medicinal plants of East and Southeast Asia: Attributed properties and uses. MIT Press Cambridge. London. UK; 1980.
69. Kaewseejan N, Puangpronpitag D, Nakornriab M. Evaluation of phytochemical composition and antibacterial property of *Gynura procumbens* extract. Asian Journal of Plant Sciences. 2012;11:77-82.
70. Vanijajiva O, Kadereit JW. A revision of gynura (Asteraceae: Senecioneae). Journal of Systematics and Evolution. 2011;49(4):285-314.
71. Iskander MN, Song Y, Coupar IM, Jiratchariyakul W. Antiinflammatory screening of the medicinal plant *Gynura procumbens*. Plant Foods for Human Nutrition. 2002;57:233-244.
72. Wiart C. Medicinal plants of Southeast Asia (No. 2. ed.). Prentice Hall; 2002.
73. Song XQ, Wu XY, Zhu SS, Ren Q, Wu TF. The rapid propagation of tissue culture on *Gynura procumbens* [J]. Journal of Guizhou Normal University (Natural Sciences). 2011;S4:002.
74. Keng CL, Lee LS, Pin PL. Micropropagation of *Gynura procumbens* (Lour.) Merr. An important medicinal plant. Journal of Medicinal Plants Research. 2009;3(3):105-111.
75. Rahman AFMM, Al Asad MS. Chemical and biological investigations of the leaves of *Gynura procumbens*. International Journal of Biosciences. 2013;3(4):36-43.
76. Davies FG. The genus *Gynura* (Compositae) in Malesia and Australia. Kew Bulletin. 1980;711-734.
77. Bhore SJ, Ravichantar N, Loh CY. Screening of endophytic bacteria isolated from leaves of Sambung Nyawa [*Gynura procumbens* (Lour.) Merr.] for cytokinin-like compounds. Bioinformation. 2010; 5(5):191.
78. Akowuah GA, Sadikun A, Mariam A. Flavonoid identification and hypoglycemic studies of butanol fraction from *Gynura procumbens*. Pharmaceutical Biology. 2002;40:405-410.
79. Wiedenfeld H. Two pyrrolizidine alkaloids from *Gynura scandens*. Phytochemistry. 1982;21(11):2767–2768.
80. Liang XT, Roeder E. Senecionine from *Gynura segetum*. Planta Medica. 1984; 50(4):362.
81. Matheson JR, Robins DJ. Pyrrolizidine alkaloids from *Gynura sarmentosa.* Fitoterapia. 1992;63(6):557.
82. Takahira M, Kondo Y, Kusano G, Nozoe S. Four new 3α-hydroxy spirost-5-ene derivatives from Gynura Japonica makino. Tetrahedron Letters. 1977;18(41):3647-3650.
83. Bohlmann F, Zdero C. Gynuron, ein neues terpencumarin-derivat aus *Gynura*

crepioides. Phytochemistry. 1977;16(4): 494-495.

84. Yoshitama K, Kaneshige M, Ishikura N, Araki F, Yahara S, Abe K. A stable reddish purple anthocyanin in the leaf of *Gynura aurantiaca* cv. (Purple Passion). Journal of Plant Research. 1994;107(3):209-214.
85. Akowuah GA, Sadikunand A, Mariam A. Structural analysis of quercetin and rutin from *Gynura procumbens*. Journal of Tropical Medicinal Plants. 2001;2(2):193-199.
86. Yam M, Sadikun A, Asmawi M. Antioxidant potential of *Gynura procumbens*. Pharmaceutical Biology. 2008;46(9):616-625.
87. Sadikum A, Aminah I, Ismail N, Ibrahim P. Sterols and sterol glycosides from the leaves of *Gynura procumbens*. Natural Product Sciences (Korea Republic); 1996.
88. Hew CS, Gam LH. The identification of high abundant proteins in the leaves of *Gynura procumbens*. Biotechnology and Biotechnology Equipment. 2010;24:2132–2136.
89. Puangpronpitag D, Chaichanadee S, Naowaratwattana W, Sittiwet C, Thammasarn K, Luerangand A, Kaewseejan N. Evaluation of nutritional value and antioxidative properties of the medicinal plant *Gynura procumbens* Extract. Asian Journal of Plant Sciences. 2010;9:146-151.
90. Yam MF, Sadikun A, Ahmad M, Akowuah GA, Asmawi MZ. Toxicology evaluation of standardized methanol extract of *Gynura procumbens*. Journal of Ethnopharmacology. 2009;123(2):244-249.
91. Perry LM. Medicinal plants of East and Southeast Asia: Attributed properties and uses. 1st Edn., The MIT Press, Cambridge, Massachusetts and London; 1980.
92. Hew CS, Khoo BY, Gam LH. The anti-cancer property of proteins extracted from *Gynura procumbens* (Lour.) Merr. PloS One. 2013;8(7):e68524.
93. Lokhande A, Ingale SL, Lee SH, Sen S, Khong C, Chaeand BJ, Kwon IK. Effects of dietary supplementation with *Gynura procumbens* (Merr.) on egg yolk cholesterol, excreta microflora and laying hen performance. British Poultry Science. 2014;55(4):524-531.
94. Hakim P, Sani HA, Noor MM. Effects of *Gynura procumbens* extract and glibenclamide on sperm quality and specific activity of testicular lactate dehydrogenase in streptozotocin-induced diabetic rats. Malaysian Journal of Biochemistry and Molecular Biology. 2008; 16(2):10-14.
95. Zahra AA, Kadir FA, Mahmood AA, Alhadi AA, Suzy SM, Sabri SZ, Latif II, Ketuly AA. Acute toxicity study and wound healing potential of *Gynura procumbens* leaf extract in rats. Journal of Medicinal Plants Research. 2011;5(12):2551-2558.
96. Hoe SZ, Lee CN, Mok SL, Kamaruddinand MY, Lam SK. *Gynura procumbens* Merr. decreases blood pressure in rats by vasodilatation via inhibition of calcium channels. Clinics. 2011;66(1):143-150.
97. Ng HK, Poh TF, Lam SK, Hoe SZ. Potassium channel openers and prostacyclin play a crucial role in mediating the vasorelaxant activity of *Gynura procumbens*. BMC Complementary and Alternative Medicine. 2013;13:188-199.
98. Kaur N, Kumar R, Yam MF, Sadikun A, Abdul Sattar MZ, Aswami MZ. Antihypertensive effect of *Gynura Procumbens* water extract in spontaneously hypertensive rats. International Journal of Applied Research in Natural Products. 2013;6(3):20-27.
99. Abrika OSS, Yam MF, Asmawi MZ, Sadikun A, Dieng H, Hussain EA. Effects of extracts and fractions of *Gynura procumbens* on rat atrial contraction. Journal of Acupuncture and Meridian Studies. 2013;6(4):199-207.
100. Jarikasem S, Charuwichitratana S, Siritantikorn S, Chantratita W, Iskander M, Frahm AW, Jiratchariyakul W. Antiherpetic effects of *Gynura procumbens*. Evidence-Based Complementary and Alternative Medicine; 2013.
101. Zhang XF, Tan BKH. Effects of an ethanolic extract of *Gynura procumbens* on serum glucose, cholesterol and triglyceride levels in normal and streptozotocin-induced diabetic rats. Singapore Medical Journal. 2000;41:9-13.
102. Hassan ZM, Ahmad M, Pausi M, Yusof SR, Naidu G, Kumar S, Umachigi SP. Hypoglycaemic effects of aqueous extract of *Gynura procumbens.* Pharmacologyonline. 2008;1:30-50.

103. Nisa F, Hermawan A, Murwanti R, Meiyanto E. Antiproliferative effect of gynura procumbens (lour.) Merr. Leaves etanolic extract on 7, 12-dimethylbenz(a)antracene induced male rat liver. Advanced Pharmaceutical Bulletin. 2012;2(1):99-106.
104. Nurulita NA, Meiyanto E, Matsuda E, Kawaichi M. Gynura procumbens modulates the microtubules integrity and enhances distinct mechanism on doxorubicin and 5-flurouracil-induced breast cancer cell death. Oriental Pharmacy and Experimental Medicine. 2012;12(3):205-218.
105. Wang H, Zhou JW, Fu DH, Zhou Y, Cheng WZ, Liu ZL. Gynura procumbens ethanolic extract suppresses osteosarcoma cell proliferation and metastasis in vitro. Oncology Letters. 2013;6(1):113-117.
106. Vijayakumar M, Priya K, Nancy FT. Noorlidah A, Ahmed ABL. Biosynthesis, characterization and anti-bacterial effect of plant-mediated silver nanoparticles using *Artemisia nilagirica*. Industrial Crops and Products. 2012;41:235-240.
107. Raju AJS, Raju VK, Victor P, Naidu SA. Floral ecology, breeding system and pollination in *Antigonon leptopus* L. (Polygonaceae). Plant Species Biology. 2001;16:159-164.
108. Mabberley DJ. Mabberley's plant-book third edition (2008). Cambridge University Press: UK; 2008.
109. Burke JM, DiTommaso A. Corallatia (*Antigonon leptopus*): International Introduction of a plant with documented invasive capability. Invasive Plant Science and Management. 2011;4:265-273.
110. Acevedo-Rodríguez P, Strong MT. Monocotyledons and gymnosperms of Puerto Rico and the Virgin Islands. Contributions from the United States National Herbarium. 2005;52(1).
111. Mulabagal V, Alexander-Lindo RL, DeWitt DL, Nair MG. Health-beneficial phenolic aldehyde in Antigonon leptopus tea. Evidence-Based Complementary and Alternative Medicine; 2011.
112. Kawasaki M, Kanomata T, Yoshitama K. Flavonoids in the leaves of twenty-eight polygonaceous plants. The botanical magazine= Shokubutsu-gaku-zasshi. 1986;99(1):63-74.
113. Battu G, Raju NJ. Studies in preliminary phytochemical and antimicrobial activity of *Antigonon leptopus* Hook. International Journal of Chemical Science. 2009;7(4):2900-2904.
114. Carey MW, Babu DJM, Rao NV, Krishna Mohan G. Study of anti-inflammatory activity of *Antigonon leptopus* Hook. et Arn roots. Journal of Pharmacy and Chemistry. 2008;2(3):133-138.
115. Graveson R. Plants of Saint Lucia: A Pictorial Flora of Wild and Cultivated Vascular Plants; 2012.
116. Cheyl L. Ethnomedicines used in Trinidad and Tobago for urinary problem and Diabetes mellitus. J Ethnobiol Ethnomedicine. 2006;13:45-51.
117. Wu J. Manufacture of traditional Chinese medicine with Anti viral, Anti-inflammatory and detoxicating effects. Faming Zhuanli Shenqing Gongkai Shuomingshu CN. 2006;1:840.
118. Gupta AVN, Rao R, Jyothirmai B, Jagarlamu B, Bhogavalli PK. Studies on anti-microbial activity of flower extracts of Antigonon leptopus against common dental pathogens. Annals of Biological Research. 2011;2(2):99-103.
119. Carey MW, Rao NV, Ravikumar B, Krishna Mohan G. Preliminary studies of analgesic and anti-inflammatory properties of Antigonon Leptopus Hook. & Arn, roots in experimental models. Journal of Health Science. 2008;54(3):281-286.
120. Chistokhodova N, Nguyen C, Calvino T, Kachirskaia I, Cunningham I, Miles DH. Antithrombin activity of medicinal plants from central Florida. Journal of Ethnopharmacol. 2002;81:277-280.
121. Ranjan P, Tripathy K. *Antigononleptopus:* An Review. European Journal of Pharmaceutical and Medical Research. 2015;2(2):473-483.
122. Rani SV, Sujatha S, Mohanand SK, Kumar RB. Antidiabetic effect of *Antigononleptopus* Hook & Arn. leaf on Streptozotocin-induced diabetic rats. Pharmacologyonline. 2010;2:922-931.
123. Raju JN, Rao GB. Anthelmintic Activities of Antigonon leptopus Hooks and Mussaenda Erythrophylla Lam. International Journal of Pharmacy and Pharmaceutical Sciences. 2011;3(1):68-69.
124. Priya, KS, Satyavathi K, Bhojaraju P, Kumari YR, Prasad DV, Durga MSS,

Kanthal LK. GC-MS profiling and anthelmintic activity of *Antigonon leptopus* LEAVES. International Journal of Pharmaceutical Sciences and Research. 2014;5(5):1914.

125. Hooshyar H, Talari S, Feyzi F. Therapeutic Effect of *Hedera helix* alcoholic extract against cutaneous leishmaniasis caused by leishmania major in Balb/c Mice. Jundishapur Journal of Microbiology. 2014;7(4).
126. Metcalfe DJ. *Hedera helix L*. Journal of Ecology. 2005;93(3):632-648.
127. McAllister HA, Rutherford A. *Hedera helix* L. and *H. hibernica* (Kirchner) bean (Araliaceae) in the British Isles. *Watsonia*. 1990;18:7-15.
128. Clapham AR, Tutin TG, Moore DM. Flora of the British isles. CUP Archive; 1990.
129. Guelcin İ, Mshvildadze V, Gepdiremen A, Elias R. Antioxidant activity of saponins isolated from ivy: Alpha-hederin, hederasaponin-C, hederacolchiside-E and hederacolchiside-F. *Planta medica*. 2004;70(6):561-563.
130. Gaillard Y, Blaise P, Darré A, Barbier T, Pépin G. An unusual case of death: Suffocation caused by leaves of common ivy (*Hedera helix*). Detection of Hederacoside C, α-Hederin, and Hederagenin by LC-EI/MS-MS. Journal of analytical toxicology. 2003;27(4):257-262.
131. Snow B, Snow D. Bird and berries. A study of An Ecological Interactions. T&A. D. Poyser, London; 1988.
132. Barnea A, Harborne JB, Pannel C. What parts of fleshy fruits contain secondary compounds toxic to birds and why? Biochemical Systematics and Ecology. 1993;21:421-429.
133. Baysal Ö, Zeller W. Extract of *hedera helix* induces resistance on apple rootstock m26 similar to acibenzolar-s-methyl against fire blight (*erwinia amylovora*). Physiological and Molecular Plant Pathology. 2004;65(6):305-315.
134. Mosch J, Zeller W, Rieck M, Ullrich W. Further studies on plant extracts with a resistance induction effect against *Erwinia amylovora*. In VII International Workshop on Fire Blight. 1995;411:361-366.
135. Mosch J, Klingauf F, Zeller W. On the effect of plant extracts against fireblight (*Erwinina amylovora*). In V International Workshop on Fire Blight. 1989;273:355-362.
136. Thomas V. Do modern-day medical herbalists have anything to learn from Anglo-Saxon medical writings? Journal of Herbal Medicine. 2011;1(2):42-52.
137. Mills S, Bone K. Principles and practice of phytotherapy: Modern herbal medicine. Edinburgh: Churchill Livingstone; 2000.
138. Süleyman H, Mshvildadze V, Gepdiremen A, Elias R. Acute and chronic antiinflammatory profile of the ivy plant, *Hedera helix*, in rats. Phytomedicine. 2003;10(5):370-374.
139. Häberlein H. Hedera helix-mode of action evidenced by cell biologicals and biophysical investigation. Przewodnik Lekarski. 2008;1:255-256.
140. Cioaca C, Margineanu C, Cucu V. The saponins of hedera helix with antibacterial activity. Die Pharmazie. 1978;33(9):609.
141. Eguale T, Tilahun G, Debella A, Feleke A, Makonnen E. *Haemonchus contortus*: In vitro and *in vivo* anthelmintic activity of aqueous and hydro-alcoholic extracts of *Hedera helix*. Experimental Parasitology. 2007;16(4):340-345.
142. Mendel M, Chłopecka M, Dziekan N, Wiechetek M. The effect of the whole extract of common ivy (*Hedera helix*) leaves and selected active substances on the motoric activity of rat isolated stomach strips. Journal of Ethnopharmacology. 2011;134(3):796-802.
143. Bedir E, Kirmizipekmez H, Sticher O, Calis I. *Triterpene saponins* from the fruits of *Hedera helix*. Phytochemistry. 2000;53(8): 905-909.
144. Fazio S, Pouso J, Dolinsky D, Fernandez A, Hernandez M, Clavier G, Hecker M. Tolerance, safety and efficacy of *Hedera helix* extract in inflammatory bronchial diseases under clinical practice conditions: A prospective, open, multicentre postmarketing study in 9657 patients. Phytomedicine. 2009;16(1):17-24.
145. Hofmann D, Hecker M, Völp A. Efficacy of dry extract of ivy leaves in children with bronchial asthma - A review of randomized controlled trials. Phytomedicine. 2003;10: 213-220.
146. Körner O, Bakker MJ, Heuvelink E. Daily temperature integration: A simulation study to quantify energy consumption.

Biosystems Engineering. 2004;87(3):333-343.

147. Pollet B, Steppe K, Dambre P, Van Labeke MC, Lemeur R. Temperature integration of *Hedera helix* L.: Quality aspects and growth response. Scientia Horticulturae. 2009;120(1):89-95.
148. Ottelé M, van Bohemen HD, Fraaij AL. Quantifying the deposition of particulate matter on climber vegetation on living walls. Ecological Engineering. 2010;36(2):154-162.
149. Sternberg T, Viles H, Cathersides A, Edwards M. Dust particulate absorption by ivy (*Hedera helix* L) on historic walls in urban environments. Science of the Total Environment. 2010;409(1):162-168.
150. Demir F, Özcan M. Chemical and technological properties of rose (*Rosa canina* L.) fruits grown wild in Turkey. Journal of Food Engineering. 2001;47(4):333-336.
151. Ercisli S. Rose (*Rosa* spp.) germplasm resources of Turkey. Genetic Resources and Crop Evolution. 2005;52(6):787-795.
152. Özcan M. Nutrient composition of rose (*Rosa canina* L.) seed and oils. Journal of Medicinal Food. 2002;5(3):137-140.
153. Roman I, Stănilă A, Stănilă S. Bioactive compounds and antioxidant activity of *Rosa canina* L. biotypes from spontaneous flora of Transylvania. Chemistry Central Journal. 2013;7(1):73.
154. Demir N, Yildiz O, Alpaslan M, Hayaloglu AA. Evaluation of volatiles, phenolic compounds and antioxidant activities of rose hip (*Rosa* L.) fruits in Turkey. LWT-Food Science and Technology. 2014;57(1):126-133.
155. Dogan A, Kazankaya A. Fruit properties of rose Hip species grown in Lake Van basin (eastern Anatolia region). Asian Journal of Plant Sciences. 2006;5(1):120-122.
156. Jabłońska-Ryś E, Zalewska-Korona M, Kalbarczyk J. Antioxidant capacity, ascorbic acid and phenolics content in wild edible fruits. J. Fruit Ornam. Plant Res. 2009;17(2):115-120.
157. Winther K, Kharazmi A, Rein E. A powder made from a subspecies of rosehip (*Rosa canina*) reduces WOMAC symptoms scores as well as cholesterol levels in patients suffering from osteoarthritis. Osteoarthritis Cartilage. 2004;13:S93.
158. Winther K, Rein E, Kharazmi A. The anti-inflammatory properties of rose-hip. Inflammopharmacology. 1999;7(1):63-68.
159. Christensen R, Bartels EM, Altman RD, Astrup A, Bliddal H. Does the hip powder of *Rosa canina* (rosehip) reduce pain in osteoarthritis patients?–a meta-analysis of randomized controlled trials. Osteoarthritis and Cartilage. 2008;16(9):965-972.
160. Wenzig EM, Widowitz U, Kunert O, Chrubasik S, Bucar F, Knauder E, Bauer R. Phytochemical composition and in vitro pharmacological activity of two rose hip (*Rosa canina* L.) preparations. Phytomedicine. 2008;15(10):826-835.
161. Orhan N, Aslan M, Hosbas S, Deliorman OD. Antidiabetic effect and antioxidant potential of *Rosa canina* fruits. Pharmacognosy Magazine. 2009;5(20): 309.
162. Nojavan S, Khalilian F, Kiaie FM, Rahimi A, Arabanian A, Chalavi S. Extraction and quantitative determination of ascorbic acid during different maturity stages of *Rosa canina* L. fruit. Journal of Food Composition and Analysis. 2008;21(4): 300-305.
163. Kültür Ş. Medicinal plants used in Kırklareli province (Turkey). Journal of Ethnopharmacology. 2007;111(2):341-364.
164. Sadigh-Eteghad S, Tayefi-Nasrabadi H, Aghdam Z, Zarredar H, Shanehbandi D, Khayyat L, Seyyed-Piran SH. *Rosa canina* l. fruit hydro-alcoholic extract effects on some immunological and biochemical parameters in rats. BioImpacts: BI. 2011;1(4):219.
165. Mitchell BL, Ulrich CM, McTiernan A. Supplementation with vitamins or minerals and immune function: Can the elderly benefit?. Nutrition Research. 2003;23(8): 1117-1139.
166. Štajner D, Popović BM, Čanadanović-Brunet J, Đilas S, Ćetković G. Nutritive composition and free radical scavenger activity of honey enriched with of *Rosa* spp. LWT-Food Science and Technology. 2014;55(1):408-413.
167. Fujii T, Ikeda K, Saito M. Inhibitory effect of rose hip (*Rosa canina* L.) on melanogenesis in mouse melanoma cells and on pigmentation in brown guinea pigs. Bioscience, Biotechnology, and Biochemistry. 2011;75(3):489-495.

168. Montazeri N, Baher E, Mirzajani F, Barami Z, Yousefian S. Phytochemical contents and biological activities of *Rosa Canina* fruit from Iran. J Med Plant Res. 2011;5(18):4584-4589.
169. Winther K, Falk-Rønne J, Kharazmi A, Hansen AV, Hansen EW. 69 Does Litovet, a Herbal Remedy Made From *Rosa Canina*, Act As An Anti-Inflammatory Agent In Horses Exposed To Strenuous Exercise – A Randomized, Placebo-Controlled, Parallel, Double-Blinded Study On The Immune System Of Horses, Their Working Capacity And Behaviour. Osteoarthritis and Cartilage. 2008;16:S44-S45.
170. González CV, Fanzone ML, Cortés LE, Bottini R, Lijavetzky DC, Ballaré CL, Boccalandro HE. Fruit-localized photoreceptors increase phenolic compounds in berry skins of field-grown *Vitis vinifera* L. cv. Malbec. Phytochemistry. 2014;110:46-57.
171. Handoussa H, Hanafi R, Eddiasty I, El-Gendy M, El Khatib A, Linscheid M, Ayoub N. Anti-inflammatory and cytotoxic activities of dietary phenolics isolated from *Corchorus olitorius* and *Vitis vinifera*. Journal of Functional Foods. 2013;5(3): 1204-1216.
172. Gonçalves J, Silva CL, Castilho PC, Câmara JS. An attractive, sensitive and high-throughput strategy based on microextraction by packed sorbent followed by UHPLC-PDA analysis for quantification of hydroxybenzoic and hydroxycinnamic acids in wines. Microchemical Journal. 2013;106:129-138.
173. Prodanov M, Vacas V, Hernández T, Estrella I, Amador B, Winterhalter P. Chemical characterisation of Malvar grape seeds (*Vitis vinifera* L.) by ultrafiltration and RP-HPLC-PAD-MS. Journal of Food Composition and Analysis. 2013;31(2): 284-292.
174. Baker E, Ulucam E, Cerkezkayabekir A. Investigation of the protective effects of proanthocyanidin and vitamin E against the toxic effect caused by formaldehyde on the liver tissue. Journal of Environmental Toxicology. 2015;30(12):1406-15.
175. Bakar E, Ulucam E, Cerkezkayabekir A. Protective effects of proanthocyanidin and vitamin E against toxic effects caused by formaldehyde in the kidney tissue. Biotechnic and Histochemistry. 2015;90(1): 69-78.
176. Hilbert G, Temsamani H, Bordenave L, Pedrot E, Chaher N, Cluzet S, Richard T. Flavonol profiles in berries of wild *Vitis* accessions using liquid chromatography coupled to mass spectrometry and nuclear magnetic resonance spectrometry. Food Chemistry. 2015;169:49-58.
177. Anastasiadi M, Chorianopoulos N, Nychas G, Haroutounian S. Antilisterial activities of polyphenol-rich extracts of grapes and vinification byproducts. Journal of Agricultural and Food Chemistry. 2009;57(2):457-463.
178. Pan QH, Wang L, Li JM. Amounts and subcellular localization of stilbene synthase in response of grape berries to UV irradiation. Plant Science. 2009;176(3): 360-366.
179. Bavaresco L, Civardi S, Pezzutto S, Vezzulli S, Ferrari F. Grape production, technological parameters, and stilbenic compounds as affected by lime-induced chlorosis. Vitis. 2005;44(2):63-65.
180. Bavaresco L, Vezzulli S, Battilani P, Giorni P, Pietri A, Bertuzzi T. Effect of ochratoxin A-producing *Aspergilli* on stilbenic phytoalexin synthesis in grapes. Journal of Agricultural and Food Chemistry. 2003;51(21):6151-6157.
181. Bavaresco L, Pezzutto S, Ragga A, Ferrari F, Trevisan M. Effect of nitrogen supply on trans-resveratrol concentration in berries of *Vitis vinifera* L. cv. Cabernet Sauvignon. Vitis. 2001;40(4):229-230.
182. Deluc LG, Decendit A, Papastamoulis Y, Mérillon JM, Cushman JC, Cramer GR. Water deficit increases stilbene metabolism in Cabernet Sauvignon berries. Journal of Agricultural and Food Chemistry. 2010;59(1):289-297.
183. Fernandes F, Ramalhosa E, Pires P, Verdial J, Valentão P, Andrade P, Pereira JA. *Vitis vinifera* leaves towards bioactivity. Industrial Crops and Products. 2013;43: 434-440.
184. Castellarin SD, Di Gaspero G, Marconi R, Nonis A, Peterlunger A, Paillard ES, Testolin R. Colour variation in red grapevines (*Vitis vinifera* L.): Genomic organisation, expression of flavonoid 3'-hydroxylase, flavonoid 3', 5'-hydroxylase genes and related metabolite profiling of red cyanidin-/blue delphinidin-based anthocyanins in berry skin. BMC Genomics. 2006;7(1):12.

185. Guendez R, Kallithraka S, Makris DP, Kefalas P. Determination of low molecular weight polyphenolic constituents in grape (*Vitis vinifera* sp.) seed extracts: Correlation with antiradical activity. Food Chemistry. 2005;89(1):1-9.
186. Kuhn N, Guan L, Dai ZW, Wu BH, Lauvergeat V, Gomès E, Delrot S. Berry ripening: Recently heard through the grapevine. Journal of Experimental Botany. 2014;65(16):4543-4559.
187. Koundouras S, Marinos V, Gkoulioti A, Kotseridisand Y, van Leeuwen C. Influence of vineyard location and vine water status on fruit maturation of nonirrigated cv. Agiorgitiko (*Vitis vinifera* L.). Effects on wine phenolic and aroma components. Journal of Agricultural and Food Chemistry. 2006;54(14):5077-5086.
188. Stagos D, Kazantzoglou G, Magiatis P, Mitaku S, Anagnostopoulos K, Kouretas D. Effects of plant phenolics and grape extracts from Greek varieties of *Vitis vinifera* on Mitomycin C and topoisomerase I-induced nicking of DNA. International Journal of Molecular Medicine. 2005;15(6):1013-1022.
189. Shrotriya S, Deep G, Gu M, Kaur M, Jain A, Inturi S, Agarwal R, Agarwal C. Generation of reactive oxygen species by grape seed extract causes irreparable DNA damage leading to G2/M arrest and apoptosis selectively in head and neck squamous cell carcinoma cells. Carcinogenesis. 2012;33(4):848-858.
190. Muhamad ZMAM, Mustafa AM. Traditional Malay medicinal plants. Kuala Lumpur: Penerbit Fajar Bakti Sdn Bhd. 1994;460-465.
191. Parekh J, Chanda S. *In-vitro* antimicrobial activities of extracts of *Launaea procumbens* roxb. (Labiateae), *Vitis vinifera* l. (Vitaceae) and *Cyperus rotundus* l. (Cyperaceae). African Journal of Biomedical Research. 2006;9(2):89-93.
192. Brown JC, Huang G, Haley-Zitlin V, Jiang X. Antibacterial effects of grape extracts on *Helicobacter pylori*. Applied and Environmental Microbiology. 2009;75(3): 848-852.
193. Soleas GJ, Grass L, Josephy PD, Goldberg DM, Diamandis EP. A comparison of the anticarcinogenic properties of four red wine polyphenols. Clinical Biochemistry. 2002;35(2):119-124.
194. Marikar FMMT, Guanghui J, Wang S, Dingyuan M, Zichun H. Metallothionein 2A an interactive protein linking phosphorylated FADD to NF-kB pathway leads to colorectal cancer formation. Journal of Chinese Clinical Oncology. 2016;5(6):1-15.
195. Anastasiadi M, Pratsinis H, Kletsas D, Skaltsounis AL, Haroutounian SA. Bioactive non-coloured polyphenols content of grapes, wines and vinification by-products: Evaluation of the antioxidant activities of their extracts. Food Research International. 2010;43(3):805-813.
196. Lakshmi BVS, Sudhakar M, Anisha M. Neuroprotective role of hydroalcoholic extract of *Vitis vinifera* against aluminium-induced oxidative stress in rat brain. Neurotoxicology. 2014;41:73-79.
197. Apostolou A, Stagos D, Galitsiou E, Spyrou A, Haroutounian S, Portesis N, Kouretas D. Assessment of polyphenolic content, antioxidant activity, protection against ROS-induced DNA damage and anticancer activity of *Vitis vinifera* stem extracts. Food and Chemical Toxicology. 2013;61:60-68.
198. Khan AV, Ahmed QU, Khan MW, Khan AA. Herbal cure for poisons and poisonous bites from Western Uttar Pradesh, India. Asian Pacific Journal of Tropical Disease. 2014;4:S116-S120.
199. Rivero-Cruz JF, Zhu M, Kinghorn AD, Wu CD. Antimicrobial constituents of Thompson seedless raisins (*Vitis vinifera*) against selected oral pathogens. Phytochemistry Letters. 2008;1(3):151-154.
200. Botella C, Diaz A, De Ory I, Webb C, Blandino A. Xylanase and pectinase production by *Aspergillus awamori* on grape pomace in solid state fermentation. Process Biochemistry. 2007;42(1):98-101.
201. Brenes A, Viveros A, Goni I, Centeno C, Sáyago-Ayerdy SG, Arija I, Saura-Calixto F. Effect of grape pomace concentrate and vitamin E on digestibility of polyphenols and antioxidant activity in chickens. Poultry Science. 2008;87(2):307-316.
202. Braga FG, Silva FAL, Alves A. Recovery of winery by-products in the Douro demarcated region: Production of calcium tartrate and grape pigments. American Journal of Enology and Viticulture. 2002;53(1):41-45.

203. Silva ML, Malcata FX. Effects of time of grape pomace fermentation and distillation cuts on the chemical composition of grape marcs. Zeitschrift für Lebensmitteluntersuchung und-Forschung A. 1999;208(2):134-143.

204. Cheng VJ, Bekhit AEDA, McConnell M, Mros S, Zhao J. Effect of extraction solvent, waste fraction and grape variety on the antimicrobial and antioxidant activities of extracts from wine residue from cool climate. Food Chemistry. 2012;134(1):474-482.

205. Barcia MT, Pertuzatti PB, Rodrigues D, Gómez-Alonso S, Hermosín-Gutiérrez I, Godoy HT. Occurrence of low molecular weight phenolics in *Vitis vinifera* red grape cultivars and their winemaking by-products from São Paulo (Brazil). Food Research International. 2014;62:500-513.

206. Molva C, Baysal AH. Antimicrobial activity of grape seed extract on *Alicyclobacillus acidoterrestris* DSM 3922 vegetative cells and spores in apple juice. LWT-Food Science and Technology. 2015;60(1):238-245.

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