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Review Article

Alternanthera sessilis: A Review of Literature on the Phytoconstituents, Traditional Usage and Pharmacological Activities of Green and Red Cultivar

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ABSTRACT

The weed *Alternanthera sessilis*, having Green (ASG) and Red (ASR) cultivars, is a member of the Amaranthaceae. Both cultivars are known to possess high medicinal and nutraceutical values as they are widely utilized in traditional medicine. Populations from various Asian regions commonly consume this medicinal weed as part of diet and as therapeutic agent. In general, both cultivars have been employed for treating a broad range of human ailments including cardiovascular diseases, diabetes, hypertension, and inflammatory disorders such as asthma, bronchitis and hepatitis apart from its administration as a painkiller. Following its ethnomedicinal uses, an attempt was made to review and consolidate the phytochemical constituents of ASG and ASR discovered from previous studies that utilized advanced technologies, respective traditional application among different ethnicities of Asia and their established pharmacological properties. All the information in this study was acquired through a literature search of research databases, namely ScienceDirect, Scopus, PubMed and Google Scholar using keywords such as *Alternanthera sessilis, Alternanthera sessilis* red, dwarf copperleaf and sessile joyweed. The results of each study were reviewed to identify its relevance and the cultivar that was being investigated. All relevant studies were collected and its subsequent results were reported and discussed to provide insights into the health enhancing qualities of ASG and ASR. Inspection of phytoconstituents in ASG and ASR showed the presence of polyphenol, flavonoid, carotenoid, terpenes and alkaloid with polyphenol being the major chemical group found in both cultivars. It was also revealed that whilst ASR is traditionally consumed in China, Malaysia, Singapore, and Taiwan, indigenous usage of ASG is more common in nations such as Sri Lanka, India, and Indonesia. Both ASG and ASR showed potent anti-oxidant, anti-hyperglycemic, antimicrobial, antifungal and hepatoprotective effects while the anti-inflammatory, anti-cancer and analgesic properties were disclosed in ASG only. Further processing and commercialization of this remedial weed as a product benefiting the wellbeing of humans is recommended as *Alternanthera sessilis* has high potential to be utilized as a curative agent while being a vital ingredient that can be included in daily consumption.

Keywords: *Alternanthera sessilis*, Dwarf copperleaf, Sessile joyweed, Phytoconstituents, Pharmacological properties.

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INTRODUCTION

Complementary and Alternative Medicines (CAMs) which includes acupuncture, homeopathy, aromatherapy, phytotherapy, and meditation are treatments that are not a part of conventional healthcare. Nevertheless, phytotherapy, defined as the application of herbs and plants to treat diseases, has gained attention among researchers lately with diverse plant extracts being examined on a large scale and receiving approval for usage as natural remedies to impede and cure various ailments. The gradual increase in evidence from scientific research is proving the significance of medicinal plants in primary healthcare. In addition, World Health Organisation (WHO) has confirmed three-fourths of the population globally opted for folk medicine as their main form of healthcare where most of its therapies utilizes plant extracts and their respective bioactive constituents.[1] This is due to the fact that such plants are found easily and inexpensive to obtain, therefore, supporting its extensive employment in treating diseases. In addition to being used for treatments, medicinal plants are regularly consumed by individuals around the globe, especially those from rural regions, as a supplement to their usual

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diet and as an alternative source of nutrition during food crises and poverty.[2]

Alternanthera sessilis (*A. sessilis*) is a weed existing in two cultivars, Green (ASG) and Red (ASR) categorized according to their aerial colour. Both the green and red cultivars emerge from the similar Amaranthaceae family.[3] The difficulty to differentiate between these two cultivars is very minimal based on morphology, as primarily both have different aerial colors. However, most researchers rarely state the type of *Alternanthera sessilis* used in their research. This situation may lead to misunderstanding and misinterpretation of the resulting biological activities from the investigated cultivar. Owing to divergent origins and distribution of both cultivars, the phytochemical constituents presented in both weeds slightly differ, thus, manipulating their traditional usage and pharmacological actions. Hence, this study seeks to objectively examine and distinguish the morphology and distribution of ASG and ASR while also accumulating information about their phytochemical components, traditional usage, and individual pharmacological actions. It also discusses the prospects for further developing these medicinal weeds as therapeutic agents.

METHODOLOGY

The literature review was conducted using a variety of scientific search engines such as Scopus (https://www.scopus.com/home.uri), PubMed (https://pubmed.ncbi.nlm.nih.gov), ScienceDirect (https://www.sciencedirect.com) and Google Scholar (https://scholar.google.com). *Alternanthera sessilis*, dwarf copperleaf, and sessile joyweed were the keywords used to retrieve related information regarding the green cultivar. To collect relevant details on the red cultivar, a separate keyword was used which is *Alternanthera sessilis* red since the terms *Alternanthera sessilis*, dwarf copperleaf and sessile joyweed were referring to green cultivar mostly. The literature survey was done from the year 2000 to 2022 with a total of 63 reference articles in English being recovered inclusive of scientific reports and issued books. Evaluation and accumulation of data on the phytoconstituent, traditional application and pharmacological properties of green and red cultivars were performed. Apart from reporting the related studies, existing gaps identified during the literature review were mentioned as well. This might offer information on prospective study directions for more in-depth investigation involving both cultivars.

Alternanthera sessilis and its Origin

Alternanthera sessilis (L.) R. Br. Ex DC, also known as *Alternanthera denticulate* R. Brown and *Alternanthera nodiflora* R. Brown, is usually found in damp and moist areas or wetlands.[4,5] It favors areas with continual or intermittent high humidity while still having the ability to endure extremely dry climate.[6] The term anthera indicates flowers while sessilis specify the natural form of the plant that lacks a stalk therefore appearing as inflorescences. The term *alterna* means alternate.[7] The plant is commonly referred to as sessile joyweed or dwarf copperleaf.[8] However, both ASG and ASR also have several local names depending on their existing regions as listed in Table 3. For ASG, it is popularly known as Keremak or Kermak putih in Malaysia.[9] In the southern region of India, it is referred to as Ponnankanni, Citai or Koduppai. Bai Hua Zi (白花子) or Lian Zi Cao (莲子草) are the names given in China while Daun Tolod is its domestic name in Indonesia.[10] Mukunuwenna or Ponnankanni are the local names given by people of Sri Lanka.[11] On the other hand, ASR is known by names such as Red Sessile Joyweed, Hongtian Wu (红田乌) or Hongtian Wu Grass (红田乌草) in Singapore. Bayam Keremah Merah and Horngtyan Wu are the regional names in Malaysia and Taiwan respectively.[12] Both ASR and ASG branch from the domain of Eukaryote followed by Kingdom Plantae, phylum Spermatophyta, subphylum Angiospermae, class of Dicotyledonae and thereby being classified into family of Amaranthaceae having genus Alternanthera.[5] ASG is a shrub that is thought to originate from tropical America and is also known as the wild-type *A. sessilis* species.[13] On the other hand, ASR is commonly found in the tropical and sub-tropical climates of Malaysia and Singapore.[3] Moreover, another two studies reported different origins of *A. sessilis*. There are several species of *Alternanthera* spp., including *A. sessilis*, which are native to the Old World, and occurring in Africa, Asia, and Australia.[14] Another researcher reported them to be native to China and while also existing in nations such as India, Nepal, Vietnam, Laos, Cambodia, Malaysia, Philippines, Thailand, Bhutan, Myanmar, Indonesia and Sikkim.[15] Both studies, however, did not specify the cultivars investigated, either green or red.

Morphological Description

Generally, *A. sessilis* is a widespread species that grows quickly and has leaf shape ranging from elliptical to oval. Furthermore, the appearance of these inflorescences are axillary, sessile and clustered.[16] Looking into the morphology of both cultivars, ASG is visibly dissimilar to ASR in which the green cultivar has greenish short sessile leaves with an acute blunt apex and glabrous (fine, thin, articulate hairs) margins shown in Figure 1.[17] It also has a cylindrical light brown prostrate stem and produces white flowers that have small axillary sessile heads with pink tinge.[18] The plant grows to 0.2–1 m in height and has strong taproots with numerous erect branches. White flowers produced by this weed blooms during a specific time of the year, that is from December to March.[19] The fruit is 2–2.5 mm long with a small, flattened, indehiscent utricle enclosing the seed. The seeds having a shiny outlook and disc-shaped are brownish-black in colour with a diameter of 0.8–1 mm.[5,8,20] Its root sprouts from the stem's node.[13] Based on whether the weed is growing on terrestrial or aquatic areas, its seeds are distributed by wind or water.[4,5,8] Meanwhile, ASR has reddish purple leaves and stems while its flowers are pink or yellow in colour displayed by Figure 2.[21]

Phytochemical Constituent

Due to the divergence in geographical location, the phytoconstituents identified in both ASR and ASG are slightly different attributable to nutrient availability, humidity, soil type, intensity of light received and climate of the specific region varying between the locale of ASG and ASR. Nonetheless, both plants show the presence of various active phytoconstituents as listed in Tables 1 and 2. The phytochemical compounds are obtained from the Gas Chromatography-Mass Spectrometry (GCMS), Liquid Chromatography-Mass Spectrometry (LCMS) and High Performance Liquid Chromatography (HPLC) analyses done in previous studies.

Traditional Usage

A. sessilis regarded as a traditional medicinal weed, is consumed regularly with diet or as medicine by Asians.[29] Due to its health benefits, traditional medicine practitioners from Asia generally use the plant to treat many illnesses and diseases. For example, liver disease, spleen disease, diarrhea, as well as improving eyesight, curing headache, fever, and gastrointestinal problems.[12,30] The use of *A. sessilis* in several regions of Asia were presented in Table 3. ASG is traditionally used as a therapeutic agent in India, Indonesia and Sri Lanka and partly in Malaysia. Hazli *et al.* (2019) stated that ASG is consumed as ulam in Malaysia to lower blood glucose levels. In India, the plant was also used as a galactagogue, cholagogue, pain killer and antidote for snakebite apart from treating malaria, hypothermic, ulcer, hepatitis, bronchitis and asthma when consumed as cooked vegetables.[31,32] Consequently, ponnankanni name is given to this plant in India due to the fact that Indians from the south part belief that it can give the body a "golden sheen".[33] In Indonesia, ASG is employed to treat disorders of intestines such as dysentery and stomach related disease.[34,35] ASG was also used to treat indigestion associated with a poor functioning liver, bile related issue, persisting liver congestion, inflamed kidney pelvis, inflamed bladder, strangury, gonorrhea and snakebites in Sri Lanka.[36] Besides the aforementioned uses, the poultice of freshly pounded ASG is good for mild conjunctivitis, fractures, blisters, dermatitis, abscess and eczema.[29] Not only that, the plant's infusion is suggested as a natural treatment for diabetes, bronchitis, wounds, vomiting, diarrhea, nausea, cough and gas trouble.[29] Its roots can be used to treat inflamed wounds, while shoots of the weed with its green leaves can be consumed in the form of tea to heal hypertension.[37,38]

Figure 1: *Alternanthera sessilis* green.

In contrast to ASG, the literature available on the traditional use of red cultivar is finite, probably due to its demographic. ASR is consumed frequently in countries such as Malaysia, Taiwan and Singapore. A study from Tan and Kim (2013), claimed that ASR is traditionally consumed raw by Malaysians to lower the likelihood of cardiovascular diseases. It is also occasionally taken as tea or a decoction. In Taiwan, it is used to treat renal diseases and is claimed to have hepatoprotective effects.[39] Furthermore, another study documented that the Chinese population in Singapore consumes ASR as herbal medicine. It is drunk as tea or decoction to boost immunity, lowering the level of cholesterol and promotes blood circulation thereby fostering good health qualities. It is also claimed to help with hyperlipidemia, hypertension, and bleeding of the nose.[40] In China, ASR is stir-fried or cooked in soup. This practice is prevalent in the Chinese food therapy known as Yao Shan.[24]

Pharmacological Properties of ASG and ASR

Anti-cancer Activities

ASG contains gallic acid, a polyphenol that has been linked to anti-cancer effects. Gallic acid is excellent at preventing cellular mutations while being toxic to cancerous cells and non-toxic to healthy cells, according to numerous studies.[41] Studies that experimented the anti-cancer activities of ASG were listed in Table 4. A 3-4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium bromide (MTT) colorimetric assay was used to assess the cytotoxicity of the whole ASG plant extracted using ethanol on HeLa (cervix adenocarcinoma) cells. Outcome of the experiment revealed cytotoxic activities of less than 40% activity at 500 µg/mL.[42] Another scientific analysis conducted using three different extracts of ASG - the residue of methanol from the methanolic extraction, the petroleum-ether partitionate from methanolic extraction and the chloroform partitionate from methanolic extraction, showed cytotoxicity against pancreas epithelioid carcinoma (Panc-1 cell), where the chloroform partitionate from the methanolic extraction induced over 80% of cell apoptosis at 100 µg/mL concentration.[43] Since chloroform partitionate from methanolic extraction had the greatest response, it was further tested on two other cancerous pancreatic cell lineages, Capan-1 and MIA PaCa-2. According to its results, the extract exhibited strong cytotoxicity against both cell lineages having IC_{50} values of 34.82 ± 2.20 µg/mL and 13.08 ± 10.40 µg/mL for Capan-1 and MIA PaCa-2 and respectively.[43] Another study extracted different parts of ASG—the aerial part, leaf, and stem—using ethanol as a solvent and tested them on the human cancerous cell

line of colon, HT-29.[44] Anti-cancer properties for each part of plant extract were assessed using MTT assay.

Overall, it can be deduced that ASG leaves extracted using ethanol were the most effective at treating colon cancer. This possessed ability is attributable to carbonic acid, hexadecanoic acid, linoleic acid, phytol, octadecadienoic acid, heptadecanone, neophytadiene, and octadecyne present in ASG.[44] These bioactive compounds have strong pro-inflammatory, antioxidant, and anti-angiogenesis properties that enable the therapeutic activity of ASG against cancerous colon cells. Besides, research based on nanomedicines that primarily focuses on cancer cell lines offers the capability to combat drug resistance and boost chemotherapy treatment effectiveness. Biosynthesized gold (Au) nanoparticles produced from water extraction of ASG leaves at dosages of 10 to 15 mg/mL substantially lowered the expansion HeLa cell in a study conducted. By altering intrinsic apoptotic pathways, ASG-Au nanoparticles also cause apoptosis in HeLa cells.[45] When silver (Ag) nanoparticles were biosynthesized using extracts of ASG leaves, the MTT assay employed in this study demonstrated the anti-proliferative quality of ASG on PC3 prostate cancerous cells in concentration dependent manner starting at 1.56 µg/mL to 25 µg/mL while having 6.85 µg/mL IC_{50} value. ASG was claimed to assist the Ag nanoparticles in triggering apoptosis and being cytotoxic to cancerous prostate cells.[46] When compared to the standard reference drug, cisplatin, the aqueous extracts of ASG aerial used to synthesize silver nanoparticles demonstrated anti-proliferative effect on MCF-7 cancerous breast cell line by having 3.04 g/mL IC_{50} value.[47] However, to date, no study has documented the anti-cancer properties of ASR.

Anti-inflammatory Activities

Inflammation in tissues is an important aspect indicating the body's response towards harmful substances. It is part of the body's defense system that limits the invasion or elimination of harmful substances from the body. Cytokines being the inflammation regulatory molecules regulate an intricate network involving the immunological, physiological and behavioral events to generate inflammatory responses. Eicosanoids, vasodilating amines and peptides, cytokines and proinflammatory mediators are only a few of the signaling molecules implicated in the inflammatory response. By preventing additional tissue injury, they can promote healing and reintroduce the function of tissues.[48] Although it is a protective mechanism, there are complex events and pathways, which may also induce, maintain, or aggravate many diseases. Scientific investigations that discover the capability of ASG in expressing its anti-inflammatory effect are presented in Table 5. According to Babu *et al.* (2018), the cooked ASG exhibited lower anti-inflammatory properties compared to uncooked ASG when 20 mg/mL concentration of each sample was tested for protein denaturation assay. The difference in efficacy of the cooked and uncooked ASG might be due to some of the compounds denatured during the cooking process that eventually caused

Figure 2: *Alternanthera sessilis* red.

Table 1: Phytoconstituent of ASG.

Chemical Group	Chemical compounds	References
Phytosterols	α- spinasterol	[5]
	stigmasterol	
	campesterol	
Polyphenols	Vanillic acid	[12]
	Catechin	
	Ferulic acid	
	Epigallocatechin	
	Ethyl gallate	
	Chlorogenic acid	
	Apigenin	
	Daidzein	
	4-hydroxybenzoic	
	Gallic acid	[20]
	Quercetin	[22]
Alkaloid	Berberine	
Triterpene	Lup-20(29)-en-3-one (Lupenone)	[23]
Carotenoid	Astaxanthin	[24]
	Carotene	
	β-carotene	
	Zeaxanthin	
	Violaxanthin	
	Neoxanthin	
	Lutein	
Diterpene	Phytol	[25]
	Geranylgeraniol	
	Neophytidiene	
	Gibberellin	

Note: ASG: Alternanthera sessilis green.

Table 2: Phytoconstituent of ASR.

Chemical Group	Chemical Compounds	References
Polyphenols	Gallic acid	[12]
	Chlorogenic acid	
	4-hydroxybenzoic acid	
	Ethyl gallate	
	Myricetin	
	Daidzein	
	Rutin	[24]
	Ferulic acid	
	Quercetin	
	Apigenin	
	Epigallocatechin	[26]
	Vanillic acid	
	Catechin	[27]
Carotenoids	Carotene	[24]
	Xanthophyll	
	Rhodoxanthin	[25]
	4-ketonostoxanthin 3-sulfate	
Betalains	Betanin	[24]
	Amaranthin	
	Betaxanthin	
Rhodoxanthin	Xanthophylls	[25]
Xanthonoid	Dihydrogambogic acid	
	Tetrahydrogambogic acid	
Flavanoid	Carpelastofuran	
Isoflavanoid	Lonchocarpic acid	
	Euchrenone b2 and Euchrenone b3	
Caffeic acid glucoside	1-Caffeoyl-beta-D-glucose	
Flavones and Flavanols	Fulvinervin B, 5,6-Dihydroxy-7,8,4' -trimethoxyflavanone	
	Scutellarein 7-glucuronide-6-ferulate	
	Patuletin 3-glucoside-7- sulfate	
	Quercetin 3-(2'''-galloylglucosyl)-(1->2)-alpha-L-arabinofuranoside	
	Patuletin 3-(60 '-(E)-feruloylglucoside)	
	Vitexin 2' '-O-rhamnoside 6' '-acetate	
	Veronicafolin 3-glucosyl-(1->3)-galactosid	
Hydroxycoumarin	Lonchocarpenin	
Flavanones	5-Hydroxy-7-methoxy-6,8-di -C-methylflavanone	
Lignan	Dehydrodieugenol	
Isoflavans	Millinol B	
Isoflavone	7-Prenyloxy-3',4' -dimethoxyisoflavone	
Hydroxybenzoate	Lithospermic acid	
Chalcone glycoside	4' -O-gentobioside	
	Chalconaringenin 2'-O-glucoside	
Diterpene	Phytol	[28]
	Isophytol	
Oxygenated diterpene	1,1,1,5,5,5-hexamethyl-3,3-bis[trimethylsilyl) oxy]trisiloxane	
Monoterpene	2,6-dimethyl-7-octen-3-ol	
Sugar alcohol	Scyllo-inositol	

Note: ASR: Alternanthera sessilis red.

a reduced anti-inflammatory activity. Protein denaturation is associated with an inflammatory reaction contributing to various inflammatory disorders including diabetes, cancer and rheumatoid arthritis.[49] Hence, a compound's apparent capacity for anti-inflammation is indicated by its ability to halt protein degradation. Anti-inflammatory activity by ethanol extracts of ASG via membrane stabilization and protein denaturation assays, *in vitro*, were revealed as well.[50] The study showed that ASG possessed anti-inflammatory activities in all the assays in a concentration-dependent manner (100–500 ug/mL). Two other studies documented the anti-inflammatory properties of ASG in animal models having paw edema initiated by carrageenan. Given that this model of inflammation comprises a number of inflammatory mediators including bradykinin, histamine, prostaglandins, and serotonin, it is commonly employed to assess the anti-inflammatory efficacy of medicinal plants, as well as manufactured medications. Suppression of paw edema might indicate that the tested sample inhibited inflammatory mediators thus preventing inflammation. Both studies proved that aqueous, ethanolic, chloroform, and petroleum ether extracts could suppress carrageenan-induced paw edema.[51,52] Also, 200 µg/mL concentration of ASG extracted using ethanol solvent has significantly ($p<0.05$) decreased the hyperpermeability of human aortic endothelial cells caused by TNF- alpha when compared to its control group.[53] Evidently, ASG's significant anti-inflammatory qualities are the main reason it is employed in the traditional system of medicine. Gibberellin, an anti-inflammatory terpene, and polyphenols including p-hydroxybenzoic acid, kaempferol monosulfate, daidzein, protocatechuic acid and apigenin-6,8-di-C-D-glucopyranoside were discovered from extracted ASG stem.[54] However, no study has determined the anti-inflammatory properties of ASR till date.

Table 3: Consumption of *A. sessilis* locally and its respective ethnopharmacological properties.

Country	Local name given	Type of Cultivar	Method of consumption	Illness cured	References
Malaysia	Bayam Keremah Merah	Red cultivar	Uncooked vegetables as side dish or consumed as decoction and tea	Cardiovascular Disease	[3]
	Keremak, Kermak putih	Green cultivar	Ulam/salad	Blood glucose level	[24]
China	Lian Zi Cao Bai Hua Zi	Red cultivar	Vegetable stir fry/soup	NA	
India	Ponnankanni, Citai, or Koduppai	Green cultivar	Cooked vegetable	Galactagogue, cholagogue, pain killer, fever, malaria, hypothermic, ulcer, hepatitis, bronchitis, asthma, and as an antidote for snakebite.	[31,32]
Indonesia	Daun Tolod	Green cultivar	NA	Stomach disorders and dysentery.	[34,35]
Sri Lanka	Mukunuwenna, or Ponnankanni.	Green cultivar	Vegetable/salad	Indigestion associated with a poor functioning liver, bile related issue, persisting liver congestion, inflamed kidney pelvis, inflamed bladder, strangury, gonorrhea and snakebites.	[36]
Taiwan	Horngtyan Wu	Red cultivar	NA	Renal diseases and has hepatoprotective effects.	[39]
Singapore	Red sessile, joyweed, Hong Tian Wu or Hongtian Wu Grass	Red cultivar	Decoction and tea	Hypertension, cholesterol lowering, hyperlipidemia, treats bleeding of the nose, enhances circulatory system and provides immunity.	[40]

Note: NA: Not Available.

Table 4: Anti-cancer properties of ASG.

Part use	Type of extraction	Type of cell lines	Concentrations used	Duration of treatment	IC_{50}	References
Whole plant	80% Ethanol	HeLa	250 and 500 µg/mL	24 hr	NA	[42]
		PANC-1			27.19 ± 3.01 µg/mL	
Leaf	Chloroform fraction of Methanol extract	MIA PaCa-2	0.1, 1, 10, 100 µg/mL	24 hr	13.08 ± 10.40 µg/mL	[43]
		Capan-1			34.82 ± 2.20 µg/mL	
Aerial					> 500 µg/mL	
Stem	Ethanol	HT-29	25, 50, 100, 200, 300, 400, 500 µg/mL	72 hr	< 200 µg/mL	[44]
Leaf					< 200 µg/mL	
Leaf	Aqueous leaf extract for synthesis of gold nanoparticles.	HeLa	1, 2.5, 5, 7.5, 10, 12.5, 15 µg/mL	24 hr	> 10 µg/mL	[45]
Leaf	Aqueous leaf extract for synthesis of silver nanoparticles.	PC3	1.56, 3.12, 6.25, 12.5, 25 µl/mL	48 hr	6.85 µg/mL	[46]
Aerial	Aqueous aerial extract for synthesis of silver nanoparticles.	MCF-7	1.56, 3.12, 6.25, 12.5, 25 µl/mL	48 hr	3.04 µg/mL	[47]

Note: ASG: *Alternanthera sessilis* green; NA: Not available; IC_{50}: Half maximal inhibitory concentration; PC3: Prostate cancer cells; MCF-7: Breast cancer cells; HT-29: Human colon cancer cells; Capan-1: Human pancreatic ductal adenocarcinoma cell; MIA PaCa-2: Human pancreatic cancer cell; PANC-1: Human pancreatic cancer cell; HeLa: Cervix adenocarcinoma cells.

Table 5: Anti-inflammatory effects of ASG.

Part use	Type of extraction	Type of assays	Concentrations used	Duration of treatment	IC_{50}	Result	References
Leaf	Cooked and extracted with methanol.	Protein denaturation assay.	NA	NA	NA	uncooked > cooked.	[47]
	Uncooked and extracted with methanol.						
Leaf	Ethanol	Membrane stabilization assay.	100, 200, 300, 400 and 500 µg/mL	30 min	NA	73.8% rate of suppression for 500 µg/mL.	[50]
		Bovine serum denaturation assay.	100, 200, 300, 400 and 500 µg/mL	23 min		75.43% rate of suppression for 500 µg/mL.	
		Egg albumin denaturation assay.	100, 200, 300, 400 and 500 µg/mL	20 min		84.34% rate of supression for 500 µg/mL.	
Leaf	Chloroform.	Edematous Paw initiated by Carrageenan.	100 and 200 mg/kg	60 min	NA	67% and 50% rate of suppression for 200 and 100 mg/kg respectively.	[51]
	Petroleum ether.		100 and 200 mg/kg			47% and 38% rate of suppression for 200 and 100 mg/kg respectively.	
Aerial	Aqueous	Edematous Paw initiated by Carrageenan.	200 and 400 mg/kg	60 min	NA	57% highest suppression rate for 400 mg/kg.	[52]
	90% ethanol		200 and 400 mg/kg			64% highest inhibition rate at 400 mg/kg.	
Whole plant	Ethanol	FITC-Dextran Permeability Assay.	25, 50, 100 and 200 *µ*g/mL	24 hr	NA	Impediment of enhanced permeability induced by TNF-alpha at 200 *µ*g/mL.	[53]

Note: ASG: *Alternanthera sessilis* green; NA: Not available; IC_{50}: Half maximal inhibitory concentration.

Antioxidant Properties

Increased production of oxygen radicals may result in Deoxyribonucleic Acid (DNA) degradation and alteration that could potentially cause aging-related diseases and cancers.[55] Natural remedies, particularly herbal antioxidants, have been effectively used as rejuvenators to cure illnesses or diseases driven by oxidative stress for many years. This is due to antioxidants being a highly valuable compound in defending the body from harm induced by free radical oxidative stress. The antioxidant properties of ASG and ASR extracted using various solvents have been examined using a number of different techniques.[26] A number of investigations found a favorable link between flavonoid and polyphenol phytoconstituent with effects of antioxidants, hinting that *A. sessilis*' antioxidant activity might be attributable to these polyphenolic substances.[11] Various extracts from ASG and ASR can reduce oxidants *in vitro* listed in Tables 6 and 7 respectively. Aerial ASR ethanolic extract demonstrated more antioxidant capability in comparison to the other three (the water extract of ASR and ASG with the ethanol extract of ASG) using Oxygen Radical Absorbance Capacity (ORAC), beta-carotene bleaching, Ferric Reducing Ability Assays (FRAP) and 2,2′-azi no-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS). Although the ethanol extract of ASG exhibited a higher antioxidant percentage in the 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) assay, it was not significant compared to the ethanol extract of ASR.[26] In another study conducted, activity of catalase and superoxide dismutase enzymes in human aortic endothelial cells increased following the administration of ethanol extracted whole-plant ASG at concentrations 25–200 g/mL and 50–200 g/

Table 6: Antioxidant properties of ASG.

Part use	Type of extraction	Type of assays	Concentrations used	IC_{50}	Result	References
Aerial	Aqueous	β-carotene bleaching	NA	NA	34% antioxidant activity	[26]
		ORAC	NA	NA	0.1 mmol TE/ 100g FW sample	
		DPPH	0.02 -0.1 mg/mL	NA	27.50%	
		ABTS	NA	NA	NA	
		FRAP	NA	NA	0.4 mmol $FeSO_4.7H_2O$/100g FW sample	
	Ethanol	β-carotene bleaching	NA	NA	36% antioxidant activity	
		ORAC	NA	NA	1.5 mmol TE/ 100g FW sample	
		DPPH	0.02 -0.1 mg/mL	NA	86.90%	
		ABTS	NA	NA	70%	
		FRAP	NA	NA	2.9 mmol $FeSO_4.7H_2O$/100g FW sample.	
Whole plant	Ethanol	SOD activity	50, 100 and 200 µg/mL	> 400 µg/mL	Increased effect of SOD in dose-dependent manner (120.7 ± 3.15%, 123.2 ± 6.67%, and 136.1 ± 4.01% of control).	[53]
		CAT activity	25, 50 and 200 µg/mL		Increased effect CAT in a non-dose dependent manner (112.5 ± 8.65%, 96.84 ± 8.46%, and 110.1 ± 1.28% of control).	

Note: ASG: *Alternanthera sessilis* green; NA: Not available; IC_{50}: Half maximal inhibitory concentration; DPPH: 2,2-diphenyl-1-picryl-hydrazyl-hydrate; FRAP: Feric reducing ability of plasma; ORAC: Oxygen Radical Antioxidant Capacity; ABTS: 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); SOD: Superoxide dismutase; CAT: Catalase.

mL respectively. These enzymes had previously decreased due to oxidative stress brought on by H_2O_2.[53]

On the other hand, Chai *et al.* (2016) conducted an extensive study to compare the DPPH radical scavenging activities of leaf and callus solvent fractions of ASR. By comparing the leaf and callus extracts of ASR, the callus water fraction had a greater scavenging ability with an EC_{50} value of 354.64 ± 29.12 µg/mL followed by the callus hexane fraction. With an EC_{50} value of 115.51 ± 7.56 g/mL, the leaf chloroform extract demonstrated the greatest scavenging activity of all the leaf solvent extracts.[27] Khan *et al.* (2016) conducted a comparable study involving the scavenging potential of ASR flowers and leaves with the leaves showing slightly higher DPPH activity compared to the flower, 179 ± 0.06 µg/mL and 170 ± 0.02 µg/mL IC_{50} values respectively. The ferric reduction activity of ASR leaf extracts from ethyl acetate and ethanol on hepatocellular carcinoma HepG2 cells was observed in dose-dependent manner (5-20 µg/mL). 5 µg/mL of ethyl acetate ASR leaf extract successfully suppressed oxygen radicals and lowered peroxidation of lipids triggered in HepG2 by H_2O_2.[25]

Antimicrobial and Antifungal Activities

Flavonoids, alkaloids, saponins, quinones, tannins, phenolic acids, coumarins, and terpenoids are phytochemicals that have antimicrobial characteristics. ASG comprises bulk of these phytochemicals.[56] The reported antifungal and antimicrobial effects of ASG and ASR were indicated in Table 8. According to Kumari and Krishna (2016), the potentiality of ASG water extracts exhibiting anti-fungal and anti-bacterial properties could be determined using the agar well diffusion method. The study selected a few bacteria, including *Escherichia coli, Bacillus pumillus, Bacillus subtilis, Salmonella typhi, Pseudomonas aeruginosa* and *Staphylococcus aureus*. Interestingly, the result showed zones of inhibitions against *Bacillus pumillus, Salmonella typhi* and *Bacillus subtilis* while *Staphylococcus aureus, Escherichia coli*, and *Pseudomonas aeruginosa* did not show any significant difference. Negative results were obtained in the antifungal assay where two of the fungal strains, *Candida albicans* and *Aspergillus niger*, were not inhibited.[57] However, from another study, the aqueous extract of ASG tested on several microorganisms exhibited an obvious inhibitory impact. The results revealed

Table 7: Antioxidant properties of ASR.

Part use	Type of extraction	Type of assays	Concentrations used	EC_{50}/IC_{50}	Result	References
Leaf	Ethanol	FRAP	5 - 20 µg/mL	IC_{50}: > 400 µg/mL	33% of antioxidant activity.	[25]
	Ethyl Acetate				40% antioxidant activity.	
Aerial	Aqueous	ORAC	NA	NA	0.8 mmol TE/ 100g FW sample.	[26]
		DPPH	0.02 -0.1 mg/mL	NA	7.80%	
		ABTS	NA	NA	NA	
		FRAP	NA	NA	4.5 mmol $FeSO_4.7H_2O$/100g FW sample.	
	Ethanol	β-carotene bleaching	NA	NA	54% antioxidant activity.	
		ORAC	NA	NA	13.8 mmol TE/ 100g FW sample.	
		DPPH	0.02 -0.1 mg/mL	NA	83.30%	
		ABTS	NA	NA	84%	
		FRAP	NA	NA	29.3 mmol $FeSO_4.7H_2O$/100g FW sample.	
Leaf	Hexane	DPPH	NA	EC_{50}: 93.37 ± 5.64 µg/mL	NA	[27]
	Chloroform		NA	EC_{50}: 115.51 ± 7.56 µg/mL	NA	
	Ethyl acetate		NA	EC_{50}: 10.81 ± 0.29 µg/mL	NA	
	Butanol		NA	EC_{50}: 35.71 ± 1.24 µg/mL	NA	
	Water		NA	EC_{50}: 35.96 ± 1.28 µg/mL	NA	
Callus	Hexane		NA	EC_{50}: 171.97 ± 3.53 µg/mL	NA	
	Chloroform		NA	EC_{50}: 34.12 ± 0.67 µg/mL	NA	
	Ethyl acetate		NA	EC_{50}: 43.87 ± 0.39 µg/mL	NA	
	Butanol		NA	EC_{50}: 57.11 ± 0.13 µg/mL	NA	
	Water		NA	EC_{50}: 354.64 ± 29.12 µg/mL	NA	
Leaf	Essential oil	DPPH	50 - 200 µg/mL	IC_{50}: 179 ± 0.06 µg/mL	NA	[28]
Flower				IC_{50}: 170 ± 0.02 µg/mL	NA	

Note: ASR: *Alternanthera sessilis* red; NA: Not available; IC_{50}: Half maximal inhibitory concentration; EC_{50}: Half maximal effective concentration, DPPH: 2,2-diphenyl-1-picryl-hydrazyl-hydrate; FRAP: Ferric reducing ability of plasma; ORAC: Oxygen Radical Antioxidant Capacity; ABTS: 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid).

Table 8: Antimicrobial and anti-fungal properties of ASG and ASR.

Part use	Type of extraction	Type of microbial	Concentrations used	MIC/MBC	Result (zon inhibition)	References
ASG						
Whole plant	Aqueous	*Bacillus pumillus*	NA	Nil	12 mm	[57]
		Salmonella typhi	NA	Nil	12 mm	
		Bacillus subtilis	NA	Nil	10 mm	
		Escherichia coli	NA	Nil	Nil	
		Staphylococcus aureus	NA	Nil	Nil	
		Pseudomonas aureginosa	NA	Nil	Nil	
		Aspergillus niger	NA	Nil	Nil	
		Candida albicans	NA	Nil	Nil	
Whole plant	Aqueous	*Staphylococcus aureus*	10, 25 and 50 µg	Nil	1.8 mm	[58]
		Staphylococcus heamolyticus		Nil	1.8 mm	
		Enterococcus faecalis		Nil	1.3 mm	
		Bacillus subtilis		Nil	1.0 mm	
		Klebsiella pneumoniae		Nil	1.6 mm	
		Escherichia coli		Nil	1.6 mm	
		Proteus vulgaris		Nil	0.9 mm	
		Proteus mirabilis		Nil	1.5 mm	
		Candida albicans		Nil	1.5 mm	
Leaf	Ethanol	*Escherichia coli*		MIC: 252.7 µg/mL	25.3 mm	[59]
		Staphylococcus aureus	10 uL	MIC: 252.5 µg/mL	17.7 mm	
		Candida albicans		MIC: 252.5 µg/mL	16.3 mm	
ASR						
Leaf	Ethanol	*Bacillus cereus*	NA	MIC: 12.5 mg/mL; MBC: 25 mg/mL	NA	[60]
		Staphylococcus aureus	NA	MIC: 0.2 mg/mL; MBC: 0.4 mg/mL	NA	

Note: ASG: *Alternanthera sessilis* green; ASR: *Alternanthera sessilis* red; NA: Not available; MIC: Minimum inhibitory concentration; MBC: Minimum bactericidal concentration; NIL: Non-existent.

the ability of ASG extracted using water to inhibit the growth of *Staphylococcus aureus* and *Staphylococcus haemolyticus* species with 1.8 mm zone inhibition for 50 µg concentration.[58] Aqueous leaf extract revealed the existence of flavonoid, steroid, alkaloid, anthraquinone, and tannin through phytoconstituent analysis.[58] Another study from Sivakumar and Sumathi (2016), tested the ASG extracted using ethanol. Growth of *Candida albican, Staphylococcus aureus* and *Escherichia coli* was seen to be inhibited by the ASG ethanolic extract.[59] The differing solvent extraction techniques utilized in these two research may have contributed to the divergent results, with the ethanolic extract perhaps having more active chemicals than aqueous extract thus effectively preventing the proliferation of fungus and bacteria. Hence, the ASG extracted using ethanol solvent might have a higher diffusion rate or a higher degree of sensitivity to the tested microorganisms. Another investigation employing the disk diffusion assay method, reported susceptibility of Gram-positive *Staphylococcus aureus* and *Bacillus cereus* to the ethanolic leaf extract of ASR.[60] The Minimum Inhibitory Concentrations (MIC) of 0.2 mg/mL and 12.5 mg/mL were reported for *Staphylococcus aureus* and *Bacillus cereus* respectively. A Minimum Bactericidal Concentration (MBC) of 0.4 mg/mL and 25 mg/mL was reported for *Staphylococcus aureus* and *Bacillus cereus* respectively. Such findings recommend exploitation of ASR leaves to be developed into a new class of antibacterial agents.[60]

Table 9: Antidiabetic activities of ASG and ASR.

Part use	Type of extraction	*In vivo*/ *In vitro*	Type of assays	Concentrations used	Mode of administration	Duration of treatment	IC_{50}	Result	References
ASG									
Leaves	95% ethanol after being defatted by petroleum ether.	Wistar albino rats	Diabetic rats induced by Streptozotocin.	200 and 400 mg/kg	Oral	Single dose for 1,2 and 4 hr.	NA	73% and 72% rate of inhibition for 400 and 200 mg/kg respectively.	[61]
						Multidose; once daily for 10 consecutive days.	NA	25% and 22% inhibition rate for 400 and 200 mg/kg respectively.	
Leaves	95% Ethanol	Wistar Rats	Diabetic rats induced by Streptozotocin	100 and 200 mg/kg	Oral	Daily once for 15 days.	NA	59% and 51% inhibition rate at 100 and 200 mg/kg on day 15th, respectively.	[62]
ASR									
Aerial	Ethyl acetate fraction	Male Sprague-Dawley	Diabetic rats induced by Streptozotocin.	150 mg/kg	Oral	Daily once for 15 days.	NA	Fasting blood glucose level of ASR-treated group was significantly ($p < 0.05$) reduced compared to the negative control group, however the level of insulin in serum collected from ASR treated groups failed to reveal a marked difference than the negative control group.	[3]
Leaf	Hexane fraction	*In vitro*	α-glucosidase inhibitory activity.	NA	NA	NA	6.31 ± 1.70 mg/mL	NA	[27]
	Chloroform fraction			NA	NA	NA	4.89 ± 1.67 mg/mL	NA	
	Ethyl acetate fraction			NA	NA	NA	0.55 ± 0.00 mg/mL	NA	

Part use	Type of extraction	*In vivo*/ *In vitro*	Type of assays	Concentrations used	Mode of administration	Duration of treatment	IC_{50}	Result	References
	Butanol fraction			NA	NA	NA	2.95 ± 0.31 mg/mL	NA	
	Water fraction			NA	NA	NA	NA	NA	
Callus	Hexane fraction			NA	NA	NA	0.67 ± 0.05 mg/mL	NA	
	Chloroform fraction			NA	NA	NA	0.90 ± 0.11 mg/mL	NA	
	Ethyl acetate fraction			NA	NA	NA	0.25 ± 0.01 mg/mL	NA	
	Butanol fraction			NA	NA	NA	NA	NA	
	Water fraction			NA	NA	NA	NA	NA	

Note: ASG: *Alternanthera sessilis* green; ASR: *Alternanthera sessilis* red; NA: Not available; IC_{50}: Half maximal inhibitory concentration.

Table 10: Hepatoprotective effect of ASG and ASR.

Part use	Type of extraction	*In vivo*	Type of assays	Concentrations used	Mode of administration	Duration of treatment	IC_{50}	Result	References
ASG									
Whole plant	Methanol	Wistar albino rats	CCl_4- induced liver damage.	50,200 and 500 mg/kg	Intraperitoneal injection.	Single dose every 24h for 3 consecutive days.	NA	The administration with methanolic extract of *A. sessilis*, especially 500mg/kg, significantly reduced the higher levels of cholesterol and billirubin in serum compared to the CCl_4-induced group.	[9]
Aerial	Ethanol	Wistar albino rats	Paracetamol -induced liver damage.	200 and 400 mg/kg	Oral	Daily once for 7 consecutive days.	NA	400 mg/kg concentration of ASG significantly reduced SGOT, SGPT, ALP, bilirubin, lipid peroxidation and cholesterol level while upregulating SOD, CAT and GSH compared to paracetamol-induced group.	[31]

Part use	Type of extraction	*In vivo*	Type of assays	Concentrations used	Mode of administration	Duration of treatment	IC_{50}	Result	References
ASR									
Whole plant	Aqueous	ICR strain mice	CCl_4- induced liver damage.	300 mg/10 mL/kg	Oral	Single dose at 2, 6 and 10h after liver damage induction.	NA	Significantly reduced SGPT and SGOT ($p < 0.05$). Histologically, the visibility of improved hepatic cords and necrosis of the collar with moderate inflammation surrounding the central veins indicated that ASR ameliorated liver injury. In addition, the extent of hepatocytes necrosis reduced noticeably.	[39]
		ICR strain mice	Paracetamol-induced liver damage.	300 mg/10 mL/kg		Single dose at 2, 6 and 10h after liver damage induction.	NA	SGOT and SGPT ($p < 0.05$) significantly suppressed by ASR compared to induction group. Histopathologically, ASR restored the paracetamol-induced liver injuries, with little bleeding and hardly any vacuolization or localised necrosis present.	
		Wistar albino rats	D(+)-galactosamine-induced liver damage.	300 mg/10 mL/kg		Single dose at 2, 6 and 10h after liver damage induction.	NA	ASR significantly suppressed SGOT and SGPT compared to induction group. ASR was able to preserve a similar hepatic structural pattern as the control group, with slight inflammation and necrosis in the portal tract.	

Note: ASG: *Alternanthera sessilis* green; ASR: *Alternanthera sessilis* red; NA: Not available; IC_{50}: Half maximal inhibitory concentration; SGOT: Serum glutamate oxaloacetic transaminase; SGPT: Serum glutamate pyruvic transaminase; ALP: Alkaline phosphatase; CCL_4: Carbon tetrachloride.

Anti-hyperglycemia Activities

The anti-hyperglycemic capability of ASG and ASR reported from previous studies were listed in Table 9. Das *et al.* (2015) along with Rayilla and Goverdhan (2017) investigated the anti-diabetic activities of ASG. The leaves of ASG were employed in both investigations, but they used different extraction techniques. One was extracted using 95% ethanol after being defatted by petroleum ether.[61] The other was macerated in 90% ethanol.[62] According to the data from single and multi-dose studies and subacute investigation done for 15 days, ASG leaf extracts employed in both studies significantly ($p<0.05$) decreased the level of glucose in diabetic rats induced by streptozotocin.[61,62] Leaf extracts of concentrations 200 mg/kg and 400 mg/kg used for the oral glucose tolerance test significantly ($p<0.05$) decreased the level of glucose in blood which could be compared to the standard medication glibenclamide (10 mg/kg) utilized in both single and multi doses study.[61] For the 15 days study conducted, it revealed an inhibition rate of 50% and 51% for concentrations 100 mg/kg and 200 mg/kg respectively on the final day.[62]

Table 11: Anagesic effect of ASG.

Part use	Type of extraction	*In vivo*	Type of assays	Concentrations used	Mode of administration	Duration of treatment	Result	References
Whole plant	Ethanol	Swiss Albino mice	Writhing induced by acetic acid.	250, 500 mg/kg	Oral	NA	500 mg/kg and 250 mg/kg concentrations were used with 59.52% and 37.28% rate of inhibition respectively.	[64]
			Hot-plate methods.		Intraperitoneal	NA	Highest reaction at 7.28 s and 6.87 s for concentrations 500 mg/kg and 250 mg/kg respectively with a total duration of 60min for the assay conducted.	
Leaf	Hydroethanolic	Swiss albino mice	Eddy's hot plate method.	250, 500 mg/kg	Intraperitoneal	NA	Highest reaction at 12.17 and 13.50 and sec for 250 mg/kg and 500 mg/kg concentrations respectively with a total duration of 60min for the assay conducted.	[65]
			Acetic acid induced writhing response.		Oral	NA	69.17% and 66.58% inhibition at doses 500 and 250 mg/kg, respectively.	

Note: ASG: *Alternanthera sessilis* green; NA: Not available.

Interestingly, ASR also possessed similar anti-diabetic activity to ASG. The study from Tan and Kim (2013), found that 150 mg/kg concentration of ASR extracted using ethyl acetate significantly ($p<0.05$) lowered glucose level in the blood of fasting obese rats having Type 2 Diabetes following administration for two weeks. These findings imply that anti-diabetic action of ASR enhances insulin tolerance and protective effects of pancreas in diabetic rats.[3] Another study reported anti-glucosidase activity in the leaf and callus ethyl acetate fractions where both were classified as inhibitors of á-glucosidase with one being competitive and the other non-competitive.[27] Alpha-glucosidase inhibitors are among the most successful class of anti-diabetic remedies that can improve and alleviate hyperglycemia, particularly postprandial hyperglycemia, over alpha-amylase inhibitors.[63] Therefore, alpha-glucosidase inhibition may account for the anti-hyperglycemic potential of ASR in obese rats having Type 2 Diabetes.[3] Overall, these results indicate the potential of both cultivars for the creation of novel oral diabetic medications.

Hepatoprotective Effects

Results of successful experiments revealing the hepatoprotective capability of ASG and ASR are summarized in Table 10. Apart from antioxidant activities, Das *et al.* (2014) also examined the hepatoprotective ability of the ASG extracted using ethanol. According to the data, the ethanolic extract of ASG given in a concentration of 400 mg/kg per day significantly ($p < 0.05$) reduced liver injury induced by paracetamol given at a concentration of 500 mg/kg per day. Both the ASG ethanolic extract treatment and paracetamol administration was given for 7 days. ASG at 400 mg/kg protected the liver by reducing the level of total cholesterol, bilirubin, serum enzymes and peroxidation of lipid *in vivo* while significantly ($p < 0.05$) enhancing activities of High Density Lipoprotein (HDL) cholesterol, Superoxide

Dismutase (SOD), Glutathione (GSH) and Catalase (CAT) compared to concentration of 200 mg/kg.[31] In comparison to silymarin, the standard reference drug employed in Carbon Tetrachloride (CCL_4) induced liver damage, the hepatoprotective action of methanol extract *in vivo* at a dosage of 500 mg/kg BW (Body Weight) successfully lowered the level of serum bilirubin, cholesterol, Alkaline Phosphatase (ALP), Serum Glutamate Oxaloacetic Transaminase (SGOT) and Serum Glutamate Pyruvic Transaminase (SGPT). The action demonstrated by ASG whole plant extracted using methanol solvent was marked significant, justifying its traditional use in managing liver disorders.[9]

On the other hand, Lin *et al.* (2004) tested the aqueous extract of ASR *in vivo* for hepatotoxin induced hepatic damage. The hepatotoxins utilised in the investigation were 188 mg/kg of D(+)-galactosamine in rats and 31.25 µL/kg of carbon tetrachloride or 600 mg/kg paracetamol in mice. 300 mg/kg of ASR was able to decrease the elevated activity of SGPT and SGOT at 2, 6, and 10 hr (observed for a total duration of 24 hr) following the administration of aforementioned hepatotoxins.[39] Further confirmation was made via histopathological examination, where the ASR extract showed significant improvement in reducing presence of eosinophils, pyknotic nuclei, necrosis of centrilobular and degeneration of hepatocytes microvesicular.[39]

Analgesic Activities

Only a few studies have investigated the analgesic potential of ASG and their results are listed in Table 11. Both Mondal *et al.* (2014) and Mohapatra *et al.* (2018) investigated the analgesic activity of ASG using the same animal model and test protocols, but with a different method of extraction. The ASG extracted using ethanol was able to impede acetic acid-induced writhing when 500 mg/kg and 250 mg/kg concentrations were used with 59.52% and 37.28% rate of inhibition respectively.[64] Moreover, the extract also exhibited its highest reaction at 7.28 s and 6.87 s for concentrations 500 mg/kg and 250 mg/kg respectively when a 60 min hot-plate test was conducted. In contrast, the other study used the hydroethanolic extract of ASG.[65] They reported the same results as Mondal *et al.* (2014) where the extract significantly ($p<0.05$) suppressed writhing initiated by acetic acid in mice revealed through the hot-plate test when concentrations of 500 mg/kg and 250 mg/kg were employed. These results further confirm that ASG contains active phytoconstituents that contribute towards analgesic activities. At present, no research has identified ASR's analgesic capabilities.

CONCLUSION

A. sessilis exists in two different colors, one with green aerial parts known as green cultivar and the other having red aerial parts known as red cultivar. Both plants have various active phytoconstituents including polyphenol, terpenes, alkaloid, flavonoids, and carotenoids that exhibit a variety of pharmacological activities. The plants also have gallic acid, which may contribute to anti-cancer properties. The other bioactive compounds in the plants exhibit strong pro-inflammatory, antioxidant, wound healing, analgesic, and anti-angiogenesis properties. Extracts from different portions of *A. sessilis* such as leaves, aerial and stem as well as the whole plant can be exploited to develop novel antioxidants, anti-diabetic, anti-bacterial, anti-inflammation, anti-cancer, hepatoprotective and analgesic agents. However, it is necessary to understand that *A. sessilis* properties require more in-depth studies to detect the mechanism action and safety of its phytoconstituents since *in vitro* studies are still in its early phases. Further *in vivo* and clinical studies are needed, particularly to investigate its anti-cancer properties over a wider range of concentrations. Despite the fact that a lot of scientific publications tend to focus on the green cultivar, presumably because it is so widely available, further research on the red cultivar is necessary since it displays characteristics that are comparable to those of the green cultivar. Further processing and commercialization of this remedial weed as a product benefiting the wellbeing of humans is recommended as *A. sessilis* has high potential to be utilized as a curative agent while being a vital ingredient that can be included in daily consumption. Companies that manufacture products containing *A. sessilis* should include relevant information on its bioactive components and any additional nutritional elements added to the products and their concentration to raise awareness among consumers about the safety of nutraceutical products.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

***A. sessilis*:** *Alternanthera sessilis*; **ABTS:** 2,2′-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid; **Ag:** Silver; **ALP:** Alkaline phosphatase; **ASG:** Alternanthera sessilis green; **ASR:** Alternanthera sessilis red; **Au:** Gold; **CAM:** Complementary and alternative medicines; **Capan-1:** Human pancreatic ductal adenocarcinoma cell; **CAT:** Catalase; **CCl_4:** Carbon tetrachloride; **DNA:** Deoxyribonucleic Acid; **DPPH:** 2,2-diphenyl-1-picryl-hydrazyl-hydrate; **FRAP:** Ferric reducing ability assays; **GCMS:** Gas chromatography-mass spectrometry; **GSH:** Glutathione; **HDL:** High density lipoprotein; **HeLa:** Cervix adenocarcinoma cells; **HPLC:** High performance liquid chromatography; **HT-29:** Human colon cancer cells; **LCMS:** Liquid chromatography-mass

spectrometry; **MBC:** Minimum bactericidal concentration; **MCF-7:** Breast cancer cells; **MIA PaCa-2:** Human pancreatic cancer cell; **MIC:** Minimum inhibitory concentrations; **MTT:** 3-4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium bromide; **ORAC:** Oxygen radical absorbance capacity; **PANC-1:** Human pancreatic cancer cell; **PC3:** Prostate cancer cells; **SGOT:** Serum glutamate oxaloacetic transaminase; **SGPT:** Serum glutamate pyruvic transaminase; **SOD:** Superoxide dismutase; **WHO:** World Health Organisation.

AUTHOR CONTRIBUTIONS

Conceptualization: O.R., S.C.C., Y.E.G., V.L. and Y.K.Y.; Methodology: V.L. and Y.K.Y.; validation, V.L. and Y.K.Y.; Formal analysis: O.R., S.C.C., Y.E.G., V.L. and Y.K.Y.; Investigation: O.R., S.C.C., Y.E.G., V.L. and Y.K.Y.; Data curation: O.R., S.C.C. and Y.E.G.; Writing—original draft preparation: O.R., S.C.C. and Y.E.G.; Writing—review and editing: O.R., S.C.C., Y.E.G., V.L. and Y.K.Y.; Supervision: Y.K.Y.; Project administration: O.R., S.C.C. and Y.E.G.; Funding acquisition: Y.K.Y. All authors have read and agreed to the published version of the manuscript.

REFERENCES

1. Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. Front Pharmacol. 2014;4(177):177. doi: 10.3389/fphar.2013.00177, PMID 24454289.
2. Ulian T, Diazgranados M, Pironon S, Padulosi S, Liu U, Davies L, *et al.* Unlocking plant resources to support food security and promote sustainable agriculture. Plants People Planet. 2020;2(5):421-45. doi: 10.1002/ppp3.10145.
3. Tan KH, Kim KH. *Alternanthera sessilis* Red ethyl acetate fraction exhibits antidiabetic potential on obese Type 2 diabetic rats. Evid Based Complement Alternat Med. 2013;2013:1-8. doi: 10.1155/2013/845172.
4. Arollado EC, Osi MO. Hematinic activity of *Alternanthera sessilis* (L.) R. Br. (Amaranthaceae) in mice and rats. Int Sci Res J. 2010;2(2):110-7.
5. Walter TM, Merish S, Tamizhamuthu M. Review of *Alternanthera sessilis* with reference to traditional Siddha medicine. Int J Pharmacogn Phytochem Res. 2014;6(2):249-54.
6. Sun Y, Ding J, Frye MJ. Effects of resource availability on tolerance of herbivory in the invasive *Alternanthera philoxeroides* and the native *Alternanthera sessilis*. Weed Res. 2010;50(6):527-36. doi: 10.1111/j.1365-3180.2010.00822.x.
7. Chen Y, Zhou Y, Yin TF, Liu CX, Luo FL. The invasive wetland plant *Alternanthera philoxeroides* shows a higher tolerance to waterlogging than its native congener *Alternanthera sessilis*. PLOS ONE. 2013;8(11):e81456. doi: 10.1371/journal.pone.0081456, PMID 24303048.
8. Anitha T, Mary JR. A study on the cooking quality, biochemical and nutritive value of edible green leaf vegetable: *Alternanthera sessilis* L. R. Br. Ex. DC. Int J Appl Res. 2016;2(4):28-30.
9. Bachok MF, Yusof BNM, Ismail A, Hamid AA. Effectiveness of traditional Malaysian vegetables (ulam) in modulating blood glucose levels. Asia Pac J Clin Nutr. 2014;23(3):369-76. doi: 10.6133/apjcn.2014.23.3.01, PMID 25164446.
10. Bhuyan B, Baishya K, Rajak P. Effects of *Alternanthera sessilis* on liver function in carbon tetra chloride induced hepatotoxicity in Wister rat model. Indian J Clin Biochem. 2018;33(2):190-5. doi: 10.1007/s12291-017-0666-1, PMID 29651210.
11. Hwong CS, Leong KH, Aziz AA, Junit SM, Noor SM, Kong KW. *Alternanthera sessilis*: uncovering the nutritional and medicinal values of an edible weed. J Ethnopharmacol. 2022;298:1-15. doi: 10.1016/j.jep.2022.115608.
12. Othman A, Ismail A, Hassan FA, Yusof BNM, Khatib A. Comparative evaluation of nutritional compositions, antioxidant capacities, and phenolic compounds of red and green sessile joyweed (*Alternanthera sessilis*). J Funct Foods. 2016;21:263-71. doi: 10.1016/j.jff.2015.12.014.
13. Louppe D. Plant resources of tropical Africa (PROTA). PROTA.
14. Robertson KR. The genera of Amaranthaceae in the southeastern United States. J Arnold Arbor. 1981;62(3):267-313. doi: 10.5962/bhl.part.11251.
15. Fan S, Yu D, Liu C. The invasive plant *Alternanthera philoxeroides* was suppressed more intensively than its native congener by a native generalist: implications for the biotic resistance hypothesis. PLOS ONE. 2013;8(12):e83619. doi: 10.1371/journal.pone.0083619, PMID 24386236.
16. Nikam SR, Namdas DDD. Preliminary phytochemical analysis of *Alternanthera sessilis* Leaves (Linn). R.Br. Ex. DCYMER Digital. YMER. 2022;21(1):220-5. doi: https://doi.org/10.37896/YMER21.01/2010.37896/YMER21.01/20.
17. Rojas SJ, Acevedo RP. *Alternanthera sessilis* (sessile joyweed). CABI compendium; 2022.
18. Sravani VL, Abbas Z, Surya P. A review on *Alternanthera sessilis*. Indo-. Am J Pharmacol Sci. 2017;4(09):2845-52. doi: 10.5281/zenodo.888221.
19. Waisundara VY. Traditional herbal remedies of Sri Lanka. CRC Press; 2019.
20. Gupta HV, Raj J, Rathi AK, Sundaram E, Kumar S, Manchanda RK. Morpho-anatomy of leaf, stem and root of *Alternanthera sessilis* (L.) R. Br. ex DC and *Alternanthera pungens* Kunth (Amaranthaceae) and its significance in drug identification. Indian J Res Homoeopathy. 2012;6(4):1-7. doi: 10.53945/2320-7094.1700.
21. Natl Parks2023, February. *Alternanthera sessilis* red.Available from: https://www.nparks.gov.sg/florafaunaweb/flora/3/4/3433. 2023, February.
22. Manalo RAM, Arollado EC, Heralde FM. *Alternanthera sessilis* leaf fractions possess *in vitro* inhibitory activities in mammalian α-amylase and α-glucosidase. Pharm Sci Asia. 2020;47(3):279-86. doi: 10.29090/psa.2020.03.019.0076.
23. Suganya D, Banupriya R, Maheswari AU, Elumalai S. Studies on biological activity of aqueous extract of *Alternanthera sessilis* (Linn) for developing potential herbal drug formulation of ocular diseases. Med Aromat Plants. 2019;08(01):1-10.
24. Mohd Hazli UHAM, Abdul-Aziz A, Mat-Junit S, Chee CF, Kong KW. Solid-liquid extraction of bioactive compounds with antioxidant potential from *Alternanthera sesillis* (red) and identification of the polyphenols using UHPLC-QqQ-MS/MS. Food Res Int. 2019;115:241-50. doi: 10.1016/j.foodres.2018.08.094, PMID 30599938.
25. Mohd Hazli UHAM, Hwong CS, Abdul-Aziz A, Mat-Junit S, Leong KH, Kong KW. Effects of *Alternanthera sessilis* red leaf extracts on hydrogen peroxide-induced oxidative stress in HepG2 cells and identification of phytochemicals using HPLC-QToF-MS/MS. S Afr J Bot. 2022;151:440-50. doi: 10.1016/j.sajb.2022.04.056.
26. Azizah O, Amin I, Fouad AR. Antioxidant properties of *Alternanthera sessilis* red and green. Acta Hortic. 2015;1106(1106):131-6. doi: https://doi.org/10.17660/ActaHortic.2015.1106.2010.17660/aActahHortic.2015.1106.20.
27. Chai TT, Khoo CS, Tee CS, Wong FC. Alpha-glucosidase inhibitory and antioxidant potential of antidiabetic herb *Alternanthera sessilis*: comparative analyses of leaf and callus solvent fractions. Pharmacogn Mag. 2016;12(48):253-8. doi: 10.4103/0973-1296.192202, PMID 27867265.
28. Khan MM, Yusufzai SK, Kaun LP, Shah MR, Idris R. Chemical composition and antioxidant activity of essential oil of leaves and flowers of *Alternanthera sessilis* red from Sabah. J App Pharm Sci. 2016;6(12):157-61. doi: 10.7324/JAPS.2016.601222.
29. Anitha R, Kanimozhi S. Pharmacognostic evaluation of *Alternanthera sessilis* (L.) R. Br. Ex. Pharmacogn J. 2012;4(28):31-4. doi: 10.5530/pj.2012.28.6.
30. Hossain AI, Faisal M, Rahman S, Jahan R, Rahmatullah M. A preliminary evaluation of antihyperglycemic and analgesic activity of *Alternanthera sessilis* aerial parts. BMC Complement Altern Med. 2014;14(1):169. doi: 10.1186/1472-6882-14-169, PMID 24885344.
31. Das M, Ashok D, Das A. Hepatoprotective activity of ethanolic extract of *Alternanthera sessilis* Linn. on paracetamol induced hepatotoxic rats. Int J Pharm Pharm Sci. 2014;4(4):91-6.
32. Lalitha ST, Vijayalakshmi K. Evaluation of vitamins and antinutrients in the leaves of traditional medicinal plant *Alternanthera sessilis* (L.) R. Br. Ex. DC. Int J Health Sci Res. 2018;8:244-53.
33. Vani M, Rahaman SA, Prameela Rani AP. Detection and quantification of major phytochemical markers for standardization of *Talinum portulacifolium, Gomphrena serrata, Alternanthera Ssessilis* and *Euphorbia heterophylla* by HPLC. Pharmacogn J. 2018;10(3):439-46. doi: 10.5530/pj.2018.3.72.
34. Azam FMS, Biswas A, Mannan A, Afsana NA, Jahan R, Rahmatullah M. Are famine food plants also ethnomedicinal plants? An ethnomedicinal appraisal of famine food plants of two districts of Bangladesh. Evid Based Complement Alternat Med. 2014;2014:741712. doi: 10.1155/2014/741712, PMID 24701245.
35. Kumar MS, Rani GS, Kumar SS, Astalakshmi N. Screening of aqueous and ethanolic extracts of aerial parts of *Alternanthera sessilis* Linn. R. Br. Ex. DC. for nootropic activity. J Pharm Sci Res. 2011;3(6):1294-7.
36. Jayaweera DMA. Medicinal Plants (Indigenous and exotic) used in Ceylon. J Nat Sci Found. 2002;1:42-3.
37. Acharya E, Pokhrel B. Ethno-medicinal plants used by Bantar of Bhaudaha, Morang, Nepal. Our Nat. 2007;4(1):96-103. doi: 10.3126/on.v4i1.508.
38. Hosamani KM, Ganjihal SS, Chavadi DV. HosamaniK MGanjihalS SChavadi V *Alternanthera triandra* seed oil: A moderate source of ricinoleic acid and its possible industrial utilisation. Ind Crops Prod. 2004;19(2):133-6. doi: 10.1016/j.indcrop.2003.07.009.
39. Lin S, Lin Y, Shyuu S, Lin C. Hepatoprotective effects of Taiwan folk medicine: *Alternanthera sessilis* on liver damage induced by various hepatotoxins. Phytother Res. 1994;8(7):391-8. doi: 10.1002/ptr.2650080703.
40. Siew YY, Zareisedehizadeh S, Seetoh WG, Neo SY, Tan CH, Koh HL. Ethnobotanical survey of usage of fresh medicinal plants in Singapore. J Ethnopharmacol. 2014;155(3):1450-66. doi: 10.1016/j.jep.2014.07.024, PMID 25058874.
41. Gupta R, Singh HK. Detection and quantitation of gallic acid in *Alternanthera sessilis* and *Clerodendrum infortunatum* by HPTLCMOJPH. MOJPH. 2016;4(6):467-71. doi: 10.15406/ppij.2016.04.00097.

42. Sowemimo A, Van De Venter M, Baatjies L, Koekemoer T. Cytotoxic activity of selected Nigerian plants. Afr J Trad Complement Altern Med. 2010;6(4):526-8. doi: 10.4314/ajtcam.v6i4.57186.
43. George S, Bhalerao SV, Lidstone EA, Ahmad IS, Abbasi A, Cunningham BT, *et al*. Cytotoxicity screening of Bangladeshi medicinal plant extracts on pancreatic cancer cells. BMC Complement Altern Med. 2010;10(1):52. doi: 10.1186/1472-6882-10-52, PMID 20849608.
44. Gothai S, Muniandy K, Mohd Esa N, Subbiah S, Arulselvan P. Anticancer potential of *Alternanthera sessilis* extract on HT-29 human colon cancer cells. Asian Pac J Trop Biomed. 2018;8(8):394. doi: 10.4103/2221-1691.239427.
45. Qian L, Su W, Wang Y, Dang M, Zhang W, Wang C. Synthesis and characterization of gold nanoparticles from aqueous leaf extract of *Alternanthera sessilis* and its anticancer activity on cervical cancer cells (HeLa). Artif Cells Nanomed Biotechnol. 2019;47(1):1173-80. doi: 10.1080/21691401.2018.1549064, PMID 30942109.
46. Firdhouse MJ, Lalitha P. Biosynthesis of silver nanoparticles using the extract of *Alternanthera sessilis*—antiproliferative effect against prostate cancer cells. Cancer Nanotechnol. 2013;4(6):137-43. doi: 10.1007/s12645-013-0045-4, PMID 26069509.
47. M JF, P L. JFP LApoptotic efficacy of biogenic silver nanoparticles on human breast cancer MCF-7 cell lines. Prog Biomater. 2015;4(2-4):113-21. doi: 10.1007/s40204-015-0042-2, PMID 26566469.
48. Abdulkhaleq LA, Assi MA, Abdullah R, Zamri-Saad MZ, Taufiq-Yap YH, Hezmee MNM. The crucial roles of inflammatory mediators in inflammation: a review. Vet World. 2018;11(5):627-35. doi: 10.14202/vetworld.2018.627-635, PMID 29915501.
49. Babu NR, Divakar J, Krishna UL, Vigneshwaran C. Study of antimicrobial, antioxidant, anti-inflammatory activities and phytochemical analysis of cooked and uncooked different spinach leaves. J Pharmacogn Phytochem. 2018;7(5):1798-803.
50. Sunmathi D, Sivakumar R, Ravikumar K. *In vitro* anti-inflammatory and antiarthritic activity of ethanolic leaf extract of *Alternanthera sessilis* (L.) R. Br. ex DC. and *Alternanthera philoxeroides* (Mart.) Griseb. International Journal of Advances in Pharmacy, Biology and Chemistry. 2016;5(2):109-15.
51. Subhashini T, Krishnaveni B, Reddy CS. Anti-inflammatory activity of leaf extracts of *Alternanthera sessilis*. Hygeia J Drugs. Med. 2010;2(1):54-6.
52. Sahithi B, Rajani GP, Sowjanya K, Gupta D. Anti-inflammatory activity of ethanolic and aqueous extracts of *Alternanthera sessilis* Linn. Pharmacol Online. 2011;1:1039-43.
53. Mohd Razali NN, Teh SS, Mah SH, Yong YK, Ng CT, Lim YM, *et al.* Protective effects of *Alternanthera sessilis* ethanolic extract against TNF-α or H_2O_2-induced endothelial activation in human aortic endothelial cells. Evid Based Complement Alternat Med. 2022;2022:1128738435. doi: 10.1155/2022/8738435, PMID https://www.ncbi.nlm.nih.gov/pubmed/3525121635251216.
54. Muniandy K, Gothai S, Badran KMH, Suresh Kumar S, Esa NM, Arulselvan P. Suppression of proinflammatory cytokines and mediators in LPS-induced RAW 264.7 macrophages by stem extract of Alternanthera sessilis via the inhibition of the NF-κB pathway. Suppression of Proinflammatory Cytokines and Mediators in LPS-Induced RAW 264.7 Macrophages by Stem Extract of *Alternanthera sessilis* via the Inhibition of the NF-κB Pathway. J Immunol Res. 2018;2018:3430684. doi: 10.1155/2018/3430684, PMID 30155492.
55. Vallejo MPRJ, Salazar L, Grijalva M. Oxidative stress modulation and ROS-mediated toxicity in cancer: a review on *in vitro* models for plant derived compounds. Oxid Med Cell Longev. 2017;2017:586068. doi: 10.1155/2017/4586068, PMID 29204247.
56. Gayathri BM, Balasuriya K, Gunawardena GSP, Rajapakse RPVJ, Dharmaratne HRW. Toxicological studies of the water extract of green leafy vegetable Sessile joy weed (*Alternanthera sessilis*). Curr Sci. 2006;91(11):1517-20.
57. Kumari MEVN, Krishnan V. Antimicrobial activity of *Alternanthera sessilis* (L.) R. Br. Ex. DC. and *Alternanthera philoxeroides* (Mart.) GrisebAlternanthera philoxeroides. World J Res Rev. 2016;3(3):78-81.
58. Monroy AEM, Limsiaco CL. Phytochemical and antimicrobial Analysis of "Lupo" (*Alternanthera sessilis* L.R.BR.). West Visayas State Univ Res J. 2016;5(2):21-34.
59. Sivakumar R, Sunnathi D. Phytochemical screening and antimicrobial activity of ethanolic leaf extract of *Alternanthera sessilis* (L.) R. Br. Ex. DC. and *Alternanthera Philoxeroides* (Mart.) GrisebAlternanthera Philoxeroides. Eur J Pharm Sci. 2016;3(3):409-12.
60. Kulasingam K. Antimicrobial studies on *Alternanthera sessilis* red leaves; 2014 [[Master's thesis]. Malaysia: International Medical University]. International Medical University Malaysia Central Digital Repository. http://localhost:8080/xmlui/handle/123456789/1519.
61. Das M, Kumar AD, Mastanaiah K, Das A. Evaluation of antidiabetic activity of ethanolic extract of *Alternanthera sessilis* Linn. streptozotocin-induced diabetic rats. Int J Pharm Sci Res. 2015;6(7):1027-32.
62. Rayilla D, Goverdhan P. Antidiabetic and antihyperlipidemic activities of *Alternanthera sessilis* in experimentally induced Type 2 diabetesIOSRPBS. IOSRJPBS. 2017;12(3):44-7. doi: 10.9790/3008-1203064447.
63. Joshi SR, Standl E, Tong N, Shah PK, Kalra S, Rathod RH. Therapeutic potential of α-glucosidase inhibitors in type 2 diabetes mellitus: an evidence-based review. Expert Opin Pharmacother. 2015;16(13):1959-81. doi: 10.1517/14656566.2015.1070827, PMID 26255950.
64. Mondal H, Saha S, Awang K, Hossain H, Ablat A, Islam MK, *et al*. Central-stimulating and analgesic activity of the ethanolic extract of *Alternanthera sessilis* in mice. BMC Complement Altern Med. 2014;14(1):398. doi: 10.1186/1472-6882-14-398, PMID 25315440.
65. Mohapatra SS, Kafle A, Chatterjee J, Mohan P, Roy RK, Reddy I. Analgesic activity of hydroethanolic extract of *Alternanthera sessilis* in mice. J Pharmacogn Phytochem. 2018;7(4):1836-9.

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