

Muntingia Calabura (Jamaica Cherry): An Overview

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ABSTRACT

Muntingia, or *Jamaica Cherry*, is a small, fast-growing tree that can reach up to 40 ft. tall at full maturity. The soft leaves are evergreen and have an alternate phyllotaxy. Leaves are dark green on top and light green underneath. The small, white flowers feature yellow stamens in the center. The small, round fruits are abundant, and depending on the variety, have a red or yellow color. Fruits are edible raw or made into jam. The fruit possessed potent anti-inflammatory activity. The flowers have antiseptic and antispasmodic qualities, and are made into medicinal teas. The *M. calabura* leaves exhibited potential anti-proliferative and antioxidant activities. The present study on Muntingia is to give an overview on traditional uses and pharmacological activity.

Key words : Muntingia calabura, Antiproliferative, Antioxidant, Antiseptic, Antispasmodic

INTRODUCTION

There has been an increased urgency to discover novel antibiotics/anti microbial compounds due to emergence of drug resistant microorganisms. Therefore, an infection caused by antibiotic resistant microbes complicates conventional treatment causing prolonged illness and increases the death risks. Many medical practitioners also employ traditional (Ayurvedic) medicine, in Western and other developing nations like India, in complementary to modern medicines. Today also, as a testament to its persistence, over 80% of people in the world still utilize traditional medicine for primary healthcare. Many underdeveloped countries are rich in biodiversity hotspots like Southeast Asia, Africa, Central and Southern America. Among all the natural resources, plants are the single largest source for traditional medicines, accounting for 25% of new drugs components being tested for clinical trials (Singh et al.,2017).

Cherry leaves (*Muntingia calabura*) contain antioxidants that generally form by phenolic or pholifenols, the sinamat acid derivatives, flavonoids, tocopherols, coumarin and polifungsional acids. Flavonoids that have an antioxidant activity consist of flavonol, flavanon, flavones, isoflavones, catechins and kalkon. Phenolic compounds that have

antioxidant activity can be known through the way of extraction. Extractions are a way to separate a desired substance when it is mixed with others. The mixture is brought into contact with a solvent in which the substance of interest is soluble, but the other substances present are insoluble. Components of active compounds from plants or animals can be extracted based on "Like Dissolved Like Theory", compounds will be extracted depends on solubility (Triswaningsih et al.,2017).

Medicinal plants are sources of important therapeutic aid for alleviating human ailments. Approximately 80% of the people in the developing countries all over the world depend on the traditional medicine for their primary health-care. Interestingly, approximately 85% of traditional medicine involves the use of plant extracts. Interest in phytomedicine started in the last 20 years and with increasing awareness of the health hazards and toxicities associated with unsystematic use of synthetic drugs and antibiotics, interest in the use of plants and plant-based drugs has revived throughout the world. However, a large number of medicinal plants remain to be investigated for their possible pharmacological value. One of the plants that has recently gained a medicinal plant status is *Muntingia calabura* L. (Elaeocarpaceae).

Muntingia, or *Jamaica Cherry*, is a small, fast-growing tree that can reach up to 40 ft. tall at full maturity. The soft leaves are evergreen and have an alternate phyllotaxy. Leaves are dark green on top and light green underneath. The small, white flowers feature yellow stamens in the center. The small, round fruits are abundant, and depending on the variety, have a red or yellow color (Mahmood et al., 2014).

SYSTEMIC CLASSIFICATION

Kingdom: *Plantae*

Order: *Malvales*

Family: *Muntingiaceae*

Genus: *Muntingia L.*

Species: *M. Calabura*

GENERAL HISTORY

Muntingia, also known as *Jamaica Cherry*, is widely grown in the tropics and subtropics worldwide. By the early 1900s, Muntingia was popular in Southeast Asia, and in 1922, the USDA introduced several trees to Hawaii, USA. In 1926, Dr. David Fairchild collected seeds from a yellow-fruit variety in Ceylon, and by the 1930s, Muntingia could be found in home gardens throughout south Florida. Today, Muntingia is very popular throughout Southeast Asia, especially in the Philippines, but is not very widespread in south Florida.

ORIGIN AND DISTRIBUTION :

The Jamaica cherry is indigenous to southern Mexico, Central America, tropical South America, the Greater Antilles, St. Vincent and Trinidad. The type specimen was collected in Jamaica. It is widely cultivated in warm areas of the New World and in India, south-east Asia, Malaya, Indonesia, and the Philippines, in many places so thoroughly naturalized that it is thought by the local people to be native.

Macmillan says that it was first planted in Ceylon about 1912. Several trees were introduced into Hawaii by the United States Department of Agriculture in 1922. Dr. David Fairchild collected seeds of a yellow-fruited form in the Peradeniya. Botanic Gardens, Ceylon, in 1926. The tree has been grown in southern Florida for its fruits and as quick shade for nursery plants. It is seldom planted at present. Volunteers from bird-distributed seeds

spring up in disturbed hammocks and pinelands. The author supplied seeds requested by the Kenya Agriculture Research Institute, Kihuyu, in 1982. The Jamaica cherry is said to grow better than any other tree in the polluted air of Metropolitan Manila. It runs wild on denuded mountainsides and on cliffs and is being evaluated for reforestation in the Philippines where other trees have failed to grow and also for wildlife sanctuaries since birds and bats are partial to the fruits.

The fruits are sold in Mexican markets. In Brazil, they are considered too small to be of commercial value but it is recommended that the tree be planted on river banks so that the abundance of flowers and fruits falling into the water will serve as bait, attracting fish for the benefit of fishermen. In Malaya, the tree is considered a nuisance in the home garden because fruit-bats consume the fruits and then spend the day under the eaves of houses and disfigure the porch and terrace with their pink, seedy droppings.

MEDICINAL USES

Antioxidant activity, improvement in endothelial function, vascular function and insulin sensitivity; as well as attenuation of platelet reactivity and reduction in blood pressure. Moreover proper scientific screening of potential bio actives of these plants followed by chemical investigations is necessary to make these herbal remedies more viable. In this context, the present study was undertaken to evaluate the antioxidant of *Muntingia calabura*(raw fruit).

TRADITIONAL USES :

The emergences of various types of diseases, both infectious and non-infectious, nowadays have become a major global burden. Various pharmaceutical drugs have been developed and prescribed to patients to help cure those diseases. Unfortunately, conventional drugs have also been associated with various unwanted side effects. For example, morphine has been known to cause phenomenon such as tolerance and dependence while the appearance of antibiotic-resistance bacteria such as methicillin- and vancomycin-resistance bacteria have been well documented. Due to these problems, patients have been looking for

other alternative to treat their diseases, where complementary and alternative medicine (CAM), particularly the plant based medicines, has been one of the sources of the CAM used. One of the plants that have recently gained attention among researchers throughout the world is *M. calabura*



Muntingia calabura fruit and flower



Muntingia calabura tree

Based on the literature searches carried out, this plant has limited traditional uses throughout the world with medicinal uses recorded in, particularly, Peru, Colombia, Mexico, Vietnam and Philippines.

This might explain why *M. calabura* medicinal value is not well documented in Malaysia and why it is considered as a neglected plant. Despite the lack of traditional claims, various parts of the plant have been used to treat different types of illnesses. In Peruvian folklore medicine, the flowers and barks are used as an antiseptic and to reduce swelling in lower extremities while the leaves, either boiled or steeped in water, are used to reduce gastric ulcer and swelling of prostate gland, and to alleviate headache and cold. Moreover, the boiled barks can be used as a wash to reduce swelling in the lower extremities. In Colombia, the infusion of the flowers is used as a tranquillizer and tonic. In Mexico, the plant is used to treat measles, mouth pimples and stomach ache. In Philippines, the flowers is also used to treat headache and incipient cold or as tranquillizers, antispasmodics and antidyspeptics. Other than that, the roots of *M. calabura* have been used as an emmenagogue in Vietnam and as an abortifacient in Malaysia.

Other than for medicinal uses, the fruit, which are sometimes eaten fresh, are frequently cooked in tarts or made into jam, while the leaf infusion is drunk as a tea-like beverage.

OTHER USES:

Wood: The sapwood is yellowish, the heartwood red-dish-brown, firm, compact, fine-grained, moderately strong, light in weight, durable indoors, easily worked, and useful for interior sheathing, small boxes, casks, and general carpentry. It is valued mostly as fuel, for it ignites quickly, burns with intense heat and gives off very little smoke. Jamaicans seek out trees blown down by storms, let them dry for a while and then cut them up, preferring this to any other wood for cooking. It is being evaluated in Brazil as a source of paper pulp.

Bark: The bark is commonly used for lashing together the supports of rural houses. It yields a very strong, soft fiber for twine and large ropes.

Medicinal Uses: The flowers are said to possess antiseptic properties. An infusion of the flowers is valued as an antispasmodic. It is taken to relieve headache and the first symptoms of a cold.

CHEMICAL CONSTITUENTS OF *M. calabura*

Since 1991 to date, various phytochemical constituents have been isolated from different parts

of *M. calabura*. Kaneda et al. (1991) were the first to isolate bioactive compounds from the roots of *M. calabura*. They reported on the isolation of 12 flavonoids from methanol extract of *M. calabura* roots (MEMCR) namely (2S)-5'-hydroxy-7,3',4'-trimethoxyflavan (1), (2S)-7,8,3',4',5'-pentamethoxyflavan (2), (2S)-2'-hydroxy-7,8,3',4',5'-pentamethoxyflavan (3), (2S)-5'-hydroxy-7,8,3',4'-tetramethoxyflavan (4), (2S)-8-hydroxy-7,3',4',5'-tetramethoxyflavan (5), (2S)-8,2'-dihydroxy-7,3',4',5'-tetramethoxyflavan (6), (2S)-8,5'-dihydroxy-7,3',4'-trimethoxyflavan (7), 7,8,3',4',5'-pentamethoxyflavone (8), (M),(2S),(2''S)-, (P),(2S),(2''S)-8,8''-5'-trihydroxy-7,7'-3',3'''-4',4'''-5'''-heptamethoxy-5,5'''-biflavan (9), 5'-hydroxy-7,8,3',4'-tetramethoxyflavone (10), (M),(2S),(2''S)-, (P),(2S),(2''S)-8,8''-5'-5'''-tetrahydroxy-7,7'-3',3'''-4',4'''-hexamethoxy-5,5'''-biflavan (11) and 8,5'-dihydroxy-7,3',4'-trimethoxyflavone (12) (Consolacion et al.,2015).

PHARMACOLOGICAL ACTIVITIES AND CLINICAL TRIALS

Antibacterial activity

The first attempt to study the antibacterial activity of *M. calabura* was carried out by using the leaves and fruits collected in the State of Puebla and State of Veracruz, Mexico. The MEMCL and methanol extract of *M. calabura* fruits (MEMCFr) diluted in 100 mg/mL of DMSO concentration were subjected to two-fold serial dilutions and then tested against *Escherichia coli* (C600) and *Staphylococcus aureus* (209 P) using the micro-dilution assay. Both MEMCL and MEMCFr exhibited antibacterial activity against *E. coli* and *S. aureus* with the recorded MIC of 512 and 1024 mg/mL, and 128 and 256 mg/mL, respectively. This was followed by another antibacterial activity report by Zakaria et al. (2007b), who studied the antibacterial properties of MEMCL, aqueous (AEMCL), and chloroform (CEMCL) extract of *M. calabura* leaves, collected from Shah Alam Selangor, Malaysia, between January and February 2005. These extracts, prepared at various concentrations (10 000, 40 000, 70 000 and 100 000 ppm), were tested against *Corney bacterium diphtheria*, *S. aureus*, *Bacillus cereus*, *Proteus vulgaris*, *Staphylococcus epidermidis*, *Kosuria rhizophila*, *Shigella flexneri*, *E. coli*, *Aeromonas hydrophila*, and *Salmonella typhi* using the in vitro disc diffusion

method. The results showed that CEMCL was less effective as compared with the AEMCL and MEMCL. At all concentrations tested, AEMCL inhibited the growth of *S. aureus* and *K. rhizophila* while MEMCL exerted antibacterial activity against *S. flexneri*, *B. cereus*, *S. aureus*, *P. vulgaris*, *A. hydrophila*, and *K. rhizophila* (Consolacion et al.,2015).

M. calabura as Insecticidal activity

Only one study related to investigation of insecticidal activity of *M. calabura* was recorded using the flowers and fruits collected from the Universidade Rural Federal de Pernambuco (UFRPE), Recife, Brazil. The authors prepared two types of extracts from *M. calabura* flowers and fruits, namely ethanol extracts [flowers (EEMCFI) and fruits (EEMCFr)], and hexane extracts [flowers (HEMCFI) and fruits (HEMCFr)], at concentrations ranging from 0.25 to 30.0 mg/mL, and tested them against *Plutella xylostella* larvae and pupae using leaf disc immersion assay. All extracts were reported to be toxic to the larvae and pupae of *P. xylostella*. Moreover, the EEMCFI and EEMCFr were the most toxic against first instar *P. xylostella* larvae with the recorded LC50 of 0.61 mg/mL and 1.63 mg/mL, respectively. This is followed by the HEMCFr (LC50¼5.5 mg/mL) and HEMCFI (LC50¼18.9 mg/mL). When comparing their relative toxicities, it is worth highlighting that EEMCFI was 31.0-fold more toxic than HEMCFI, and 4.2 - and 8.9-fold more toxic than EEMCFr and HEMCFr, respectively. Overall, these extracts were more effective than cordycepin, the reference drug, which produced 100% mortality only at 500 mg/mL in 72 h (Zakaria et al., 2010).

Anti-nociceptive activity

The first attempt to investigate the antinociceptive activity of *M. calabura* was made using the leaves collected from Shah Alam, Selangor, Malaysia, between January and February, 2004, AEMCL was prepared in concentrations of 10, 50, and 100% strength that is equivalent to 27, 135, and 270 mg/kg, was subjected to the acetic acid induced abdominal constriction test followed by another studies to determine the role of L-arginine/nitric oxide/cyclic-guanosine monophosphate (L-arginine/NO/cGMP) pathway in the observed antinociceptive activity of AEMCL. From the results obtained, AEMCL exerted a significant and

concentration-dependent antinociceptive activity when assessed using the abdominal constriction test. Pre-treatment with L-arginine significantly blocked the antinociceptive activity of the extract at the highest concentration while pretreatment with NG-nitro-L-arginine methyl esters (L-NAME) significantly enhances the antinociceptive effects at low concentration but inhibit its effect at higher concentration of AEMCL. Methylene blue (MB) significantly enhanced AEMCL antinociceptive activity at all concentrations used. Co-treatment of L-arginine with L-NAME or MB together significantly reversed the antinociceptive activity of AEMCL at low concentration without affecting other concentrations of the AEMCL. These findings suggested the involvement of Larginine/NO/cGMP pathway in modulating the antinociceptive activity of AEMCL. Acetylsalicylic acid (ASA), in the dose of 100 mg/kg, was used as the reference drug (Zakaria et al., 2007).

A year later, another report on the antinociceptive activity of *M. calabura* leaves was released. This time, the leaves were collected between July and August, 2005 from Shah Alam, Selangor, Malaysia, and prepared as CEMCL, in the concentrations of 10, 50, and 100% strength. CEMCL was tested for its antinociceptive activity using the abdominal constriction test, the hot plate test, and the formalin test. In the abdominal constriction test, the extract exhibited a concentration-dependent activity with CEMCL at the highest concentration producing 49.5% analgesia while CEMCL at 50% concentration produced an activity that was equieffective to that of 100 mg/kg ASA (the reference drug). The extract also exerted an antinociceptive effect, but in a concentration-independent manner, when assessed using the hot plate test with the onset of activity depending on the concentration of CEMCL. However, the activity exerted by CEMCL, at all concentrations used, was overshadowed by the activity exhibited by 5 mg/kg morphine. The extract also demonstrated antinociceptive activity when assessed using the formalin test, which was seen in both early and late phases of the test. However, the concentration-dependent activity by CEMCL was observed only in the early phase of the formalin test. The reference drugs used in the formalin test were 5 mg/kg morphine for the early and late phase, and 100 mg/kg ASA, for the late phase (Preethi et al., 2011).

Anti-inflammatory activity

The leaves were prepared as CEMCL, in the concentrations of 10, 50, and 100%, and tested using the carrageenan-induced paw edema test. ASA (100 mg/kg) was used as a reference drug. All concentrations of CEMCL exerted an inconsistent anti-inflammatory activity that was less effective than the ASA. Another report on the anti-inflammatory activity of *M. calabura* leaves was also published while attempting to determine the antinociceptive activity of AEMCL. In this study AEMCL was prepared in the concentrations of 10, 50, and 100% (equivalent to the doses of 27, 135, and 270 mg/kg, respectively) and subjected to the carrageenan-induced paw edema assay. The results obtained demonstrated that the extract exhibited concentration-independent anti-inflammatory activity. The anti-inflammatory activity of the 10 and 50% AEMCL were completely lost after 7 h of its administration while the anti-inflammatory activity of 100% AEMCL was lost after only 6 h of its administration. It is worth mentioning that the anti-inflammatory activity of AEMCL, at the concentrations of 10 and 50%, was significantly greater than the reference drug, 100 mg/kg ASA, at the interval of 3 and 4 h after their administration. In the recent attempt to study the pharmacological properties of the fruits of *M. calabura*, the MEMCFr and AEMCFr were prepared in doses of 200 and 400 mg/kg and tested using the carrageenan-induced paw edema test (Preethi et al., 2012a). The results obtained demonstrated that both extracts exerted dose-dependent inhibition of carrageenan induced localized edema at 4 h after the administration of extracts. The significant anti-inflammatory activity was recorded at 24.5 and 44.2% for both doses of MEMCFr and at 20.4 and 46.2% for both doses of AEMCFr. Indomethacin, in the dose of 10 mg/kg, was used as the reference drug and caused 84.3% inhibition of carrageenan-induced edema formation in comparison with the extracts (Zakaria et al., 2007).

Antipyretic activity

The first attempt to determine the antipyretic potential of *M. calabura* was made by using the leaves that was prepared as CEMCL. The extract, at the concentrations of 10, 50, and 100%, was tested using Brewer's yeast (BY)-induced pyrexia test. The

extract exhibited a concentration-independent antipyretic activity. Comparison made against the 100 mg/kg ASA, as the reference drug, showed that the CEMCL antipyretic activity was less effective than the drug. Another report on the antipyretic activity of another extract of *M. calabura*, namely AEMCL, while studying the antinociceptive and anti-inflammatory activities. The AEMCL exerted a concentration-independent antipyretic effect with the onset of effects of 27 and 135 mg/kg AEMCL was recorded after 240 min of their administration. Overall, the antipyretic activity of AEMCL was less effective than the reference drug, 100 mg/kg ASA (Preethi et al., 2010).

Ant ulcer activity

The investigation of antiulcer potential of *M. calabura* was initiated with one study. This preliminary study was carried out by involving the use of *M. calabura* leaves obtained from a company, Ethno Resources Sdn. Bhd., Selangor, Malaysia. The leaves were prepared as EEMCL, in the dose of 250 and 500 mg/kg, and assayed only against the ethanol-induced gastric ulcer model. The extract demonstrated significant and dose-dependent antiulcer activity indicated by the reduction in the areas of gastric ulcer injuries (112.5 ± 2.11 and $95.08 \pm 2.18 \text{ mm}^2$) in comparison with the negative control group ($735.25 \pm 2.12 \text{ mm}^2$) and 20 mg/kg omeprazole-treated group (the reference drug; $90.33 \pm 2.02 \text{ mm}^2$). Further study on the ethanol-treated stomach samples revealed that the EEMCL reduces the acidity of gastric content while increases the mucus production of gastric mucosa when compared with the negative control. Moreover, the subsequent microscopic observations supported the macroscopic findings. Another study on the antiulcer potential of *M. calabura* leaves was studied. In this study, the leaves were prepared as MEMCL and subjected to ethanol- and indomethacin-induced gastric ulcers wherein in the former assay the doses of 25, 50, 100, 250, and 500 mg/kg were used while in the later assay, the doses of 100, 250, and 500 mg/kg were used. The discrepancy in the range of doses used was attributed to preliminary findings using the ethanol-induced gastric ulcer model wherein the extract exerted a dose-independent antiulcer activity. Therefore, an additional study using lower doses (25 and 50 mg/kg) was performed

(Sridhar et al., 2011). Moreover, the role of NO and sulfhydryl groups in mediating the antiulcer activity of MEMCL was also investigated using the ethanol-induced gastric ulcer. From the results obtained, MEMCL, at all doses tested, exhibited a significant and dose-dependent reduction of ethanol-induced gastric ulcer formation with the percentage of antiulcer ranging between 63 and 95% in comparison with the reference drug, 100 mg/kg ranitidine, that produced 70% protection. In addition, all doses of MEMCL exerted significant and dose dependent inhibition of indomethacin-induced gastric ulcer formation with the percentage of protection ranging between 47 and 69%. In comparison, 100 mg/kg ranitidine exhibited 78% antiulcer activity. Histopathological evaluation revealed the extract potential to reverse the toxic effect of ethanol and indomethacin and returned the stomach to almost normal mucosal architecture that is comparable with protection exerted by ranitidine. Moreover, pre-treatment with 70 mg/kg L-NAME significantly worsened the gastric ulcers in MEMCL- and 100 mg/kg carbenoxolone-treated groups and this unwanted effect of L-NAME was reversed by 200 mg/kg L-arginine. These findings indicate the participation of NO in the antiulcer potential exerted by MEMCL. Pre-treatment with 10 mg/kg NEM, in contrast, significantly reversed the antiulcer activity of MEMCL and increased the gastric ulcer formation in comparison with saline pretreated group that is also receiving MEMCL. These findings indicate the participation of endogenous sulfhydryl compounds in the gastroprotective activity demonstrated by MEMCL (Sani et al., 2012).

Antidiabetic activity

The leaves of *M. calabura*, collected from Station Ghanpur, Warangal, Andhra Pradesh, India, were prepared as MEMCL, in doses of 300 and 500 mg/kg, and subjected to the antidiabetic studies. Firstly, the serum glucose level was observed at 2, 4, 6, and 8 h after the administration of the extract. The results showed that both doses of MEMCL produced significant hypoglycemic effects after 6 and 4–8 h, respectively, in the normal fasted rats. The 500 mg/kg of MEMCL caused significant reduction in the blood glucose level from 83.19 mg/dL at 0 h to 62.62 mg/dL (24.81%) at the end of the 6 h. In comparison, the reference drug, 5 mg/kg glipizide, caused

significant reduction in the blood glucose level after 2 h of administration that lasted for another 6 h. In the second study, the effect of 500 mg/kg MEMCL on the oral glucose tolerance test (OGTT) was also investigated. The results showed that pre-treatment with 500 mg/kg MEMCL caused significant reduction in the rise of blood glucose at 1 h interval (116.46 ± 6.94 mg/dL) when compared with the control group pre-treated with 5% gum acacia, which showed a rapid increase of blood glucose (144.73 ± 7.86 mg/dL). For the standard group (glipizide 5 mg/kg), the glucose levels reached the fasting values at the end of 1 h interval (72.09 ± 2.98 mg/dL). In the third study, the 500 mg/kg MEMCL was subjected to the alloxan-induced diabetic assay. Following the experiments, 500 mg/kg of MEMCL significantly reduced the alloxan-induced hyperglycemia with maximum effect observed at 6 h (27%) in comparison with the reference drug, 5 mg/kg glipizide, which produced 37% reduction in blood glucose level (Zakaria et al., 2007).

Antihypertensive activity

The leaves of *M. calabura* were collected in June, 2001, from Kaohsiung City, Taiwan and prepared as a methanol extract (MEMCL). The crude MEMCL was then partitioned using dH₂O and chloroform in the ratio of 1:1, and the aqueous fraction obtained was further fractionated sequentially using a mixture of dH₂O and n-butanol (1:1). The water-soluble fraction (WSF) was collected, prepared in the dose range of 10, 25, 50, 75, and 100 mg/kg, and systemically injected into the femoral vein of the animals. In the first study, the mean systemic arterial pressure (MSAP), heart rate (HR), baseline blood pH, gas (partial pressure of CO₂ and O₂), and electrolytes (Na⁺, K⁺, hematocrit) were measured for 3 h from blood samples withdrawn from the arterial blood following pre-treatment with isotonic normal saline, 5 mg/kg acetylcholine (the reference drug), or WSF (10, 25, 50, 75, or 100 mg/kg). In the second study, the plasma nitrate level was measured using blood samples withdrawn from the femoral artery using the chemiluminescence assay (Zakaria et al., 2007). In the third study, the biochemical analysis involving protein extraction and Western blot analysis were carried out. The apical heart or segment of thoracic aorta was rapidly removed from sacrificed rats and later subjected to Western blot analysis of iNOS,

eNOS, nNOS, or b-actin protein. Another study was performed to delineate the causative relationship between NO and *M. calabura*-induced cardiovascular responses wherein the temporal change in MSAP or HR elicited by 50 mg/kg WSF was measured for 180 min in rats subjected to pretreatment with L-NAME, L-NIO, SMT, 7-NI, or ODQ administered 20 min prior to administration of WSF. The findings revealed that intravenous administrations of WSF significantly and dose dependently caused an immediate decrease in MSAP (initial phase) that returned to the pre-injection baseline within 10 min post-injection without affecting the HR. The decrease in MSAP was followed by a delayed hypotensive effect (delayed phase) that started at 90 min and lasted for approximately 180 min post-injection. Acetylcholine (5 mg/kg) also caused a significant decrease in MSAP that reached its peak within the first 30 s and lasted for less than 5 min post-administration. The authors also reported that treatment with a 50 mg/kg WSF caused no significant change to the baseline systemic arterial blood gases, electrolytes, Hct, and pH when measured at 10, 30, 60, 120, and 180 min post-injection as seen with saline and WSF, at the doses of 25, 75, and 100 mg/kg. Moreover, intravenous pretreatment with 0.65 mg/kg/min, as well as 0.13 and 0.35 mg/kg/min L-NAME, a non-selective NOS inhibitor, significantly attenuated both the initial and delayed phases of hypotension induced by the WSF.^[16] An inhibitor of eNOS, L-NIO, given intravenously at the dose of 1.0 mg/kg/min, significantly suppressed only the initial phase of WSF-induced hypotension while, to the contrary, 0.5 mg/kg/min SMT, a selective inhibitor of iNOS, given through the same route strongly inhibited only the delayed phase of the same response. Of all doses of L-NAME, L-NIO, 7-NI or SMT used, only L-NMAE, at the highest dose (0.65 mg/kg/min), given alone evoked a significant and transient increase in MSAP by 12% and a decrease in HR by 11%. In addition, 0.2 mg/kg/min ODQ, an sGC inhibitor that had no significant effect on baseline MSAP or HR when given alone, markedly suppressed both the initial and delayed phases of WSF-decreased MSAP. WSF also induced a significant increase in iNOS, but not eNO or nNOS, protein expression in the heart or aorta detected at 90 or 180 min post-administration (Zakaria et al., 2007).

Cardioprotective activity

Using the AEMCL, of which the location and period of leaves collection were not given, the authors studied the extract ability to attenuate isoproterenol-induced myocardial infarction in rats. Several parameters (e.g., aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH), and creatinine phosphokinase (CK)) were estimated in both the serum and heart tissues, and the serum uric acid level was also estimated. From the results obtained, AEMCL caused significant reduction in the activity of marker enzymes (AST, ALT, CK, and LDH) and the level of uric acid when compared with the isoproterenol-induced myocardial infarction group. In all parameters estimated, only 200 and 300 mg/kg AEMCL exerted significant effects (Zakaria et al., 2008; Zakaria et al., 2010).

CONFLICTS OF INTEREST: None

ACKNOWLEDGEMENT: The authors are grateful to the management and group of Institution Shri Venkateshwara College of Pharmacy, Ariyur, Puducherry to carry out the work.

CONCLUSION

Current attention towards the pharmacological potential of medicinal plants have been escalating globally as indicated by the increase in publications on the pharmacological potential of various traditionally claimed or newly discovered medicinal plants. In an attempt to find a pure and effective lead from plants. It is worth mentioning that according to the World Health Organization (1999), a medicinal plant is any plant which, in one or more of its parts, contains substances that can be used for therapeutic purposes, or which are precursors for semisynthesis of chemo-pharmaceutical. Such a plant will have its parts including leaves, flowers, stems, barks, roots, rhizomes, fruits, grains or seeds, employed in the control or treatment of a disease condition and, therefore, contains chemical components that are medically active. Regard of *M. calabura*, all parts of the plant, namely the leaves, fruits, flowers, stem bark, bark, and roots have been used traditionally to treat various ailments.

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