Potent bioactivities of the endemic Annonaceae heighten its dire conservation status

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Abstract: Sri Lanka records 17 endemic species of the Annonaceae family. Worldwide, the Annonaceae are known to possess compounds with pharmaceutically important properties such as anticancer and insecticidal actions. In an attempt to investigate the mosquito larvicidal and antioxidant activities of the endemic Annonaceae plants, twelve plant species were collected. Of the 71 extracts investigated from various plant parts, five plants showed significant larvicidal activity with the CH2Cl2 extracts of the leaves of G. hookeri and G. gardneri (LC50 at 48 h = 0.4 and 0.3 ppm, respectively) exhibiting potency compared to the known larvicide (4S)-4-methyl-2-(11-dodecynyl)-2-butenolide (LC50 = 0.3 ppm). Compared to the percent radical scavenging activity of the standard dl-α tocopherol (55.84), the MeOH extracts of the stem of A. hortensis (56.30), the leaves of U. semecarpifolia (57.33), and the seeds of X. nigricans (62.06) showed very promising activity. Significantly, it is recorded that two of the Sri Lankan endemic Annonaceae plants are extinct (P. moonii and A. hortensis) and the rest, except for U. sphenocarpa, are critically endangered, endangered, vulnerable or near threatened. These grim statistics highlight not only the urgency and the importance of biodiversity conservation of the endemic Annonaceae of Sri Lanka but also of investigating the plants for new phamacophores.

Keywords: Annonaceae, antioxidant activity, biodiversity conservation, endemic species, mosquito larvicidal activity.

INTRODUCTION

In an estimated number of the 270,000 species of vascular flora, 12 % are threatened (Walter & Gillett, 1998) and these plants are scattered in 369 families found in 200 countries. Because of the lack of information due to, either poor taxonomic knowledge or gaps in field work, the number could be much higher. When the sample assessed is the population within a species, or when there is genetic erosion among species, the situation becomes grimmer (Harper & Hawksworth, 1994; Gaston, 1996). In Sri Lanka, of the 3314 listed flowering plants, 455 are threatened with about 70 plants having become extinct by 1997 (Walter & Gillett, 1998).

The World Conservation Monitoring Center has designated Sri Lanka as a ‘hotspot’ in terms of rich biodiversity and threats faced (Caldecott et al., 1994). About 25 % of the flowering plant species are endemic to the island (Gunatilleke & Gunatilleke, 1990). The relict rainforest plant taxa of Gondwana-Deccan ancestry are now found only in some isolated forest pockets in Penninsular India and Southwestern Sri Lanka. The Deccan flora evolved in isolation in the late Cretaceous and early Tertiary periods, during the drifting of the Indian plate (Jayasekara, 1997). It has been hypothesized that biotic impoverishment, prior absence followed by colonization and later speciation has led to the tremendous endemic diversity in the island (Biswas, 2008). Except for a few reports (Bandara et al., 1989; Hewage et al., 1997; Hewage et al., 1998), there has not been a large-scale systematic search for bioactive agents from Sri Lankan flora so far. Although endemic plants such as Salacia reticulata var. diandra (Celastraceae) have underscored the potential of Sri Lankan plants (Gunatilaka et al., 1993; Dhanabalasingham et al., 1996; Yoshikawa et al., 1997), in general the bioactivity potential of Sri Lankan endemics remains relatively unknown. As such, there is an urgent need to investigate their therapeutic potential before they disappear forever.
The Annonaceae are woody trees, shrubs and vines comprising about 130 genera and 2,300 species worldwide. Considering its large size, it is chemically one of the least known of the tropical plant families (Leboeuf et al., 1982). However, plants of the Annonaceae have received increased phytochemical and pharmacological attention in recent years; this is mostly due to the discovery of Annonaceous acetogenins, a class of natural products with a variety of biological activities (Cave et al., 1997; Kojima & Tanaka, 2009; Liaw et al., 2010). In Sri Lanka, Annonaceae is centered in the lowland rainforests (Dassanayake & Fosberg, 1980). They extend to the dry and lower montane zones, but are absent from elevations above 1500 m. Due to extensive deforestation in the humid regions, many species have become rare. In Sri Lanka, 17 endemic species, namely, Desmos zeylanica Hook. f. & Thoms., Desmos elegans (Thwaites) Saff., Uvaria semecarpifolia Hook. f. & Thom., Uvaria sphenocarpa Hook. f. & Thom., Sagarea thwaitesi Hook. f. & Thom., Phoenicanthus coriacea (Thw.) H. Huber, Phoenicanthus obliqua (Hook. f. & Thoms.) Alston, Alphonsea hortensis H. Huber, Polyalthia persicaefolia (Hook. f. & Thom.) Thw., Polyalthia moonii Thwaites, Miliusa zeylanica ex Hook. f. & Thom., Enicosanthum acuminata (Thw.) Airy-Shaw, Xylopia nigricans Hook. f. & Thom., Goniothalamus gardneri Hook. f. & Thom., Goniothalamus hookeri Thw., Goniothalamus thomsonii and Goniothalamus salicina Hook. f. & Thom., belonging to ten genera are recorded (Dassanayake & Fosberg, 1980), although many have not been collected for decades. It is in this backstop, that the antioxidant and mosquito larvicidal activities of the extracts of 12 Annonacea belonging to 8 genera are reported in the present investigation. However, five endemic Annonaceae species could not be collected during plant collection between 2004 to 2010, which may have disappeared from their known habitats.

METHODS AND MATERIALS

Endemic Annonaceae plants were collected from Central Sri Lanka during 2004 - 2010 (Table 1) and identified and deposited at the National Herbarium of Royal Botanic Gardens, Peradeniya.

Air dried, ground plant materials (100 - 500 g) were extracted sequentially for 24 h at room temperature with CH,OCl, followed by MeOH (500 - 1500 mL each) by using a bottle shaker. The combined extracts were concentrated in vacuo at 35 °C to obtain the respective crude extracts.

The mosquito larvicidal assay was carried out according to Ratnayake et al. (2001), with solutions of 0.5 mg/mL (500 ppm) of the plant extracts using second instar larvae of Aedes aegypti. The potent larvicide, (4S)-4-methyl-2-(11-dodecynyl)-2-butenolide was used as the positive control (Ratnayake et al., 2001). LC50 values at 48 h (mean ± SD) in ppm, were based on 4 concentrations and 4 replicates and were determined by using MiniTab statistical software.

Radical scavenging activity (antioxidant activity) of plant extracts against stable DPPH radicals was determined spectrophotometrically by the slightly modified methods of Miliauskas et al. (2004) and Yen and Duh (1994). dl-a tocopherol was used as the positive control. All the determinations were performed in 3 replicates and averaged.

RESULTS AND DISCUSSION

Out of the 71 extracts studied, 25 extracts showed toxicity against A. aegypti. The extracts of G. gardneri and G. hookeri demonstrated exceptionally high larvicidal activity while A. hortensis, E. acuminata, X. championii, U. sphenocarpa and U. semecarpifolia showed significant activity (Table 1). The most active was the dichloromethane leaf extracts of G. hookeri and G. gardneri (LC50 at 48 h = 0.4 and 0.3 ppm, respectively). Significantly, larvicidal potency of extracts of G. hookeri and G. gardneri were comparable with the potent larvicide (4S)-4-methyl-2-(11-dodecynyl)-2-butenolide (Ratnayake et al., 2001). Although no reports of either bioactivity or use in traditional medicine exists for these two plants in Sri Lanka, plants of the genus Goniothalamus are known for the presence of cytotoxic acetogenins and styryl-lactones (Leboeuf et al., 1982). However, of the large majority of the 166 Goniothalamus plants known globally, only 22 species have so far been investigated (Wiart, 2007).

Several extracts exhibited potent percent antioxidant activity. For example, MeOH extract of the stem of A. hortensis (56.30), the leaves of U. semecarpifolia (57.33), and the seeds of X. nigricans (62.06) showed higher radical scavenging activity compared to the standard dl-a-tocopherol (55.84). In recent times, free radicals have been implicated in inflammation processes, cardiovascular disease, rheumatoid arthritis, neurodegenerative disease, and the ageing process (Hollman & Katan, 1999). X. nigricans, X. parvifolia and X. championii, of which the latter two are non-endemic, are rich in isooquinoline alkaloids where some have shown potent antioxidant activity (Wijeratne et al., 1996, 2001; Puvenendran et al., 2008, 2010).
| Genus Botanical name | Habit | Locality | Habitat | Plant part(s) | Type of extract(s) | % Mortality | % AOA |
|----------------------|-------|----------|---------|---------------|-------------------|-------------|-------|
| *Alphonsea Tr* Kandy Southwestern lowland | Lf | CH₂Cl₂ | 100 (114 ± 0.32) | 40.62 ± 0.24 |
| *A. hortensis* H. Huber | Lf | MeOH | 35 | 32.81 ± 0.28 |
| | Sd | MeOH | 100 | 30.31 ± 0.04 |
| | St | CH₂Cl₂ | 100 (46.9 ± 0.12) | 13.69 ± 0.22 |
| | St | MeOH | 85 | 56.30 ± 0.05 |
| | SBk | MeOH | 100 (46.9 ± 0.6) | 35.12 ± 0.24 |
| *Desmos Tl* Kandy Wettest parts of the lowland hill country at elevation between 200 and 800 m | Lf | CH₂Cl₂ | 100 | 2.49 ± 0.35 |
| *D. zeylanica* Hook. f. & Thoms | Lf | MeOH | 85 | 9.70 ± 0.50 |
| | Sd | MeOH | 100 (44.64 ± 0.08) | 4.61 ± 0.06 |
| | St | CH₂Cl₂ | 100 | 7.03 ± 0.12 |
| | St | MeOH | 95 | 5.84 ± 0.07 |
| | SBk | MeOH | 20 | 19.25 ± 0.12 |
| *Enicosanthum Tr* Matale Low elevation of both primary and secondary forests | Lf | CH₂Cl₂ | 100 (41.5 ± 0.14) | 8.20 ± 0.16 |
| *E. acuminata* (Thw.) Airy-Shaw | Lf | MeOH | 100 | 36.52 ± 0.05 |
| | St | CH₂Cl₂ | 100 | 13.52 ± 0.06 |
| | St | MeOH | 00 | 19.69 ± 0.25 |
| | SBk | CH₂Cl₂ | 00 | 6.92 ± 0.10 |
| | SBk | MeOH | 100 | 45.59 ± 0.15 |
| *Goniothalamus Tl* Kandy Secondary and disturbed primary rainforests | Lf | CH₂Cl₂ | 100 (0.3 ± 0.34) | 23.45 ± 0.32 |
| *G. gardneri* Hook. f. & Thoms. | Lf | MeOH | 100 (38.4 ± 0.86) | 43.45 ± 0.14 |
| | St | CH₂Cl₂ | 100 (1.4 ± 0.32) | 12.45 ± 0.05 |
| | St | MeOH | 100 (5.3 ± 0.22) | 14.65 ± 0.21 |
| | Rt | MeOH | 100 (3.7 ± 0.54) | 26.63 ± 0.17 |
| | SBk | CH₂Cl₂ | 100 (3.1 ± 0.04) | 19.85 ± 0.31 |
| | Rt | MeOH | 100 (3.3 ± 0.82) | 26.97 ± 0.52 |
| | Fl | CH₂Cl₂ | 100 (29.5 ± 0.45) | 14.74 ± 0.87 |
| | Fl | MeOH | 100 (14.4 ± 0.68) | 17.91 ± 0.37 |
| *G. hookeri* Thw. | Lf | CH₂Cl₂ | 100 (0.4 ± 0.37) | 4.50 ± 0.50 |
| Tr Galle Primary and secondary rainforests at low elevations | Lf | MeOH | 100 (45.6 ± 0.75) | 14.03 ± 0.25 |
| | SBk | CH₂Cl₂ | 100 (1.9 ± 0.12) | 3.39 ± 0.35 |
| | SBk | MeOH | 00 (2.1 ± 0.64) | 12.43 ± 0.93 |
| *G. salicina* Hook. f. & Thoms. | Lf | CH₂Cl₂ | 100 (4.5 ± 0.35) | 10.97 ± 0.41 |
| TI Adam’s Peak Very local on hill sides and ridges in mixed dipterocarp forests | Lf | MeOH | 100 (38 ± 0.68) | 59.98 ± 0.57 |
| | St | CH₂Cl₂ | 80 | 9.79 ± 0.53 |
| | St | MeOH | 20 | 34.93 ± 0.65 |
| | SBk | CH₂Cl₂ | 100 | 11.47 ± 0.21 |
| | SBk | MeOH | 00 | 40.85 ± 0.43 |
| *Phoenicanthus Tr* Kandy An understorey tree of mid-mountain in forests along the Western and Southern edge of the main block | Lf | CH₂Cl₂ | 100 (132 ± 0.45) | 13.21 ± 0.69 |
| *P. coriacea* (Thw.) H. Huber | Lf | MeOH | 70 | 17.33 ± 0.81 |
| | St | CH₂Cl₂ | 100 | 15.13 ± 0.23 |
| | St | MeOH | 00 | 35.95 ± 0.54 |
| | SBk | CH₂Cl₂ | 60 | 13.84 ± 0.91 |
| | SBk | MeOH | 00 | 37.58 ± 0.47 |

- Continued
Sri Lankan Annonaceae, *P. persicifolia*, *P. moonii*, *A. hortensis*, *G. thomsonii*, *M. zeylanica*, *P. coriacea*, *P. obliqua*, *U. semecarpifolia* and *X. nigricans*, were considered indeterminate (Table 2), while *G. hookeri*, *S. thwaitesii* and *E. acuminata* were considered vulnerable. On the other hand, *D. elegans*, a species is considered nationally threatened when it is evaluated to be critically endangered (CR), endangered (EN), or vulnerable (V) (Walter & Gillett, 1998). Globally, it is estimated that 9.2 % of Annonaceae species are threatened (Walter & Gillett, 1998). In 1997, among the Sri Lankan Annonaceae, *P. persicifolia*, *P. moonii*, *A. hortensis*, *G. thomsonii*, *M. zeylanica*, *P. coriacea*, *P. obliqua*, *U. semecarpifolia* and *X. nigricans*, were considered indeterminate (Table 2), while *G. hookeri*, *S. thwaitesii* and *E. acuminata* were considered vulnerable. On the other hand, *D. elegans*,

| Genus Botanical name | Habit* | Locality | Habitat | Plant part(s)* | Type of extract(s) | % Mortality † | % AOA * |
|----------------------|--------|----------|---------|----------------|-------------------|-------------|---------|
| *P. obliqua* Hook. f. & Thoms. | Tr | Kandy | A tree in the South west of Sri Lanka | Lf | CH₃Cl₂ | 80 | 11.24 ± 0.78 |
| | St | CH₃Cl₂ | 100 | 14.56 ± 0.37 |
| | St | MeOH | 20 | 27.90 ± 0.54 |
| *Sageraea* Hook. f. & Thoms. | Tr | Nuwara Eliya | A tree found in the entire country | Lf | CH₃Cl₂ | 70 | 10.87 ± 0.65 |
| *Sageraea thwaitesii* Hook. f. & Thoms. | Lf | MeOH | 20 | 40.64 ± 0.82 |
| | St | CH₃Cl₂ | 80 | 32.96 ± 0.32 |
| | St | MeOH | 40 | 16.63 ± 0.43 |
| *Uvaria* Hook. f. & Thoms. | Cl | Kandy | Local in both dry and wet parts of the island at elevations between sea level and 720 m | Lf | CH₃Cl₂ | 70 | 6.08 ± 0.20 |
| *U. sphenocarpa* Hook. f. & Thoms. | Lf | MeOH | 00 | 1.49 ± 0.06 |
| | St | CH₃Cl₂ | 00 | 4.24 ± 0.10 |
| | St | MeOH | 00 | 42.93 ± 0.80 |
| | SBk | CH₃Cl₂ | 70 | 3.52 ± 0.23 |
| | SBk | MeOH | 00 | 23.66 ± 0.17 |
| *U. semecarpifolia* Hook. f. & Thoms. | Cl | Kegalle | Rather uncommon both in primary rainforests and secondary regrowth at elevations between 70 to 600 m | Lf | CH₃Cl₂ | 00 | 19.31 ± 0.20 |
| | Lf | MeOH | 00 | 57.33 ± 0.42 |
| | SBk | CH₃Cl₂ | 65 | 33.23 ± 0.12 |
| | SBk | MeOH | 00 | 26.66 ± 0.60 |
| *X. nigricans* Hook. f. & Thoms. | Tr | Matale | Rare tree of the dry and intermediate zones at low elevations | Lf | CH₃Cl₂ | 45 | 21.03 ± 0.39 |
| | Lf | MeOH | 00 | 33.92 ± 0.40 |
| | Sd | CH₃Cl₂ | 50 | 14.33 ± 0.67 |
| | Sd | MeOH | 00 | 62.06 ± 0.33 |
| | St+SBk | MeOH | 100 (142.5 ± 0.81) | 25.58 ± 0.43 |
| | St+SBk | CH₃Cl₂ | 00 | 9.18 ± 0.32 |
| *X. championii* Hook. f. & Thoms. | Tr | Kithulgala | Wet parts of the country in the intermediate zones | Lf | CH₃Cl₂ | 65 | 27.82 ± 0.35 |
| | Lf | MeOH | 55 | 48.45 ± 0.19 |
| | SBk | CH₃Cl₂ | 100 (137.5 ± 0.75) | 26.28 ± 0.04 |
| | SBk | MeOH | 100 (104.0 ± 0.42) | 25.18 ± 0.6 |

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| a | Tr, Tree; Tl, Treelet; Cl, Climber. b | Lf, Leaf; Sd, Seed; St, Stem; SBk, Stembark; Rt, Root; Fl, Flower. c | Average of four replicates, each beaker containing five second instar larvae of *A. aegypti*; % Mortality at 48 h with 500 ppm solution of extract; Solutions with no extract was used as a negative control; (4S)-4-methyl-2-(11-dodecynyl)-2-butenolide, which gives 100 % mortality at 1 ppm was used as positive control. d | LC₅₀ values stated as Mean ± SD, in ppm, were based on four concentrations and four replicates. e | Percentage antioxidant activity (AOA) is based on three replications and is stated as Mean ± SD. The absorbance of the DPPH radical without antioxidant (negative control) and the reference compound DL-α-tocopherol (positive control) which exhibited activity at 55.84 ± 0.05 were also measured.

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Bioactives from endemic Sri Lankan Annonaceae

D. zeylanica, G. gardneri, G. salicina and U. sphenocarpa were considered not threatened. However, by 2011 (Weerakoon & Wijesundara, 2012), the situation had dramatically shifted (Table 3) with P. moonii being extinct; G. salicina and P. coriacea considered endangered; D. zeylanica, E. acuminata, G. gardneri, G. hookeri, G. thomsonii and S. thwaitesii being vulnerable; D. elegans, X. nigricans, G. thomsonii and S. thwaitesii being near threatened. The only species apparently out of danger is U. sphenocarpa. Thus, the majority of the 17 endemic Annonaceae species are nationally threatened and one is extinct. This dire situation far exceeds the global average (9.2 %) of threatened species calling attention to a crisis situation. During the collection attempts, D. elegans, P. persicafelia, G. thomsonii, P. moonii and M. zeylanica could not be located due to their disappearance from recorded sites.

In conclusion, this study reveals the richness of bioactivity of the endemic Annonaceae of Sri Lanka, and its very promising potential as a source of plant medicines. However, it also highlights the grim conservation status of the endemic Annonaceae. If urgent remedial action is not undertaken towards their conservation, these plants will be well on their way towards extinction. This work also highlights the importance of screening the endemic flora of the South Asian region for potential drugs before they are threatened by deforestation and other anthropogenic factors.

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Table 2: Endemic Annonaceae conservation status in 1997

| Indeterminate | Vulnerable | Not threatened |
|---------------|------------|----------------|
| P. persicafelia | G. hookeri | D. elegans |
| P. moonai | S. thwaitesii | D. zeylanica |
| A. hortensis | E. acuminata | G. gardneri |
| G. thomsonii | G. salicina | |
| M. zeylanica | U. sphenocarpa | |
| P. coriacea | P. obliqua | |
| U. semecarpfolia | X. nigricans | |

Source: Walter and Gillett, 1998

Table 3: Endemic Annonaceae conservation status in 2010

| EX | CR | EN | V | NT | LC |
|----|----|----|---|----|----|
| A. hortensis | P. persicafelia | G. salicina | D. zeylanica | D. elegans | U. sphenocarpa |
| P. moonai | M. zeylanica | G. gardneri | X. nigricans |
| P. coriacea | G. hookeri | U. semecarpfolia |
| G. thomsonii | S. thwaitesii | P. obliqua |
| E. acuminata | |

Source: Weerakoon & Wijesundara, 2012.
EX (Extinct); CE (Critically Endangered); E (Endangered); V (Vulnerable); NT (Near Threatened); LC (Least Concerned)

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