Original Research Article

Screening of fifteen mangrove plants found in Sri Lanka for *in-vitro* cytotoxic properties in breast (MCF-7) and hepatocellular carcinoma (HepG2) cells.

ABSTRACT

Aims:
Evaluation of cytotoxic potential of leaf and stem bark extracts of 15 mangrove plants grown in Sri Lanka in breast cancer (MCF -7) and hepatocellular (Hep G2) carcinoma cells grown in Sri Lanka.

Place and Duration of Study:
At the Institute of Biochemistry, Molecular Biology and Biotechnology, University of Colombo between 1st of February 2014 to April 2015.

Methodology:
Leaves and stem barks of 15 mangrove plants were extracted with hexane, chloroform, ethyl acetate and methanol. Resulting extracts were screened for cytotoxic activity against MCF-7 and HepG2 cells using the Sulforhodamine B (SRB) assay.

Results:
Of the 15 plants tested, *Phoenix paludosa, Avicennia officinaliss* and *Scyphiphora hydrophyllacea* showed highest cytotoxic properties in cancer cells. Chloroform extract of stem bark of *S. hydrophyllacea*, *Bruguiera gymnorrhiza* (chloroform, ethyl acetate and methanol extracts of leaves), hexane and ethyl acetate extracts of leaves of *Aegiceras corniculatum*, methanol extracts of leaves and stem bark of Nypa *fruticans* and *Rhizophora mucronata,* methanol extract of stem bark of *Sonneratia alaba* and *Rhizophora apiculata* and methanol extract of bark of *A. officinails* exerted selective cytotoxicity to HepG2 cells. The hexane extract of leaves of *B. gymnorrhiza*, chloroform extract of leaves of *N. fruticans*, ethyl acetate extract of stem bark of *Lumnitzera littorea*, chloroform extract of leaves of *Rhizophora apiculata* and chloroform extract of leaves of *Pemphis acidula* showed selective cytotoxic effects against MCF-7 cells. Out of the 120 mangrove extracts tested, 82 extracts showed no significant cytotoxic effects (IC_{50}>100 µg/mL) against MCF 7 or Hep G2 cells.

Conclusion:
The cytotoxic activities demonstrated by some of the solvent extracts of some mangrove plants provide scientific evidence for their therapeutic potentials and further studies are needed to identify active compounds responsible for cytotoxic effects.

Keywords: *Mangrove, cytotoxicity, MCF-7, HepG2*

1. Introduction

Mangroves belong to twelve plant families and they are botanically diverse. Almost all the mangroves are holophytic species, well adapted to grow in wet soil conditions and usually possess some amount of viviparity [1, 2]. The mangroves grown in Sri Lanka belong to true mangroves (14 species) and mangrove associates (12 species) [3]. In Sri Lanka mangroves are extensively found in Puttalam,

Kalpitiya, Koggala, Kalamatiya and Kokilai areas in association with estuaries [4]. Mangroves have diverse uses: For example, they are used to obtain timber and tannins; they behave as coastal stabilizers; root system in mangroves provides shelter for many commercially important fishes and prawns, etc. [5]. These mangrove plants can survive in extremely high salinity, high temperature, high moisture, strong winds and high and low tides of water. In order to survive in these hostile environments, changes in their physiological activities have occurred ensuing in the bio-synthesis of novel secondary metabolites [6]. These secondary metabolites provide proper protection to these mangrove plants against various biotic and abiotic stresses conditions [7]. A wide range of natural compounds, including novel chemical compounds have been isolated from mangroves and mangrove associates. Alkaloids, alcohols, amino acids, fatty acids, lipids, phenolic compounds, steroids, tannins, flavonoids, halogenated compounds, pheromones, phorbol esters and triterpins are among these isolated compounds [8, 9]. Some isolated compounds from mangroves are considered to have bioactivities that may be beneficial to improve human health and these compounds might be very useful in new drug discovery process [10]. Mangrove plants have also been used as a folklore medicine and extracts from mangroves have been reported to have biological activities including cytotoxic, anti-bacterial, anti-viral and anti-inflammatory, etc as shown in Table 1. However, there is no data available on *in-vitro* cytotoxic properties of leaves and stem bark of most of the mangroves grown in Sri Lanka in breast (MCF-7) and hepatocellular carcinoma (HepG2) cells. Therefore, the main aim of this study was to evaluate the cytotoxic potential of leaves and stem bark of 15 selected mangroves/mangrove associates grown in Sri Lanka by evaluating of their effects in breast (MCF-7) and hepatocellular carcinoma (HepG2) cells.

Botanical name	Traditional use of the plant	Reported biological activities	References
Aegiceras corniculatum***	Used to treat for diabetes, asthma and in fish poisoning.	Toxic effects to fish, influence on the growth of fungi and some anti-viral activity	[11], [12], [13], [14], [15] , [16], [17]
Avicennia officinails ***	Used to treat for leprosy, hepatitis and as a diuretic.	Bio-toxic effects on fingerlings of fish and some anti-viral activity	[18],[19],[20], [21], [22],[23], [24]
Bruguiera	Used to treat for eye	Tested as growth	[25],[26], [27],[28]

gymnorrhiza***	diseases.	hormones on plants	
Excoecaria Indica*	As a pain killer and in fish poisoning.	-	[29]
Heritiera littoralis*	Used to treat for diarrhea and to control mosquitoes.	Antifungal, antifeedant activity and bio-toxic effects on some fish	[30], [31], [32], [33]
Lumnitzera littorea*	Used to treat for Celiac disease.	-	[34]
Lumnitzera racemosa*	Used to treat for asthma, diabetes and infertility.	Antiviral activity	[35], [36],[37], [38]
Nypa fruticans*	Used to treat for diabetes, asthma, snake bites leprosy and rheumatoid arthritis.		[39], [40]
Pemphis acidula*	Used to treat for reproduction related diseases.	Spasmolytic and oestrogenic activity	[41], [42]
Phoenix paludosa*	Used to treat for diarrhea	Cytotoxic activity	[43], [44]
Rhizophora apiculata***	Used to treat for diarrhea, nausea, vomiting, typhoid, and hepatitis.	Antimicrobial activity, antiviral activity, antifungal, antifeedant and studies on HIV.	[45],[46],[47], [48]
Rhizophora mucronata*	Used to treat for elephantiasis, hepatitis, ulcers and hematoma.	Studies on HIV, as growth hormone on plants, bio-toxicity on fish.	[49], [50], [51], [52]
Scyphiphora hydrophyllacea*	-	Cytotoxic properties of isolated compounds	[53], [54]
Sonneratia alba*	Used to treat swellings and sprains.		[55], [56], [57]
Sonneratia caseolaris*	Used to treat for hemorrhages.	Toxic effects mosquito larvae	[58], [59], [60]

Table 1. Botanical names, traditional uses and reported biological activities of studied mangroves grown in Sri Lanka.

*** mangroves; ** mangrove minors; * mangrove associates

2. Materials and methods

2.1. Chemicals

Fetal bovine serum (FBS), trypsin-EDTA, strep-penicillin, HepG2 cells, MCF-7 cells and Dulbecco's modified Eagle's medium (DMEM) were purchased from American Type Culture Collection (ATCC),

USA. All the chemicals used in the study were purchased from Sigma-Aldrich (St Louis, MO, USA) unless otherwise specified.

2.2 Plant material

Healthy leaves and barks of 15 selected mangrove plants were collected from the mangrove park, Kadolkele, Negombo in the Western Province of Sri Lanka and Kalpitiya area in the North Western Province of Sri Lanka. Plants were identified by the Botanists at the National Herbarium, Royal Botanical Garden, Peradeniya, Sri Lanka and by Mr. W.A. Sumanadasa, of the National Aquatic Resources Research and Development Agency (*NARA*), Negombo. Voucher specimens were deposited in the National Herbarium, Royal Botanical Garden, Peradeniya, Sri Lanka and Institute of Biochemistry Molecular Biology and Biochemistry, University of Colombo Sri Lanka (Table 2).

2.3 Preparation of plant extracts

Collected mangrove leaves and barks were dried at room temperature for 4-7 days and ground into powder. Ground leaf and bark samples (10 g each) were extracted sequentially in to hexane, chloroform, ethyl acetate and methanol respectively by sonication at room temperature. All the resulting extracts (sixty leaf extracts and fifty six stem bark extracts) were filtered and concentrated under vacuum in a rotary evaporator (Rotavapor® R-/ BUCHI, Switzerland). Stock solutions were prepared by dissolving all extracts in dimethyl sulfoxide (DMSO).

2.4 Cell culture maintenance

HepG2 and MCF-7 cells were maintained in Dulbecco's modified Eagle's medium supplemented with 10% (v/v) fetal bovine serum and 50 IU/mL penicillin and 50 µg/mL streptomycin at 37 ºC in a humidified environment (95 % air ;5 % CO_2). At 80 % confluency, cancer cells were trypsinized and seeded ($5x10^3$ cells/well) in 96-well cell culture plates and incubated for 24 h.

2.5 Assessment of cytotoxicity

After 24 h incubation, cells were exposed to leaf and bark extracts (doses ranging from 25 to 400 µg/mL and in triplicates) of mangroves for 24 and 48 h and cytotoxicity assessed by Sulforhodamine B assay (SRB) as previously described by us [61, 62]. Briefly, treated cells were washed three times with PBS and fixed with Trichloroacetic acid (10%). Fixed cells were washed with tap water five times and then SRB (0.4 %) was added to each well and incubated for 20 min. Unbound dye was removed by washing with acetic acid and bound dye was solubilized with Tris base (10 mM; pH 7.5). Plates were then kept on a plate shaker for 1 h and absorbance was taken at 540 nm using Synergy™ HT Multi-Mode Microplate Reader (BioTek, USA).

2.6 Statistical analysis

All the experiments in this study were carried out at least three times in triplicate. Data were analyzed using Prism 5.0 (Graph pad Prism) statistical software package and results were expressed as mean ± standard deviation (SD).

3. Results

A total of 116 solvent extracts (hexane, chloroform, ethyl acetate and methanol extracts of leaf and stem bark) representing 15 mangrove/mangrove associates and mangrove minors collected from Sri Lanka were tested for their cytotoxic effects on MCF 7 and HepG2 cells. The cytotoxic activities of mangrove extracts have been summarized in Table 2. Extracts with IC_{50} value < 100 µg/mL were considered to be cytotoxic, while those with IC_{50} value > 100 µg/mL were considered to be low/non-cytotoxic.

3.1 Selective cytotoxic effects of mangrove extracts

Among the 116 extracts tested in MCF-7 and HepG2 cells, chloroform extract of stem bark of *Scyphiphora hydrophyllacea*, *Bruguiera gymnorrhiza* (chloroform, ethyl acetate and methanol extracts of leaves), hexane and ethyl acetate extracts of leaves of *Aegiceras corniculatum*, methanol extracts

of leaves and stem bark of *N. fruticans* and *Rhizophora mucronata,* methanol extracts of stem bark of *Sonneratia alba* and *Rhizophora apiculata* showed selective cytotoxicity to HepG2 cells. However, the hexane extract of leaves of *B. gymnorrhiza*, chloroform extracts of leaves of *N. fruticans*, ethyl acetate extract of stem bark of *Lumnitzera littorea*, chloroform extract of leaves of *R. apiculata* and chloroform extract of leaves of *Pemphis acidula* showed selective cytotoxic effects against MCF-7 breast cancer cells.

3.2 Non-selective cytotoxic effects of mangrove extracts

Hexane extracts of leaves and stem bark of *S. hydrophyllacea*, methanol extract of leaves of *P. paludosa* and ethyl acetate extract of stem bark of *A. officinalis* showed non-selective cytotoxic activity against both cancer cell lines tested.

3.3 Low or no cytotoxic effects of mangrove extracts

Out of the 116 mangrove extracts tested, 84 extracts showed no significant cytotoxic effects (IC_{50}>100 µg/mL) against MCF 7 and HepG2 cancer cells (Table 2).

Table 2. Cytotoxic effects of leaves and stem bark of mangrove plants and their voucher specimen numbers: IC_{50} values of plant extracts on MCF 7 and HepG2 cells as determined by SRB assay at 24 and 48 h post incubation periods.

Botanical name of the mangrove plant and voucher specimen number.	Part used	Extract	IC_{50} value (µg/mL) at 24 h post incubation		IC_{50} value (µg/mL) at 48 h post incubation	
			MCF-7	HepG2	MCF-7	HepG2
Aegiceras corniculatum (C-7)	Leaves	Hexane	145.1	73.99	139.1	64.0
		Chloroform	109.6	98.72	93.8	80.2
		Ethyl acetate	166.9	82.91	133.2	71.6
		Methanol	283.1	426.2	200.5	408.1
	Stem/ bark	Hexane	256.1	951.2	148.4	867.6
		Chloroform	189.0	260.2	44.69	159.7
		Ethyl acetate	466.7	148.1	302.8	100.7
		Methanol	>1000	163.6	826.8	100.1
Avicennia officinalis (C-11)	Leaves	Hexane	259.78	158.7	198.3	109.4
		Chloroform	418.89	184.7	336.1	132.2
		Ethyl acetate	267.39	241.1	227.9	180.5
		Methanol	198.9	221.2	153.2	182.3
	Stem/ bark	Hexane	230.6	>1000	189.9	>1000

		Chloroform	81.38	155.4	67.2	140.0
		Ethyl acetate	65.08	54.8	56.3	27.91
		Methanol	276.3	47.2	207.7	27.5
Bruguiera gymnorrhiza (C-3)	Leaves	Hexane	98.43	764.9	90.2	730.3
		Chloroform	146.8	74.98	130.5	69.2
		Ethyl acetate	154.5	98.08	142.3	88.4
		Methanol	296.6	63.37	230.6	60.3
	Stem/ bark	Hexane	>1000	>1000	576.5	152.9
		Chloroform	240.1	143.3	245.9	97.07
		Ethyl acetate	180.5	105.9	167.9	89.71
		Methanol	428.4	157.8	463.2	103.3
Excoecaria Indica (S-15)	Leaves	Hexane	>1000	>1000	>1000	>1000
		Chloroform	733.5	654.4	680.9	554.1
		Ethyl acetate	437.1	303.7	378.3	247.7
		Methanol	239.3	260.4	221.3	200.2
	Stem/ bark	Hexane	499.9	>1000	419.9	>1000
		Chloroform	252.0	143.2	222.5	100.9
		Ethyl acetate	286.3	200.4	146.2	141.7
		Methanol	252.6	211.3	112.2	135.7
Heritiera littoralis (C-5)	Leaves	Hexane	939.9	>1000	883.7	>1000
		Chloroform	859.8	>1000	820.0	>1000
		Ethyl acetate	904.5	969.4	829.8	907.2
		Methanol	>1000	>1000	>1000	>1000
	Stem/ bark	Hexane	>1000	>1000	>1000	>1000
		Chloroform	>1000	>1000	>1000	>1000
		Ethyl acetate	>1000	>1000	>1000	>1000
		Methanol	670.8	458.1	463.2	300.8
Lumnitzera littorea (S-2)	Leaves	Hexane	>1000	>1000	>1000	>1000
		Chloroform	323.0	377.7	298.2	358.0
		Ethyl acetate	286.3	288.9	247.2	260.1
		Methanol	200.3	264.3	148.6	234.1
	Stem/ bark	Hexane	>1000	>1000	>1000	>1000
		Chloroform	395.2	402.5	355.9	337.8
		Ethyl acetate	120.2	250.2	88.4	251.0
		Methanol	166.6	394.5	114.6	344.8
Lumnitzera racemosa (C-4)	Leaves	Hexane	347.6	700.2	300.8	640.0
		Chloroform	170.1	230.1	123.3	169.4
		Ethyl acetate	541.6	440.7	499.0	394.0
		Methanol	765.87	777.98	752.1	701.9
	Stem/ bark	Hexane	820.7	1020.5	582.9	66.46
		Chloroform	180.7	150.2	128.7	66.98
		Ethyl acetate	>1000	>1000	>1000	>1000
		Methanol	231.0	321.8	136.3	235.6
Nypa fruticans	Leaves	Hexane	139.2	264.2	108.9	210.4

(S-3)		Chloroform	90.36	277.7	77.2	240.3
		Ethyl acetate	166.9	203.2	154.8	164.2
		Methanol	390.98	74.27	120.4	64.2
	Stem/ bark	Hexane	744.4	329.3	687.2	324.2
		Chloroform	460.5	566.8	419.0	417.2
		Ethyl acetate	>1000	>1000	>1000	>1000
		Methanol	160.2	103.6	140.3	71.52
Pemphis acidula (C-14)	Leaves	Hexane	154.5	135.9	122.3	109.4
		Chloroform	163.5	132.7	129.6	112.9
		Ethyl acetate	395.1	368.9	377.5	362.2
		Methanol	632.1	734.6	597.3	704.6
	Stem/ bark	Hexane	189.7	138.4	154.6	111.8
		Chloroform	73.03	188.3	60.9	152.8
		Ethyl acetate	195.4	305.8	149.7	245.5
		Methanol	414.8	197.9	402.1	157.6
Phoenix paludosa (S-10)	Leaves	Hexane	369.2	889.3	319.9	840.1
		Chloroform	590.5	732.9	550.0	769.2
		Ethyl acetate	487.2	621.3	465.2	602.8
		Methanol	36.71	49.0	33.19	44.2
	Stem/ bark*	Hexane	-	-	-	-
		Chloroform	-	-	-	-
		Ethyl acetate	-	-	-	-
		Methanol	-	-	-	-
Rhizophora apiculata (C-12)	Leaves	Hexane	567.98	278.2	540.0	244.3
		Chloroform	678.89	598.4	629.3	509.7
		Ethyl acetate	765.87	1272	700.2	>1000
		Methanol	765.99	720.5	678.3	667.9
	Stem/ bark	Hexane	>1000	303.6	>1000	235.5
		Chloroform	104.9	465.3	83.5	355.6
		Ethyl acetate	1004	460.5	980.4	420.2
		Methanol	245.9	133.6	204.5	96.91
Rhizophora mucronata (C-13)	Leaves	Hexane	908.78	801.2	820.0	720.6
		Chloroform	547.67	491.6	480.3	405.5
		Ethyl acetate	>1000	>1000	>1000	>1000
		Methanol	176.98	82.93	140.3	67.0
	Stem/ bark	Hexane	716.6	821.8	640.5	745.1
		Chloroform	>1000	>1000	>1000	>1000
		Ethyl acetate	358.6	679.0	283.0	613.2
		Methanol	204.3	89.4	162.2	46.59
Scyphiphora hydrophyllacea (C-10)	Leaves	Hexane	87.97	83.74	66.3	62.16
		Chloroform	109.4	118	94.2	62.01
		Ethyl acetate	752.6	528.5	730.6	651.0
		Methanol	544.6	791.0	503.4	>1000
	Stem/ bark	Hexane	90.3	84.74	80.9	56.7
		Chloroform	120.5	89.93	106.3	80.2

		Ethyl acetate	>1000	>1000	1031.0	>1000
		Methanol	900.4	861.4	474.2	803.5
Sonneratia alba (S-4)	Leaves	Hexane	764.92	678.9	673.9	598.2
		Chloroform	879.9	675.89	855.2	597.3
		Ethyl acetate	>1000	>1000	>1000	>1000
		Methanol	987.12	560.78	900.7	507.0
	Stem/ bark	Hexane	695.4	332.5	565.6	255.6
		Chloroform	152.6	159.0	112.4	100.2
		Ethyl acetate	326.2	>1000	300.3	>1000
		Methanol	201.4	144.7	172.3	94.92
Sonneratia caseolaris (C-16)	Leaves	Hexane	>1000	630.6	>1000	600.3
		Chloroform	632.6	420.3	583.5	301.3
		Ethyl acetate	365.8	399.2	366.4	320.5
		Methanol	600.6	487.7	580.4	434.4
	Stem/ bark	Hexane	>1000	>1000	>1000	>1000
		Chloroform	289.3	184.6	250.3	115.4
		Ethyl acetate	500.1	308.4	457.2	105.4
		Methanol	636.8	425.3	602.8	292.8

4. Discussion

Mangrove forests are considered to be the most productive ecosystems in the world [63]. However, mangroves grow under conditions such as high salinity, strong winds, extreme tides, high temperatures and extreme muddy soils etc. Thus, mangrove plants possess physiological, biological, ecological and morphological adaptations to extreme conditions [64]. Even though mangrove ecosystems have been studied broadly, there is a critical need to understand them better and care must be taken to prevent degradation and destruction of mangrove eco systems.

Results of the present study with the leaf and stem bark extracts of fifteen mangrove species grown in Sri Lanka indicates that some of them have cytotoxic properties in breast (MCF -7) and hepatocellular carcinoma (HepG2) cells. Some mangrove plant extracts showed selective cytotoxic effects against breast and hepatocellular carcinoma cells, whereas some extracts showed non-selective cytotoxicity against both cancer cell lines or were not cytotoxic (IC_{50} >100 µg/mL) against any of the cell lines tested. Among the extracts tested, the methanolic extract of *P. paludosa* leaves showed the highest cytotoxicity in the two cancer cell lines tested. We have previously shown cytotoxic activity of different leaf extracts (hexane, chloroform, ethyl acetate and methanol) of *P. paludosa* in several cancer cell lines and normal cell lines [65]. Ethyl acetate extract of *A. officinalis* stem bark showed second

highest cytotoxic properties in the two cancer cell lines tested. Previous studies by other researchers have shown that, *A. officinailis* leaf extracts have cytotoxic effects to Ehrlich ascites carcinoma (EAC) and human promyelocytic leukemia cell lines (HL 60) [66]. Hexane extract of *S. hydrophyllacea* leaves showed third highest cytotoxic properties in the two cancer cell lines tested and several cytotoxic compounds have been reported to be isolated from the mangrove plant *S. hydrophyllacea* [67]. *S. hydrophyllacea* (hexane and chloroform extracts of stem bark), *B. gymnorrhiza* (chloroform, ethyl acetate and methanol extracts of leaves), *Aegiceras coniculatum* (hexane and ethyl acetate extracts of leaves), *N. fruticans* (methanol extract of leaves and stem bark), *S. alaba* (methanol extract of stem bark), *A. officinalis* (methanol extract of bark), *R. apiculata* (methanol extract of stem bark) and *R. mucronata* (methanol extracts of leaves and stem bark) showed selective cytotoxic properties to HepG2 cells. Moreover, *B. gymnorrhiza* (hexane extract of leaves), *N. fruticans* (chloroform extract of leaves), *L. littorea* (ethyl acetate extract of stem bark), *R. apiculata* (chloroform extract of leaves) and *P. acidula* (chloroform extract of leaves) showed selective cytotoxic effects against MCF-7 breast cancer cells (IC_{50}< 100 µg/mL). Among these plants, *A. corniculatum*, which was cytotoxic to HepG2 cells, has been used as a medicinal plant in Bangladesh for asthma, diabetes and rheumatism. Extracts of this plant have reported to be cytotoxic to human gastric adenocarcinoma cells (AGS), colorectal adenocarcinoma cells (HT-29) and breast carcinoma cells (MDA-MB-435S) [68]. *Avicennia officinalis* and *B. gymnorrhiza* which was cytotoxic to HepG2 cells in the present study have been used in traditional medicine to treat for leprosy, hepatitis, as a diuretic and for eye disease respectively. Extracts of these plants have also shown cytotoxic properties in cancer cells [69]. None of the extracts obtained from *Lumnitzera racemosa, Heritiera littoralis, Excoecaria indica* and *Sonneratia caseolaris* showed significant cytotoxic properties (IC_{50} >100 µg/mL) in the two cancer cell lines tested.

This is the first study on screening of cytotoxic properties of leaf and bark of 15 listed mangrove plants grown in Sri Lanka against human breast and hepatocellular cancer cell lines. This study supports the reported cytotoxic activities of *S. hydrophyllacea*, *A. corniculatum*, *A. officinalis* and *B. gymnorrhiza.* Cytotoxic properties of *B. gymnorrhiza*, *P. paludosa*, *N.fruticans*, *S. alba*, *L. littorea*, *R. apiculata*, *R. mucronata* and *P. acidula* have not been reported previously. This study offers baseline data to focus on further studies into the isolation and characterization of novel secondary metabolites and to

197 determine anti-cancer mechanism of such metabolites from mangrove plants grown in Sri Lanka.
198 Mangrove plants that were found to be cytotoxic in the present study will be very useful as a source of
199 new anti- cancer drug leads for drug discovery to fight against cancer.

200 **5. CONCLUSION**

201 Screening of leaves and stem barks of 15 selected mangrove plants growing in Sri Lanka, for
202 cytotoxic activity in MCF -7 breast cancer cells and HepG2 hepatocellular carcinoma cells have
203 demonstrated. Some mangrove plant extracts can exert selective cytotoxic properties to MCF -7 and
204 HepG2 cells, whereas a few plant extracts showed non-selective cytotoxic properties, while a few
205 others demonstrated no cytotoxic properties. The overall results indicate that some mangrove species
206 found in Sri Lanka have the potential to be developed to isolate novel drugs that can be used in
207 cancer therapy.
208

209 **CONSENT**

210 Not applicable.

211 **ETHICAL APPROVAL**

212 Not applicable.

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