Effects of Plant Extracts on HIV-1 Protease

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Effects of Plant Extracts on HIV-1 Protease

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Abstract: Acquired immunodeficiency syndrome (AIDS) is one of the most important public health problems, affecting many people every day. This syndrome is caused by the human immunodeficiency virus (HIV) and the HIV-1 protease plays an essential role by promoting virus maturation and thus infecting new cells. The HIV-1 protease is one of the main targets for anti-HIV drug therapy. The present work is a literature survey of plant extracts whose activity has been studied on HIV-1 protease. Here we list 275 species of medicinal plants, distributed in 99 families, with their place of origin, part used, type of extract, concentration and activity. We aim with this work to provide data that could be used in the research and development of new therapeutic agents for AIDS treatment.

Keywords: Review, natural products, plants, AIDS, HIV-1 Protease, Anti-HIV drugs.

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is one of the most important public health problems now a day. At the end of 2007, about 33 million people were estimated to be infected and 25 million individuals have died from this disease [1]. Every day, over 6800 people become infected with the human immunodeficiency virus (HIV), the causative agent of AIDS, and over 5700 people die from AIDS, mostly because of inadequate access to HIV prevention and treatment services. In addition, HIV infected people are affected by emotional, behavioural, and psychosocial complications [2, 3].

In regard to HIV biology, the virus interacts with target cells using envelope glycoproteins that are recognized by CD4 receptors and CCR5 (macrophage) or CXCR4 (T cell) co-receptors leading to membrane fusion followed by virus entry and subsequent integration to the host genome [1]. The HIV-1 protease is a member of the aspartyl-protease family that performs an essential step in the life cycle of the virus by promoting the maturation of the envelope proteins from cleaved precursors. Therefore the inhibition of this enzyme produces immature and non-infectious virions [4-6].

Because of its fundamental importance on virus biology, HIV-1 protease has emerged as one of the main targets for anti-HIV drug therapy. HIV-1 protease inhibitors have been successfully used on AIDS therapy. However, the development of drug resistance by the virus represents an important problem on AIDS-chemotherapy. Additionally, there is not yet a definitive cure for this disease [7].

Thus, the search for new anti-HIV effective therapies remains a challenge for the scientists. Therefore around the world many researches have focused on natural products as a source of structurally novel chemicals. Medicinal plants are characterized by the presence of several bioactive constituents and research with plants and natural products may provide new compounds for anti-HIV drug therapy [8].

Several reports have shown the action of medicinal plants and its constituents against various diseases such as: allergy [9, 10], cancer [11], pain [12], malaria [13], osteoporosis [14], Parkinson's disease [15], leishmania [16], hyperglycemia [17], inflammation [18], fungal and bacterial infection [19], hypertension [20], diabetes [21], obesity [22] and ulcer [23]. Here, we reviewed the literature related to plants with anti HIV-protease activity.

MATERIALS AND METHODS

The search was carried out on PubMed, Biological Abstracts and NAPRALERT (acronym for Natural Products ALERT – the data bank of the University of Illinois at Chicago) updated until November 2009, using ''HIV-protease'' as legend. Plants extract with complete information (place, part used, type of extract, concentration and activity) were selected for this work. The references found in the search were later consulted for details on the models or mechanism-based bioassays used for testing the plant extracts against HIV- 1 protease.

RESULTS AND DISCUSSION

As result for our search we list 275 species of medicinal plants studied, which were distributed in 99 families, including Asteraceae, Fabaceae, Rosaceae and Lamiaceae with 33, 19, 20 and 11 plants, respectively. Hence 205 of the plants studied, showed some degree of activity depending on the part used, the type of extract and the concentration on which they were used. About 70 species were inactive against HIV-1 protease enzyme. Based on this search it was also possible to classify the effect of the extracts as active, strongly active, weakly active or inactive (Table **1**).

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Table 1. Plants with Anti-HIV Protease Activity

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Acanthaceae					
Andrographis paniculata (Burm. F.) Nees	China	CSBk	H_2O Ext. - 200 μg/ml	Inactive	[45]
Baphicacanthus cusia (Nees) Bremek	China	DRh	H_2O Ext. - 200 μg/ml	Weak activity	[45]
Actinidiaceae					
Actinidia arguta (Siebold & Zuccarini) Planchon ex Miquel	South Korea	Lf + Sm	MeOH Ext. - 100 μg/ml	Inactive	[46]
Alismataceae					
Alisma plantago-aquatica L. var *orientales* Samuels	Singapore	Rh	Hot H_2O Ext. - 250 μg/ml	Active	[24]
Amaryllidaceae					
Crinum macowani Baker	South Africa	Bb	H_2O Ext. - 48 μg/ml	Inactive	[39]
	South Africa	Bb	EtOH Ext. - 48 μg/ml	Inactive	[39]
Anacardiaceae					
Rhus acuminata DC.	India	DGl	H_2O Ext. - 200 μg/ml	Weak activity	[35]
Rhus javanica L.	Singapore	Gl	Hot H_2O Ext. - 250 μg/ml	Active	[24]
Apiaceae					
Aciphylla aurea Mt. St. Bathans	New Zealand	AP	EtOH (75%) Ext. - 50 μg/ml	Active	[29]
Aciphylla glaucescens W. R. B. Oliv	New Zealand	AP	EtOH (75%) Ext. - 50 μg/ml	Active	[29]
Ammi visnaga (L.) Lam.	Sudan	CSF	H_2O Ext. - 100 μg/ml	Weak activity	[26]
Anethum graveolens L.	India	DSm	H_2O Ext. - 200 μg/ml	Inactive	[35]
		DF	H_2O Ext. - 200 μg/ml	Inactive	[35]
Bupleurum longeradiatum Turcz.	South Korea	DRt	MeOH Ext. - 100 μg/ml	Weak activity	[46]
Cryptotaenia japonica Hassk.	South Korea	DEP	MeOH Ext. - 100 μg/ml	Inactive	[46]
Ledebouriella divaricata (Turcz.) Hiroe	China	CSAF	H_2O Ext. - 200 μg/ml	Inactive	[45]
Apocynaceae					
Parameria laevigata (A. L. Juss.) Moldenke	Singapore	Bk	Hot H_2O Ext. - 25 μg/ml	Inactive	[24]
Araliaceae					
Eleutherococcus chiisanensis (Nakai) C. H. Kim & B.Y. Sun	South Korea	DSm	MeOH Ext. - 100 μg/ml	Weak activity	[46]
Eleutherococcus koreanus Nakai	South Korea	DRt	MeOH Ext. - 100 μg/ml	Active	[46]
Panax pseudoginseng Wall.	China	CSRt	MeOH Ext. - 200 μg/ml	Strong activity	[45]
Pseudopanax simplex (G. Forst.) Philipson	New Zealand	Lf + Sm	EtOH (75%) Ext. - 50 μg/ml	Active	[29]
Arecaceae					
Areca catechu L.	China	CSESd	H_2O Ext. - 200 μg/ml	Active	[45]
Aristolochiaceae					
Aristolochia bracteolate Retz.	Sudan	CSRt	H_2O Ext. - 100 μg/ml	Weak activity	[26]
		CSESd	H_2O Ext. - 100 μg/ml	Inactive	[26]
Asclepiadaceae					
Solenostemma argel (Del.) Hayne	Sudan	CSRt	H_2O Ext. - 100 μg/ml	Weak activity	[26]
Asphodelaceae					
Bulbine alooides (L.) Willd.	South Africa	Rt	H_2O Ext. - 48 μg/ml	Active	[39]
			EtOH Ext. - 48 μg/ml	Active	[39]
Asteraceae					
Arctium lappa L.	China	DF	H_2O Ext. - 200 μg/ml	Inactive	[45]
Artemisia capillaries Thunb.	Singapore	Sd	Hot H_2O Ext. - 250 μg/ml	Active	[24]
Artemisia caruifolia Buch. Ham. ex Roxb.	China	DAP	MeOH Ext. - **	Active	[47]

(Table 1) contd…..

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Artemisia iwayomogi Kitam.	South Korea	DRt	MeOH Ext. - 100 µg/ml	Inactive	[46]
Artemisia princeps Pamp.	Singapore	Lf	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Aster korainensis Nakai.	South Korea	DLf	MeOH Ext. - 100 µg/ml	Weak activity	[46]
Aster tataricus L. F.	Singapore	Rt	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Atractylodes lancea (Thunb.) DC.	Singapore	Rh	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Carpesium abrotanoides L.	South Korea	DEP	MeOH Ext. - 100 µg/ml	Weak activity	[46]
Celmisia dallii Buch.	New Zealand	EP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Celmisia spectabilis Hook. F.	New Zealand	EP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Centaurea scoparia Sieb.	Egypt	DRt	**	Active	[48]
Chrysanthemum indicum L.	China	CSFwH	MeOH Ext. - 200 µg/ml	Inactive	[45]
Craspedia uniflora G. Forster	New Zealand	EP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Dendranthema morifolium (Ramat.) Tzvelev.	China	CSFwH	H_2O Ext. - 200 µg/ml	Strong activity	[45]
			MeOH Ext. - 200 µg/ml	Active	[45]
	Singapore	Fw	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Eclipta alba (L.) *Hassk.*	India	DLf	H_2O Ext. - 200 µg/ml	Inactive	[35]
Elephantopus scaber L.	Singapore	Lf	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Helianthus tuberosus L.	South Korea	DAP	MeOH Ext. - 100 µg/ml	Weak activity	[46]
Helichrysum aggregatum Yeo	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Helichrysum filicaule Hook. F.	New Zealand	EP	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Helichrysum parvifolium Yeo	New Zealand	AP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Leucogenes leontopodium (Hook. F.) Beauverd	New Zealand	EP	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Olearia arborescens (G. Forst.)	New Zealand	Lf + Sm	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Olearia lacunosa var *alpina* Hook. F.	New Zealand	Lf + Sm	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Olearia traversii (F. Muell.) Hook. F.	New Zealand	Lf + Sm	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Pachystegia rufa Molloy	New Zealand	Lf + Sm	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Raoulia species	New Zealand	EP	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Raoulia tenuicaulis Hook. Fil.	New Zealand	EP	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Senecio scandens Ham.	China	CSEP	H_2O Ext. - 200 µg/ml	Strong activity	[45]
Serratula coronate L.	South Korea	DRt	MeOH Ext. - 100 µg/ml	Inactive	[46]
Sigesbeckia pubescens (Makino) Makino	South Korea	DEP	MeOH Ext. - 100 µg/ml	Active	[46]
Taraxacum mongolicum Hand. Mazz.	Singapore	Bk	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Taraxacum officinale Weber ex F. H. Wigg.	South Korea	DFw	Lyophilized Ext. - 100 µg/ml	Weak activity	[49]
Berberidaceae					
Epimedium sagittatum (Siebold. & Zucc.) Maxim.	Singapore	Lf	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Nandina domestica Thunb.	Singapore	Lf	Hot H_2O Ext. - 25 µg/ml	Weak activity	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
Bignoniaceae					
Campsis grandiflora (Thunb.) K. Schum.	South Korea	DLf + Sm	MeOH Ext. - 100 µg/ml	Inactive	[46]
		DRt	MeOH Ext. - 100 µg/ml	Inactive	[46]
Blechnaceae					
Blechnum discolor (G. Forst.) Keyserl.	New Zealand	Fd	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Blechnum species	New Zealand	Fd	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Brainia insignis J. Sm	Singapore	Rh	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Woodwardia orientalisi Sw. & Schrad.	Singapore	Fp	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Woodwardia unigemmata (Makino) Nakai	China	CSRh	H_2O Ext. - 200 µg/ml	Active	[45]
			MeOH Ext. - 200 µg/ml	Strong activity	[45]

(Table 1) contd…..

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Boraginaceae					
Cordia spinescens L.	Panama	DLf	Hot H_2O Ext. - **	Weak activity	[38]
Lithospermum erythrorhizon Siebold & Zuccarini	China	CSRt	H_2O Ext. - 200 µg/ml	Weak activity	[45]
		CSESd	H_2O Ext. - 200 µg/ml	Active	[45]
			MeOH Ext. - 200 µg/ml	Active	[45]
Burseraceae					
Boswellia carteri Birdw.	Egypt	DRE	**	Active	[48]
Campanulaceae					
Platycodon grandiflorum (Jacq.) A. DC.	Singapore	Rt	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Cannabaceae					
Cannabis sativa L.	Singapore	F	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Capparidaceae					
Crateva religiosa Forst.	India	DBk	H_2O Ext. - 200 µg/ml	Inactive	[35]
Polanisia icosandra L. DC.	India	DSd	H_2O Ext. - 200 µg/ml	Inactive	[35]
Caprifoliaceae					
Lonicera japonica Thunb.	Singapore	FwB	Hot H_2O Ext. - 25 µg/ml	Weak activity	[24]
		Fb	Hot H_2O Ext. - 250 µg/ml	Weak activity	[24]
	China	CSFwB	H_2O Ext. - 200 µg/ml	Inactive	[45]
Caryophyllaceae					
Melandrium firmum (Siebold et Zucc.) Rohrb.	South Korea	DEP	MeOH Ext. - 100 µg/ml	Weak activity	[46]
Celastraceae					
Euonymus alatus (Thunb.) Sieb.	South Korea	DSm	MeOH Ext. - 100 µg/ml	Inactive	[46]
Maytenus senegalensis (Lam.) Exell.	Sudan	CSSd	H_2O Ext. - 100 µg/ml	Active	[26]
	Sudan	CSSd	MeOH Ext. - 100 µg/ml	Active	[26]
Combretaceae					
Terminalia arjuna (Roxb. ex DC.) Wight & Arn.	Singapore	Fp	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
	India	DSBk	H_2O Ext. - 200 µg/ml	Active	[35]
			MeOH Ext. - 200 µg/ml	Active	[35]
Terminalia bellerica Roxb.	Singapore	F	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Terminalia chebula Retz.	Singapore	AP	Hot H_2O Ext. - 25 µg/ml	Active	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
	India	DF	H_2O Ext. - 200 µg/ml	Weak activity	[35]
Terminalia horrida	Egypt	DRE	**	Active	[48]
Convolvulaceae					
Cuscuta chinensis Lam.	South Korea	DF + Sm	MeOH Ext. - 100 µg/ml	Active	[46]
Coriariaceae					
Coriaria species	New Zealand	EP	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Cornaceae					
Griselinia littoralis Broadway Mint	New Zealand	Lf + Sm	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Cunoniaceae					
Weinmannia racemosa L. F.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]

(Table 1) contd…..

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Cyatheaceae					
Cyathea smithii Hook. Fil.	New Zealand	Fd	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Cynomoriaceae					
Cynomorium songaricum Rupr.	China	DSm	CH_2Cl_2 Ext. - 100 µmols	Active	[50]
Cyperaceae					
Baumea teretifolia (R.Br.) Palla	New Zealand	EP	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Carex secta	New Zealand	EP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Cyperus rotundus L.	Singapore	Rh	H_2O Ext. - 25 µg/ml	Inactive	[24]
Schoenus tendo (Hook. F.) Hook. F.	New Zealand	EP	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Dennstaedtiaceae					
Hypolepis ambigua (A. Rich.) Brownsey & Chinnock	New Zealand	Fd	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Paesia scaberula (A.Rich.) Kuhn	New Zealand	Fd	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Dioscoreaceae					
Discorea hispida Dennst.	Singapore	Rh	Hot H_2O Ext. - 25 µg/ml	Active	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
Dioscorea birmanica Pierre ex. Prain & Burkill	Thailand	DEP	H_2O Ext. - 100 µg/ml	Inactive	[41]
			EtOH Ext. - 100 µg/ml	Inactive	[41]
Dioscorea membranacea Pierre ex. Prain & Burkill	Thailand	DEP	EtOH Ext. - 48 µg/ml	Strong activity	[41]
			EtOH Ext. - 100 µg/ml	Inactive	[41]
Dryopteridaceae					
Cyrtomium fortune J. Sm.	Singapore	Rh	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Matteuccia struthiopteris (L.) Todaro var. *pensylvanica* (Willd.) C. V. Morton	Singapore	Rh	Hot H_2O Ext. - 25 µg/ml	Weak activity	[24]
Elaeocarpaceae					
Elaeocarpus grandiflorus Smith.	Singapore	F	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
Ephedraceae					
Ephedra sinica Stapf.	Singapore	Sm	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Ericaceae					
Pernettya macrostigma (Colenso.) Middleton.	New Zealand	Lf + Sm	EtOH (75%) Ext. - **	Active	[29]
Euphorbiaceae					
Croton tiglium L.	Egypt	DSd	**	Active	[48]
Croton zambesicus Müll.Arg.	Sudan	CSESd	H_2O Ext. - 100 µg/ml	Weak activity	[26]
Euphorbia granulate Forsk.	Sudan	CSLf	MeOH Ext. - 100 µg/ml	Active	[26]
Euphorbia prostrata Ait.	Sudan	CSLf	H_2O Ext. - 100 µg/ml	Inactive	[26]
Phyllanthus amarus L.	New Zealand	AP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Phyllanthus emblicai L.	India	DF	H_2O Ext. - 200 µg/ml	Inactive	[29]
Ricinus communis L.	India	DLf	H_2O Ext. - 200 µg/ml	Inactive	[29]
Fabaceae					
Abrus precatorius L.	Indonesia	DSd	H_2O Ext. - **	Inactive	[51]
Acacia mearnsii De Wild.	New Zealand	Bk	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Acacia nilotica (L.) Willd. ex Delile	Sudan	CSP	H_2O Ext. - 100 µg/ml	Active	[26]

(Table 1) contd…..

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Astragalus membranaceus Moench.	Singapore	Rt	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Cassia fistula L.	Singapore	Bk	Hot H_2O Ext. - 250 µg/ml	Active	[24]
	India	DBk	H_2O Ext. - 200 µg/ml	Inactive	[35]
Cassia obtusifolia L.	Sudan	CSAP	H_2O Ext. - 100 µg/ml	Inactive	[26]
Dolichos biflorus L.	India	DSd	H_2O Ext. - 200 µg/ml	Inactive	[35]
Lotus corniculatus L.	New Zealand	Lf	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Lotus pedunculatus Cav.	New Zealand	Lf	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Nothofagus cliffortioides (Hook. F.) Poole	New Zealand	Lf + Sm	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Pongamia glabra Vent. Sans.	India	DRt	H_2O Ext. - 200 µg/ml	Inactive	[35]
Pueraria lobata (Willd.) Ohwi	China	CSRt	H_2O Ext. - 200 µg/ml	Strong activity	[45]
Saraca indica Linn.	India	DBk	H_2O Ext. - 200 µg/ml	Active	[35]
Sophora flavescens Ait.	South Korea	DAP	Lyophilized Ext. - 100 µg/ml	Active	[49]
	China	CSRt	H_2O Ext. - 200 µg/ml	Inactive	[45]
Sophora japonica L.	Singapore	Rt	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Sophora subprostrata Chun. & T. Chen.	Singapore	Rh	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Sophora tonkinensis Gapnep.	China	CSRt	H_2O Ext. - 200 µg/ml	Strong activity	[45]
Spatholobus suberectus Dunn.	Singapore	EP	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
	China	CSRh	MeOH Ext. - 200 µg/ml	Strong activity	[45]
Tephrosia purpurea Linn. Pers.	India	DRt	H_2O Ext. - 200 µg/ml	Inactive	[35]
Gentianaceae					
Gentiana macrophylla Pall.	Singapore	Rt	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Gentiana montana G. Forst.	New Zealand	EP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Gentiana scabra L.	Singapore	Rh + Rt	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Gleicheniaceae					
Sticherus cunninghamii (Hook.) Ching	New Zealand	Fd	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Goodeniaceae					
Selliera radicans Cav.	New Zealand	AP	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Hymenophyllaceae					
Hymenophyllum demissum (G.Forst.) Sw.	New Zealand	EP	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Hypoxidaceae					
Hypoxis sobolifera var. *sobolifera* (Jacq.) Nel	South Africa	Cs	H_2O Ext. - 48 µg/ml	Active	[39]
Iridaceae					
Belamcanda chinensis (L.) DC	Singapore	Rh	Hot H_2O Ext. - 25.0 µg/ml	Active	[24]
Juglandaceae					
Juglans mandshurica Maxim.	South Korea	DF	MeOH Ext. - 100 µg/ml	Weak activity	[46]
Lamiaceae					
Isodon excises var *coreanus*	South Korea	DAP	MeOH Ext. - 100 µg/ml	Weak activity	[46]
		DRt	MeOH Ext. - 100 µg/ml	Weak activity	[46]
Leonotis leonurus (L.) R.Br.	South Africa	Lf	EtOH Ext. - 48 µg/ml	Active	[39]
	South Africa	Lf	H_2O Ext. - 48 µg/ml	Active	[39]
Leonurus sibiricus L.	South Korea	DEP	MeOH Ext. - 100 µg/ml	Weak activity	[46]
Lycopus lucidus Turcz. Var Hirtus Regel	Singapore	EP	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Mentha haplocalyx Briq.	China	CSEP	H_2O Ext. - 200 µg/ml	Active	[45]

(Table 1) contd…..

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Perilla frutescens (L.) Britt. var. *acuta* (Thunb.) Kudo	China	CSLf	H_2O Ext. - 200 µg/ml	Active	[45]
			MeOH Ext. - 200 µg/ml	Active	[45]
Pogostemon heyneanus Benth.	India	DLf	H_2O Ext. - 200 µg/ml	Weak activity	[35]
Prunella vulgaris Linn.	China	CSEP	H_2O Ext. - 200 µg/ml	Strong activity	[45]
Salvia miltiorrhiza Bunge.	Singapore	Rt	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Scutellaria baicalensis Georgi.	China	CSRt	H_2O Ext. - 200 µg/ml	Strong activity	[45]
			MeOH Ext. - 200 µg/ml	Active	[45]
	Singapore	Sd	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Vitex lucens T. Kirk	New Zealand	Lf + Sm	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Lauraceae					
Cinnamomum zeylanicum Blume	India	DLf	H_2O Ext. - 200 µg/ml	Inactive	[35]
Lindera erythrocarpa (Makino) Rehd.	South Korea	DLf	MeOH Ext. - 100 µg/ml	Active	[46]
Lindera strychnifolia Sieb. et Zucc.	China	CSRt	MeOH Ext. - 200 µg/ml	Strong activity	[45]
Litsea sebifera Pers.	India	DBk	H_2O Ext. - 200 µg/ml	Weak activity	[35]
Liliaceae					
Anemarrhena asphodeloides Bunge.	Singapore	Rhz	Hot H_2O Ext. - 250 µg/ml	Active	[24]
	South Korea	DRt	MeOH Ext. - 100 µg/ml	Inactive	[46]
Fritillaria cirrhosa D. Don.	China	CSRh	H_2O Ext. - 200 µg/ml	Inactive	[45]
Fritillaria thunbergii Miq.	Singapore	Rh	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Hemerocallis fulva L.	South Korea	DAP	Lyophilized Ext.- 100 µg/ml	Weak activity	[49]
Phormium tenax J. R. Forst. et G. Forst.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 500 µg/ml	Active	[29]
Tulbaghia violacea Harv	South Africa	Bb	H_2O Ext. - 48 µg/ml	Inactive	[39]
	South Africa	Bb	EtOH Ext. - 48 µg/ml	Inactive	[39]
Loranthaceae					
Loranthus parasiticus L. Merr.	Singapore	EP	Hot H_2O Ext. - 25 µg/ml	Weak activity	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
Viscum coloratum (Kom.) Nakai.	South Korea	DRt	MeOH Ext. - 100 µg/ml	Inactive	[46]
Lycopodiaceae					
Lycopodium laterale R. Br.	New Zealand	AP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Lythraceae					
Woodfordia floribunda Salisb.	Indonesia	DFw + Lf	H_2O Ext. - **	Active	[51]
			MeOH Ext. - **	Active	[51]
	Singapore	Rh	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Magnoliaceae					
Magnolia fargesii Cheng	Singapore	FwB	Hot H_2O Ext. - 25 µg/ml	Active	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
Magnolia obovata Thunb.	Singapore	Bk	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Magnolia officinalis Rehder & E. H. Wilson	Singapore	Bk	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Malvaceae					
Hibiscus hamabo Sieb. et Zucc.	South Korea	DR	Lyophilized Ext. - 100 µg/ml	Weak activity	[49]
Plagianthus divaricatus J. R. & G. Forst.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Sida cordifolia L.	India	DRt	H_2O Ext. - 200 µg/ml	Inactive	[35]
Sida racemosa	Singapore	Fb	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]

(Table 1) contd…..

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Meliaceae					
Azadirachta indica A. Juss.	Sudan	CSLf	H_2O Ext. - 100 µg/ml	Inactive	[26]
Khaya senegalensis (Desr.) A. Juss.	Sudan	CSLf	H_2O Ext. - 100 µg/ml	Weak activity	[26]
Trichilia emetic A. Vahl.	Sudan	CSBk	H_2O Ext. - 100 µg/ml	Inactive	[26]
Menispermaceae					
Coscinium fenestratum (Gaertn.) Colebr.	India	DGl	H_2O Ext. - 200 µg/ml	Inactive	[35]
Sinomenium acutum (Thunb.) Rehd. & Wils.	South Korea	DEP	MeOH Ext. - 100 µg/ml	Inactive	[46]
Monimiaceae					
Hedycarya arborea J. R. Forst. et G. Forst.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Moraceae					
Ficus edelfeltii King	Singapore	Bk	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Ficus religiosa L.	India	DBk	H_2O Ext. - 200 µg/ml	Weak activity	[35]
Myoporaceae					
Myoporum laetum Forst. fil.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Myristicaceae					
Myristica fragrans Houtt.	India	DA	H_2O Ext. - 200 µg/ml	Weak activity	[35]
Myrsine australis (A.Rich.) Allan.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Myrtaceae					
Metrosideros excels Sol. ex Gaertn.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Syzygium cumini (L.) Skeels	India	DBk	MeOH Ext. - 200 µg/ml	Active	[35]
Syzygium maire (A.Cunn.) Sykes et Garn. Jones	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Oleaceae					
Ligustrum lucidum W.T. Aiton.	China	CSF	MeOH Ext. - 200 µg/ml	Strong activity	[45]
Nestegis apetala (Vahl.) L. Johnson	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Nestegis cunninghamii (Hook. F.) L. A. S. Johnson	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Onagraceae					
Oenothera biennis L.	New Zealand	Sd	EtOH (75%) Ext. - 50 µg/ml	Active	[29]
Orchidaceae					
Pterostylis oliveri Petrie	New Zealand	AP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Paeoniaceae					
Paeonia moutan Sims.	China	CSRt	H_2O Ext. - 20 µg/ml	Active	[45]
			MeOH Ext. - 200 µg/ml	Strong activity	[45]
	Singapore	RtBk	Hot H_2O Ext. - 25 µg/ml	Active	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
Phyllocladaceae					
Phyllocladus alpinus Hook. F.	New Zealand	Lf	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Phyllocladus trichomanoides D. Don.	New Zealand	Lf	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Pinaceae					
Pseudotsuga menziesii (Mirbel) Franco	New Zealand	Bk	EtOH (75%) Ext. - **	Active	[29]
Pittosporaceae					
Pittosporum anomalum Laing & Gourlay	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Pittosporum eugenioides Cunn.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]

(Table 1) contd…..

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Poaceae					
Andropogon muricatus Retz.	India	DRt	H_2O Ext. - 200 µg/ml	Inactive	[35]
Coix lacryma-jobi L.	Singapore	Sd	Hot H_2O Ext. - 25 µg/ml	Weak activity	[24]
Podocarpaceae					
Prumnopitys taxifolia (Banks & Sol. ex D. Don) de Laub.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Polygonaceae					
Polygonum cuspidatum Siebold & Zucc.	Singapore	Rh + Rt	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Polygonum multiflorum Thumb.	China	CSRt	MeOH Ext. - 200 µg/ml	Strong activity	[45]
Rheum palmatum L.	Singapore	Rh	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Rumex cyprius Murb.	Egypt	DF	**	Active	[48]
Polypodiaceae					
Drynaria fortune (Kunze) J. Sm.	Singapore	Rh	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
Portulacaceae					
Portulaca oleracea L.	Singapore	EP	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Primulaceae					
Samolus repens (J. R. Forst. & G. Forst.) Pers.	New Zealand	EP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Punicaceae					
Punica granatum L.	Singapore	RtBk	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Ranunculaceae					
Aconitum ferox Wall. ex Ser.	India	DT	H_2O Ext. - 200 µg/ml	Inactive	[35]
Cimicifuga heracleifolia Komar.	Singapore	Rh	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Clematis apiifolia DC.	South Korea	DEP	MeOH Ext. - 100 µg/ml	Inactive	[46]
Clematis chinensis L.	Singapore	Rt	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
	China	CSRt	H_2O Ext. - 200 µg/ml	Inactive	[45]
Clematis heracleifolia DC.	South Korea	DAP	MeOH Ext. - 100 µg/ml	Inactive	[46]
Coptis chinensis Franch. var. *chinensis*	Singapore	Rh	Hot H_2O Ext. - 250 µg/ml	Active	[24]
	China	CSRh	MeOH Ext. - 200 µg/ml	Strong activity	[45]
Nigella sativa L.	Egypt	DSd	**	Active	[48]
	India	DSd	H_2O Ext. - 200 µg/ml	Inactive	[35]
Pulsatilla chinensis (Bunge) Regel	Singapore	Rt	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Ranunculus chinensis Bunge.	South Korea	DRt	H_2O Ext. - 100 µg/ml	Inactive	[46]
Rhamnaceae					
Berchemia berchemiaefolia (Makino) Koidz.	South Korea	DBk	MeOH Ext. - 100 µg/ml	Active	[46]
Discaria toumatou Raoul.	New Zealand	Lf + Sm	EtOH(75%) Ext. - 50 µg/ml	Active	[29]
Sageretia theezans (Vahl) Brongn.	South Korea	DLf	Lyophilized Ext.-100 µg/ml	Active	[49]
Rosaceae					
Crataegus pinnatifida Bunge	South Korea	DLf	MeOH Ext. - 100 µg/ml	Active	[52]
		DSm	MeOH Ext. - 100 µg/ml	Active	[46]
Eriobotrya japonica Lindl.	South Korea	DFw	MeOH Ext. - 100 µg/ml	Inactive	[46]
Geum japonicum Thunb.	Singapore	EP	Hot H_2O Ext. - 250 µg/ml	Active	[24]
	Japan	EP	EtOAc Ext.. - 0.017 mg/ml	Active	[53]
			MeOH Ext. - 0.017 mg/ml	Active	[53]

(Table 1) contd…..

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Prunus armeniaca Linn.	Singapore	Sd	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Prunus mume Sieb. et Zucc.	Singapore	F	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Prunus persica (L.) Batsch.	Korea	Lf	MeOH Ext. - 100 µg/mL	Active	[40]
Prunus sargentii Rehder	Korea	Lf	MeOH Ext. - 100 µg/mL	Strong activity	[40]
		Sm	MeOH Ext. - 100 µg/mL	Active	[40]
Raphiolepis umbellate L.	South Korea	DSd	Lyophilized Ext.-100 µg/ml	Weak activity	[49]
Rosa acicularis Lindl.	Korea	Lf	MeOH Ext. - 100 ug/mL	Active	[40]
		Sm	MeOH Ext. - 100 ug/mL	Active	[40]
Rosa davurica Pall.	South Korea	DLf	H_2O Ext. - 100 µg/ml	Weak activity	[54]
		DPE	H_2O Ext. - 100 µg/ml	Inactive	[54]
		DR	H_2O Ext. - 100 µg/ml	Weak activity	[54]
		DS	H_2O Ext. - 100 µg/ml	Weak activity	[54]
Rosa maximowicziana Regel	Korea	Sm	MeOH Ext. - 100 µg/mL	Active	[40]
Rosa rugosa Thunb.	Korea	Rt	MeOH Ext. - 100 µg/mL	Strong activity	[40]
Rosa wichuraiana Crépin.	Korea	Sm	MeOH Ext. - 100 µg/mL	Active	[40]
Rubus cissoids A. Cunn.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Rubus corchorifolius L. f.	Korea	Lf	MeOH Ext. - 100 µg/mL	Active	[40]
Rubus crataegifolius Bunge	Korea	Sm	MeOH Ext. - 100 µg/mL	Active	[40]
Rubus fruticosus L.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Sorbus alnifolia Siebold & Zucc.) K. Koch	Korea	Sm	MeOH Ext. - 100 µg/mL	Active	[40]
Sorbus commixta Hedl.	South Korea	DLf + Tw	MeOH Ext. - 100 µg/ml	Weak activity	[46]
Stephanadra incisa (Thunb.) Zabel	Korea	Sm	MeOH Ext. - 100 µg/mL	Active	[40]
Rubiaceae					
Coprosma foetidissima J. R. et G. Forst.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Coprosma rhamnoides A. Cunn.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Nauclea latifoliai Smith	Sudan	CSF	H_2O Ext. - 100 µg/ml	Weak activity	[26]
Nertera depressa Gaertn.	New Zealand	EP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Oldenlandia diffusa (Willd.) Roxb.	Singapore	EP	Hot H_2O Ext. - 25 µg/ml	Weak activity	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
	China	CSEP	H_2O Ext. - 200 µg/ml	Strong activity	[45]
Serissa japonica (Thunb.) Thunb.	South Korea	Lf	Lyophilized Ext.-100 µg/ml	Inactive	[49]
Rutaceae					
Aegle marmelos L. Correa	India	DBk	H_2O Ext. - 200 µg/ml	Inactive	[35]
Dictamnus dasycarpus Turcz.	South Korea	DRt	MeOH Ext. - 100 µg/ml	Inactive	[46]
	Singapore	RtBk	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Euodia rutaecarpa (Juss.) Benth.	Singapore	F	Hot H_2O Ext. - 25 µg/ml	Inactive	[24]
Haplophyllum tuberculatum (Forssk.) A. Juss.	Sudan	CSAP	H_2O Ext. - 100 µg/ml	Weak activity	[26]
		CSRt	H_2O Ext. - 100 µg/ml	Weak activity	[26]
Melicope simplex A. Cunn.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Phellodendron amurense Rupr.	Singapore	Bk	Hot H_2O Ext. - 25 µg/ml	Active	[24]
Zanthoxylum bungeanum Maxim.	Singapore	Fp	Hot H_2O Ext. - 25 µg/ml	Weak activity	[24]
Zanthoxylum schinifolium Sieb. et Zucc.	Singapore	Fp	Hot H_2O Ext. - 250 µg/ml	Active	[24]

(Table 1) contd…..

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Salvadoraceae					
Salvadora persica L.	Sudan	CSLf	H_2O Ext. - 100 µg/ml	Inactive	[26]
		CSSd	H_2O Ext. - 100 µg/ml	Inactive	[26]
Santalaceae					
Exocarpus bidwillii Hook. F.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Sapindaceae					
Xanthoceras sorbifolia Bunge	China	Wd	MeOH Ext. - 200 µg/ml	Active	[55]
Schisandraceae					
Schisandra chinensis (Turcz.) Bail.	Singapore	F	Hot H_2O Ext. - 25 µg/ml	Weak activity	[24]
Scrophulariaceae					
Hebe canterburiensis (J. B. Armstr.) L. B. Moore	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Hebe glaucophylla (Cockayne) Cockayne	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Hebe salicifolia (G. Forst.) Pennell	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Hebe subsimilis (Cockayne) Cockayne & Allan var. *astonii* (Petrie) Ashwin	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Parahebe diffusa (Hook. F.) W. R. B. Oliv.	New Zealand	EP	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Simaroubaceae					
Brucea javanica (Linn.) Merr.	Singapore	Sd	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Smilacaceae					
Smilax corbularia Kunth	Thailand	DEP	H_2O Ext. - 100 µg/ml	Inactive	[41]
			EtOH Ext. - 100 µg/ml	Inactive	[41]
Smilax glabra Roxb.	Thailand	DEP	H_2O Ext. - 100 µg/ml	Inactive	[41]
			EtOH Ext. - 100 µg/ml	Inactive	[41]
Solanaceae					
Datura stramonium L.	Egypt	DSd	**	Active	[48]
Solanum dubium Fresen	Sudan	CSF	H_2O Ext. - 100 µg/ml	Inactive	[26]
Sterculiaceae					
Helicteres isora Linn	Indonesia	DF	H_2O Ext. - **	Inactive	[28]
Theaceae					
Camellia japonica L.	South Korea	DPE	Butanol Ext. - 100 µg/ml	Active	[49]
Stewartia koreana Nakai ex Rehd.	South Korea	DSd	MeOH Ext. - 100 µg/ml	Active	[46]
Tiliaceae					
Entelea arborescens R. Br.	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Tilia amurensis Ruprecht	South Korea	DLt	MeOH Ext. - 100 µg/ml	Active	[46]
Typhaceae					
Typha angustata L.	South Korea	DAP	MeOH Ext. - 100 µg/ml	Active	[46]
Valerianaceae					
Patrinia villosa Juss	Singapore	Rt	Hot H_2O Ext. - 25 µg/ml	Weak activity	[24]
			Hot H_2O Ext. - 250 µg/ml	Active	[24]
Verbenaceae					
Pygmaeopremna herbacea Roxb.	Thailand	DEP	H_2O Ext. - 100 µg/ml	Inactive	[41]
	Thailand	DEP	EtOH Ext. - 100 µg/ml	Inactive	[41]
Violaceae					
Viola yedoensis Makino	China	CSEP	H_2O Ext. - 200 µg/ml	Active	[45]
			MeOH Ext. - 200 µg/ml	Active	[45]

(Table 1) contd…..

Family and Botanical Name	Place	Part of Plant	Type of Extract and Dose	Activity	Refs.
Winteraceae					
Pseudowintera colorata (Raoul) Dandy	New Zealand	Lf + Sm	EtOH (75%) Ext.- 50 µg/ml	Active	[29]
Zingiberaceae					
Alpinia officinarum Hance	Singapore	Rh	Hot H_2O Ext. - 250 µg/ml	Active	[24]
Zygophyllaceae					
Balanites aegyptiaca (L.) Delile	Sudan	CSBk	H_2O Ext. - 100 µg/ml	Weak activity	[26]
		CSF	H_2O Ext. - 100 µg/ml	Weak activity	[26]
Tribulus terrestris Linn	Sudan	CSAP	H_2O Ext. - 100 µg/ml	Inactive	[26]

**Incomplate date derived from an abstract; AP = Aerial Parts; Bb = Bulb; Bk = Bark; Cs = Corms; CSAF = Commercial Sample of Aerial Fungus; CSAP = Commercial Sample of Aerial Parts; CSBk = Commercial Sample of Bark; CSEP = Commercial Sample of Entire Plant; CSESd = Commercial Sample of Entire Seed; CSF = Commercial Sample of Fruit; CSFb = Commercial Sample of Fruitbody; CSFwH = Commercial Sample of Flower Heads; CSFwB = Commercial Samples of Flower Buds; CSLf = Commercial Sample of Leaf; CSP = Commercial Sample of Pod; CSRh = Commercial Sample Rhizome; CSRt = Commercial Sample of Root; CSSd = Commercial Sample of Seed; CSSm = Commercial Sample of Stem; DA=Dried Arillus; DAP = Dried Aerial Parts; DBk = Dried Bark; DEP = Dried Entire Plant; DF = Dried Fruit; DFb = Dried Fruitbody; DFp = Dried Fruitpell; DFw = Dried Flowers; DGl = Dried Galls; DLf = Dried Leaf; DLt = Dried Latex; DPE = Dried Pericarp; DRE = Dried Resin; DRh = Dried Rhizome; DRt = Dried Root; DSd = Dried Seed; DSm = Dried Stem; DSmBk = Dried Stembark; DT = Dried Tuber; EP = Entire Plant; F = Fruit; Fb = Fruitbody; Fd = Frond; Fp = Fruitpell; Fw = Flowers; FwB = Flower Buds; Gl = Galls; Lf = Leaf; Rh = Rhizome; Rt = Root; RtBk = Rootbark; Sd = Seed; Sm = Stem; Tw = Twigs; Wd = Wood; Lf + Sm = Leaf + Stem; Rh + Rt = Rhizome + Root.

Most of protease assays were carried out based on the cleavage of a peptide substrate, to simulate a natural processing site between the matrix and capsid polypeptides of *gag* precursor for HIV-1 protease. Enzymes and substrates reacted over appropriated conditions such as temperature, pH, and medium. After reaction the hydrolysate and remained substrate were quantified and analyzed by HPLC or fluorogenic assay [24-26].

Plants were studied mainly in countries of Asia (China, Japan, Indonesia, India, South Korea and Singapore) and a few in America (Panama), Africa (Egypt and Sudan) and Oceania (New Zealand). Many of these countries are known by their traditional medicine, which made them attractive for search of natural products with anti-HIV activity [27-29].

In searching for natural products with anti-HIV properties, Xu *et al.* [24] selected and examined typical traditional medicines from China, Japan and Indonesia for possible inhibitory activity of their aqueous extracts against HIV-1 protease, and as result over 77% of them were active in the tests performed. One interesting observation was that different species of plant within a genus can vary in their effects, e.g. within the *Magnolia* genus, *M. fargesii* was active against HIV-1 protease, whereas *M. obovata* and *M. oficinalis* were not. Among *Terminalia* species, *T. arjuna* and *T. chebula* were active while *T. belerica* was inactive, indicating that inhibitors of HIV-1 protease are quite widely distributed among various crude extract of plants. Although *T. arjuna* was active at concentration of 250 µg/ml, at 25 µg/ml it was not, confirming that a plant can or cannot show activity depending on the concentration of the extract.

Aqueous extracts of most crude drugs are likely to contain many phenolic compounds and tannins. Some plants, such as *Geum japonicum, Punica granatum, Rhus javanica, T. arjuna, T. chebula*, *Woodwardia orientalis* and *W. unigemmata* have been reported to contain tannins and other phenolic compounds which have known antiviral properties and thus may be responsible for the activity of these plants [30-34].

Hussein *et al.* [26] investigated for the first time plants used in the folk medicine in Sudan targeting their inhibitory effects on HIV-1 replication and HIV-1 protease enzyme. Although these plants had never been investigated for their antiviral activity, 19 extracts showed inhibitory effects on the viral replication and 5 extracts showed considerable inhibitory effects against HIV-1 protease. The antiviral effect of the other plants may reflect an inhibitory activity on enzymes other than the protease or through inhibition of other essential steps in the viral life cycle. The authors also found that phenolic compounds isolated from *Maytenus senegalensis*, especially those glycosylated showed inhibitory activity, suggesting that the glucose moiety may have a potentiating effect on the activity of these compounds against HIV-1 protease enzyme.

India is known for Ayurvedic traditional medicine and it is used by several people in the world to treat various diseases. In view of its importance in therapy, Kusumoto *et al.* [35] made a screening of the inhibitory effects of plants used in Ayurveda on HIV-1 protease. Plants as *Areca catechu*, *Eugenia jambolana*, *Saraca indica* and *Terminalia arjuna* inhibited the HIV-1 protease activity by more than 70% at a concentration of 0.2 mg/ml. *A. catechu* showed the most potent inhibition and its isolated procyanidin arecatannin B1 is one of the compounds possibly responsible for the inhibitory activity of this plant.

Despite the great biodiversity of the American continent, we only found one plant studied. *Cordia spinescens* (Boraginaceae) used in Central America to relieve fever and headache [36]. A leave extract of this plant presented potential protease inhibition [37]. The magnesium lithospermate, calcium rosmarinate and magnesium rosmarinate compounds were isolated and identified as potent reverse transcriptase inhibitors. However, these compounds showed weak protease activity, indicating that substances bearing a protease inhibitory effect still remained in the fractions and need to be isolated and tested [38].

A screening of New Zealand plant extracts for inhibitory activity against HIV-1 protease was made for Wan *et al.* [29]. *Pseudotsuga menziesii* was one of the active plants and

a polyphenol compound was the causative compound for the inhibitory activity. These data demonstrated once more the importance of this class of metabolites on HIV-1 protease inhibition.

New studies are being made now a day. Several reports have identified plants and isolated compounds as potential inhibitors of the enzyme HIV-1 protease [39-44]. In this article we reviewed the studies of many plant extracts able to inhibit the HIV-1 protease, some of which presented strong activity. In addition, phenolic compounds isolated from some of the studied plants also showed to be active, which emphasizes the importance of isolating and testing new structures on HIV-1 protease. Thus, research with natural products may provide new therapeutic agents for AIDS treatment.

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