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Revisão

Natural products inhibitors of the enzyme acetylcholinesterase

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RESUMO: "Produtos naturais inibidores da enzima acetilcolinesterase". A Doença de Alzheimer (DA) é uma patologia neurodegenerativa, progressiva, que afeta principalmente a população idosa, responsável por 50-60% dos casos de demência em pessoas com mais de 65 anos de idade. Os principais sintomas associado a DA envolve deficiência orgânica cognitiva, principalmente perda de memória. Outras características associadas com os estágios avançados de DA inclui déficit na linguagem, depressão, problemas de comportamento, inclusive agitação, alterações de humor e psicose.Um dos mais promissores caminhos para tratar esta doença é aumentar o nível de acetilcolina no cérebro usando inibidores da acetilcolinesterase (AChE). Este trabalho teve como objetivo revisar a literatura das plantas e substâncias encontradas nas plantas, inibidores da enzima acetilcolinesterase. Foram levantadas 309 plantas e 260 substâncias isoladas de plantas que foram classificados em grupos químicos adequados, os modelo testados, e suas atividades. Foram consultados 175 referências.

Unitermos: Inibidores da Acetilcolinesterase, AchE, doença de Alzheimer, distúrbios neurodegenetivos, plantas medicinais, produtos naturais, revisão.

ABSTRACT: Alzheimer's disease (AD) is a progressive, neurodegenerative pathology that primarily affects the elderly population, and is estimated to account for 50-60% of dementia cases in persons over 65 years of age. The main symptoms associated with AD involve cognitive dysfunction, primarily memory loss. Other features associated with the later stages of AD include language deficits, depression, behavioural problems including agitation, mood disturbances and psychosis. One of the most promising approaches for treating this disease is to enhance the acetylcholine level in the brain using acetylcholinesterase (AChE) inhibitors. The present work reviews the literature on plants and plant-derived compounds inhibitors of enzyme acetylcholinesterase. The review refers to 309 plant extracts and 260 compounds isolated from plants, which are classified in appropriate chemical groups and model tested, and cites their activity. For this purpose 175 references were consulted.

Keywords: Acetylcholinesterase inhibitors, AChE, Alzheimer's disease, neurodegenerative disorders, medicinal plants, natural products, review.

INTRODUCTION

The enzyme acetylcholinesterase (AChE) catalyses the hydrolysis of the ester bound of acetylcholine (ACh) to terminate the impulse transmitted action of ACh through cholinergic synapses (Stryer, 1995). Although the basic reason of Alzheimer's disease (AD) is not clear so far, AD is firmly associated with impairment in cholinergic transmission. A number of AChE inhibitors have been considered as candidates for the symptomatic treatment of AD as the most useful relieving strategy (Howes et al., 2003).

Reversible inhibitors of cholinesterase are currently used in clinical trials examining the treatment of Alzheimer's disease. Anticholinesterase may interact with the central cholinergic system to improve memory and cognitive deficits of the patients by diminishing the breakdown of acetylcholine at the synaptic site in the brain. However, the therapeutic window is small, and testing of the inhibitory effect on acetylcholinesterase (AChE) in erythrocytes has been proposed as a guide to the efficacy and safety of putative therapies.

Alzheimer's disease is a progressive degenerative neurologic disorder resulting in impaired memory and behavior. Epidemiological data indicate a potentially considerable increase in the prevalence of the disease over the next two decades (Johnson et al., 2000). AD affects up to 5% of people over 65 years, rising to 20% of those over 80 years (Camps et al., 2000a). Most treatment strategies have been based on the cholinergic hypothesis which postulated that memory impairments in patients suffering from this disease result from a

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deficit of cholinergic function in brain. Cholinergic neurotransmission is specially affected in patients with Alzheimer's disease. One of the most promising approaches for treating this disease is to enhance the acetylcholine level in brain using acetylcholinesterase inhibitors (Enz et al., 1993). Several AChE inhibitors are being investigated for the treatment of Alzheimer's disease. However, only tacrine (**1**), donezepil (**2**), rivastigmine (**3**) and galanthamine (**4**) have been approved by the Food and Drug Administration in the United States (Zarotsky et al., 2003). Among the other strategies under investigation, monoamine oxidase B (MAO-B) inhibitors have also been proposed for the treatment of AD. Recent studies have shown that MAO-B activity can increase up to 3-fold in the temporal, parietal and frontal cortex of AD patients compared with controls. This increase in MAO-B activity produces an elevation of brain levels of hydroxyl radicals, which has been correlated with the development of Aβ plaques. Aβ is the main component of the senile plaques found in AD brains and any compound able to inhibit its aggregation might be regarded as potentially useful in the treatment of the disease (Bruhlmann et al., 2001).

Nature is a rich source of biological and chemical diversity. The unique and complex structures of natural products cannot be obtained easily by chemical synthesis. A number of plants in the world have been used in traditional medicine remedies. Huperzine A (**5**) is a natural compound first isolated from Chinese medicine *Huperzia serrata* (Thumb.) in 1986, is a potent, reversible and selective inhibitor of AChE.

In a previous paper this research group has reviewed crude plant extracts and chemically defined molecules with potential antitumor activity for mammary (Moura et al., 2001), cervical (Moura et al., 2002) and ovarian neoplasias (Silva et al ., 2003), as inhibitors of HMG CoA reductase (Gonçalves et al., 2000), central analgesic activity (Almeida et al., 2001), employed in prevention of osteoporosis (Pereira et al., 2002), for the treatment of Parkinson's disease (Morais, 2003), with antileishmanial (Rocha et al., 2005), hypoglycaemic (Barbosa-Filho et al., 2005) and antiinflammatory activity (Falcão et al., 2005, Barbosa-Filho et al., 2006). The present work reviews the literature on plants and plant-derived compounds inhibitors of enzyme acetylcholinesterase.

MATERIALS AND METHODS

The keywords used for this review were medicinal plants, natural products, and acetylcholinesterase inhibitors. The search perfound using Chemical Abstracts, Biological Abstracts and the data bank of the University of Illinois at Chicago, NAPRALERT (Acronym for NAtural PRoducts ALERT), updated to December 2004. The references obtained were later consulted.

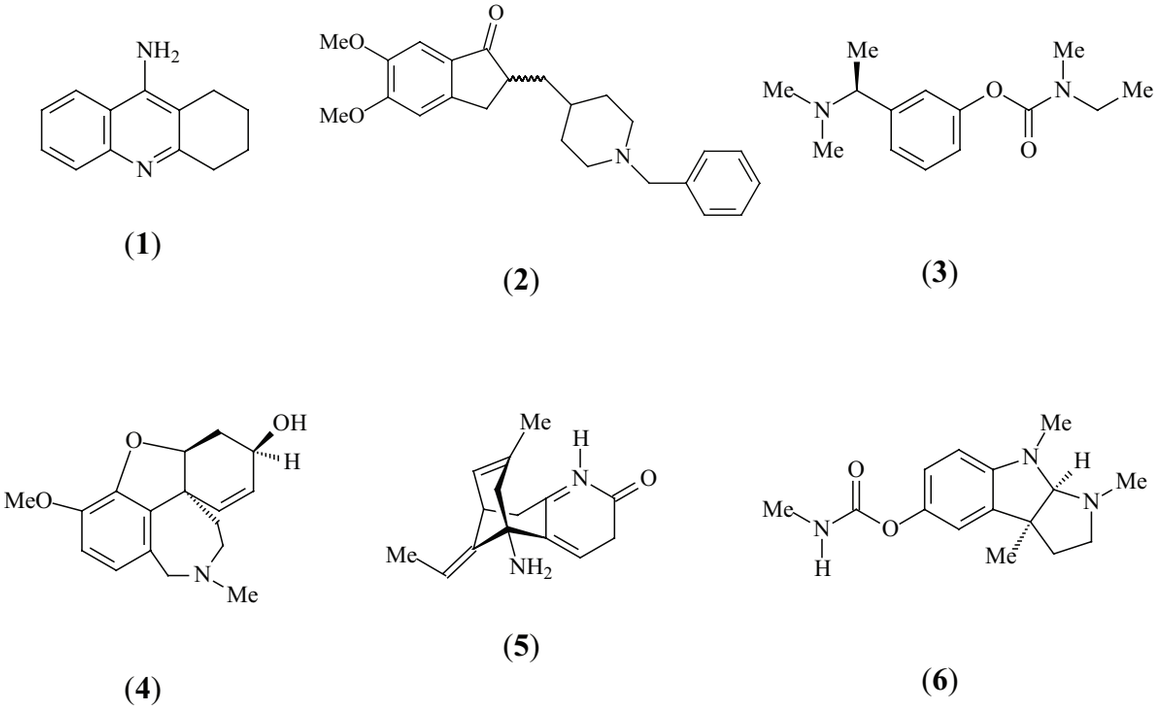

Figure 1. Representative examples of synthetic **(1-3)** and natural **(4-6)** products inhibitors of the enzyme acetylcholinesterase

RESULTS AND DISCUSSION

Consultation of various types of literature sources resulted in elaboration of a list of natural products (Table 1 and 2) evaluated specifically for acetylcholinesterase inhibition. It should be noted that most of references cited are not first-hand observations, but secondary sources. For details on the models or mechanism-based bioassays utilized for selecting plant extracts and pure compounds against acetylcholinesterase, the original references should be consulted.

Plant extracts inhibitors of acetylcholinesterase enzyme

Acetylcholine is a neurotransmitter inhibited primarily by acetylcholinesterase (AChE) and secondly by butyrylcholinesterase (BChE), considered to play a role in the pathology of AD (Hebert et al., 1995). Despite the unknown etiology of AD, elevation of acetylcholine amount through AChE enzyme inhibition has been accepted as the most effective treatment strategy against AD. Therefore, AChE inhibitors have become the remarkable alternatives in treatment of AD. However, the present drugs (tacrine, rivastigmine and donezepil) with AChE inhibitory activity possess some side effects (Schneider, 2001). Consequently, it is compulsory to develop new drugs in order to combat AD (Viegas-Junior et al., 2004).

The history of drug discovery showed that plants are highly rich sources in the search for new active compounds and they have become a challenge to modern pharmaceutical industry. Many synthetic drugs owe their origin to plant-based complementary medicine. Since AD, one of the most common cause of death worldwide, has become a threaten to public health, new treatment strategies based on medicinal plants have been focused (Howes et al., 2003; Orhan et al., 2004).

A recent study with Brazilian plants showed excellent results for the species *Amburana cearensis, Lippia sidoides, Paullinia cupana, Plathymiscium floribundum* and *Solanum asperum* (Trevisan; Macedo, 2003). Since the plants have been used in treatment of memory disfunction in some folk medicines since centuries the present study presents a review of 309 plants belong to 92 botanical families tested against acetylcholinesterase inhibition. The plants are listed in Table 1, in alphabetical order of their family, scientific name, country, plant part used, type of extract, dose/ concentration, result and references.

Chemically-defined molecule as inhibitors of acetylcholinesterase enzyme

The prototype for the centrally acting AChE inhibitors was tacrine, the first drug to be approved in the United States (Cognex®) for the treatment of AD. However, its severe side effects such hepatotoxicity and gastrointestinal upset, represent an important drawback (Camps et al., 2000). The results of the studies on tacrine spurred the development of other centrally acting reversible AChE inhibitors, such as the recently marketed galanthamine (Nivalin®), donezepil (Aricept®) and rivastigmine (Exelon®) or the natural product (-)-huperzine A, which is currently undergoing extensive clinical trials, showing considerable promise for the palliative treatment of AD.

Galanthamine, a long acting, selective, reversible and competitive AChE inhibitor, is considered to be more effective in the treatment of AD and to have fewer limitations (Rhee et al., 2001). Recently it has reported wich because of bioavailability problems and possible side-effects, there still is great interest in finding better AChE inhibitors.

Donezepil was developed in order to overcome the disadvantages of physostigmine and tacrine, and later approved by the FDA for treatment of AD. It is highly selective for acetylcholinesterase with a significantly lower affinity for butyrylcholinesterase (Racchi et al., 2004).

Rivastigmine is a carbamilating, pseudo-irreversible acetylcholinesterase inhibitor which in preclinical biochemical studies has shown a significant nervous system selectivity (Racchi et al., 2004).

(-)-Huperzine A is a natural compound first isolated from Chinese medicine *Huperzia serrata* (Thumb.) in 1986. It is a potent, reversible and selective inhibitor of AChE with a rapid absorption and penetration into the brain in animal tests. Compared to tacrine, physostigmine (**6**), galanthamine and donezepil, huperzine A possesses a longer duration of action and higher therapeutic index, and the peripheral cholinergic side effects are minimal at therapeutic doses (Camps et al., 2000; Li et al., 2004). Huperzine A possesses higher selectivity and has almost no effect on butyrylcholinesterase. In China, huperzine A has already been approved as a palliative drug for AD (Högenauer et al., 2001).

We founded 260 chemically defined natural molecules reported in the literature, which have been evaluated for acetylcholinesterase inhibition. The compounds tested, which have been isolated and identified belong to the classes of alkaloids (139), monoterpenes (27), coumarins (18), triterpenes (17), flavonoids (14), benzenoids (13), diterpenes (8), oxygen heterocycles (5), sesquiterpenes (5), stilbenes (3), lignans (2), sulfur compounds (2), proteids (2), polycyclic (1), quinoid (1), benzoxazinone (1), carotenoid (1) and alycyclic (1).

CONCLUSION

The present work shows that most of the plant extracts tested showed inhibitory activity against acetylcholinesterase and they could be considered for

further studies in the treatment of AD. In particular, the species belonging to Amaryllidaceae, Apiaceae, Asteraceae, Fabaceae and Fumariaceae were the most studied. Since most of acetylcholinesterase inhibitors are known to contain nitrogen, the higher activity of these extracts may be due to their rich alkaloidal content. The alkaloids are the major compounds isolated from this species and shows inhibitory activity for the acetylcholinesterase. More research is needed to further explore the actions of this alkaloids in the search of promising treatment for AD.

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Table 1. Plant extracts showing acetylcholinesterase inhibition

Family and botanical name	Origin	Part used	Extract	Dose/Concent.	Result	References
Acanthaceae						
Justicia gendarussa	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Trianthema portulacastrum	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Adiantaceae						
Adiantum capillus-veneris	India	Leaf/Stem/Root	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Agavaceae						
Dracaena deremensis	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Polianthes tuberosa	USA	Dried bulb	MeOH	Variable	Inactive	Rhee et al., 2001
			Toluene	Variable	Inactive	Rhee et al., 2001
Alismataceae						
Alisma orientale	China	Root	EtOH-H_2O 50%	0.02 mg/mL	Inactive	Howes et al., 1999
			H_2O ext.	9.5 mcg/mL	Inactive	Howes et al., 1999
Alisma plantago	South Korea	Rhizome	MeOH	Not stated	Weak activity	Lee et al., 1997
Amaranthaceae						
Achyranthes japonica	South Korea	Root	MeOH	Not stated	Active	Lee et al., 1997
Amaryllidaceae						
Amaryllis belladona	USA	Dried bulb	MeOH	Variable	Active	Rhee et al., 2001
			Toluene	Variable	Active	Rhee et al., 2001
Chlidanthus fragrans	USA	Dried bulb	MeOH	Variable	Active	Rhee et al., 2001
			Toluene	Variable	Active	Rhee et al., 2001
Crinum powellii	Netherlands	Dried bulb	EtOH 70%	10.0 mg/mL	Active	Rhee et al., 2003
	USA	Dried bulb	MeOH	Not stated	Active	Rhee et al., 2001
			Toluene	Variable	Active	Rhee et al., 2001
	Switzerland	Fresh bulb	EtOH 95%	15.0 mcg/disc	Active	Marston et al., 2002
Eucharia amazonica	Netherlands	Bulb	EtOH 70%	10.0 mg/mL	Active	Rhee et al., 2003
		Dried bulb	MeOH	Variable	Active	Rhee et al., 2001
			Toluene	Variable	Active	Rhee et al., 2001
Galanthus nivalis	Netherlands	Dried bulbs	EtOH 70%	10.0 mg/mL	Active	Rhee et al., 2003
	Switzerland	Fresh bulbs	EtOH 95%	15.0 mcg/disc	Active	Marston et al., 2002
Habranthus robustus	USA	Dried bulb	MeOH	Variable	Inactive	Rhee et al., 2001
			Toluene	Variable	Inactive	Rhee et al., 2001
Hippeastrelia sp	USA	Dried bulb	MeOH	Variable	Weak activity	Rhee et al., 2001
			Toluene	Variable	Weak activity	Rhee et al., 2001
Hymenocallis festalis	USA	Dried bulb	MeOH	Variable	Active	Rhee et al., 2001
			Toluene	Variable	Weak activity	Rhee et al., 2001
Hymenocallis sp	USA	Dried bulb	MeOH	Variable	Weak activity	Rhee et al., 2001
			Toluene	Variable	Inactive	Rhee et al., 2001
Ismene festalis	Switzerland	Fresh bulb	EtOH 95%	15.0 mcg/disc	Active	Marston et al., 2002
Leucojum vernum	Switzerland	Entire plant	EtOH 95%	15.0 mcg/disc	Active	Marston et al., 2002
Narcissus pseudo-narcissus	Switzerland	Fresh bulb	EtOH 95%	15.0 mcg/disc	Active	Marston et al., 2002

Narcissus tazzeta	USA	Dried bulb	MeOH	Variable	Inactive	Rhee et al., 2001
Nerine bowdenii	Netherlands	Dried bulb	EtOH 70%	10.0 mg/mL	Active	Rhee et al., 2003
	USA	Dried bulb	MeOH	Variable	Active	Rhee et al., 2001
			Toluene	Variable	Active	Rhee et al., 2001
	Switzerland	Dried bulb	Fresh bulb	15.0 mcg/disc	Active	Marston et al., 2002
Rhodophiala bifida	USA	Dried bulb	MeOH	Variable	Inactive	Rhee et al., 2001
			Toluene	Variable	Inactive	Rhee et al., 2001
Sprekelia formosissima	USA	Dried bulb	MeOH	Variable	Inactive	Rhee et al., 2001
			Toluene	Variable	Inactive	Rhee et al., 2001
		Fresh bulb	EtOH 95%	15.0 mcg/disc	Inactive	Marston et al., 2002
Zephyranthes candida	USA	Dried bulb	MeOH	Variable	Weak activity	Rhee et al., 2001
Anacardiaceae						
Anacardium occidentale	Brazil	Bark	EtOH	2.3 mg/mL	Inactive	Trevisan; Macedo, 2003
Mangifera indica	India	Leaf	EtOH	2 mm sl	Inactive	Gupta et al., 1997
Annonaceae						
Polyalthia longifolia	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Apiaceae						
Angelica gigas	South Korea	Root	MeOH	Not stated	Inactive	Lee et al., 1997
			MeOH	100.0 mcg/mL	Active	Khang et al., 2001
Angelica sinensis	South Korea	Root	Dichloromethane	200.0 mcg/mL	Active	Park et al., 1996
Anthriscus sylvestris	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
Bupleurum chinense	China	Entire plant	Saponin fraction	Not stated	Active	Wu and yu, 1984
Bupleurum falcatum	South Korea	Root	MeOH	Not stated	Inactive	Lee et al., 1997
Bupleurum scorzonerifolium	South Korea	Root	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Centella asiatica	India	Leaf	EtOH-H_2O 50%	0.05 mg/mL	Active	Howes et al., 1999
Cnidium officinale	South Korea	Rhizome	MeOH	Not stated	Active	Lee et al., 1997
Daucus carota	India	Root	EtOH	2 mm sl	Inactive	Gupta et al., 1997
Foeniculum vulgare	South Korea	Fruit	MeOH	Not stated	Weak activity	Lee et al., 1997
Glehnia littoralis	South Korea	Root	MeOH	Not stated	Inactive	Lee et al., 1997
Ledebouriella seseloides	South Korea	Not specified	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Ligusticum wallichii	South Korea	Rhizome	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Notopterygium incisum	South Korea	Root	Dichloromethane	200.0 mcg/mL	Active	Park et al., 1996
Ostericum koreanum	South Korea	Root	MeOH	Not stated	Inactive	Lee et al., 1997
Thevetia peruviana	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Apocynaceae						
Apocynum lancifolium	Not stated	Leaf	EtOH-H_2O 50%	0.05 mg/mL	Active	Howes et al., 1999
Catharanthus roseus	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Ervatamia coronaria	Thailand	Root	MeOH	0.1 mg/mL	Weak activity	Ingkaninan et al., 2003
Araceae						
Colocasia esculenta	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Pinellia ternata	South Korea	Tuber	MeOH	Not stated	Weak activity	Lee et al., 1997
			MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Philodendron imbe	Brazil	Leaf	Hexane:$CHCl_3$	1.4 mg/mL	Inactive	Trevisan; Macedo, 2003

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Verbesina diversifolia	Brazil	Flower	EtOH	1.6 mg/mL	Inactive	Trevisan; Macedo, 2003
Vernonia conyzoides	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Bombacaceae						
Bombax ceiba	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Boraginaceae						
Auxemma glazioviana	Brazil	Stem	$CHCl_3$	2.5 mg/mL	Active	Trevisan; Macedo, 2003
			EtOAc	0.6 mg/mL	Inactive	Trevisan; Macedo, 2003
Cordia piauhiensis	Brazil	Root	$CHCl_3$	2.7 mg/mL	Inactive	Trevisan; Macedo, 2003
Heliotropium ramosissimum	Iraq	Aerial parts	Acid-EtOH	0.4 mg/mL	Active	Mahmoud et al., 1987
Lithospermum erythrorhizon	South Korea	Root	MeOH	Not stated	Inactive	Lee et al., 1997
Burseraceae						
Commiphora wightii	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Protium heptaphyllum	Brazil	Resin	Hexane	3.3 mg/mL	Active	Trevisan; Macedo, 2003
		Essential oil	-	17 mg/mL	Active	Trevisan; Macedo, 2003
Campanulaceae						
Codonopsis pilosula	China	Root	EtOH-H_2O 50%	0.3 mg/mL	Inactive	Howes et al., 1999
Platycodon grandiflorum	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
		Root	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Cannabaceae						
Cannabis sativa	South Korea	Seed	MeOH	Not stated	Weak activity	Lee et al., 1997
	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Caprifoliaceae						
Lonicera japonica	South Korea	Flowers	MeOH	0.5 mg/mL	Weak activity	Lee et al., 1997
Sambucus nigra	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Caricacaceae						
Carica papaya	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Caryophyllaceae						
Stellaria media	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Celastraceae						
Celastrus paniculatus	India	Seed oil	Seed oil	200 mg/kg	Inactive	Gattu et al., 1997
Clavicipitaceae						
Cordyceps scarabaeicola	South Korea	Pericarp+Seeds	Lyophilized	Not stated	Inactive	Yu et al., 2003
Combretaceae						
Quisqualis indica	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Commelinaceae						
Tradescantia virginiana	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Convolvulaceae						
Evolvulus nummularius	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Ipomoea nil	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Crassulaceae						
Kalanchoe pinnata	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Cucurbitaceae						
Mormodica charantia	Brazil	Stem	Hexano	1.5 mg/mL	Inactive	Trevisan; Macedo, 2003

Trichosanthes kirilowii	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
Cupressaceae						
Biota orientalis	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Cycadaceae						
Cycas revoluta	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Cyperaceae						
Cyperus rotundus	South Korea	Rhizome	MeOH	Not stated	Weak activity	Lee et al., 1997
Scirpus fluviatilis	South Korea	Rhizome	MeOH	Not stated	Weak activity	Lee et al., 1997
Dioscoreaceae						
Dioscorea batatas	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
Ephedraceae						
Ephedra foliata	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Ephedra sinica	South Korea	Aerial parts	MeOH	0.1 mg/mL	Weak activity	Lee et al., 1997
Equisetaceae						
Equisetum ramosissimum	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Euphorbiaceae						
Acalypha indica	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Codiaeum variegatum	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Croton urucunama	Brazil		Latex	1.5 mg/mL	Active	Trevisan; Macedo, 2003
Dalechampia fernanendesii	Brazil	Leaf + Fruit	EtOH	0.6 mg/mL	Inactive	Trevisan; Macedo, 2003
Euphorbia hirta	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Euphorbia milii	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Euphorbia neriifolia	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Euphorbia pulcherrima	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Euphorbia royleana	India	Fresh latex	Latex	Variable	Active	Sing and Agarwal, 1984
Jatropha integerrima	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Phyllanthus fraternus	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Putranjiva roxburghii	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Ricinus communis	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Securinega suffruticosa	South Korea	Leaf	Alkaloid fract	IC_{50} 27.3 mcg/mL	Active	Jang et al., 2003
			H_2O ext.	IC_{50} >80 mcg/mL	Inactive	Jang et al., 2003
			MeOH	IC_{50} 49.5 mcg/mL	Active	Jang et al., 2003
Fabaceae						
Aeschynomene indica	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Albizia julibrissin	South Korea	Bark	MeOH 80%	200.0 mcg/ml	Inactive	Park et al., 1996
Amburana cearensis	Brazil	Stem bark	EtOH	2.3 mg/mL	Active	Trevisan; Macedo, 2003
Astralagus membranaceus	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
		Root	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Bauhinia chyilantha	Brazil	Leaf	EtOH	1 mg/mL	Inactive	Trevisan; Macedo, 2003
Bowdichia virgilioides	Brazil	Bark	Hexane	0.6 mg/mL	Inactive	Trevisan; Macedo, 2003
Butea superba	Thailand	Rootbark	MeOH	0.1 mg/mL	Weak activity	Ingkaninan et al., 2003
Caesalpinia pulcherrima	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Caesalpinia sappan	South Korea	Wood	MeOH	0.1 mg/mL	Weak activity	Lee et al., 1997

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Caragana chamlagu	South Korea	Root	MeOH	Not stated	Active	Sung et al., 2002
Cassia fistula	Thailand	Root	MeOH	0.1 mg/mL	Weak activity	Ingkaninan et al., 2003
Cassia occidentalis	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Cassia siamea	Thailand	Leaf	H_2O soluble fraction	IC_{50} 1.31 mg/mL	Active	Permtermsin et al., 2001
Crotalaria juncea	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Dolichos lablab	South Korea	Seed	MeOH	Not stated	Weak activity	Lee et al., 1997
Glycine max	South Korea	Seed	MeOH	Not stated	Active	Lee et al., 1997
	Italy	Seed oil	Seed oil	15% of diet	Inactive	Salvati et al., 1996
Glycyrrhiza uralensis	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
Leucaena leucocephala	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Lonchocarpus sericeus	Brazil	Stem bark	EtOH	2.5 mg/mL	Inactive	Trevisan; Macedo, 2003
Mimosa acustipula	Brazil	Stem bark	EtOH	1.8 mg/mL	Active	Trevisan; Macedo, 2003
Mimosa pudica	India	Root	EtOH 100%	100.0 mcg/mL	Inactive	Mahanta; Mukherjee, 2001
			H_2O ext.	100.0 mcg/mL	Active	Mahanta; Mukherjee, 2001
			Hot H_2O ext.	100.0 mcg/mL	Active	Mahanta; Mukherjee, 2001
			MeOH	100.0 mcg/mL	Inactive	Mahanta; Mukherjee, 2001
Plathymiscium floribundum	Brazil	Heartwood	EtOH	2.8 mg/mL	Active	Trevisan; Macedo, 2003
Pterodon polygalaeflorus	Brazil	Seed	EtOAc	2.3 mg/mL	Inactive	Trevisan; Macedo, 2003
Pueraria thunbergiana	South Korea	Root	MeOH	Not stated	Inactive	Lee et al., 1997
Sesbania sesban	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Vanilosmopsis arborea	Brazil	Not stated	EtOH	1.2 mg/mL	Active	Trevisan; Macedo, 2003
Fumariaceae						
Fumaria asepala	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria bastardii	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria boissieri	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria bracteosa	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria capreolata	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria cilicica	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria densiflora	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria flabellata	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria gaillardotii	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria judaica	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria kralikii	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria macrocarpa	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria microcarpa	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria officinalis	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria parviflora	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria petteri	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria rostellata	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria schleicheri	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Fumaria vailantii	Turkey	Aerial parts	Alkaloid fract.	Not stated	Active	Sener, 2002
Gentianaceae						
Gentiana scabra	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997

Ginkgoaceae						
Ginkgo biloba	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Hydrocharitaceae						
Hyderilla verticillata	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Lamiaceae						
Agastache rugosa	South Korea	Aerial parts	MeOH	Not stated	Weak activity	Lee et al., 1997
Coleus blumei	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Mentha arvensis	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
Ocimum sanctum	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Perilla frutescens	South Korea	Aerial parts	MeOH	Not stated	Weak activity	Lee et al., 1997
Prunella vulgaris	South Korea	Aerial parts	MeOH	0.2 mg/mL	Weak activity	Lee et al., 1997
Rosmarinus officinalis	England	Leaf	EtOH-H_2O 50%	0.089 mg/mL	Weak activity	Howes et al., 1999
Salvia lavandulaefolia	England	Essential oil	Essential oil	IC_{50} 0.03 µL/mL	Active	Perry et al., 2000
				20.0 µL/animal	Active	Perry et al., 2002
Salvia miltiorrhiza	South Korea	Root	MeOH	0.2 mg/mL	Weak activity	Lee et al., 1997
	China	Root	EtOH-H_2O 50%	0.1 mg/mL	Active	Howes et al., 1999
			H_2O ext.	9.5 mcg/mL	Active	Howes et al., 1999
Schizonepeta tenuifolia	South Korea	Aerial parts	MeOH	Not stated	Weak activity	Lee et al., 1997
Scutellaria baicalensis	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
Scutellaria baicalensis	South Korea	Root	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Lardizabalaceae						
Akebia quinata	South Korea	Stem	MeOH	Not stated	Weak activity	Lee et al., 1997
Lauraceae						
Cinnamomum cassia	South Korea	Bark	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
		Branchlets	MeOH	Not stated	Inactive	Lee et al., 1997
Cinnamomum japonicum	South Korea	Wood	MeOH	Not stated	Active	Lee et al., 1997
Liliaceae						
Allium sativum	India	Dried bulb	Essential oil	Not stated	Active	Thomas; Pal, 1974
	Iran	Dried bulb	H_2O	50.0 mg/kg	Active	Sharifi et al., 2003
Anemarrhena aspodheloides	South Korea	Rhizome	MeOH	Not stated	Active	Lee et al., 1997
Asparagus cochinchinensis	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
Liriope platyphylla	South Korea	Tuber	MeOH	1.0 mg/mL	Weak activity	Lee et al., 1997
Lycopodiaceae						
Lycopodium alpinum	Turkey	Aerial parts	MeOH-$CHCl_3$	1.0 mg/mL	Inactive	Orhan et al., 2003
Lycopodium annotinum	Turkey	Aerial parts	Not specified	1.0 mg/mL	Inactive	Orhnan et al., 2003
Lycopodium clavatum	Turkey	Aerial parts	MeOH-$CHCl_3$	1.0 mg/mL	Weak activity	Orhan et al., 2003
Lycopodium complantum	Turkey	Aerial parts	MeOH-$CHCl_3$	1.0 mg/mL	Inactive	Orhan et al., 2003
Lycopodium selago	Turkey	Aerial parts	MeOH-$CHCl_3$	1.0 mg/mL	Inactive	Orhan et al., 2003
Lythraceae						
Lawsonia inermis	India	Dried leaf	MeOH	Not stated	Inactive	Lahon; Singh, 1977
Magnoliaceae						
Magnolia kobus	South Korea	Flowers	MeOH	Not stated	Weak activity	Lee et al., 1997
Magnolia obovata	South Korea	Bark	MeOH	Not stated	Weak activity	Lee et al., 1997

Magnolia officinalis	South Korea	Bark	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Malvaceae						
Gossypium herbaceum	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Hibiscus rosa-sinensis	India	Leaf/Stem	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Malva verticillata	South Korea	Leaf	MeOH	Not stated	Inactive	Lee et al., 1997
Meliaceae						
Melia azedarach	India	Leaf	EtOH	2 mm sl	Inactive	Gupta et al., 1997
Menispermaceae						
Stephania suberosa	Thailand	Root	MeOH	0.1 mg/mL	Weak activity	Ingkaninan et al., 2003
Stephania tetrandra	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
Moraceae						
Cecropia anguria	Brazil	Stem	Hexane	1.8 mg/mL	Inactive	Trevisan; Macedo, 2003
Cecropia pachystachya	Brazil	Leaf	EtOH	1.1 mg/mL	Inactive	Trevisan; Macedo, 2003
Ficus elastica	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Ficus krishnae	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Musaceae						
Musa parasidiaca	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Myrtaceae						
Callistemon lanceolatus	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Psidium guajava	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Syzygium aromaticum	South Korea	Root	MeOH	200.0 mcg/mL	Inactive	Park et al., 1996
Nyctaginaceae						
Boerhavia diffusa	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Bougainvillea glabra	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Olacaceae						
Ptychopetalum olacoides	Brazil	Root	EtOH	100 mg/kg	Active	Siqueira et al., 2003
Oleaceae						
Forsythia suspensa	South Korea	Fruit	MeOH	Not stated	Weak activity	Lee et al., 1997
Olea europaea	Spain	Fruit fixed oil	Fixed oil	10.0% of diet	Active	De La Cruz et al., 2000
Oleandraceae						
Nephrolepis biserrata	India	Stem/Root	EtOH	2 mm slices	Active	Gupta et al., 1997
Orchidaceae						
Gastrodia elata	South Korea	Rhizome	MeOH	Not stated	Weak activity	Lee et al., 1997
Oxalidaceae						
Oxalis corniculata	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Paeoniaceae						
Paeonia albiflora	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
Paeonia moutan	South Korea	Bark	MeOH	Not stated	Active	Lee et al., 1997
Paeonia obovata	South Korea	Root	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Papaveraceae						
Argemone mexicana	India	Stem	EtOH	2 mm sl	Inactive	Gupta et al., 1997
Chelidonium majus	Switzerland	Aerial parts	EtOH 95%	15.0 mcg/disc	Active	Marston et al., 2002
Corydalis ternata	South Korea	Tuber	$CHCl_3$-MeOH (2:1)	5.0 mcg/mL	Active	Hwang et al., 1996
			H2O fraction	10.0 mcg/mL	Inactive	Hwang et al., 1996
			MeOH	5.0 mcg/mL	Active	Hwang et al., 1996

Papaver somniferum	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Parazoanthidae						
Parazoanthus axinellae	Organism Adriatic Sea	Not specified	EtOH 75%	IC_{50} 110.0 mg/mL	Active	Turk et al., 1995
Piperaceae						
Piper betle	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Piper interruptum	Thailand	Stem	MeOH	0.1 mg/mL	Weak activity	Ingkaninan et al., 2003
Piper nigrum	Thailand	Seed	MeOH	0.1 µmols/mL	Weak activity	Ingkaninan et al., 2003
Plantaginaceae						
Plantago asiatica	South Korea	Seed	MeOH	Not stated	Weak activity	Lee et al., 1997
Poaceae						
Coix lacryma-jobi	South Korea	Seed	MeOH	Not stated	Inactive	Lee et al., 1997
Cynodon dactylon	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Hordeum vulgare	South Korea	Fruit	MeOH	Not stated	Active	Lee et al., 1997
Phyllostachys nigra	South Korea	Caules	MeOH	1.0 mg/mL	Weak activity	Lee et al., 1997
Triticum aestivum	South Korea	Entire plant	MeOH	Not stated	Weak activity	Lee et al., 1997
		Seed	MeOH	Not stated	Inactive	Lee et al., 1997
Polygalaceae						
Polygala tenuifolia	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
	China	Root	EtOH-H_2O 50%	0.3 mg/mL	Inactive	Howes et al., 1999
	South Korea	Root	H_2O ext.	9.5 mcg/mL	Inactive	Howes et al., 1999
			MeOH 80%	200.0 mcg/mL	Weak activity	Park et al., 1996
Polygonaceae						
Antigonon leptopus	India	Leaf/Stem	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Polygonum multiflorum	South Korea	Root	MeOH	0.1 mg/mL	Weak activity	Lee et al., 1997
	China	Root	EtOH-H_2O 50%	0.2 mg/mL	Inactive	Howes et al., 1999
	South Korea	Root	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Rheum ondulatum	South Korea	Rhizome	MeOH	0.1 mg/mL	Weak activity	Lee et al., 1997
Polyporaceae						
Polyporus umbellatus	South Korea	Entire plant	MeOH	Not stated	Weak activity	Lee et al., 1997
Poria cocos	South Korea	Entire plant	MeOH	Not stated	Weak activity	Lee et al., 1997
		Fruitbody	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Pontederiaceae						
Eichhornia crassipes	India	Stem/Branch	EtOH	2 mm slices	Active	Gupta et al., 1997
Portulacaceae						
Portulaca quadrifida	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Pteridaceae						
Pteris multifida	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Punicaceae						
Punica granatum	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Ranunculaceae						

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Aconitum carmichaelii	South Korea	Root	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
		Tuber	MeOH	Not stated	Active	Lee et al., 1997
Cimicifuga heracleifolia	South Korea	Rhizome	MeOH	Not stated	Weak activity	Lee et al., 1997
Cimicifuga racemosa	USA	Rhizome	EtOH 70%	10.0 mg/mL	Inactive	Rhee et al., 2003
Coptis chinensis	South Korea	Rhizome	Dichloromethane	200.0 mcg/mL	Active	Park et al., 1996
			MeOH 80%	200.0 mcg/mL	Active	Park et al., 1996
Coptis japonica	South Korea	Rhizome	MeOH	0.1 mg/mL	Weak activity	Lee et al., 1997
Rhamnaceae						
Ziziphus jujuba	South Korea	Fruit	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
	China	Seed	MeOH	Not stated	Weak activity	Lee et al., 1997
	South Korea	Seed	EtOH-H_2O 50%	0.05 mg/mL	Inactive	Howes et al., 1999
		Fruit	H_2O ext.	0.03 mg/mL	Inactive	Howes et al., 1999
			MeOH	Not stated	Weak activity	Lee et al., 1997
			MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Rosaceae						
Crataegus pinnatifida	South Korea	Fruit	MeOH	Not stated	Weak activity	Lee et al., 1997
Eriobotrya japonica	South Korea	Leaf	MeOH	1.0 mg/mL	Weak activity	Lee et al., 1997
Prunus armeniaca	South Korea	Seed	MeOH	Not stated	Weak activity	Lee et al., 1997
Prunus persica	South Korea	Seed	MeOH	Not stated	Weak activity	Lee et al., 1997
Rubus coreanus	South Korea	Fruit	MeOH	Not stated	Weak activity	Lee et al., 1997
Rubiaceae						
Gardenia jasminoides	South Korea	Fruit	MeOH	0.2 mg/mL	Weak activity	Lee et al., 1997
Ixora coccinea	India	Leaf	EtOH	2 mm sl	Inactive	Gupta et al., 1997
Rubia cordifolia	South Korea	Root	MeOH	Not stated	Inactive	Lee et al., 1997
Uncaria rhynchophylla	South Korea	Branchlets	MeOH	0.2 mg/mL	Weak activity	Lee et al., 1997
Rutaceae						
Citrus aurantiifolia	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Citrus aurantium	South Korea	Fruit	MeOH	Not stated	Weak activity	Lee et al., 1997
Citrus paradisi	USA	Essential oil	Essential oil	IC_{50} 0.13 mcg/mL	Active	Miyazawa et al., 2001
Citrus unshiu	South Korea	Pericarp	MeOH	Not stated	Weak activity	Lee et al., 1997
Euodia officinalis	South Korea	Fruit	MeOH	Not stated	Weak activity	Lee et al., 1997
Euodia rutaecarpa	South Korea	Aerial parts	Dichloromethane	200.0 mcg/mL	Active	Park et al., 1996
Phellodendron amurense	South Korea	Bark	MeOH	Not stated	Inactive	Lee et al., 1997
Poncirus trifoliata	South Korea	Fruit	MeOH	Not stated	Weak activity	Lee et al., 1997
			Dichloromethane	200.0 mcg/mL	Active	Park et al., 1996
Triphasia trifolia	Brazil	Leaf	Hexane	1.1 mg/mL	Inactive	Trevisan; Macedo, 2003
			$CHCl_3$	1.4 mg/mL	Active	Trevisan; Macedo, 2003
			EtOAc	1.8 mg/mL	Inactive	Trevisan; Macedo, 2003
			MeOH	2.1 mg/mL	Active	Trevisan; Macedo, 2003
Vitis vinifera	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Santalaceae						
Santalum album	South Korea	Wood	MeOH	Not stated	Weak activity	Lee et al., 1997

Euphoria longana	South Korea	Arillus	MeOH	Not stated	Weak activity	Lee et al., 1997
Paullinia cupana	Brazil	Not stated	EtOH	1.5 mg/mL	Active	Trevisan; Macedo, 2003
Schisandraceae						
Schisandra chinensis	South Korea	Fruit	MeOH	Not stated	Inactive	Lee et al., 1997
		Fruit	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Scrophulariaceae						
Mazus pumilus	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Rehmannia glutinosa	South Korea	Root	MeOH	Not stated	Inactive	Lee et al., 1997
		Root	MeOH 80%	200.0 mcg/mL	Inactive	Park et al., 1996
Scrophularia buergeriana	South Korea	Root	MeOH	Not stated	Weak activity	Lee et al., 1997
Verbascum chinense	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Simaroubaceae						
Simarouba versicolor	Brazil	Fruit	EtOH	1.5 mg/mL	Inactive	Trevisan; Macedo, 2003
Solanaceae						
Datura innoxia	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Lyceum chinense	South Korea	Bark	MeOH	Not stated	Weak activity	Lee et al., 1997
Nicotiana rustica	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Physalis minima	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Solanum asperum	Brazil	Leaf	EtOH	1.4 mg/mL	Active	Trevisan; Macedo, 2003
Solanum nigrum	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Withania somnifera	India	Root	EtOH-H_2O 50%	0.15 mg/mL	Active	Howes et al., 1999
		Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Tiliaceae						
Corchorus aestuans	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Tropeolaceae						
Tropaeolum majus	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Verbenaceae						
Lantana camara	India	Leaf	EtOH	2 mm slices	Inactive	Gupta et al., 1997
Lippia alba	Brazil	Leaf	EtOH	2.1 mg/mL	Inactive	Trevisan; Macedo, 2003
Lippia sidoides	Brazil	Leaf	MeOH	2.8 mg/mL	Active	Trevisan; Macedo, 2003
			EtOH	2.2 mg/mL	Active	Trevisan; Macedo, 2003
Nictanthes arbor-tristis	India	Leaf	EtOH	2 mm sl	Inactive	Gupta et al., 1997
Vitex agnus castus	Brazil	Leaf	MeOH	1.7 mg/mL	Inactive	Trevisan; Macedo, 2003
Vitex rotundifolia	South Korea	Fruit	MeOH	Not stated	Inactive	Lee et al., 1997
Zamiaceae						
Dioon edule	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Dioon spinulosum	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Zamia furfuraceae	India	Leaf	EtOH	2 mm slices	Active	Gupta et al., 1997
Zingiberaceae						
Amomum xanthioides	South Korea	Seed	MeOH	Not stated	Inactive	Lee et al., 1997
Curcuma zedoaria	South Korea	Rhizome	MeOH	Not stated	Weak activity	Lee et al., 1997
Zingiber officinale	South Korea	Rhizome	MeOH	Not stated	Inactive	Lee et al., 1997

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Table 2. Chemically defined natural compounds showing acetylcholinesterase inhibition

Chemical name	Class	Model	Dose/Concent.	Result	References
Acetophenone	Benzenoid	In vitro	Not stated	Inactive	Miyazawa et al., 1998
Akuammicine	Alkaloid	In vitro	IC_{50} 221 µmols	Active	Mroue et al., 1996
Akuammidine	Alkaloid	In vitro	IC_{50} 188 µmols	Active	Mroue et al., 1996
Alkaloid C	Alkaloid	In vitro	IC_{50} 48.6 µmols	Active	Rahman et al., 2003
Allicin	Sulfur compound	In vivo/ Brain	LC_{50} 2.88 mg/L	Active	Singh; Singh, 1996
		In vitro	12 mcg	Active	Singh; Singh, 1996
Almazole D, (+)	Alkaloid	In vitro	Not stated	Inactive	N'Diaye et al., 1996
Alopecuridine	Alkaloid	In vitro	Not stated	Active	Hirasawa et al., 2003
Anabasamine	Alkaloid	In vitro	Not stated	Active	Tilyabaev; Abduvakhabov, 1998
Anabasine	Alkaloid	In vitro	Not stated	Active	Tilyabaev; Abduvakhabov, 1998
Anatoxin A	Alkaloid	In vivo/ Brain	0.016 mg	Inactive	Astrachan et al., 1980
		In vivo/ Blood	0.016 mg	Inactive	Astrachan et al., 1980
Anisodamine	Alkaloid	In vitro	Not stated	Active	Guo et al., 1992
Arisugacin	Triterpene	In vitro	IC_{50} 1.0 nmols	Active	Omrua et al., 1995
Arisugacin A	Triterpene	In vitro	IC_{50} 1.0 nmols	Strong activity	Kuno et al., 1996
		In vitro	IC_{50} 0.001 µmols	Strong activity	Otoguro et al., 2000
Arisugacin B	Triterpene	In vitro	IC_{50} 25.8 nmols	Active	Kuno et al., 1996
		In vitro	IC_{50} 0.026 µmols	Strog activity	Otoguro et al., 2000
Arisugacin C	Triterpene	In vitro	IC_{50} 2.5 µmols	Active	Otoguro et al., 2000
Arisugacin D	Triterpene	In vitro	IC_{50} 3.5 µmols	Active	Otoguro et al., 2000
Arisugacin E	Triterpene	In vitro	Not stated	Inactive	Otoguro et al., 2000
Arisugacin F	Triterpene	In vitro	Not stated	Inactive	Otoguro et al., 2000
Arisugacin G	Triterpene	In vitro	Not stated	Inactive	Otoguro et al., 2000
Arisugacin H	Triterpene	In vitro	Not stated	Inactive	Otoguro et al., 2000
Atherospermoline	Alkaloid	In vitro	IC_{50} 4.0 µmols	Active	Ogino et al., 1997
Atherospermoline, 12-*O*-acetyl	Alkaloid	In vitro	IC_{50} 10.0 µmols	Active	Ogino et al., 1997
Atherospermoline, 2'-*N*-nor	Alkaloid	In vitro	IC_{50} 2.5 µmols	Active	Ogino et al., 1997
Auraptene	Coumarin	In vitro	0.16 mcg/mL	Active	Miyazawa et al., 2001
Axillaridine A	Alkaloid	In vitro	IC_{50} 5.21 µmols	Active	Rahman et al., 2002
Axillarine C	Alkaloid	In vitro	IC_{50} 227.9 µmols	Weak activity	Rahman et al., 2002
Axillarine F	Alkaloid	In vitro	IC_{50} 182.0 µmols	Weak activity	Rahman et al., 2002
Baccabolivic acid	Diterpene	In vitro	10.0 ppm	Active	Calderon et al., 2001
Barakol	Oxygen heterocycle	In vitro	IC_{50} 0.4 mmols	Active	Permtersin et al., 2001
		In vitro	IC_{50} 0.21 mmols	Active	Permtersin et al., 2001
Benzoxazin-3-one, 1,4: 2,4-dihydroxy-7-methoxy	Benzoxazinone	In vitro	5.0 mmols	Weak activity	Cuevas; Niemeyer, 1993
		In vitro	1.0 mmols	Active	Cuevas; Niemeyer, 1993
		In vitro	10.0 mmols	Weak activity	Cuevas; Niemeyer, 1993
		In vitro	10.0 mmols	Equivocal	Cuevas; Niemeyer, 1993
		In vitro	5.0 mmols	Active	Cuevas; Niemeyer, 1993

Berberine	Alkaloid	In vitro	IC_{50} 167.4 µmols	Weak activity	Schmeller et al., 1997
		In vitro	0.1 mmols	Active	Shin et al., 1993
		In vitro	0.125 µmols	Active	Hwang et al., 1996
		In vitro	0.52 mcg/mL	Active	Jang et al., 2003
		In vitro	0.98 µmols	Active	Ulrichova et al., 1985
		In vitro	0.30 mcg/mL	Active	Chun et al., 1979
		In vitro	ID_{50} 0.98 µmols	Strong activity	Ulrichova et al., 1983
Berberine, 13-ethyl	Alkaloid	In vitro	IC_{50} 0.91 µmols	Active	Ulrichova et al., 1985
Berberine, 13-methyl	Alkaloid	In vitro/ Brain	ID_{50} 8.0 µmols	Strong activity	Ulrichova et al., 1983
Berberine, epi: pseudo	Alkaloid	In vitro/ Brain	ID_{50} 5.1 µmols	Strong activity	Ulrichova et al., 1983
Bicuculline, (+)	Alkaloid	In vivo/ Spinal	5.0 mg/Kg	Inactive	Nistri et al., 1974
Buxahejramine, (-)	Alkaloid	In vitro	IC_{50} 162.0 µmols	Active	Rahman et al., 2001
Buxahyrcanine, *N*-isobutyroyl	Alkaloid	In vitro	Not stated	Inactive	Choudhary et al., 2003
Buxahyrcanine, *N*-tygloyl: (+)	Alkaloid	In vitro	IC_{50} 443.6 µmols	Active	Choudhary et al., 2003
Buxahyrcawine, *N*-benzoyl: (+)	Alkaloid	In vitro	Not stated	Inactive	Choudhary et al., 2003
Buxakarachiamine, (-)	Alkaloid	In vitro	IC_{50} 143.0 µmols	Active	Rahman et al., 2001
Buxakashmiramine, (-)	Alkaloid	In vitro	IC_{50} 25.4 µmols	Active	Rahman et al., 2001
Buxaminol E	Alkaloid	In vitro	IC_{50} 33.0 µmols	Active	Kvaltinova et al., 1991
Calystegine B2	Alkaloid	In vitro	1.0 mmols	Inactive	Asano et al., 1996
Calystegine N1	Alkaloid	In vitro	1.0 mmols	Inactive	Asano et al., 1996
Camphor	Monoterpene	In vitro	Not stated	Inactive	Perry et al., 2000
Carotene, β	Carotenoid	Stomach tissue	0.02% of diet	Inactive	Man et al., 1996
Carvacrol	Monoterpene	In vitro	1.0 mmols	Active	Gracza, 1985
Carvone, (+)	Monoterpene	In vitro	IC_{50} 1.85 mmols	Active	Miyazawa et al., 1997
		In vitro	1.0 mmols	Active	Gracza, 1985
Carvone, (-)	Monoterpene	In vitro	IC_{50} 1.38 mmols	Active	Miyazawa et al., 1997
Castoramine, (-)	Alkaloid	In vitro	0.5 mmols	Active	Miyazawa et al., 1998b
Chaconine, α	Alkaloid	In vivo	10.0 mg/Kg	Active	Alozie et al., 1979
		In vivo	30.0 mg/ Kg	Active	Alozie et al., 1979
		In vivo	60.0 mg/ Kg	Weak activity	Alozie et al., 1979
		In vitro	8.3 µmols	Active	Alozie et al., 1979
		In vitro	0.016 mol	Active	Alozie et al., 1979
Chelerythrine	Alkaloid	In vitro	IC_{50} 9.40 µmols	Active	Ulrichova et al., 1985
		In vitro/ Brain	ID_{50} 9.4 µmols	Strong activity	Ulrichova et al., 1983
Chelilutine	Alkaloid	In vitro/ Brain	ID_{50} 0.02 mmols	Active	Ulrichova et al., 1983
Chelirubine	Alkaloid	In vitro/ Brain	ID_{50} 0.09 mmols	Active	Ulrichova et al., 1983
Cimicidine	Alkaloid	In vitro	IC_{50} 197 mmols	Active	Mroue et al., 1996
Cimicine	Alkaloid	In vitro	IC_{50} 241.0 µmols	Active	Mroue et al., 1996

Cineol, 1,8	Monoterpene	In vitro	0.67 mmols	Active	Perry et al., 2000
		In vitro	1.0 mmols	Active	Gracza, 1985
		In vitro	Not stated	Inactive	Antonious et al., 1983
Coptisine	Alkaloid	In vitro/ Brain	ID_{50} 5.8 µmols	Strong activity	Ulrichova et al., 1983
Cordifoline	Alkaloid	In vitro	Dose variable	Inactive	Cardoso et al., 2004
Cordifoline, desoxy	Alkaloid	In vitro	Dose variable	Active	Cardoso et al., 2004
Cotisine, pseudo	Alkaloid	In vitro/ Brain	ID_{50} 0.011 mmols	Active	Ulrichova et al., 1983
		In vitro	IC_{50} 1.30 µmols/L	Active	Ulrichova et al., 1985
		In vitro	ID_{50} 1.3 µmols	Strong activity	Ulrichova et al., 1983
Coumarin, 7-hydroxy-3,4-dimethyl	Coumarin	In vitro	17.6 µmols	Active	Bruhlmann et al., 2001
Coumarin, 7-hydroxy-6-(2(R)-hydroxy-3-methyl-but-3-enyl	Coumarin	In vitro	IC_{50} 0.13 mmols	Active	Kang et al., 2001
Coumarin, 7-methoxy-5-prenyl-oxy	Coumarin	In vitro	IC_{50} 0.24 mmols	Active	Kang et al., 2001
Crooksiine	Alkaloid	In vitro	3.06 mcg/mL	Active	Mroue; Alam, 1991
Curcumin	Benzenoid	In vitro	20.0 µmols	Active	Korutla; Kumar, 1994
Cyclomicrophylline A	Alkaloid	In vitro	IC_{50} 235.0 µmols	Active	Rahman et al., 2001
Cyclopenin	Alkaloid	In vitro	IC_{50} 2.04 µmols	Weak activity	Kuno et al., 1996
Cyclophostin	Oxygen heterocycle	In vitro	IC_{50} 76.0 nmols	Active	Kuno et al., 1996
		In vitro	IC_{50} 76.0 nmols	Active	Kurokawa et al., 1993
Cycloprotobuxin C	Alkaloid	In vitro	IC_{50} 38.8 µmols	Active	Rahman et al., 2001
Cyclovirobuxeine A	Alkaloid	In vitro	IC_{50} 105.7 µmols	Active	Rahman et al., 2001
Cymene, para	Monoterpene	In vitro	1.2 mmols	Weak activity	Miyazawa et al., 1997
Cysteine, S-allyl	Proteid	In vitro	400.0 mcg/mL	Weak activity	Welch et al., 1992
Decursin	Coumarin	In vitro	IC_{50} 0.39 mmols	Active	Kang et al., 2001
Decursinol	Coumarin	In vitro	IC_{50} 28.0 µmols	Active	Kang et al., 2001
Deguelin	Flavonoid	In vitro	0.40 mcg/mL	Weak activity	Ashack et al., 1980
Delavine	Alkaloid	In vitro	IC_{50} 105.5 µmols	Active	Rahman et al., 2002b
Derrisic acid	Benzenoid	In vitro/ Ileum	Not stated	Inactive	Ashack et al., 1980
Elagic acid	Coumarin	In vitro	Not stated	Active	Ho et al., 1999
Embelin	Quinoid	In vivo	20.0 mg/kg	Active	Dhar et al., 1986
Evodiamine, dehydro	Alkaloid	In vitro	IC_{50} 37.8 µmols	Active	Park et al., 1996
Fagaronine	Alkaloid	In vitro	IC_{50} 1.5 µmols/L	Active	Ulrichova et al., 1986
Faleoconitine	Alkaloid	In vitro	20.0 microliters	Active	Rahman et al., 2000
Fangchinoline	Alkaloid	In vitro	IC_{50} 3.2 µmols	Active	Ogino et al., 1997
Fangchinoline, 2'-nor	Alkaloid	In vitro	IC_{50} 10.0 nmols	Active	Ogino et al., 1992
Fangchinoline, 2,2'-*N,N*-dinor	Alkaloid	In vitro	IC_{50} 5.8 µmols	Active	Ogino et al., 1997
Fangchinoline, 2-*N*-nor	Alkaloid	In vitro	IC_{50} 6.2 µmols	Active	Ogino et al., 1997

Fasciculin 2	Proteid	In vitro	Not stated	Active	Tai et al., 2002
Fawcettimine	Alkaloid	In vitro	Not stated	Weak activity	Tan et al., 2000
Fenchone	Monoterpene	In vitro	1.0 mmols	Active	Gracza, 1985
Fenfangjine E	Alkaloid	In vitro	IC_{50} 3.9 µmols	Active	Ogino et al., 1997
Flavanone, 2(S): 2',5-dihydroxy-5',7-dimethoxy	Flavonoid	In vitro	IC_{50} 28.0 µmols	Active	Ahmad et al., 2003
Flavone, 2',4',5,7-tetrahydroxy-3,5',6,8-tetramethoxy	Flavonoid	In vitro	50.0 ppm	Weak activity	Calderon et al., 2001
Flavone, 2',5,7-trihydroxy-3,4',5',6,8-pentamethoxy	Flavonoid	In vitro	50.0 ppm	Weak activity	Calderon et al., 2001
Flavone, 2',5-dihydroxy-3,4',5',6,7,8-hexamethoxy	Flavonoid	In vitro	50.0 ppm	Equivocal	Calderon et al., 2001
Flavone, 4',5,7-trihydroxy-3,6,8-trimethoxy	Flavonoid	In vitro	50.0 ppm	Weak activity	Calderon et al., 2001
Forticine	Alkaloid	In vitro	Not stated	Inactive	Rahman et al., 2002b
Funtumafrine C	Alkaloid	In vitro	IC_{50} 45.75 µmols	Active	Kalauni et al., 2002
Funtumine, *N*-methyl	Alkaloid	In vitro	IC_{50} 97.61 µmols	Active	Kalauni et al., 2002
Galanthamine	Alkaloid	In vitro	Not stated	Active	Greenwood, 1998
		In vitro/ Brain	0.01 mmols	Active	Tonkopii; prozorovskii, 1976
		In vivo	4.0 mg/kg	Active	Tonkopii; prozorovskii, 1976
		In vivo	Not stated	Active	Prozorovskii et al., 1996
		In vitro/ Brain	IC_{50} 40.0 µmols	Active	Harvey, 1995
		In vivo/ Plasma	3.0 mg/kg	Active	Pak et al., 2001
		In vivo/ Brain	3.0 mg/ kg	Active	Pak et al., 2001
		In vitro	0.01 mcg/plate	Active	Marston et al., 2002
		In vitro	0.01 mcg/mL	Active	Rhee et al., 2001
		In vitro	0.6 mcg/plate	Active	Rhee et al., 2001
		In vitro	0,2 mcg/plate	Active	Rhee et al., 2001
Galanthamine, (-)	Alkaloid	In vitro	Not stated	Active	Greenblatt et al., 1999
Geraniol	Monoterpene	In vitro	Not stated	Inactive	Perry et al., 2000
Gingerol, 6	Benzenoid	In vitro	LC_{50} 5.96 mg/mL	Active	Singh et al., 1999
Ginsenoside RB-1	Triterpene	In vitro	1.0 µmols	Inactive	Benishin et al., 1991
Haplophytine	Alkaloid	In vitro	IC_{50} 225.0 µmols	Active	Mroue et al., 1996
Harman-3-carboxylic acid	Alkaloid	In vitro	Dose variable	Inactive	Cardoso et al., 2004
Heliotrine	Alkaloid	In vitro	0.5 mg/mL	Active	Mahmoud et al., 1987
Heliotropamide	Alkaloid	In vitro	Not stated	Active	Guntern et al., 2003
Herniarin, 3,4-dimethyl	Coumarin	In vitro	Not stated	Active	Bruhlmann et al., 2001

Hispidone	Flavonoid	In vitro	IC_{50} 11.6 µmols	Active	Ahmad et al., 2003
Huperzine A	Alkaloid	In vitro	1.0 µmols/L	Active	Tan et al., 2000
		In vitro	0.082 µmols	Active	Tan et al., 2002
		In vivo	0.5 mg/kg	Active	Cheng; Tang, 1998
		In vivo	0.5 mg/kg	Active	Cheng; Tang, 1998
		In vivo	Not stated	Active	Anon, 1992a
		In vivo	0.5 mg/kg	Active	Grunwald et al., 1994
		In vitro	0.02 µmols	Active	Kozikowski et al., 1995
		In vivo	Not stated	Active	Anon, 1992b
		In vivo	0.1 mg/kg	Active	Wang et al., 2000
		In vitro	5.9 nmols	Active	Rajendran et al., 2000
		In vitro	0.024 µmols	Active	Hogenaurer et al., 2001
		In vitro	7.0 nmols	Active	Zhao; Tang, 2002
		In vitro	Not stated	Active	Li et al., 2004
		In vitro	0.1 µmols	Active	Kozikowski et al., 1991
		In vivo	0.25 mg/kg	Active	Anon, 1991
Huperzine A, (+)	Alkaloid	In vitro	IC_{50} 3.153 µmols	Weak activity	Zhang et al., 2002b
		In vitro	IC_{50} 1448 nmols	Inactive	Yamada et al., 1991
		In vitro	Not stated	Inactive	Mc-Kinney et al., 1991
Huperzine A, (-)	Alkaloid	In vivo/ Brain	0.5 mg/Kg	Active	Tang et al., 1994
		In vitro	IC_{50} 0.1 µmols	Active	Tang et al., 1994
		In vitro	IC_{50} 260.0 nmols	Active	Camps et al., 2000a
		In vitro	IC_{50} 65.0 n mols	Active	Zhang et al., 2002b
		In vitro	IC_{50} 475.0 nmols	Active	He et al., 2003
		In vitro	IC_{50} 44.5 nmols	Active	Yamada et al., 1991
		In vitro	Not stated	Active	Mc-Kinney et al., 1991
Huperzine A, (DL)	Alkaloid	In vivo/ Brain	0.5 mg/kg	Active	Tang et al., 1994
		In vitro	IC_{50} 0.3 µmols	Active	Tang et al., 1994
		In vitro	IC_{50} 0.074 µmols	Active	Camps et al., 2000b
		In vitro	IC_{50} 71.5 nmols	Active	Yamada et al., 1991
		In vitro	IC_{50} 0.3 µmols	Active	Kozikowski et al., 1991
		In vitro	Not stated	Active	Mc-kinney et al., 1991
		In vitro	IC_{50} 71.5 nmols	Active	Kozikowski et al., 1991b
Huperzine A, 1-methyl	Alkaloid	In vitro	6.48 µmols/L	Active	Wang et al., 1999
Huperzine A, 10,10-dimethyl	Alkaloid	In vitro	Not stated	Active	Kozikowski et al., 1996
Huperzine A, *cis*: (DL)	Alkaloid	In vitro	IC_{50} 6.0 µmols	Active	Kozikowski et al., 1990
Huperzine B	Alkaloid	In vitro	IC_{50} 0.54 µmols	Strong activity	Liu et al., 1999
Huperzine C	Alkaloid	In vitro	Not stated	Active	Liu and Huang, 1994
Huperzine D	Alkaloid	In vitro	Not stated	Inactive	Liu and Huang, 1994
Huperzine P	Alkaloid	In vitro	Not stated	Weak activity	Tan et al., 2000

Huperzine R	Alkaloid	In vitro	IC_{50} 0.082 µmols	Strong activity	Tan et al., 2002
		In vitro	95.0 µmols	Weak activity	Tan et al., 2002
Huperzinine	Alkaloid	In vitro	Not stated	Weak activity	Liu; Huang, 1994
Hyrcanine, (-)	Alkaloid	In vitro	IC_{50} 10.0 µmols	Inactive	Rahman et al., 1998
Iantheran A	Oxygen heterocycle	In vitro	IC_{50} 3.0 µmols	Active	Okamoto et al., 2001
Iantheran B	Oxygen heterocycle	In vitro	IC_{50} 3.0 µmols	Active	Okamoto et al., 2001
Imperatorin, iso	Coumarin	In vitro	IC_{50} 69.0 µmols	Active	Kang et al., 2001
Imperialine	Alkaloid	In vitro	Not stated	Inactive	Rahman et al., 2002b
Impericine	Alkaloid	In vitro	IC_{50} 67.97 µmols	Active	Rahman et al., 2002b
Ionone, α	Sesquiterpene	In vitro	IC_{50} 36.7 mcg/mL	Active	Miyazawa et al., 1998
Ionone, β	Sesquiterpene	In vitro	IC_{50} 53.3 mcg/mL	Active	Miyazawa et al., 1998
Isatin	Alkaloid	In vitro/ Brain	1.5 mmols	Active	Kumar et al., 1993
Jasmine, *cis*	Alicyclic	In vitro	IC_{50} 78.3 mcg/mL	Weak activity	Miyazawa et al., 1998
Kobophenol A	Benzenoid	In vitro	IC_{50} 115.8 µmols	Active	Sung et al., 2002
Lanceomigine	Alkaloid	In vitro	IC_{50} 383.0 µmols	Weak activity	Mroue et al., 1996
Leurocristine	Alkaloid	In vivo	1.5 mcg/animal	Active	Kozik et al., 19831
Limonene, (+)	Monoterpene	In vitro	1.2 mmols	Equivocal	Miyazawa et al., 1997
Limonene, (-)	Monoterpene	In vitro	1.2 mmols	Equivocal	Miyazawa et al., 1997
Linalool, (DL)	Monoterpene	In vitro	Not stated	Inactive	Perry et al., 2000
Lupinine	Alkaloid	In vitro	Not stated	Active	Tilyabaev; Abduvakhabov, 1998
Lupinine, epi	Alkaloid	In vitro	Not stated	Active	Tilyabaev; Abduvakhabov, 1998
Lycoposerramine A	Alkaloid	In vitro	200.0 µmols	Inactive	Takayama et al., 2001
Marmesin	Coumarin	In vitro	IC_{50} 67.0 µmols	Active	Kang et al., 2001
Melochinine, (-): (R)	Alkaloid	In vitro	100.0 mg/L	Active	Breuer et al., 1982
Menth-1-ene, *para*: (+)	Monoterpene	In vitro	IC_{50} 1.64 mmols	Active	Miyazawa et al., 1997
Menthol, (+)	Monoterpene	In vitro	IC_{50} 2.0 mmols	Active	Miyazawa et al., 1997
Menthol, (-)	Monoterpene	In vitro	1.2 mmols	Weak activity	Miyazawa et al., 1997
Menthol, iso: (+)	Monoterpene	In vitro	1.2 mmols	Equivocal	Miyazawa et al., 1997
Menthone, (-)	Monoterpene	In vitro	IC_{50} 1.42 mmols	Active	Miyazawa et al., 1997
Menthone, iso: (+)	Monoterpene	In vitro	IC_{50} 1.57 mmols	Active	Miyazawa et al., 1997
Moenjodaramine	Alkaloid	In vitro	IC_{50} 10.0 µmols/mL	Strog activity	Rahman et al., 1998
Moenjodaramine, homo	Alkaloid	In vitro	IC_{50} 10.0 µmols/mL	Active	Rahman et al., 1998
Murranganon	Coumarin	In vitro	IC_{50} 79.14 µmols	Active	Choudhary et al., 2002
Murrangatin, 2'-*O*-ethyl	Coumarin	In vitro	Not stated	Inactive	Choudhary et al., 2002
Mutarotenone	Flavonoid	In vitro	0.24 mcg/mL	Weak activity	Ashack et al., 1980
Naphtyl ketone, β-methyl	Polycyclic	In vitro	IC_{50} 55.0 mcg/mL	Active	Miyazawa et al., 1998
Nepapakistanamine A	Alkaloid	In vitro	IC_{50} 50.1 µmols	Active	Kalauni et al., 2001
Nodakenin	Coumarin	In vitro	IC_{50} 68.0 µmols	Active	Kang et al., 2001
Nootkatone	Sesquiterpene	In vitro	0.16 mcg/mL	Active	Miyazawa et al., 2001

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Nupharidine, 7-epi: deoxy (-)	Alkaloid	In vitro	0.5 mmols/L	Strong activity	Miyazawa et al., 1998b
Nupharidine, deoxy	Alkaloid	In vitro	Not stated	Active	Shimosaka, 1955
Nupharmine, (-)	Alkaloid	In vitro	0.5 mmols	Weak activity	Miyazawa et al., 1998b
Nupharolutine	Alkaloid	In vitro	0.5 mmols/L	Active	Miyazawa et al., 1998b
Onocerin, α	Triterpene	In vitro	IC_{50} 5.2 µmols	Active	Orhan et al., 2003
Pachycarpine	Alkaloid	In vivo	Dose variable	Inactive	Zhu et al., 1982
Pachysamine, epi: 2-β-hydroxy	Alkaloid	In vitro	IC_{50} 78.2 mmols	Active	Rahman et al., 2002
Palmatine	Alkaloid	In vitro	IC_{50} 124.5 µmols	Weak activity	Schmeller et al., 1997
Paniculatin	Flavonoid	In vitro	IC_{50} 31.65 µmols	Active	Choudhary et al., 2002
Pericyclivine, 10-methoxy-*N*-1-methyl	Alkaloid	In vitro	IC_{50} 0.135 mmols	Active	Mroue et al., 1996
Persicanidine A	Alkaloid	In vitro	IC_{50} 352.2 µmols	Active	Rahman et al., 2002b
Peucedanone	Coumarin	In vitro	IC_{50} 0.18 mmols	Active	Kang et al., 2001
Phlegmariunine B	Alkaloid	In vitro	Not stated	Weak activity	Tan et al., 2000
Physostigmine	Alkaloid	In vitro	IC_{50} 31.65 µmols	Active	Choudhary et al., 2002
		In vitro	0.01 mcg/plate	Active	Marston et al., 2002
		In vitro	IC_{50} 61.0 nmols	Active	Yu et al., 1988
Physostigmine, (+)	Alkaloid	In vitro	Not stated	Active	Brossi et al., 1986
Physostigmine, (-)	Alkaloid	In vitro	Not stated	Active	Brossi et al., 1986
Physostigmine, nor	Alkaloid	In vitro	IC_{50} 56.0 nmols	Active	Yu et al., 1988
Pimara-7,15-dien-1-one, iso: 14α-hydroxy	Diterpene	In vitro	0.2 mcg/mL	Active	Rasomiaranjanahary et al., 2003
Pimara-7,15-diene, iso: 1β-14α-dihydroxy	Diterpene	In vitro	25.0 mcg/plate	Weak activity	Rasomiaranjanahary et al., 2003
Pimara-8,15-dien-14-one, iso: 7β-hydroxy	Diterepene	In vitro	0.5 mcg/plate	Active	Rasomiaranjanahary et al., 2003
Pinene, α	Monoterpene	In vitro	IC_{50} 0.63 mmols	Active	Perry et al., 2000
Pinene, β	Monoterpene	In vitro	4.7 mmols	Active	Perry et al., 2000
Pinosylvin monomethyl ether	Stilbene	In vitro	10.0 nmols	Inactive	Suga et al., 1993
Protoberberine	Alkaloid	In vitro/ Brain	0.034 mmols	Active	Ulrichova et al., 1983
Ptilosarcenone	Diterpene	In vitro	Not stated	Active	Wratten et al., 1977
		In vitro	0.36 mmols	Active	Wekell; Liston, 1978
Ptilosarcone	Diterpene	In vitro	Not stated	Active	Wratten et al., 1977
		In vitro	1.5 mmols	Active	Wekell; Liston, 1978
Pulegole, iso: (-)	Monoterpene	In vitro	IC_{50} 2.0 mmols	Active	Miyazawa et al., 1997
Pulegone, (+)	Monoterpene	In vitro	IC_{50} 0.89 mmols	Active	Miyazawa et al., 1997
Resorcinol, dimethoxy-pentadecyl	Benzenoid	In vitro	IC_{50} 62.0 µmols	Active	Kozubck et al., 1992
Resorcinol, heptadecenyl	Benzenoid	In vitro	IC_{50} 25.0 µmols	Active	Kozubck et al., 1992
Resorcinol, heptadecyl	Benzenoid	In vitro	IC_{50} 65.0 µmols	Active	Kozubck et al., 1992
Resorcinol, pentadecyl	Benzenoid	In vitro	IC_{50} 90.0 µmols	Active	Kozubck et al., 1992
Resorcinol, tricosenyl	Benzenoid	In vitro	IC_{50} 24.0 µmols	Active	Kozubck et al., 1992
Resorcinol, tricosyl	Benzenoid	In vittro	IC_{50} 18.0 µmols	Active	Kozubck et al., 1992
Resveratrol	Stilbene	In vitro	Not stated	Inactive	Sung et al., 2002
Rhapontin	Stilbene	In vitro	Not stated	Inactive	Sung et al., 2002
Rotenone	Flavonoid	In vitro/ Ileum	0.4 mcg/mL	Inactive	Ashack et al., 1980

Rotenone, dehydro	Flavonoid	In vitro/ Ileum	Not stated	Inactive	Ashack et al., 1980
Rotenone, dihydro	Flavonoid	In vitro/ Ileum	0.155 mcg/mL	Weak activity	Ashack et al., 1980
Rotenone, iso	Flavonoid	In vitro/ Ileum	0.62 mcg/mL	Weak activity	Ashack et al., 1980
Saligcinnamide	Alkaloid	In vitro	IC_{50} 19.99 µmols	Active	Rahman et al., 2002
Salignenamide A	Alkaloid	In vitro	IC_{50} 50.64 µmols	Active	Rahman et al., 2002
Salignenamide C	Alkaloid	In vitro	IC_{50} 61.3 µmols	Active	Rahman et al., 2002
Salignenamide D	Alkaloid	In vitro	IC_{50} 185.2 µmols	Active	Rahman et al., 2002
Salignenamide E	Alkaloid	In vitro	IC_{50} 6.21 µmols	Active	Rahman et al., 2002
Salignenamide F	Alkaloid	In vitro	IC_{50} 6.357 µmols	Active	Rahman et al., 2002
Salonine A	Alkaloid	In vitro	IC_{50} 33.4 µmols	Active	Rahman et al., 2003
Salonine B	Alkaloid	In vitro	Not stated	Inactive	Rahman et al., 2003
Sanguilutine	Alkaloid	In vitro/ Brain	ID_{50} 0.011 mmols	Active	Ulrichova et al., 1983
Sanguinarine	Alkaloid	In vitro	IC_{50} 10.9 µmols	Weak activity	Schmeller et al., 1997
		In vitro/ Brain	Not stated	Active	Ulrichova et al., 1984
		In vitro/ Brain	ID_{50} 0.035 mmols	Active	Ulrichova et al., 1983
Sanguirubine	Alkaloid	In vitro/ Brain	ID_{50} 0.06 mmols	Active	Ulrichova et al., 1983
Saracodine, *N*(3)-demethyl	Alkaloid	In vitro	IC_{50} 204.2 µmols	Weak activity	Rahman et al., 2002
Sarcophine	Diterpene	In vitro/ Ileum	0.2 mg/L	Active	Ne'Eman et al., 1974
Sarcorine	Alkaloid	In vitro	IC_{50} 69.99 µmols	Active	Rahman et al., 2002
Sarsalignenone	Alkaloid	In vitro	IC_{50} 5.83 µmols	Active	Rahman et al., 2002
Sarsalignone	Alkaloid	In vitro	IC_{50} 7.02 µmols	Active	Rahman et al., 2002
Schisandrin	Lignan	In vivo	3.0 mg/Kg	Active	Itoh et al., 1989
Scirpus fluviatilis trimer	Benzenoid	In vitro	2.88 mcg/mL	Active	Akiyama et al., 1991
Secodine, tetrahydro: decarbomethoxy	Alkaloid	In vitro	0.21 µmols	Active	Mroue et al., 1993
		In vitro	IC_{50} 0.203 mmols	Active	Mroue et al., 1996
Securinine, dihydro	Alkaloid	In vitro	IC_{50} 18.9 mcg/mL	Active	Jang et al., 2003
Semperviraminol	Alkaloid	In vitro	Not stated	Inactive	Rahman et al., 2001
Sieboldine A	Alkaloid	In vitro	IC_{50} 2.0 µmols	Active	Hirasawa et al., 2003
Silymarin	Flavonoid	In vivo	100.0 mg/kg	Inactive	Tyutyulkova et al., 1981
Sinularia cembranoid 1	Diterpene	In vitro	IC_{50} 63.0 µmols	Active	Reddy et al., 1993
Sparteine	Alkaloid	In vivo	Dose variable	Inactive	Zhu et al., 1982
Strictosidine	Alkaloid	In vitro	Dose variable	Inactive	Cardoso et al., 2004
Strictosidine, 5α-carboxy	Alkaloid	In vitro	Dose variable	Inactive	Cardoso et al., 2004
Strictosidine, 3,4-dehydro	Alkaloid	In vitro	Dose variable	Inactive	Cardoso et al., 2004
Strictosidinic acid	Alkaloid	In vitro	Dose variable	Inactive	Cardoso et al., 2004
Strictosidinic acid, 3,4-dehydro	Alkaloid	In vitro	Dose variable	Inactive	Cardoso et al., 2004
Strychnine	Alkaloid	In vivo	5.0 mg/kg	Inactive	Nistri et al., 1974
Suberogorgin	Sesquiterpene	In vitro	4.03 mol	Active	Peng et al., 1996
		In vitro	4.92 mol	Active	Peng et al., 1996
		In vitro/ Ileum	0.1 mmols	Active	Xu et al., 1992
Suberosin, 7-demethyl	Coumarin	In vitro	IC_{50} 2.4 mmols	Active	Kang et al., 2001
Syringaresinol	Lignan	In vitro	IC_{50} 200.0 mcg/mL	Active	El-Hassan et al., 2003
Terpinen-4-ol, (+)	Monoterpene	In vitro	1.2 mmols	Equivocal	Miyazawa et al., 1997
Terpinen-4-ol, (-)	Monoterpene	In vitro	1.2 mmols	Equivocal	Miyazawa et al., 1997

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Terpinene, α	Monoterpene	In vitro	IC_{50} 1.0 mmols	Active	Miyazawa et al., 1997
Terpinene, γ	Monoterpene	In vitro	1.2 mmols	Equivocal	Miyazawa et al., 1997
		In vitro	4.7 mmols	Inactive	Perry et al., 2000
Terpineol	Monoterpene	In vitro	4.7 mmols	Inactive	Perry et al., 2000
Terreulactone A	Sesquiterpene	In vitro	IC_{50} 0.2 µmols	Active	Kim et al., 2002
Territrem A'	Triterpene	In vitro	0.5 ng/mL	Active	Ling et al., 1986
Territrem B	Triterpene	In vitro	IC_{50} 7.6 nmols	Active	Omrua et al., 1995
		In vitro	IC_{50} 7.6 nmols	Strong activity	Kuno et al., 1996
		In vitro	IC_{50} 0.008 µmols	Strong activity	Otoguro et al., 2000
		In vitro	IC_{50} 0.26 µmols	Active	Peng, 1995
Territrem B'	Triterpene	In vitro	5.0 ng/mL	Active	Ling et al., 1986
Territrem C	Triterpene	In vitro	IC_{50} 6.8 nmols	Active	Omrua et al., 1995
		In vitro	IC_{50} 6.8 nmols	Strong activity	Kuno et al., 1996
		In vitro	IC_{50} 0.007 µmols	Strong activity	Otoguro et al., 2000
Thiocyanate, iso: benzyl	Sulfur compound	In vitro	300.0 µmols	Inactive	Kumar et al., 1991
Thymol	Monoterpene	In vitro	LC_{50} 2.89 mg/L	Active	Singh et al., 1999
		In vitro	1.0 mmols	Active	Gracza, 1985
Toosendanin	Triterpene	In vitro	Not stated	Inactive	Zhang and Chiu, 1992
Tubotaiwine	Alkaloid	In vitro	IC_{50} 108.0 µmols	Active	Mroue et al., 1996
Turbinatine	Alkaloid	In vitro	Dose variable	Active	Cardoso et al., 2004
Turbotoxin A	Alkaloid	In vitro	IC_{50} 28.0 µmols	Active	Kigoshi et al., 2000
Ulosantoin	Alkaloid	In vitro	IC_{50} 0.01 µmols	Active	Van-Wagenen et al., 1993
Umbelliferone	Coumarin	In vitro	IC_{50} 29.0 mmols	Weak activity	Kang et al., 2001
Ursolic acid	Triterpene	In vitro	IC_{50} 7.5 nmols	Active	Chung et al., 2001
Vaganine A	Alkaloid	In vitro	IC_{50} 8.59 µmols	Active	Rahman et al., 2002
Vaganine D, (-)	Alkaloid	In vitro	IC_{50} 46.9 µmols	Active	Kalauni et al., 2001
Vinervine, 16-decarbomethoxy	Alkaloid	In vitro	IC_{50} 57.0 µmols	Active	Mroue et al., 1996
Viniferin, α	Benzenoid	In vitro	IC_{50} 2.0 µmols	Active	Sung et al., 2002
Xanthotoxin	Coumarin	In vitro	IC_{50} 54.0 µmols	Active	Kang et al., 2001
Xanthyletin	Coumarin	In vitro	IC_{50} 0.15 mmols	Active	Kang et al., 2001
Xyloketal A	Oxygen heterocycle	In vitro	1.5 µmols	Active	Lin et al., 2001
Zoanthoxanthin, pseudo	Alkaloid	In vitro	4.0 µmols	Active	Turk et al., 1995