

Natural products inhibitors of the angiotensin converting enzyme (ACE). A review between 1980 - 2000

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RESUMO: “Produtos naturais inibidores da enzima conversora de angiotensina (ECA). Uma revisão entre 1980 - 2000”. A inibição da Enzima Conversora da Angiotensina (ECA) é um alvo terapêutico moderno e eficaz no tratamento da hipertensão arterial. Na cascata enzimática que envolve o sistema renina-angiotensina, a ECA promove a remoção dos aminoácidos histidil-leucina da angiotensina I para formar o octapeptídio angiotensina II, a qual é fisiologicamente ativa em diversos sistemas, e considerado como um dos mais potentes vasoconstritores endógenos conhecido. Portanto, uma racionalidade no tratamento da hipertensão seria administrar drogas ou compostos de origem natural que inibam seletivamente a ECA. O presente estudo constitui uma revisão da literatura sobre plantas e moléculas de origem natural com potencial anti-hipertensivo, baseado na inibição *in vitro* da ECA. A revisão referencia 321 plantas, partes usadas, tipo de extrato e se é ativo ou não. Inclui ainda o nome de 158 compostos isolados de plantas superiores, esponjas e algas marinhas, fungos e venenos de cobra. Alguns aspectos de pesquisa recente com produtos naturais direcionados à produção de drogas anti-hipertensivas também são discutidos. Nesta revisão 148 referências foram consultadas.

Unitermos: Enzima conversora da angiotensina, efeito anti hipertensivo, agentes hipotensivos.

ABSTRACT: Inhibition of Angiotensin Converting Enzyme (ACE) is a modern therapeutic target in the treatment of hypertension. Within the enzyme cascade of the renin-angiotensin system, ACE removes histidyl-leucine from angiotensin I to form the physiologically active octapeptide angiotensin II, one of the most potent known vasoconstrictors. Therefore, a rationale for treating hypertension would be to administer drugs or natural compounds which selectively inhibit ACE. The present work constitutes a review of the literature of plants and chemically defined molecules from natural sources with *in vitro* anti-hypertensive potential based on the inhibition of ACE. The review refers to 321 plants, the parts utilized, type of extract and whether they are active or not. It includes also the names of 158 compounds isolated from higher plants, marine sponges and algae, fungi and snake venom. Some aspects of recent research with natural products directed to produce anti-hypertensive drugs are discussed. In this review, 148 references were cited.

Keywords: Angiotensin converting enzyme, anti-hypertensive effect, hipotensive agents.

INTRODUCTION

The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure defines hypertension as systolic blood pressure (SBP) of 140 mm Hg or greater, diastolic blood pressure (DBP) of 90 mm Hg or greater, or taking anti-hypertensive medication. The objective of identifying and treating high blood pressure is to reduce the risk of cardiovascular disease and associated morbidity and mortality. To that end, it is useful to provide a classification of adult blood pressure for the purpose of identifying high-risk individuals and to provide guidelines for treatment. The positive relationship between SBP and DBP and cardiovascular risk has long been recognized.

This relationship is strong, continuous, graded, consistent, independent, predictive, and etiologically significant for those with and without coronary heart disease (Stamler, 1991, Flack et al., 1995). Therefore, although classification of adult blood pressure is somewhat arbitrary, it is useful to clinicians who must make treatment decisions based on a verification of factors including the actual level of blood pressure. Hypertension detection begins with proper blood pressure measurements. Repeated blood pressure measurements will determine whether initial elevations persist and require prompt attention or have returned to normal. According to the National Heart, Lung and Blood Institute (1997), heart disease and stroke remain the first and third leading causes of death, respectively, in the United States and impose an enormous financial and

social burden on Americans. In particular, the continued high prevalence of hypertension and hypertension-related complications of stroke, heart failure, and end-stage renal disease in the southeastern United States makes these diseases a public health concern for all who reside in this region, particularly African Americans (Hall et al., 1997). Approximately 50 million adult Americans have hypertension and are still unaware that they have high blood pressure (Burt et al., 1995). In addition, most persons with hypertension have additional risk factors for cardiovascular disease (Furster; Pearson, 1996). Thus, prevention and treatment of hypertension and target organ disease remain important public health challenges that must be addressed as we enter the new millennium.

There are different ways to treat the problem related to arterial hypertension. Treatment leading to lower levels may be useful, particularly to prevent stroke (Du et al., 1997), to preserve renal function (Lazarus et al., 1997) and to prevent or slow heart failure progression (Krumholz et al., 1997, Neaton et al., 1993). The goal may be achieved by lifestyle modification, alone or with pharmacological treatment.

Non-Pharmacological treatment of arterial hypertension

The main objective of hypertensive treatment is to reduce the high morbidity and mortality. As well as reducing the pressure, an important objective of treatment is to control other cardiovascular risk factors. Lifestyle modifications offer the potential for preventing hypertension, have been shown to be effective in lowering blood pressure, and can reduce other cardiovascular risk factors at little cost and with minimal risk (Appel et al., 1997). Even when lifestyle modifications alone are not adequate in controlling hypertension, they may reduce the number and dosage of anti-hypertensive medications needed to manage the condition (Neaton et al., 1993, Singer et al., 1995).

Pharmacological treatment of arterial hypertension

Main lifestyle modifications for hypertension prevention and management.

Main Lifestyle Modifications

- Lose weight if overweight.
- Limit alcohol intake
- Increase aerobic physical activity
- Reduce sodium intake to no more than 100 mmol per day
- Maintain adequate intake of dietary calcium and magnesium for general health
- Stop smoking
- Reduce intake of dietary saturated fat and cholesterol for overall cardiovascular health.

Reducing blood pressure with drugs clearly decreases cardiovascular morbidity and mortality. Protection has been demonstrated for stroke, coronary events, heart failure, progression of renal disease,

progression to more severe hypertension, and all-cause mortality (Psaty et al., 1997, Moser; Hebert, 1996).

Actually, there are a lot of alternatives available to treat arterial hypertension, both in schemes of monotherapy and/or combined therapy. The efficacy, security and effects of the different drugs are fundamental criteria to be considered in choosing the anti-hypertensive treatment scheme for each patient. In Table 1 the conventional pharmacological anti-hypertensive medications are presented, further details see references.

Mechanism of anti-hypertensive effect based on the inhibition of the angiotensin converting enzyme (ACE)

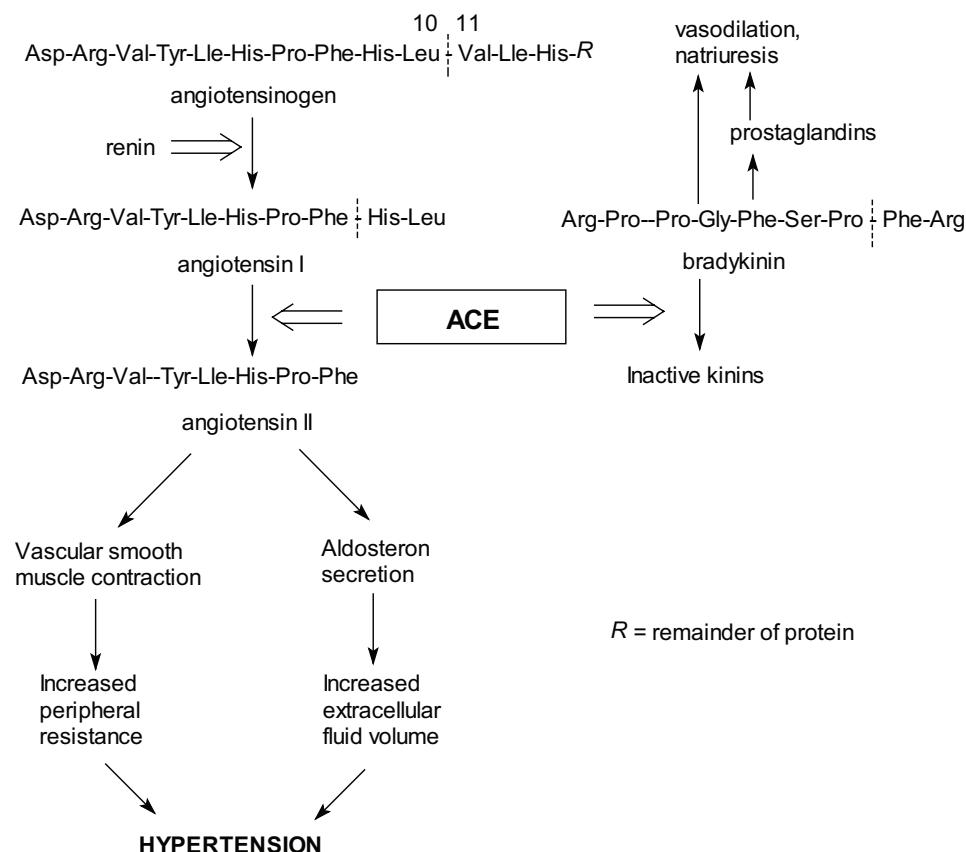
The renin-angiotensin-aldosterone system plays a pivotal role in the maintenance of vascular tone *vis à vis* peripheral resistance. Renin produced from the juxtaglomerular apparatus of the kidney, splits angiotensinogen to produce the inactive decapeptide angiotensin I. The latter is then converted to the powerful octapeptide vasoconstrictor, angiotensin II by the action of angiotensin converting enzyme (ACE). Angiotensin II also stimulates the synthesis and release of aldosterone from the adrenal cortex, which increases blood pressure by promoting sodium retention (and thereby water retention) in the distal tubules (Ahnfelt-Ronne, 1991). Research suggests that angiotensin II stimulates the production of superoxide anion and hydrogen peroxide in the polymorphonuclear leucocytes, which inactivates the vasodilatory compounds endothelial derived vascular relaxing factor (nitric oxide – NO) and prostacyclin (PGI_2) (Kumar; Das, 1993). ACE also inactivates the vasodilating nonapeptide bradykinin, which theoretically contributes to the hypertensive effects of ACE activity (Ahnfelt-Ronne, 1991) (Figure 1).

Therefore, a good rationale for treating hypertension would be to administer drugs or natural compounds which selectively inhibit ACE. Such selective inhibitors would be capable of decreasing blood pressure and producing natriuresis and diuresis.

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

Table 1. Conventional anti-hypertensive medication

Drugs	References
Diuretics	Kaplan, 1996
Beta-blockers	Heintzen; Strauer, 1994
Alpha ₁ -blockers	Grimm, 1989; Lasagna, 2000
Alpha ₂ -adrenoceptor agonists	Wallin; Frisk-Holmberg, 1981
Calcium channel-blockers	Wenzel et al., 2000; Zannad, 2000
Angiotensin II receptor antagonists	Burnier; Maillard, 2001; Chung, 1999
Inhibitors of the angiotensin converting enzyme (ACE)	Waeber, 1998; Gustafsson et al., 1998

**Figure 1.** The suggested hypertensive mechanism of angiotensin. Adapted from Hansen et al., 1995 and Hansen et al., 1996a.

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), hypoglycemic (Barbosa-Filho et al., 2005), antiinflammatory activity (Falcão et al., 2005, Barbosa-Filho et al., 2006a) and inhibitors of the enzyme acetylcholinesterase (Barbosa-Filho et al., 2006b).

In this work we present such natural products, in other words, plant extracts, semi purified fractions, chemically defined molecules isolated from plants and

metabolites from fungi that act specifically inhibiting the angiotensin converting enzyme (ACE), which is one of the most powerful known vasoconstrictors.

MATERIAL AND METHODS

The keyword for this revision was ACE (Angiotensin Converting Enzyme). We made a data search in the Chemical Abstracts, Biological Abstracts and the NAPRALERT (trademark, NATural PRoducts ALERT) database at the Illinois University, Chicago. The specialized magazines referenced were then searched.

Table 2. Percentage inhibition of angiotensin converting enzyme (ACE) activity by *Euphorbia hirta* extracts at doses of 500 µg and 150 µg

Extract and dose	Mean percentage inhibition of ACE
<i>Crude methanol</i>	
150 µg	55.4 ± 0.02
500 µg	90.3 ± 0.50
<i>Fraction at 150 µg</i>	
Petroleum ether (non-polar compounds)	18.2 ± 2.5
Chloroform (medium polar)	43.7 ± 4.5
Methanol (polar)	48.6 ± 0.9
Water (very polar)	45.4 ± 1.8

RESULTS AND DISCUSSION

Plants which inhibit the angiotensin converting enzyme

Screening for anti-hypertensive effects in traditional medicines has been performed over many years and several animal models have been used (Villar et al., 1986). In western medicine, drug development has become increasingly more mechanistic in focus with the aim of excluding unwanted side-effects. The rationale behind this approach is to identify a molecular target (receptor or enzyme) which has an essential role in the regulation of the disease and then search for ligands, substrates or inhibitors of the target.

In the treatment of hypertension, inhibition of the angiotensin converting enzyme (ACE) is established as a modern therapeutic principle.

Elbl and Wagner (1991) introduced an *in vitro* assay for the detection of ACE inhibitors in plant extracts. This method is based on the ACE-catalyzed cleavage of the chromophore-fluorophore labelled substrate, dansyltriglycine, into dansylglycine, which is quantitatively measured by HPLC (high performance liquid chromatography). By using this technique, a number of plant species have been found to be active (Elbl; Wagner, 1991).

Williams et al. (1997) using another bioassay, but also involving ACE inhibition, verified that the leaves and stems of *Euphorbia hirta* inhibited the activity of angiotensin converting enzyme by 90% and 50% at 500 µg and 150 µg respectively using enzyme linked immunosorbent assay (ELISA). The data are presented in Table 2. The study also revealed that the most active ACE inhibitory compounds were present in the polar and very polar fractions of the medium.

The results of the literature survey are presented in Table 3, which lists the effects on angiotensin converting enzyme of 321 plant extracts. The plants are arranged in alphabetical order. Each entry gives the following information in sequence: botanical name, family, part used, type of extract or fraction, whether active or not and reference.

From these studies, it appears to be the possible, using biomonitoring phytochemical methods, to find out new substances potentially active, which may prove important for the development of new substances inhibitors of the angiotensin converting enzyme.

Chemically defined molecules inhibitors of the angiotensin converting enzymes

Synthetic drugs such as captopril (Ondetti et al., 1977) or tetrodotoxin (Ferreira, 1965), a nonapeptide isolated from the venom of *Bothrops jararacussu* with established ACE inhibiting activity are used as first line drugs in both secondary and primary hypertension. The rising cost of these and other imported anti-hypertensive drugs stimulates the evaluation of new products as a source of cheaper agents. Several classes of ACE inhibitory compounds were isolated from plants, for example, flavonoids (Wagner et al., 1991; Wagner; Elbl, 1992; Hansen et al., 1996b), xanthones (Chen et al., 1992), secoiridoids (Hansen et al., 1996a). For a comprehensive review of these compounds, see Hansen (1995).

The results of the literature are presented in Table 4, which lists the effects on angiotensin converting enzyme of 158 chemically defined molecules. The compounds are arranged in alphabetical order. Each entry gives the following information in sequence: chemical name, class, whether active or not and reference.

CONCLUSION

This revision focussed initially on the search for information about natural product inhibitors of the angiotensin converting enzyme (ACE). From the literature searched, 321 species of plants and 158 natural substances which inhibit ACE were identified. These natural products may become important for human clinical treatments.

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Table 3. Plant extracts summary showing inhibition of angiotensin converting enzyme

Species	Family	Part used	Extract	Activity	Reference
<i>Abies cantoniensis</i>	Fabaceae	Dried aerial	H ₂ O	Inactive	Han et al., 1991
<i>Abutilon indicum</i>	Malvaceae	Root	Acetone EtOH (95%)	Weak	Hansen, 1995
		Root	H ₂ O	Inactive	Hansen, 1995
		Root	Acetone	Weak	Hansen, 1995
<i>Achyranthes aspera</i>	Amaranthaceae	Aerial parts	EtOH (95%)	Active	Hansen, 1995
		Aerial parts	H ₂ O	Weak	Hansen, 1995
		Dried root	MeOH-H ₂ O (1:1)	Inactive	Inokuchi et al., 1984
		Root	MeOH	Inactive	Oh et al., 1997
<i>Achyranthes bidentata</i>	Amaranthaceae	Aerial parts	Acetone	Weak	Hansen, 1995
<i>Achyranthes japonica</i>	Amaranthaceae	Aerial parts	EtOH (95%)	Weak	Hansen, 1995
<i>Achyranthes ruibrofusca</i>	Amaranthaceae	Tuber	MeOH	Inactive	Oh et al., 1997
		Root	MeOH	Inactive	Oh et al., 1997
<i>Aconitum koreanum</i>	Ranunculaceae	Rhizome	MeOH	Inactive	Oh et al., 1997
<i>Aconitum locznamnum</i>	Ranunculaceae	Dried rhizome	H ₂ O	Weak	Han, 1991
<i>Acorus gramineus</i>	Araceae	Fruit	MeOH	Inactive	Inokuchi et al., 1984
		Dried entire plant	MeOH-H ₂ O (1:1)	Active	Oh et al., 1997
<i>Actinidia arguta</i>	Actinidiaceae	Aerial parts	MeOH	Inactive	Inokuchi et al., 1984
<i>Actinostemma lobatum</i>	Cucurbitaceae	Dried entire plant	MeOH-H ₂ O (1:1)	Inactive	Inokuchi et al., 1984
<i>Agrimonia pilosa</i>	Rosaceae	Dried stem	MeOH-H ₂ O (1:1)	Inactive	Inokuchi et al., 1984
<i>Ajuga decumbens</i>	Lamiaceae	Bark	MeOH	Inactive	Oh et al., 1997
<i>Alkebia</i> sp.	Lardizabalaceae	Dried bark	H ₂ O	Equivocal	Han, 1991
<i>Albizia julibrissin</i>	Fabaceae	Dried rhizome	MeOH-H ₂ O (1:1)	Inactiva	Inokuchi et al., 1984
		Rhizome	H ₂ O	Active	Han, 1991
<i>Alisma orientale</i>	Aismataceae	Fresh bulb	MeOH	Inactive	Oh et al., 1997
		Fresh bulb	Lyophilized	Inactive	Sendl et al., 1992
		Fresh leaf	Lyophilized	Inactive	Sendl et al., 1992
		Branches	Hexane	Inactive	Arisawa et al., 1989
		Branches	CHCl ₃	Inactive	Arisawa et al., 1989
		Branches	BuOH	Active	Arisawa et al., 1989
		Branches	H ₂ O	Active	Arisawa et al., 1989
		Rhizome	MeOH	Inactive	Oh et al., 1997
		Dried root	EtOH (95%)	Active	Ham et al., 1996
		Dried root	Decotion	Active	Kanetoshi et al., 1993
		Dried root	EtOH (95%)	Active	Ham et al., 1996
		Root	MeOH	Weak	Oh et al., 1997
		Dried leaf	EtOH (80%)	Active	Shimizu et al., 1999
<i>Anemarrhena asphodeloides</i>	Liliaceae				
<i>Angelica acutiloba</i>	Apiaceae				
<i>Angelica gigas</i>	Apiaceae				
<i>Angelica keiskei</i>	Apiaceae				

<i>Angelica koreana</i>	Apiaceae	Rizome	MeOH	Inactive
<i>Angelica pubescens</i>	Apiaceae	Dried root	MeOH-H ₂ O (1:1)	Inactive
<i>Angelica sinensis</i>	Apiaceae	Dried root	H ₂ O	Weak
<i>Angelica species</i>	Apiaceae	Dried root	H ₂ O	Equivocal
<i>Angelica tenuissima</i>	Apiaceae	Rizome	MeOH-H ₂ O (1:1)	Inactive
<i>Arcium lappa</i>	Asteraceae	Dried fruit	MeOH	Inactive
		Dried fruit	MeOH-H ₂ O (1:1)	Inactive
		Seed	H ₂ O	Equivocal
<i>Areca catechu</i>	Arecaceae	Dried seed	MeOH	Inactive
		Dried seed	Chromatog. fraction	Active
		Dried seed	MeOH-H ₂ O (1:1)	Active
		Dried seed	Tannin fraction	Active
		Rizome	MeOH	Inactive
		Dried rizome	H ₂ O	Active
		Aerial parts	MeOH	Inactive
		Dried root	H ₂ O	Active
		Dried stem	H ₂ O	Weak
		Stem	Acetone	Active
		Stem	EtOH (95%)	Active
		Stem	H ₂ O	Active
		Bark	EtOH (95%)	Active
		Aerial parts	MeOH	Inactive
		Aerial parts	MeOH	Inactive
		Dried entire	MeOH-H ₂ O (1:1)	Inactive
		Dried aerial	H ₂ O	Active
		Aerial parts	MeOH	Inactive
		Dried aerial	H ₂ O	Active
		Dried entire plant	MeOH-H ₂ O (1:1)	Inactive
		Dried root	H ₂ O	Inactive
		Aerial parts	MeOH	Inactive
		Dried root	MeOH-H ₂ O (1:1)	Inactive
		Aerial parts	MeOH	Active
		Rhizome	CHCl ₃	Weak
		Rhizome	H ₂ O	Weak
		Rhizome	MeOH	Weak
		Dried rhizome	H ₂ O	Equivocal
		Dried rhizome	MeOH-H ₂ O (1:1)	Inactive
		Dried root	H ₂ O	Equivocal
		Seed	MeOH	Weak
		Aerial parts	MeOH	Inactive
		Aerial parts	MeOH	Inactive
<i>Aristotelia chilensis</i>	Elaeocarpaceae			
<i>Artemisia apiaecae</i>	Asteraceae			
<i>Artemisia capillaris</i>	Asteraceae			
<i>Asarum heterotropoides</i>	Aristolochiaceae			
<i>Asarum sieboldii</i>	Aristolochiaceae			
<i>Asarum sp.</i>	Aristolochiaceae			
<i>Asparagus cochinchinensis</i>	Liliaceae			
<i>Astilbe chinensis</i>	Saxifragaceae			
<i>Astragalus membranaceus</i>	Fabaceae			
<i>Astragalus sinicus</i>	Fabaceae			
<i>Atractylodes japonica</i>	Asteraceae			
<i>Atractylodes macrocephala</i>	Iridaceae			
<i>Belamcanda chinensis</i>	Cucurbitaceae			
<i>Benincasa hispida</i>	Polygonaceae			
<i>Bistorta suffulta</i>	Urticaceae			
<i>Boehmeria nivea</i>				

<i>Boehmeria tricuspis</i>	Urticaceae	Aerial parts	MeOH	Inactive
<i>Boerhavia diffusa</i>	Nyctaginaceae	Root	Acetone	Weak
		Root	EtOH (95%)	Weak
		Root	H ₂ O	Active
<i>Bupleurum falcatum</i>	Apiaceae	Root	CHCl ₃	Weak
		Root	H ₂ O	Inactive
		Root	MeOH	Weak
		Flowers	MeOH	Inactive
<i>Camellia japonica</i>	Theaceae	Green leaf	Acetone	Active
<i>Camellia sinensis</i>	Theaceae	Dried leaf	Acetone	Inactive
<i>Cardiospermum halicacabum</i>	Sapindaceae	Aerial parts	Acetone	Weak
		Aerial parts	EtOH (95%)	Inactive
<i>Cardus crispus</i>	Asteraceae	Aerial parts	H ₂ O	Weak
<i>Carpusium abrotanoides</i>	Asteraceae	Aerial parts	MeOH	Inactive
<i>Carsella bursa-pastoris</i>	Brassicaceae	Aerial parts	MeOH	Inactive
<i>Cassia obtusifolia</i>	Fabaceae	Dried entire plant	MeOH-H ₂ O (1:1)	Inactive
<i>Cassia sp.</i>	Fabaceae	Dried seed	H ₂ O	Inactive
<i>Cavratia japonica</i>	Vitaceae	Dried seed	MeOH-H ₂ O (1:1)	Inactive
<i>Celastrus orbiculatus</i>	Celastraceae	Aerial parts	MeOH	Inactive
<i>Centella asiatica</i>	Apiaceae	Root	MeOH	Inactive
		Aerial parts	Acetone	Active
		Aerial parts	EtOH (95%)	Active
		Aerial parts	H ₂ O	Active
		Dried aerial	H ₂ O	Inactive
<i>Centipeda minima</i>	Asteraceae	Dried entire plant	MeOH-H ₂ O (1:1)	Inactive
<i>Chenopodium album</i>	Chenopodiaceae	Flowers	MeOH	Inactive
<i>Chrysanthemum indicum</i>	Asteraceae	Dried flowers	H ₂ O	Active
<i>Chrysanthemum lavandulaceum</i>	Asteraceae	Dried rhizome	MeOH-H ₂ O (1:1)	Inactive
<i>Cimicifuga foetida</i>	Ranunculaceae	Rhizome	MeOH	Inactive
<i>Cinnamomum cassia</i>	Lauraceae	Bark	MeOH	Inactive
		Dried bark	Tannin fraction	Active
		Dried twig	H ₂ O	Inactive
<i>Cinnamomum zeylanicum</i>	Lauraceae	Dried bark	Chromatog. fraction	Active
		Dried bark	MeOH-H ₂ O (1:1)	Active
<i>Cirsium japonicum</i>	Asteraceae	Aerial parts	MeOH	Inactive
<i>Citrus aurantium</i>	Rutaceae	Dried fruit	H ₂ O	Inactive
<i>Citrus unshiu</i>	Rutaceae	Frass	MeOH	Inactive
<i>Clematis apifolia</i>	Ranunculaceae	Aerial parts	MeOH	Inactive
<i>Clematis chinensis</i>	Ranunculaceae	Dried root	MeOH	Inactive
<i>Clematis heracleifolia</i>	Ranunculaceae	Aerial parts	MeOH	Inactive
<i>Clematis mandshurica</i>	Ranunculaceae	Root	MeOH	Inactive

<i>Clerodendrum trichotomum</i>	Aerial parts	MeOH	Weak
	Rhizome	MeOH	Inactive
	Dried rhizome	MeOH-H ₂ O (1:1)	Inactive
	Dried seed	H ₂ O	Equivocal
	Dried organism	H ₂ O	Inactive
	Dried root	MeOH-H ₂ O (1:1)	Inactive
	Fruit	MeOH	Inactive
	Fresh fruit	MeOH-H ₂ O (1:1)	Inactive
	Tuber	MeOH	Inactive
	Aerial parts	MeOH	Inactive
<i>Cnidium officinale</i>	Dried fruit	H ₂ O	Active
	Seed	MeOH	Inactive
	Flowers	Acetone	Inactive
	Flowers	EtOH (95%)	Inactive
	Flowers	H ₂ O	Weak
	Fresh fruit	MeOH-H ₂ O (1:1)	Active
	Tuber	MeOH	Inactive
	Dried fruit	Flavonoid fraction	Active
	Dried rhizome	H ₂ O	Inactive
	Dried root	H ₂ O	Weak
<i>Cnidium sp.</i>	Dried aerial	Infusion	Active
	Dried rhizome	H ₂ O	Inactive
	Dried organism	H ₂ O	Weak
	Dried wood	H ₂ O	Active
	Dried flowers	MeOH-H ₂ O (1:1)	Equivocal
	Dried organism	Acetone	Inactive
	Root	EtOH (95%)	Active
	Root	H ₂ O	Active
	Leaf + Stem	Acetone	Active
		EtOH (95%)	Active
<i>Cnidoscolus ssp.</i>	Dried seed	MeOH-H ₂ O (1:1)	Inactive
	Aerial parts	MeOH	Inactive
	Dried bark	H ₂ O	Inactive
	Blood	MeOH	Weak
	Dried root	H ₂ O	Inactive
	Dried leaf	MeOH-H ₂ O (1:1)	Inactive
	Calix	MeOH	Equivocal
	Dried root	H ₂ O	Equivocal
	Rhyzone	H ₂ O	
<i>Cynometra variabilis</i>	Caryophyllaceae		
	Cupressaceae		
	Hypoxidaceae		
	Amaranthaceae		
	Cucurbitaceae		
	Cyperaceae		
	Polyporaceae		
	Fabaceae		
	Thymelaeaceae		
	Orchidaceae		
<i>Cyperus rotundus</i>	Fabaceae		
	Cynostemma pentaphylla		
	Cyperus rotundus		
	Daedaleopsis confragosa		
	Dalbergia odorifera		
	Daphne genkwa		
	Dendrobium sp.		
	Desmodium gangeticum		
	Desmodium sphaerocarpum		
<i>Dianthus superbus</i>	Fabaceae		
	Caryophyllaceae		
	Saxifragaceae		
	Rutaceae		
	Dioscoreaceae		
	Ebenaceae		
	Dissacaceae		
	Polypodiaceae		
<i>Dichroa febrifuga</i>			
<i>Dictamnus dasycarpus</i>			
<i>Dioscorea opposita</i>			
<i>Diospyros kaki</i>			
<i>Dipsacus asper</i>			
<i>Drynaria fortunei</i>			

<i>Echinops setifer</i>	Asteraceae	Root	MeOH	Inactive
<i>Eleutherococcus divaricatus</i>	Araliaceae	Dried stembark	BuOH	Active
<i>Eleutherococcus gracilisylphus</i>	Araliaceae	Dried bark	H ₂ O	Weak
		Dried root	H ₂ O	Equivocal
		Dried stem	CHCl ₃	Active
<i>Eleutherococcus senticosus</i>	Araliaceae	Bark	MeOH	Inactive
<i>Eleutherococcus sessiliflorus</i>	Araliaceae	Dried aerial parts	H ₂ O	Weak
<i>Elsholtzia splendens</i>	Lamiaceae	Seed	Acetone	Weak
<i>Entada purpuretha</i>	Fabaceae	Seed	EtOH (95%)	Active
		Seed	H ₂ O	Active
<i>Ephedra sinica</i>	Ephedraceae	Dried aerial parts	Tannin fraction	Active
<i>Ephedra</i> sp.	Ephedraceae	Dried entire plant	Chromatog. fraction MeOH-H ₂ O (1:1)	Active
		Dried entire plant	Tannin fraction	Active
<i>Epimedium alpinum</i>	Berberidaceae	Dried aerial parts	H ₂ O	Active
<i>Epimedium brevicornum</i>	Berberidaceae	Not specified	Chromatog. fraction MeOH-H ₂ O (1:1)	Active
<i>Epimedium macranthum</i>	Berberidaceae	Dried entire plant	MeOH-H ₂ O (1:1)	Active
		Dried entire plant	H ₂ O	Active
		Dried stem	EtOH (100%)	Active
<i>Equisetum hyemale</i>	Equisetaceae	Dried leaf	EtOH (96%)	Weak
<i>Erythroxylum laurifolium</i>	Erythroxylaceae	Aerial parts	MeOH-H ₂ O (1:1)	Inactive
<i>Grossularia myriooides</i>	Grossulariaceae	Dried bark	H ₂ O	Inactive
<i>Eucommia ulmoides</i>	Eucommiaceae	Dried bark	CHCl ₃	Weak
<i>Euodia officinalis</i>	Rutaceae	Fruit	H ₂ O	Inactive
		Fruit	MeOH	Weak
		Bark	MeOH	Inactive
		Dried aerial parts	H ₂ O	Equivocal
		Dried leaf	MeOH	Active
<i>Eupatorium fortunei</i>	Asteraceae	Dried aerial parts	H ₂ O	Active
<i>Euphorbia hirta</i>	Euphorbiaceae	Dried aerial parts	CHCl ₃	Weak
<i>Euphorbia humifusa</i>	Euphorbiaceae	Dried aerial parts	H ₂ O	Inactive
<i>Euphorbia kansui</i>	Euphorbiaceae	Dried aerial parts	MeOH	Weak
		Dried fruit	H ₂ O	Weak
<i>Euphorbia longana</i>	Sapindaceae	Dried organism	H ₂ O	Weak
<i>Flammulina velutipes</i>	Tricholomataceae	Dried organism	H ₂ O	Inactive
<i>Fomes fomentarius</i>	Polyporaceae	Dried organism	H ₂ O	Inactive
<i>Fomitopsis pinicola</i>	Polyporaceae	Dried organism	H ₂ O	Equivocal
<i>Forsythia suspensa</i>	Oleaceae	Dried fruit	MeOH-H ₂ O (1:1)	Active
<i>Fritillaria</i> sp.	Liliaceae	Dried bulb	H ₂ O	Active
<i>Fuchsia magellanica</i>	Onagraceae	Aerial parts	MeOH	Weak
<i>Gaultheria verum</i>	Rubiaceae	Aerial parts	H ₂ O	Inactive
<i>Ganoderma lipsiense</i>	Ganodermataceae	Dried organism		

<i>Ganoderma lucidum</i>	H ₂ O	Weak	Han et al., 1991
<i>Gardenia jasminoides</i>	MeOH-H ₂ O (1:1)	Inactive	Inokuchi et al., 1984
	MeOH	Inactive	Oh et al., 1997
	H ₂ O	Equivocal	Han et al., 1991
	H ₂ O	Inactive	Melzig et al., 1996
	MeOH-H ₂ O (1:1)	Inactive	Inokuchi et al., 1984
	H ₂ O	Equivocal	Han et al., 1991
	MeOH	Inactive	Oh et al., 1997
	H ₂ O	Equivocal	Hansen et al., 1995
	H ₂ O	Inactive	Han et al., 1991
	MeOH	Inactive	Oh et al., 1997
	H ₂ O	Equivocal	Han et al., 1991
	MeOH	Inactive	Oh et al., 1997
	H ₂ O	Active	Hansen et al., 1995
	H ₂ O	Inactive	Han et al., 1991
	MeOH	Inactive	Oh et al., 1997
	H ₂ O	Equivocal	Han et al., 1991
	MeOH	Inactive	Oh et al., 1997
	H ₂ O	Inactive	Han et al., 1991
	BuOH	Active	Hansen et al., 1995
	EtOAc	Active	Hansen et al., 1995
	EtOH (95%)	Active	Hansen et al., 1995
	H ₂ O	Active	Han et al., 1991
	MeOH	Inactive	Oh et al., 1997
	H ₂ O	Inactive	Melzig et al., 1996
	Acetone-H ₂ O (1:1)	Strong	Hansen et al., 1995
	EtOH (95%)	Active	Hansen et al., 1995
	H ₂ O	Equivocal	Han et al., 1991
	MeOH	Equivocal	Oh et al., 1997
	Acetone	Active	Hansen et al., 1995
	EtOH (95%)	Active	Hansen et al., 1995
	H ₂ O	Active	Hansen et al., 1995
	MeOH	Equivocal	Han et al., 1991
	H ₂ O	Inactive	Inokuchi et al., 1984
	MeOH-H ₂ O (1:1)	Inactive	Melzig et al., 1996
	H ₂ O	Inactive	Oh et al., 1997
	MeOH	Equivocal	Han et al., 1991
	H ₂ O	Active	Somanadhan et al., 1998
	CH ₂ Cl ₂	Active	Somanadhan et al., 1998
	Chromatog. fraction	Active	Somanadhan et al., 1998
	EtOAc	Active	Somanadhan et al., 1998
	H ₂ O	Active	Oh et al., 1997
	MeOH	Inactive	Inokuchi et al., 1991
	MeOH	Inactive	Somanadhan et al., 1998
	MeOH	Inactive	Somanadhan et al., 1998
	MeOH	Inactive	Oh et al., 1997
	MeOH	Inactive	Oh et al., 1997
	H ₂ O	Equivocal	Han et al., 1991
		Inactive	Juncaceae
		Inactive	Araliaceae
		Inactive	Rubiaceae
		Inactive	Saninidaeae

<i>Kuehneromyces mutabilis</i>	Strophariaceae	Dried organism	H ₂ O	Inactive
<i>Lactarius deterrimus</i>	Russulaceae	Dried entire plant	H ₂ O	Inactive
<i>Leonurus sibiricus</i>	Lamiaceae	Aerial parts	MeOH	Inactive
		Dried entire plant	MeOH-H ₂ O (1:1)	Inactive
<i>Lepisorus thanbergianus</i>	Polypodiaceae	Aerial parts	MeOH	Inactive
<i>Lespedeza capitata</i>	Fabaceae	Dried leaf	Flavonoid fraction	Active
<i>Lilium brownii</i>	Liliaceae	Dried bulb	H ₂ O	Equivocal
<i>Lindera strychnifolia</i>	Lauraceae	Dried root	H ₂ O	Weak
<i>Liriopé platyphylla</i>	Liliaceae	Tuber	MeOH	Inactive
<i>Lonicera japonica</i>	Caprifoliaceae	Flowers	MeOH	Inactive
<i>Loranthus parasiticus</i>	Loranthaceae	Dried flowers	H ₂ O	Weak
		Aerial parts	MeOH	Inactive
<i>Luffa aegyptiaca</i>	Cucurbitaceae	Dried entire plant	H ₂ O	Inactive
<i>Lycium chinense</i>	Solanaceae	Dried seed	MeOH-H ₂ O (1:1)	Inactive
		Dried fruit	MeOH-H ₂ O (1:1)	Inactive
		Dried leaf	MeOH-H ₂ O (1:1)	Inactive
		Dried rootback	Not stated	Active
		Fruit	MeOH	Inactive
		Dried rootbark	CHCl ₃	Active
		Dried rootbark	MeOH-H ₂ O (1:1)	Inactive
<i>Lycopus coreanus</i>	Lamiaceae	Aerial parts	MeOH	Inactive
<i>Lygodium japonicum</i>	Schizaeaceae	Dried aerial parts	H ₂ O	Active
<i>Lysimachia barystachys</i>	Primulaceae	Aerial parts	MeOH	Inactive
<i>Machilus thunbergii</i>	Lauraceae	Bark	CHCl ₃	Active
		Bark	H ₂ O	Inactive
		Bark	MeOH	Active
		Dried organism	H ₂ O	Weak
		Flowers	MeOH	Inactive
		Dried bark	MeOH-H ₂ O (1:1)	Inactive
		Dried flowers	MeOH-H ₂ O (1:1)	Inactive
		Dried leaf	H ₂ O	Equivocal
		Aerial parts	MeOH	Inactive
		Fruit	MeOH	Inactive
		Aerial parts	MeOH	Inactive
		Aerial parts	MeOH	Inactive
		Dried organism	H ₂ O	Inactive
		Aerial parts	Acetone	Active
		Aerial parts	EtOH (95%)	Active
		Aerial parts	H ₂ O	Active
		Dried seed	MeOH-H ₂ O (1:1)	Inactive
		Seed	MeOH	Inactive
<i>Macrolepiota rhacodes</i>	Lepiotaceae			
<i>Magnolia densata</i>	Magnoliaceae			
<i>Magnolia sp.</i>	Magnoliaceae			
<i>Mahonia bealei</i>	Berberidaceae			
<i>Malus baccata</i>	Rosaceae			
<i>Melia azedarach</i>	Meliaceae			
<i>Menispermum dauricum</i>	Menispermaceae			
<i>Mentha arvensis</i>	Lamiaceae			
<i>Meripilus giganteus</i>	Polyporaceae			
<i>Merremia tridentata</i>	Convolvulaceae			
<i>Mormodica cochinchinensis</i>	Cucurbitaceae			

<i>Morus alba</i>	Moraceae	Bark	CHCl ₃	Inactive
		Dried bark	H ₂ O	Weak
		Dried fruit	H ₂ O	Equivocal
		Dried leaf	MeOH	Weak
		Dried leaf	MeOH-H ₂ O (1:1)	Inactive
		Dried leaf	MeOH-H ₂ O (1:1)	Active
		Seed	MeOH	Inactive
		Dried seed	H ₂ O	Inactive
		Dried root	H ₂ O	Weak
		Seed	Seed oil	Active
		Dried root	H ₂ O	Equivocal
		Root	MeOH	Inactive
		Fruitbody	MeOH	Weak
		Dried root	H ₂ O	Active
		Dried bark	MeOH	Active
		Dried bark	MeOH-H ₂ O (1:1)	Inactive
		Dried bark	Tannin fraction	Active
		Root	MeOH	Active
		Rhizome + root	Polysacchar. fraction	Inactive
		Dried root	MeOH-H ₂ O (1:1)	Weak
		Dried root	H ₂ O	Equivocal
		Dried entire plant	H ₂ O	Active
		Dried root	H ₂ O	Weak
		Root	MeOH	Inactive
		Dried organism	CHCl ₃	Weak
		Aerial parts	H ₂ O	Weak
		Aerial parts	MeOH	Weak
		Aerial parts	CHCl ₃	Weak
		Seed	MeOH	Weak
		Aerial parts	CHCl ₃	Weak
		Root	H ₂ O	Weak
		Root	MeOH	Weak
		Dried organism	H ₂ O	Weak
		Bark	MeOH	Inactive
		Root	MeOH	Inactive
		Dried organism	H ₂ O	Inactive
		Aerial parts	MeOH	Inactive
		Dried entire plant	CHCl ₃	Active
		Aerial parts	MeOH	Weak
		Root	CHCl ₃	Weak
		Root	H ₂ O	Weak
		Root	MeOH	Weak
		Dried organism	H ₂ O	Weak
		Bark	MeOH	Inactive
		Root	MeOH	Inactive
		Dried organism	H ₂ O	Inactive
		Aerial parts	MeOH	Inactive
		Dried entire plant	CHCl ₃	Active
		Aerial parts	MeOH	Weak
		Root	CHCl ₃	Weak
		Root	H ₂ O	Weak
		Hymenochaetaceae	MeOH	Weak
		Rutaceae	MeOH	Inactive
		Lamiaceae	MeOH	Inactive
		Strophariaceae	MeOH	Inactive
		Phrymaceae	MeOH	Inactive
		Euphorbiaceae	MeOH	Inactive
		Sinarouhiaeae	MeOH	Active
		Serophulariaceae	MeOH	Weak
		<i>Phaeolus schweinitzii</i>	MeOH	Inactive
		<i>Phellodendron amurense</i>	MeOH	Inactive
		<i>Phlomis umbrosa</i>	MeOH	Inactive
		<i>Pholiota squarrosa</i>	MeOH	Inactive
		<i>Phryma leptostachya</i>	MeOH	Inactive
		<i>Phyllanthus niruri</i>	MeOH	Active
		<i>Picrasma quassoides</i>	MeOH	Weak
		<i>Picrorhiza kurroa</i>	MeOH	Inactive

<i>Pinellia ternata</i>	Araceae	Dried rhizome	H ₂ O	Active	Han et al., 1991
<i>Pinus pinastre</i>	Pinaceae	Tuber	MeOH	Inactive	Oh et al., 1997
<i>Pinus tabulaeformis</i>	Pinaceae	Dried bark	Flavonoid fraction	Inactive	Blaszo et al., 1996
<i>Piper futoakadsura</i>	Piperaceae	Aerial parts	MeOH	Inactive	Oh et al., 1997
<i>Piptoporus betulinus</i>	Polyporaceae	Dried aerial parts	H ₂ O	Active	Han et al., 1991
<i>Pistacia lentiscus</i>	Anacardiaceae	Dried organism	H ₂ O	Inactive	Melzig et al., 1996
<i>Plantago asiatica</i>	Plantaginaceae	Dried aerial parts	Flavonoid fraction	Active	Sanz et al., 1993
<i>Plantago</i> sp.		Dried seed	H ₂ O	Equivocal	Han et al., 1991
<i>Platycarya strobilacea</i>	Juglandaceae	Entire plant	H ₂ O	Active	Inokuchi et al., 1984
<i>Platycodon grandiflorum</i>	Campanulaceae	Entire plant	Acetone	Active	Hansen et al., 1995
		Entire plant	EtOH (95%)	Active	Hansen et al., 1995
		Entire plant	H ₂ O	Active	Hansen et al., 1995
		Dried leaf	MeOH-H ₂ O (1:1)	Inactive	Inokuchi et al., 1984
		Dried seed	MeOH	Inactive	Hansen et al., 1995
		Fruit	CHCl ₃	Weak	Hansen et al., 1995
		Root	H ₂ O	Weak	Hansen et al., 1995
		Root	MeOH	Inactive	Oh et al., 1997
		Fruitbody	Not stated	Active	Ikenizu et al., 1995
		Root	MeOH	Inactive	Oh et al., 1997
		Dried root	H ₂ O	Equivocal	Han et al., 1991
		Dried aerial parts	Tannin fraction	Active	Inokuchi et al., 1985
		Dried entire plant	Chromatog. fraction	Inactive	Inokuchi et al., 1984
		Dried entire plant	MeOH-H ₂ O (1:1)	Active	Inokuchi et al., 1984
		Dried rhizome	MeOH-H ₂ O (1:1)	Inactive	Inokuchi et al., 1984
		Dried rhizome	H ₂ O	Inactive	Han et al., 1991
		Root	MeOH	Inactive	Oh et al., 1997
		Dried root	H ₂ O	Active	Han et al., 1991
		Aerial parts	MeOH	Inactive	Oh et al., 1997
		Dried organism	H ₂ O	Weak	Metzig et al., 1996
		Dried organism	H ₂ O	Equivocal	Han et al., 1991
		Dried aerial parts	Tannin fraction	Active	Inokuchi et al., 1985
		Aerial parts	MeOH	Inactive	Oh et al., 1997
		Dried entire plant	Chromatog. fraction	Active	Inokuchi et al., 1984
		Dried entire plant	MeOH-H ₂ O (1:1)	Active	Inokuchi et al., 1984
		Aerial parts	H ₂ O	Weak	Han et al., 1991
		Dried aerial parts	MeOH-H ₂ O (1:1)	Inactive	Inokuchi et al., 1984
		Dried inflores.	MeOH	Inactive	Oh et al., 1997
		Fruit	Acetone	Active	Hansen et al., 1995
		Root	EtOH (95%)	Strong	Hansen et al., 1995
		Root	H ₂ O	Weak	Hansen et al., 1995

<i>Pseudarthria viscida</i>	Fabaceae	Root	Acetone	Weak
		Root	EtOH (95%)	Active
		Root	H ₂ O	Active
		Dried fruit	H ₂ O	Weak
<i>Psoralea corylifolia</i>	Fabaceae	Dried root	H ₂ O	Weak
		Root	Acetone	Weak
<i>Pueraria lobata</i>	Fabaceae	Root	EtOH (95%)	Active
		Dried root	MeOH-H ₂ O (1:1)	Inactive
<i>Pueraria pseudo-hisuta</i>	Fabaceae	Dried aerial parts	H ₂ O	Inactive
<i>Pulsatilla chinensis</i>	Ranunculaceae	Aerial parts	MeOH	Inactive
<i>Pyrola japonica</i>	Pyrolaceae	Entire plant	Acetone	Active
<i>Pyrrosia lingua</i>	Polypodiaceae	Entire plant	EtOH (95%)	Active
<i>Quinchamalium chilense</i>	Santalaceae	Entire plant	H ₂ O	Active
<i>Ranunculus japonicus</i>	Ranunculaceae	Aerial parts	EtOH (95%)	Active
<i>Rauvolfia serpentina</i>	Apocynaceae	Aerial parts	MeOH	Inactive
<i>Rehmannia glutinosa</i>	Scrophulariaceae	Dried root	MeOH-H ₂ O (1:1)	Inactive
<i>Rheum palmatum</i>	Polygonaceae	Dried root	H ₂ O	Weak
<i>Rheum</i> sp.	Polygonaceae	Dried rhizome	Tannin fraction	Active
<i>Rosa multiflora</i>	Rosaceae	Dried rhizome	MeOH	Weak
<i>Salvia miltiorrhiza</i>	Lamiaceae	Dried rhizome	MeOH	Inactive
<i>Sanguisorba officinalis</i>	Rosaceae	Dried root	Chromatog. fraction	Active
<i>Sapium sebiferum</i>	Euphorbiaceae	Fruit	MeOH-H ₂ O (1:1)	Active
<i>Sasa borealis</i>	Poaceae	Dried root	MeOH	Inactive
<i>Saussurea lappa</i>	Asteraceae	Root	MeOH	Inactive
<i>Schinus latifolius</i>	Anacardiaceae	Dried root	MeOH-H ₂ O (1:1)	Active
	Bark	Root	MeOH	Inactive
	Bark	Dried root	MeOH	Inactive
	Bark	Aerial parts	MeOH	Inactive
	Bark	Dried root	MeOH	Active
	Bark	Root	MeOH	Inactive
	Bark	Dried aerial parts	EtOH-H ₂ O (7:3)	Active
	Bark	Dried root	H ₂ O	Equivocal
<i>Schizonepeta tenuifolia</i>	Lamiaceae	Dried root	MeOH-H ₂ O (1:1)	Inactive
<i>Scrophularia ningpoensis</i>	Scrophulariaceae	Root	MeOH	Inactive
<i>Scutellaria baicalensis</i>	Lamiaceae	Dried root	CHCl ₃	Weak
		Root	H ₂ O	Weak
		Root	MeOH	Weak

<i>Sedum sarmentosum</i>	Crassulaceae	Entire plant	Acetone	Active
		Entire plant	EtOH (95%)	Active
		Entire plant	H ₂ O	Active
		Root	Acetone	Active
		Root	EtOH (95%)	Weak
<i>Sida acuta</i>	Malvaceae	Entire plant	H ₂ O	Active
		Root	Acetone	Active
		Root	EtOH (95%)	Active
<i>Sida cordifolia</i>	Malvaceae	Entire plant	H ₂ O	Active
		Root	Acetone	Active
		Root	EtOH (95%)	Weak
<i>Sida retusa</i>	Malvaceae	Entire plant	H ₂ O	Active
		Root	Acetone	Active
		Root	EtOH (95%)	Weak
<i>Sigesbeckia orientalis</i>	Asteraceae	Dried aerial parts	H ₂ O	Active
		Rhizome	MeOH	Inactiv
		Rhizome	H ₂ O	Weak
		Dried root	MeOH	Inactiv
		Rhizome	MeOH	Inactive
		Rhizome + stem	MeOH-H ₂ O (1:1)	Inactive
		Dried aerial parts	H ₂ O	Active
		Aerial parts	MeOH	Inactive
		Root	MeOH	Inactive
		Flower	MeOH	Inactive
		Dried root	H ₂ O	Weak
		Root	MeOH	Inactive
		Bark	MeOH	Inactive
		Dried root	H ₂ O	Weak
		Rhizome	MeOH	Inactive
		Dried stem	H ₂ O	Inactive
		Root	MeOH	Inactive
		Dried root	H ₂ O	Inactive
		Aerial parts	MeOH	Inactive
		Seed	MeOH	Inactive
		Aerial parts	MeOH	Inactive
		Aerial parts	MeOH	Inactive
		Aerial parts	CHCl ₃	Weak
		Aerial parts	H ₂ O	Inactive
		Aerial parts	MeOH	Weak
		Dried flowers	H ₂ O	Equivocal
		Aerial parts	MeOH	Inactive
		Dried seed	H ₂ O	Inactive
		Leaf	MeOH	Inactive
<i>Smilax china</i>	Liliaceae			
<i>Sinomenium acutum</i>	Menispermaceae			
<i>Solanum nigrum</i>	Solanaceae			
<i>Solidago virgaurea</i>	Asteraceae			
<i>Sophora flavescens</i>	Fabaceae			
<i>Sophora japonica</i>	Fabaceae			
<i>Sophora subprostrata</i>	Fabaceae			
<i>Sorbus amurensis</i>	Rosaceae			
<i>Sparganium stoloniferum</i>	Sparganiaceae			
<i>Spatholobus suberectus</i>	Fabaceae			
<i>Stemonia japonica</i>	Stemonaceae			
<i>Stemonia sessilifolia</i>	Stemonaceae			
<i>Stephanandra incisa</i>	Rosaceae			
<i>Loganiaeae</i>	Loganiaceae			
<i>Syringa max-yomica</i>	Syracaceae			
<i>Syrrax japonicus</i>	Symplocaceae			
<i>Symplocos chinensis</i>	Asteraeae			
<i>Taraxacum mongolicum</i>				
<i>Taxus cuspidata</i>	Taxaceae			
<i>Thuja orientalis</i>	Cupressaceae			

<i>Torilis japonica</i>	Apiaceae	Fruit	CHCl ₃	Weak
<i>Torreya nucifera</i>	Taxaceae	Fruit	H ₂ O	Inactive
<i>Trachomitum venetum</i>	Apocynaceae	Seed	MeOH	Inactive
<i>Trachycarpus excelsus</i>	Aracaceae	Dried entire plant	MeOH-H ₂ O (1:1)	Inactive
<i>Trametes hirsuta</i>	Polyporaceae	Dried leaf	MeOH-H ₂ O (1:1)	Inokuchi et al., 1984
<i>Trametes versicolor</i>	Polyporaceae	Dried organism	H ₂ O	Melzig et al., 1996
<i>Trichosanthes kirilowii</i>	Cucurbitaceae	Dried organism	H ₂ O	Melzig et al., 1996
		Dried fruit	H ₂ O	Han et al., 1991
		Root	MeOH	Oh et al., 1997
<i>Tricholoma populinum</i>	Tricholomataceae	Dried organism	H ₂ O	Melzig et al., 1996
<i>Tricholoma portentosum</i>	Tricholomataceae	Dried organism	H ₂ O	Melzig et al., 1996
<i>Tricholopsis rutilans</i>	Tricholomataceae	Dried organism	H ₂ O	Melzig et al., 1996
<i>Triumfetta rhomboidea</i>	Tiliaceae	Root	Acetone	Hansen et al., 1995
		Root	EtOH (95%)	Hansen et al., 1995
<i>Tropaeolum majus</i>	Tropaeolaceae	Dried aerial	H ₂ O	Weak
<i>Tussilago farfara</i>	Asteraceae	Dried flowers	H ₂ O	Inactive
<i>Ulmus parvifolia</i>	Ulmaceae	Root	MeOH	Inactive
<i>Uncaria rhynchophylla</i>	Rubiaceae	Dried branchets	MeOH-H ₂ O (1:1)	Inokuchi et al., 1984
		Root	Acetone	Hansen et al., 1995
		Root	EtOH (95%)	Hansen et al., 1995
		Root	H ₂ O	Active
		Dried seed	H ₂ O	Active
		Dried aerial parts	H ₂ O	Weak
<i>Vaccaria segatalis</i>	Caryophyllaceae	Aerial parts	MeOH	Equivocal
<i>Verbena officinalis</i>	Verbenaceae	Dried bark	EtOH-H ₂ O (1:1)	Inactive
<i>Veronicastrum sibiricum</i>	Scrophulariaceae	Dried fruit	Flavonoid fraction	Active
<i>Viburnum opulus</i>	Caprifoliaceae	Dried organism	H ₂ O	Active
<i>Vitis vinifera</i>	Vitaceae	Dried seed	H ₂ O	Weak
<i>Vohvariella speciosa</i>	Pluteaceae	Dried fruit	MeOH-H ₂ O (1:1)	Equivocal
<i>Xanthium sibiricum</i>	Asteraceae	Fruit	MeOH	Inactive
<i>Xanthium strumarium</i>	Asteraceae	Dried organism	H ₂ O	Inactive
<i>Xylaria polymorpha</i>	Xylariaceae	Aerial parts	MeOH	Inokuchi et al., 1984
<i>Youngia japonica</i>	Asteraceae	Fruit	MeOH	Oh et al., 1997
<i>Zathoxylum piperitum</i>	Rutaceae	Rhizome	MeOH	Oh et al., 1997
<i>Zingiber officinale</i>	Zingiberaceae	Fruit	MeOH	Oh et al., 1997
<i>Ziziphus jujuba</i>	Rhamnaceae	Dried seed	MeOH-H ₂ O (1:1)	Weak
<i>Ziziphus spinosa</i>	Rhamnaceae			Oh et al., 1997

Table 4. Chemically defined natural compounds showing inhibition of angiotensin converting enzyme

Chemical name	Class	Source	Activity	Reference
Actinomadura antibiotic 15B1	Proteid	<i>Actinomadura</i> sp.	Active	Kidd et al., 1984
Actinomadura antibiotic 15B2	Proteid	<i>Actinomadura</i> sp.	Active	Kidd et al., 1984
Actinomyces antibiotic 1582	Proteid	<i>Actinomyces</i> sp.	Active	Kidd, et al., 1985
Actinomyces antibiotic K-26	Proteid	<i>Actinomyces</i> sp.	Active	Yamato et al., 1986
Afzelin	Flavonoid	<i>Erythroxylum laurifolium</i>	Active	Hansen et al., 1995
Aismol	Sesquiterpene	<i>Alisma orientale</i>	Inactive	Yamahara et al., 1989
Ancovenin	Proteid	<i>Streptomyces</i> sp.	Active	Kidd et al., 1983
Angiotensin compound	Proteid	<i>Streptomyces</i> sp.	Active	Wakamiya et al., 1985
Anisomelic acid	Diterpene	<i>Vipera aspis aspis</i>	Active	Komori et al., 1990
Anisomelic acid, 4-methylene-5-oxo	Diterpene	<i>Anisomeles indica</i>	Weak	Monose et al., 1994
Arginine, L	Proteid	<i>Anisomeles indica</i>	Inactive	Arisawa et al., 1986
Arrivacin A	Sesquiterpene	Commercial	Active	Higashi et al., 1995
Arrivacin B	Sesquiterpene	<i>Ambrosia psilostachya</i>	Active	Chen et al., 1991
Arphamenine B	Alkaloid	<i>Ambrosia psilostachya</i>	Active	Chen et al., 1991
Aspergillomarasmine A	Proteid	<i>Chromobacterium violaceum</i>	Inactive	Aoyagi et al., 1986
Aspergillomarasmine B	Proteid	<i>Aspergillus oryzae</i>	Active	Mikami et al., 1983
Asperoside	Cardenolide	<i>Aspergillus oryzae</i>	Active	Mikami et al., 1983
Astragalin	Flavonoid	<i>Eucommia ulmoides</i>	Active	Yamada et al., 1992
Attractylenolide I	Sesquiterpene	<i>Diospyros kaki</i>	Active	Kameda et al., 1987
Attractylenolide III	Sesquiterpene	<i>Attractyloides japonica</i>	Inactive	Sakurai et al., 1993
Attractylodiolol	Oxygen heterocycle	<i>Attractyloides japonica</i>	Inactive	Sakurai et al., 1993
Attractylone	Coumarin	<i>Attractyloides japonica</i>	Active	Sakurai et al., 1993
Bergenin	Proteid	<i>Attractyloides japonica</i>	Inactive	Arisawa et al., 1989
Bestatin	Diterpene	<i>Allophyllus edulis</i>	Inactive	Aoyagi et al., 1986
Capsianoside A	Diterpene	<i>Streptomyces olivoreticuli</i>	Active	Yahara et al., 1990
Capsianoside C	Diterpene	<i>Capsicum</i> spp.	Active	Izumitani et al., 1990
Capsianoside I	Diterpene	<i>Capsicum</i> spp.	Weak	Inokuchi et al., 1996b
Capsianoside II	Diterpene	<i>Capsicum</i> spp.	Inactive	Yahara et al., 1990
Catechin, (+)	Flavonoid	<i>Allophyllus edulis</i>	Active	Cho et al., 1993
Catechin, <i>epi</i> (-)	Flavonoid	<i>Allophyllus edulis</i>	Inactive	Inokuchi et al., 1996b
Catechin-3-O-gallate, <i>epi</i> (-)	Flavonoid	<i>Areca catechu</i>	Inactive	Arisawa, et al., 1989
Cochinmicin I	Proteid	Korean green tea	Active	Cho et al., 1993
Cochinmicin II	Proteid	<i>Microbispora</i> sp.	Inactive	Uchida et al., 1987
Cochinmicin III	Proteid	<i>Microbispora</i> sp.	Weak	Lam et al., 1992
Corilagin	Tannin	<i>Microbispora</i> sp.	Weak	Lam et al., 1992
		<i>Phyllanthus niruri</i>	Active	Ueno et al., 1988

Coriolic acid, (DL)	Lipid	Active
Cycloaniisomelic acid, 4,7-oxy	Diterpene	Inactive
Cymene, allo	Monoterpene	Weak
Cytosporin A	Oxygen heterocycle	Commercial
Cytosporin B	Cytospora sp.	Cytospora sp.
Cytosporin C	Cytospora sp.	Cytospora sp.
Daphnodorin A	Daphne odora	Daphne odora
Daphnodorin B	Daphne odora	Daphne odora
Daphnodorin C	Daphne odora	Daphne odora
Dimorphheolic acid, <i>alpha</i>	Lycium chinense	Lycium chinense
Dimorphheolic acid, <i>alpha</i> (DL)	Fritillaria verticillata	Fritillaria verticillata
Dimorphheolic acid, <i>beta</i> (DL)	Fritillaria verticillata	Fritillaria verticillata
Doratomyces antibiotic WF-10129	Doratomyces patredinis	Doratomyces patredinis
Ellagic acid	Phyllanthus niruri	Phyllanthus niruri
Evocarpine	Evodia rutaecarpa	Evodia rutaecarpa
Excelsioside	Flaxinus excelsior	Flaxinus excelsior
Fagopyrum tripeptide	Fagopyrum sp.	Fagopyrum sp.
Fangchinolium hydroxide	Stephania tetrandra	Stephania tetrandra
Fenfangjine F	Stephania tetrandra	Stephania tetrandra
Fenfangjine G	Stephania tetrandra	Stephania tetrandra
Fenfangjine H	Stephania tetrandra	Stephania tetrandra
Fenfangjine I	Stephania tetrandra	Stephania tetrandra
Ficus oligopeptide FLP-1	Ficus carica	Ficus carica
Ficus oligopeptide FLP-2	Ficus carica	Ficus carica
Ficus peptide FLP-3	Ficus carica	Ficus carica
Ficus peptide FLP-1	Ficus carica	Ficus carica
Ficus peptide FLP-2	Ficus carica	Ficus carica
Ficus peptide FLP-3	Ficus carica	Ficus carica
Fisetin	Commercial	Commercial
Gallic acid	Phyllanthus niruri	Phyllanthus niruri
Gallocatechin, (+)	Korean green tea	Korean green tea
Gallocatechin, <i>epi</i> (-)	Korean green tea	Korean green tea
Gallocatechin, <i>epi</i> , 3-O-gallate (-)	Korean green tea	Korean green tea
Gallocatechin-3-O-gallate (-), <i>epi</i> (-)	Phyllanthus niruri	Phyllanthus niruri
Geraniin	Allophylus edulis	Allophylus edulis
Glu-Asn-Trp, P	Proteid	Trimeresurus flavoviridis
Glu-Gln-Trp, P	Proteid	Trimeresurus okinavensis
		Trimeresurus flavoviridis
		Trimeresurus okinavensis

Glu-Lys-Trp-P	Proteid	<i>Trimeresurus flavoviridis</i>	Weak
Gossypol	Sesquiterpene	<i>Trimeresurus okinavensis</i>	Weak
Kaempferol-3-O-galloyl-glucose	Flavonoid	<i>Gossypium</i> sp.	Active
Kapakahine A	Proteid	<i>Cribochalinia olenda</i>	Active
Lanosten (20-R)	Triterpene	<i>Diospyros kaki</i>	Inactive
Lanosten (20-S)	Triterpene	<i>Schinus molle</i>	Active
Ligstroside	Iridoid	<i>Schinus molle</i>	Active
Ligustuloside B	Monoterpene	<i>Ligustrum japonicum</i>	Inactive
Liriiodendrin	Lignan	<i>Eucommia ulmoides</i>	Active
Lycurumin A	Proteid	<i>Lycium chinense</i>	Active
Lycurumin B	Proteid	<i>Lycium chinense</i>	Active
Microginin	Proteid	<i>Lycium chinense</i>	Active
Microginin 299-C	Proteid	<i>Microcystis aeruginosa</i>	Active
Microginin 299-D	Proteid	<i>Microcystis aeruginosa</i>	Active
Micromonospora ACE K-13	Iridoid	<i>Micromonospora halophytica</i>	Inactive
Molihiaside A	Alkaloid	<i>Jasminum azoricum</i>	Active
Monocrotaline		<i>Crotalaria</i> sp.	Inactive
Morrisonide	Iridoid	<i>Crotalaria</i> sp.	Active
Muracein A	Proteid	<i>Sambucus nigra</i>	Inactive
Muracein B	Proteid	<i>Noardia orientalis</i>	Active
Muracein C	Proteid	<i>Noardia orientalis</i>	Active
Myrcene	Monoterpene	<i>Noardia orientalis</i>	Active
Myriceron-cafeoyl-ester	Triterpene	Comercial	Active
Nicotinamide	Proteid	<i>Myrica cerifera</i>	Inactive
		Soy sauce	Active
		<i>Corchorus olitorius</i>	Active
		<i>Streptomyces</i> sp.	Inactive
		<i>Tryptospermum lanceolatum</i>	Active
		<i>Lycium chinensis</i>	Active
		<i>Fritillaria verticillata</i>	Active
	Xanthone		
Norathyriol			
Ociadeca-10-trans-[2-cis-15-cis]-trienoic acid, 9-hydroxy	Lipid		
Ociadeca-9-trans-11-trans-dienoic hydroxy	acid,	13- Lipid	
Oleacein	Iridoid	<i>Olea europaea</i>	Active
Oleoside	Iridoid	<i>Olea europaea</i>	Weak
Oleoside-11-methyl ester	Iridoid	<i>Olea lancea</i>	Weak
		<i>Olea europaea</i>	Weak
		<i>Olea lancea</i>	Weak

Oleuropein	Iridoid	<i>Olea europaea</i>	Weak	Hansen et al., 1996a
Ovatodiolide	Diterpene	<i>Olea lancea</i>	Weak	Hansen et al., 1996a
		<i>Anisomeles indica</i>	Inactive	Arisawa et al., 1986
		<i>Anisomeles indica</i>	Inactive	Monose et al., 1994
		<i>Anisomeles indica</i>	Inactive	Arisawa et al., 1986
		<i>Anisomeles indica</i>	Weak	Monose et al., 1994
Ovatodiolide, 4,5-deoxy	Diterpene	<i>Anisomeles indica</i>	Weak	Aoyagi et al., 1986
Ovatodiolide, 4,5- <i>o</i> -epoxy	Diterpene	<i>Anisomeles indica</i>	Active	Ferreira et al., 1992
Pepstatin	Proteid	<i>Bothrops jararacussu</i>	Active	Bush et al., 1984
Peptide P	Proteid	<i>Streptomyces tanashiensis</i>	Active	Tsi et al., 1997
Phenacein	Alkaloid	<i>Aojium graveolens</i>	Active	Morishita et al., 1991
Phthalide, 3- <i>N</i> -butyl]	Misc lactone	<i>Aureobasidium</i> sp.	Inactive	Wagner et al., 1992
Polysaccharide HS-142-1	Carbohydrate	<i>Lespedeza capitata</i>	Active	Uchida et al., 1987
Procyanidin B-1	Flavonoid	Korean green tea	Active	Wagner et al., 1992
Procyanidin B-2, 3,3'-di- <i>O</i> -gallate	Flavonoid	<i>Lespedeza capitata</i>	Active	Cho et al., 1993
Procyanidin B-3	Flavonoid	Korean green tea	Active	Uchida et al., 1987
Procyanidin B-3, 3- <i>O</i> -gallate	Flavonoid	Korean green tea	Active	Wagner et al., 1992
Procyanidin B-5, 3,3'-di- <i>O</i> -gallate	Flavonoid	<i>Lespedeza capitata</i>	Active	Uchida et al., 1987
Procyanidin B-6	Flavonoid	Korean green tea	Active	Wagner et al., 1992
Procyanidin C-1, 3,3',3''-tri- <i>O</i> -gallate	Flavonoid	<i>Lespedeza capitata</i>	Active	Wagner et al., 1992
Procyanidin C-2	Flavonoid	<i>Phoma</i> sp.	Inactive	Harris et al., 1993
Pycnidione		<i>Pinus maritima</i>	Active	Paecker et al., 1999
Pycnogenol		<i>Diospyros kaki</i>	Active	Kameda et al., 1987
Quercetin-3- <i>O</i> -(2'',- <i>O</i> -galloyl)-glucoside	Flavonoid	<i>Diospyros kaki</i>	Active	Arisawa et al., 1989
Quercetin-3- <i>O</i> -beta-D-glucoside	Flavonoid	<i>Allophlyus ecdalis</i>	Active	Arisawa et al., 1989
Quercitrin	Flavonoid	<i>Erythroxylum laurifolium</i>	Active	Hansen et al., 1996b
Quercitrin, iso	Flavonoid	<i>Diospyros kaki</i>	Active	Kameda et al., 1987
Quinolone, 1-methyl-2-[(<i>cis</i> -4- <i>cis</i> -7)-4,7-trideca-dienyl]	Alkaloid	<i>Evodia rutaecarpa</i>	Active	Lee et al., 1998
Quinolone, 1-methyl-2-[pentadeca- <i>cis</i> -6- <i>cis</i> -9-dienyl]			Active	Lee et al., 1998
Sambacein I	Iridoid	<i>Jasminum azoricum</i>	Active	Somanadhan et al., 1998
Sambacein II	Iridoid	<i>Jasminum azoricum</i>	Active	Somanadhan et al., 1998
Sambacein III	Iridoid	<i>Jasminum azoricum</i>	Active	Somanadhan et al., 1998
Sambacoside A	Iridoid	<i>Jasminum azoricum</i>	Active	Somanadhan et al., 1998
Sollasin C	Sesquiterpene	<i>Poecilastra solasaki</i>	Active	Killday et al., 1993
Sollasin D	Sesquiterpene	<i>Streptomyces chromofuscus</i>	Active	Mynderse et al., 1985
Streptomyces antibiotic A-58365-A	Alkaloid	<i>Streptomyces chromofuscus</i>	Active	Mynderse et al., 1984
Streptomyces antibiotic A-58365-B		<i>Streptomyces chromofuscus</i>	Active	O'Connor et al., 1985
		<i>Streptomyces chromofuscus</i>	Active	Mynderse et al., 1985
		<i>Streptomyces chromofuscus</i>	Active	Mynderse et al., 1984

Streptomyces antibiotic WS-7338-B	Proteid	<i>Streptomyces</i> sp.	Weak
Streptomyces antibiotic WS-9826-A	Proteid	<i>Streptomyces violaceusniger</i>	Weak
Syringin	Phenylpropanoid	<i>Eucommia ulmoides</i>	Active
Taxol	Diterpene	<i>Taxus brevifolia</i>	Active
Terpinene, <i>alpha</i>	Monoterpene	Commercial	Weak
Terpinene, <i>gamma</i>	Monoterpene	Commercial	Weak
Terpineol, <i>alpha</i>	Monoterpene	Commercial	Weak
Tetradeca- <i>trans</i> -6- <i>trans</i> -12-diene-8,10-diene-1,3-diol	Alkynone	<i>Attractylodes japonica</i>	Inactive
Tetradeca- <i>trans</i> -6- <i>trans</i> -12-diene-8,10-diene-1,3-diol diacetate	Alkynone	<i>Attractylodes japonica</i>	Inactive
Tetrandrine, (+)	Alkaloid	<i>Stephania tetrandra</i>	Active
Tetrandrine-2N- <i>beta</i> -oxide	Alkaloid	<i>Stephania tetrandra</i>	Active
Variecolin	Sesterterpene	<i>Aspergillus variecolor</i>	Active
Veratridine	Alkaloid	<i>Veratrum</i> sp.	Active
Vicenin 2	Flavonoid	<i>Allophylus edulis</i>	Active
Vitexin	Flavonoid	<i>Allophylus edulis</i>	Active
Vitexin, iso	Flavonoid	<i>Allophylus edulis</i>	Active
Vitexin-2''-O- <i>alpha</i> -L-rhamnoside	Flavonoid	<i>Allophylus edulis</i>	Active
Xanthone, 1,3,5,6-tetrahydroxy	Xanthone	<i>Tripteropeltatum lanceolatum</i>	Active
Xanthone, 1,3,6,7-tetrahydroxy	Xanthone	<i>Tripteropeltatum lanceolatum</i>	Weak
Xanthone, 2,3,6,7-tetrahydroxy	Xanthone	<i>Tripteropeltatum lanceolatum</i>	Weak
Xanthone, 3,4,5,6-tetrahydroxy	Xanthone	<i>Tripteropeltatum lanceolatum</i>	Weak
Xanthone, 3,4,6,7-tetrahydroxy	Xanthone	<i>Tripteropeltatum lanceolatum</i>	Active