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Angiotensin-Converting Enzyme Inhibitory Action of Selected Plants

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Hypertension is the fourth leading cause of morbidity in the Philippines affecting more than 20% of Filipino adults (DOH 2013). Recognized as the "silent killer", it gradually destroys the body without any symptoms. Untreated hypertension may lead to stroke, blindness, heart attack, and kidney and heart failure (Chobanian et al. 2003).

Angiotensin-converting enzyme (ACE) is a key metalloprotease in the renin-angiotensin-aldosterone system. It catalyzes two reactions: conversion of the inactive decapeptide Angiotensin I into the vasoconstrictor and salt-retaining octapeptide Angiotensin II, and the hydrolysis of the vasodilator bradykinin which is contributory in lowering blood pressure. These lead to the elevation of blood pressure in an individual (Ferrario 2010). Inhibition of ACE is central in preventing hypertension (Cushman et al. 1977). One way to lower blood pressure is through the use of ACE inhibitors (Chobanian et al. 2003).However, its usage is associated with unwanted side effects, such as nephrotoxicity and congenital malformations (Adhiyaman et al. 2001; Cooper et al. 2006).It is necessary to look for other blood pressure lowering compounds that are equally effective but with minimal side effects.

Several studies have tried to look for other potential ACE inhibitors from various plant sources (Adsersen and Adsersen 1997; Tsutsumi et al. 1998; Duncan et al. 1999; Somanadhan et al. 1999; Oh et al. 2002; Loizzo et al. 2007). In this study, extracts from *Bixa orellana* (Bixaceae), *Artocarpus heterophyllus* (Moraceae), *Morus alba* (Moraceae), *Nymphaea pubescens* (Nymphaeacea) and *Syzygium samarangense (*Myrtaceae) were evaluated for their anti-hypertensive potential using an ACE-inhibitory colorimetric assay.

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The yields of the different extracts from the five plants are reported in Table 1. Results of the ACE inhibitory assay are shown in Figure 1. Table 2 shows the outcomes of the phytochemical screening of the different methanol extracts.

Table 1. Percent yield of leaves and extracts

Plant	Weight of dried leaves (g)	Yield methanol extract (%)	Yield hexane extract (%)	Yield ethyl acetate extract (%)
A. heterophyllus	184.56	3.41	34.27	19.66
B. orellana	177.19	8.95	24.58	20.38
M. alba	171.21	6.61	17.31	5.77
N. pubescens	104.93	11.58	19.93	4.86
S. samarangense	162.3	5.67	16.54	16.54

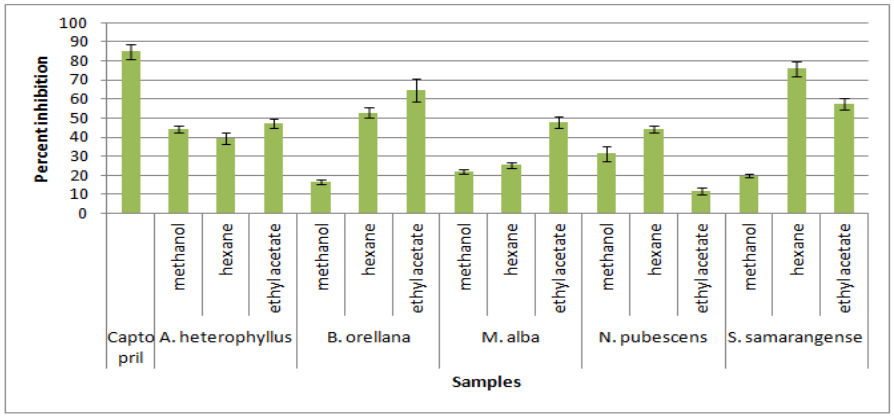

Figure 1. Average percent inhibition of the various extracts.

Table 2. Phytochemical profile of the methanol extracts

Plant	Saponins	Flavonoids	Cardiac Glycosides	Phenolic Compounds	Alkaloids	Terpenoids	Tannins
A. heterophyllus	+	-	+	+	+	+	+
B. orellana	+	+	+	+	-	+	-
M. alba	+	-	-	+	+	+	+
N. pubescens	+	-	+	+	+	+	+
S. samarangense	-	+	-	-	+	+	-

The hexane and ethyl acetate extracts of *B. orellana* and *S. samarangense* exhibited significant inhibition of ACE activity, with their percent inhibition values exceeding 50%. It is notable that these two plants are positive for the presence of flavonoids. This is consistent with previous findings attributing effective ACE inhibitory activity to flavonoids (Lacaille-Dubois et al. 2001; Perez-Viscaino et al. 2009; Jimenez-Ferrer et al. 2010; Balasuriya and Rupasinghe 2011; Balasuriya and Rupasinghe 2012). Flavonoids were previously identified from the leaves of *S. samarangense* (Nair et al. 1999). Other *Syzygium* species were found to contain flavonoids (Samy et al. 2014). Flavonoid bisulphates were previously identified from the extracts of *B. orellana* (Harborne 1975). Several ACE inhibitory flavonoids were isolated and identified from the ethanol extract of *Erythroxylum laurifolium* leaves (Hansen et al. 1996). Flavan-3-ols and procyanidins displayed inhibitory activity against ACE and the effect was observed to be dependent on the number of the epicatechin units forming the procyanidin (Actis-Goretta et al. 2003)

Epidemiological studies have shown the link between food consumption and protective effect of compounds against cardiovascular disease. Several lines of evidence support that dietary intake of flavonoids from cocoa have a wide range of health benefits including endothelial function, blood pressure, inflammation, and oxidative stress (Grassi and Ferri 2014). In a double-blind, placebo-controlled, parallel trial, chokeberry flavonoids were shown to have a clinical potential in preventing ischemic heart disease because of their ability to reduce the severity of inflammation (Naruszewicz et al. 2007).

Isolation and identification of the compounds responsible for the inhibition of ACE activity are ongoing. The activities of the *B. orellana* and *S. samarangense* extracts in hypertensive-induced mice will be evaluated using the non-invasive tail-cuff blood pressure measurement method.

SUPPLEMENTARY MATERIAL

Review of literature pertinent to the plants and experimental details relating to this paper are available online.

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