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Hypotensive effect of *Ficus sycomorus* L. on the arterial blood pressure of rabbits

Samia M. El-Sayyad[1], Makboul A. Makboul[1], Rofida M. Ali[1], Salwa F. Farag[1]*
[1]Faculty of Pharmacy, Pharmacognosy Department, Assiut University, Assiut 71526, Egypt

Research Article

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*For Correspondence

Salwa Farouk Farag, Faculty of Pharmacy, Pharmacognosy Department, Assiut University, Assiut, Egypt; Phone: +02 088 2080711

E-mail: farag_s@yahoo.com

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ABSTRACT

The hypotensive effect of the different extracts of *Ficus sycomorus* L. (FS) on blood pressure was evaluated in normotensive male rabbits for the first time. Anaesthetized rabbits were intraperitoneally injected with the tested extract in a dose of 400 mg/kg. The unripe fruit extract (FSFE) produced the greatest fall in the mean arterial blood pressure (MABP) from 181±5.22 to 65±11.56 mmHg. The wood extract (FSWE) caused significant and sustained hypotension and reduced MABP from 198±4.53 to 79±2.41 mmHg. The stem bark extract (FSBE) demonstrated slight fall in the MABP, it reduced MABP from 186±1.43 to 122±2.65 mmHg. The leaf extract (FSLE) showed fluctuation in the MABP. Hence, it can be concluded that *F. sycomorus* L. exerts a hypotensive effect suggesting its potential to be utilized as a therapeutic alternative for hypertension. Also, phytochemical screening of ethanolic extracts of the different parts of *F. sycomorus* L. revealed the presence of carbohydrates and/or glycosides, unsaturated sterols and/or triterpenoids, flavonoids, tannins and coumarins in addition to traces of saponins.

INTRODUCTION

The genus *Ficus* belongs to family Moraceae (mulberry family). The members of this family are mainly tropical or subtropical, monoecious or dioecious trees, shrubs or herbs, with milky latex. It comprises about seventy three (73) genera and over one thousand (1,000) species [1].

Ficus sycomorus L. is grown in Egypt and called sycamore or gimmei [2]. The fruit is edible and the extracts obtained from the different parts of the plant are used traditionally for treatment of various diseases such as diarrhea, dysentery, skin infections, stomach disorders, liver diseases, jaundice, chest conditions, cough and scrofula, tuberculosis, inflammations, throat pain, fungal diseases, epilepsy, lactation disorders, helminthiasis, mental disorders, infertility and sterility [3-6]. In addition, a decoction of the bark is used for excessive menstrual flow [7].

Phytochemical investigations on a number of *Ficus* species identified phenolics and flavonoids as major compounds [8].

It had been reported that, *F. sycomorus* exhibited antitumor activity,[9,10] antimicrobial activity,[5,9-13] analgesic and antiinflammatory activities,[14] anticonvulsant and inhibitory effect on muscle contraction,[15] sedative and anticonvulsant properties,[5] increased sperm cell production in rats,[6] antidiabetic activity,[16] hepatoprotective activity,[4,17,18] antidiarrheal activity,[19] antioxidant activity [13,20] and insecticidal and acaricidal activities [21]. *F. sycomorus* sap from the plant stem decreased the area covered by psoriatic plaques in psoriatic patients [22].

As an alternative to drug therapy, it is desirable to change dietary style and use medicinal plant products for the prevention and treatment of hypertension (HT) and thereby to avoid the adverse side-effects of organically synthesized drugs as well as the high cost of drug therapy. In this regard, the use of plants as medicines dates back to the earliest years of human life [23]. The hypotensive effect of *F. exasperata* Vahl. and *F. racemosa* L. had been reported [24,25]. In the present study, a qualitative

phytochemical analysis of ethanolic extracts of the different parts of *F. sycomorus* L. was performed for the detection of carbohydrates and/or glycosides, cardienolides, unsaturated sterols and/or triterpenes, flavonoids, saponins, alkaloids, tannins, anthraquinones, coumarins and iridoids. Also, we investigated the hypotensive effect of the different extracts of *F. sycomorus* L. (FS) on blood pressure in normotensive male rabbits.

MATERIALS AND METHODS

Plant Material

Fresh samples of *Ficus sycomorus* L. including leaves, stems and unripe fruits were collected in the period of February to April 2010, from the Experimental Station of Ornamental Plants, Faculty of Agriculture, Assiut University and kindly identified and authenticated by the late Prof. Dr. Naeem E. Keltawy, Professor of Ornamental Horticulture and Floriculture, Faculty of Agriculture, Assiut University. A voucher sample (no. 2010 FS) has been deposited in the Herbarium of Pharmacognosy Department, Faculty of Pharmacy, Assiut University, Assiut, Egypt.

Animals

Adult Boscat healthy rabbits (1-1.5 Kg) of both sex were used. The animals were bred and housed under standardized environmental conditions in Pre-clinical Animal House, Pharmacology Department, Faculty of Medicine, Assiut University. They were fed with standard diet and allowed free access to drinking water. The animals were randomly assigned to groups according to the experimental design.

Chemicals

Tween 80 was purchased from Sigma Chemical Co., St. Louis, USA. Normal saline 0.9% was obtained from (El-Nasr pharmaceutical and chemical Co., Egypt). All other chemicals used were of analytical grade and purchased locally.

Preparation of Extracts

The air-dried powdered leaves (1.0 kg), stem bark (0.5 kg), wood (1 kg) and fresh unripe fruit (1.5 kg) of *F. sycomorus* L. were separately extracted with 70% aqueous ethanol by maceration at room temperature. The extracts were concentrated under reduced pressure to give the corresponding extract 60 g, 60g, 60g and 50 g, respectively. Three grams of each of the dried extract of leaves, stem bark, wood and fresh unripe fruit was prepared as an emulsion in normal saline containing 3% (v/v) Tween 80.

Phytochemical Analysis

The extracts of leaves, stem bark, wood and fresh unripe fruit were tested by standard phytochemical methods [26-28] for the presence of alkaloids, flavonoids, anthraquinones, tannins, saponins, iridoids, steroids, triterpenoids, carbohydrates and/or glycosides.

Measurement of Blood Pressure

The hypotensive activity of the extracts of leaves, stem bark, wood and fresh unripe fruits of *F. sycomorus* L. was performed according to the reported method [29,30].

Rabbits were divided into four groups of 3 animals each. They were anaesthetized with intraperitoneal administration of urethane solution (25%) in a dose of 1.0 g/kg. Animal was fixed in supine position on a dissecting table. A small mid-tracheal incision (approx. 1 cm) was made to expose trachea, and left carotid artery. The trachea was exposed and cannulated with a plastic cannula to facilitate spontaneous respiration and cleaned from time to time. Arterial blood pressure was recorded *via* the left carotid artery; the latter was cannulated to elcomatic EM 751 blood pressure transducer. Soon after the carotid artery was cannulated, 500 I.U./kg of heparin, was injected to prevent intravascular blood clotting. Blood pressure was recorded by using a universal oscillograph (Harvard apparatus limited, Kent, U.K.). Following 15 min period of equilibrium (the blood pressure and heart rate had remained constant); rabbits were intraperitoneally injected with tested extract in a dose of 400 mg/kg body weight. The dose was separated by an interval of 30 min. Blood pressure was recorded before and after administration of the dose for 2 hrs. The mean arterial blood pressure (MABP) was calculated as [31]:

$$\text{MABP (mm Hg)} = \frac{(2 \times \text{diastolic blood pressure}) + \text{systolic blood pressure}}{3}$$

Change in blood pressure was expressed as percentage of control value obtained immediately before administration of tested extract.

$$\%\ \text{Change in MABP} = \frac{\text{MABP of experiment} - \text{MABP of control}}{\text{MABP of control}}$$

Statistical analysis

The results were expressed as mean ± S.E. (n=3 animals). Student's t-test was used to test the significance of difference between the treated and control group. The results were regarded as significant when $P<0.05$.

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RESULTS AND DISCUSSION

The phytochemical analysis showed that different extracts of *F. sycomorus* L. contained carbohydrates and/or glycosides, unsaturated sterols and/or triterpenes and flavonoids, tannins and coumarins in addition to traces of saponins **(Table 1).** Cardenolides, alkaloids and/or basic nitrogenous compounds, anthraquinones (free or combined) and iridoids were not detected.

The unripe fruit extract of *F. sycomorus* L. produced the greatest fall in MABP from an initial level of 181 ± 5.22 mmHg to 65 ± 11.56 mmHg at the end of the experiment. This hypotensive effect continued up to 120 min. However, the extract caused marked abnormalities to the heart pulse in the form of arrhythmia that appeared after 60 min and lasted throughout the rest of the experiment **(Table 2, Figure 1).**

Table 1. Results of phytochemical screening of different extracts of *F. sycomorus* L.

Plant constituent	Relative level			
	L.	B.	F.	W.
Carbohydrates and/or glycosides	+++	+++	+++	+++
Cardienolides	-	-	-	-
Unsaturated sterols and/or triterpenes	+++	+++	+++	+++
Flavonoids	++	++	++	++
Saponins	+	+	+	+
Alkaloids and/or basic nitrogenous compounds	-	-	-	-
Tannins	+++	+++	+++	+++
Anthraquinones	-	+	-	-
Coumarins	++	++	++	++
Iridoids	-	-	-	-

+++ = major ++ = moderate + = traces − = absent
L. =Leaves B. =Stem bark F. = Unripe fruits W. =Wood

Table 2. Effect of the different extracts of *F. sycomorus* L. on the Mean Arterial Blood Pressure (MABP) of anaesthetized normotensive rabbits.

Time (min) / Extract	0 (control)	30		60		90		120	
	MABP	MABP	%Change	MABP	%Change	MABP	%Change	MABP	%Change
Unripe fruit	181±5.22	102±5.00**	-43.60	93±6.20**	-48.62	47±7.90**	-74.03	65±11.56**	-64.09
Wood	198±4.53	142±5.35**	-28.28	122±5.33**	-38.38	95±2.60**	-52.02	79±2.41**	-60.10
Stem bark	186±1.43	181±2.57	-2.68	149±4.01**	-19.89	154±3.51**	-17.20	122±2.65**	-64.00
Leaf	201±4.98	213±4.11	+6.00	214±3.00*	+6.00	182±8.03*	-10.00	207±5.42	+3.00

*$P < 0.05$ versus control; **$P < 0.01$ versus control

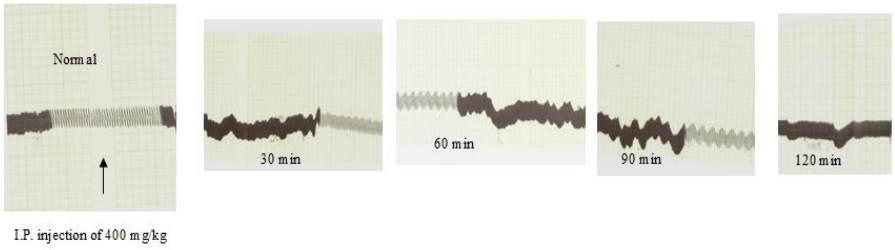

Figure 1. The effect of the ethanolic extract of *F. sycomorus* L. unripe fruits on the blood pressure of normal rabbit.

The wood extract of *F. sycomorus* L. caused significant and sustained hypotension. The mean arterial blood pressure dropped from an initial level of 198±4.53 mmHg to 79±2.41 mmHg at the end of the experiment. The extract didn't affect heart rate and rhythm **(Table 2, Figure 2).**

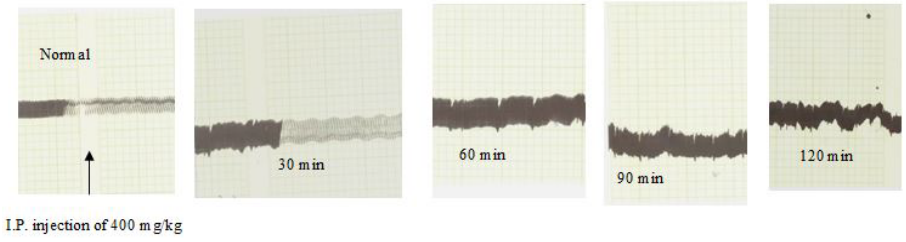

Figure 2. The effect of the ethanolic extract of *F. sycomorus* L. wood on the blood pressure of normal rabbit.

The stem bark extract demonstrated the least hypotensive effect, causing a fall from an initial level of 186 ± 1.43 mmHg to 122 ± 2.65 mmHg at the end of the experiment. There was no marked effect on heart rate and rhythm **(Table 2, Figure 3).**

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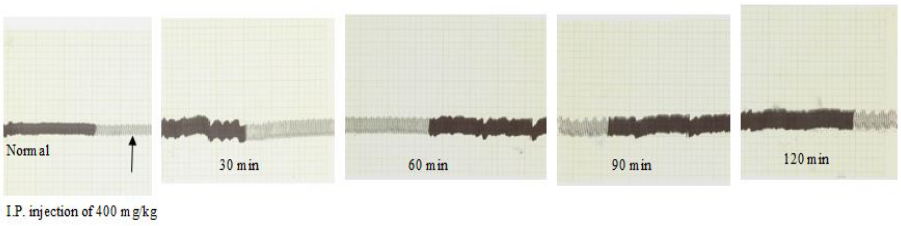

Figure 3. The effect of the ethanolic extract of *F. sycomorus* L. stems bark on the blood pressure of normal rabbit.

The leaf extract showed slight increase in the MABP from initial level 201 ± 4.98 mmHg to 214 ± 3.00 mmHg in the first hour of the experiment. Then, it caused slight decrease in the MABP to 192 ± 8.03 at 60-90 min followed by increase in the MABP to 207 ± 5.42 at 90-120 min **(Table 2, Figure 4).** Concerning the heart rate and rhythm, there was no effect.

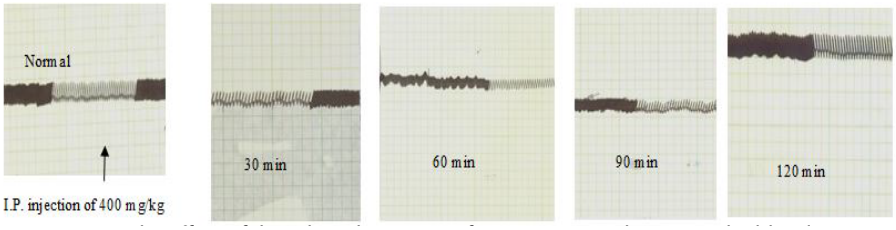

Figure 4. The effect of the ethanolic extract of *F. sycomorus* L. leaves on the blood pressure of normal rabbit.

The extracts of unripe fruits, wood and stem bark induced significant hypotensive effect when administered intraperitoneally to anesthetized normal rabbits. This may be due to its direct or indirect effect on cardiac pump or vascular tissues responsible for reduction in vascular muscle tone, leading to vasodilatation [32]. Care should be taken when using the unripe fruit extract because it caused marked arrhythmia.

Flavonoids, coumarins, tannins and steroids/triterpenoids and their glycosides have been reported as constituents of this genus [20]. Literature data reported that, flavonoids, terpenoids and coumarins exhibited activities in cardiovascular system [33-36]. Presence of such compounds in *F. sycomorus* L. might possibly contribute in the hypotensive effects of the plant extracts. The fluctuation in the MABP caused by leaf extract may be due to competition between constituents that increase and those which decrease it.

CONCLUSION

This is the first report for the hypotensive activity of the unripe fruits, wood and stem bark extracts of *F. sycomorus* L. in normotensive rabbits suggesting its potential to be utilized as a therapeutic alternative for hypertension. Care should be taken when using the unripe fruits extract because it caused marked arrhythmia.

The phytochemical constituent's flavonoids, triterpenoids, flavonoids and coumarins of *F. sycomorus* L. extracts might possibly contribute in the hypotensive effects in normotensive male rabbits suggesting it's potential to be utilized as a therapeutic alternative for hypertension.

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