PHARMACOLOGICAL ACTION OF *EUCOMMIA ULMOIDES*, OLIV.

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Eucommia ulmoides, Oliv. is a deciduous tree that grows wildly in Shu Chuan, Fu Pei Shêng, China. The medicinal portion are contained in the bark that has been dried after peeling, the thickness of the bark being 1 to 5 mm and of varying dimensions in size. The external surface is grey or dark grey in color, shows well marked longitudinal rugosity and cutaneous pores. The inner surface is smooth, dark violet in color, and the structure coarse. When broken into pieces white threads are produced.

FIG. 1. *Eucommia ulmoides*, Oliv. (Actual size)

According to Pen Ts'ao Kang Mu of Li Shih-Chên (1) *Eucommia ulmoides*, Oliv. is highly efficacious in lumbago resulting from cold. It is comparatively recently that *Eucommia ulmoides*, Oliv. began to be used in Chinese medicine, and even in Pen Ts'ao Kang Mu its use is not widely taken up. However, in recent years, since Hsü Pang-Hsien (2) and Chang Chi-Yu (3) pointed out the efficacy of this drug in hypertension it has come to draw attention in China and at the Pharmaceutical Research Laboratory of the Chinese Science Academy (4) saponin and potassium sulphocyanide have been isolated from it. In Japan Minatodani and Ishiguro (5) have extracted gutta percha from the bark,

No investigations have yet been made regarding the pharmacological properties of *Eucommia ulmoides*, Oliv., and the present studies were undertaken, therefore, with this in mind.

EXPERIMENTAL MATERIALS

Eucommia ulmoides, Oliv. examined here was a product of Shu Chuan Shêng, China. It was cut into small pieces and infused for 3 hours with about 3 times its volume of water in a water bath. After cooling it was filtered, and the sediment was reinfused with a similar amount of water over a warm bath. The filtrates were collected together and dried by evaporation over a water bath. The aqueous extract obtained was employed in the experiments conducted.

Amount recovered: 10.4%.

Properties: A dark brown mass soluble in water. The aqueous extract was weakly acid in reaction, gave off an aromatic odor, was sweet, faintly pungent, and reduced Fehling's solution. The pH was 4.4. Complete hemolysis with a dilution of 1 in 160 and incomplete hemolysis with a 1 in 320 dilution resulted.

EXPERIMENTAL RESULTS

A. General Toxic Symptoms

First, general toxicity of the aqueous extract of *Eucommia ulmoides*, Oliv. was examined for frogs, mice and rabbits.

1) Experiments with frogs

Into frogs of about 10 g body weight, various quantities of a 10% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. in 0.6% saline were injected into the abdominal lymph sac, and the general toxicity was observed.

No abnormality was noted with 0.5 c.c. With 1 c.c. the frogs became quiet after 5 minutes but no changes were noted in the respiration, and after one hour there was noted recovery to normal.

2) Experiments with mice

Various amounts of a 10% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. in 0.9% saline were injected subcutaneously, and the general toxic signs were observed.

No abnormalities were noted with amounts below 0.1 c.c. With 0.2 c.c. the animals became somewhat active in movement, but no abnormality was noted later. With 0.5 c.c. the animals remained quiet but at the end of 1 hour returned to normal.

3) Experiments with rabbits

Varying quantities of a 20% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. in 0.9% saline were injected into the ear vein of rabbits weighing about 1 kg and the general toxic signs were observed.

With 1.0 c.c. there were noted a tendency for the body temperature to rise and slight dilation of the ear blood vessels. No other abnormalities were noted. With 2.0 c.c. the

body temperature rose slightly, and there were noted slight dilation of the ear vessels and slight contraction of the pupils. However after one hour there was recovered to normal. Almost similar results were noted with 5.0 c.c.

As has been described above the general toxic sings resulting from an administration of an aqueous extract of *Eucommia ulmoides*, Oliv. are extremely weak.

B. Effect on the Circulatory and Respiratory Systems

1) Experiments on the blood pressure and respiration

As was described early in this paper, in China the efficacy of *Eucommia ulmoides*, Oliv. in hypertension has been demonstrated and it has hence become widely used for this condition. Such has been responsible for our interest in this drug and the reason for conducting this series of experiments. Firstly we therefore paid attention on whether *Eucommia ulmoides*, Oliv. really lowers the blood pressure and, if so, to discover the reason for this.

Rabbits weighing about 2 kg were anesthetized with injections of 5.0 c.c. per kg body weight of a 10% aqueous solution of urethane, and the blood pressure and respiration were recorded in the conventional manner on smoked paper. Next, varying amounts of a 10% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. in 0.9% saline were injected into the ear vein, and the changes were observed. With 5.5 c.c. there was noted a fall in blood pressure that was maintained for a long period. No changes were noted in the respiration.

FIG. 2. Movements of the rabbits respiration and arterial pressure. Intravenous injection of 10% aqueous extract of *Eucommia ulmoides*, Oliv. 5.4 c.c.

Next, after the blood pressure had been lowered by an injection of the aqueous extract of *Eucommia ulmoides*, Oliv. the abdomen was pressed with the fingers when the blood pressure began to rise and returned to the previous level.

When rabbits weighing about 1 kg were previously injected with 0.5 mg of atropine sulphate into the ear vein, an injection of the aqueous extract of *Eucommia ulmoides*, Oliv. produced no fall in blood pressure. No changes were also noted in the respiration.

FIG. 3. Movements of the rabbits respiration and arterial pressure. Intravenous injection of 0.5 mg atropine sulphate, later, injection of 10% aqueous extract of *Eucommia ulmoides*, Oliv. 5.5 c.c.

Again after the blood pressure had been lowered with an aqueous extract of *Eucommia ulmoides*, Oliv. and atropine sulphate injected, the blood pressure immediately began to rise and returned to the previous level. No changes were noted in the respiration.

From the above experiments it became clear that an aqueous extract of *Eucommia ulmoides*, Oliv. lowers the blood pressure, but that this fall is removed by atropine sulphate. Hence it appears that an aqueous extract of *Eucommia ulmoides*, Oliv. has an excitatory action on the parasympathetic nerves.

2) Experiments with the frog's heart preparation

Varying concentration of the aqueous extract in Ringer's solution were examined by Straub's method.

No changes were noted with a concentration of 0.005% and below. With 0.01–0.05% no changes were noted in frequency of the heart beat but there was a slight decrease in amplitude. With a concentration of 0.1–0.2% there resulted a decrease in amplitude due to the weakening in contraction, and with a 0.5% there resulted not only decrease in amplitude but an eventual fall in frequency of 1/2 to 1/3. With concentrations of 1.0% and above the heart came to rest in a state of diastole. The arrested heart, however, began to beat again after washing with Ringer's solution. When stimulated with the tip of a tweezer there resulted a single movement, while barium chloride solution produced a contraction,

To the heart previously treated with 0.004% atropine sulphate a 1.0% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. was made to act but no marked changes were demonstrated.

Again the heart brought to rest with a 1.0% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. was acted upon by 0.004% atropine sulphate when the heart began to beat again.

FIG. 4. Excised heart of frog.

FIG. 5. Excised heart of frog.

From the above experiments it became clear that the aqueous extract of *Eucommia ulmoides*, Oliv. acts suppressively on the movements of the heart preparation of the frog, and that this suppressive action is inhibited by atropine sulphate. Hence it would seem that a solution of the aqueous extract of *Eucommia ulmoides*, Oliv. stimulates the parasympathetic nerves.

3) Experiments on the peripheral blood vessels

Employing the Laewen-Tredelenburg's method the hind legs of the frog were perfused, and varying concentrations in Ringer's solution of the aqueous extract of *Eucommia ulmoides*, Oliv. were made to act on the preparation. Similarly employing Krawkow-Pissemiski's method the blood vessels of the ear of the rabbit were perfused, and varying concentrations in Locke's solution of the aqueous extract of *Eucommia ulmoides*, Oliv. were made to act on the vessels.

With 0.005% there resulted no marked changes, but with concentrations of above 0.01%, there was seen an increase in the number of drops, the increase being proportional to the strength of solution employed. In other words, solutions of the aqueous extract of *Eucommia ulmoides*, Oliv. dilated the blood vessels.

When the preparations are first perfused with a 0.02% solution of atropine sulphate there results a decrease in the number of drops. If next perfusion is conducted with 0.02% atropine sulphate plus 0.1% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. there results no increase in the number of drops.

Again when first perfusion is made with a 0.1% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. there results an increase in number of drops, but when this is followed by perfusion with 0.1% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. in combination with a 0.02% solution of atropine sulphate the number of drops decreases.

Thus the dilation of blood vessels brought about by an aqueous extract of *Eucommia ulmoides*, Oliv. is inhibited by atropine sulphate.

FIG. 6. Perfusion of blood vessels of the hind legs of the frog.

↓ : 0.02% atropine sulphate
↑ : 0.02% atropine sulphate + 0.1% *Eucommia*-extract

FIG. 7. Perfusion of ear vessels of the rabbit.

↓ : 0.1% *Eucommia*-extract
↑ : 0.1% *Eucommia*-extract + 0.02% atropine sulphate

When primary perfusion with a 0.0000001% solution of epirenamine (adrenaline) is made there results a conspicuous decrease in the number of drops, but when this is followed by perfusion with 0.0000001% solution of epirenamine in combination with 0.1% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. there results an increase in the number of drops.

When perfusion is made first with a 0.1% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. there is noted an increase in the number of drops, but when this is followed by perfusion with a 0.1% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. plus 0.0000001% solution of epirenamine the number of drops decreases. The degree of decrease is not marked when compared with that resulting when perfusion is made with only 0.0000001% solution of epirenamine.

FIG. 8. Perfusion of blood vessels of the hind legs of the frog.

↓ : 0.0000001% epirenamine
↑ : 0.0000001% epirenamine + 0.1% *Eucommia*-extract

FIG. 9. Perfusion of ear vessels of the rabbit.

↓ : 0.1% *Eucommia*-extract
↑ : 0.1% *Eucommia*-extract + 0.0000001% epirenamine

Thus it would seem that the dilatation of vessels resulting from the aqueous extract of *Eucommia ulmoides*, Oliv. is not influenced by epirenamine.

C. Action on the Smooth Muscles

1) Experiments with the excised rabbit's intestine

The effects of varying concentrations of the aqueous extract of *Eucommia ulmoides*, Oliv. were examined by Magnus' method, employing the excised intestine of rabbits.

No marked changes were noted with a concentration of 0.005%, but with concentrations of 0.01 to 0.05% there resulted some enhancement of tension. With concentrations of 0.1 to 1.0% there resulted a transitory rise in tension but the amplitude was small and gradually relaxation appeared with a fall in tension.

When the intestine previously treated with 0.004% atropine sulphate was acted upon by a 0.5% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. there was not seen the increase in tension due to the latter.

If the tension produced temporarily by a 0.5% solution of the aqueous extract of *Eucommia ulmoides*, Oliv. is now acted upon by a 0.004% solution of atropine sulphate there results an immediate fall in tension.

FIG. 10. Excised intestine of the rabbit.

FIG. 11. Excised intestine of the rabbit.

Thus the increase in tension brought about by the aqueous extract of *Eucommia ulmoides*, Oliv. is inhibited by atropine sulphate.

2) Experiments with the excised uterus of the rabbit

The effects of varying concentrations in Locke's solution of the aqueous extract of *Eucommia ulmoides*, Oliv. was examined by Magnus' method employing the excised uterus of the rabbit.

No marked changes were noted with a concentration of 0.005%, but there was increase in tension with concentrations of 0.01 to 0.05%. The amplitude also increased. With concentrations of 0.1 to 0.5% there was an immediate increase in tension followed by rigidity. With concentrations of more than 1.0% there resulted stasis immediately after a transitory rigidity, followed gradually by a fall in tension.

The relation between the actions of the aqueous extract of *Eucommia ulmoides*, Oliv. and atropine sulphate on the excised rabbit's uterus was not so distinct as in the case of experiments with the excised rabbit's intestine.

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D. Action on the Excised Eyeball of the Frog

Varying concentrations in Ringer's solution of the aqueous extract of *Eucommia ulmoides*, Oliv. were made to act on the excised eyeball of the frog, employing the method of Ehrmann.

With concentrations of 0.05% and below no marked changes were noted. With concentrations of 0.1 to 0.5% there resulted a marked contraction of the pupil. With higher concentrations the pupillary contraction was rather weak.

TABLE 1. Excised eyeball of the frog.

Time (min)		0			5			10			15		
Concentration	Diameter (mm)	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
NaCl	L	2.00	2.50	5.00									
0.1% <i>Eucommia</i>	R	2.00	2.50	5.00									
NaCl	L	2.00	2.50	5.00							1.75	3.00	5.25
0.1% <i>Eucommia</i>	R	2.00	3.00	6.00							1.25	2.50	3.13
NaCl	L	2.00	3.00	6.00							2.00	3.00	6.00
0.2% <i>Eucommia</i>	R	2.00	3.00	6.00							1.75	2.75	4.81
NaCl	L	1.75	2.50	4.38							1.75	2.50	4.38
0.2% <i>Eucommia</i>	R	1.75	2.50	4.38							1.50	2.25	3.38
NaCl	L	1.50	2.25	3.38							1.50	2.25	3.38
0.5% <i>Eucommia</i>	R	1.50	2.25	3.38							1.25	2.00	2.50
NaCl	L	2.00	3.00	6.00									
0.5% <i>Eucommia</i>	R	2.00	3.00	6.00									

Time (min)		20			30			40			50			60		
Concentration	Diameter (mm)	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
NaCl	L	1.75	2.50	4.38				1.75	2.50	4.38	1.75	2.25	3.93	1.75	2.25	3.93
0.1% <i>Eucommia</i>	R	1.50	2.00	3.00				1.25	1.75	2.20				1.25	1.75	2.20
NaCl	L	1.25	3.00	3.75										1.25	3.00	3.75
0.1% <i>Eucommia</i>	R	1.25	2.50	3.13										1.25	2.25	2.81
NaCl	L				2.00	2.75	5.50				2.00	2.75	5.50	1.75	2.75	4.81
0.2% <i>Eucommia</i>	R				1.50	2.50	3.75				1.50	2.25	3.38	1.50	2.25	3.38
NaCl	L				1.75	2.50	4.38				1.50	2.25	3.38	1.50	2.25	3.38
0.2% <i>Eucommia</i>	R				1.25	2.25	2.81				1.00	2.00	2.00	1.00	2.00	2.00
NaCl	L				1.50	2.25	3.38	1.25	2.00	2.50	1.25	2.00	2.50	1.00	2.00	2.00
0.5% <i>Eucommia</i>	R				1.00	1.75	1.75	1.00	1.75	1.75	0.25	1.50	0.38	0.25	1.50	0.38
NaCl	L				2.00	3.00	6.00	1.75	3.00	5.25	1.75	3.00	5.25	1.75	3.00	5.25
0.5% <i>Eucommia</i>	R				1.75	2.75	4.81	1.75	2.75	4.81	1.50	2.75	4.12	1.50	2.50	3.75

L: Left eyeball, l: Length
R: Right eyeball, w: Width

If both eyes are previously acted upon by 0.01% atropine sulphate the pupils dilate. After 15 minutes one eye was acted upon by 0.1%, 0.2%, and 0.5% solutions of the aqueous

extract of *Eucommia ulmoides*, Oliv., while another was left untreated. But no differences were noted in the size of the pupils.

TABLE 2. Excised eyeball of the frog.

Time (min)		0			5			10			15		
Diameter (mm)	Concentration	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.01% atropine sulphate	L	1.00	2.00	2.00	1.00	2.00	2.00	1.25	2.25	2.81	1.50	2.50	3.75
0.1% <i>Eucommia</i>	R	1.00	2.00	2.00	1.00	2.00	2.00	1.25	2.25	2.81	1.50	2.50	3.75
	L	1.25	2.50	3.75				1.75	2.50	4.48	2.00	2.50	5.00
0.2% <i>Eucommia</i>	R	1.25	2.50	3.75				1.75	2.50	4.48	2.00	2.50	5.00
	L	1.00	1.75	1.75	1.25	1.75	2.19	1.25	2.00	2.50	1.25	2.00	2.50
0.5% <i>Eucommia</i>	R	1.00	1.75	1.75	1.25	1.75	2.19	1.25	2.00	2.50	1.25	2.00	2.50

Time (min)		20			30			40			50			60		
Diameter (mm)	Concentration	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.10% atropine sulphate	L	1.50	2.50	3.75	1.75	2.50	3.75	1.75	2.50	4.58	1.75	2.75	4.81	1.75	3.00	5.25
0.1% <i>Eucommia</i>	R	1.50	2.50	3.75				1.50	2.50	3.75				1.50	2.50	3.75
	L	2.25	2.50	5.63				2.50	2.50	6.25				2.50	2.75	6.88
0.2% <i>Eucommia</i>	R	2.00	2.50	5.00										2.00	2.50	5.00
	L	1.25	2.50	2.81	1.50	2.50	3.75	1.50	2.50	3.75	1.75	2.50	4.58	1.75	2.75	4.81
0.5% <i>Eucommia</i>	R	1.25	2.00	2.50										1.25	2.00	2.50

L: Left eyeball, l: Length
R: Right eyeball, w: Width

Both eyes are acted upon by 0.01% atropine sulphate, after 15 minutes one eye was acted upon by 0.1%, 0.2% and 0.5% solution of the aqueous extract of *Eucommia ulmoides*, Oliv.

There was thus no contraction of the pupils.

If now both eyes are acted upon by 0.1%, 0.2%, and 0.5% solutions of the aqueous extract of *Eucommia ulmoides*, Oliv. there results contraction of the pupils. After 15 minutes when one eye is treated with a 0.01% solution of atropine sulphate the pupil dilates.

TABLE 3. Excised eyeball of the frog.

Time (min)		0			5			10			15		
Diameter (mm)	Concentration	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.1% <i>Eucommia</i>	L	1.50	2.00	3.00				1.25	1.75	2.19			
0.01% atropine	R	1.50	2.00	3.00				1.25	1.75	2.19	1.25	1.75	2.19
0.2% <i>Eucommia</i>	L	1.00	2.00	2.00				1.00	1.75	1.75			
	R	1.00	2.00	2.00				1.00	1.75	1.75	1.00	1.75	1.75
0.5% <i>Eucommia</i>	L	1.50	3.00	4.50				1.25	3.00	3.75	1.25	2.25	2.81
	R	1.50	3.00	4.50				1.25	3.00	3.75	1.25	2.25	2.81

Time (min)		20			30			40			50			60		
Concentration	Diameter (mm)	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.1% <i>Eucommia</i>	L				1.00	1.50	1.50							1.00	1.25	1.25
0.01% atropine	R	1.25	1.75	2.19				1.50	1.75	2.63				1.50	2.00	3.00
0.2% <i>Eucommia</i>	L				1.00	1.50	1.50				1.00	1.25	1.25	0.75	1.00	0.75
	R	1.00	2.00	2.00	1.25	2.00	2.50	1.25	2.25	2.81				1.25	2.25	2.81
0.5% <i>Eucommia</i>	L				1.00	2.25	2.25	1.00	2.00	2.00				1.00	1.75	1.75
	R	1.50	2.75	4.12										1.50	2.75	4.12

L: Left eyeball, l: Length
R: Right eyeball, w: Width

Both eyes are acted upon by 0.1%, 0.2% and 0.5% solution of the aqueous extract of *Eucommia ulmoides*, Oliv., after 15 minutes one eye was acted upon by 0.01% atropine sulphate.

If both eyes are previously treated with a 0.001% solution of epirenamine this pupils dilate. Next, 15 minutes later on one eye 0.1%, 0.2% and 0.5% solutions of the aqueous extract of *Eucommia ulmoides*, Oliv. are made to act, while another eye is left untreated.

TABLE 4. Excised eyeball of the frog.

Time (min)		0			5			10			15		
Concentration	Diameter (mm)	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.0000001% epirenamine	L	1.25	2.00	2.50				1.50	2.25	3.38	1.50	2.50	3.75
0.1% <i>Eucommia</i>	R	1.25	2.00	2.50							1.50	2.50	3.75
0.2% <i>Eucommia</i>	L	1.00	2.00	2.00				1.25	2.00	2.50	1.50	2.50	3.75
	R	1.00	2.00	2.00				1.25	2.00	2.50	1.50	2.50	3.75
0.5% <i>Eucommia</i>	L	1.25	2.50	3.13	1.25	2.75	3.44	1.50	2.75	4.11	1.75	2.75	5.48
	R	1.25	2.50	3.13	1.25	2.75	3.44	1.50	2.75	4.11	1.75	2.75	5.48

Time (min)		20			30			40			50			60		
Concentration	Diameter (mm)	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.0000001% epirenamine	L	1.50	2.75	4.12	1.75	2.75	4.81	1.75	3.00	5.25				2.00	3.00	6.00
0.1% <i>Eucommia</i>	R	1.50	2.25	3.38							1.25	2.25	2.81	1.25	2.25	2.81
0.2% <i>Eucommia</i>	L				1.75	2.75	4.81				1.75	3.00	5.25	2.00	3.00	6.00
	R	1.50	2.50	3.75										1.50	2.21	3.38
0.5% <i>Eucommia</i>	L	1.75	3.00	5.25				1.75	3.00	5.25	2.00	3.00	6.00	2.25	3.00	6.75
	R	1.75	2.50	4.38							1.50	2.50	3.75	1.50	2.50	3.75

L: Left eyeball, l: Length
R: Right eyeball, w: Width

Both eyes are acted upon by 0.001% solution of epirenemine, after 15 minutes one eye was acted upon by 0.1%, 0.2% and 0.5% solution of the aqueous extract of *Eucommia ulmoides*, Oliv.

In this case there is noted a difference in the degrees of dilatation of the pupils, namely the pupils contract.

If, on the contrary, both eyes are acted upon by 0.1%, 0.2% and 0.5% solutions of the aqueous extract of *Eucommia ulmoides*, Oliv. the pupils contract. At the end of 15 minutes on one eye a 0.001% solution of epirenamine is made to act when the pupils dilate.

TABLE 5. Excised eyeball of the frog.

Time (min)		0			5			10			15		
Diameter (mm)	Concentration	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.1% <i>Eucommia</i>	L	2.00	3.00	6.00							1.75	2.75	4.81
0.0000001% epirenamine	R	2.00	3.00	6.00							1.75	2.75	4.81
0.2% <i>Eucommia</i>	L	1.50	2.25	3.38				1.25	2.00	2.25	1.25	2.00	2.25
	R	1.50	2.25	3.38				1.25	2.00	2.25	1.25	2.00	2.25
0.5% <i>Eucommia</i>	L	2.00	3.00	6.00				1.75	3.00	5.25	1.50	2.75	4.12
	R	2.00	3.00	6.00				1.75	3.00	5.25	1.50	2.75	4.12

Time (min)		20			30			40			50			60		
Diameter (mm)	Concentration	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.1% <i>Eucommia</i>	L				1.50	2.75	4.13				1.25	2.50	3.75	1.25	2.50	3.75
0.0000001% epirenamine	R	1.75	2.75	4.81	2.00	3.00	6.00	2.25	3.00	6.75				2.25	3.00	6.75
0.2% <i>Eucommia</i>	L				1.00	1.75	1.75				1.00	1.50	1.50	1.00	1.25	1.25
	R	1.50	2.00	3.00	1.75	2.25	3.93	1.75	2.50	4.58	2.00	2.50	5.00	2.00	3.00	6.00
0.5% <i>Eucommia</i>	L	1.50	2.50	3.75							1.50	2.50	3.75	1.25	2.25	2.81
	B	1.75	3.00	5.25							2.00	3.50	7.00	2.00	3.50	7.00

L: Left eyeball, l: Length

R: Right eyeball, w: Width

Both eyes are acted upon by 0.1%, 0.2% and 0.5% solution of the aqueous extract of *Eucommia ulmoides*, Oliv., after 15 minutes one eye was acted upon by 0.001% solution of epirenemine.

When both eyes are acted upon by a 0.1% solution of cocaine hydrochloride the pupils dilate. Fifteen minutes later one eye was acted upon by 0.1%, 0.2% and 0.5% solutions of the aqueous extract of *Eucommia ulmoides*, Oliv., while another eye was left untreated. In this case there was noted a difference in the sizes of the pupils, and they contracted.

If, on the contrary, when both eyes are acted upon by 0.1%, 0.2% and 0.5% solutions of the aqueous extract of *Eucommia ulmoides*, Oliv. the pupils contract. Fifteen minutes later one eye was acted upon by a 0.1% solution of cocaine hydrochloride when there resulted dilation of the pupils.

From the above experiments it was found that the contraction of pupils of the excised frog's eye brought about by an aqueous extract of *Eucommia ulmoides*, Oliv. is suppressed by

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atropine sulphate, but not by solutions of epirenamine and cocaine. It will be thus clear that solutions of the aqueous extract of *Eucommia ulmoides*, Oliv. stimulate the parasympathetic nerves.

TABLE 6. Excised eyeball of the frog.

Time (min)		0			5			10			15		
Diameter (mm)	Concentration	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.1% cocaine	L	1.00	1.75	1.75				1.50	2.00	3.00	1.75	2.00	3.55
0.1% <i>Eucommia</i>	R	1.00	1.75	1.75				1.50	2.00	3.00	1.75	2.00	3.55
0.2% <i>Eucommia</i>	L	1.00	2.50	2.50				1.50	2.25	3.38	1.75	2.50	4.38
	R	1.00	2.50	2.50				1.50	2.25	3.38	1.75	2.50	4.38
0.5% <i>Eucommia</i>	L	1.50	2.75	4.12				1.75	3.00	5.25	1.75	3.00	5.25
	R	1.50	2.75	4.12				1.75	3.00	5.25	1.75	3.00	5.25

Time (min)		20			30			40			50			60		
Diameter (mm)	Concentration	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.1% cocaine	L				2.00	2.50	5.00				2.00	2.75	5.50	2.00	2.75	5.50
0.1% <i>Eucommia</i>	R	1.75	2.00	3.55	1.50	2.00	3.00							1.25	2.00	2.50
0.2% <i>Eucommia</i>	L	2.00	3.00	6.00	2.25	2.75	6.26				2.50	3.00	7.50	2.50	3.25	8.13
	R	1.75	2.50	4.38	1.75	2.50	4.38				1.50	2.50	3.75	1.50	2.50	3.75
0.5% <i>Eucommia</i>	L				2.00	3.00	6.00	2.50	3.00	7.50				2.75	3.00	8.25
	R	1.75	3.00	5.25							1.75	2.75	4.81	1.75	2.75	4.81

L: Left eyeball, l: Length
R: Right eyeball, w: Width

Both eyes are acted upon by 0.1% solution of cocaine hydrochloride, after 15 minutes one eye was acted upon by 0.1%, 0.2% and 0.5% solution of the aqueous extract of *Eucommia ulmoides*, Oliv.

TABLE 7. Excised eyeball of the frog.

Time (min)		0			5			10			15		
Diameter (mm)	Concentration	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.1% <i>Eucommia</i>	L	2.00	2.50	5.00				1.75	2.50	4.38			
0.1% cocaine	R	2.00	2.50	5.00				1.75	2.50	4.38	1.75	2.50	4.38
0.2% <i>Eucommia</i>	L	2.00	2.50	5.00				2.00	2.25	4.50	1.75	2.25	3.94
	R	2.00	2.50	5.00				2.00	2.25	4.50	1.75	2.25	3.94
0.5% <i>Eucommia</i>	L	2.00	3.00	6.00				1.75	3.00	5.25	1.50	2.75	4.12
	R	2.00	3.00	6.00				1.75	3.00	5.25	1.50	2.75	4.12

Time (min)		20			30			40			50			60		
Diameter (mm)	Concentration	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w	l	w	l×w
0.1% <i>Eucommia</i>	L				1.50	2.50	3.75				1.50	2.25	3.38	1.50	2.25	3.38
0.1% cocaine	R	1.75	2.50	4.58				2.00	2.50	5.00	2.25	2.50	5.63	2.25	2.75	6.26
	L	1.75	2.00	3.56				1.50	2.00	3.00	1.25	2.00	2.50	1.25	1.75	2.19
0.2% <i>Eucommia</i>	R	2.00	2.25	4.50				2.25	2.50	5.62				2.50	2.75	6.88
	L				1.25	2.75	3.44				1.25	2.50	3.13	1.25	2.25	2.81
0.5% <i>Eucommia</i>	R	1.50	3.00	4.50	1.75	3.00	5.25	2.00	3.00	6.00				2.00	3.00	6.00

L: Left eyeball, l: Length
R: Right eyeball, w: Width

Both eyes are acted upon by 0.1%, 0.2% and 0.5% solution of the aqueous extract of *Eucommia ulmoides*, Oliv., after 15 minutes one eye was acted upon by 0.1% solution of cocaine hydrochloride.

E. Experiments with Water Leech Muscle

Water leech muscle reacts with contraction to solution of drugs (cholinergic substances) that stimulate the parasympathetic nerved. Hence it is used in determinations of acetylchline chloride (6).

According to Yoshida and Yoshimura (7), there are no marked changes with a 0.00005% solution of acetylcholine chloride, but with concentration of 0.0001 to 0.001% water leech muscles show always an immediate contraction.

The writer prepared varying strengths in Ringer's solution of the aqeous extract of *Eucommia ulmoides*, Oliv. and examined their actions on leech muscle, employing the method of Fühner.

No marked changes resulted with 0.002%, but with 0.005% there was seen a slight contraction, while with concentrations of 0.01 to 0.05% there was noted marked contraction after about 2 to 5 minutes, with rise in tension and active motility that returned to the former state after 20 to 30 minutes. With strengths of 0.1% and above, contractions were weak and the increase in tension was not marked.

FIG. 12. Experiments with water leech muscle.

With the excised rabbit's intestine and uterus concentrations of 0.01 to 0.05% were required to produce a rise in tension but with water leech muscle a concentration of 0.005% produced contractions.

From the above experiments it is believed that aqueous extract of *Eucommia ulmoides*, Oliv. possesses an action that stimulates the parasympathetic nerves.

F. Experiments on the Movements of the Ciliary Body of the Esophagus of the Frog

Movements of the ciliary bodies are brought about by acetylcholine chloride, and essentially there are no nerve cells and practically no nerve fibers in the mucosa. Instead there is present a cholinesterase, and by the synthesis of acetylcholine by non-nervous tissues movements of the ciliary bodies are said to be caused.

The writer prepared with Ringer's solution varying concentrations of acetylcholine chloride and of the aqueous extract of *Eucommia ulmoides*, Oliv., and the speeds of movement of the ciliary bodies of the frog's esophagus were estimated by Burn's method (8).

With a strength of 0.0000005% acetylcholine chloride no marked changes were elicited, but with concentrations of 0.0000001% to 0.0001% movements of the ciliary bodies of the esophagus were accelerated.

With a strength of 0.002% of the aqueous extract of *Eucommia ulmoides*, Oliv. no marked changes were noted, but with a concentration of 0.05% there was a slight increase in speed of movement of the ciliary bodies, and marked motility was elicited with a strength of 0.01 to 1.0%.

FIG. 13 A. Experiments on the movements of the ciliary body of the esophagus of the frog.
 — : 0.0001%, 0.000001% acetylcholine chloride
 - - : Ringer's solution

FIG. 13 B. Experiments on the movements of the ciliary body of the esophagus of the frog.
 — : 0.02%, 0.005% aqueous extract of *Eucommia ulmoides*, Oliv.
 - - : Ringer's solution
 Each point indicated on plan is average quantity of 10 times examined.

From the above experiments it became clear that the aqueous extract of *Eucommia ulmoides*, Oliv. increases the speeds of movement of ciliary bodies of the esophagus of the frog. Hence it can be said that it has an action that stimulates the parasympathetic nerves.

G. *Effective Constituents of Eucommia ulmoides, Oliv.*

In order to extract the effective constituents of *Eucommia ulmoides*, Oliv. and to study them the following experiments were undertaken.

1) *Ether extract of Eucommia ulmoides, Oliv.*

Eucommia ulmoides, Oliv. was cut into small pieces and these were infused in cold ether for 2 to 3 days, then the ether was removed and an extract was obtained. This procedure was repeated 5 times.

Amount recovered: 10.1%.

Characteristics: Dark brown in color, tasteless and odorless, caramel-like in nature and with marked mucosity. Insoluble in water. Soluble in propylene glycol, but when water is added to this solution there is return of mucosity which renders experiments impossible.

2) *Alcohol extract of Eucommia ulmoides, Oliv.*

Small pieces of *Eucommia ulmoides*, Oliv. were placed in 5 l its volume of alcohol, and extracted over a water bath for 3 to 5 hours. This procedure was repeated 7 times.

Amount recovered: 11.7%.

Characteristics: Black brown mass with an aromatic odor. Insoluble in water but soluble in propylene glycol. However when water is added there is reproduced a mass which renders experiments impossible.

3) *Aqueous extract prepared from the sediments obtained after ether and alcohol extraction*

The sediments left after the ether and alcohol extracts were prepared, were treated

FIG. 14. Movements of the rabbits respiration and arterial pressure. Intravenous injection of 100 mg *Eucommia ulmoides*, Oliv.

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with 3 times their volume of water and extracted over a water bath 2 to 3 times. The filtrates obtained were collected together and dried by evaporation over a water bath. An aqueous extract was next prepared and its action on rabbit's blood pressure and respiration was examined. It was then found that it lowers markedly the blood pressure and this action was maintained for a long time. No changes were noted on the respiration.

SUMMARY

1. The toxicity of the aqueous extract of *Eucommia ulmoides*, Oliv. for frogs, mice and rabbits is extremely low.
2. The aqueous extract of *Eucommia ulmoides*, Oliv. lowers the blood pressure of rabbits. No marked changes are noted in the respiration.
3. The aqueous extract of *Eucommia ulmoides*, Oliv. acts inhibitorily on the excised heart of the frog.
4. The extract dilates the blood vessels of the hind legs of the frog and the ear veins of the rabbit.
5. It produces a rise in tension of the excised intestine and uterus of rabbits.
6. It contracts the pupils of the excised eyeball of the frog.
7. It produces a conspicuous contraction of the muscles of the water leech.
8. It accelerates the movements of the ciliary bodies of the esophagus of the frog.
9. The action of the aqueous extract of *Eucommia ulmoides*, Oliv. is inhibited by atropine sulphate, but not by other drugs examined. Hence it may be said that the aqueous extract of *Eucommia ulmoides*, Oliv. stimulates the parasympathetic nerves.
10. An aqueous extract of the sediment resulting after extraction of *Eucommia ulmoides*, Oliv. with ether and alcohol, produces a marked fall in the blood pressure of rabbits.

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