

*Some Pharmacological Effects of the Roots of Pteryxia  
Terebinthina (Hook.) Coult. & Rose Var. Terebinthina,  
and of Pteryxin, a Substance Isolated from the Roots*

TRACEY G. CALL<sup>1</sup>

*School of Pharmacy  
Montana State University  
Missoula, Montana*

and

EARL B. FISCHER

*University of Minnesota  
Minneapolis, Minnesota*

SEVERAL BENZOPYRONE compounds have been used in medical practice in recent years. Some of these compounds which have been used as anticoagulants have become very well established in therapy, while the value of others used as smooth muscle spasmolytics and as coronary vasodilators is the subject of considerable controversy.

The *Umbelliferae* family has yielded a number of benzopyrone compounds of medicinal interest. Khellin is probably the best known of these. In a search for plants containing khellin-like substances, the roots of *Pteryxia terebinthina* (Hook.) Coult. & Rose var. *terebinthina* were collected near the Columbia River in Sherman County, Oregon. Of the numerous species of *Umbelliferae* tested by one of us (Call), this species was selected for further study because of the high yield of crystalline material from some of its extracts. Herbarium specimens were determined by Dr. Lincoln Constance and were deposited in the herbaria at the University of California and at the University of Minnesota.

*Experimental*

*Roots.* After the roots were dried to a moisture content of less than 10 per cent, they were milled to a 30-mesh fineness. Most of the essential oil was removed by spreading the powder in a thin layer and exposing this powder to a current of air at 39° C. until dried to a constant weight.

Chronic toxicity studies of the powdered root were made by mixing the powdered root with powdered Purina dog pellets and feeding the mixture to mice. Swiss-strain albino mice, 29-31 days of age and weighing 16 to 18 grams, were divided into eight lots. Each lot contained litter mates consisting of three female mice or of three male mice. Six mice were used as controls, and six

<sup>1</sup> Present address: Sunkist Growers Inc., Research Department, Box 215, Corona, California.

TABLE 1. PER CENT MORTALITY OVER 12-WEEK OBSERVATION PERIOD

Controls	5% Diet	10% Diet	15% Diet
0	0	33	50

mice were fed on each of diets containing 5 per cent, 10 per cent, and 15 per cent pteryxia root.

The per cent mortality at the end of 12 weeks is shown in Table 1.

All deaths occurred during the first three weeks of the diet.

A difference in growth rates between the controls of each sex and the treated mice indicated the possible presence of a hormonal effect. Further studies are planned with larger numbers of animals under conditions especially arranged to determine whether or not this effect is statistically significant.

The blood-coagulation time was determined, using the McGowen modification of the capillary tube method (Bray, 1951) on each of the mice that survived at the end of the 12-week diet period. The results of these determinations are presented in Table 2.

At the end of this experiment, the animals were sacrificed. The livers of the mice that survived on the 10 and 15 per cent diets were considerably darker than those of the controls. Wakim *et al.* (Krantz and Carr, 1951) state that animals killed by dicoumarol, an anticoagulant, exhibit dark and congested livers.

*Pteryxin, a substance from the pteryxia root.* Pteryxin, a crystalline substance, was isolated from the roots by several extraction procedures. Several chemical properties and reactions, together with its toxicity to fish, indicate that pteryxin is probably a benzopyrone compound, possibly a furanobenzopyrone. Pteryxin has a melting point of about 81° C., a molecular weight of

TABLE 2. BLOOD-COAGULATION TIME OF MICE ON DIET FOR 12 WEEKS

Group	No. of Mice	Av. Coagulation Time, Minutes	Av. Deviation Minutes	Per Cent Deviation
Control	6	4.75	0.50	10.5
5% diet	6	6.75	0.75	11.1
10% diet	4	10.00	2.50	25.0
15% diet	3	15.33	1.56	10.2

about 400, and a probable molecular formula of  $C_{22}H_{24}O_7$ . (Chemical studies of this compound are to be published elsewhere.)

Tests were made to compare the acute toxicity of pteryxin with some benzopyrone compounds and rotenone. Fresh water tropical fish, *Lebistes reticulatus* Peters, were used for the tests. A method similar to that used by Späth and Kuffner (1936) in their studies was followed. Four adult male fish were used for each dose level for each substance. The results of this study are presented in Table 3.

TABLE 3. ACUTE TOXICITY OF PTERYXIN AND SOME OTHER SUBSTANCES TO FISH

Substance Tested	Total Time Elapsed						
	5 Min.	10 Min.	20 Min.	40 Min.	80 Min.	160 Min.	320 Min.
Rotenone 1:400,000		+	+	+			
		+	+	+			
			+	+			
Xanthotoxin 1:40,000			+	+			
			+	+			
			+	+			
Pteryxin 1:40,000			+	+	+		
			+	+	+		
			-	-	+		
Imperatorin 1:30,000		-	-	+	+		
		-	-	+	+		
		-	-	-	+		
		-	-	-	+		
Coumarin 1:5,000	-	-	-	+	+		
	-	-	-	+	+		
	-	-	-	+	+		
	-	-	-	-	+		
Khellin 1:5,000		-	-	+	+		
		-	-	+	+		
			-	+	+		
			-	-	+		

- Equilibrium completely lost.

+ Dead.

Determinations of the acute oral toxicity of pteryxin were made using adult Swiss-strain white mice. Oral doses of pteryxin suspended in a 6 per cent acacia emulsion were administered by means of a dose syringe. Four mice were given 0.5 Gm./Kg., three were given 1.0 Gm./Kg., and three were given 2.0 Gm./Kg. No deaths had occurred at the end of 24 hours.

Effect of pteryxin on smooth muscle was determined *in vitro* by the use of Magnus-type smooth muscle preparations. Spontaneously contracting, isolated rat uteri were used for most of these studies. Details of the materials and methods used in these determinations have been previously described by Call and Green (1956). The effect of pteryxin was compared with those of papaverine HCl, atropine sulphate and khellin (an antispasmodic from *Ammi visnaga* L., family *Umbelliferae*). The results of the atropine series were inconsistent. Under the condition of these tests, pteryxin possesses slightly more than four times the spasmolytic activity of papaverine HCl and twice the activity of khellin. A representative kymograph record is presented as Figure 1.

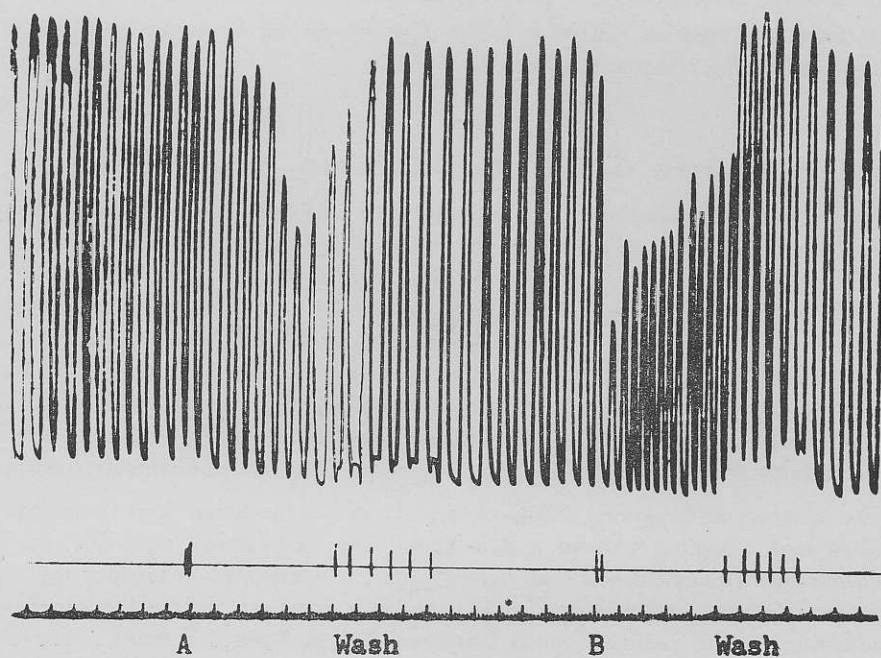


Figure 1. Kymograph record comparing the effect of papaverine hydrochloride and of pteryxin on a spontaneously contracting rat uterus. A = Papaverine HCl 1:100,000. B = Pteryxin 1:400,000. Time-marker intervals 10 seconds and 1 minute.

### *Summary*

Pteryxia root, at a 15 per cent dietary level, killed 50 per cent of the mice in one to three weeks. The blood-coagulation time of the surviving mice was significantly increased.

Pteryxin killed guppies within 80 minutes in a concentration of 1:40,000. Oral toxicity to mice was low. Pteryxin possesses a spasmolytic activity twice that of khellin and four times that of papaverine HCl on spontaneously contracting rat uteri *in vitro*.

### *Acknowledgment*

This study was partially supported by a grant from the American Foundation for Pharmaceutical Education.

### *Literature Cited*

- Bray, W. E. 1951. Clinical laboratory methods. The C. V. Mosby Co., St. Louis.
- Call, Tracey G. and John Green. 1956. Spasmolytics from plants. I: Suksdorfia A and Columbianin. Proceedings of the Montana Academy of Sciences, 16:49-51.
- Krantz, John C., Jr. and C. Jelleff Carr. 1951. The pharmacologic principles of medical practice, Second edition. The Williams and Wilkins Co., Baltimore.
- Späth, Ernst and Fredrich Kuffner. 1936. Die natürlichen Cumarine und ihre Wirkung auf Fische. Monatsh. Chem., 69: 75-144.

### *Forest Soils Group Holds Summer Field Meeting*

Forty-seven foresters representing industry, state and federal agencies, and colleges and universities of Oregon, Washington, and British Columbia attended the annual summer meeting and field tour at Centralia, Washington, on June 12 to 14. The Weyerhaeuser Timber Company, through its Centralia Forestry Research Center, played host for the group and conducted a two and one-half day tour over its Clemson and Vail-McDonald tree farms. Company research specialists William Cummings, Jim King, and Gene Steinbrenner showed the foresters soil-profile and forest-tree-growth plots and studies. Soil-site correlations from this work are expected eventually to provide specific guides to forest growth potential for various physiographic, soil, and climatic conditions.

The members of the group, which has been known as the Forest Soils Committee of the Douglas-fir Region, adopted a new name. The Committee's new title is: The Northwest Forest Soils Council. The new designation is expected to broaden the scope of the group's work and influence to include forest areas east of the Cascade Range. Commenting on this change Council Chairman George Schroeder stated: "The ever-increasing interest in forest soils problems and work is evidenced by the number of foresters attending the Committee meetings and requesting assistance and information on this subject. The Council stands ready to assist any group or organization in the Northwest in furthering forest soils studies and forest resource improvement."