

A NOTE ON THE ACTIONS OF "ERIOCOMINE," A CONSTITUENT OF ERIOCOMA FLORIBUNDA.*

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In a recent paper in THIS JOURNAL, G. G. Colin¹ reported on the active constituents and actions of *Eriocoma floribunda*, which is extensively employed by the laity as an abortifacient and is used by physicians, in Mexico. According to Colin, the exact nature of the active constituent, which he has named "eriocomine," is not understood, but apparently it is not an alkaloid. A summary of general actions with reports on clinical cases is given in a thesis by R. Torres.² The significant claims of Colin and of Torres for "eriocomine" are as follows: temporary slight anæsthetic action on the tongue, local irritant action on subcutaneous and intramuscular injection but not on oral administration, congestion of viscera and genitalia in animals, abortion in pregnant animals, stimulation of contractions of excised and intact uteri of guinea-pigs, oxytocic action similar to the actions of ergot and pituitary, and a definite usefulness in controlling post-partum hemorrhage. Its use during labor is contraindicated. According to these claims, "eriocomine" would be an unusual uterine hemostatic.

Unfortunately, the data supplied by Colin and Torres are indefinite and inconclusive, but they do suggest a possible indirect and undesirable uterine action. During the routine of other researches, we have taken the opportunity of testing "eriocomine" on the uterus, circulation and blood of animals. The "eriocomine" was supplied by Mr. Colin as a 10 per cent aqueous solution of the supposedly active fraction of eriocoma. A brief summary of the results obtained follows.

CIRCULATION.

Injected intravenously into dogs and cats, "eriocomine" had no effect on blood pressure and pulse rate until very large amounts were given. Doses of 19 and 36 mg. per kilo did nothing, 77 mg. per kilo caused a 23 per cent fall of blood pressure, and 100 mg. per kilo in three cats caused variable effects. This large dose killed one cat by cardiac paralysis, lowered the blood pressure 42 per cent and increased the pulse 20 per cent in another cat, and had no definite effect in still another cat. Since the total oral dose recommended for patients is only 300 mg., our results would indicate that this clinical dose would be insufficient to cause any direct circulatory response even if it were injected directly into the blood stream. This confirms Colin's claim that the drug has little or no effect on the circulation, and shows that it is also unable to stimulate smooth muscle in the blood vessels.

INTESTINE AND UTERUS.

Applied directly to excised strips of rabbit intestine, according to the Magnus technic, a 1 : 10,000 concentration of "eriocomine" did nothing, while 1 : 5000

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¹ G. G. Colin, *Jour. A. Ph. A.*, 18 (1929), 876.

² R. Torres, *Estudio sobre la aplicación terapeutica, de la Eriocomina en Ginecologia*, Thesis, National Univ. of Mexico (1929), 54.

paralyzed the preparation. The non-pregnant cat uterus was depressed by a concentration of 1 : 3333 and gave no response with lower concentrations. The non-pregnant guinea-pig uterus was not stimulated, no definite response being obtained with the maximum concentration (1 : 2500) tried. With the pregnant guinea-pig uterus, the results were still more disappointing; no stimulation was observed with concentrations ranging from 1 : 10,000 to 1 : 500. When the uterine movements of cats were recorded *in situ*, using Jackson's method, doses of 19, 77 and 100 mg. per kilo intravenously failed to elicit contractions of the uterus, although good contractions in the same animals were obtained after injections of epinephrine, ergot and pituitary extract. From these results it is concluded that "eriocomine" had no direct stimulant action on excised intestinal and uterine muscles and on the uterus *in situ*, even with the highest tolerated dosage. Therefore, we were unable to confirm the claim that "eriocomine" is a uterine stimulant comparable to ergot and pituitary.

GENERAL PROPERTIES AND EFFECTS ON BLOOD.

A striking feature of the claims was that "eriocomine" caused marked gastrointestinal irritation, and even hemorrhagic enteritis. It also caused marked irritation when injected locally. The irritation after oral administration would result in engorgement and hyperemia of the entire abdominal region, including the uterus, and thus cause uterine stimulation and abortion. Such an indirect action would explain why the uterus of cats was not stimulated *in situ* when the drug was injected intravenously. This mechanism of action would be in keeping with that of other irritants, such as cantharides and the various ecboic volatile oils. Due to limitation of material, we were unable to make life tests for the irritant action of "eriocomine," but certain tests were made *in vitro*.

Colorimetric estimations of acidity in the 10 per cent solution showed a p_H of 6.9 to 7.0, *i. e.*, neutrality. The product was non-irritating to the tongue. A test for the presence of saponins was made by adding sodium chloride in isotonic concentration (0.9 per cent) to "eriocomine," and incubating this mixture with washed rabbits' red blood cells. However, 24 hours' incubation of the red cells in concentrations of "eriocomine" ranging from 0.025 to 5.0 per cent failed to cause detectable hemolysis. There was some darkening and agglutination of the red cells which might be accounted for by the colloidal nature of the material. In a parallel series, concentrations of pure saponin as low as 0.0001 per cent hemolyzed the cells within 1 hour. The conclusion would seem to be justified that the irritant constituent of "eriocomine" is not free saponin, acid or alkali.

CONCLUSIONS.

1. "Eriocomine," a constituent of *Eriocoma floribunda*, when injected intravenously in animals, was found to have no action on blood pressure and pulse rate, except in toxic and fatal doses.

2. No direct smooth muscle stimulation was demonstrated with "eriocomine," even in maximum doses, on the excised intestine and pregnant and non-pregnant uterus, and on the non-pregnant uterus *in situ*.

3. "Eriocomine" possessed a neutral reaction, was non-irritating to the tongue, and did not hemolyze red blood cells, indicating absence of saponin.

4. "Eriocomine" lacks the properties which would justify regarding it as a possible oxytocic and uterine hemostatic comparable to ergot and pituitary, but it may act as an irritant ecboic.

COMPARATIVE MARRUBIIN CONTENT IN MARRUBIUM VULGARE FROM EUROPEAN VS. AMERICAN SEED.

BY ADELIA MCCREA.*

Marrubium vulgare L., the perennial white horehound, is a common garden plant. While it is frequently used as a potherb and for flavoring, it is also of some interest medicinally. This is probably due to its glucoside content, the crystalline principle marrubiin; and it was in regard to this property that the tests herein described were made.

It has been considered that, in its characteristic physiological activity, European marrubium was better than American plants which were stated to be without marrubiin. Since it is the same species, botanically, ours having been naturalized from Europe, so marked a difference was difficult to explain; hence an experiment was designed to give further comparative data.

For this, seed was obtained from three sources: France, Germany and American-grown (Michigan). A light, slightly acid, sandy soil was chosen, as the plant seems to prefer such a type; and the seed lots were planted in adjacent beds. The French seed germinated first, then the American, and lastly the German; but at harvest time all beds were closely approximate in growth, and no distinction was visible in herbage or bloom.

As marrubium belongs to the *Labiatae*, it was considered probable that maximum yields would be obtained from flowering plants, as is true of other mints. All were therefore cut while in bloom, using the flowering parts, with a minimum of stems. They were carefully dried at a moderate temperature, about 40° C., until brittle; then ground to a fine powder and processed for the glucoside.¹ All were found to be practically identical in physical appearance and melting points, as shown in the tabulation below; but there is considerable variation in the amount of marrubiin present.

Seed source.	Per cent of marrubiin.	RELATIVE MARRUBIIN VALUES.	
		Melting point.	Remarks.
French	0.34%	156-159° C.	Readily freed from waxes
German	1.00%	156-158.5° C.	Readily freed from waxes
American	0.47%	156-158° C.	Separated with difficulty.

It is interesting to note that all three samples possess a good content of the characteristic glucoside, the French running lowest of the three instead of highest as had been expected. It is therefore concluded that the reported lack of marrubiin in American marrubium has been due to faulty methods of culture, to failure in separating the waxes, or to both of these factors. Certainly, it is present in plants grown and harvested under proper conditions.

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¹ Chemical extraction and testing were done by W. F. Kamm of this Laboratory.