Salivary counts and white blood cell counts were taken simultaneously in 5 cases of myelogenous leucemia, during treatment with Roentgen ray irradiation and with Fowler's solution. Marked fluctuations which occurred in the white blood cell counts of these individuals were not accompanied by any consistent change in the number of salivary leucocytes. Further, no constant relationship between leucocytes of saliva and peripheral blood were seen in observations made in other pathological conditions, including agranulocytic angina, thrombocytopenic purpura with chronic granulocytopenia, carcinoma of stomach, carcinoma of breast, Hodgkin's disease, lymphatic leucemia and lobar pneumonia.

Similar conclusions were reached by Elliott and Jenkinson,[3] who followed the saliva of patients with myelogenous leucemia treated with irradiation.

Conclusions. In a series of 512 enumerations of leucocytes in saliva and peripheral blood in 20 normal and 17 abnormal individuals, no correlation has been observed between the total number of white blood cells in the peripheral blood and in the saliva.

7360 C

Comparative Pharmacology of Isomeric Saligenins and Their Bromine Derivatives.

DAVID I. MACHT AND H. A. B. DUNNING, JR.

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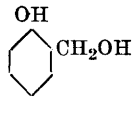
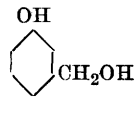
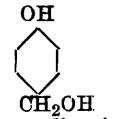
Macht and Dunning described the chemical and physiological properties of mono-brom-hydroxy-benzyl alcohol, or mono-brom-saligenin.[1] This compound, which has been named *Bromsalizol,* was the mono-brom derivative of ortho-hydroxy-benzyl alcohol. Inasmuch as 3 isomers of saligenin with the hydroxyl OH and benzyl CH_2OH groups in the ortho, meta and para positions, respectively, are possible, they and their mono-brom derivatives were prepared in these laboratories and investigated with regard to their comparative pharmacology. The structural formulae of the 3 saligenin isomers and their corresponding mono-brom derivatives are as follows:

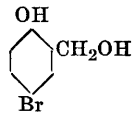
[3] Elliott, A. R., and Jenkinson, E. L., *Med. Clinics of N. Am.*, 1933, **17**, 327.

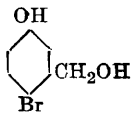
[1] Macht and Dunning, PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 465.

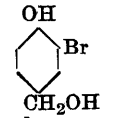

ortho-saligenin


meta-saligenin


para-saligenin


2 oxy-5 brom-benzyl alcohol (Bromsalizol)


mono-brom-meta-saligenin


mono-brom-para-saligenin

The melting point of ortho-saligenin was 85°-87°; of meta-saligenin, 70°-71°; of para-saligenin, 116°; of mono-brom-ortho-saligenin, 108°-109°; of mono-brom-meta-saligenin, 124°; and of mono-brom-para-saligenin, 128°.*

A pharmacodynamic comparison of the compounds mentioned above was made by studying (1) their effect and that of controls on the growth of *Lupinus* seedlings in plant physiological solutions; (2) their action on the muscular coordination and respiration of goldfish, *Carassius auratus;* (3) their influence on the behavior of mice, injected intraperitoneally; and (4) of rats, also injected intraperitoneally; (5) their local anesthetic effect on the cornea of the rabbit's eye and on frog-skin; (6) their action on surviving preparations of smooth muscle from the intestine of the cat and uterus of the guinea pig; (7) on the kidney function of rabbits after administration by mouth; (8) on the circulation and respiration of etherized cats after intravenous injection; (9) their antipyretic effect on rabbits and rats; and ascertaining (10) the killing intravenous dose for cats. Most of the results obtained are summarized in Table I.

It was found in each case that the mono-brom-saligenins were more potent pharmacologically than their corresponding mother saligenins. The di-brom-saligenins and other halogen derivatives are under investigation and will be described later. Most of the physiological reactions obtained demonstrated that the ortho-saligenin was more active than the meta-saligenin and the meta- more active than the para-saligenin. Similarly, the brominated ortho-saligenin was more active than the brominated meta-saligenin, and the latter was more potent than the brominated para-saligenin. The single exception to this rule was the effect produced on smooth

* Complete data regarding the chemical and physical properties of these compounds are to be published by one of the authors (H. A. B. D.) in his dissertation for a doctorate in chemistry.

TABLE I.
Pharmacology of Saligenin and Brom-Saligenin Isomers.**

Compound	Effect on *Lupinus Albus* Seedlings of Solutions of		Effect on Goldfish, *Carassius Auratus*		Effect on Mice of Intraperitoneal Injections of	Dose Inhibiting Contractions of Intestinal Segment mg.	Anesthesia of Frogskin†	Minimal Lethal Dose on Intravenous Injection in Cats mg. per kilo
	1: 5,000 %	1: 10,000 %	Incoordination	Respiratory paralysis				
Ortho-saligenin	27 (20)	52 (20)	15 min. 1:10,000 (10)	50 min. 1:10,000 (10)	15 mg. coma in 5 min.; dead in 2 hours (10)	50 (15)	.200 (20)	532 (2)
Meta-saligenin	62 (10)	77 (10)	no effect 1:2,500 (6)	no effect 1:2,500 (6)	30 mg. coma in 20 min. recovery in 2 hours (6)	45 (6)	.040 (5)	615 (2)
Para-saligenin	81 (10)	90 (10)	no effect 1:2,500 (6)	no effect 1:2,500 (6)	30 mg. coma in 25 min. recovery in 1 hour (6)	65 (6)	.006 (5)	934 (2)
Brom-ortho-saligenin, Bromsalizol	22 (20)	50 (20)	25 min. 1:10,000 (10)	80 min. 1:10,000 (10)	10 mg. coma in 2 min. dead in 20 hours (6)	3 (15)	1.000 (20)	250 (2)
Brom-meta-saligenin	41 (10)	80 (10)	62 min. 1:10,000 (6)	120 min. 1:10,000 (6)	10 mg. semiconsciousness in 14 min. recovery in 1½ hrs (6)	2 (6)	.400 (5)	153 (2)
Brom-para-saligenin	71 (10)	100 (10)	120 min. 1:10,000 (6)	150 min. 1:10,000 (6)	20 mg. slight depression in 20 min. recovery in 1 hour (6)	30 (6)	.170 (5)	361 (6)

** Figures in parenthesis indicate number of experiments.

† The anesthetic efficiency of Bromsalizol being regarded as 1.000, the relative efficiency of the other compounds is expressed as decimals of that standard.

muscle. The brominated meta-saligenin was more powerful than the brominated ortho-saligenin. On the other hand, the toxicity of the brom-meta-saligenin for cats was considerably greater. None of the saligenins or of their brominated derivatives produced impairment of the kidney function of rabbits after administration by stomach tube of as much as 250 mg. per kilo weight. The saligenins themselves exhibited a slightly antipyretic effect on rabbits in which hyperpyrexia had been produced by injections of hay infusion. The brominated compounds, however, showed a definite antipyretic effect in such animals. Experiments with injections of camphorated oil revealed that the brominated saligenins, and especially Bromsalizol, antagonized the convulsant

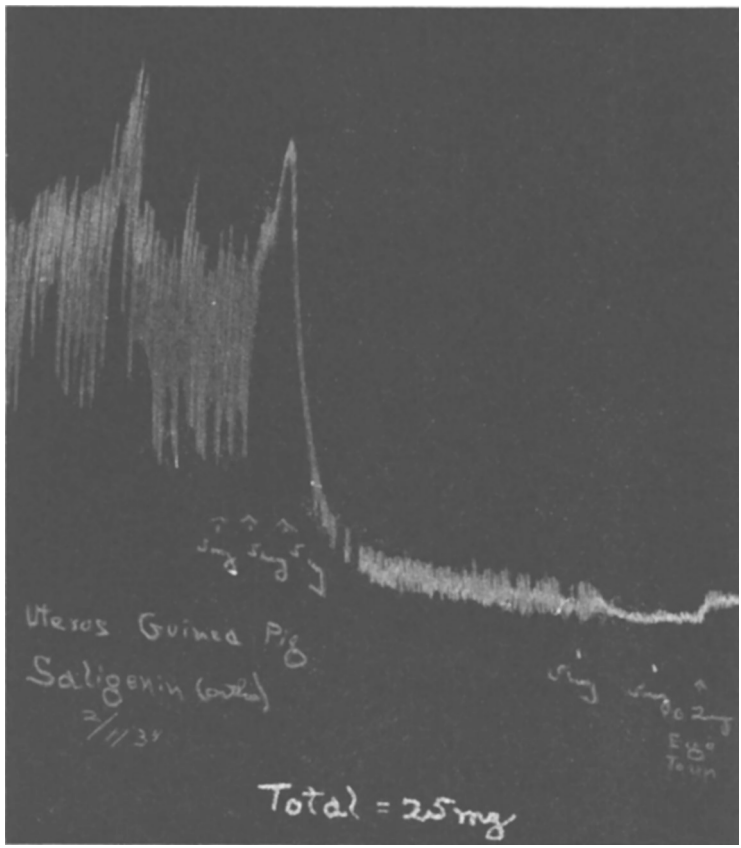


FIG. 1.

Preparation of uterine muscle from the guinea pig. Effect of repeated doses of ortho saligenin in 50 cc. of Locke's solution until complete inhibition of contractions results.

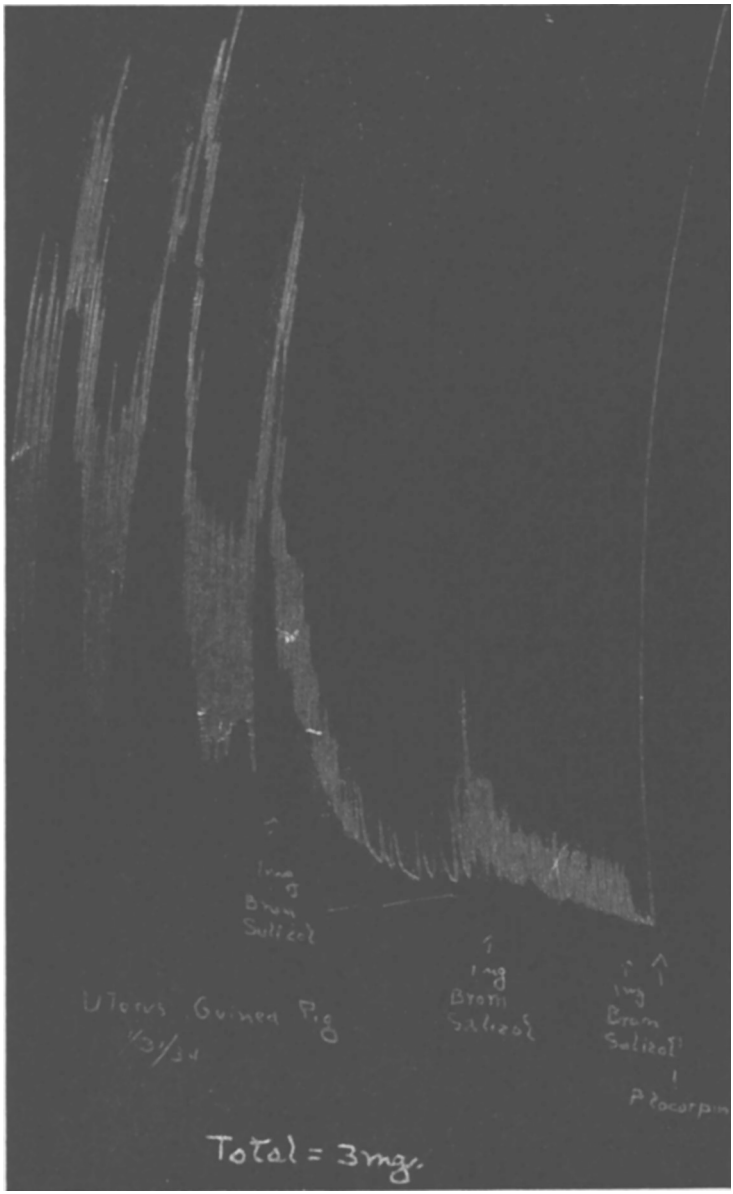


FIG. 2.

Preparation of uterine muscle from guinea pig. Effect of mono-brom-ortho saligenin, or Bromsalizol. 3 mg. in 50 cc. of Locke's solution produce inhibition of contractions but not death, as is indicated by response of preparation to pilocarpine.

effects of camphor injections in rats and guinea pigs. Such an antagonism was not produced by ortho-saligenin itself, thus indicating that the brominated compound produced some sedation of the cerebrum.

The comparative study of the two kinds of isomers mentioned above strikingly emphasizes the selective, quantitative differences in the action of chemical isomers. Figures 1 and 2 illustrate the effect of ortho-saligenin and its mono-brom derivative, Bromsalizol, on surviving preparations of the guinea pig uterus. It will be observed that the brominated compound, as an antispasmodic, is 8 times more

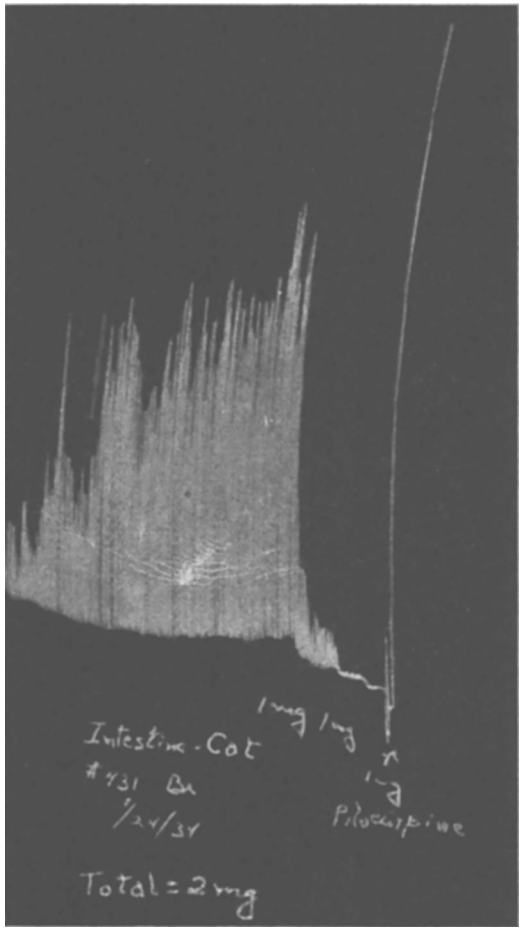


FIG. 3.

Intestinal segment of cat. 2 mg. of mono-brom-meta saligenin in 50 cc. of Locke's solution inhibit contractions.

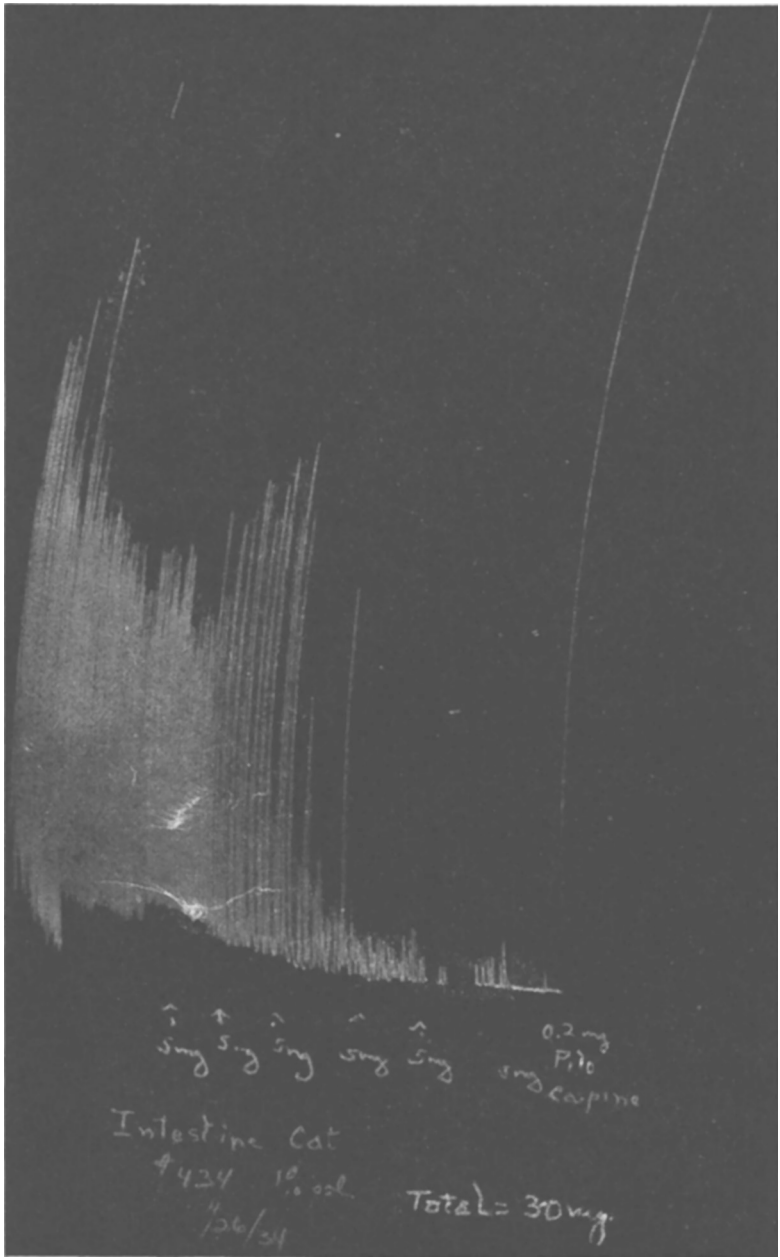


FIG. 4.

Intestinal preparation of cat. Effect of mono-brom-para saligenin. It required 30 mg. in 50 cc. of Locke's solution to inhibit contractions.

powerful than saligenin itself. Figures 3 and 4 illustrate the difference between the effects of brom-meta-saligenin and brom-para-saligenin on isolated intestinal segments from the same cat. Again, it will be noted that the brom-meta compound is 15 times more potent than the corresponding brom-para compound as a sedative for smooth muscle. Clinical studies have already been made with regard to the antispasmodic effects of the above mentioned compounds and are now being conducted especially with mono-brom-ortho-saligenin, or Bromsalizol, which, as appears from the table, offers the widest margin of safety as well as the most efficient therapeutic index.

7361 C

Vitamin A of Serum Following Administration of Haliver Oil in Normal Children and in Chronic Steatorrhea.

JACK CHESNEY AND AUGUSTA B. McCOORD. (Introduced by S. W. Clausen.)

From the School of Medicine, University of Rochester, New York.

After the ingestion of an oil of high vitamin A content, such as haliver oil, a marked increase in the intensity of the Price-Carr reaction for vitamin A is observed in the blood serum of normal persons. The degree of this increase may indicate the ability of the individual to absorb vitamin A. The amount of vitamin A in the serum is stated in colorimetric units which are purely arbitrary. Using a 10% solution of copper sulphate as a standard, serum of sufficient content in vitamin A to match the standard when acted upon by the antimony trichloride reagent is considered to contain 100 units of vitamin A per 100 cc. Each colorimetric unit is equivalent to 2.9 biological units.

To 12 afebrile children who were considered to have no disorder in the absorption of fats, 2 cc. of haliver oil* were administered while the children were fasting. Throughout the remainder of the 24-hour test period, the children ate meals with low vitamin A content at the usual times. Blood was taken for analysis before the ingestion of the oil, and 2, 4, 6, 9, 12, and 24 hours afterwards. The maximum concentration of vitamin A is observed at 4 hours and is approximately 9 times the fasting level. (Table I.) The level at 24 hours is about 50% above the original level.

* Furnished by the courtesy of the Abbott Laboratories.