SUGAR ALCOHOLS XIV.

THE ISOLATION OF POLYGALITOL FROM *POLYGALA SENEGA* AND THE PHYSICOCHEMICAL AND BIOLOGICAL PROPERTIES OF POLYGALITOL.*

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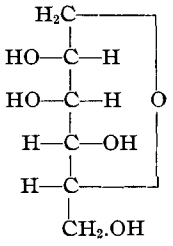
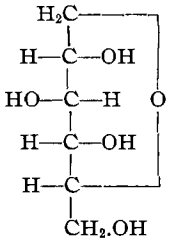
Polygalitol has been isolated from the leaves and stems of *P. Amara* by Chodat (1), from *P. vulgaris* by Picard (2) and from *P. Tennuifolia* by Shinoda, Sato and Sato (3). This anhydride was extracted from the fresh plants as a white crystalline compound m. p. 142–143° C., $[\alpha]_D^{16} = +47.81°$. Polygalitol has been shown to have the following formula and is isomeric with styracitol synthesized from glucose. Both compounds yield the same glucosazone m. p. 208° C. (4).[2]



Polygalitol



Styracitol

During the preparation of polygalitol in this laboratory in large quantities for animal experiments an improved method of isolation was developed. Since European species were difficult to obtain, it was of some interest to try local varieties of polygala. *Polygala Senega*, senega snakeroot, was selected because as an official drug it was more readily available. Price (5) has reported a sugar-like substance in extracts of senega root that he did not identify. In 1894 Guillaume-Gentil (6) reported a substance which he had obtained from *P. Senega* having a m. p. of 138° C. and suggested that it was similar to the "sugar" Chodat had isolated from the leaves of *P. Amara* six years before. In 1896 Schraeder (7) found sucrose in the root of *P. Senega* to the extent of 5 per cent and reported the presence of a small amount of sweet impure crystals in his preparation that he was unable to identify. Kain in 1898 (8) in Germany and Bienfang in this country in 1934 (9) also have reported sucrose as a constituent of senega root. Procter in 1860 (10) undoubtedly isolated a small amount of polygalitol from extracts of *P. Senega* although he did not report the physical properties. Since the roots only were used in these experiments, the leaves and stem as well as the root were used in this investigation. Jacobs and Isler (11) have recently made an exhaustive study of the sapogenins of *P. Senega* root.

EXPERIMENTAL.

1. Fresh Plant.—About 150 Gm. of fresh plant collected in the vicinity of Oakland, Md., on June 19, 1937, and identified pharmacognostically by Dr. Joseph E. Harned, were placed im-

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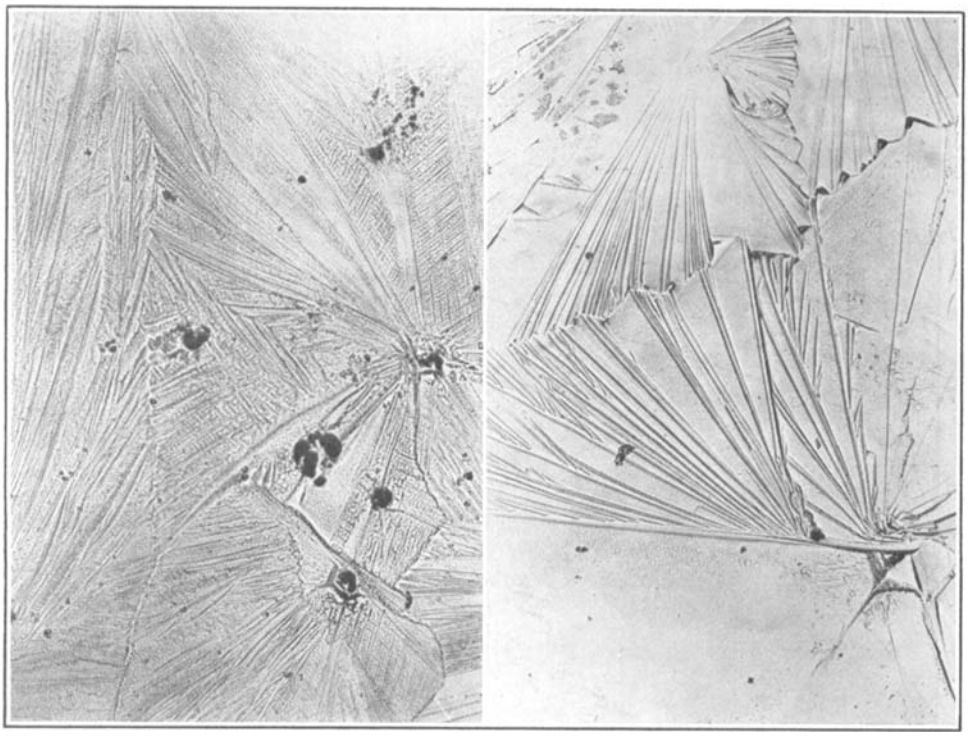
[2] Since this paper was submitted for publication Freudenberg and Rogers (*J. A. C. S.*, 59, 1602 (1937) have reported polygalitol as 1–5 anhydrosorbitol and styracitol, 1–5 anhydromannitol. These authors also were able to isolate 2 2 Gm. of crude polygalitol from dried *P. Senega*.

mediately in two liters of alcohol. The whole flowering plants deprived of their roots were used. After 36 hours the alcohol was recovered in a vacuum at low temperature until a light brown syrup remained. The syrup was dissolved in 100 cc. of water and lead subacetate was added until no further precipitation occurred, it was filtered and the excess lead was removed as sulfide. The clear lead-free filtrate was evaporated under reduced pressure to a syrup and was vigorously extracted with a mixture of 70 per cent ether in alcohol, filtered and evaporated to dryness. After standing in a desiccator for a week crystals of polygalitol formed as characteristic feathery rosettes. The crystals were purified by dissolving in water, adding charcoal, filtering and evaporating on a water-bath. Approximately 3 Gm. of impure crystals were obtained, which yielded 2 Gm. of pure polygalitol, m. p. 142–143° C. $[\alpha]_D^{16} + 47.3°$

2. *Dried Root.*—One pound of dried, powdered senega root from commercial sources was extracted with 50 per cent boiling alcohol until exhausted and the percolate evaporated and extracted



Crystals from *P. Senega.* Crystals from *P. Amara.*

Plate I.

as before. The alcohol-soluble fractions, after repeated purification with the ether-alcohol mixture and charcoal, yielded a colorless syrup which crystallized upon long standing in a desiccator. This product after recrystallization gave the characteristic melting point for polygalitol. Approximately 1 Gm. of pure compound was obtained. Plate I shows the characteristic feathery crystals of polygalitol from alcohol obtained from *P. Amara* and *P. Senega.* Armstrong has pointed out that the appearance of a 1–5 oxide ring in the alcohols is of interest, possibly indicating an intermediate stage in the synthesis of sugar alcohol from glucose (4).

Chodat in isolating polygalitol in 1888 reported the compound as an aldose which reduced Fehling's solution. Later Picard showed that the sugar alcohol he had isolated from *P. vulgaris* was identical with Chodat's compound. In these studies we have found a 70 per cent ether-alcohol mixture invaluable in removing traces of a reducing sugar-like substance that prevents complete purification. This material undoubtedly was the substance that led Chodat to believe polygalitol to possess a reducing group.

The yield of polygalitol reported by other workers varies from 0.85 to 2.2 per cent of air-dried plants deprived of their roots. Our yields have varied from 0.67 to 3.5 per cent of air-dried *P. Amara*, later methods of extraction yielding the higher value.

PHYSICOCHEMICAL PROPERTIES OF POLYGALITOL.

Polygalitol possesses a pleasant sweet taste which is followed by a very weak bitter taste. Repeated recrystallization failed to remove the bitter taste. The relative sweetness of polygalitol has been studied along with other sugar alcohols and certain of their anhydrides and previously reported (12). Polygalitol is the only anhydride of mannitol that possesses a sweet taste. The relative sweetness is in the ratio of 75 to 100, sucrose having an assigned value of 100, *d*-mannitol was found to possess a value of 57. The removal of water from a sugar alcohol with the formation

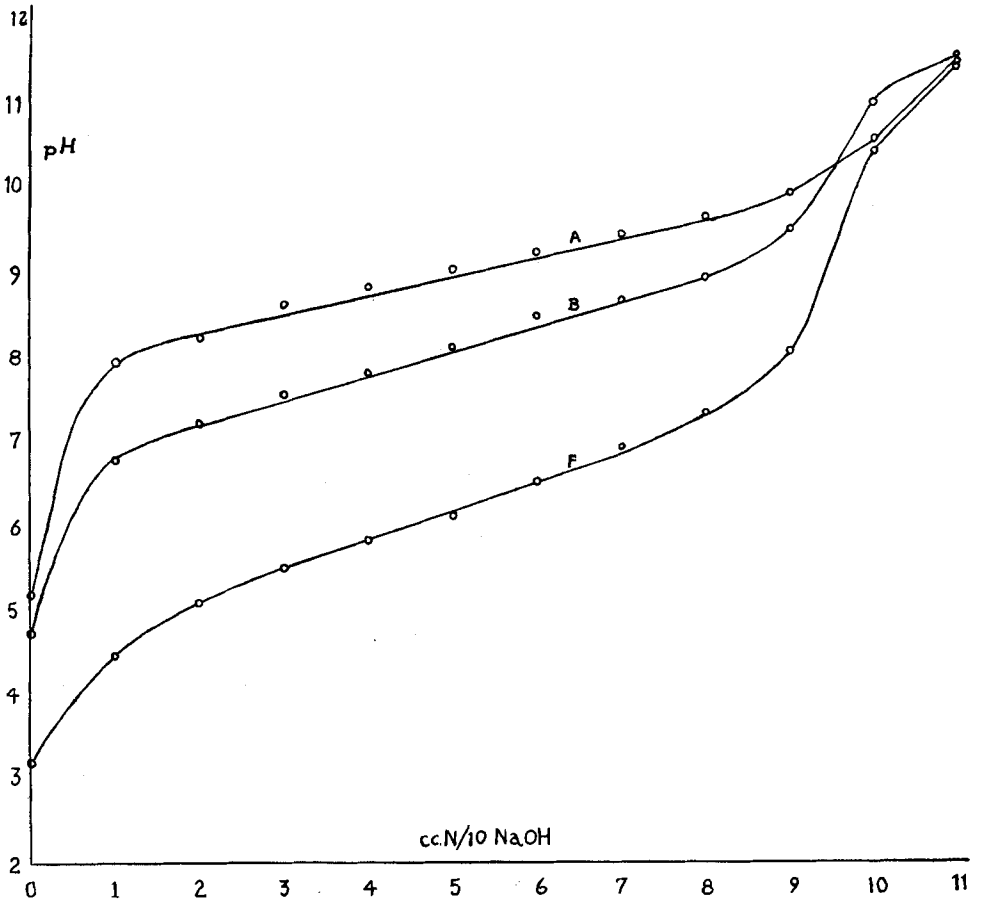


Fig. 1.—The effect of sugar alcohols on the dissociation of boric acid; Curve A, $M/10$ boric acid; curve B, $M/10$ boric acid + 4 per cent Mannitan or Glycerol; curve F, $M/10$ boric acid + 4 per cent Mannitol. The addition of 4 per cent Polygalitol to $M/10$ boric acid gives a curve approximating A.

of the anhydride as a rule destroys the sweet taste of the former. Polygalitol does not reduce Fehling's solution before or after hydrolysis. Upon ignition the compound yielded 0.87 per cent ash. The p_H of a 4 per cent aqueous solution of polygalitol gave a value of 6.7. The effect of the sugar alcohols and their anhydrides on the dissociation of boric acid has been studied previously (13, 14). Chart I shows the effect of polygalitol and mannitol on the dissociation of boric acid. In general, the anhydrides of the sugar alcohols potentiate the dissociation of boric acid to a lesser degree than do the parent substances. Polygalitol conforms perfectly to this generalization.

BIOLOGICAL PROPERTIES OF POLYGALITOL.

In former communications the authors have presented studies on the metabolism of the sugar alcohols and certain of their anhydrides in the animal body (15, 16, 17). No reports have been found in the literature regarding the metabolism of polygalitol, although its isomer, styracitol, has been partially investigated (18). Accordingly the authors investigated this problem. The results are summarized in Table I. In general polygalitol resembles the other anhydrides of

TABLE I.—SUMMARY OF RESULTS.

Glycogen Storage in Livers and Tissues of Rats after Polygalitol Diet.

Number of Animals.	Average Gm. Polygalitol Consumed.	Liver Glycogen Per Cent Mean.	Tissue Glycogen Per Cent Mean.
11	1.9	0.18	0.08
8	Controls	0.18	0.05

Respiratory Quotients during Fasting and after Polygalitol.

	Number of Animals.	Gm. O_2 per 100 Gm. per Hr.	R. Q.
Fasting	27	0.179	0.732
Polygalitol	27	0.185	0.745

Influence of Polygalitol on Blood-Sugar Level of Rabbits.

Number of Animals.	Mg. per 100 Cc. Blood. Fasting.	1/2 Hr.	1 Hr.	2 Hr.s	3 Hr.s	4 Hrs.	5 Hrs.
4	103	121	110	115	119	105	114
Glucose control							
4	97	179	255	243	197		
Water control							
2	88	101	112	114	125		

Influence of Polygalitol in Insulin Shock in Mice.

Number of Animals.	Hrs. Fasting.	Units per 100 Gm. Mouse.	Cc. 15 Per Cent Sol.	Recovery.
19 (Polygalitol)	12	5	1.4 to 4	None
20 (Glucose)	12	5	1.5	18

mannitol in that the white rat is incapable of storing glycogen or utilizing the compound as a carbohydrate to elevate the fasting respiratory quotient. Polygalitol is also without influence on the fasting blood-sugar level of the rabbit and is incapable of relieving the convulsions of insulin hypoglycemia. The details of these experiments will be published elsewhere.

The utilization of the sugar alcohols and their anhydrides by various microorganisms has been investigated (19). A study of these results compared with our previous findings reveals the interesting fact that although neither acid nor gas was formed from the anhydrides of mannitol, *i. e.*, mannitan, mannide, isomannide, both acid and gas were produced from the 1–5 anhydride, polygalitol. This sweet-tasting anhydride stands as an exception to the generalization that the removal of a molecule of water from the sugar alcohol molecule prevents their utilization by many organisms.

CONCLUSIONS.

1. Polygalitol, the 1–5 anhydride of mannitol, has been isolated from the fresh leaves and stem and from the dried root of *Polygala Senega* in pure form.

2. This anhydride occurs in the fresh flowering plant to the extent of approximately 2 per cent. Calculated on the basis of air-dried plant this concentration is considerably higher than that previously reported for other polygala species.

3. The discovery of this anhydride in other polygala species may be anticipated.

4. Polygalitol is one of the few anhydrides of the sugar alcohols that possesses a sweet taste.

5. Polygalitol, in accord with theory does not potentiate the dissociation of boric acid.

6. Polygalitol is not utilized as a carbohydrate in the animal body and in this respect resembles the other anhydrides of mannitol.

7. Certain bacteria possess the ability to utilize polygalitol with the production of acid and gas but are unable to utilize the other anhydrides of mannitol.

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RAPID CITY, SOUTH DAKOTA, OPENS HISTORICAL MUSEUM.

The Rapid City Historical Museum, Rapid City, South Dakota, was opened May 1st. Its field is Indian and pioneer material. The building is 134 by 41 feet, of native Minelusa limestone. The roof is supported entirely on the 18-inch walls, leaving the floor space unobstructed by structural elements. The cost was $30,000, of which two-thirds was furnished by the Works Progress Administration. The northern section houses the John A. Anderson collection of Indian material; the southern section includes space for the exhibition of pioneer material and an office for the custodian.

The AMERICAN PHARMACEUTICAL ASSOCIATION met in Rapid City in 1929.
