any increase in volume of the material, but only the liquid imbibed by the solid substance causes swelling. Detmer states that imbibition is by no means capillarity; a fluid entering by capillarity occupies previously existing spaces, while when imbibition takes place, the molecules of the liquid push in between the micelles actually making space for themselves and thus bringing about an increase in volume. These considerations make clear how a liquid may be absorbed in quantity in the open spaces in the plant tissues and yet may not cause appreciable swelling either because the micelles are already distended as in fresh wood or because the liquid does not have the properties facilitating imbibition as distinguished from capillarity. Steel (13) takes the view that when a substance absorbs a liquid without swelling, the cohesion of the molecules of the substance is too great to permit them to be forced apart by the liquid.

In studying the data concerning the effect of water and other liquids on blocks of woody tissues dried to constant weight, we find that recovery of original size occurs to a greater extent and at a more rapid rate with the blocks dried at room temperature than with the ones dried in an oven at 90° C. These results are in accord with the general rule of colloid chemistry that gels which have been partially dehydrated have a lowered capacity for reimbibing water. This has sometimes been explained on the basis that during drying the salts and other dissolved substances are finally left in a concentrated form on the tissue surfaces, and thus affect imbibition in a different manner than when diffused in dilute form.

Effect of Thickness of Woody Tissue on Swelling.—MacDougal (4) showed that in thin sections, the coefficient of expansion is relatively high and solvation is attained quickly. Our results are in agreement; thus the chestnut wood blocks increased only 7 per cent in thickness while the thin sections (0.05 mm.) increased 20 per cent in width. Cells at or near the surface of a section or block may swell until the forces causing swelling are counter-balanced by the elastic force of the stretched cell wall. Cells on the interior of a block, in order to swell, must overcome not only the elastic forces of their own cell walls but also the restrictions of the surrounding cells; in blocks possessing considerable rigidity it can be readily understood that the inner cells must swell less than the outer cells and thus the coefficient of expansion is relatively low in thick pieces or blocks. In a block the outer layers would cause the greater amount of swelling. This is in accord with our results, which show that the greater part of the swelling of blocks took place in considerably shorter time than was necessary for the liquids to penetrate to the center of the blocks. (*To be continued.*)

STUDIES ON STRYCHNINE. III. THE EFFECTIVENESS OF SUCROSE, SACCHARIN AND DULCIN IN MASKING THE BITTERNESS OF STRYCHNINE.[*,1]

BY JUSTUS C. WARD, JAMES C. MUNCH,[2] H. J. SPENCER AND F. E. GARLOUGH.

Earlier papers in this series (1, 2) on the masking of the bitter taste of strychnine gave the results of experiments with a number of chemically unrelated substances. The results obtained with 1.5 and 10 per cent sucrose solutions suggested the desirability of continuing and extending studies with sucrose as well as with other sweetening agents.

In the series of tests reported in this communication, strychnine alkaloid, sulphate and hydrochloride were obtained from several manufacturers. Chemical tests showed the purity of the products used. The sucrose was a sample of factory-run beet sugar. Soluble saccharin and *p*-phenetylurea (dulcin) were obtained from commercial sources. The technic used in our previous studies was followed here. Five cc. of a solution of strychnine and 5 cc. of a solution of the sweetening agent

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* Scientific Section, Miami meeting, 1931.

1 Bureau of Biological Survey, U. S. Department of Agriculture.

2 Sharp and Dohme, Glen Olden, Penna.

were mixed. The mixture was retained in the mouth for exactly one minute and then ejected. Two principal observations were made: (1) the instant at which the bitter taste was first perceptible, and (2) the effect of the bitterness on the strength of the sweet taste. Two individuals (W and S) were consistently available, so most of the figures presented are averages of the results obtained by them. The other investigators made similar studies, but not in such detail. Their results are in substantial agreement. A considerable period of time was allowed to elapse between taste tests to avoid the possible potentiation of strychnine taste. In a series of studies on this point we have found that an interval of fifteen to thirty minutes between tastes is desirable.

The threshold taste limens of the sweetening agents and of the strychnine compounds were first determined. The concentration of the sweetening agent was then increased to 10, 20, 30, 40, 50, 60, 80 and 100 times its threshold, and the limen for the strychnine compound determined at each sweetness concentration. The experiments to determine the efficiency of each of the three sweetening agents in masking bitter taste were conducted as separate tests. The thresholds for the unmixed solutions are given in Table I. The values for the strychnine products are in substantial agreement with the average values obtained upon five individuals in the previous tests, and on forty students tested at Temple University during the last two years.

TABLE I.—THRESHOLD TASTE LIMENS OF HUMAN BEINGS.

Product.	Threshold Concentration. Millimols/Liter.	Gamma/5 Cc.
Sucrose	22.20	38,000
Saccharin	0.067	80
Dulcin	0.10	90
Strychnine as:		
Alkaloid	0.00347	5.8
Sulphate	0.00323	5.4
Hydrochloride	0.00323	5.4

TABLE II.—TASTE LIMENS FOR SUCROSE-STRYCHNINE TESTS.

Concentrations as millimols/liter.

Sucrose.	Strychnine in the Form of: Alkaloid.	Sulphate.	Hydrochloride.
0	0.00347	0.00323	0.00323
22	0.00333	0.00333	0.00323
222	0.00363	0.00348	0.00363
444	0.00572	0.00500	.....
667	0.00800	0.00616	0.00667
890	0.01142	0.01142	.....
1110	0.02000	0.02000	0.01820
1330	0.03330	0.02500	.....
1785	0.03330	0.03640	0.03640
2220	0.05000	0.05720	0.04440

The relative sweetness of saccharin and of dulcin in terms of sucrose has been studied by previous investigators, and divergent conclusions reached because of the variations in concentrations used as "isodulceous" standards. Saccharin has been reported to be 200 to 700 times as sweet as sucrose (3) and the threshold concentrations reported to be 10 mg. per liter. This would correspond to 50 gamma of saccharin in the 5-cc. portion tasted in our technic. We find the absolute quantity of saccharin detectable under our conditions to be 80 gamma. The threshold taste concentrations for sucrose reported in the literature vary from 5 mg. to 60 mg. in 5 cc., although the absolute quantities claimed to have been detected are 3 gamma and 58 gamma. In our experiments 38 mg. (38,000 gamma) proved to be the limiting quantity. This would mean that saccharin is 38,000/80 or 475 times as sweet as sucrose under our testing conditions.

Similarly, dulcin has been reported to be 70 to 350 times as sweet as sucrose, according to the sucrose concentration with which it was compared. In our tests the threshold was 90 gamma, or it was 38,000/90 or 420 times as sweet as sucrose. It is probable that the sample of dulcin used in these tests was purer than the samples used by other investigators.

The detailed findings of the taste limens for strychnine in the form of the alkaloid, the sulphate and the hydrochloride in sucrose solutions are given in Table II. The first line shows the concentration in millimols per liter in aqueous solution which just produced the characteristic strychnine bitterness taste. The succeeding figures show the thresholds with increasing concentrations of sucrose. A sucrose solution, ten times its threshold concentration, had only a slight masking action. A concentration twenty times the threshold shows a beginning protection, which increases rather irregularly with further increase in sucrose concentration. The highest concentrations of sucrose studied appeared to give somewhat greater masking effects on the strychnine sulphate solution than on the alkaloid and somewhat less on the hydrochloride. It is not felt, however, that these differences are necessarily significant. The solution of sucrose 100 times its threshold masked 14 to 18 times the threshold of strychnine and its salts.

TABLE III.—TASTE LIMENS FOR SACCHARIN-STRYCHNINE TESTS.

Concentrations as millimols/liter.

	Strychnine in the Form of:		
Saccharin.	Alkaloid.	Sulphate.	Hydrochloride.
0	0.00347	0.00323	0.00323
0.067	0.00333	0.00363	0.00351
0.667	0.00363	0.00400	0.00400
1.333	0.00400	0.00470	.....
2.000	0.00444	0.00616	0.00533
2.67	0.00500	0.00667	.....
3.33	0.00533	0.00800	0.00800
4.00	0.00572	0.01000	.....
5.33	0.00667	0.01600	0.01000
6.67	0.00800	0.02220	0.01600

The detailed findings of the taste limens for strychnine and its salts in saccharin solutions are given in Table III. Increasing concentrations of saccharin again proved effective in masking the bitterness of strychnine. A marked difference was found, however, in tests upon the alkaloid and upon the salts. The 100-fold saccharin solution masked somewhat more than two times the threshold of the alkaloid, but five times the concentration of strychnine as the hydrochloride and seven times the threshold as the sulphate. Our previous studies have shown the "common ion effect" produced by sodium salts (2), although we did not obtain as great an effect as this. It is also conceivable that these strong solutions through influences on the osmotic pressure may influence the rates of absorption.

Because of the limited solubility of dulcin, it was not possible to obtain so extensive a series of solutions. The detailed data are given in Table IV. In general, dulcin tends to resemble saccharin; that is, there is an increased masking effect with an increase in dulcin concentration, and the masking action is about twice as great against the salts as against the alkaloid. The strongest solution tested, which was twenty times the threshold for dulcin, protected against somewhat less than two times the threshold for the alkaloid and against somewhat more than three times the threshold for strychnine as the sulphate or hydrochloride.

TABLE IV.—TASTE LIMENS FOR DULCIN-STRYCHNINE TESTS.

Concentrations as millimols/liter.

Dulcin.	Strychnine in the Form of: Alkaloid.	Sulphate.	Hydrochloride.
0	0.00347	0.00323	0.00323
0.10	0.00333	0.00348	0.00348
1.00	0.00363	0.00421	0.00470
2.00	0.00572	0.01000	0.01000

TABLE V.—MASKING POWER OF SWEETENING AGENTS AGAINST STRYCHNINE.

Gm. required to mask 1 Gm. of strychnine.

Threshold Concentration of Strychnine.	Saccharin. Strychnine as: Alkaloid.	Sulphate.	Dulcin. Strychnine as: Alkaloid.	Sulphate.	Sucrose. Strychnine as: Alkaloid.	Sulphate.
1	14.3	13.2	16.1	15.5	6,790	6,790
10	131	120	147.5	128.5	62,350	63,400
20	240	204	188	188	79,100	90,500
30	326	234	...	...	74,000	110,050
40	382	290	...	...	79,600	79,500
50	452	260	...	...	57,000	57,000
60	502	288	...	...	40,700	54,400
80	578	240	...	...	54,350	50,000
100	522	216	...	...	45,500	39,800

For the practical application of these results, Table V has been prepared to show the number of grams of each sweetening agent required to mask the bitter taste of one Gm. of strychnine as alkaloid or as sulphate in various multiples of the threshold bitter taste. For example, the threshold concentration of strychnine having a bitter taste is 5.8 gamma per 5 cc., or 1.16 mg. per liter. If 1 Gm. of strychnine is dissolved in 862 liters of water to give a concentration of 1.16 mg. per liter (the threshold concentration recorded in Table V) it would be necessary to dissolve in this solution 14.3 Gm. of saccharin, 16.1 Gm. of dulcin or 6790 Gm. of sucrose to mask its bitter taste. As the concentration of strychnine is increased, the sweetening agents become relatively more effective. Saccharin appears to be the most efficient of these sweetening agents, but tremendous amounts are required for masking purposes.

As the concentration of strychnine in a sweetening agent was increased, loss in sweetness developed before any bitter taste could be detected. This was particularly noticed with strong concentrations. When solutions of sucrose fifty times the threshold, or stronger, were mixed with strychnine in any form, marked nausea was noted by one of us. This was observed even though the solution was almost tasteless from neutralization of the sweet and bitter tastes. When strychnine in any form was mixed with solutions of saccharin or of dulcin at concentrations fifty times their sweetness threshold or above, a peculiar metallic flavor resembling dental amalgam was observed.

Variation of individuals in speed of bitterness perception was again confirmed. One of us was able to identify the bitter taste of strychnine at a given concentration in two to ten seconds, another required fifteen to twenty seconds. The opposite condition prevailed for detecting sweet tastes, the "bitter-slow" being "sweet-fast." These differences in rate of apperception were not associated with any marked variation in absolute threshold taste limen, which is in accord with our previous findings (2).

CONCLUSIONS.

1. Sucrose, saccharin and dulcin mask the bitter taste of strychnine as the alkaloid, sulphate or hydrochloride.
2. Sucrose masks the bitterness of the alkaloid and the salts to about the same extent, a concentration one hundred times its sweetness threshold masking fourteen to eighteen times the strychnine threshold.
3. A solution of saccharin one hundred times its threshold masks somewhat more than two times the threshold of the alkaloid, and five to seven times the thresholds of the salts.
4. A solution of dulcin twenty times its threshold masks somewhat less than two times the threshold of strychnine alkaloid, and somewhat more than three times the thresholds of the salts.
5. Increasing concentrations of sweetening agents increased their masking effects.

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PHARMACOLOGICAL AND CHEMICAL STUDIES OF THE DIGITALIS GROUP. I. ADONIS, APOCYNUM AND CONVALLARIA.*

BY JAMES C. MUNCH[1] AND JOHN C. KRANTZ, JR.[2]

Although a very large number of papers have been published dealing with various phases of studies conducted upon digitalis, no systematized and concerted investigation of the pharmacology and chemistry of other members of the digitalis

* Preliminary reports at Miami meeting, 1931, and Washington meeting, 1934.

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