STUDIES ON STRYCHNINE.

2. The Action of Certain Substances in Masking the Taste of Strychnine.

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The threshold for detection of the bitter taste of strychnine in distilled water was 5.4 micrograms; when dissolved in Denver city water the threshold was found to be 6.5 micrograms. This discrepancy directed the authors' attention to the possibility of masking the bitter taste of strychnine by the addition of various salts, sugar and other substances. The method of determining the threshold limen was described in a previous communication (2).

A series of solutions of strychnine in the form of the alkaloid, the sulphate and the hydrochloride were prepared in various solvents. The minimum quantity of strychnine in terms of the alkaloid which was just detected is given in Table I.

TABLE I.—THRESHOLD TASTE LIMENS OF HUMANS FOR STRYCHNINE.

Results in Micrograms of Alkaloid.

Solvent.	Concentration per cent.	Strychnine in form of: Alkaloid.	Sulphate.	Hydrochloride.
Distilled Water	.....	5.6	5.4	5.8
City Water	.....	6.1	6.4	6.3
Sodium Bicarbonate	0.000,053	5.3	....	....
Alum	0.000,63	6.3	....	....
Borax	0.000,69	6.9	....	....
Sodium Chloride	0.6	7.1	7.0	8.5
Sodium Chloride	0.9	7.2	7.2	9.5
Saccharin	0.000,019	7.5	....	....
Sucrose	1.0	8.9	7.2	7.2
Sucrose	5.0	11.1	8.5	9.5
Sucrose	10.0	17.5	14.8	14.3
Yerba Santa	1.0	16.7	....	....
Yerba Santa	5.0	36.4	....	....

Using distilled water as a solvent the threshold of strychnine in the form of the sulphate was found to be 5.4 micrograms; as the alkaloid, 5.6 micrograms and as the hydrochloride, 5.8 micrograms. When dissolved in Denver city water the thresholds were found to be 6.4 micrograms, 6.1 micrograms and 6.3 micrograms, respectively. When dissolved in 0.6 and 0.9 per cent sodium chloride solutions the thresholds were increased to between 7.0 and 7.2 micrograms for strychnine in the form of the alkaloid or of the sulphate. For the hydrochloride the thresholds were greatly increased, namely, 8.5 and 9.5 micrograms. The authors believe that the greater masking action upon the hydrochloride resulted from the "common ion effect."

Greater masking was produced by one, five and ten per cent solutions of sucrose. The degree of masking was the greatest for the alkaloid; while it was less, and approximately the same for strychnine in the form of both the sulphate and the hydrochloride. The reason for this discrepancy is being investigated further.

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A second series of experiments was then undertaken to determine the degree of masking effect produced by the use of sodium bicarbonate, alum and other products with results given in Table I. Only strychnine alkaloid was used in this series of tests. It was found that sodium bicarbonate in an amount equal to one-half of the quantity of strychnine present somewhat intensified the bitter taste. The threshold was found to be 5.3 micrograms. A number of tests were conducted which demonstrated that this intensification was real and not apparent. The authors do not believe that this intensification is a function of the hydrogen-ion concentration, since borax masked rather than intensified the bitter taste. The greatest degree of masking was produced by an extract of yerba santa. With a five per cent solution of yerba santa the threshold quantity giving just detectable bitterness was increased to 36.4 micrograms, which is approximately seven times the threshold for strychnine in distilled water.

In a further study of the "common-ion effect" investigations were undertaken with strychnine in the form of the sulphate, hydrochloride and nitrate. Solutions were prepared using potassium, sodium, calcium and magnesium sulphate, hydrochloride and nitrate as solvents. For uniformity, concentrations of 0.1 per cent of the SO_3, Cl and NO_2 anions were prepared. These test solutions were tasted in accordance with the authors' technic to determine the threshold of bitter taste with the results given in Table II.

TABLE II.—THRESHOLD TASTE LIMENS OF HUMANS FOR STRYCHNINE AS SULPHATE IN SALINE SOLUTIONS.

Results in Micrograms of Alkaloid.

Anion.	Cation. Potassium.	Sodium.	Calcium.	Magnesium.
Sulphate	5.5	6.2	...	9.3
Chloride	5.6	5.5	6.3	10.0
Nitrate	5.6	5.9	7.2	9.7
Average:	5.6	5.9	6.8	9.7
Per cent of normal threshold	102	108	125	178

The average quantity detected in the potassium solutions and in the sodium solutions was 5.6 and 5.9 micrograms, respectively. These values are but slightly larger than the threshold in distilled water, indicating only 2 per cent and 8 per cent masking efficiency. Calcium chloride and nitrate solutions gave an average of 25 per cent in masking efficiency. Magnesium salts showed a materially greater efficiency. The average for the three salts tested was 9.7 micrograms, or a masking efficiency of 78 per cent, which proves that magnesium exerts the most potent masking action, followed in order by calcium, sodium and potassium.

When the threshold quantities were determined for the sulphates, chlorides and nitrates, no particular or significant differences were noted in the average values. It was concluded that the cations and not the anions were the significant factors in masking the taste of strychnine. The conclusions of Parker (1) regarding the lack of masking effect of potassium nitrate and of magnesium sulphate upon the bitter taste at the base of the tongue were not confirmed in our work.

In this series of experiments, attention was also directed to the time interval between application of the solution to the tongue and the first perception of a bitter taste. Tests were conducted upon three to five individuals. Individual sensitivity

of the taste buds was observed to vary considerably, although the minimum threshold could in no way be associated with sensitivity of any given area. In some individuals the bitter taste was first observed at the tip, in others at the base or sides of the tongue and on the soft palate. This difference in locus was not associated with differences in time of perception nor with differences in acuity. The interval in seconds between the application and the first detection of bitter taste ranged from five seconds to forty seconds. The average values ranged from twelve to twenty-eight seconds. The detailed report of these time intervals is given in Table III.

TABLE III.—SPEED OF RECOGNITION OF BITTER TASTE OF STRYCHNINE AS SULPHATE.

Time in Seconds.

Product.	Subject Number. 1	2	3	4	5
	10	20	30	10	15
Distilled Water					
Potassium:					
Sulphate	20	20	20	8	..
Chloride	15	25	25	..	..
Nitrate	5	35	20	..	..
Average	13	27	22	8	..
Sodium:					
Sulphate	5	12	40	10	4
Chloride	10	22	40	20	..
Nitrate	20	20	25	..	..
Average	12	18	35	15	4
Calcium:					
Chloride	5	20	10	..	..
Nitrate	30	25	30	..	..
Average	18	22	20	..	..
Magnesium:					
Sulphate	5	20	15	15	..
Chloride	30	22	10	..	..
Nitrate	10	20	15	..	..
Average	15	21	13	15	..
Average for cations	14	22	22	13	4

No significant effect in delaying the time when the bitter taste was first noted could be attributed to the anion or to the cation present. The correlation coefficient between the threshold quantity detected and the time until the bitter taste was first noted was found to be -0.03 ± 0.11. This demonstrates conclusively the lack of relationship between perception and rate of development of taste.

CONCLUSIONS.

1. The bitter taste of strychnine may be masked by a number of chemically unrelated substances: salts, sucrose and yerba santa extract.

2. The cation and not the anion is the significant factor in the masking action of salts.

3. Of the cations studied, the masking efficiency decreased in the order magnesium, calcium, sodium to potassium. The average masking action of magnesium salts was 78 per cent; calcium 25 per cent; sodium 8 per cent and potassium 2 per cent.

4. No consistent masking effect could be attributed to the anions studied.

5. Taste buds for detecting bitterness are located on the tip as well as on the base and sides of the tongue.

6. No relationship was found between acuity and speed of perception of the bitter taste of strychnine ($r = -0.03 \pm 0.11$).

7. The addition of sodium bicarbonate increases the bitterness of strychnine.

8. The addition of five per cent yerba santa extract increased the threshold of strychnine from its normal value of 5.4 micrograms to a value of 36.4, or approximately seven times the threshold concentration in distilled water. This was the most efficient masking action observed.

BIBLIOGRAPHY.

(1) G. H. Parker, "Smell, Taste and Allied Senses in the Vertebrates," page 154.

(2) J. C. Ward and J. C. Munch, "Studies on Strychnine. 1. The Relative Sensitivity of Certain Chemical and Physiological Tests," JOUR. A. PH. A., 19 (1930), 954.

LABORATORY NOTES ON ALCOHOL DETERMINATIONS.*

BY R. E. SCHOETZOW.

While, in general, the determination of alcohol in pharmaceutical preparations appears simple, yet difficulties do arise. At times, due to "bumping" and foaming on distillation, or to difficulties encountered in removing volatile substances, it appears that it is art, not science, that is required to make the determination. Some of our experiences may be of interest to others. Our methods, of course, are based on the method given in the tenth revision of the United States Pharmacopœia. This method is a general one. The Pharmacopœia gives appropriate steps to be taken, when some substances are present, but it seems to us that the next Pharmacopœia might with benefit give more detailed directions, perhaps a method for each class of products such as, spirits, liniments, tinctures, fluidextracts and collodions.

The first step in the Pharmacopœial Method is the distillation of the alcohol from the preparation, which has been diluted with an appropriate amount of water, but some mixtures such as Tincture Benzoin Compound, will "bump" violently on being distilled. They will "bump" so violently that the liquid may pass over into the condenser, or that the apparatus is broken.

We have tried all the ordinary remedies, such as glass beads, broken porcelain, etc., without much success. We do find, however, that if an alkali is added, not an excess since that would cause foaming, but an amount sufficient to combine with the resins present that, after allowing the mixture to stand for some time, the distillation will proceed quietly. We have found Milk of Magnesia with its low soluble alkalinity to be very suitable for use as an alkali.

Other preparations, like the Soap Liniments, or Fluidextract of Sarsaparilla, will foam to such an extent that the distillation cannot be performed. The addition of capryllic alcohol, will restrain the foaming, but not sufficiently. We have found, however, that calcium chloride added to slight excess will by precipitating or combining with the foam-producing constituents, enable the distillation to be carried out successfully.

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