(38) Henderson, *Am. J. Physiol.*, 86, 82 (1928).
(39) Magee and Southgate, *J. Physiol.*, 65, Proc. VII (1928).
(40) Whitehead, *Am. J. Physiol.*, 89, 253 (1929).
(41) von Oettingen, *Ibid.*, 90, 464 (1929).
(42) Salant and Brodman, *J. Pharmacol. and Exper. Therap.*, 37, 55 (1929).
(43) Frédericq, *Arch. de internat. Pharmacodyn. et de Thérapie*, 38, 438 (1930).
(44) Waucomont, *Ibid.*, 36, 285 (1930).
(45) Komant, *Naunyn-Schmiedeberg's Arch. f. exper. Path. u. Pharmakol.*, 163, 635 (1932).
(46) Salant and Parkins, *J. Pharmacol. and Exper. Therap.*, 45, 315 (1932).
(47) Rabbeno and Cisbani, *Arch. de internat. Pharmacodyn. et de Thérapie*, 43, 268 (1932).
(48) Epstein, *Ibid.*, 45, 251 (1933).
(49) Bernheim, *Am. J. Physiol.*, 104, 433 (1933).
(50) Hockett, *Newman and Thienes, Arch. de Pharmacodyn. et de Thérapie*, 46, 363 (1933).
(51) Hoyt, Patek and Thienes, *Ibid.*, 47, 228 (1934).
(52) Verzár and McDougall, "Absorption from the Intestine," Longman's, Green and Co., London (1936).
(53) Emerson, *Proc. Soc. Exper. Biol. and Med.*, 35, 376 (1936).
(54) Van Liere and Emerson, *Arch. de internat. Pharmacodyn. et de Thérapie*, 57, 45 (1937).
(55) Reynolds, *Physiol. Rev.*, 17, 304 (1937).
(56) Cheney, *Proc. Soc. Exper. Biol. and Med.*, 37, 572 (1937).
(57) Donatelli, *Arch. de internat. Pharmacodyn. et de Thérapie*, 58, 27 (1938).
(58) Singh, *J. Physiol.*, 94, 1, 322 (1938).
(59) Fischer, *J. Cellular and Comp. Physiol.*, 12, 85 (1938).
(60) Farmer, *Proc. Soc. Exper. Biol. and Med.*, 39, 204 (1938).
(61) McLachlin, *J. Pharmacol. and Exper. Therap.*, 64, 243 (1938).
(62) Lazarus, *J. Physiol.*, 93, Proc. 32-P (1938).
(63) Beard and Pizzolato, *J. Pharmacol. and Exper. Therap.*, 63, 306 (1938).
(64) Franklin and Maher-Loughnan, *J. Physiol.*, 94, 426 (1938).
(65) Eichler, Kaffee und Koffein, *Verlag von J. Springer*, Berlin, 58, 91 (1938).

A STUDY OF THE STABILITY OF ALKALOIDAL POISONS IN THE PRESENCE OF PRESERVATIVES.*

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The stability of alkaloids under various conditions has been the subject of many investigations. Among the more important of these are the very few studies undertaken in the interest of forensic medicine. These deal primarily with the fate of alkaloids when in contact with dead tissue, either preserved with one of several common preserving materials or allowed to decompose. The conditions of contact between the alkaloid and contaminating substance were generally controlled to simulate as nearly as possible one or more actual toxicological situations. One of the earliest investigations of this type carried out was by Tidy (1) who studied the durability of morphine sulfate when exposed to the processes of tissue decomposition within the human body. Little significant work on the stability of alkaloids under circumstances involving legal toxicological investigation has been done since. The recent studeis of Rising and Lynn (2, 3, 4, 5), while dealing in part with alkaloids, were principally on poisons of non-alkaloidal nature.

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In a time when technical evidence in prosecutions of criminal poisonings and litigation over the control of industrial poisoning is of particular importance, there should certainly be more data added to our knowledge concerning the stability of various poisons under all conditions of toxicological interest. Such information concerning alkaloidal poisons would be especially pertinent.

It is to aid in filling these gaps in the field that the following data are presented and their method of collection briefly outlined.

The principal object of the study to be described was to determine the destructive power, if any, on certain poisons, of several substances commonly used by coroners, morticians and others to preserve bodies which might contain a poison. Specimens of viscera are frequently preserved for analysis without thought or knowledge of what effect the preserving agent might have on any poison present. Further, little thought is given to possible interferences in the analytical work due to preservative used. A second object of the study was to investigate this factor.

Since forensic toxicology also involves unembalmed and otherwise unpreserved cadavers, it was deemed highly desirable to determine the stability of poisons in contact with decomposing tissue. Search for such information was made a third phase of the study.

Salts of morphine, codeine, narcotine, pilocarpine, sparteine and veratrine were the poisons chosen for investigation. Cavity fluid, 95 per cent ethyl alcohol, 4 per cent formaldehyde, 1 per cent mercuric chloride and 1 per cent arsenic trioxide were the preservatives selected. Stomachs from freshly killed sheep were made the carriers for the alkaloids.

The specimens for investigation were composed of either the alkaloidal salt in aqueous solution with or without a preservative, or the alkaloidal salt intimately mixed with minced sheep stomach and the mixture covered with a preservative or permitted to decompose. Each sample was contained in a four ounce, clear-glass, wide-mouth bottle closed with a cork and paraffin seal. Certain of the unpreserved samples were left unsealed. All of the unpreserved specimens were allowed to face the exigencies of weather outside. No precaution was taken to keep constant the temperature of those stored inside, nor was the sunlight shut out. Table I shows the conditions to which each alkaloidal salt was subjected.

In order to develop the data desired a complete set of specimens covering each of the conditions under investigation for each poison was analyzed at approximately three-month intervals Tables II to XIII give the results of these determinations.

The methods of extraction and estimation together with a discussion of interfering substances has been presented (6).

TABLE I.

No. of Condition.	Amt. of Alk. Salt.	Volume of Preservative.	Preservative.	Amt. of Sheep Stomach.	Storing Conditions.
1	100.0 mg.	50.0 cc.	Cavity fluid	50.0 Gm.	Sealed
2	100.0 mg.	50.0 cc.	95% alcohol	50.0 Gm.	Sealed
3	100.0 mg.	50.0 cc.	4% HCHO	50.0 Gm.	Sealed
4	100.0 mg.	50.0 cc.	1% As_2O_3	50.0 Gm.	Sealed
5	100.0 mg.	50.0 cc.	1% $HgCl_2$	50.0 Gm.	Sealed
6	100.0 mg.	none	none	50.0 Gm.	Sealed and outside of bldg.
7	100.0 mg.	none		50.0 Gm.	Unsealed and outside of bldg.
8	100.0 mg.	25.0 cc.	Cavity fluid	none	Sealed
9	100.0 mg.	25.0 cc.	95% alcohol	none	Sealed
10	100.0 mg.	25.0 cc.	4% HCHO	none	Sealed
11	100.0 mg.	25.0 cc.	1% As_2O_3	none	Sealed
12	100.0 mg.	25.0 cc.	1% $HgCl_2$	none	Sealed
13	100.0 mg.	25.0 cc.	none	none	Sealed

TABLE II.—STABILITY OF MORPHINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION.

Months.	Per Cent of Recovery.					
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.8	98.6	98.7	98.7	98.0	98.8
3	92.1	93.1	95.0	92.8	94.3	95.2
6	80.4	85.0	86.1	84.3	86.7	89.2
9	76.4	81.2	83.2	79.8	79.3	84.2
12	74.2	77.5	79.3	75.8	75.9	80.5
15	73.5	76.3	77.4	74.3	74.1	78.5
18	71.2	74.3	74.1	72.6	71.7	73.5
21	70.5	73.1	72.5	71.4	70.2	70.1
24	67.7	69.6	68.7	68.8	67.3	68.4

TABLE III.—STABILITY OF MORPHINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

Months.	Per Cent of Recovery.						
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	94.8	94.1	96.1	95.7	96.0	96.4	96.4
3	87.2	86.2	87.9	88.0	87.7	91.5	89.2
6	74.0	78.2	80.4	79.3	78.3	78.2	76.7
9	70.2	73.7	72.8	71.5	70.6	73.4	72.4
12	68.3	68.9	68.1	68.3	68.0	76.4	71.3
15	62.7	65.6	66.3	66.1	62.1	68.3	66.7
18	60.6	61.3	61.4	61.7	60.2	63.7	58.8
21	58.2	58.8	59.6	62.1	59.6	59.4	56.9
24	53.7	54.1	56.2	56.3	57.1	55.7	53.2

TABLE IV.—STABILITY OF CODEINE PHOSPHATE IN CONTACT WITH PRESERVATIVE SOLUTION.

Months.	Per Cent of Recovery.					
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.2	98.7	98.7	98.6	98.8	98.8
3	95.5	98.1	98.2	96.3	95.7	98.0
6	94.2	97.7	97.3	95.1	95.4	98.0
9	93.9	97.4	97.0	94.7	95.1	97.6
12	93.4	96.0	96.7	93.5	93.8	97.3
15	92.3	94.7	95.6	92.1	91.9	96.1
18	91.7	93.2	94.8	90.1	91.4	95.3
21	91.4	93.0	94.1	89.3	90.6	94.8
24	90.8	92.7	93.8	88.5	89.4	93.6

TABLE V.—STABILITY OF CODEINE PHOSPHATE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

Months.	Per Cent of Recovery.						
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	95.3	94.3	95.0	94.2	94.1	94.1	94.1
3	90.6	91.4	90.7	89.2	91.0	89.2	91.7
6	87.2	88.7	86.4	85.7	87.4	86.2	85.6
9	84.6	84.6	83.7	82.2	84.6	83.5	82.4
12	79.4	80.2	82.3	80.7	83.3	79.7	79.8
15	76.3	78.6	79.2	80.3	81.3	78.2	77.1
18	75.5	74.0	78.7	78.9	79.2	76.7	75.2
21	72.4	75.5	76.2	77.5	78.7	74.1	73.6
24	70.1	71.2	72.7	74.3	75.8	70.4	69.3

TABLE VI.—STABILITY OF NARCOTINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION.

	Per Cent of Recovery.					
Months.	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.9	98.6	98.7	98.6	98.8	98.7
3	94.4	92.1	94.2	93.1	91.5	96.2
6	87.4	87.2	92.2	90.8	90.2	95.4
9	84.2	85.2	91.0	87.1	88.2	94.2
12	81.0	82.7	89.7	86.4	85.5	93.5
15	77.2	79.3	87.1	84.7	84.0	91.9
18	74.2	77.6	86.2	83.0	82.3	91.5
21	92.5	75.5	84.5	81.2	80.8	91.0
24	71.9	74.0	82.6	78.8	78.7	89.7

TABLE VII.—STABILITY OF NARCOTINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

	Per Cent of Recovery.						
Months.	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	93.1	95.1	93.7	94.6	94.2	95.0	95.0
3	85.1	89.1	88.6	90.0	89.1	90.3	89.5
6	78.2	81.3	82.7	84.7	80.8	82.4	83.1
9	71.4	74.1	75.0	77.9	74.3	75.9	76.5
12	65.3	71.8	70.7	72.4	70.8	71.3	71.2
15	60.0	64.7	66.5	66.8	67.4	66.5	66.7
18	51.6	60.3	64.0	61.7	63.1	63.7	62.4
21	47.5	58.6	56.8	58.1	58.3	59.6	56.8
24	44.2	55.8	53.6	54.7	55.5	54.4	53.2

TABLE VIII.—STABILITY OF PILOCARPINE NITRATE IN CONTACT WITH PRESERVATIVE SOLUTION

	Per Cent of Recovery.					
Months.	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.6	98.7	98.9	98.8	98.1	98.8
3	93.2	94.1	96.1	95.7	96.0	95.4
6	88.0	98.6	92.7	94.0	92.3	91.1
9	85.6	86.2	89.2	93.8	89.4	87.4
12	83.4	83.2	88.5	93.3	87.7	85.1
15	82.2	82.7	87.1	91.2	86.2	84.2
18	80.2	81.8	84.4	90.1	86.0	83.3
21	77.7	80.5	82.1	89.5	83.0	82.0
24	76.5	78.7	81.6	87.2	81.0	81.3

TABLE IX.—STABILITY OF PILOCARPINE NITRATE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

	Per Cent of Recovery.						
Months.	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	93.3	94.0	94.5	93.7	95.1	94.2	94.2
3	85.2	87.6	87.5	88.2	87.7	88.3	87.4
6	77.3	76.8	78.4	80.1	76.9	77.1	76.2
9	67.5	68.6	72.4	73.6	71.3	72.7	70.6
12	62.4	64.7	66.7	68.0	65.6	64.8	67.2
15	58.7	59.1	62.8	61.7	61.1	60.3	62.4
18	53.8	55.3	57.3	57.4	57.6	56.8	55.3
21	47.6	53.8	54.6	54.1	54.7	52.5	52.1
24	43.2	49.7	51.2	52.8	50.9	49.4	51.7

TABLE X.—STABILITY OF SPARTEINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION.

Months.	Per Cent of Recovery. $HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.5	98.7	98.8	98.7	98.1	98.8
3	95.2	96.3	96.3	97.1	94.3	95.6
6	93.3	93.7	93.5	94.3	90.9	91.1
9	90.6	92.1	91.7	93.6	89.4	91.0
12	88.1	90.4	91.2	93.2	90.3	90.3
15	84.6	87.3	89.8	92.5	88.8	90.2
18	79.4	86.7	88.1	92.4	87.2	90.0
21	77.1	83.5	86.5	90.2	85.0	89.3
24	75.3	83.5	85.1	89.4	84.2	88.1

TABLE XI.—STABILITY OF SPARTEINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

Months.	Per Cent of Recovery. $HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	93.1	94.3	94.8	94.9	94.1	95.1	95.1
3	83.5	88.2	87.3	86.4	87.3	88.7	89.1
6	72.4	77.5	78.3	79.3	79.0	78.5	76.4
9	66.7	68.2	68.5	69.5	72.4	70.4	69.3
12	57.3	62.3	60.2	62.6	67.7	64.4	65.7
15	50.1	57.8	56.7	58.5	61.5	57.9	58.3
18	45.7	55.2	52.5	52.7	54.6	53.6	52.6
21	40.2	52.3	49.7	46.1	49.8	48.7	48.5
24	38.7	48.2	47.5	44.7	47.4	46.1	45.7

TABLE XII.—STABILITY OF VERATRINE HYDROCHLORIDE IN CONTACT WITH PRESERVATIVE SOLUTION.

Months.	Per Cent of Recovery. $HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.6	98.6	98.8	98.8	98.7	98.8
3	95.3	96.1	96.0	95.6	95.4	94.8
6	93.6	93.5	94.7	94.1	93.5	92.2
9	90.4	91.7	91.0	92.5	91.9	91.4
12	89.6	89.2	90.3	91.0	90.2	91.2
15	87.4	88.3	89.7	89.8	89.8	89.4
18	86.1	86.7	88.3	87.6	87.3	88.2
21	84.7	85.2	86.7	87.7	85.6	86.7
24	84.1	83.0	85.1	86.4	84.7	86.3

TABLE XIII.—STABILITY OF VERATRINE HYDROCHLORIDE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

Months.	Per Cent of Recovery. $HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	93.3	95.8	94.1	95.1	94.6	96.2	96.2
3	87.2	88.7	90.1	91.7	91.2	91.9	90.4
6	84.1	85.6	87.6	87.8	86.3	87.1	87.8
9	80.0	81.2	86.7	83.6	81.5	82.3	85.7
12	75.7	76.6	82.3	80.1	77.6	89.1	80.2
15	72.4	72.7	76.5	75.3	74.2	77.8	77.1
18	68.6	69.1	74.3	72.4	71.8	73.6	72.8
21	64.3	66.5	72.9	69.8	69.0	72.3	70.7
24	62.4	65.3	71.4	68.4	69.7	70.2	69.8

TABLE XIV.—BEST PRESERVATIVE FOR ALKALOIDAL SALT IN SOLUTION.

Alkaloidal Salt.	Preservative.	Per Cent of Alkaloidal Salt Remaining at End of 2 Years.
Morphine Sulfate	4% formaldehyde	69.6
Codeine Phosphate	1% arsenic trioxide	93.8
Narcotine Sulfate	1% arsenic trioxide	82.6
Pilocarpine Nitrate	95% alcohol	87.2
Sparteine Sulfate	95% alcohol	89.4
Veratrine Hydrochloride	95% alcohol	86.4

TABLE XV.—POOREST PRESERVATIVE FOR ALKALOIDAL SALT IN SOLUTION.

Alkaloidal Salt	Preservative.	Per Cent of Alkaloidal Salt Remaining at End of 2 Years.
Morphine Sulfate	Cavity fluid	67.3
Codeine Phosphate	95% alcohol	88.5
Narcotine Sulfate	1% mercuric chloride	71.9
Pilocarpine Nitrate	1% mercuric chloride	76.5
Sparteine Sulfate	1% mercuric chloride	75.3
Veratrine Hydrochloride	4% formaldehyde	83.0

TABLE XVI.—BEST PRESERVATIVE FOR ALKALOIDAL SALTS IN CONTACT WITH ANIMAL TISSUE.

Alkaloidal Salt.	Preservative.	Per Cent of Alkaloidal Remaining at End of 2 Years.
Morphine Sulfate	Cavity fluid	57.1
Codeine Phosphate	Cavity fluid	75.8
Narcotine Sulfate	4% formaldehyde	55.8
Pilocarpine Nitrate	95% alcohol	52.8
Sparteine Sulfate	4% formaldehyde	48.2
Veratrine Hydrochloride	1% arsenic trioxide	71.4

TABLE XVII.—POOREST PRESERVATIVE FOR ALKALOIDAL SALTS IN CONTACT WITH ANIMAL TISSUE.

Alkaloidal Salt.	Preservative.	Per Cent of Alkaloidal Remaining at End of 2 Years.
Morphine Sulfate	1% mercuric chloride	53.7
Codeine Phosphate	1% mercuric chloride	70.1
Narcotine Sulfate	1% mercuric chloride	44.2
Pilocarpine Nitrate	1% mercuric chloride	43.2
Sparteine Sulfate	1% mercuric chloride	38.7
Veratrine Hydrochloride	1% mercuric chloride	62.4

SUMMARY

Data are presented showing the stability of morphine sulfate, codeine phosphate, narcotine sulfate, pilocarpine nitrate, sparteine sulfate and veratrine hydrochloride under various toxicological conditions.

REFERENCES.

(1) Tidy, *Med. Times and Gaz.*, 1, 497 (1868); Witthaus and Becker, *Medical Jurisprudence, Forensic Medicine and Toxicology*, Vol. 4.

(2) Rising and Lynn, JOUR. A. PH. A., 20, 9 (1931).

(3) Rising and Lynn, *Ibid.*, 21, 138 (1932).

(4) Rising and Lynn, *Ibid.*, 21, 225 (1932).

(5) Rising and Lynn, *Ibid.*, 21, 334 (1932).

(6) Wilson and Rising, *Ibid.*, 28, 146 (1939).