

soaps, fats, edible oils and to a host of other commodities, give some idea of the extent of the field surveyed; and in addition, the theoretical side is by no means ignored. Unfortunately, as the author points out, the outbreak of World War II has made it practically impossible to obtain a complete coverage of adsorbents of foreign manufacture.

This bibliography, compiled by Mr. Deitz as research associate at the National Bureau of Standards, for the U. S. Cane Sugar Refiners, is a masterpiece of thorough, careful and painstaking labor, and an excellent example of how such a task should be undertaken and carried through. It has no rivals in its field, and is clearly indispensable to all chemists interested in solid adsorbents, a subject which, directly or indirectly, concerns a large proportion of the profession.

Its industrial sponsors are twelve of our leading sugar-refining corporations and four outstanding chemical firms. The research committee by whom it is published, and of which James M. Brown is chairman, is made up of one representative from the National Bureau of Standards (Bates) and eight from industry. The volume is dedicated to Frederick John Bates, chief of the Optics Division of the Polarimetry Section of the National Bureau of Standards and president of the International Commission for Uniform Methods of Sugar Analysis, under whose personal supervision and direction, and in whose section, the experimental work was carried out by a staff of research associates.

As explained by Director Lyman J. Briggs in a foreword, this publication constitutes the beginning

of a broad program of basic research in the study of sugar-refining problems.

After a "History of Commercial Adsorbents in Relation to the Sugar Refining Industry," including a descriptive list of some 165 solid adsorbents, there follow chapters on I, Adsorption of Gases and Vapors on Solid Adsorbents (196 pp.); II, Adsorption from Solutions on Solid Adsorbents (152 pp.); III, Thermal Effects in Adsorption Processes (26 pp.); IV, Theories of Adsorption (58 pp.); V, Refining of Sugars and Other Applications of Adsorbents (256 pp.); VI, General Information on Adsorbents and Special Methods of Investigation (80 pp.); and VII, Preparation of Carbon Adsorbents (38 pp.). These chapters give classified citations to 6,002 original articles. The abstract which follows every entry has been prepared from either the original article, *Chemical Abstracts*, *British Chemical Abstracts*, *Journal of the Society of Chemical Industry Abstracts*, *Journal of the Chemical Society Abstracts*, *Science Abstracts* or the *Chemisches Zentralblatt*, and the abstract reference follows each journal reference.

The sources of the bibliography are given, with a key to periodical abbreviations, an author index, a subject index and a list of the abbreviations used in the abstract text complete the volume. Attractive in appearance, with excellent paper and press work, fundamentally important in its content, with its subject-matter well organized, clearly and compactly presented, it will be a conspicuously valuable addition to any chemical library.

MARSTON TAYLOR BOGERT

COLUMBIA UNIVERSITY

SPECIAL ARTICLES

PREVENTION AND TREATMENT OF d-TUBOCURARINE POISONING

It is generally considered that the anticholinesterases, *e.g.*, physostigmine and neostigmine, antidote curare poisoning¹; in-appropriate doses they re-establish the electrical excitability of the motor nerves of curarized animals. It is also well known that both of these drugs in larger doses have a peripheral paralyzing action which differs from curare in that it is not annulled by potassium.² After administration of epinephrin to the partially curarized or curarized-neostigminized cat muscle (Rosenblueth, Lindsley and Morison) an indirect activation of the muscle caused a marked transitory increase in electric and mechanical responses. Following curare administration, epinephrin had a negligible effect on the response to di-

rect stimulation of the cat muscle.³ It has also been ascertained that the contractility of the frog gastrocnemius muscle is slightly increased by treatment with a 0.1 per cent. ephedrine solution (antioxidase?).⁴

The purpose of the study was to find methods by which paralysis and death of the intact animal by the newly introduced active curare principle, d-tubocurarine chloride, could be prevented.

EXPERIMENTAL

Rabbits were used for these experiments, and all injections were given into the marginal ear vein. d-tubocurarine chloride,^{5,6} dissolved in water with chlorobutanol added as a preservative, was used in

³ A. Rosenblueth, D. B. Lindsley and R. S. Morison, *Am. Jour. Physiol.*, 115: 53, 1936.

⁴ H. Kreitmair, *München. Med. Wchnschr.*, 74: 190, 1927.

⁵ The supply of d-tubocurarine chloride by Dr. H. Sid-

¹ J. Pál, *Centralbl. f. Physiol.*, 10: 18, 1900.

² A. Schweitzer and S. Wright, *Jour. Physiol.*, 89: 384, 1937.

the experiments. Each ml of this solution has the potency equivalent to 20 units of Standard Intocostarin.⁷

Table 1 summarizes the effects of anticholinesterases and long-acting sympathetic stimulants on the prevention of paralysis and death by d-tubocurarine. Small

TABLE 1

THE PREVENTION OF d-TUBOCURARINE POISONING BY ANTICHOLINESTERASES AND SYMPATHETIC STIMULANTS

No. of rabbits	d-tubocurarine in standard Intocostarin units per kg	Physostigmine mg per kg	Neostigmine mg per kg	Ephedrine mg per kg	Tyramine mg per kg	Results
8	1.5	Died in < 10 min.
2	2.0	Died in < 5 min.
2	1.5	2.5	...	Died in < 10 min.
2	1.5	2.5	Died in < 10 min.
2	1.5	0.1	No paralysis; survived.
2	1.5	...	0.05	No paralysis; all survived.
2	1.5	0.1	All died in < 15 min.
2	1.5	...	0.05	All died in < 15 min.
3	2.0	0.1	...	2.5	...	No paralysis; all survived.
3	2.0	...	0.05	2.5	...	No paralysis; all survived.
3	2.0	...	0.05	...	2.5	No paralysis; all survived.
3	2.0	0.1	2.5	No paralysis; all survived.
3	3.0	0.1	...	2.5	...	Two survived; one died.
2	3.0	...	0.05	...	2.5	One survived; one died.
6	1.5	0.25	All died in < 10 min.
4	1.5	...	0.15	All died in < 10 min.

doses of physostigmine and neostigmine prevented paralysis and death following doses of 1.5 units of d-tubocurarine; increase of the dose of the anticholinesterases alone did not antagonize toxic effects from increased doses of d-tubocurarine; in fact, they aggravated rather than alleviated the symptoms of curare poisoning. Ephedrine and tyramine up to toxic doses did not antidote d-tubocurarine at the lethal dose level of 1.5 units, whereas a combination of small doses of the anticholinesterases and ephedrine or tyramine antidoted 2 and even 3 units of d-tubocurarine.

In the second series of experiments, not included in this table, d-tubocurarine was given first and the antidote injected only when complete muscular paralysis had been produced. Six rabbits received 1.5 units of d-tubocurarine and three of these received 0.05 mg of neostigmine and the other three 0.10 mg of physostigmine. All these rabbits recovered from the paralysis within a few minutes.

ney Newcomer, of E. R. Squibb and Sons, N. Y., is gratefully acknowledged.

⁶ O. Wintersteiner and J. D. Dutcher, *SCIENCE*, 97: 467, 1943.

⁷ The dose of d-tubocurarine is expressed in terms of Standard Intocostarin units per kilogram body weight, and all other doses are expressed in terms of mg per kg of body weight.

Rabbits receiving 2.0 units of d-tubocurarine could not be resuscitated by any dose of the anticholinesterases, but three animals receiving this dose quickly recovered when treated with a mixture containing 2.5 mg ephedrine, 0.05 mg physostigmine and 0.025 mg of neostigmine.

COMMENT

Most studies on curare antidotes have been done with impure curare samples and by using muscle-nerve preparations. Such studies have not been altogether free of objection since it has been shown that all impure curare samples, including Intocostarin, possess cholinesterase-inhibitory activity. However, recent experiments have shown that chemically pure d-tubocurarine chloride is devoid of this inhibitory action.⁸ Cowan has shown that physostigmine-like compounds restored the response of partially curarized frog preparations to nerve stimulation with 100 shocks per second⁹; and Briscoe has shown in the nerve-muscle preparation of cats that large doses of physostigmine depressed the muscle twitch following nerve stimulation as did moderate doses of curare; both types of depression are antagonized by smaller doses of the other depressant.¹⁰ Similar observations were made in this laboratory.¹¹ We were able to show the limits of the antidotal action of physostigmine and neostigmine in the intact animal and the fact that the antidotal action of these compounds can not be increased by increasing their doses, but by the addition of ephedrine and tyramine and probably other similar compounds.

Wilson and Stoner have recently shown that the serum of myasthenia gravis patients, when tested on isolated nerve-muscle preparations, produced a block in nerve-muscle transmission, and since this blocking effect appeared to be due to an alcohol-soluble substance which may be responsible for the causation of myasthenia gravis,¹² a comparison between d-tubocurarine poisoning and myasthenia gravis is justified. A treatment of myasthenia gravis using anticholinesterases and long-acting sympathetic stimulants simultaneously in similar ratios as used in the above experiments is recommended for clinical trial.

THEODORE KOPPANYI

A. EARL VIVINO

DEPARTMENT OF PHARMACOLOGY
AND MATERIA MEDICA,
GEORGETOWN UNIVERSITY
SCHOOL OF MEDICINE

⁸ A. R. McIntyre and Rae E. King, *SCIENCE*, 97: 69, 1943.

⁹ S. L. Cowan, *Jour. Physiol.*, 93: 215, 1938.

¹⁰ G. Briscoe, *Jour. Physiol.*, 93: 194, 1938.

¹¹ F. W. Maurer, *Jour. Pharm. and Exp. Ther.*, 66: 25, 1939.

¹² A. Wilson and H. Berrington Stoner, *Quart. Jour. of Med.*, 13: 1, 1944.