

A SURVEY OF CHEMOTHERAPEUTIC RESEARCHES IN PROGRESS
IN THE UNITED STATES, AND THE PROMOTION OF COÖPERATION
BETWEEN ORGANIC CHEMISTS AND PHARMACOLOGISTS.

BY MARSTON TAYLOR BOGERT.*

In an endeavor to bring about more frequent and more intimate coöperation between organic chemists and pharmacologists, the following letter, accompanied by a suitable questionnaire sheet, was mailed to 793 scientists thought likely to be interested:

NATIONAL RESEARCH COUNCIL.

Division of Chemistry and Chemical Technology, Committee on Chemical Research
on Medicinal Substances.

COÖPERATION BETWEEN CHEMISTS AND PHARMACOLOGISTS.

With the steady progress of scientific investigation, the rôle of the fundamental science of chemistry in the service of the healing art becomes increasingly important and fascinating, and the time seems opportune to endeavor to bring about closer and more frequent coöperation between our chemists and our pharmacologists, in the belief that this will lead to the discovery of products of sufficient therapeutic promise to justify their further testing by clinicians and that thus some real contribution will be made to the alleviation of human suffering and the cure of the sick.

In our own country it happens frequently to-day that chemists who have prepared new compounds possessing therapeutic possibilities know not where to turn in order to have such products tested pharmacologically and, similarly, pharmacologists who have become interested in the physiological effects of a certain group of compounds have difficulty in finding a chemist willing and able to prepare for them the substances desired. This kind of coöperation has been far commoner in Europe than here and is one of the reasons why so many valuable modern remedies are of European origin.

Our Committee of the National Research Council will feel that it is performing a useful and patriotic service if it can function as a sort of clearing house to bring together these two groups of workers. The Committee has no thought of attempting to direct or interfere in any way with the research work of any one, but will endeavor to aid by supplying information likely to be of value and which the recipient can utilize as he thinks best. There is much of inspiration to be derived from the knowledge that our investigations are being watched with deep interest by others.

The purpose of the enclosed questionnaire, therefore, is threefold:

1. To secure a list of chemists and pharmacologists pursuing investigations in these fields, with the record of the researches they have under way.
2. To ascertain which of these investigators are interested in the type of coöperation proposed.
3. To learn what institutions have special facilities to offer in these fields, so that prospective students and research workers may be informed.

It is suggested that those coöperating in these investigations agree that if any of their products proves to be a useful drug, it shall be placed on the market under conditions which are acceptable to the Council of Pharmacy and Chemistry of the American Medical Association for inclusion in their list of new and non-official remedies. This will not prevent the patenting of the product, should the investigator so desire, but will require that the substance shall be given a trade name which indicates its true chemical nature, that the structural formula shall be given if known, that the literature used in circulating the remedy shall not contain any false, fraudulent or exaggerated claims as to its efficacy, and that the substance shall be sold only through the medium of reputable physicians and not marketed directly to the public.

* Chairman, Committee on Chemical Research on Medicinal Substances, Division of Chemistry and Chemical Technology, National Research Council.

If you believe that what we are trying to accomplish is really worth while, and that our Committee of the National Research Council is an appropriate body to undertake it, we hope that you will be good enough to assist us by supplying the information requested on the accompanying sheet.

MARSTON TAYLOR BOGERT, *Chairman.*

The replies to this appeal have been most encouraging and we now have records of over 300 scientists who are either already engaged in coöperation of the kind mentioned or are willing to engage in it. Even in the case of many not yet in a position to participate, we have received most cordial endorsement of the undertaking and expressions of their desire to coöperate whenever the opportunity occurs.

The information thus accumulated is enabling us to bring into mutually advantageous contact fellow workers in the same or closely related fields, and we believe that in thus functioning as a sort of clearing house for information of this kind we are performing a useful service. I will cite but a few illustrations of how this operates practically. Three communications recently passed through my hands within a few days of one another. Two of these were from distinguished medical men, one in the South and the other in the West. One of these gentlemen was interested in a certain group of dyestuffs in the treatment of diseases affecting the human kidneys; the other happened to be interested in the same group of dyestuffs for combating infections in the gall bladder; while the third communication was a manuscript from certain of our organic colleagues reporting investigations in this same group of dyes. The way was thus opened to apprise each of these gentlemen of the fact that the others were interested in the same field and the particular direction in which their investigations were proceeding. In another instance, two scientists who had begun the compilation of bibliographies covering the same ground, each ignorant of the other's undertaking, were brought together and a coöperative effort replaced what would otherwise have been duplication. Every week opportunities occur for service of this character, and they are likely to increase with the rapidly growing interest in this vitally important field of research, if we can maintain an efficient organization for handling the business. What such a central office can accomplish will be determined chiefly by the extent of the financial support accorded the undertaking. During the past year, the only aid received has been that from the National Research Council who supplied the necessary stationery and postage. It is obvious that the work cannot be continued unless provision is made at least for clerical assistance.

The researches reported are arranged alphabetically below and will suffice to give a conspectus of present activities in the study of medicinal products along chemical and pharmacological lines. It is appreciated that the record is incomplete but, so far as the writer knows, it is the only attempt which has been made within recent years to gather and classify information of this kind, and may be regarded as representing the situation on or about July 1, 1926.

The list is as follows:

1. Acetanilide with reference to its cardiac effects.
2. Acetophenones, amino derivatives, as drugs for raising blood pressure.
3. Acetylsalicylic acid (Aspirin).
4. Acids, organic, from toxic plants of the Rocky Mountain region.

5. Aconite and its bio-assay.
6. Acridines, especially those related to Proflavine, Acriflavine, Rivanol, etc.
7. Adrenaline (Adrenine or Suprarenine), its bio-assay and derivatives.
8. Alcohols, including those optically active and those containing the $-CCl_3$ group.
9. Alimentary functions, drugs influencing it.
10. Alkaloids, of aconite, death camas, lupine, larkspurs, veratrum, of the Rocky Mountain region, and the relation of the physiological effect of alkaloids to acid-base equilibrium and to other physico-chemical properties.
11. Amines and their derivatives, amines containing sulfur, amine oxides, sympathomimetic amines and their action on the circulation.
12. Anemia, experimental anemia and its treatment, synthetic drugs for anemia, the use of dyes in the treatment of pernicious anemia.
13. Anesthetics, general; including acetylene and ethylene, and the synthesis of new ones.
14. Anesthetics, local; benzyl compounds, derivatives of *p*-hydroxymethyl benzoic acid, the synthesis of new types.
15. Anthraquinone derivatives as substitutes for natural cathartics, chemical composition of natural anthraquinone drugs and their evaluation.
16. Antibodies, their purification in immune sera, pneumonia antibody solutions, protein-free diphtheria antitoxin.
17. Antimonials, organic antimonials, including antimonyl tartrates and antimony derivatives of gallic acid.
18. Antiseptics, Disinfectants and Germicides; their standardization, relation of their physiological effect to acid-base equilibrium and to other physico-chemical constants, intestinal antiseptics, urinary antiseptics, phenolic antiseptics (including derivatives of resorcinol, syringic acid, etc.), antiseptic dyes, chlorine and hypochlorite antiseptics (chloramines, etc.), and mercurial antiseptics.
19. Antispasmodics, especially the benzyl derivatives.
20. Antisyphilitics (Antilutics), the synthesis and pharmacological examination of new ones.
21. Arecoline, its synthesis and the synthesis of satisfactory substitutes.
22. Arsenicals, organic, acyclic and cyclic, for syphilis, neurosyphilis and trypanosomiasis, arsonic acids and arseno compounds, arspenamine (Salvarsan) types, arsino diacetone glucose, arsenic derivatives of thiazoles and of selenazoles.
23. Arthritis, chronic, synthetic remedies.
24. Autonomic and muscular drugs, their action on the cold-blooded heart.
25. Azo dyes, especially those prepared with H acid, for use as drugs.
26. Bacteria, the chemistry of specific substances of bacterial origin, the neutralization of bacterial toxins, chemical investigation of tubercle bacilli.
27. Barbituric acid and derivatives, including barbital (veronal) and phenobarbitals (luminals).
28. Benzaldehyde.
29. Benzoic acid and benzoates.
30. Bismuth, organic derivatives.
31. Bitter principles, especially the castelamarin of *Castela nicholsoni*, Hooker.
32. Blood, influence of drugs upon the volume of its flow, drugs for causing its coagulation and for raising or lowering its pressure.
33. Bromides.
34. Caffeine and its citrate, their cardiac effects.
35. Calomel, its pharmacology.
36. Camphor and its derivatives.
37. Camphoric acid and its esters.
38. Cannabis and its bio-assay.
39. Carbon tetrachloride and its pharmacology.
40. Cardiac effects and drugs, including electrocardiographic methods for cardiac and circulatory drugs, and heart tonics.
41. Carvacrol and its derivatives.

42. Cascara, its chemical standardization, and the connection between chemical constitution and physiological effects in the case of cascara and of related drugs.
43. Cathartics, their standardization, connection between cathartic action and fineness of subdivision, phenolphthalein cathartics.
44. Cevadine.
45. Chaulmoogric and Hydnocarpic acids, their synthesis and study, including homologs, derivatives and related compounds, chaulmoogra oil.
46. Chelidonine.
47. Chenopodium, especially western oils.
48. Chloramines, organic.
49. *Cicuta occidentalis* as a toxic agent.
50. Cinchonas.
51. Cinchophens (atophans), including quinazoline, thiazole and selenazole types, and arsenic derivatives.
52. Circulation, effect of aromatic amines and other drugs upon same.
53. Citrus products, citric acid and citrates.
54. Cocaine and the cocaine-tyramine antagonism.
55. Cod-liver oil, its chemical and pharmacological examination, and the isolation of its active principles.
56. Colloids and their rôle in pharmacology.
57. Colorimetric methods and standards for pharmaceuticals.
58. *Datura stramonium*.
59. Dehydration and dehydrogenation, by catalytic methods, for the preparation of synthetic drugs.
60. Delirifacients.
61. Diabetes, synthetic remedies, odd-carbon fatty acids (Intarvin) for diabetics.
62. Diamines and their use as hair-dyes.
63. *Digitalis*, its chemical, colorimetric and bio-assay, its leaves, stems and seeds, Kansas *digitalis*.
64. Diphenic acids.
65. Dyes, synthetic; as pharmaceuticals, fluorescent dyes, antiseptic dyes, mercury derivatives of dyes, azo dyes, triphenylmethane dyes, thiazole dyes, phthalein dyes, acridine dyes, the selective bacteriostatic properties of dyes, use of dyes in pernicious anemia, relation of colloidal state of dyes to inflammatory exudates and blood, excretion of dyes by the kidneys, food colors.
66. Edema and drugs for its prevention.
67. Embalming agents and their effects upon the determination of alkaloids and other toxic agents.
68. Emetin.
69. Emulsions, effects of ions and of alkaloids.
70. Endocrine secretions.
71. Enzymes of animals, yeasts, pepsin and its assay, trypsin, physico-chemical investigation of enzymes.
72. Epilepsy, drugs for its treatment.
73. Ergot and its bio-assay.
74. Essential oils, the therapeutic efficiency of natural and synthetic volatile oils upon pathogenic fungi.
75. Esters and their pharmacological investigation.
76. Ether and its pharmacological investigation.
77. Fluorenone carboxylic acid derivatives.
78. Fluorides, inorganic and organic.
79. Gallic acid and derivatives.
80. *Gaultheria Shallon*.
81. Genito-urinary infections and drugs for their treatment.
82. Germanium derivatives, especially the dioxide and sodium germanate.

83. Glandular products, animal glands of all kinds, ovarian products, extracts of corpus luteum, follicular fluid.
84. Glucosides, of the Rocky Mountain region, of *Triglochina maritima*, the castelin of *Castela Nicholsoni*, Hooker.
85. Gold, organic derivatives for the treatment of protozoal infections.
86. Guanidines, acyclic and cyclic.
87. Hormones, ovarian, follicular, suprarenal, of the thyroid, parathyroid, liver (hepar-mone), spleen, testicles, action of hormones on urogenital system.
88. Hydrazines, organic, and their study in connection with the production of anemia or of red cell regeneration.
89. Hydrocarbons and their use as general anesthetics, especially methylene, ethylene and propylene.
90. Hyoscyamus.
91. Hypnotics (soporifics), urethane types, barbituric acid derivatives.
92. Hypochlorites, of high test, for use as antiseptics.
93. Insulin, its chemical examination and purification, use of electrophoresis in its purification, its pharmacology and therapy.
94. Iodine and iodides, effects upon nitrogen metabolism, iodamines as antiseptics, iodo-toluidines.
95. Ipecac, its preparations and alkaloids.
96. Irritants, their chemical and pharmacological study.
97. Ketones, for use in medicine.
98. Lachrymators.
99. Lactic acids.
100. Lead, organic derivatives, especially lead tetraethyl.
101. Licorice; glycyrrhizin and other licorice products.
102. Liver, its hormones, liver extract, drugs acting upon the liver, substances in the liver which reduce blood pressure.
103. Logwood; hematoxylin and other logwood products as staining media.
104. Magnesium, organic derivatives, Grignard reactions in drug syntheses.
105. Malonic acid and ethylidene malonic esters.
106. Membrane potentials and their study with reference to the preferential osmotic effects exhibited by certain animal tissues.
107. Mercurials, organic mercury derivatives of dyes, of naphthalene and naphthoic acids, of substituted benzoic acids, mercurials for the treatment of syphilis, neurosyphilis and trypano-somiasis, excretion of mercury, micro-analytical methods for the determination of mercury in organic compounds.
108. Metabolism; drugs affecting human or animal metabolism in such manner that the effects can be estimated by the changes in the chemical composition of the blood, urine, body fluids or tissues; carbohydrate and fat metabolism and adjuvants thereto; drugs influencing total or nitrogen metabolism.
109. Metals, pharmaceuticals containing the heavy metals.
110. Micro-analysis, ultra balances and Pregl methods.
111. Molecules, their size and shape with reference to their physiological effects.
112. Mountain Ash berries.
113. Mustard Gas.
114. Mustard Oils.
115. Mydriatics and their bio-assay.
116. Naphthylamines as antispasmodics and blood pressors.
117. Narcotics.
118. Onium compounds, connection between their structure and physiological effects.
119. Optical isomers, optically active alcohols and drugs, resolution of racemic forms and physiological properties of optical isomers.
120. Drugs indigenous to the Pacific coast.
121. Pectin.
122. Peristalsis and drugs which influence it

123. Petroleum, medicinals obtainable therefrom.
124. Phenanthridones.
125. Phenols, substituted phenols, phenolic compounds from Rocky Mountain poisonous plants, from the woody aster and other plants, *n*-hexyl resorcinol (Caprokol) and related compounds, phenolic analogy of Position 3 in the glucose molecule, connection between constitution, physiological and bactericidal action.
126. Phenoxyacetic acid and derivatives.
127. Phthaleins, simple and substituted, their chemistry and pharmacology.
128. Piperidine and its methyl derivatives.
129. Pituitary liquor and its bio-assay, aqueous extracts of posterior lobe of cattle pituitary.
130. Podophyllum.
131. Pressor drugs, including amines, and the pressor principle of *Capsella bursa pastoris*.
132. Pyridine carboxylic acids and their amino esters.
133. Pyrrole derivatives and their function in the production of anemia or of red cell regeneration.
134. Quinazoline drugs.
135. Quinidine and its derivatives, and the cardiac action of quinidine sulfate.
136. Quinine and its derivatives, and the cardiac action of quinine.
137. Quinoline, hydroxyquinolines as antiseptics, amino ester of quinoline carboxylic acids.
138. Renal function and drugs affecting it.
139. Respiration and drugs affecting it.
140. Salicylic acid and derivatives.
141. Scopolamine.
142. Secretagogues, especially gastrin and secretin.
143. Selenium, organic derivatives, selenazoles, arsenic selenium organic compounds.
144. Septicemia and new synthetics for its treatment.
145. Silicotungstic acid as an alkaloidal reagent.
146. Solvents; new solvents for the extraction and purification of drugs.
147. Squill and its bio-assay.
148. *Strophanthus*, its chemistry and bio-assay, chemical study of strophanthin.
149. Styptics.
150. Sulfur compounds; aromatic sulfur compounds, thiotoluidines related to "Intramin," thiazoles; pharmacology of sulfur, sulfur dioxide and sulfites.
151. Terpenes and terpene derivatives.
152. Thioureas.
153. Thymol and derivatives.
154. Thyroxin and related compounds.
155. Tin, organic derivatives.
156. Toxics, from plants or animals.
157. Urea and derivatives.
158. *Veratrum California*, and veratrine.
159. Vesicants.
160. Vitamins, especially the antineuritic vitamin B, its isolation, identification, physiological effects, and study of its derivatives.
161. War gases.

Of course, some duplication and overlapping is unavoidable in such a compilation, but this has been held down as much as seemed consistent with the information sought to be conveyed.

Those who have not received copies of the circular letter and questionnaire, and who would like to take part in this coöperative undertaking, whether as chemists or as pharmacologists, will please communicate with Professor Marston T. Bogert, Havemeyer Hall, Columbia University, New York, N. Y.

A somewhat similar census, but covering pharmaceutical research, has just been completed by Professor H. V. Army of the Columbia University College of

Pharmacy, as chairman of the Conference on Pharmaceutical Research, and has appeared in the *JOUR. A. PH. A.*, Vol. 15, pp. 690-700 (Aug. 1925). It supplements in a very valuable way our own survey, and the two taken together give an excellent picture of present-day trends in these closely related fields of scientific investigation.

The cordiality of the response to our efforts may be gleaned from the following quotations from the questionnaires returned and gives some idea of the kind of coöperation offered in reply to the query concerning "special facilities:"

"A colony of albino rats (3000-4000) of known heredity and kept under constant environmental and dietary conditions."

"Complete equipments for chemical and animal work; representation at a large city hospital and opportunities of making clinical observations; skilled assistants; experienced coöperation with the Council of Pharmacy and Chemistry over several years."

"Well equipped pharmacological laboratory, well outfitted for chemical synthesis and for both animal experimentation and bacteriological or other forms of technic. Connection with clinicians of several hospitals for clinical trial. A number of graduate and medical students as assistants to pursue subsidiary investigations."

"Close coördination of the departments of biochemistry, pharmacology and physiology with the medical wards of the hospital."

"A laboratory equipped to do nearly any kind of pharmacological work."

"Opportunity to coöperate with a distinguished urologist in our college of medicine, through whose efforts some very important remedies have been introduced into urology."

"We have unlimited quantities of citrus fruit available and will furnish raw material or partly or completely purified derivatives for other investigators."

As to special fellowships and scholarships, the only ones reported were as follows:

University of Chicago.—The Seymour Coman Research Fellowship, of \$2000-\$3000 per annum, in chemistry applied to medicine.

Columbia University.—The Ferguson Fellowship, of \$1000 per annum, for investigation and research in synthetic drugs and medicines, awarded every other year.

A Research Assistantship for the current year, of \$1800, for the synthesis and investigation of organic compounds containing both arsenic and selenium.

Northwestern University.—About 12 fellowships for graduate students, with stipends up to \$1000-\$1200 per annum, for researches on the organic chemistry of arsenic and of mercury.

ORGANIC LABORATORIES,
COLUMBIA UNIVERSITY,
November 15, 1926.

Samuel L. Hilton presented two excellent papers in which he pointed out that great commercial advantage will be gained by pharmacists by taking up the study of filling and sterilization of ampuls and working with the physician in bringing about a better service for the patients and thereby he will also advance his own standing as a professional man.