

PHARMACEUTICAL RESEARCH AS A PUBLIC SERVICE.*

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The relation of research to the public is sometimes as difficult to define as it would be to predict what lad in school this year will be elected President of the United States in 1960. But even as the acorn gives promise of the mighty oak to those viewing that glans with the eye of faith, so may a piece of research of purely theoretical character hold within it infinite possibilities of practical achievement.

Who for instance among those who were delving thirty years since into the secret of the Hertzian waves could have imagined that a Marconi would arise to utilize them to send our thought pulsations over all the world. Again little did Nernst, the mildest of men, albeit now of malodorous memory as the instigator of the German poison gas attacks, think when he began in the cloistered quiet of his Göttingen laboratory, his study of the conductivity of rare metals that it would develop into that vast industry the manufacture of tungsten lamps. In the same way, any piece of pharmaceutical research, no matter how simple or fragmentary may lead the investigator or others into paths of infinite possibilities.

There are some who belittle pharmaceutical research; who think that pharmacy and especially American Pharmacy has accomplished little of merit; who seem to think that no investigation is worthy of the name "research" unless it proves the structure of a complex organic substance or presents a new plant which the investigator may have the pleasure of christening. For my part I have an entirely different idea of pharmaceutical research, I consider every paper reporting results of original work as a piece of research; I feel that an improved recipe, the result of real experimentation may be a more valuable piece of research than many a more ambitious effort; I deplore the fact that in these days of chasing after the nimble dollars so needed to pay for shelter, food, and raiment, the retail pharmacist seems less interested in making his contributions to pharmaceutical knowledge than did his predecessors of a quarter or a half century ago.

To turn to our scoffer of pharmaceutical research, permit me to point out to him some of the achievements along the line of pharmaceutical investigation. Let us take up some instances that are now classic. Let us think a moment of the pharmacist Scheele,¹ who in the laboratory of his apothecary shop isolated chlorine and oxygen and extracted from plants fruit acids and other principles. Let us ponder over the pharmacist Linné² who converted plant lore into the science of botany. Let us turn to the apothecary Sertürner³ obtaining from opium morphium the first discovered alkaloid. Let us give credit to the pharmacists Pelletiere and Caventou⁴ for their extraction of quinine, that tremendously valuable and widely used alkaloid. Let us sing the praises of the modern pharmaceutical teacher, Bourquelot⁵ and his pupils for their striking work on glucosides, enzymes, and glucosidal synthesis. Let us acknowledge the greatness of Tschirch,⁶ not only in pharmacognosy but also in phytochemistry.

"But," says the scoffer, "what has this to do with American pharmaceutical research?"

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This is in truth the *raison d'être* of this paper and were I to give you a truly comprehensive picture of what American pharmacy has contributed to human knowledge of human welfare I would tire you out before I was half through the illustrious list. So a few outstanding examples must suffice.

Let us take pepsin for example. This enzyme was first studied by the French pharmacists Boudault⁷ and Payen⁸ and after this the work was taken up by the American pharmacists Scheffer,⁹ Fairchild,¹⁰ and Webber¹¹ their work bringing relief to thousands of sufferers, and wealth to many.

Let us think of the pharmacists Duhamel and William Proctor, Jr.,¹² the pharmacist E. R. Squibb,¹³ the pharmacist Joseph P. Remington¹⁴ and the pharmacist C. Lewis Diehl¹⁵ bringing to fruition the work on percolation begun by the French pharmacists Boullay¹⁶ and Robiquet,¹⁷ so perfecting this method of drug extraction, that in Europe it is called the "American method of percolation" and by its use bringing into being that valuable, distinctly American and enormously used class of galenicals, fluid extracts. Then let us turn to compressed tablets. While these were originally devised by the Englishman Brookedon¹⁸ as a method of compressing black lead and while a few compressed tablets of medicaments drifted into this country from England in the fifties it was the American pharmacist Jacob Dunton who first manufactured tablets in a practically commercial way, thus starting the enormous tablet industry which the pharmacist justly views with some alarm as the machine-made cause of the decline of the old-fashioned art of dispensing pharmacy. The pharmaceutical development of the tablet industry is almost entirely American, and upon the roll of workers we find first the pharmacist Dunton, the pharmacists Wyeth, Fraser, Mulford and many others cited in Kebler's¹⁹ remarkable compilation of the literature of tablets. Let it be borne in mind, that the general use of tablets upon the continent of Europe, a matter occurring during the last twenty years, is largely due to the efforts of the pharmacists Burroughs and Wellcome, Americans, even though their manufacturing plants are established in England.

Then let us consider emulsions. It is true that the first pharmaceutical emulsions were apparently prepared by the English²⁰ and French²¹ pharmacists but we seldom stop to realize the work done in this line by the Americans, Procter and Maisch²², Diehl²³ and Painter.²⁴ Nor has the scientific side of emulsion making been neglected by the American pharmacists. There is no more interesting and important chapter of physical chemistry than the subject of emulsions and the best work in this line, as far as oil in water emulsions are concerned, is that done recently by the pharmacist Roon²⁵ and the pharmacist Crockett²⁶ under the guidance of their teacher Oesper.

"Ah!" but the critic may say, "what you cite is largely commercial." I am one who from sad experience knows that the establishing of the feasibility of a certain line of investigation is one thing and the putting of the idea into practical, workable, fool-proof shape is another. I also realize from actual experience that the latter work is oft-times more difficult than the former; that the conversion of a good idea into an accomplished commercial fact requires brains, patience, time and money. Hence I deny the allegation that research ceases to be research when it becomes commercially successful.

But if one insists upon pure research, the American pharmacist is ready with the proof of his ability in this direction. Let us first turn to the most altruistic work done in American pharmacy, the revising of the Pharmacopoeia. Here we have research performed as a labor of love by the members of the Revision Committee, "here a little, there a little" frequently done anonymously, always done with no thought in mind save the bettering of our national standard. Upon the roll of honor of pharmacopoeial research workers, we find first of all, William Procter, Jr.,²⁷ who in 1841 was Chairman of a Special Committee of the Philadelphia College of Pharmacy working upon the invitation of the, then entirely medical, Committee on Revision to assist the latter in its work on the pharmaceutical side, of the 1840 Pharmacopoeia. Then comes Chairman Charles Rice,²⁸ Sanskrit scholar, hospital apothecary and pharmaceutical historian; then let us pause to think of our unforgettable Joseph P. Remington²⁹ upon whose grave should be planted as symbols *Brunella vulgaris* (all heal) for his work, *Passiflora incarnata* for his sacrifices for pharmacy, and *Gnaphalium polycephalum* for "the promise of things hoped for"; then let us give credit to the present galaxy, LaWall,³⁰ Cook,³¹ Beringer,³² Raubenheimer³³ and Scoville.³⁴ Before closing the subject of pharmacopoeial research, permit me to suggest that the old idea that this type of work should be impersonal if not confidential, should be replaced with the newer thought that referees should be encouraged to publish their findings, not so much for their own credit as to give the publicity to the vast labor incurred in preparing our national standard and as explanatory of why certain pharmacopoeial changes are made.

Turning to the so-called "pure sciences" American pharmacy has the right to be proud of the contribution of its workers along these lines. In the field of plant research there was Maisch,³⁵ beloved teacher and American winner of the Hanbury medal; there is Rusby³⁶ the botanical explorer, introducer of South American drugs and the world authority on Bolivian flora, there is Kraemer³⁷ whose work on starches and on systematic classification of powdered drugs has brought him international fame; to say nothing of a score of the younger pharmacognosists whose work adorns the pages of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

Then think of the achievement of American pharmacists in research along the line of phytochemistry, beginning with the work of early eclectic practitioners,³⁸⁻³⁹ medical and pharmaceutical; the investigations of Maisch,³⁵ and Trimble⁴⁰ and their students at the Philadelphia College of Pharmacy; the brilliant work of Schlotterbeck⁴¹ on papaveraceous plants; the recent investigations of Viehoever, Ewing and Clevenger⁴² at the Bureau of Chemistry; the study of anthraquinone drugs by Beal;⁴³ leaving as the last word the achievements of our own Dr. F. B. Power⁴⁴ and his co-workers, our British cousins, at the Wellcome Research Laboratory.

If we turn to volatile oils, we find among the valuable contributions to our knowledge of this difficult line, the early American work of F. B. Power, the researches of Edward Kremers⁴⁵ and his pupils, culminating in the intensely practical application of Kremers' great knowledge in this subject in the reports on the commercial possibilities of oil production, that have emanated from the Wisconsin Pharmaceutical Experiment Station. And lastly in my enumeration

of the achievements of pharmaceutical research, in the field of colloidal chemistry, American Pharmacy not only has a master, but a pioneer, in the person of John Uri Lloyd,⁴⁶ an acknowledgment of this being recently made by Ostwald in his journal, *Kolloidchemische Beihefte* in which he gives credit to Professor Lloyd as one of the pioneers in colloidal chemistry and pays him the great compliment of publishing in full translations of the papers that Lloyd read before the American Pharmaceutical Association at its meetings in 1879, 1881, 1882, 1883, 1884 and 1885.

Do not the forty-six names cited above prove the case for American pharmacy? To enumerate more would be boresome and yet in closing the list I am aware that I am omitting the names of many of my friends, some of them present at this time, whose investigations merit recognition in the compilation of American pharmaceutical research. The scientific investigations on the part of American pharmacists is not merely a thing of the glorious past, but is in effect in this the living present (as attested to by the splendid collection of papers presented at this meeting) and will continue in the greater future that lies before us. Of this I am certain as I note the contributions of younger men in American Pharmacy which appear in the *JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION*, *The American Journal of Pharmacy*, the journals of the *American Chemical Society*; contributions which I have the pleasure of assembling in abstracted and permanent form in the *YEAR BOOK OF THE AMERICAN PHARMACEUTICAL ASSOCIATION*.

THE PROMISE OF THE FUTURE.

But what of the future of American Pharmaceutical Research? At times, like most of us who have passed across the half-century line, I feel discouraged and think that these times are not as rich as old times. But in more optimistic moments, I see that truth ever presses onward and to-day is not only better than yesterday but that to-morrow will be best of all. In the first place each year we live upon this globe each of us finds it more difficult to live as one apart. Combined work, a system of mutual helpfulness, is replacing the individualistic system of the days gone by and for us the most hopeful sign of the future is the fact that American Pharmacy now realizes that if it is to measure up in the future to achievements of the past, it must do this by means of coöperative work.

This is the spirit that now animates the Research Committee of the American Pharmaceutical Association. Organized in 1918 with one specific duty of recommending the annual award of grants from the A. Ph. A. Research Fund, we have now begun work toward bringing into one central national committee, the research workers of all of our national drug associations and I hope to see the idea so developed that the proposed national committee will eventually include representatives of the "papers and queries" committees of our several State associations.

That there is still an abundance of material in the field of pharmaceutical research is proven by the energetic efforts in this direction made by scientists without pharmaceutical training. The great Rockefeller Institute, the chemists of the great dyestuff plants, university professors of organic chemistry and teachers of pharmacology in medical schools are attaching pharmaceutical problems that we are neglecting and oft-times I am fearful lest pharmacy will sit idly by and let our more energetic confreres capture our pharmaca field.

Recently talking with a scientific friend he asked, "What is there to do in the field of pharmaceutical research?" My answer was substantially what I have given above as to what American Pharmacy has done in the past; what non-pharmaceutical scientists are now doing along the lines of pharmaceutical chemistry; and then I added a list of problems along the lines of pharmaceutical chemistry that are as yet unsolved. Among these I cited:

(a) The condition of the "available chlorine" in the pharmaceutical chlorinated solutions, thus taking up the work where Odling left off.

(b) The application of phytochemistry to the large number of southern plants that have been used in rural districts as medicines. Remarkable though the work of Power and his associates as well as that of other investigators have been, there are still a number that should be studied, among them *Parthenium hysterophorus*, *Cephalanthus occidentalis*, *Saururus cernuus* and *Sarracenia flava*.

(c) An investigation of the possibilities of establishing a systematic scheme of separation of plant principles in galenical preparations. Beal has shown the possibilities of such a plan of separations as far as anthraquinone drugs are concerned and my own commercial work shows that this plan could be extended to limits almost rivalling in usefulness, the well known tables of separation of the metals in inorganic analytic chemistry.

(d) Similar work in preparing a table of systematic separation of synthetic drugs continuing the excellent work already begun by Miller.⁴⁷

(e) Improved methods of alkaloidal assay and particularly careful investigations of the factors aiding or hindering alkaloidal extraction. There is much for us to learn about alkaloidal assays, as recent work of Beal has shown.

(f) Study of the possibilities of the accurate assay of minute quantities of alkaloids in galenicals such as the morphine content of paregoric. In this line, the possibilities of colorimetric assay have been scarcely touched.

(g) A thorough study of colorimetric assays as relates to pharmaceuticals with special reference to more exactitude in laying down the minutiae of a colorimetric test. My work up to the present time shows that the usual methods of colorimetric assay now in vogue are as inaccurate as it would be to run acidimetric assays with $n\text{KOH}$ V. S. made by dissolving 56 grammes of commercial potassium hydroxide in water enough to make 1 liter.

(h) Study of synthetic chemicals used in medicine and preparation of still better types of such medicinal chemicals.

The topics I have just suggested are but seven of one hundred lines which could keep one hundred investigators busy for years along the lines of pharmaceutical chemistry and then let us recall that pharmaceutical chemistry is but a small part of research. Let us realize the unsolved problems of galenical pharmacy and let us think of the vast possibilities offered in the field of pharmaceutical botany and pharmacognosy. If one doubts the latter statement let him study the list of subjects needing research submitted at the last meeting of the American Conference of Pharmaceutical Faculties by Chairman Albert Schneider of the Conference Committee on Research. This list includes twenty-seven topics embracing such diversified subjects as the micro-analysis of drugs, seed germination tests of

drug plants, composition of dusting powders and face powders, microbial contaminants of pharmaceuticals, drug plant cultivation and even such intensely practical subjects as drug store sanitation and diseases of soda fountain syrups.

The enumeration of pharmaceutical achievement given above should be the earnest of what we will do in the future and while we rejoice in the interest shown in pharmaceutical problems by our friends in other lines, we must bestir ourselves and do our share of the work which is rightly our heritage. We teachers should inspire our pupils with the spirit of research; we workers of the every day world should publish our findings, however small they may seem, even as our predecessors did, we organization men should see that our associations encourage research. Then and only then will pharmacy maintain its right to be called not merely a trade, not merely an art, but also a profession in the truest sense of the term.

In conclusion let me take the liberty of appending to this paper a partial bibliography containing references to the papers published by the investigators cited above as those of which American Pharmacy is proud. Only those papers which I consider as among the best efforts of the authors are given in the bibliography as the preparation of a complete list would have consumed much time and would be tiresome to my hearers.

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THE NATIONAL RESEARCH COUNCIL.*

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The National Research Council is a novel institution, something new in our national life; a thing full of the very greatest promise for scientific research and I sincerely hope that there may be coming out of the discussion here some means by which the American Pharmaceutical Association may be brought into a position to engage in research work in connection with our organization.

I will sketch briefly over the history of the Council. Doubtless many of you are more or less familiar with it, but every day those connected directly with its operation find that something new comes up. I think it would be wise therefore if I did not assume, on your part, too much knowledge concerning this organization. It is one of the "war babies" and came into existence through the necessity of our Country meeting the highly organized scientific research work of our recent enemy. The Council is not so recent, however, in one sense. During the Civil War the Government of this country felt the need of advice from scientific people and President Lincoln called into existence the National Academy of Science. The Academy was to advise the Government in problems of science and art, and has served very effectively during and since the Civil War. I recall, for instance, the Forest Service which was established through the advice of this scientific body.

When it seemed that we were being drawn into the world war, President Wilson called upon the National Academy to prepare itself for service again, and on this occasion the men in charge felt that it would be most advisable to enlarge in their connections. The Academy is not a large body and has grown to be a sort of honorary society, and was therefore not of sufficient size to accomplish the purpose which the President wished to carry out. Accordingly the Academy advised that there be created an auxiliary body to be called the National Research Council. The President accepted this advice and asked the Academy to organize such a body. This was done by the most direct means possible. The Academy called scientific men of prominence from all parts of the country to Washington and put them to work or allowed them to remain where they were in

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