this impression. A second important factor to be considered is the increase of toxicity due to increase in lipoid solubility as one goes higher in this homologous series. Toxicity when the material is injected into the blood stream is no doubt greatly dependent upon the latter factor, which here may become more important than the protein coagulating factor. Macht has presented data for the iso-alcohols (isopropyl, isobutyl, and isoamyl) in respect to toxicity when injected into the blood stream, the relative toxicities observed being 1 : 2.75 : 9.6 which yield the ratios 1 : 3.4 : 14 when expressed as moles.

A natural question that now arises is this: To what extent will this semi-quantitative generalization hold among the higher homologues? This is to be answered experimentally, although one may predict that the higher homologues which approach closer and closer to the hydrocarbons in their physical properties, will be so slightly soluble in water that they may not admit of being subjected to a legitimate test. This limit will no doubt be found between the range C_6–C_{10}.

The above "rule of three" is of interest especially because Traube[1] has shown that such a relation exists between the relative surface tensions of aqueous solutions of these alcohols, and, what is still more important, he has also shown that hypnotic action of certain classes of compounds, particularly the urethanes, obeys this same numerical rule.

Although within a given homologous series of alcohols both toxicity and hypnotic action increase regularly with increasing molecular weight, the opposite may be found true in comparing alcohols falling in different homologous series. Thus the normal primary, secondary, iso, and tertiary alcohols, respectively, *decrease* in toxicity as we go from the straight chain to the branched molecule. On the other hand, hypnotic action fortunately *increases* in the same order.

The present treatment of the subject, directed toward the simplest class of alcohols, and only to the lower members in this class, is intended simply as an elementary basis for later work.

CONTRIBUTION NO. 2,
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PARKE, DAVIS & CO.

PHARMACEUTICAL RESEARCH.*

BY GEORGE M. BERINGER.

The most ancient records available show that from time immemorial the progressive peoples of each period recognized that the preparation and dispensing of medicines was an important vocation to be entrusted only to those specially trained and educated to perform such duty to society. In ancient Egypt, the priests of Isis alone compounded and dispensed the prescriptions of the physician priests. The Israelites evidently held the apothecaries in high esteem as the Biblical records contain a number of references to them and their work. The holy anointing oil and the incense were both directed to be "compounded after the art of the apothecary." To Eleazar of the priesthood, the son of Aaron, were entrusted the services and duties at that time performed by the apothecary.

[1] Pflügers *Arch. Physiol.*, 105, 559.

* Address delivered before the New York Branch of the American Pharmaceutical Association, January 10, 1921.

So we as pharmacists can take just pride in that we are engaged in a most ancient and honored calling.

The student of the history of pharmacy is soon brought to realize that pharmacy has played no small part in the world's progress and that pharmacists have made many valuable contributions to the knowledge of materia medica, botany, chemistry and allied sciences and that some of these, of the greatest benefit to mankind, are constantly employed in the professions and industries. He likewise becomes painfully aware of the fact that ofttimes the credit is given to, or taken by, other branches of science. The writers of Encyclopoedia articles and similar works of reference are especially faulty in their failure to recognize the importance of the contributions of the unobtrusive workers in science despite the services of incalculable value that these have rendered to mankind. To most of these authors and compilers the activities of the warrior, the statesman, or politician, so often destructive of the world's progress, and even of the novelist, seem to be of paramount importance for perpetuation. Since the influence of pharmacy has been quite commonly overlooked by these general historians, it remains as one of the duties of pharmacists to see that the scattered data and facts concerning the lives and contributions of pharmacists are collected, preserved and published so that it shall be established beyond peradventure as to whom credit is justly due.

Throughout the medieval period, and especially that portion which is referred to as the age of the alchemist, the contributions to the sciences were largely made by the investigators in medicine and the apothecaries who were aiming to improve the methods of preparing their remedies and of discovering new substances of therapeutic value.

Among the English-speaking nations there has been unfortunately a too apparent disposition to disparage the work of the apothecaries, and during the fourteenth century they were commonly referred to as the "physician's cooks," and even in comparatively recent times, as the "physician's handmaids." It is evident to the student of history that a relatively small percentage of medical practitioners have been engaged in actual research work, and that a goodly number of pharmacists have carried on research in behalf of pharmacy that will compare favorably with any that has emanated from the medical branch.

I cannot at this time delve too deeply into the debt of the world to pharmacy, for I conceive that a discussion of that topic would occupy the entire evening and preclude the consideration of the subject that has been assigned for this time. Nevertheless, it has such a close association with the subject of research that I cannot refrain from giving a few illustrations that must serve the purpose of the present occasion.

The study of the sciences undertaken by Davy as an apprentice to a surgeon-apothecary no doubt gave him his first insight into chemistry and determined the bent of his mind toward chemical research. The results of these investigations won for him reward and undying fame as the discoverer of a number of the important chemical elements.

That peerless, indefatigable experimenter and ideal research worker, Karl Wilhelm Scheele, is constantly referred to as the "great Swedish chemist," and his name is scarcely ever associated with pharmacy. Yet he studied pharmacy, and for the major part of his comparatively short life depended upon this calling

for his livelihood. During the last eleven years of his life, he owned and managed a pharmacy, and was supported thereby while carrying on some of his most successful experiments. His activities and investigations cover a very wide range of topics of the utmost importance to mankind. The discoveries of chlorine; barium; manganese and the investigations of its applications to the glass industry; of tartaric acid; arseniureted hydrogen; his studies of the cyanides such as Prussian blue and hydrocyanic acid; and of the composition of the atmosphere, are but some of the contributions of this pharmacist to the world's progress. These can be traced largely to contact with the wares and the problems of his chosen vocation. Who is prepared to estimate the world's indebtedness to this studious, observing and painstaking worker, many of whose discoveries are still in daily application in our industries?

Klaproth is another apothecary whose early investigations of the composition of pitchblende led him to the discovery of uranium, and this was the initial step that has led up to the discovery of that remarkable group, the radio-active elements.

In the field of organic chemistry important contributions to our knowledge can be traced to pharmacists and numerous are the illustrations available. I must here content myself with only citing for your attention the fundamental work of Sertürner and of Pelletier and Caventou upon the alkaloids. The galaxy of brilliant investigations emanating from pharmacists who have engaged in research in this interesting domain covers nearly every civilized nation, and the results have been of inestimable value in the practice of medicine.

Research is best defined as a careful search for the truth, and so it can be safely asserted—that no authoritative work is accomplished, no scientific investigation or discovery is made, and no theory that is sound is propounded that is not based upon research.

Research is generally subdivided into that which is "pure" and that which is "applied." The distinction is made upon the basis of the latter being undertaken with a specific need in view and that the results will be applicable to the solving of some industrial and commercial problem, usually of monetary advantage. Practical application is commonly the reason that actuates the establishing of research departments in most of our large industries. No one can take exception to this as, eventually, the discoveries and inventions made are disseminated to the advantage of all. Yet there is a feeling held by the real scientists that personal interests should not blind one to the obligation of true citizenship, to contribute his full share toward public welfare and scientific progress.

While the truly scientific and enthusiastic research worker engages in "pure research," possibly with the thought of clearing up some abstruse question that, although advancing our sum of human knowledge, may at the time have no apparent practical application, it happens ofttimes that his work and discoveries become of exceedingly great value and unexpected important application. The discoverer of the Herzian waves had no thought of the utilitarian value of his discovery and the later application thereof to wireless telegraphy. The investigation of our own Prof. John Uri Lloyd on the subject of precipitates in fluidextracts was undertaken because the question was deemed a pharmaceutical problem of the time demanding attention, and his publications were then considered simply from a pharmaceutical view-point. We are now proud of the association and the

distinction awarded these by Dr. Wolfgang Ostwald as fundamental and important early studies in colloidal chemistry and claim the credit for priority of publication in the Proceedings of the American Pharmaceutical Association.

Recently we had the pleasure of listening to a lecture by Prof. Edward Kremers of the University of Wisconsin, in which he detailed the investigations carried on for upwards of twenty-five years on certain American species of Monarda. His studies of the aromatic principles and the other constituents of these plants constitute an elaborate piece of pharmaceutical research that is destined to become a classic contribution to phyto-chemistry. While this may be viewed as a pure scientific investigation, whose main value will be as a pioneer and in its suggestion for similar investigations directed to other groups of plants, it has cleared up a number of points relating to the source, composition and production of some of the important aromatic plant constituents, and I predict that it will prove of material assistance and pecuniary value to the industries engaged in preparing these on a commercial scale.

The history of Cinchona cultivation is an interesting narrative of scientific research applied to every phase of the subject. The selection of the species and varieties of Cinchona yielding alkaloids; the study of the alkaloidal content of the different barks; the problems of soil, climate, and altitude, and their influence upon the character and percentage of alkaloidal content of the bark; the production of varieties yielding the largest percentage of quinine; the study of the localization of the alkaloids in different parts of the plant, the effect of climate, season, etc., upon these, and their transformation from amorphous to the crystalline state during the development of their plant organs; the discovery of the value of partial stripping, the best time for this operation, and the renewal of the bark by mossing; the modern methods of marketing the bark and alkaloids; the improved process of manufacturing the alkaloids in a high degree of purity; these are some of the problems that had to be worked out scientifically and the value of the results from either a commercial or a humanitarian view-point is beyond calculation. It is a gigantic example of practical applied scientific research. Notwithstanding all that has been accomplished by the study and scientific investigation of the Cinchonas, the subject is not exhausted. The paper by Howard and Chick on "Some Recent Samples of Grey Cinchona Bark"[1] demonstrates the necessity for a thorough reinvestigation of the grey cinchonas of Peru to determine positively by newly collected authentic specimens the species yielding the bark containing the high percentage of cinchonine reported, and whether this was due to the altitude at which the trees grew. This paper presents the possibilities for duplicating the cultivation of the Ledgeriana variety of *Cinchona Calisaya* in which quinine almost alone is present to a high percentage by the cultivation of a selected Cinchona of the grey bark group for the production of cinchonine.

In addition to the classification of research as "pure" and "applied," I would advocate a further subdivision as especially applicable to pharmacy; namely, major and minor investigations in both pure and applied research. Every apothe-

[1] *The Pharmaceutical Journal and Pharmacist*, July 24, 1920. Reprinted in *The American Journal of Pharmacy*, October 1920.

cary has opportunities from time to time to note improvements in formulas, methods of manipulation and niceties in compounding, what our friend Thomas McElhenie calls "wrinkles." These observations, although they may appear individually as comparatively insignificant, yet, if they be but suggestions for improvement, in the aggregate they will make toward a substantial advancement in the art of pharmacy. As a part of his collegiate training and to inculcate the faculty of observation and deduction, every student in pharmacy should have assigned some topic of pharmaceutic interest for special study, investigation and report, even though these subjects be but very elementary problems in pharmaceutic research.

Notable events have a marked influence in stimulating the character of research and the results achieved. The foundation of a school of pharmacy in America for the systematic education of pharmacists had a decisive effect in the development of such characters as Daniel B. Smith and Dr. George B. Wood, and this event was the stimulus to which may be attributed the preparation of that masterwork, the United States Dispensatory.

The introduction of the process of displacement made the subject of percolation and the preparation of the various classes of galenicals by this method, topics demanding extensive experimentation, and as a result we have recorded the classical investigations of Procter, Squibb, Diehl, Lloyd and others as contributions of great practical worth to pharmacy.

The events of the Civil War presented new opportunities for pharmaceutical research and the further development of such pharmacists as Maisch and Squibb. The southern States were compelled to rely much upon their natural resources. To meet this necessity Dr. Francis P. Porcher wrote his book on "The Resources of the Southern Fields and Forests, Medical, Economical and Agricultural," and this work is still frequently referred to as an authority. Dr. Charles Mohr, a southern pharmacist, likewise made many valuable scientific investigations of the natural products and resources of several of the southern States and his contributions to our literature are of practical value to medicine and pharmacy as well as to botany.

The organizers of the American Pharmaceutical Association in 1852 had in mind as main purposes, the improvement of the quality of drugs imported and the better education and protection of pharmacists. The objects announced suggested research, and this organization has ever since been the nucleus around which has been gathered the principal research workers in pharmacy, and its publications have been the mediums for disseminating the far-reaching results.

The great World War forcefully demonstrated the necessity for coördinated scientific research, applicable to the industries as well as to modern warfare. As a war measure, the National Research Council was organized in 1916 primarily for the purpose of stimulating and coördinating research on war problems. In 1918, by executive order of the President of the United States, this was reorganized as a permanent body, and the announcement was officially made that "its essential purpose is the promotion of scientific research and of the application and dissemination of scientific knowledge for the benefit of the national strength and well being." It is now chartered as the National Academy of Science. Despite the far-reaching possibilities and effects of pharmaceutical research and the im-

portance to mankind of a thorough knowledge of all remedial substances, and that pharmacists are the logical persons for the carrying on of such investigations, it remains a fact that so far pharmacy has not been recognized in the plans of the National Research Council, and that there is no evidence that pharmaceutical research is to be given any encouragement.

The thorough study of the numerous medicinal products supplied by pharmacists, and the processes employed in securing and preparing medicines will open up boundless fields for study with innumerable research problems, the possibilities of which and the value thereof to mankind cannot be estimated. Suffice it to proclaim that "the sum of scientific knowledge for the benefit of the national strength and well being" acquired thereby, will hold no secondary place.

The practical issue at this time and the important question before American pharmacists is how pharmaceutical research can be systematized and organized so that the importance of the coöperation of this branch of scientific investigation will be fully recognized, and an appropriate place in the scheme of the National Research Council be assigned to pharmacy.

The field open to pharmaceutical research is now not more restricted than formerly, but on the contrary is continually expanding and it is but a fair inference to assert that the value of the past investigations can be more than duplicated by those of the future. There is no lack of opportunity for pharmacists to engage in study and research, and the present generation should not let the imputation rest that there is now less desire. An observing writer has recently stated that pharmacy has never been more in need of research upon strictly pharmaceutical problems than at the present time.

There is scarcely a topic associated with the practice of pharmacy on which the available knowledge can be said to be complete. Innumerable are the questions requiring further study arising from the natural kingdoms and all quarters of the globe from which medicines are obtained. The methods and processes employed in pharmacy are not yet sufficiently understood, and despite all the work done on percolation, and all that has been written thereon, the last word has not yet been spoken. The value of the various solvents and their appropriate use in the extraction of different drugs is still an open question meriting further extensive investigations involving in each drug a study of its active constituents and their behavior to solvents *in situ* and after extraction. The revisions of our national standards, the Pharmacopoeia and National Formulary, call for continuous research along many lines. The tests and assay processes are constantly undergoing revision and must be considered on the whole as tentative and requiring much further review and improvement. The botanical source of some of the official vegetable drugs is still undetermined even though these may have been in use for many generations. The proper time for collection of vegetable drugs and the approved methods for their preservation; drug plant cultivation, the effect of soil, climate conditions, altitude, etc.; the percentage of active constituents and the study of the localization of these in the respective plants remain fertile fields for study. The voluminous and excellent work of such men as Tschirch, Oesterle, Moeller, Dragendorff, Flückiger, Koch, Zörnig, Hanbury, Holmes, Greenish, Collin, Maisch, Kraemer, Bastin and Trimble in developing the knowledge of pharmacognosy and plant chemistry, but serves to demonstrate

the vastness of the field yet unexplored. The enzymes; the ferments; the vitamines; the animal organ drugs, such as the endocrine gland products; the synthetic chemicals; as well as the new remedies that are being continually introduced into medical practice, present an endless variety of topics demanding the attention and investigation of pharmacists. The textbooks, and even the legally recognized official standards, contain statements that are in need of verification, and it is an imperative duty that these be critically examined and that each erroneous or misleading statement be either corrected or eliminated.

In citing these various lines of research open to pharmacy, it must be understood that I have offered these merely as examples and not as an enumeration of the extensive field of exploration available for the application of systematic pharmaceutical research.

The need is that pharmacists themselves, as well as scientists engaged in other fields of research, should have a correct view of the possibilities and the comprehensiveness of pharmaceutical research. The investigations properly coming under this classification have many points of contact with other fields of research, and therein is the need for coördination and coöperation, and the reason why pharmacy should be properly represented in any plans for national scientific research. The problems arising in the laboratory of the manufacturing pharmacist are, of course, important and should receive searching study and investigation, but not from a selfish standpoint alone. His problems can best be solved by coöperation not only with his fellow manufacturers, but by that of research workers in the sciences involved in the questions at issue, and the benefits of such research belong to "the national strength and well being." However, to limit pharmaceutical research to such a narrow field would be to have it serve only the selfish ends of a few.

Many of the problems arising in pharmacy are of a chemical nature, but to limit pharmaceutical research to chemical problems would be a very narrow construction. Likewise, it is important that the pharmacologic action of synthetic remedies should be carefully studied and their therapeutic value accurately defined, but to limit the field of pharmaceutical research to such pharmacological investigation, as was at one time proposed, evidences a lack of conception of true pharmaceutical research and its proper scope. True, all of these and many more lines of scientific investigations are points of contact and coöperation of pharmacists with other research workers. Pharmacy research cannot, however, be classified with medicine, nor with chemistry or with any of the other lines of research so far recognized. It performs a distinct duty to the public and should be accorded recognition as a distinct vocation with problems of national interest and welfare peculiar to its field of service. All of the propositions for pharmaceutical research that have so far emanated from those outside of pharmacy have only demonstrated the insufficiency of the view, and a failure to comprehend the extensive fields awaiting organized pharmaceutical research.

Pharmacists themselves must have a proper conception of the present and a broad vision of the future possibilities. The salvation of pharmacy and its establishment upon a solid basis as a profession founded upon scientific studies and investigation, rests entirely upon the pharmacists themselves. The investigations of the past have been largely carried on by the individual workers engaged

as teachers in the schools of pharmacy, or as experts in the laboratories of the manufacturers, and by a few retail pharmacists. There has been no systematic attempt to coördinate pharmaceutic research or make it a coöperative division of a national comprehensive research plan. Pharmacy has been like an ocean-going steamer with good engines and compass, but no navigator. We must now realize the changed condition of the times resulting partly from the war necessities, and partly from the advanced position assumed by those who have been placed in charge of the National Research Council. This organization is composed of those associations or societies that have as a basis for membership, research Consequently, if pharmacy would seek a part in the scheme of this coöperative national movement, it must organize its research committee, association, or section composed of the workers and those interests in pharmacy that are concerned in research, so that scientific pharmaceutic investigation will be stimulated and properly directed.

It would appear that the American Pharmaceutical Association is the proper body to organize pharmaceutical research, that it may be assigned to its proper field of usefulness and correlated in the scheme of the National Research Council, and the Committee on Research is charged with this duty. The American Pharmaceutical Association is acknowledged to be the scientific support of the drug industries and the organization of research must now become another means of exhibiting its leadership and useful activity in behalf of pharmacy. It must hold aloft the torch of learning and transmit the knowledge acquired from the contributions of the past with increased brightness and added store and energy to the future generations.

Upon the colleges of pharmacy we must rely for support. Not only should their faculties be composed of enthusiastic research workers capable of carrying on scientific investigation, but every student in the higher or post-graduate courses should be given training in original investigations of problems pharmaceutic. This is a feasible plan by which the work of the past can be perpetuated and the needed army of research workers in pharmacy may be gradually built up of the proper material.

In closing permit me to refer to the Biological Exploration of the Amazon Basin under Dr. H. H. Rusby. While the newspapers have very commonly spoken of this as an expedition of chemists, it is organized, controlled and financed by pharmacists, and to a very large degree it is a pharmaceutical research expedition, and is typical of many more extensive pieces of research that would become feasible under an organized pharmaceutical research endowment.

"We all have personal responsibilities in things outside our own individual lives.

"The great art—the great art of human relationships—must be considered and practiced by every man in business to-day. We must hang together with the other fellow in order to bring things out right. It has been every man for himself which has given us our profiteers and human gougers. It must be *every man for the next fellow as well as himself* which will bring us into the condition of right human relationships without which no amount of spot prosperity will help.

"Get into the get together spirit and see how it works.

"It does."—PAULL HAYDEN, *N. Y. Commercial.*