

Quality Versus Quantity

By
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Reprinted from Eclectic Medical Journal

NOTE: John Uri Lloyd (1849-1936) founded Lloyd Brothers Pharmacy in Cincinnati, and was responsible for the formulation of a body of plant extracts called Specific Medicines (following the recommendations of Scudder). The pharmacy closed in the early 1960's, but his legacy is still present as the Lloyd Library, the largest library of medical plant books in the world, his pioneering work in colloidal chemistry, and several works of fiction, including "Stringtown on the Pike (A bestseller of its day) and the mystical "Etidorhpa".

The culmination of his work (in my opinion) was the Third Revision of "King's American Dispensatory" in 1898, 2200 pages of the best PLANT Pharmacy ever assembled. When he published this pamphlet the Eclectic medical movement was moribund. Its single surviving medical school would close forever 3 years after Lloyd's death and the withdrawal by his heirs of his long-time financial support for this tattered remnant of a century-year long experiment in Medical Populism. For the last 20 years of his life, he expended his near-mythic reputation in pharmacy writing curmudgeonly *emeriti*-type articles in Pharmaceutical journals in futile attempts (similar to this publication) to draw his fellow pharmacists away from chemical reductionism and back into viewing plants as *entities*, not sources of drug compounds. That these fell on increasingly deaf ears can be surmised by his gently-ironic postscript.

He was perhaps the only true American alchemist. Michael Moore

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* The demand for these articles has exhausted both the reprints and the journals carrying the articles. The subjects are apparently so important that we reprint the series, beginning: with this number of the JOURNAL.—EDITOR.

#I

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October, 1909, I wrote an editorial titled "Strength versus Quality." This briefly considered certain important phases of a problem that has long been a feature of my study of plant products and educts, and which in various directions have been voiced in times gone by in my lectures on pharmacy and pharmaceutical chemistry. In order that this further contribution ("Quality versus Quantity") to a very important subject be connected with the editorial to which I refer, I reproduce the same, as follows:

"Strength versus Quality.—An error common to a superficial, as well as to a one-sided or fragmentary conception of pharmacy, is that of considering *strength* and *quality* as synonymous terms. As we have said, it is a common error, but it is one established by very high authority. The truth is that, although more or less related, the constituent that gives the factor *strength* is often less important than are the attributes that go to make up *quality*, which, perhaps more than does strength, leads to high excellence.

"Let us define *strength* as a dominating something that stands out boldly, and which, in toxic drugs, produces a violent or energetic action, as does the poisonous something that produces death when an overdose of a toxic drug is administered. Let us define quality as a balanced combination of other something, with just enough of the toxic agent to make a complex product that, as a whole, has wider functions than are possible if the single death-dealing substance dominates. But we need not confine ourselves to toxic drugs, for, from all time, in many familiar directions, such as tea, coffee, spices, tobacco, etc., standards of strength have been differentiated from those of quality.

"For example, the *strength* of wine lies in its alcoholic proportion, but the *quality* of wine depends on the attributes imparted by accompanying congeners, such as water, potassium salts, ethers, acids, tannates and such. These, if balanced, the one in proportion to the other, produce wine of varying qualities. Indeed, no less an authority than Solomon drew a fine line when he excluded the red tannates: 'Look not upon the wine when it is red.'

"The dominating, poisonous agent in nux vomica is a strychnine compound, and on this substance rests the official (U. S. P.) strength of the drug. But nux vomica contains other alkaloidal structures and essential oils, as well as other organic complexities, which, balanced in Eclectic pharmacy and thus used in Eclectic therapy, are necessary to the quality of the Eclectic nux vomica. In the standardizing of nux vomica, the U. S. Pharmacopoeia recognizes strychnine only, whilst the Eclectic physician considers strychnine, in undue proportion, objectionable in that it dangerously overbalances *quality*.

"In like manner, the poisonous strength of *podophyllum* root is, by such authority, due to its resin; of belladonna, to its structural atropine; of aconite, to its structural aconitine; of hydrastis, to its structural hydrastine; and of jalap to its structural resin, etc., etc. In all these, and in others similar, the Eclectic depends on no such standards, but places *quality*, not *strength*, foremost.

"Nor is a standard of strength difficult to attain, whereas that of excellence, based on quality, is too often vainly sought, or reprehensibly neglected. It is easy, and not, as a rule, expensive, to double or treble the amount of the strength principle of a compound in which the congeneric substances that make for quality are elusive. A boy can add an ounce of alcohol to a pint of wine, and thus, for a few cents, double its *strength*, but a vintage of exceptional quality, with less alcoholic strength, commands a price far above that of pure alcohol. A novice in pharmacy can add seventy grains of

strychnine to a U.S.P. fluid extract of nux vomica, and thus double its pharmacopeial strength. An apprentice in pharmacy can, from *dried root* of gelsemium, make a preparation very poisonous by excess of the alkaloids, but yet very deficient in quality as contrasted with a preparation of the recent root of less alkaloidal strength.

"In our opinion, the attempt to standardize a preparation by a single dominating constituent is but a struggle towards a pharmaceutical standard of excellence, in which *therapeutic quality* should be the ideal. This fact Eclectic physicians have recognized for more than half a century.—LLOYD, E. M. JOURNAL, October, 1909.

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With the above before us, a further step may well take our further thought in the direction of quality in contradistinction to quantity as applied to therapy. And it much pleases us all to appreciate that not alone the physician, the pharmacist and the manufacturer, but the purely scientific chemist as well, is now directing his careful attention upon this problem, whose outreaching possibilities uprise before us all. And to me, particularly, comes the pleasant reflection that, with the extension of thought in these directions, arises naturally a liberality of action in opponents of other days, in which the old-style resistance to pharmaceutical investigation in outside lines is fast being relinquished. And, strange as it may seem, this toleration, now extended toward the "irregular" and his empirical works, is bred of pure scientific thought and investigation.

Chief among the factors of this liberation of good men from prejudice is the new chemistry known as "Colloidal Chemistry." In this "new chemistry" the best minds of the world are now studying, although the foundation of the work laid by Graham in the beginning of the last century has been constantly augmented by others in the passing along.

But, it may be asked, what has this to do with our subject? To such a question I would reply, "*Everything!*" Colloidal chemistry is based upon the fact that quantity is but one factor in many directions that involve both chemical and therapeutic action. The condition of a substance is a mighty factor as concerns its action as a thing, and necessarily, in this case, becomes a dominating agent in its therapeutic application. But even this is not new. Did not the United States Dispensatory record, fifty years ago, that six ounces of mercury swallowed by a man with suicidal intent produced no appreciable action of mercury, whereas, a few grains of mercury, finely divided, forms the active agent, *blue mass*. The first recorded dose of resin of podophyllum was

a lump of resin as large as the first joint of the thumb, and from this the patient recovered. Had the remedy been triturated to a fine division it is safe to say that no human being could have withstood even a portion of that heroic dose. Physicians comprehend full well the increased activity of subdivided substances, such as mineral salts and resins. The works of clinical observers, such as Webster, Scudder, Ellingwood, Fyfe, Felter, Thomas and others of our school, testify to this fact, whilst every page of any work devoted to Homeopathic therapy teems with living examples.

And yet such powders as these do not comprehend, other than in very minute traces, colloidal dispersion. In these triturates physical division prevails. Colloidal ultimates are practically unreachd. And yet so marked is the energetic increase of triturated drugs as to have established the fact of their intrinsic values in clinical therapy beyond the shadow of a doubt. The *quality* of a drug depends not alone on the weight of the materials; its *physical condition* is all-important. With this thought in mind, consider how physicians of all schools direct their prescription mixtures of dry drugs to be made into "a fine powder." Note how desirable are the triturates of milk sugar with a selected salt or resin.

And yet we have not as yet reached colloidal structures that stand in liquids without settling, that pass through the filter paper, that are so finely dispersed as to even receive the name, "*colloidal solutions*."

Let me repeat that a consideration of such as this is not new to those who, in times gone by, have honored me by listening to my lectures. Although the experiments of Graham were used as texts for definitions, we together passed into outreaches that surely will make familiar to those who listened in those days the principles of "colloidal activity," now looming up as a mighty factor in the evolution of medicine, and which is liberating from bondage the man who believes that quality is necessarily dependent on quantity, that the factors that confront the pharmacist are to be fully explained by symbols, formulae and equations.

QUALITY VERSUS QUANTITY—II.

JOHN URI LLOYD, CINCINNATI, O.

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Let me take as my text a sentence that reads as follows, from the article in the February number of the *ECLECTIC MEDICAL JOURNAL*: The quality

of a drug depends not alone on the weight of the materials; its physical condition is all-important."

Then let me ask that this be connected with my continuous contributions in the direction of plant pharmacy, in which, during the past forty years, one line of thought has been persistently presented to my readers, this being in turn threaded by a continuous line of self-questioning. The kernel of it all has, however, been to the effect that plant pharmacy is not a superficial problem, but a mighty study, based on the art of natural structural aggregations that exist in plant complexities, the art of the chemist being largely restricted to the destruction of these natural structures, together with the study and description of the factors evolved there from. I have continually urged the utilization of neutral solvents designed to liberate and to separate structural entities that are so easily affected by heroic chemistry, be it of any form or description. I have been irresistibly forced, with increasing evidences before me, to conclude that the art of pharmacy in the direction of plant complexities is the reverse of the art of the applied chemical processes of the past. It must, however, be recognized that the pharmacist has privileges in recognized chemical channels, and that the chemist cannot ignore many of the factors embraced in the term "pharmaceutical compounds."

The pharmacist's province in plant structures seems thus to me, primarily, the investigation and preservation of the qualities of natural associates that need be preserved as such, and differentiated from each other, with the aim of utilizing those that are useful. The art of the chemist seems to be that of applying destructive processes to plant structures, by means of such reagents as acids and alkalies, and by such processes obtaining from these structures ultimates that are definite entities in themselves, usually crystalline, and that can be graphically pictured by means of symbols expressing their atomic composition, and even their molecular arrangement.

Whilst I did not in the least underrate the field of the chemist, and the great work that the chemist accomplished in these directions, I considered that the field of the pharmacist, with his undefined "compounds," offers a legitimate phase of scientific research of no less importance. I have, therefore, accepted, as voiced in all my writings since 1879, that a duty of the pharmacist is that of studying *undefined* combinations in which no chemical equivalents are possible. These aggregate masses of materials are, in their vegetable host, dove-tailed together into balanced structures, each possessed of individualities of its own, but united with and interlaced with others, *physical attractions* between groups being a conspicuous factor. Such compounds

serve either as nutrients to conserve animal life, or as definite therapeutic agents to be utilized for the correction of abnormal conditions in disease expression. These symbolless structures of "pharmaceutical compounds" are, as a rule, non-crystalline, amorphous and shapeless, in the fresh plant, remaining colloidal when dried, if decomposition does not (create) liberate crystalline products.

But this shapelessness, due to colloidal condition, does not in the least detract from their activity or usefulness. Shapeless bodies, as yet outside the realm of systematic chemical equations, may possess most pronounced toxic qualities, or be of special nutritive value. The most active resins, the vegetable astringents and acrid gums, the toxic "extractives," are examples of such as these. These many years ago I even presumed to argue that the most pronounced forms of animal food products are these elusive colloidal combinations, and not the chemical ultimates that may be broken there from, and that the therapeutically helpful, the physiologically active, the nutritive structures of vegetation, are likewise non-crystalline, colloidal bodies. These arguments, however, are familiar and need not be referred to here, an example of this line of thought being the paper contributed by me to the semi-annual meeting of the American Pharmaceutical Association, 1902, titled "Organized Water as a Food."

More than once have I felt somewhat humiliated over the seeming neglect by my friends of the outreaches offered the student in pharmacy through investigations in these directions, which appeared to me to be no less scientific as a study, and no less helpful in the evolution of a perfected pharmacy, than are those of the chemist, who, by shattering natural combinations and picking out isolated fragments made thereby, is accomplishing a work of unquestioned scientific value, as well as of great therapeutic usefulness.

With the foregoing as an introduction, may I not in this paper, which is designed as a second contribution under the title that heads the article, refer to a paper written by me in 1890, at the request of Dr. Charles Rice and Dr. Fred Hoffman, and read by me before the New York College of Pharmacy? In this connection it may not be out of place for me to say, furthermore, that that paper was presented with misgivings, not because I feared that I was materially wrong in any of the premises, but because I felt that I stood practically alone in my pleading for the scientific opportunity of the student involved in plant pharmacy. I felt that, under the trend of the ideals of those involved in chemical pharmacy, my plea for recognition, based upon the arguments presented,

might be considered in an unfriendly manner by my hearers. This, even though my intent was of the kindest, and my offered examples such as I believed should be accepted, even by those wrapped up in other lines of research.

Both Dr. Hoffman and Dr. Rice reviewed the paper before its presentation to the society, and each insisted that it needed no change whatever in either argument or the examples cited. And thus the address, "Infinities in Pharmacy," was delivered a quarter of a century ago. Let us now connect with the present paper a few of the problems then presented. As concerns the simplest of living plants, it was then stated:

"Painful as the admission may be, we stand dumb before the mystery of the simplest plant, in its living entirety. And when we turn to its crude fragments—as gums, resins, barks, leaves, etc.—we have scarce the first clue to their true relationships. Or, when at last we crush this thing of life that refuses to deliver its secrets, and obtain by certain processes alkaloids, glucosides, oils, starches, sugars, acids, tannins, and other substances, all of which are more or less related and dependent one upon the other, yet we know not what infinity of other results is possible to other forms of manipulation."

With this thought in mind, the pharmacist was contrasted with the chemist, somewhat as a dealer in living animals might be contrasted with him who deals in the *flesh* of animals.

"Nor, while the different parts of the same plant are so divergent in their affinities, are we prepared to deny unperceived affinities in different plants? The spots on the distant sun may produce meteorological disturbances in an area of our globe that would not respond to the wildest commotions in another portion of the same globe.

"But in this Holy of Holies we dare not attempt to lift the veil. Leaving its awful arcana undisturbed we turn to consider plant disturbances as they come to us when the life has fled; for, as the butcher deals in flesh, not in animals, so the pharmacist deals with vegetable remains, not with the plants themselves."

Comes now a plea for further light, the argument being that no product or educt made by destruction of a plant structure had, in its living function, been thoroughly comprehended by the investigator:

"I doubt if any thorough pharmacist, whatever his accomplishments, is today satisfied with a single plant examination that is recorded."

The next sentence asks if any plant of the many hundred thousands known had been exhausted by the world's chemists and pharmacists, as

regards its phyto-chemical mysteries:

"Is there in this world a plant that has been exhausted of its material and its connected phyto-chemical mysteries? Every page of your dispensatory is vocal with pleas for light, further light. Your pharmacopoeia has been rewritten again and again, and is now woefully imperfect. Its pages do not bear record of a single crude vegetable structure in which the inner unknown does not merge into and envelop the known, and usually there is so little of the known that the crude drug is considered as an entirety, the committee of revision of the pharmacopoeia not venturing the attempt to mention the several constituents of the drug."

Passing next to two drugs to which, perhaps, more scientific effort had been directed than to any others known, the question was asked:

"Select an example from among the vegetable drugs that have been longest recognized as therapeutical agents, and first developed in regard to proximate constituents. Naturally, opium is named (a product only), or perhaps cinchona is preferred as the more important. Each has been subjected to lifetimes of conscientious investigation, but are not talented specialists, with the focused light of all these years of investigation before them, still searching into their mysteries? Are they not severally shrouded in the mist of that pharmaceutical infinity which embraces the domains of molecular and atomic space, those unfathomed depths of molecular motions that, under the influence of plant vitalities, produce substances which in themselves are perhaps marvels of simplicity, on the one hand, and of equal complexity on the other?"

Then, with the eye focused upon the questions of the investigators who have devoted their lives in such directions, a plea is made for the men involved in such complexities, the sentence ending with the question, "Are we sure that the conditions in which any of even the best known alkaloids naturally exist are known?"

"We should not underestimate the achievements of the unremitting toilers who have freely given their lives to these investigations, men now with us and those who have gone before; but no man can be injured by comparing his work with Omnipotence, and probably I do not go beyond many when I say that the natural plant conditions of such presumably well-known alkaloids as morphine and quinine are today shrouded in obscurity, for some of us cannot concede that we have learned even the interstructural associations or combinations of these labor-ridden substances. Are we sure that the conditions in which any of the best known alkaloids naturally exist are known?"

With thought directed to the alkaloids, which have, perhaps, dominated the efforts of the chemist in the direction of plant educts, a question is asked that, even now, after twenty-five years have passed, may still stand as a question:

"And I may perhaps venture to raise the question, do we know that alkaloids undeniably exist in plants as the simple salts of acids, purely as direct acid compounds? Facts innumerable connected with the simplest of plant organizations, which this age may not bring to light, are surely veiled in these directions."

Comes now a plea for the investigators to follow an optimistic looking forward to the future. And, in this plea, and in this forward look, I ventured to hope that the pharmacist of the future might restrict his field of effort, with due respect to the analytical as well as the constructive chemist, with toleration for the errors that have been made by the experimental pharmacist, and with due credit for that which he gave to those who followed. The field of a pharmacist's study must be in restricted lines if he hopes to accomplish. He must not attempt to conquer a multitude of problems. Let me quote:

"Such reflections, perhaps, are more likely to come over the workers in pharmaceutical plant research after they have passed their period of usefulness; but probably if one could follow another in the study of a single genus of plants, the magnitude of the field is such that the third and fourth generations would see good reason to restrict themselves to still narrower confines. With due respect, therefore, to our workers of the past and present, it seems to me that elaboration of the ground already gone over in plant examination is the great and pressing demand of this day, and that this service is not of less importance to phyto-chemists than the mapping of the so-called known heavens is to astronomers."

Let such reflections as these be further recorded in the language in which they were then written:

"As a further step in this line of thought—for I have as yet considered and referred to drugs of vegetable origin only that have been longest recognized and are best known—let us enumerate, beside the plants that men have attempted to investigate, those untouched by the chemist, and which have never been studied and are not even mentioned in our records. We find that those we have examined are so insignificant in numbers as to scarce justify mention. The little group so imperfectly known to us is counterbalanced by multitudes of species, of which there are numberless varieties. The botanist is yet discovering species, yet formulating names, nor will this labor end during our generation. We have not yet become familiar with the bare names of the plants he has recorded, and so light is his work compared with our own that he has but to grasp a flowering branch, describe the connections, relationships and name it according to a system, to complete his task. Comparatively, this is a small work, and yet today the botanist is crying in despair at the problem of species and sub-species determination, of which the American field alone presents innumerable difficulties. Before the American flora can be considered

phyto-chemically, even as superficially as our work has been done to this day with a few plants, ages will have elapsed, and the names of men now foremost in the ranks will perhaps have passed from recollection. A few dozen only of American species, more or less (usually more) imperfectly, have passed under the immature methods now known to the analyst; while east of the Mississippi River alone we have doubtless ten thousand distinct flowering plants. Add to these the flora of the great west, the untold product of South America, Asia, Europe, Africa, Australia, and the islands of the seas, and we cannot but shrink before the contrast with these unexplored wilds of the little that we know. Thousands of square miles of primeval forests, dense jungles and grassy pampas, which form blank spaces on our maps, await the tread of civilized man. These wastes are unknown to the very explorer; the botanist has not yet set foot in these voids, and we have seen how far the botanist even now outstrips the phyto-chemist. Even as I pen these words there comes (in public print) a cablegram from the explorer, Stanley, a man for two years lost to sight in the 'Dark Continent':

" 'All the stretch of country between Yamuga and this place was an abso-
lutely new country. The darkest region of the earth, it is one great,
compact, remorselessly sullen forest, the growth of an untold number
of
ages.' (Signed) HENRY M. STANLEY.

"That wilderness has closed upon and absorbed this single thread of light, yet it must be part of the conquests of the pharmacy of the future."

With all this before us, the question may now be asked, "What is the connection between the title that heads this article and that of the paper from which these quotations have been made?" Furthermore, "What concern has the physician in the bringing before him of pharmaceutical problems that need, in the opinion of some persons, be the care only of the maker of medicines?" To these queries I will reply that I feel assured that the physicians who read this journal, and to whom my papers on pharmacy and connected subjects have, for over a generation, been successively presented, will fully comprehend the connection between that which is presented in this paper and my preceding paper in the February JOURNAL, and that they are likewise in a position to link the two with the paper that will follow.

We are now surely upon the threshold of a proper recognition of *structure-less* pharmacy. We have reached the "breaking dawn" of the pharmacist's opportunities. Contact action, mass action and colloidal qualities of both structureless structures and minute fragments (*not* atoms) of dispersed compounds and elements must be a scientific and recognized part of the most advanced chemico-pharmaceutical field now looming before us under the name of *colloidal chemistry*.

QUALITY VERSUS QUANTITY—III.

JOHN URI LLOYD, CINCINNATI, O.

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The preceding (two) papers consider in a general way the problem of plant structures, the aim being to suggest that to ignore natural structures is to neglect an opportunity in pharmacy. That whilst the ultimates broken out of structures are of value in therapy, the structures yielding the ultimates are possessed of qualities that in many directions make them superior to the artificial products.

It may be reasoned, also, and very consistently, that to dispossess a natural drug texture of its colloidal qualities is to alter its condition otherwise than physically. In this we believe, and in this direction we believe the art of pharmacy will yet evolve until its recognized importance will be established to all concerned in both chemistry and therapy.

Let us again repeat that in such as this no reflection is placed on either the analytical or synthetical chemist. Upon the contrary, we believe that the time will come when chemistry will recognize the fact that the beginning of the study is the consideration of such problems as may be expressed by formulae. In a time to come will also follow a scientific comprehension of the pharmacist's structures now beyond the eye of the talented men engaged in the study of the products broken out of these, as yet, voidless and formless colloidal bodies.

With these remarks as a text, it may be well for this writer to extract a few phrases bearing on this subject from past prints from his pen. (See Lloyd Brothers' Drug Treatises, 1904 to 1914).

JABORANDI (1904).

Constituents.—As might be expected, the chemistry of 'jaborandi' is in a chaotic condition. The one conspicuous product is the alkaloid *pilocarpine* (discovered independently, 1875, by E. Hardy, in France, and A. W. Gerrard, in England), but this is one constituent only, for a number of fortifying or modifying acids and bases are to be obtained from, or are present in, the plant. Practitioners of medicine know from experience that a preparation of true *Pilocarpus microphyllus* carries qualities distinct from those of the alkaloid, which, in itself, as found in commerce, is not necessarily a uniform agent and, as is shown by the melting points, as well as by observation of the substances obtained under the name *pilocarpine* from different species of plants, must be taken with much discriminative allowance. A qualified student of materia medica can distinguish the official leaf and fairly judge of its condition (no

pharmacist need ask an excuse for not knowing the true drug), but yet few can draw alkaloidal distinctions between the alkaloidal products of the various species, which, indeed, remain yet to be studied. The most abundant spurious drug (*Pilocarpus Trachylopus*) yields an alkaloid that is worse than useless, because it is antagonistic to the principal alkaloid of the official leaf, few being familiar with the chemical distinctions. The so-called active principles of the *Jaborandis* embrace the alkaloids *jaborine*, *pilocarpidine*, *jaboridline*, *jaborine*, and the acids *jaboric* and *pilocarpic*, as well as other products and educts, among which is potassium nitrate, obtained by us in crystals. The chemistry of these *Jaborandi* bodies is enough, almost, to take the life study of a specialist, and the distinctions and relationships of these products in natural association, or as separate products, are not less an enigma than are the structures themselves.

VERATRUM (1904).

"*Constituents and Products.*—No constituent representing the full therapeutical qualities of *Veratrum* has been obtained from the drug. Chemistry, as is true of most other plants, destroys, creates and alters, but does not parallel. Structural relationships that exist in the drug may be broken, new substances created, but the natural balance is not maintained by any educt, product or mixture of ultimates. A fallacy is it to even hope that test-tube juggling and heroic chemistry have broken out of *Veratrum* an educt or product to replace a preparation that represents the interstructural ultimates of *Veratrum* as nature made them and combined them, and on which the entire therapy of the drug has been established. Thirty years ago, when the writer was enthusiastic in the belief that chemical methods could isolate from plants their qualities, and in alkaloidal form could put their virtues into small compass, the study of *Veratrum* and its irrevocable lesson to the contrary was one of the shocks that came with irresistible force to dispel the illusion. No constituent or created product represented *Veratrum*. All the alkaloidal fragments broken out, these so-called derivatives mixed together, are not *Veratrum* either in structural composition or in therapeutic value. Separated, they are fallacies; antagonistic are they in their actions. Mixed, they are frauds if viewed as representing the full drug. Let us chiefly consider the record of these questionable *Veratrum* alkaloids:

"In 1835 Osgood attempted, without success, to discover the active principles of *Veratrum*. Mitchell (1837) also failed, but in 1857 Richardson found a bitter alkaloid that he considered *veratrine*. In 1865 Charles Bullock broke out a resin and two alkaloids which he named *veratroidia* and *viridia*. In 1874 Mitchell announced that *viridia* was *jervine*, once called *barytine*, and in 1876 Bullock announced that his so-called *veratroidia* (discovered 1865) was impure *jervine*, asserting now that *jervine* was the *only* alkaloid obtainable from *Veratrum viride*. In 1876 Wormley proved to his own satisfaction that *veratrine* is obtained, which was again denied (1877) by Robbins. In 1878 Wright and Luff described five alkaloids, *jervine*, *pseudojervine*, *rubijervine*, *veratralbine*, *veratrine* and *cevadine*, the last in amount greater than the *total* of all the others. In 1890 Pehkschen obtained principally *jervine*, with small amounts of *veratroidine*.

"Thus discord reigns, and as long as different men with different chemicals heroically attack the drug discord is likely to continue. In our opinion, these broken out fragments are chemically made derivatives of

Veratrum structure, not natural integral parts. The total mixed alkaloidal product of *Veratrum viride*'s interstructural unknowns will no more give the therapeutical action of *Veratrum* than will the alkaloidal unknowns and various products masquerading under the name *aconitine* give the full therapeutical effects of aconite, or the chemical ultimates of ergot replace that drug. The less chemistry *Veratrum* receives the better; no acid or alkali can be tolerated. The kindly touch of natural solvents, without other than the momentary touch of heat, is absolutely necessary to the production of a representative pharmaceutical preparation.

CHIONANTHUS (1904).

"The taste of *Chionanthus* bark is bitter, and, dominated by the odor, gives a very characteristic flavor when the bark is chewed. No analysis of the bark has been made, attempts to do so having failed for obvious reasons. Mr. R. S. Justice thought to have identified saponin, which Mr. W. von Schulz disputed, in his turn announcing a glucoside. The fact is, the most tender touches of chemistry disrupt the drug, which is so sensitive that its alcoholic tinctures and fluidextracts often disintegrate and fly into unknown products even when kept in the cold. No known separated constituent gives the energy of *Chionanthus*. The so-called *Chionanthin* of early Eclecticism was intended to be a mixture of about everything the drug afforded. In its production, heat, desiccation and heroic destructive manipulation brushed the life out of the drug, the product, a so-called concentration or resinoid of the resinoid and alkaloid craze of Eclecticism's infancy, being practically valueless. The writer of this paper has made a systematic study of *Chionanthus* for twenty-five years. It has been to him a perplexing problem, one of the most exasperating in some regards of all the materia medica drugs. The experimental details of this work would fill a volume. Be it enough to state that as a conclusion we believe the only possible therapeutical representative of the bark to be a liquid pharmaceutical preparation. Practically no heat, no chemistry, no heroic disruption methods, no acid nor alkaline solvents, can be employed in its production.

NUX VOMICA (1904).

Composition.—The dominating constituent of *Nux Vomica* is a complex compound which, in natural form, is an invaluable remedy. By means of chemical reagents it can be split into parts, embracing two intensely poisonous alkaloidal products, a glucoside and acids. These alkaloids are *strychnine*, *brucine*, and perhaps *igasurine* (yet in doubt). The main acid is *igasuric acid*, while the glucoside is named *loganin*. These are all colorless bodies, the alkaloids being very bitter and energetically poisonous, *brucine* being a poison similar to *strychnine*, acting with less violence and more slowly, but not less surely, than *strychnine*.

COLLINSONIA (1904).

Constituents.—*Collinsonia* parallels other vegetable products that as a whole are useful, but in which the isolated structural fragments are not the equivalent of the drug. No definite therapeutical agent has ever been identified in *Collinsonia* or obtained from it. Mr. Lochman (1885) obtained resin, starch, tannin and wax from the plant, mucilage from the root, and traces of a

volatile oil from the leaves, but nothing outside the usual constituents of plants. No alkaloid, essential oil, glucoside or vegetable acid carrying even an individuality of its own, has been picked out of the drug. In this it differs from *Veratrum viride* (see Drug Study No. IV), which is such a mine of richness to the chemical juggler, yielding a multitude of questionable and mysterious educts. Nor, by reason of its insipidity and its lack of odor, can *Collinsonia* be classed with such drugs as *Chionanthus*, which, although devoid of chemical equivalents, is yet possessed of strong sensible qualities both of taste and smell. *Collinsonia*, like Ergot, and most other vegetable remedies is most valuable either as a whole or in preparations carrying its united qualities. No chemistry, no heroic pharmacy can be tolerated in its manipulation.

MACROTYS (*Cimicifuga*)(1905).

Constituents.—Macrotys, like other American drugs, has been persistently and repeatedly attacked by chemists, beginning with Mears (1827), passing thence to Tilghman (1834), King (1835), Davis (1861), Conrad (1871), L. S. Beach (1876), Trimble (1878), Falck (1884), Warder (1884), and others, both contemporary with and following those named above. All authorities subsequent to King unite in saying that the most conspicuous product of Macrotys' disintegration is a compound resinous body, which was first discovered by Dr. John King in 1835. Subsequent studies have been largely devoted to the splitting of this resin into by-products, none of which as nearly represents Macrotys as does the so-called resin, which is, in itself, a complex mixture of bodies. Some of these resinous bodies exist, possibly, in a natural condition in the drug, but the majority are created by drying, chemistry and manipulation. In this connection let us say that so delicate is the structure of this drug, Macrotys, that even the touch of the atmosphere, as well as manipulation by means of solvents and subsequent drying, are sufficient to produce great changes, and result in newly constructed products.

GELSEMIUM (1904).

All this problematic chemistry of Gelsemium products is, however, a matter of indifference to the physician desiring a balanced representative preparation of Gelsemium, partly because the questionable basic products on record, as well as the resin and extractives, are obtained from the dry root and not from the green. None of them carries the qualities of the preparations of Gelsemium that have made the therapeutical reputation of the drug. If the drying process did not break the natural interstructural combination, the heroic chemistry used in splitting it into fragments would accomplish that result. These alkaloids and other products are obtained from Gelsemium, but we neither comprehend how they have been created nor what their natural relationships may be, nor yet the part they bear to the host that gives them birth, and which, as a whole, is so sensitive as to forbid even the process of drying, if one wishes the fullest and finest qualities of Gelsemium.

BELLADONNA AND SCOPOLAMINE (1905) .

Their alkaloidal constituents are naturally the subject of much controversy, both in themselves and when contrasted with those of Belladonna, and, in our opinion, are likely to remain so as long as different chemists, with different chemicals, are attacking a structure that, under various

influences, yields varying products. For example, *Scopolamine*, which was first asserted to be the characteristic alkaloid of the drug, was considered by E. Schmidt to be identical with *Hyoscine*. O. Hesse next found it to consist of two alkaloids, *Hyoscine* and *Altroscine*, and, next, Schmidt proved to his own satisfaction that *Hyoscine* was a mixture of *Scopolamine* and some other body, finally asserting that *Hyoscine* does not exist. The facts are, the broken-out fragments of these natural drug structures are interesting, and chiefly so because of the opportunity they give investigators to puzzle themselves and others over artificially made products, whose qualities, changing under the influence of chemical reagents or atmospheric action, remind one of the chameleon.

DIOSCOREA (1905).

Constituents.—Excepting saponin, obtained in 1885 by Mr. W. C. Kaltyer, there are no representative educts or products of *Dioscorea* of a definite chemical structure. The drug has been attacked by enthusiasts in destructive chemistry, but the ultimates of their antagonistic processes are of no value whatever in therapy. In the early days of Eclecticism, close following the discovery of the Resin of *Podophyllum* by Dr. King, attempts were made to obtain by a similar process an energetic principle from *Dioscorea*. The product was called *Dioscorein*, and on faith was accepted for a considerable time, in the alkaloid-resinoid-concentration craze of Eclecticism, as a worthy companion of King's energetic Resin of *Podophyllum*. It was a very inferior saponin, and, naturally, did not stand the test of time.

PODOPHYLLUM (1907).

The destructive chemist next turned his attention towards dissociating this resinous substance. By various methods several decomposition products were announced, such as *Podophyllotoxin*, *Picropodophyllin*, *Picropodophyllic Acid*, etc. These are all more or less energetic, but all are faulty, none being as reliable as the natural resinous precipitate. All attempts to force these artificial products on physicians have failed, for the very good reason that none of them equals the original drug.

SCUTELLARIA (1908).

Constituents, or Decomposition Products.—As in attempts to locate the structural ultimates of other plants in which a drug as a whole, not the fragment, plays a part, so have the efforts of the chemist failed in *Scutellaria*. In 1824 Cadet made an analysis of the drug, describing, among other usual constituents of plants, a peculiar volatile oil, and a bitter principle which seemed to be peculiar to the drug. In 1877 Howard decided that the volatile oil was the characteristic principle, but this exists in very minute amount. In 1889 Myers and Gillespie obtained the usual drug products, and also, in the form of stellar crystals, a decided amount of Cadet's bitter substance, which proved to be glucoside.

To sum it all up, in our opinion these chemists severally destroyed the plant, and from the products of disintegration obtained certain ultimates that may or may not exist in the plant tissue, and likewise may or may not, singly or collectively, have any decided therapeutical connection with the drug's

structural qualities.

SPONGIA (1911).

Constituents.—Burnt Sponge contains a large amount of combined iodine, not merely a 'trace,' as Christison states. In addition, bromine, phosphorus, sulphur and other elements in unknown combinations go to make up Burnt Sponge. Whoever reasons concerning the action of compounds made up of such substances as unknown combinations of the elements that theoretically may be formulated into chloride of sodium, calcium sulphate, sodium iodide, magnesium bromide, calcium carbonate, calcium phosphate, magnesium and iron oxides, unknown sulphides and phosphates reorganized from organic tissue and reconstructed by heat from complex organic bodies, presumes much in asserting that such combinations depend solely for their qualities upon a single substance that may, by destructive chemical processes, be isolated from the original product. The intermolecular constitution of Burnt Sponge is today unknown, and the part iodine takes in the therapy of that substance is also unknown.

Let us repeat that, in our opinion, the balanced structure, a complexity in itself, that results in the empirical production of the compound known as Burnt Sponge, cannot be molecularly established by any theoretical computation made from a review of the isolated constituents thereof. Consequently, the uses of this preparation by physicians who employ it in contradistinction to iodine or its compounds, are accepted as logically applying to a structural something, molecularly unknown, that must be very different from iodine, or a single iodine compound.

DIGITALIS (1913).

. . . From 1874 to the present date thousands of chemists have sought the secrets of Digitalis, all ignoring the natural combinations of organics and inorganics, all seeking a toxic agent as the desirable therapeutic constituent, and all, so far as we can discover, believing that agent to be organic only. Seemingly in it all, natural associations of textural relationship of the organic and inorganic are ignored. First destroy the natural substance of the drug, then from it create anew, is the idealistic process, which needs no other comment than that, after more than one hundred years of these aggressive destructive methods by the most brilliant chemists, the verdict is by many persons accepted, as by Thompson in 1811, 'still unknown.' "

* * * *

The foregoing excerpts are fairly indicative of the views of this writer concerning the subject of relationships between plant structures and chemical products created therefrom. Whilst there is no question concerning the value of such ultimates as the broken out alkaloids and glucosides, or of such elements as iodine that can be produced by the destruction of sponge, and even from animal structures such as the thyroid gland, this writer believes that neither the alkaloid nor an element such as iodine parallels the colloidal

structures from which they are made. Resin of podophyllum is not *podophyllum*, emetine is not *iphecac*, iodine is neither *thyroid* nor *sponge*. Give to the evolving chemist and his products a full modicum of credit for his great services and accomplishments, but do not take from the pharmacist his birthright, the study of structural bodies, concerning which we have as yet neither molecular knowledge nor symbolic possibilities. Let us sum this phase of the subject up by an extract from a drug treatise (1909) on "Dried Fragments of Drugs Are Not Representative of Drugs.

"An experience of more than three decades, commencing in a craze for energetic, or even poisonous, proximate principles, had, as already related, taught Eclectic physicians to their own satisfaction that a toxic constituent or a mixture of the separated dried products broken out of a drug by chemical means or created from drugs by the chemist's art, useful though each might be in its own sphere, did not typify or parallel the therapeutic qualities of the whole drug. They had learned by bitter experience that a poisonous fragment or ultimate, broken out of or created from a plant by chemistry, did not represent the therapeutic qualities of the structure from which it was derived. The once prevailing hope that a single, dominating constituent, or ultimate, or a definite substance present in or obtained from a drug, could be taken to standardize the desirable therapeutic qualities of the combined medicinal parts of a plant complexity, also passed away."

QUALITY VERSUS QUANTITY - IV.

JOHN URI LLOYD, CINCINNATI, O.

Reprinted, 1931, from the *Eclectic Medical Journal*, June, 1916.

Turn to your ECLECTIC MEDICAL JOURNAL, October, 1909, and find therein a contribution from my pen, titled "Quality Versus Quantity," this being the first of a series comprising, with the present article, eight connected contributions.* Let us briefly review the foregoing articles in order to connect therewith, intelligently, the argument found in the ending of the present contribution.

An object of the first article was to correct what, in my opinion, was a well-established fallacy concerning the application of the terms strength and quality. It was attempted therein to exemplify the fact that "quality" in a plant pharmaceutical preparation might be defined as a balanced combination of complexities that, in their natural home in the drug, were of such a nature as to require the application of discriminative pharmaceutical methods. Let us quote:

"Let us define *strength* as a dominating something that stands out boldly, and which, in toxic drugs, produces a violent or energetic action, as does the poisonous something that produces death when an overdose of a toxic drug is administered. Let us define quality as a balanced combination of other somethings, with just enough of the toxic agent to make a complex product that as a whole, has wider functions than are possible if the single, death-dealing substance dominates."

This view had for many years preceding that date dominated my thought, and in order that the problem might be presented to my readers, a comparison with a familiar substance was introduced, in which a distinction was made between the strength and quality of wine, as follows:

"For example, the *strength* of wine lies in its alcoholic proportion, but the *quality* of wine depends on the attributes imparted by accompanying congeners, such as water, potassium salts, ethers, acids, tannates and such. These, if balanced, the one in proportion to the others, produce wines of varying qualities."

"A boy can add an ounce of alcohol to a pint of wine and thus, for a few cents, double its *strength*; but a vintage of exceptional *quality*, with less alcoholic *strength*, commands a price far above that of pure alcohol."

As a connected thought it was shown that a drug might likewise be dominated by a conspicuous toxic agent which, in a pharmaceutical preparation, could be designed to carry this material in the extreme. But as a pharmaceutical preparation it could, for special purposes, be made much more valuable by decreasing the proportion of the toxic agent, in order that the less energetic associates might exert themselves. Nux vomica is thus selected as a conspicuous example:

"The dominating, poisonous agent in nux vomica is a strychnine compound, and on this substance rests the official (U.S.P.) strength of the drug. But nux vomica contains other alkaloidal structures and essential oils, as well as other organic complexities, which, balanced in Eclectic pharmacy and thus used in Eclectic therapy, are necessary to the quality of the Eclectic preparation, nux vomica. In the standardizing of nux vomica the United States Pharmacopoeia recognizes strychnine only, whilst the Eclectic physician considers strychnine, in undue proportion, objectionable, in that it then dangerously overbalances quality.

* * *

"A novice in pharmacy can add seventy grains of strychnine to a U.S.P. fluid extract of nux vomica and thus double its pharmacopeial strength."

This article closes with the kindly suggestion that the present method of standardizing a pharmaceutical preparation by making it carry the greatest

possible amount of one dominating agent is not conducive to the highest pharmaceutical thought-standard. Let us quote:

"In our opinion, the attempt to standardize a preparation by a single dominating constituent is but a struggle towards a pharmaceutical standard of excellence, in which therapeutic quality should be the ideal."

Carrying this line of thought into the next article, titled "Standards of Excellence," 1909, a plea is made for the idiosyncrasies of men possessed of other viewpoints, and especially for committees whose responsibilities necessitate their making standards on long-accepted pharmaco-therapeutic lines. This is exemplified as follows:

"A standard established by one man, or a committee of men, may be correct from their one viewpoint, but need not necessarily be a standard that, under different conditions, may prevail in the thought and action of other men."

It is next shown that pharmaceutical research needs be easily paralyzed if such an authoritative standard prevents further investigation. It is also shown that—

"A chemist or a committee, thinking only of the conspicuous agent, may ignore the milder entities, and in the glare of this one dominating light establish a very one-sided standard, which may neglect unseen qualities that lie beyond the thing that makes the standard of the man of toxic faith."

It is also shown that a chemist or a committee possessed of the power of thus establishing the value of a pharmaceutical preparation by making such an inflexible law might make a very one-sided standard. Indeed, I ventured to give my opinion of the harmful result of such authorities' rulings, could it be legalized absolutely and irrevocably:

"To make such an inflexible law would be to paralyze pharmaceutical research."

It is stated that uncharitable inflexibility as concerns the privilege of others possessed of other viewpoints, such as a belief in the usefulness of non-toxic agents, could do a mighty wrong in preventing pharmaceutical progress. Indeed, I ventured to record that—

"In accordance with this line of thought, we believe that standardization, through an honest misconception of possibilities and probabilities outside their field, is too often inclined to uncharitable error. We believe that in many cases it would be better if a smaller amount—a *much* smaller amount—of certain dominating drug constituents were present in

preparations of poisonous drugs designed for the curative treatment of certain disease expressions. Our study of several decades has taught us this lesson. In other words, because a certain drug in prime quality contains naturally a certain amount of an energetic or poisonous alkaloid, glucoside or resin, it does not necessarily follow that a pharmaceutical preparation is balanced to the best advantage, for a special therapeutic use, when it carries that full proportion of energetics, which will be, in some cases, a dominating load of poison.

* * *

"Let us repeat that the standard of *pharmaceutical excellence*, in our opinion, does not necessarily reside in the one toxic agent, but is to be found in the balanced structure of the preparation's evolution from the crude drug. Nor does *therapeutic excellence* necessarily rest on an overload of a dominating, ever-conspicuous toxic constituent of a drug."

Passing now to two contributions, titled "Concerning Albumen," we are presented with a viewpoint designed, through a consideration of this well known substance, to indicate that like substances contained in a drug and that are deemed to be inert and inactive, may, under certain conditions, become possessed of exceeding energy. Indeed, an ordinary food taken into the stomach, and universally considered as most excellent even for invalids, may, under other forms and conditions, become most unbelievably energetic. The article of Dr. Eccles, in the Medical Record of August, 1911, on "Albumen," is presented as a text. Let us quote:

"A startling recent revelation is 'that one-millionth of a cubic centimeter of a 5 per cent. solution of a three-time crystallized egg-albumen, or *one-twentieth of a millionth of a gram of protein, will sensitize a guinea-pig enough* so that distinct and typical symptoms are produced after a second injection of the same material, while one fifty-thousandth of a cubic centimeter of solution containing but one-millionth of a gram of protein sensitizes fatally.' Try to grasp the full significance of these words. Think of one grain of egg-white being divided into over 66,600 equal parts, and *one* of these parts proving as deadly to a guinea-pig as a bullet through its heart. Strychnine and prussic acid are deadly, but they are almost harmless when compared with hen's egg protein, administered intravenously after sensitization. We consume this deadly material with impunity as a constant article of diet. Friedberger tells that 'if into a guinea-pig a tenth of a milligram of the serum proteid of a sheep is injected subcutaneously, and if at a later period, as early as after ten days, five milligrams of the same proteid are injected into a vein, the animal goes into convulsions, has asphyxia, and dies.' "

In summing up the problem, wherein, if the authorities quoted be correct, a touch of pure albumen in the veins produces death almost as does an electric shock, it is, furthermore, shown that all our food-grains, such as nuts, corn, peas, beans, and certain similar products, may, in like manner, produce fatal results.

Article No. 3 attempts to connect such as the foregoing with the beliefs of physicians who accept that exceedingly dilute attenuations produce, in clinical practice, most pronounced therapeutic effects. Reference is made to the fact that not only the Homeopathic profession, but many physicians outside, were becoming imbued with a belief in the influence exerted by triturates, even of presumably inert organics, when administered under certain intervals of time. Thus we quote:

"Turn now to Webster's "Dynamic Therapeutics," written by one who had been first reared in a line of instruction in which large doses predominated. Note how this experienced practitioner proceeds to instruct the reader that small doses are often better than large ones, and that even the second or third trituration, often repeated, gives frequently an intensified therapeutic touch. Even more clearly than this is stated the fact, as demonstrated by Dr. Webster's experience, that substances like the *inorganics*, in concrete form, when taken in large quantities, have no apparent disturbing influence on life, but, when finely comminuted and given in minute amounts at short intervals, are followed by most positive influences in disease expressions. Indeed, such substances as silica (deemed practically insoluble and inert) are by him commended in very minute amount, but they must be very finely comminuted."

Indeed, it being evident that the dose of the triturated silica of Dr. Webster was immeasurably greater than the albumen that killed the dog, I made a plea for further liberality of thought, as follows:

"But still further liberality is demanded when such doses as Dr. Webster and other standard Eclectic physicians employ are contrasted with the minute amount of albumen (Eccles) has the power of not only influencing the life current of a normal creature, but of cutting the thread of life and producing death."

Then comes the next article, where, having introduced the preceding texts, we swing back to the original thought of the 1909 article, "Strength Versus Quality," finding now that the nearly paralleling title, "Quality Versus Quantity," is selected. In this the aim is to fortify the original statement by a resume of the evidence introduced in the subsequent contributions. For this purpose the major part of the 1909 article "Strength Versus Quality," was reproduced, with the following comment, in which recognition is given to the pleasure I experienced in the increasing liberality of opponents of other days, who then viewed the subject of drug study and therapeutic action differently from myself. Let us quote:

"With the above before us, a further step may well take our thought in the direction of *quality* in contradistinction to quantity, as applied to therapy.

And it much pleases us all to appreciate that not alone the physician, the pharmacist and the manufacturer, but the purely scientific chemist as well, is now directing his careful attention to this problem, whose outreaching possibilities uprise before us all. And to me, particularly, comes the pleasant reflection that, with the extension of thought in these directions, arises naturally a liberality of action in opponents of other days in which the old-style resistance to pharmaceutical investigation in outside lines is fast being relinquished."

Indeed, this phase of the subject is given a special touch, in which is made the suggestive thought that progress in this direction would necessarily extend to outsiders, and that not only a toleration as concerns their own belief, but the welcome due investigators working in other lines for a common purpose, would follow. This is tersely exhibited as follows:

"And, strange as it may seem, this toleration now extended toward the 'Irregular' and his empirical work is bred of pure scientific thought and investigation."

QUALITY VERSUS QUANTITY—V.

JOHN URI LLOYD, CINCINNATI, O.

Reprinted, 1931, from the *Eclectic Medical Journal*, July, 1916.

One of the discouraging features connected with pharmaceutical problems has been the systematic attempt, as this writer views the subject, to retard personal investigation by restricting one who is concerned in research to *authoritative* publications that, through the passing of years, become, sooner or later, inadequate. Again, it would seem that an effort is being made to put all manipulative pharmacists on a common level, it being argued that what ever is accomplished by one man can be as well accomplished by every man. Possibly these erroneous views and practices, which are conspicuous in pharmaceutical politics, have done more to discourage the young pharmacist who has aggressively attempted to individualize himself by his efforts, as well as those who are older, than any other problem that confronts the pharmacist. The fact is, even the man who follows most carefully formulas recorded in authoritative publications may, by his manipulations, produce a pharmaceutical preparation quite different from that made by some other man, and that, too, even when the ingredients employed by both are identical.

Need one, as a comparison, do more than refer to the different qualities of bread or cake, or, indeed, of any prepared food, made from the same materials by different persons working under the same formula? Is not everyone aware of the fact that quality governs in cases like these; that strength, so far as the use of materials is concerned, is incidental thereto; that from the best

of flour can be made the most unpalatable, as well as unwholesome, bread; that some people can never learn to manipulate the simplest food constituents so as to equal a product made by some other person who seemingly has the knack of palatably compounding this or that food product ?

But the question may be asked, "What has this to do with the quality of remedies made of identical materials, that are manipulated by expert pharmacists, who cannot be said to be inexperienced, awkward or careless ?" In this thought let us go a step farther and ask, "Can a single material, under varying physical conditions, become possessed of different qualities?" Let us extract from the leading article, from the pen of the writer, contributed to the ECLECTIC MEDICAL JOURNAL, April, 1914, the following sentence:

"The quality of a drug depends not alone on the weight of the materials; its physical condition is all-important."

With this thought in mind, let us introduce as a text, or as texts, the varying qualities of some element that assumes, under different physical conditions, most remarkable phases, these distinctions being qualities due to manipulations of that one element only.

First, take the element carbon, which in its commonest form is known as charcoal. Let this be purified to the ultimate by the exclusion of all foreign substances. It is now black, tasteless, odorless, insoluble. Exceedingly inflammable, it burns in the air, leaving no ash. Take now this same element, carbon, in the form known as graphite. It is still black, insoluble, odorless and tasteless, but instead of burning in the open air, as does charcoal, it so persistently refuses to unite with oxygen that it is utilized in the making of crucibles designed to stand exceedingly high temperatures, crucibles of graphite of immense size being employed in the melting of iron and other metals that require a very high heat for their liquefaction. Pass now to a third form of carbon, the *diamond*. Behold ! the carbon is no longer opaque, but brilliantly transparent. It no longer burns in the air at an ordinary temperature, but at a very high temperature it unites with oxygen and disappears, with the formation of the same gas that follows the burning of charcoal in the air. Instead of being easily powdered as is the case with charcoal and with graphite, it ranks with the hardest of known bodies, a slender edge scarcely wearing from continued use in the cutting of glass. Bear these facts in mind, because these radically different materials are simply *quality* shadings in a single element.

Second, pass now to phosphorus, which in its active form is

translucent and nearly colorless, resembling soft beeswax. If held beneath water it can be molded into different shapes; at a higher temperature, it melts and flows like oil; at a still higher temperature, it volatilizes and escapes as a gas. It dissolves in bisulphide of carbon and other similar solvents much after the manner in which substances such as paraffin dissolve. On exposure to the air, even at the ordinary temperature, it is likely to catch fire spontaneously, and, burning, entirely disappear. It is poisonous to animal life, and, if used internally, needs be administered in small doses.

Place this same material, pure phosphorus, in an air-tight cylinder, expose it to a temperature of 300 degrees F. for twenty-four hours, more or less, then cool and open the vessel. No longer is the phosphorus a waxy substance; it can be scraped out in red fragments. No longer does it ignite on exposure to the air or by the blow of a hammer; it can be powdered in a mortar without danger of combustion. It does not now dissolve in bisulphide of carbon; it is comparatively odorless as contrasted with the ordinary form of phosphorus, and in ordinary doses it is not classed among the active poisons. In fact, this new form of phosphorus—for, though physically changed, it is still phosphorus—is as unlike the other as though they were different materials or different elements.

Such rules as these apply to many other elements; in fact, had we determined the qualities of all the elements, we might find that the rule is universal and not exceptional. Metals pass from the amorphous into the crystalline form and the reverse, each state carrying qualities peculiar to itself. Thus the different qualities of aluminum are probably due to the mixtures of crystalline and amorphous aluminums. Let us quote from the *Chemical News*, London, England, May 19, 1916, as follows:

"The amount of cold work which can be done upon aluminum is limited by the formation of the amorphous state. Microscopic examination of polished and etched specimens taken at various stages during cold working shows that the crystalline structure disappears at a very early stage in the working, and unless the metal is annealed it will become fatigued, developing a species 'Forcier-krankheit.' Aluminum which has been subjected to excessive cold work shows an entire absence of structure, and has the appearance of a metal which has flowed and passed into a vitreous state. The reverse change takes place with extreme slowness, and the ordinary annealing process does not change the structure from amorphous to crystalline. Aluminum annealed at a temperature of 500 degrees C. for ten hours appears to be 'dead soft,' and has its maximum elongation; nevertheless, it is still largely amorphous in structure when examined microscopically. Aluminum which has been annealed in this way without affecting the structure, or only slightly altering it, hardens very rapidly when additional cold work is done upon the metal. The

primitive crystals are transformed into the amorphous state much more readily than the larger crystals which are developed by annealing. The results of the specific heat determination render the conclusion probable that under the influence of cold work aluminum is transformed into an amorphous variety. The conclusion is only put forward tentatively, since, at present, there is no means of determining the amount of each phase present in the hard metal, hence the results which have been obtained for hard aluminum are for a metal consisting of a mixture, in unknown proportions, of the two forms of the metal. Long annealing seems to yield a metal in the most definite condition; cast metal is greatly influenced by the casting temperature and rate of cooling."

Consider the varying qualities of such elements as nitrogen and oxygen. Consider the different conditions of gold in its various colloidal forms. Think of all these problems, many of which have been recorded a century or longer, others of which are just beginning to open to view, and then ask yourself the question, "Is not the study of '*qualities*' in pharmaceutical manipulation the dominating field of him who experiments, reasons and accomplishes therein? Is not the man who reasons from such numberless thought outreaches as we have introduced as likely to evolve a beneficial something which may be due simply to a changed physical condition of a well-known compound as is the man who searches in outside lines for useful products among the unknown compounds?"

Indeed, the problems in pharmacy that now most appeal to this writer are not so much in the line of discovering new remedial agents to supplant those now established as to give to the users of medicines the wealth that comes from manipulative pharmacy and balanced research applied directly towards the study of *qualities*.

In research such as this, mass action, structural affinities and colloidal influences become all-important factors. Need we seek modern texts? Are not those of old sufficient? Are not the qualities of active phosphorus, as contrasted with red phosphorus, and of carbon as it appears in graphite, charcoal and the diamond, or of the different forms of nitrogen and oxygen, sufficient to open the door to the pharmacist, who, applying to his own field such distinctions as these, turns his thought to the study of *qualitydistinctions* in his own field?

Can we not now, in a receptive mental position, move into a higher phase of pharmaceutical research than that based upon mere strength as governed by weight and measure of the materials manipulated? Is not higher pharmacy the art of establishing *qualitydistinctions* rather than distinctions in crude materials?

Let us take as a final text the substance known as "silica," which, in

nearly a pure form, constitutes quartz and sand. This substance, in its natural form, is considered to be practically insoluble, but in a colloidal form it becomes actively otherwise. Indeed, in the form of a triturate, carried almost to the mechanical ultimate, silica has long enjoyed a distinctive reputation with careful physicians of both the Homeopathic and Eclectic schools. Turn to "Silica," in Webster's "Dynamical Therapeutics," and note his comments on its use in the form mentioned. Then, as a final touch, read the paper of Dr. S. P. Kramer, contributed to the Research Society of Cincinnati, March 2, 1916, and published in the *New York Medical Journal*, April 8, 1916. These citations will partly, but only partly, prepare one for the results of Dr. Kramer's investigations. Let us quote:

"When solutions of colloidal silicic acid (silica) are injected into the jugular vein of rabbits or dogs, under certain conditions death of the animal occurs by intravascular clotting of the blood."

This indicates that colloidal silica has the power of *producing death*, but the amount employed is not as yet stated. Pass now to the following extract:

"In a typical experiment, a dog weighing ten pounds was killed by the jugular injection of 70 mgm. of colloidal silica in a solution containing 1.4 per cent., the solution being near gelatin—that is, opalescent."

Then ask yourself the question, "How much colloidal silica is carried in this seventy milligrams of colloidal solution, containing 1.4 per cent. of silica?" The amount, expressed in grains, would be 15/1000 of a grain, an amount less than would cover a pencil point. Pass farther along and we find that Dr. Kramer gives next the manner in which death is produced by this minute amount of silica, which, as has been said, differs from sand only by reason of its colloidal quality:

"Animals killed by these injections show the right heart and pulmonary vessels filled with clot. The lungs are infarcted and the acini show the microscopic picture of red hepatization."

Take next the explanation Dr. Kramer subsequently makes of its action on the red blood corpuscles, wherein one part of colloidal silicic acid (silica) is used as a coagulating medium. We find:

"There are other striking reactions *in vitro*. If colloidal silicic acid is added to washed sheep red corpuscles in proportion of 1 to 500,000, or even 1 to 1,000,000, a prompt precipitation of *all red corpuscles takes place*."

Bear in mind that Dr. Kramer is neither a Homeopathic nor an Eclectic physician, but a professional man, fearlessly delving into problems that come to him in connection with his profession. He openly presents to the world this line of experiments, which depend for their phenomena not on material weight, but upon dynamic qualities. His experimental processes throw a new light upon what Dr. Webster, of the Eclectic school and Dr. Dewey, of the Homeopathic school, and others, record concerning the activity of colloidal or micro-divisions of silica. With all this before us, which barely touches the question of qualities that are possible to the multitudes of substances that concern the pharmacist, we may become prepared for a receptive argument regarding the actions of colloidal bodies, because *the study of colloidal activity is primarily a study of different qualities of a material, and is mainly dependent upon different physical states or conditions of the material.*

QUALITY VERSUS QUANTITY—VI.

JOHN URI LLOYD, CINCINNATI, O.

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And now, for the first time in this series, is introduced the long neglected (by the majority) subject of what is now known as "*Colloidal Chemistry*." (I prefer the term structural affinity or mass action. Combinations in this field seem not to be governed by ultimates such as atomic and molecular weights. Valence seems to be ignored.) It may not be out of place to state that only by processes that might be called offshoots of colloidal chemistry had I been able to explain, even to myself, the discord that had come into pharmaceutical work under my laboratory care during the past forty years.

Bunching, therefore, these problems together, I stated, in the article now under consideration, "Quality Versus Quantity," March, 1914, as follows

"Chief among the factors of this liberation of good men from prejudice is the new chemistry known as 'Colloidal Chemistry.' In this 'New Chemistry' the best minds of the world are now studying, although the foundation of the work laid by Graham in the beginning of the last century has been constantly augmented by others in the passing along."

And then, more specifically, as a reply to questions now often asked concerning what colloidal chemistry has in common with plant pharmacy, came the following:

"But, it may be asked, what has this to do with our subject? To such a

question I would reply, 'Everything !' Colloidal chemistry is based upon the fact that *quantity* is but one factor, in many directions that involve both chemical and therapeutic action. The *condition* of a substance is a mighty factor as concerns its action as a *thing*, and necessarily in this case becomes a dominating agent in its therapeutic application."

With an attempt to conciliate instead of offend those who might be hostile to such a view of plant pharmacy, it was next shown that physicians of both the "old school" and the early Eclectic, as well as the Homeopath, had in their practice furnished examples that accorded with the theory of the intensified influences of materials finely divided, as contrasted with mass bulks. Let us quote:

"But even this is not new. Did not the United States Dispensatory record, fifty years ago, that six ounces of mercury swallowed by a man with suicidal intent produced no appreciable action of the mercury, whereas a few grains of mercury, finely divided, forms the active agent, *blue mass*? The first recorded dose of resin of podophyllum was a lump of resin as large as the first joint of the thumb, and from this the patient recovered. Had the remedy been triturated to a fine division, it is safe to say that no human being could have withstood even a portion of that heroic dose. Physicians comprehend full well the increased activity of subdivided substances, such as mineral salts and resins. The works of clinical observers, such as Webster, Scudder, Ellingwood, Fyfe, Felter, Thomas and others of our school testify to this fact, whilst every page of any work devoted to Homeopathic therapy teems with living examples."

Comes now an attempt to distinguish between such materials as have been mentioned and others truly colloidal. (I am not in a position to accept that I can as yet find a line of distinct separation for many substances that shade from mechanical subdivisions into colloidal dispersions. I use the term "colloidal" with this qualifying differentiation.) This needs to have been very brief, but is yet fairly comprehensive. The statement is as follows:

"And yet such powders as these do not comprehend, other than in very minute traces, colloidal dispersion. In these triturates *physical* division prevails (dominates). Colloidal ultimates are practically unreachd. And yet so marked is the energetic increase of a triturated drug as to have established the fact of their intrinsic values in clinical therapy beyond the shadow of a doubt. The quality of a drug depends not alone on the weight of the material; its *physical condition* is all-important."

With this suggestion, designed to bring the reader into harmony with the expressed thought, comes a further attempt to show that physicians, as a rule, have ever recognized the necessity of subdividing their remedies in order to obtain the fullest therapeutic value. For example:

"With this thought in mind, consider how physicians of all schools

direct their prescription mixtures of dry drugs to be made into 'a fine powder.' Note how desirable are the triturates of milk sugar with a selected salt or resin."

And with this illustration before the reader again comes the contrasting of powders such as these with truly colloidal structures, in which therapeutical and physiological problems are connected with "colloidal solutions," a term not before ventured. This is tersely illustrated in a single sentence:

"And yet (in mechanical powders) we have not as yet reached such forms of colloidal structures as stand in liquids without settling; that pass through a filter paper; that are so finely dispersed as to even receive the name 'colloidal solutions.' "

As a final reflection, I presume to ask the readers of this journal, to which this series of articles has been contributed, most of whom listened to my lessons on pharmacy in my twenty-five years or more of teaching in the Eclectic Medical Institute, and who had years ago become familiar with my view of the subject of plant pharmacy and its outreaches, to consider the plea then continually made regarding the many unsolved perplexing factors that concern the investigating pharmacist whose aim is to serve best the medical profession:

"Let me repeat that a consideration of such as this is not new to those who in times gone by have honored me by listening to my lectures. Although the experiments of Graham were used as texts for definitions, we together passed into outreaches that surely will make familiar to those who listened in those days the principles of "colloidal activity,' now looming up as a mighty factor in the evolution of medicine, and which is liberating from bondage the man who believes that quality is not necessarily dependent on quantity, that the factors that confront the pharmacist cannot be fully explained by symbols, formulae and equations."

In the third paper, "Quality Versus Quantity," a plea is made for the consideration of natural structures as well as artificial ultimates broken out of natural structures, it having been time and again argued by me to my classes, as well as in print, that plant structures, as a rule, were inexplicably interlaced, and, when normal, usually (if not universally) colloidal. Time and again, by lecture as well as in print, it was attempted to emphasize that, although *destructive* chemistry yields invaluable ultimates, *constructive* pharmacy has a field to itself:

"The preceding (two) papers of this series consider in a general way the problem of plant structures, the aim being to suggest that to ignore natural

structures is to neglect an opportunity in pharmacy. That whilst the ultimates broken out of structures are of value in therapy, the structures yielding the ultimates are possessed of qualities that in many directions make them superior to the artificial products.

"It may be reasoned, also, and very consistently, that to dispossess a natural drug-texture of its colloidal qualities is to alter its condition other wise than physically. In this we believe. And in this direction we believe the art of pharmacy will yet evolve until its recognized importance will be established to all concerned in both chemistry and therapy."

But again comes the repeated plea that such as this be not considered as a reflection, in any way, upon the efforts of investigators in other directions; indeed, the hope is expressed that when these problems are taken up by the systematically talented scientist the opening view of plant structures would become a most intensely interesting and useful study. For example:

"Let us again repeat that in such as this no reflection is placed on either the analytical or synthetical chemist. Upon the contrary, we believe that the time will come when chemistry will recognize the fact that the *beginning* of this study is the consideration of such problems as may be expressed by the formulae. In a time to come will also follow a scientific comprehension of the pharmacist's structures now beyond the eyes of the talented men engaged in the study of the products broken out of these, as yet, voidless and formless colloidal bodies.!"

The four pages of 8-point type that followed the above were reproductions of previous prints by the author, in which plant pharmacy was viewed from many different angles, all tending to illustrate that a mighty field of opportunity lay before the pharmacist who, intelligently and with an open mind, would enter into the problems that would surely become of increasing interest in the pharmacist's life of the future.

THE END.

It will be observed that many repetitions are to be found in the article as a whole. An effort was made to condense and re-arrange the subject matter so as to make a continuous article as free as possible from repetition, but the task proved to be greater than would appear to the casual reader, so it was decided to let each article stand alone as it was consecutively printed.

The author intended to present this booklet to a few of his pharmaceutical friends and correspondents. However, an attempt to do this resulted in discouragement. He could not differentiate in a society where he hopes all are friends.