

THE
AMERICAN
JOURNAL OF PHARMACY

PUBLISHED BY AUTHORITY OF THE

PHILADELPHIA COLLEGE OF PHARMACY

EDITED BY

HENRY KRAEMER

PUBLICATION COMMITTEE FOR 1910

SAMUEL P. SADTLER

M. I. WILBERT

JOSEPH W. ENGLAND

FLORENCE YAPLE

JOSEPH P. REMINGTON

CHARLES H. LAWALL

AND THE EDITOR

VOLUME 82

PHILADELPHIA

1910

weight, while the "Verduenter Weingeist" of the German Pharmacopœia contains 60 to 61 per cent. by weight of alcohol. In this test the sugar of milk is digested with diluted alcohol and the filtered liquid should remain clear after mixing with equal volume of absolute alcohol, and if evaporated on a water-bath there should not be a greater residue than 0.03 Gm.

From all the foregoing it would seem that further study must be given to the Pharmacopœia. While it is desirable that a high standard should be set for all medicinal chemicals, in accordance with the steady advance of modern times, yet the requirements should not be fixed on a plane beyond practical attainment, and such tests for purity as may be established should be so well proven that they will show the correct result when properly applied.

HISTORY OF MACERATION AND PERCOLATION.*

BY OTTO RAUBENHEIMER, PH.G., Brooklyn, N. Y.

In connection with this symposium held at the oldest College of Pharmacy in the U. S. it occurred to me that a historical sketch on maceration and percolation might be of interest to the members.

MACERATION.

Etymology of the word: In Latin it is *maceratio*, the art of soaking, derived from *macero*, to make soft, to soak, which again is derived from *macer*, lean or meagre.

This process has been in use from times immemorial.

The earliest known solvents in ancient times, besides water, were wine and wine vinegar.

Wine, as we all know, has been and is to-day used as a beverage by all nations, with the exception of the Mohammedans, being prohibited by the Koran on account of its intoxicating properties. (I am, however, informed that the Sultans drink champagne, which they do not consider as a wine.) As a medicine, wine has been and is to-day used over the entire world, and medicated wines have been employed in ancient times and continue to hold their place in the various pharmacopœias of the present.

* Read at the November Pharmaceutical Meeting, Philadelphia College of Pharmacy.

The most important solvent in classic times was undoubtedly vinegar, obtained through the acetic fermentation of wine. The ancients had the most extravagant ideas with regard to the solvent power of vinegar, not only upon vegetable but even upon mineral substances, as may be gathered from the concordant statements of Livy and Plutarch that Hannibal, the celebrated Carthagenic general, in his passage across the Alps, cleared the way of rocks by means of vinegar. I might also quote here the story which Pliny tells of Cleopatra, who in fulfilment of her wager to consume a million sesterces at one meal, dissolved some costly pearls in vinegar and drank the solution.¹

The acid plant juices were assumed by the ancients to contain vinegar, and naturally medicated vinegars were prepared by maceration and are still official in the present pharmacopœias. The Father of Medicine, the Greek physician Hippocrates, in the 5th to the 4th century B.C., already prepared acetum scillæ, vinegar of squill.²

You will ask why did the ancients not use alcohol, the great solvent, and macerate therein the various drugs, etc.? My answer to this is, that, strange as it may seem, alcohol was unknown in ancient times. Not until about 1100 is the distillation of spirit from wine mentioned by Khalaf-Ebn-Abbâs Abul Kasan. Raimundus Lullus (1235-1315) named this spirit "Aqua Ardens," from ardere, to burn, burning water, a name still in use as the "Branntwein" of the Germans and the "fire water" of our Indians. A very important event in pharmaceutical history is, that Lullus was the *first* to prepare tinctures and quintessences by macerating the different drugs in spirit.³

But not until the 16th century did these preparations come into more general use through Phillipus Aureolus Paracelsus Theophrastus von Hohenheim, that much abused and envied physician-pharmacist, chemist, philosopher, and theosoph, the founder of iatro-chemistry (medical chemistry), which in contrast to alchemy opened new paths in chemistry and medicine by joining these two sciences. Paracelsus gave a tremendous impetus to the higher development of the apothecary's calling by his generous additions of chemicals as well as tinctures, essences, and quintessences to the *materia medica*. Before his time apothecary shops were nothing more than stores for roots, herbs, syrups, plasters, cerates, and especially confections. The service which Paracelsus rendered in instigating physicians and apothecaries to busy themselves with

chemistry, etc., was indeed a great one, and A. N. Scherer in his memoir "Theophrastus Paracelsus" (St. Petersburg, 1821) rightly says: "Pharmacy owes *everything* to Paracelsus."

In olden times the apothecary collected his own drugs, roots, herbs, flowers, etc., in the proper season, and he himself prepared his waters and spirits by distillation and his tinctures by maceration. The collection of drugs by the apothecary kept him in touch with botany and pharmacognosy and was especially very educational to the young pharmacist and is far superior to the selling of herbs, flowers, and even roots of *doubtful value* in *pressed packages*, as practiced by the average druggist of to-day. The old apothecary carried on this maceration in glass bottles or jars in the front window of his shop, so that the sun would strike and thereby warm the preparations. The resulting different colored tinctures very correctly can be styled as giving origin to the colored show bottles in our windows to-day.

I beg to remind the users and advocaters of maceration that agitation must not be forgotten, and I know as a fact that it is very often forgotten in this process. For obvious reasons frequent agitation, at least once a day, is essential. It might be of interest to learn that the second edition of the Netherland Pharmacopœia 1871, in the preparation of its tinctures even ordered *continual* agitation ("agitatio continua") for *7 to 28 days!* If our admirers of this so-called *simple* and *labor-saving* maceration would have to practice the Dutch method, then I believe they would soon reach a different conclusion.

Expression must necessarily go hand in hand with maceration, especially in the case of bulky drugs, as f. i. arnica flowers, in order to remove the liquid from the marc as much as possible. This, however, can never be accomplished entirely, and the retention of *strong* menstruum in the marc and the resulting indefinite finished preparation are the chief objections to the process of maceration. To overcome these, several pharmacopœias, the Hungarian, the Rumanian, the British, and the U. S., order the expressed marc to be remacerated with menstruum and then to be expressed again so as also to obtain a definite quantity of the finished preparation, as f. i. in Tinctura Arnicæ U.S.P. VIII. As the resulting liquid will be very turbid it must, last of all, be filtered. So you can readily see that the so-called simple process of maceration consists of maceration, agitation, expression, remaceration, and filtration, not so simple after all.

The *disadvantages of maceration* can be briefly summed up as follows: (1) the shaking; (2) the expressing and filtering; (3) the retention of strong menstruum in the marc and the indefinite finished product. The *advantages of maceration* are said to be: (1) the drug does not have to be a fine and uniform powder; (2) the process requires less skill and care in the manipulation than percolation; (3) there is less loss of alcoholic menstruum than by percolation.

Before leaving the subject of maceration I will say a few words about digestion, not Cleopatra's digestion, as cited before, but *pharmaceutical* digestion. Latin: digestio, derived from digerere, to distribute, which is a maceration carried on at a higher degree of temperature. Some of the pharmacopœias specify the temperature as:

	Ph. Ned. IV	Ph. Aust. VIII	U. S. P. VIII
Maceration	15°-25°	not over 20°	15°-20° in a shady place.
Digestion	35°-45°	not over 50°	
Infusion	90°-98°		

If a higher temperature is employed, as in the case of Warburg's tincture N.F. III (65°), it is best to attach an upright or reflux condenser or simply a glass tube about 4-6 feet long, so as to prevent the loss of alcohol.

PERCOLATION.

Etymology: per, through, and colare, strain.

A vast volume of literature exists on this interesting subject, and the brightest minds of all nations have spent a "lifetime of labor" in trying to perfect percolation and to enlighten us. Among these the following deserve special mentioning: Boullay, Robiquet, Guillermond, Pelletier, Pelouze, and Soubeiran of France, where percolation is said to have been originated, which, however, I find to be fallacious; Redwood, Proctor, Maben, and Ince, of Great Britain; Dieterich, Geiger, and Marpmann, of Germany; Duhamel, Procter, Parrish, Grahame, Squibb, Diehl, Oldberg, Lloyd, and Remington, in the United States. The American Pharmaceutical Association and the Philadelphia College of Pharmacy are to be congratulated upon the many faithful workers, whose contributions on percolation have been published in the Proceedings of the A.Ph.A. and first of all in the AMERICAN JOURNAL OF PHARMACY.

The oldest forerunner of percolation was undoubtedly the *lixivation* (from lix, ash) of the ashes of plants. Aristotle, of Athens,

384–322 B.C., the celebrated Greek philosopher and founder of the peripatetic school, already described this process of obtaining crude potash. According to the plants used the resulting salt—*Sal lixivius*—was named as *Sal absinthii*, *Sal cardui benedicti*, etc. Lixiviation or leeching (German—*Auslaugen*) has been extensively practiced in various technical industries ever since. Even to-day the new Spanish and French pharmacopœias give the percolation process the name lixiviation and the French Codex devotes two and a half pages (383–385) under the title “Lixiviation.”

In 1746 Comte Claude-Toussaint-Murot de la Garaye (1675–1755) published a work in Paris: “*Chymie hydraulique pour extraire les sels des végétaux, animaux et minéraux par moyen de l'eau pure*,” in which he advocated and described the extraction of powdered vegetable drugs, etc., with water. “Sel” was not merely the name for a chemical salt but also for an extract or active principle, as can be seen by the old synonym “*Sal essentielle tartari*” which stands for tartaric acid. One of the products of the chemical and pharmacological studies and researches of this French physician and philanthropist was the preparation of the so-called “*Sal essentielle de la Garaye*,” which was a dry cinchona extract.⁴ But already in 1672 the German “Chymicus,” Joel Langelot or, as it was customary those days, Latinized to “Langelottius,” the alchemist and Court physician to the Duke of Schleswig-Holstein, recommended the very same method and also constructed a “philosophical mill” described by Joh. Christ Wiegleb, *Geschichte des Wachstums und der Erfindungen in der Chemie* (Berlin and Stettin, 1791–1792). This is by rights the forerunner of the method of displacement.

Benjamin Thompson, Count of Rumford, a born American (at Rumford now Concord, N. H.), who deserves special credit for being the first to ascertain that liquids can be boiled by means of steam, used a method of preparing coffee, resembling our present percolation, which he described in his 18th essay in *Repertory of Arts*, April and May, 1813.

In 1817 C. Johnson applied this principle to the extraction of cinchona bark in England, saying: “The machine I use is similar to the one made several years ago by Edmund Loyd & Co., 178 Strand, London, and does not differ essentially from any of those described by Count Rumford. In the Lancaster public dispensary this method is found to yield a better preparation than was formerly obtained from twice the quantity of cinchona bark” (*Annals of Philosophy*, ix, p. 451).

In 1816 the French Count Réal invented a hydrostatic extraction press or pressure percolator in which the drug is held in place by perforated disks and the solvent, contained in a tube twelve feet high, is forced through by its own pressure. Réal's process and apparatus are described in *Annalen der Pharmacie*, vol. xv, p. 80, also in Buchner's *Repertorium* and in Soubeiran's *Traité de Pharmacie*, the German translation by Schoedler which I have here for your inspection devoting seven pages (pp. 123-129) to this subject. On pages 127 and 128 the fineness of the powder and the method of packing are described by Soubeiran and the German pharmacist Geiger. Philip Lorenz Geiger, the discoverer of a number of alkaloids, as coniine, atropine, hyoscyamine, aconitine, and colchicine, also wrote a little book, *Réal's Aufloesungspresse*, Heidelberg, 1817.

A very important point in Réal's process is that he recommended to macerate the ground drug with 50 per cent. menstruum for several hours before packing it in the apparatus. No doubt the Réal process smoothed the way for the coming percolation method.

In 1834 the French pharmacist Theophile Jules Pelouze employed the process of displacement in his laboratory by extracting nutgalls in the preparation of tannic acid.

In 1835 the French pharmacist Boullay and son (the father discovered picrotoxin in 1818) published in the *Journal de Pharmacie*, vol. 21, pp. 1-22, their paper: "Considerations nouvelles sur la méthode de déplacement,"⁶ giving the experience of Soubeiran, Limonin, Boudet, Buchner, Dublanc, Pelletier, and Pelouze. In the same journal, p. 113, Robiguet criticizes Boullay's claims to priority, having used the méthode de déplacement for five to six years in his laboratory and factory. I beg to point out that in Boullay's method the drug was put dry into the apparatus.

Dr. Fr. Schoedler, the translator of Soubeiran's *Traité de Pharmacie*, states, p. 115: "The science of pharmacy has *not* been enriched through the much praised méthode de déplacement of M. Boullay nor through the experiments of Guillermond. The principle and application of their method are the same as the Réal process, which has been in use over twenty years."

An abstract of the paper of M. A. Guillermond, was reported as early as 1836 in the AMERICAN JOURNAL OF PHARMACY, vol. vii, p. 308, and I am glad to state that this JOURNAL of the Philadelphia College of Pharmacy has been the recipient of the largest portion of the literature on percolation ever since.

In 1838 the Philadelphia pharmacist, Augustine Duhamel, published in the A.J.Ph., vol. x, pp. 1-17, an essay, "Boullay's Filter and System of Displacement with Observations drawn from Experience." Duhamel deserves special credit, as he was the first to present this subject to the American pharmaceutical profession.

In 1839 A. Duhamel and Wm. Procter, Jr., published in the A.J.Ph., vol. xi, pp. 189-201: "Observations on the Method of Displacement," in which paper they state that in France this method is extensively applied and was *made official* in the *Codex 1835*, but in the U. S. it is hardly known, much less applied, and they make a plea for its introduction into the next U.S.P. And it was introduced into the U.S.P. 1840, which authority states in the preface: "As to the *kind of filtration commonly called displacement*, it is strongly recommended to those who have not made themselves practically familiar with the various sources of error in the matter of displacement to postpone its application whenever an alternative is given in this work, until they shall have acquired the requisite skill."

In 1840 this process was also sanctioned by the Edinburgh Pharmacopœia, which states: "A much superior method has been introduced which answers well for most tinctures—namely the *method of displacement by percolation*." This is the first mentioning of percolation, which word is used instead of displacement. Quite a dispute arose which pharmacopœia adopted percolation first. As a matter of fact it was made official in both pharmacopœias in their edition of 1840, but the U.S.P. 1840 did not appear until 1843 and the Edinburgh Pharmacopœia 1840 was published in 1839.

As we have seen before Réal moistened the ground drug with half its weight of menstruum, Boullay used the dry powder, and the Edinburgh Pharmacopœia moistened it sufficiently with menstruum to form a thick pulp.

The British Pharmacopœia of 1864 in which percolation was introduced gives the following, according to Ince *very unsatisfactory*, general directions: "Macerate for forty-eight hours in three-quarters of the spirit in a closed vessel, agitating occasionally; then transfer to percolator and when fluid ceases to pass, continue the percolation with the remainder of the spirit." Such an authority as Ince criticizes this method as *unnecessary, wasteful, and messy*. As this combination method is even used to-day by some druggists, I hope they will consider these criticisms and discard this process in favor of the up-to-date percolation method.

Before the A.Ph.A., in 1858, Prof. Israel G. Grahame read an excellent paper: "The Process of Percolation or Displacement, its History and Application to Pharmacy,"⁶ in which he makes the following remarks which still hold good to-day: "If I have a just conception of the principle upon which it is based, it is, that the substance to be treated and the menstruum should be presented to each other under such circumstances, that *each particle of the solvent shall be fully charged with soluble matter and immediately displaced with another particle*, to become in its turn saturated in a like manner; and if all the conditions of the process have been properly observed, these saturated particles collect and escape from the apparatus, and contain to the fullest possible extent all that the *menstruum is capable of taking up and even more than could be taken up by any other means.*" Prof. Grahame, aside from suggesting the use of the funnel as a percolator, deserves credit for advocating the use of powdered drugs of regular and definite degree of fineness, as well as the proper moistening before packing it in the percolator; both of these suggestions are even now considered indispensable to successful percolation.

A committee of the A.Ph.A., consisting of E. Parrish, I. J. Grahame, and C. T. Carney, presented a report on percolation at the 1859 meeting, giving an account of the introduction of the *kind of filtration commonly called displacement* into U.S.P. 1840, its extended use in U.S.P. 1850, and a proposed general description of *percolation* for U.S.P. 1860.⁷

Four pages (pp. 3-6) are devoted to percolation by U.S.P. 1860, "The kind of filtration known as percolation or the process of displacement," the use of a funnel being also permissible and the uniform powder being moistened with one-quarter to one-half its weight of the menstruum. In U.S.P. 1870 we find the same general description (pp. 3-6), with the exception that the powder is to be moistened with a *specified quantity* of the menstruum. In U.S.P. 1880 and 1890 this chapter has been improved by giving more explicit directions, by passing the moistened powder through a sieve, by the attachment of a long rubber tube to the percolator to regulate the flow, by directions to percolate the dregs of a tincture, and by authorizing repercolation in the preparation of fluidextracts. In U.S.P. VIII this chapter has been further improved by dividing it into distinct paragraphs, as percolators, the process, repercolation, rate of flow, and maceration, stating under the latter that percolation

is not suitable for exhausting some drugs and that the process of maceration is employed for some of the tinctures as aloes, asafetida, sweet orange peel, etc.

U.S.P. VIII has made a number of improvements in the manipulation of the percolation process. The quantity of menstruum to moisten the drug has been reduced, f. i. tinct. hydrastis: U.S.P. 1890 used 150 c.c., and U.S.P. VIII only 60 c.c.; tinct. cinchon co. U.S.P. 1890 used 200 c.c., and U.S.P. VIII only 80 c.c. Furthermore the U.S.P. 1890 directed to macerate the moistened drug for twenty-four hours and then pack it in the percolator and proceed with percolation. The U.S.P. VIII has made a great improvement in the macero-percolation process by directing to transfer the moistened drug to the percolator and, without pressing, allow it to stand, well covered, for six or in some cases twelve hours, then pack it firmly, pour on the menstruum, and when the liquid begins to drop close the lower orifice and macerate again from twenty-four to forty-eight hours and then allow the percolation to proceed slowly, in the case of tinctures from eight to fifteen drops per minute. This rate of flow in the new Swiss Pharmacopœia is twenty drops per minute, in the new Austrian Pharmacopœia thirty drops, and in the German Pharmacopœia (under *extracta fluida*) forty drops per minute. The new French Codex states that the twenty-four hours' percolate should weigh about one and a half times the amount of drug employed.

The fruitful work which Dr. E. R. Squibb has done as to percolation requires no further comment.

Repercolation or fractional percolation as called by Prof. Diehl was introduced by Squibb in 1866 with the object of saving alcoholic menstruum and to prepare strong solutions, as fluidextracts, without the application of heat. The origin of fluidextracts is generally credited to American pharmacy, and the work of Grahame,⁸ Procter,⁹ Squibb,¹⁰ and others is well known. The U.S.P. 1850 recognized seven fluidextracts, 1860, twenty-five, 1870, forty-six, 1880, seventy-nine, 1890, eighty-eight, and U.S.P. VIII, eighty-five, now under the official title "*Fluidextractum*." Besides this, fluidextracts have become official in almost all pharmacopœias and are recognized as "*liquid extracts*" in the British Pharmacopœia.

Percolation is also gradually but steadily replacing maceration in the foreign pharmacopœias. Chapters on percolation, similar to the U.S.P. process, are adopted in these books and general formulas

for fluidextracts and tinctures are given. The greatest victory, however, which percolation has gained is its recognition by the Brussels International Conference for the Unification of Pharmacopœial Formulæ for Potent Medicaments, a copy of which can be found in that excellent "Digest of Comments on U.S.P.", Bulletin No. 49, Hygienic Laboratory, by Murray Galt Motter and Martin I. Wilbert, pp. 64-68. Article 2, b, of the Protocol states: "Tinctures of potent drugs shall be prepared of the strength of 10 per cent. and by *percolation*." September 20, 1902, the day on which this agreement was signed, will be a memorable one in the annals of pharmacy—it marks the advent of a new era, the attainment of attempts covering nearly fifty years to unify the formulæ for potent medicaments throughout the world. It might be of interest to learn that when this Protocol was signed again by the duly authorized representatives of the various governments on November 29, 1906, at the Belgian ministry for foreign affairs, the Swedish government formulated the following reservation: "As the preparation of tinctures of drugs by percolation involves an increase in the price of these products, this method seems not altogether suitable for employment in a general manner in Sweden."

In connection with this subject it might be of interest to learn that the new Austrian and Swiss Pharmacopœias order tincture of opium to be prepared by maceration instead of percolation, the latter authority calling attention to this in a footnote. The new French Codex, by the way, orders this tincture to be prepared by dissolving 5 Gm. of extract of opium in 95 Gm. of 70 per cent. alcohol. Our U.S.P. VIII seems to have solved this problem in an excellent manner, by first extracting the opium with boiling water, then macerating in diluted alcohol, and lastly percolating.

In summing up I want to say that the disadvantages of maceration, *i.e.*, the shaking, expressing, and filtering, the retention of strong menstruum in the marc, and the indefinite quantity and strength of the finished product, are the principal advantages of percolation. The advantages of maceration are very little indeed. The uniform fineness of the ground drug used in percolation can be easily regulated by the sieve. The necessary skill and care in the manipulation of the percolation will certainly be acquired by the college teaching and principally by the practical experience, and I beg to remind you that the clerk who cannot conduct percolation properly ought not to be employed. As to the increased loss of alcoholic

menstruum by percolation, being left in the marc, the same can be expressed, distilled, or displaced by water.

In my experience the percolation process, and especially the improved macero-percolation method of our U.S.P. VIII, although the same cannot be used for the exhaustion of all drugs, decreases the labor and saves time and is a scientific method par excellence. When properly carried on all the advantages of maceration are obtained and furthermore it is superior to maceration, inasmuch as no strong menstruum is retained in the marc.

In conclusion I want to state that, although percolation has been originated in a foreign country, American pharmacists have greatly perfected this process and American pharmacy can justly be proud of it.

BIBLIOGRAPHY.

- ¹ Meyer-McGowan, History of Chemistry, 1906, p. 21.
- ² Schelenz, Geschichte der Pharmazie, 1904, p. 104.
- ³ *Ibid.*, p. 328.
- ⁴ *Ibid.*, p. 566.
- ⁵ Journal de Pharmacie, 1835, vol. 21, pp. 1-22.
- ⁶ Proc. A.Ph.A., vol. 7, pp. 285-294, and A.J.Ph., vol. 31, p. 354.
- ⁷ *Ibid.*, vol. 8, pp. 220-239.
- ⁸ *Ibid.* 1858.
- ⁹ *Ibid.*, 1863, vol. 11, pp. 222-248.
- ¹⁰ *Ibid.* and Percolation by Brandel and Kremers, Ph. Review, 1906, p. 363, 1908, p. 270.

MAHLON N. KLINE.

Mahlon N. Kline, President of the Smith, Kline & French Co., wholesale druggists, Philadelphia, died suddenly of heart failure on Saturday evening, November 27, while attending a meeting of the Brotherhood of St. Andrew at the Church of the Saviour, Philadelphia. Mr. Kline was so long and so intimately associated with the drug trade, both wholesale and retail, and did such excellent work in connection with drug and pharmaceutical matters that his death will be felt as a distinct loss to the industry.

Of all his other affiliations it may truly be said that none were of more deep concern to him than his relations with the Philadelphia College of Pharmacy, and his work as a member and officer reflects credit alike on his ability and loyalty to its interests. He was elected an active member in 1886 and a member of its Board of Trustees in 1897, of which latter body he became Chairman in 1901. He was elected First Vice-president of the College in 1905,