adoption of boundaries, and we have increasing confidence that further chance for definite improvement of the names by adjustment of the boundaries is slight. It is hoped, however, to enlist the aid of those who are interested in the color names used in the description of drugs and pharmaceuticals to give the present tentative systems of boundaries a final check before adopting it.

A summary of the work on powdered crude drugs has been prepared. This summary gives for each powdered drug the color name now included in the National Formulary monograph, then it gives the color name or names found from the present tentative system together with the number of samples examined. Copies of this summary are available now to all who wish them.[1] Criticism is invited of the color names yielded by the present system. If, for example, you believe from your knowledge of drugs that the term, weak Olive-Green, would be a more accurate description of Adonis than pale Olive-Brown, we hope that you will so inform us. New color names cannot be added to the system, but the boundaries can be adjusted so that another of the listed names could be applied to a given drug. Our judgment as to appropriate names has been based a good deal on the present names to be found in the National Formulary. The aim is to make available a system of color names having legal and scientific standing and, at the same time, a system which will accord with present usage of color names as much as possible. Criticisms will help to do this. They should be submitted either to the AMERICAN PHARMACEUTICAL ASSOCIATION or to the National Bureau of Standards where they will receive our interested attention.

DRUG EXTRACTION. XVII. MODIFIED REPETITION DIACOLATION.*[,1]

BY WILLIAM J. HUSA[2] AND C. L. HUYCK.

Using powdered belladonna root, experiments have been conducted to determine the efficiency of a modified repetition diacolation process as compared with the U. S. P. XI percolation and fractional percolation processes for making fluidextracts.

HISTORICAL REVIEW.

Introduction of Repetition Diacolation.—In 1930, H. Breddin (1) of Germany described a repercolation process which he called "repetition diacolation." He reported that by this method he obtained 300 Gm. of fluidextract from 300 Gm. of menstruum and 300 Gm. of drug. Glass tubes about one-half meter in length and 3.3 cm. in width were employed as percolators. To conserve alcohol, water was used in each tube toward the end of the percolation to displace the menstruum held by the marc. The 300 Gm. of drug were divided into three 100-Gm. portions. The first portion of drug was extracted with 200 Gm. of menstruum, the first 50 Gm. of percolate being reserved. The next 150 Gm. of percolate and 50 Gm. of

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[1] This paper is based on part of a dissertation presented to the Graduate Council of the University of Florida by C. L. Huyck, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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fresh menstruum were used to extract the second portion of drug, the first 50 Gm. of percolate again being reserved. The next 150 Gm. of percolate and 50 Gm. of fresh menstruum were used to extract the third portion of drug, a reserve percolate of 200 Gm. being collected. The reserves were united to make 300 Gm. of finished fluidextract.

Advantages of Repetition Diacolation.—The advantages of repetition diacolation over simple percolation were stated by Breddin (2) as follows: (*a*) economy of menstruum, (*b*) avoidance of distillation and (*c*) prevention of formation of capillary passages in the packed drug by use of cylindrical tubes as percolators. Breddin (3) also made other claims of superiority of cylindrical tubes over conical percolators. It was stated (4), (5) that by the avoidance of heat, repetition diacolation produced fluidextracts having a better odor and taste than those made by simple percolation. Breddin (6) reported that in the preparation of tinctures, repetition diacolation had an advantage over maceration in eliminating the use of a metallic tincture press, which caused contamination with tannin-bearing drugs.

Disadvantages of Repetition Diacolation.—According to H. Ihbe (7) the disadvantages of Breddin's process were found to be as follows: (*a*) full extraction was not attained in the last tube, (*b*) close observation was needed in collecting the weak percolate, (*c*) difficulty was encountered in estimating the volume of the moistened drug for the selection of tubes of the proper size.

Drugs upon Which Repetition Diacolation Was Tested and Results Obtained.—Breddin (8), (9) reported that repetition diacolation was successful in the extraction of ergot, condurango, orange peel, valerian, male fern, sabadilla, cinchona, cinnamon, digitalis and cantharides. Rademacher (10) made fluidextract of thyme by this process and stated that, on the basis of active constituents present, it clearly surpassed the fluidextract made according to the German Pharmacopœia. Gstirner (11) reported that fluidextract of ipecac made by repetition diacolation was superior in content of alkaloids and extractive matter to fluidextracts made by the pharmacopœial processes of Germany, Switzerland, Denmark, Sweden, Great Britain and the United States. It was stated by Madsen (12) that in the case of thyme, valerian and senega the fluidextracts made by repetition diacolation contained more extractive matter than those made by either simple percolation or repercolation. Brandrup (13) found that repetition diacolation produced a slightly better fluidextract of thyme than simple percolation. It was reported by Reinicke (14) that fluidextract of senega made by repetition diacolation was superior to fluidextracts made according to the pharmacopœias of Switzerland and the United States.

Variations of Repetition Diacolation.—A modification of repetition diacolation was described by Ihbe (7). In his procedure 600 Gm. of drug were divided into three equal portions. The first two tubes were provided with stop-cocks and all three were arranged so that the percolate would flow by gravity from one to the other. The first portion of drug was moistened with 45 Gm. of menstruum, the second with 67 Gm. and the third with 88 Gm. From the three portions of drug the quantities of reserve percolate collected were 45 Gm., 67 Gm. and 488 Gm., respectively. The reserves were mixed to make a total of 600 Gm. of fluidextract from 600 Gm. of drug. Ihbe stated that a one per cent solution of sodium chloride and mixtures of various organic solvents, such as acetone, chloroform and benzin,

when adjusted to the same specific gravity as that of the menstruum, were suitable for displacing the menstruum from the marc. Fluidextracts of ergot, senna and bitter orange were made by this process by Ihbe (7).

Breddin varied his process at times in different ways. In some cases he used four or five tubes, and sometimes he mixed the drug with kaolin or finely clipped cotton. Denatured alcohol and benzene colored red with a dye were used to displace the menstruum in some cases (15).

In the preparation of fluidextract of thyme, Rademacher (10) evacuated the receiver when the flow was not sufficiently rapid.

EXPERIMENTAL PART.

Preparation of Fluidextract of Belladonna Root by a Modified Repetition Diacolation Process.—In applying the repetition diacolation process to belladonna root in the present study, certain modifications were made. From previous results of the present authors (16) it was obvious that sufficient menstruum was not used in repetition diacolation to thoroughly exhaust belladonna root. For this reason the process was modified by collecting twice as much weak percolate as was recommended by Breddin. Furthermore, the menstruum remaining in the drug near the end of the percolation of each portion of drug was not displaced by water as was done by Breddin.

As directed in repetition diacolation, heavy-walled glass tubes were used as percolators, the dimension being as follows: length, 65 cm.; thickness of wall, 5 mm.; internal diameter, 4.1 cm. The lower end of each tube was fitted with a one-holed rubber stopper which was channelled so as to allow suitable drainage. The flow was regulated by use of a screw clamp.

The drug used was moderately coarsely powdered belladonna root from a 100-lb. portion previously described (16). The menstruum was a mixture of four volumes of alcohol and one volume of distilled water. The procedure, which was carried out in duplicate, was as follows. A 750-Gm. portion of drug was divided into three equal portions. The first 250-Gm. portion of drug was moistened with 62.5 cc. of menstruum, transferred to a percolator tube and allowed to stand for about fifteen minutes. The drug was then packed from the top, saturated with menstruum and allowed to macerate for about two days. Percolation was then allowed to proceed, a reserve percolate of 125 cc. and five successive 150-cc. portions of weak percolate being collected. The second portion of drug was treated in the same manner, with the exception that the various fractions of weak percolate in the order of collection were used as menstruum, followed by sufficient fresh menstruum to allow collection of 125 cc. of reserve and five 150-cc. fractions of weak percolate. The third portion of drug was then percolated with weak percolate from the second portion of drug and a reserve percolate of 500 cc. was collected. The three reserve portions of percolate were then mixed to yield 750 cc. of fluidextract from 750 Gm. of drug.

In each case the volume of the packed drug was about 650 cc. and the height of the drug column was about 47.5 cm. When menstruum was poured on the first portion of packed drug the liquid reached the lower orifice in about $7^1/_2$ hours, while in case of the second and third portions of drug 16 to 18 hours were required for the liquid to reach the lower orifice. The greater length of time required for the menstruum to flow through the drug in the latter portions is doubtless due to the greater viscosity of the weak percolate used as menstruum as compared with fresh menstruum used for the first portion; the same phenomenon was observed in other fractional percolation processes previously reported. The rate of flow of percolate was about 1.2 to 1.4 cc. per minute. Analytical data are given in Table I.

TABLE I.—ANALYTICAL DATA ON FLUIDEXTRACTS OF BELLADONNA ROOT PREPARED BY MODIFIED REPETITION DIACOLATION.

	Gm. Alkaloids in Percolates.		Gm. Total Extractive in Percalates.	
	Exp. A.	Exp. B.	Exp. A.	Exp. B.
First reserve 125 cc.	1.4	1.4	21.6	19.4
Second reserve 125 cc.	1.5	1.4	25.2	24.4
Third reserve 500 cc.	1.7	2.1	65.9	72.4
Total 750 cc.	4.6	4.9	112.7	116.2
Total calculated on 1000 cc.	6.1	6.5	150.3	154.9

In previous work (16) fluidextracts of belladonna root made from the same shipment of drug used in the present study contained 5.8 Gm. of alkaloids per L. when made by U. S. P. percolation and 5.7 Gm. of alkaloids when made by U. S. P. fractional percolation. Since the average content of alkaloids in the fluidextracts made by modified repetition diacolation was 6.3 Gm. per L., it is apparent that this process is more efficient for the extraction of the alkaloids of belladonna root than the U. S. P. XI processes.

Modified Repetition Diacolation with Oldberg Percolators.—In comparing repetition diacolation with U. S. P. fractional percolation it is seen that there are two main points of difference: (*a*) the type of percolator used, and (*b*) the relative quantities of drug in the various portions. Accordingly an experiment was carried out using the same proportions of drug and the same scheme of collection of percolates as in modified repetition diacolation, but using Oldberg percolators in place of cylindrical glass tubes. This experiment was intended to show whether the more favorable results obtained in modified repetition diacolation were due to the apparatus or to the proportions of drug and percolates.

Since the percolators, when two-thirds full, were found to hold more drug than the tubes, portions of 333.3 Gm. of drug were used instead of the 250-Gm. portions employed in the previous experiment. The method used was the same as in the preceding experiment.

The entire process was conducted in duplicate. The volume of packed drug was 800 cc. and the height of the drug column was 20.5 cm. The liquid reached the lower orifice in about 1¼ hours in the first portion and in about 6 to 7 hours in the second and third portions. The rate of flow was about 1.2 to 1.6 cc. per minute. Analytical data are given in Table II.

TABLE II.—ANALYTICAL DATA ON FLUIDEXTRACTS OF BELLADONNA ROOT PREPARED BY MODIFIED REPETITION DIACOLATION USING OLDBERG PERCOLATORS.

	Gm. Alkaloids in Percolates.		Gm. Total Extractive in Percolates	
	Exp. C.	Exp. D.	Exp. C.	Exp. D.
First reserve 167 cc.	1.7	1.7	23.7	21.3
Second reserve 167 cc.	1.9	1.8	25.7	26.1
Third reserve 666 cc.	2.5	2.6	99.7	99.7
Total 1000 cc.	6.1	6.1	149.1	147.1

In order to obtain a better comparison of the results of Tables I and II, the results of Table I were recalculated on a basis of 1000 cc. of fluidextract and averages were taken of the duplicate experiments. The comparative results are given in Table III.

TABLE III.—COMPARISON OF CYLINDRICAL TUBES AND OLDBERG PERCOLATORS IN MODIFIED REPETITION DIACOLATION.

	Gm. Alkaloids in Percolates.		Gm. Total Extractive in Percolates.	
	Cylindrical Tubes.	Oldberg Percolators.	Cylindrical Tubes.	Oldberg Percolators.
First reserve 167 cc.	1.9	1.7	27.4	22.5
Second reserve 167 cc.	1.9	1.9	33.2	25.9
Third reserve 666 cc.	2.5	2.5	92.0	99.7
Total 1000 cc.	6.3	6.1	152.6	148.1

From the results in Table III, it appears that there is a slight advantage in favor of cylindrical tubes. The total extractive was removed from the drug somewhat more rapidly in the tubes. The alkaloids were apparently extracted slightly more efficiently in the tubes although the difference was scarcely beyond the experimental error.

The fluidextracts made in Oldberg percolators by modified repetition diacolation contained 6.1-Gm. alkaloids per L. as compared with 5.7 Gm. per L. for fluidextracts made from the same shipment of drug by U. S. P. fractional percolation. Hence it appeared that the proportions of drug and percolates used in modified repetition diacolation were superior to those specified in U. S. P. XI fractional percolation. However, it seemed desirable to carry out a further experiment in order to eliminate all possible sources of error. In order to equalize such factors as temperature, etc., a portion of fluidextract was made by each of the processes at the same time in the same room. The drug used was taken from the large shipment and again thoroughly

mixed. The U. S. P. XI fractional percolation process and the modified repetition diacolation process as previously described were followed, using Oldberg percolators throughout. Experimental details and analytical data are given in Tables IV and V.

TABLE IV.—DIRECT COMPARISON OF MODIFIED REPETITION DIACOLATION AND U. S. P. FRACTIONAL PERCOLATION.

	U. S. P. Fractional Percolation.			Modified Repetition Diacolation.		
	First Portion.	Second Portion.	Third Portion.	First Portion.	Second Portion.	Third Portion.
Weight of portion of drug in Gm.	500.0	300.0	200	333.3	333.3	333.3
Volume of packed drug in cc.	1250.0	745.0	485	820.0	820.0	820.0
Height of drug column in cm.	27.5	19.5	19	23.0	23.5	22.5
Time required for liquid to reach lower orifice, in minutes	135.0	150.0	115	112.0	192	255.0
Rate of flow in cc. per minute	1.5	1.6	0.9	1.6	1.6	1.6

TABLE V.—ASSAY RESULTS ON FLUIDEXTRACTS OF BELLADONNA ROOT.

	Gm. Alkaloids in 1000 Cc.	Gm. Total Extractive in 1000 Cc.
Modified repetition diacolation	6.4	149.5
U. S. P. XI Fractional Percolation	5.9	148.5

The results on alkaloidal content of the fluidextracts in Table V confirm the conclusion that the proportions of drug and percolates used in modified repetition diacolation are superior to those specified for fractional percolation in the U. S. P. XI and N. F. VI.

DISCUSSION OF RESULTS.

Our results showing the superiority of modified repetition diacolation over Processes A and C of the U. S. P. and N. F. in the preparation of fluidextract of belladonna root are in agreement with the results of other workers on ipecac, senega, thyme and valerian (1), (12), (13), (14).

Modified repetition diacolation is a simpler process than fractional percolation of the U. S. P. and N. F. in that the drug is divided into three equal portions and the same quantities of reserve and weak percolate are collected from the first two portions of drug. When Oldberg percolators are used in both processes the convenience of operation and the time consumed are practically the same.

Since the terms "repercolation," "fractional percolation" and "divided percolation" have already been used for many years to designate percolation processes in which the drug is divided into several portions, there appears to be no necessity for the introduction of the new term "repetition diacolation." There appears to be nothing in the process of repetition diacolation of Breddin that has not been used before by others. The idea of dividing the drug into equal portions in repercolation is not new since it was used during the past fifty years by a number of workers including C. S. N. Hallberg (17), R. A. Cripps (18), F. Musset (19), D. C. Kelly (20), and J. V. Catford (21); it was also included in the British Pharmacopœia of 1914.

The use of cylindrical tubes as percolators is by no means an innovation. As far back as in 1862, Lalieu (22) conducted a repercolation process using a series of cast-iron tubes of about the same dimensions as the tubes used in repetition diacolation. Glass tubes have been used by various workers, including J. U. Lloyd (23) and J. V. Catford (21). Displacement of an alcoholic menstruum by water is not new; for example, it was used many years ago by E. R. Squibb (24).

In spite of the lack of any new features in Breddin's repetition diacolation process, it is worthy of attention from the standpoint that division of the drug into three equal portions is simpler and better than the division into three unequal portions as specified in U. S. P. fractional percolation. Apparently in modified repetition diacolation the proportion of reserve percolate to quantity of drug in the first two portions is advantageous.

On the whole, the use of cylindrical glass tubes in place of Oldberg percolators is not advantageous, particularly if one considers that the Oldberg percolators are easier to pack and clean. In the present study of modified repetition diacolation, two fluidextracts of belladonna root made in glass tubes averaged 6.3 Gm. of alkaloids per L. while four fluidextracts made in Oldberg percolators averaged 6.2 Gm. of alkaloids per L. These results are in accord with the conclusion reached by the present authors in a previous investigation (25) in which it was found that in ordinary percolation there was no appreciable advantage for either glass tubes or Oldberg percolators from the standpoint of efficiency of extraction of alkaloids.

The displacement of the alcoholic menstruum from the marc by water was not carried out in the present study because many investigations, including the recent work of Büchi and Feinstein (26) have shown that this is not successful for numerous drugs. Naturally there would always be some mixing of the two liquids and a sharp separation could not be expected. However, on the plan used in some European pharmacopœias of preparing 1000 Gm. of fluidextract from 1000 Gm. of drug there would not be such a great necessity of a sharp separation of the alcoholic liquid and the water used for displacement, because in preparing 1000 Gm. of fluidextract from 1000 Gm. of menstruum and 1000 Gm. of drug a quantity of menstruum is left in the drug equal to the weight of the total extractive matter in the finished fluidextract. While displacement is thus theoretically possible it is not always practical because water causes the marc of some drugs to swell and clog the percolator.

SUMMARY.

The proportions of drug and percolates used in modified repetition diacolation are superior to those specified for fractional percolation in the U. S. P. XI and N. F. VI. Modified repetition diacolation is simpler than fractional percolation in that the drug is divided into three equal portions and the same quantities of reserve and weak percolate are collected from the first two portions of drug.

The superiority of modified repetition diacolation over Processes A and C of the U. S. P. in the preparation of fluidextract of belladonna root as demonstrated in the present study is in agreement with the result of other workers on ipecac, senega, thyme and valerian.

The use of cylindrical glass tubes in modified repetition diacolation has no appreciable advantage over the use of Oldberg percolators.

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A PHYTOCHEMICAL AND PHARMACOLOGICAL STUDY OF SOLANUM VILLOSUM.*[1]

BY EARL PETER GUTH.[2]

CHAPTER I.

INTRODUCTION.

The family *Solanaceæ* comprises about 75 genera and 1750 species (1), the majority of which contain either alkaloids or glucosides. Among this large number are two, *viz.*, *Solanum nigrum* L. and *Solanum villosum* Mill., that attracted attention because of conflicting reports relative to the poisonous effects on domestic animals when mixed with feed or when eaten while the animals were grazing. These two species are found growing as "weeds" in Washington fields and gardens.

According to Wehmer (2), *Solanum nigrum* contains the "Alkaloidal-Glucoside" solanine and traces of a not so well-defined mydriatic alkaloid. Schutte (3) reports finding an unidentified mydriatic alkaloid.

Pammel (4) reports a case of poisoning of a sheep by *Solanum nigrum* and concludes that the leaves were poisonous. The fruit he states is used in making jam and has little toxicity. At a later date (5) Pammel reports that the ripe fruit of *Solanum nigrum* is not poisonous but that the green or unripe fruit is toxic.

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