marked on such containers must be inaccurate. There is no substitute in prescription work for an accurately graduated measure.

In conclusion, it should be added that the American-made glass graduates, in accuracy and appearance, are superior to the foreign makes, and much more likely to be in accord with U. S. P. standard.

CUDBEAR AS A PHARMACEUTICAL COLORING.*

GEORGE M. BERINGER.

Since 1874, when Hans Wilder[1] directed attention to the advantages of cudbear over cochineal and carmine as a coloring agent for pharmaceutical preparations, it has become very popular and is now extensively used. As a vegetable dye miscible with either slightly acid or alkaline solutions, with the production of acceptable shades of red, it has been used by many almost as a universal coloring where red colored liquids are wanted. Despite its extensive use and desirable tinctorial properties, one has but to note the criticisms in the phramaceutical press to learn that it has not proved entirely satisfactory.

The principal complaint has been the lack of uniformity in the color of preparations as made by formulas in which the tincture of cudbear was directed. This tincture as found in the drug stores is exceedingly variable, due in part to the variability of commercial cudbear and in a large measure to the imperfect extraction of cudbear by the official N. F. formula.

This tincture is directed in a number of the National Formulary recipes, and in the revision now in progress it has again been decided to retain cudbear as a coloring agent. The desirability of adopting a method of standardizing the tincture is obvious and a sub-committee on color standards have been giving earnest consideration to this vexing problem.

A few of the suggestions offered for this purpose may be here mentioned. One of the earlier thoughts was the publication of a color chart with the shades designated by numbers and to indicate in the formula for a preparation the number of the shade that the product should match. A similar suggestion was to color silk thread or woolen yarn to the desired shades, and chart and number these as guides. Tinted glass, especially that known as "ruby flash glass," was recommended for comparing acid solutions of cudbear. Tintometers were recommended, but these are beyond the reach of the average pharmacist and so not practicable. A novel proposition along this line was offered by Harvey I. Leith,[2] namely, that standard glass rods be prepared of definite diameter and length and colored in their manufacture according to standards established by the Committee on National Formulary. Each rod to have a groove at the top bearing a tag with a number indicating the color. A rod of the standard tint dipped into a preparation would not be discerned if the coloring matched; if the rod showed it

---

*Presented at the meeting of the New Jersey Pharmaceutical Association, Atlantic City, N. J., June 5, 1912.

[1] American Journal of Pharmacy, 1874—299.

[2] American Druggist, 1910—175.

would indicate that the preparation was off in color. None of these suggestions were found to be practicable. The question naturally arises as to the proper directions that would have to be given in such schemes to insure the manipulator matching the shade.

A more promising line of work has been the attempt to standardize dilutions of cudbear tinctures against chemical solutions of definite strength and color such as solution of iodine, solution of gold tribromide or an alkalized phenolphthalein solution. The latter, a suggestion of Mr. Otto Raubenheimer, has been more favorably considered by the committee, and will be more particularly referred to later on. Other methods suggested have been chemical, such as the determination of the tinctorial value by the amount of sulphurous acid or solution of sodium hypochlorite required to bleach out a specified volume of the tincture previously well diluted.

Chairman Diehl[3] is undoubteedly correct in his opinion "that any other than the simplest method of standardization will prove disastrous since it is not likely to be carried out by the average pharmacist." His suggestion was[4] "that comparison of the diluted tincture should be made with dilutions of the purest attainable form of the real active coloring principles." Prof. H. V. Arny[5] states that "orcein, the active principle of cudbear, was found to be of uniform tinctorial power and a solution of orcein 1 to 40,000 was found to match a dilution of 1 to 100 of a sample of tincture of cudbear."

If a purified cudbear or a satisfactory extract thereof of a uniform quality could be readily prepared, then the problem of standard red colored solutions would be simplified. Still better would be the isolation of the coloring principles in a reasonably pure condition. A tincture made with a definite proportion of such extract or coloring principle should not vary greatly and only slight difference of shades could exist in the preparations colored therewith. In the investigations of the writer he has endeavored to keep this thought continuously in mind and his experiments have been largely directed thereby.

Cudbear is one of the interesting group of dyes, orchil, cudbear and litmus, that are commercially produced from various lichens. Lichens contain in their tissues a number of different coloring principles, and E. Bachmann,[6] who studied this subject, distinguished by micro-chemical reactions sixteen different pigments, including greens, yellows, browns and reds of various shades. Moreover, various lichens contain colorless acids and ester-like compounds of orcin and closely related substances which, through the action of alkalies, air and water split to produce first *orcin,* which is itself colorless, but by the continued action of ammonia and air is converted into *orcein* and other colored substances. In former times, the ammonia needed was supplied by the use of stale urine. It is to be hoped that, with the modern methods of obtaining ammonia, this disgusting process is no longer practiced; yet the odor obtained from some samples seem to indicate the possibility of its continuance. By the use of different species of

---

[3] A. Ph. A. Bulletin, 1909—379.

[4] A. Ph. A. Bulletin, 1910—371.

[5] A. Ph. A. Bulletin, 1910—371. Also Practical Druggist, 1912—24.

[6] Pringsheim's Jahrbucher, Vol. XXI, p. 1.

lichens and modification of the process and of the alkali used, different end products are produced resulting in the commercial dyes named.

Cudbear is stated to be prepared principally from certain species of Lecanora and Variolaria. *Lecanora tartarea* of northern Europe is said to be the source of most of that in the market and hence this species has been named the cudbear plant or cudweed. The name cudbear was given to this dye in honor of Dr. Cuthbert Gordon, who introduced it as a dye into Great Britain in the latter half of the eighteenth century. As a dye it is indifferent to cotton, but valuable in the dyeing of wool and silk.

As a commercial product it is very prone to adulteration, and in pharmacy its use should be restricted to a selected article that has been carefully tested and found to comply with the standard adopted. While good cudbear yields an ash of from 5 to 12 per cent, some samples examined gave an ash equivalent to 30 per cent. This consists very largely of sodium chloride, which is a common adulterant and which according to Allen[7] "is sometimes added to reduce an unusually rich article to a uniform standard of quality." In one sample the writer found such an abundance of salt present that a portion crystallized out on evaporating the ammoniocial solution as directed in Hankey's process for ticture of cudbear.

As the coloring of cudbear is only slightly soluble in cold water I strongly advocate that all cudbear used for pharmaceutical purposes be first washed with at least five times its weight of cold water. On mixing cudbear with this amount of cold water and allowing it to macerate for a few hours, with accasional agitation before filfering, the aqueous solution removes most of the sodium chloride, some ammonium salts with their empyreumatic odor, as well as some organic products that are undesirable, such as undecomposed lichen acids, partly converted orcin and extractive. The washed cudbear is more readily extracted and loses scarcely any of its real tinctorial power. This is a simple refinement that should be introduced no matter what formula be adopted for the preparation of a standard tincture.

TINCTURE OF CUDBEAR AND ITS STANDARDIZATION.

It is impossible to entirely exhaust cudbear of its coloring, and in the preparation of the tincture it is safe to assert that the amount directed in the N. F. formula for Tinctura Persionis 125 gm. in the liter is not half extracted and that an equally satisfactory preparation would result if the cudbear be reduced one-half, and hereafter a tincture of not over 10 per cent drug strength should be directed.

The directions for the manipulation in the N. F. read exceedingly simple: "Pack the cudbear in a suitable percolator, and percolate it with a mixture of one (1) volume alcohol and two (2) volumes of water until 1000 cc. of tincture are obtained."

Cudbear is a most troublesome substance to percolate. It is difficult to moisten evenly and not infrequently a portion becomes pasty and other portions scarcely moistened, with the result that one is prone to obtain either channeling and uneven extraction, or more frequently clogging of the percolator, which may even completely stop the process. Consequently, if percolation is to be adopted, the plan

---

[7] Commercial Organic Analysis, Vol. III, pt. 1, p. 324.

of admixing with the cudbear an inert diluent must be resorted to. A number of substances, such as sand and ground pumice, which usually serve for this purpose with other refractory drugs, have not proved satisfactory with cudbear. In my experience ground cork has proved entirely satisfactory, about one-third to one-half of the weight of the cudbear being sufficient. The commercial ground cork of the factories, however, should not be used, as this is made from cork refuse and siftings and is full of foreign matters and dirt and has a musty odor. Unsightly corks, or even old corks if thoroughly cleansed by boiling with water and drying, will serve the purpose and these can readily be reduced to a powder, passing through a No. 20 to a No. 40 sieve by the use of an almond grater, a useful implement, that should be in every drug store and laboratory.

The official menstruum is likewise too weak in alcohol to serve as a solvent for the coloring matters present. Water alone is a poor solvent for these and alcohol is one of the best, and if the menstruum is to be hydro-alcoholic then a mixture of at least alcohol three volumes and water one volume is to be recommended. The coloring principles present in cudbear are in part, associated as ammonia compounds, and some are not soluble even in alcohol until alkali be added. Orcein, the most important dye constituent of cudbear, as found in the market, is but indifferently soluble in alcohol and its color is not fully developed unless ammonia or other alkali be present. Hence, ammoniacal extraction of cudbear seems to be indicated, and when the extraction is so made then the alcohol can be reduced to the amount needed as a preservative. This is the principle that has been followed in the formula for tincture proposed by Wm. T. Hankey:[8]

Cudbear 125 gm., macerate for 36 hours in a mixture of ammonia water 125 cc. and water 1877 cc., shaking at intervals, then filter and wash the residue on the filter with water until 2000 cc. of filtrate is obtained. Evaporate the filtrate to 500 cc., then add 330 cc. of alcohol and sufficient water to obtain 1000 cc. of tincture.

This is a decided improvement on the present N. F. formula, but the extraction of the cudbear is far from complete, the ammonia directed being insufficient for this purpose. Moreover, the tincture made by this formula shows a tendency to precipitate.

It has been proposed to adopt the Hankey formula in this revision of the National Formulary[9] with the modification that the tincture is to be standardized by the method proposed by Mr. Raubenheimer. The directions being that 1 cc. of the concentracted ammoniacal extract mixed with 399 cc. of water and 1 drop of 1% solution of ammonia should match the color of the Standard Pink Phenolphthalein Solution. The Standard Pink Solution is to be prepared by mixing 1 cc. of Phenolphthalein T. S., U. S. P., with 2 drops of Solution of Potassium Hydroxide and sufficient distilled water to make 100 cc.

If these match, the dilution with alcohol and water is carried out as directed in the formula. If they do not correspond, then the amount of the cudbear solution required to match the standard is determined by a repetition of the color comparison and the proper degree of dilution or concentration is thus fixed. The standard tincture should be of such a strength that 1 cc. diluted with 199 of water should match the standard pink phenolphthalein solution.

---

[8] A. Ph. A., 1908—p. 93.

[9] Bulletin of N. F. Committee No. 31—p. 363.

The writer experimented with standard color test solutions as proposed by Raubenheimer[10] and also with the solution of orcein 1 to 40,000 as proposed by Arny.[11] The latter had a more decided red tint than the dilution of the cudbear tincture prepared by the proposed formula and was more difficult to match. With some of the samples of tincture made by other formulas the dilution did not match the tints of either of these proposeed standards. It is apparent that while the amount of alkali directed to be added to the cudbear dilution (1 drop of 1% solution of ammonia) may be sufficient to develop the purplish tint desired in in a tincture made by ammoniacal extraction it would be inadequate for such a purpose in tinctures made by other formulas. This was all the more evident in the stronger tinctures resulting from my experiments. In some of these a nearer approach to an exact matching of tints was obtained by a modification of Raubenheimer's standard made by increasing the alkali and diminishing the phenolphthalein thus, 1 cc. of solution of potassium hydroxide, 0.2 cc. of phenolphthalein T.S. and distilled water sufficient to make 100 cc. Using all three of these solutions for comparison it was found difficult to accurately match some of the dilutions of the tincture. Comparisons were more readily made, however, if the standards were diluted to 200 cc., or one-half of proposed strength.

While these standards may serve the purpose for the comparison of tinctures made by the proposed N. F. formula they are not entirely satisfactory and they are of questionable value in determining the strength of cudbear tinctures made by other processes. In some of these, the directions given must be deviated from at least by the addition of more ammonia, and then it becomes difficult to determine in each case the exact amount of alkali that is required to produce the purplish pink tint to match that of the standard. An excess of alkali will produce a deep purple not at all comparable with the standards that have been proposed.

In order to make comparisons of different tinctures, the writer surmised that if sufficient alkali be added to the diluted tinctures to produce the full purple coloration then the strength of such dilution should be readily and more accurately estimated. Such a method would necessitate the selection of a standard purple solution of known value. It was hoped that the Arny orcein solution of 1-40,000 upon the addition of alkali would serve the purpose, but on trial it was found that the shade of purple it produced varied too greatly from that of cudbear solutions to be at all satisfactory. This is explained by the fact, as will be shown later, that the other color substances associated with orcein in cudbear materially influence the colors produced by the tincture and that they cannot be ignored. It is possible that a dilute solution of potassium permanganate may serve for such standard.

From the cudbear selected for the experiments, a number of samples of tincture of cudbear were prepared by different formulas. In all of these 125 gm. of the cudbear was used to the liter of tincture so as to make the comparison with the formula of the N. F. III fair. The cudbear was previously washed with 5 times its weight of water before extraction and ground cork used as the diluent. The products were tested by determining the amount necessary to be diluted to

---

[10] Bulletin Committee on N. F. No. 31—p. 364.

[11] The Practical Druggist, 1912, April—p. 24.

100 cc. to match as near as possible the proposed standards. Subsequently, a practical test was also added, the determination of the amount of each necessary to color 100 cc. of Aromatic Elixir, U. S. P., to a uniform color; 1 cc. of the sample made by the N. F. III formula being used as the basis of this test. The following tabulated statement shows the results:

No. Formula.	Arny Orcein Standard.	Raubenheimer Standard Phenolphthalein Pink Solution.	Beringer Modification.	To Color 100 cc. Aromatic Elix.
1—National Formulary III.	3. cc. after adding 3 drops NH_3 (1%).	2.4 cc. after adding 5 drops NH_3 (1%).	2.2 2.2 cc. drops NH_3 (1%).	1. cc.
2—Hankey's Recipe.	2. cc. after adding 2 drops NH_3 (1%).	1.7 cc. after adding 3 drops NH_3 (1%).	1.5 cc. after adding 2 drops NH_3 (1%).	.8 cc.
3—Menstruum—Diluted Alcohol.	1. cc. after adding 2 drops NH_3 (1%).	.8 cc. after adding 2 drops NH_3 (1%).	.6 cc. after adding 4 drops NH_3 (1%).	.3 cc.
4—Menstruum—Alcohol 3 vols. Water 1 vol.	.8 cc. Tint not well matched.	.5 cc. after adding 2 drops NH_3 (1%). Difficult to match exactly.	.5 cc. after adding 2 drops NH_3 (1%) not exactly matched.	.2 cc.
5—Menstruum—Alcohol.	1. cc. Dilution cloudy and difficult to match exactly bv addition of NH_3	.65 cc.	.65 cc.	.22 cc.
6—Menstruum—Stronger Ammonia Water 25cc.; Alcohol 975 cc.; finish with alcohol.	1.2 cc. Dilution too purple; comparison approximate only.	.8 cc.	.9 cc.	25? cc. *Not same* tint.
7—Menstruum—Ammonia Water U. S. P. 1 vol.; Water 3 vols.; percolate 4000 cc. Evaporate to 750 cc. When cold add alcohol 250 cc. and water q.s. to make 1000 cc.	.8 cc.	.57 cc. a good match.	.6 cc. good match.	.2 cc.
8—Mix the cudbear with Hydrochloric Acid 25 cc. allow to dry and then percolate with alcohol to 1000 cc.	.5 cc. after adding 4 drops NH_3 (1% .	.5 cc. after adding 4 drops NH_3 (1%).	.5 cc. after adding 4 drops NH_3 (1%).	.2 cc.

While these experiments do not permit of the exactness of determinations made by the methods of chemical analysis, they are nevertheless sufficiently instructive to permit of the following deductions: The present N. F. formula gives the poorest preparation for the reasons explained. The formula proposed for the revision is not the best that can be devised, and does not extract the cudbear nearly as thoroughly as can be done by percolation with ammonia water, as in formula No. 7. If the N. F. is to adopt a formula in which the extraction is to be made with ammonia water then formula No. 7 is to be commended. The great increase in tinctorial power obtained by using a menstruum of proper alcoholic strength is proved, and if alcoholic extraction is to be the basis of the official formula, then formula No. 4 should be approved.

Formula No. 8 is based upon the principle of neutralizing the alkaline bases present in the cudbear and then extracting the liberated colorings with alcohol. The results are pleasing, the preparation is perfectly clear and keeps without change, which cannot be reported of the samples made by ammoniacal extraction which, after keeping for several months, show more or less tendency to precipitation. The product shades toward a brick-red on account of the free acid present, but on dilution gives a bright red to cherry-red. While the acidity might prove objectionable in some preparations the results indicate a method of using cudbear to advantage in some solutions where the trace of acid is not contraindicated.

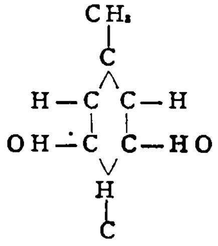
THE COLOR CONSTITUENTS OF CUDBEAR.

The text-books quite commonly are contented with the statement that the principal coloring substance present in orchil and cudbear is *orcein.* Still more common is the misleading statement that *orcin* in the presence of ammonia and air produces a colored substance *orcein.* No mention is made of any other colors produced by such exposure or oxidation and so generally the value of cudbear as a dye has been attributed entirely to the orcein content. The attempt to standardize cudbear and its tincture have likewise, in a large measure, taken the direction of comparing these with standard solutions of orcein. The assumption here again was that orcein represented all that was valuable or essential in cudbear as a coloring for pharmaceutical preparations. If such assumption was correct then the problem of obtaining uniform colored solutions with cudbear could be readily solved by the use of solution of *orcein.*

My experiments on the color constituents of cudbear were primarily undertaken with the thought of formulating a practical method of isolating the orcein in a state of sufficient purity to be used satisfactorily as a coloring in pharmacy. I have found it a most fascinating field of study, associated with peculiar and bewildering difficulties. The time at my command has not permitted of a thorough investigation of the colors isolated and the incompleteness of the investigation is admitted. Some of the results and conclusions are presented in this communication. It will be impossible to give herein all of the methods tried and many details of the experimentation are necessarily omitted.

The studies of E. Bachmann[6] indicate the complexity of the study of the lichen pigments. The numerous organic acids present in this family are in nature's laboratory largely converted into orcin. These acids have been the subject of elaborate investigations by many of the most prominent European chemists. The facility with which they form esters further complicates the study and must affect the colored products resulting from their oxidation, and present in the commercial dyes.

Orcin is not only present in many of these lichens but is increased in the process of manufacture of the dye by splitting up the organic acids and compounds by heating with alkali. It can be produced by a number of processes and when pure appears in colorless, sweet tasting crystals, containing water of crystallization and melting at 58°. It is soluble in water, alcohol and ether.[12]. Chemically orcin is dihydroxy methylbenzene or Dioxytoluol $C_6H_3(CH_3)(OH)_2 + H_2O$.



Its close relationship to benzene shows that nature had anticipated man in establishing in her laboratory dye factories that' simulated the process of the aniline dye chemists. The manufacturers of the lichen dyes have produced the same coloring materials from natural sources that can be duplicated in the chemist's laboratory by modern synthetic methods from definite chemical compounds. A priori, one could readily predict that orcin would yield a number of substitution compounds besides *orcein.*

Robiquet[13] was the first to observe that orcin in the presence of air and ammonia yielded a dye and named this body *Orcein.* This was further studied by Heeren[14] and Dumas[15] and Kane[16]. It was learned that orcein could be readily produced by exposing slightly moistened orcin in a watch crystal over a vessel containing strong solution of ammonia until it became brown and then dissolving this in water with the aid of a few drops of ammonia water and from this solution the orcein was precipitated by acetic acid.

From commercial orchil, orcein can be produced by moistening with hydrochloric acid, drying and then extracting with boiling alcohol. The alcohol is distilled off and the residue washed with water and then with ether when a carmine red powder remains.[17]

According to Liebermann[18] two dyes are produced by the action of air and ammonia on orcin. Both being brown amorphous substances with green lustre.

---

[12] Schmidt Pharm. Chem., 1012.

[13] Ann. Chem and Phys. (2), 47—238.

[14] Schweigger's Journ. of Chem., 59—page 313.

[15] Ann. Chem. Pharm., 27—145.

[16] An. Chem. Pharm., 39—25.

[17] See Die Chemie der Natürlichen Farbstoffe, Dr. Hans Rupe, to which I am indebted for many of these references.

[18] Ber. d. deutsch. chem. Ges. 7, page 247, 8, page 1649.

The one which is the chief product when the ammonia is in excess is the least soluble in alcohol and ammonia.

Especially worthy of note was the investigation of Zulkowski and Peters,[19] who found that on allowing orcin to stand for two months over ammonia that three different dyes were produced: (1) Red orcein, which crystallized from hydro-alcoholic solution in microscopic crystals, which yield a brown powder. The solution in alcohol is carmine red and with alkalies and alkaline carbonates gives a blue violet color. It is insoluble in water and ether, soluble in alcohol and acetic acid and acetone. (2) A yellow crystalline dye material, which is soluble in warm water, alcohol and ether, giving a yellow colored solution. (3) A lackmus like dye, amorphous and insoluble in alcohol.

These authors showed that these three bodies would be produced in three days by mixing 100 parts of crystallized orcein, 200 ammonia water (22% NH_3) and 1200 of hydrogen dioxide 3%. The violet mass resulting is then acidified with hydrochloric acid, the precipitated orcein is collected and washed with water until no longer acid and then dried at a moderate temperature. On concentrating the filtrate and wash water and adding sodium chloride a second precipitate of orcein can be obtained. On washing the orcein with ether the yellow dye is removed. The orcein is dissolved off the filter by boiling alcohol and there is left on the filter a lackmus like dye material insoluble in alcohol. On evaporating the alcoholic solution of orcein it is obtained as brown crystalline powder. If water be added during the evaporation the orcein is left in glistening flakes.

The method of Zulkowski and Peters with ammonia and hydrogen dioxide was tried on a small scale, using Merck's orcin and the proportion of ingredients as stated. After allowing the mixture to stand for five days, the purple colored mass was solidified with hydrochloric acid and the precipitated orcein washed on to a filter with distilled water and the washing continued until the filtrate was free from acid. The filtrate was still of a bright red color and was washed with several portions of ether, when the latter became a deep orange color and yielded on evaporation a reddish orange residue and this was no doubt the yellow described by these authors. A small portion of this orange residue was soluble in chloroform and the chloroform was colored a distinct yellow not orange, and the residue from evaporation of the chloroform was much lighter in color and had much less tinctorial power. This would indicate that the yellow of these authors was composed of two compounds, the one soluble in chloroform and the other scarcely soluble in chloroform but very soluble in ether and present in relatively large amount.

The chloroform soluble yellow gave with ammonia a lilac-pink, and with hydrochloric acid a light yellow coloration. With alcohol the solution was yellow. It dyed silk in ammoniacal bath only an indistinct faint light pink, and in acid bath a maize yellow. For wool it had little affinity, and failed to dye in alkaline bath and in acid bath only a very pale yellow. The tinctorial value of this yellow was very slight. Owing to the small amount of material obtained the results were not satisfactory.

The orcin orange, the ether soluble yellow, in contradistinction gave orange

---

[19] Monatsh f. Chem. 11, page 227.

colored solutions in water and alcohol. With ammonia it gave a bright violet color, and hydrochloric acid changed this to light scarlet-yellow. The tinctorial strength was very marked. In acid bath it dyed both silk and wool a deep rich mandarin orange, and in ammoniacal solution silk was dyed a salmon pink.

The precipitated *orcein*, after washing free from acid, was dried on the filter and then washed with ether. The ether extracted considerable of the yellow dyes which had been carried down with the orcein and these reacted the same as that obtained from the wash water. The orcein was then extracted by washing the filter with hot alcohol and on evaporation the alcohol solution yielded a glistening residue which gave a red brown powder. There still remained on the filter a very small amount of precipitate not soluble in the alcohol. This gave with alkalies a distinct litmus like blue and with acids a red, and corresponds to the "lackmus like" dye reported by Zulkowski and Peters.

The orcein so obtained was almost insoluble in water and ether, and with alcohol gave a deep carmine red colored solution and in acetone a cherry red. With alkalies it gave a blue-purple and with hydrochloric acid a red coloration. It possessed strong tinctorial properties and dyed silk in acid bath Bordeaux red, and in alkaline bath purple. It dyed wool in acid bath a brownish-red, and in alkaline bath a violet blue.

The wash water from this experiment was still of a deep red color, even after having twice precipitated the orcein and washing with ether to extract the yellows, and showed that it still retained much coloring. It was washed with warm amyl alcohol, which removed nearly all of the coloring, leaving the wash water only slightly colored. The amyl alcohol solution was separated and washed with water to remove dissolved salts, and then evaporated on a water bath. It yielded a copious reddish purple residue. This was soluble in water and more readily in alcohol giving red-purple solutions. With ammonia the solution became intensely purple, and with hydrochloric acid reddish purple. It possessed powerful tinctorial value and dyed silk and wool, either in acid or in alkaline baths, beautiful shades of purple. This dye appears to have escaped the attention of other investigators, although present in considerable quantity, probably because they failed to examine the wash waters. Provisionally we will name it *Orcin purple.*

In order to determine the conditions under which orcin purple is formed and whether the presence of hydrogen dioxide influenced its production, a few test tube experiments were tried. It was learned that orcin in the presence of potassium hydroxide and water yielded largely the yellow dye. In the presence of ammonia in excess, and without any hydrogen dioxide being added, and allowing the oxidation to proceed only two or three days and not to completion, all three dyes, red, yellow, and purple were produced, the yellow and especially the purple exceeding the amount of orcein. Moreover, that the purple dye was soluble in ether when in ammoniacal solution and could be partly recovered in this way even before acidifying and precipitating the red. Excess of ammonia and incomplete oxidation are conditions that are to be expected in the process of manufacturing cudbear. It will be thus seen that orcein is not the only product resulting from the oxidation of orcin. While the blue or lackmus like dye and the yellow readily soluble in chloroform are present in such small quantity that they can probably be ignored, the orange is present in notable amount and modifies the color of the red with the production of brighter shades. Under certain conditions the orcin purple is produced in quantity sufficient to materially affect the color.

Before taking up the Zulkowski and Peters' paper and process for experimentation, the writer had tried a number of methods for separation of the color materials from cudbear and some of these merit recording. The original thought was to obtain the coloring by precipitation as a lake with a metallic salt. Lead subacetate was found to most completely precipitate the coloring.

Process A—50 gm. of cudbear previously washed with 250 cc. of cold water was treated with successive portions of diluted ammonia water by maceration and the filtered solutions concentrated and solution of lead subacetate added so long as a precipitate was formed. The precipitate was washed by decantation and then on a filter until free from soluble lead salt. It was then suspended in water and a current of hydrogen sulphide passed through until the lead was entirely converted into sulphide. The mixture was then evaporated to dryness and the resulting mass powdered and divided into two equal portions. The one was extracted with warm alcohol and it was attempted to extract the other with diluted ammonia water. It was found, however, that the ammonia water softened the filter paper so that the lead sulphide passed through, and even after repeated evaporations and resolution the lead sulphide persisted in the filtrate. The alcoholic solution from the other half was evaporated and yielded a red powder. The yield was exceedingly small, and the tediousness of this process precludes its recommendation. The residue gave a bright red solution in alcohol, and with ammonia a purple coloration. The alcoholic solution had a pecliar fluoresence. To ether it yielded a yellow dye and from the ether extract water removed traces of a substance which on concentrating the aqueous solution and adding potassium hydroxide gave a pale yellow iridescent liquid with pale green and pink shadings. This was attributed to traces of organic lichen acids, and a similar reaction was obtained from the washings of the cudbear, and from other extractions.

Process B—50 gm. of cudbear was washed as previously directed, mixed with 10 cc. hydrochloric acid, dried and then extracted for 12 hours in a Soxhlet apparatus with alcohol. The extraction even then was not complete. The alcohol was distilled off and the residue evaporated to dryness on the water bath and reduced to powder. It was then of a purple-brown color and weighed 8 gm., equivalent to 16 per cent of the cudbear taken. This will be referred to as extract by acid alcoholic process. Five gm. was purified by washing with water and then with ether, as recommended in the published process. The ether was colored yellow and on evaporation gave the orange yellow dye. Associated with it was a small amount of a violet-red dye that was insoluble in chloroform.

The purified extract was now of a dull red color and weighed 1.75 gm. It gave with alkalies the blue purple coloration and dyed silk and wool the orcein shades. In accordance with the published statement it should be orcein. It was, however, far from pure and, although made by alcoholic extraction, was no longer entirely soluble in alcohol; a portion dissolved readily in alcohol and a smaller amount was very scarcely soluble even in boiling alcohol. This portion dissolved readily in ammonia water yielding a purple solution, but when reprecipitated by the addition of acid its solubility in alcohol, even in this freshly precipitated state, was not increased. This portion was likewise much weaker in tinctorial value.

Process C—50 gm. of cudbear was washed as in previous processes, then mixed with 25 gm. of ground cork and percolated with a mixture of ammonia water 1 volume, water 3 volumes, until 3500 cc. of percolate was obtained and the cudbear was fairly well extracted although not exhausted. The percolate was concentrated to 500 cc. and sufficient hydrochloric acid (25 cc.) was added to make the solution decidedly acid, then warmed and set aside for 24 hours for the precipitate to settle. The precipitate was collected on a filter and washed till free from acid, then dried and powdered. It yielded a red brown powder, which gave a purple solution with alkalies, and dyed silk in acid bath a light purplish red, corresponding to what is listed by silk manufacturers as crushed strawberry, and in alkaline bath a red violet. This impure orcein we will designate as *Perseo Red.* It is composed of two red coloring substances, one soluble in alcohol with a carmine red solution, the other practically insoluble in alcohol but soluble in ammonia water and the ammoniacal solution on evaporation yields a shining lustrous purple powder, which is insoluble in alcohol, but soluble in diluted alcohol to deep purple red solution. The experience with these red dyes obtained in both processes B and C seems to confirm the statement of Liebermann[20] as to the existence of two red dyes produced by oxidation of orcin with ammonia and air.

The filtrate and wash water from the precipitated perseo red was concentrated and extracted with ether, which extracted the yellow dye. Subsequent extraction with amyl alcohol yielded a brownish red solution and on evaporating off the amyl alcohol there remained a lustrous brown powder. This was soluble in water and in alcohol, yielding purple-red solutions, which on the addition of ammonia became a brighter red but not purple. It dyed silk in acid bath a heliotrope, and in alkaline bath an "old-pink" shade.

In attempting to isolate the different coloring matters present in cudbear, either by precipitation or by the use of immiscible solvents, one must recognize the difficulty of their separation in an absolutely pure state. Traces of the associated colorings are almost sure to adhere, and modify the shades produced in dyeing. Nevertheless, there are several well defined and distinct colors which are evidenced in every one of these methods and prove that in cudbear we have to deal with the orcein like reds, a yellow and the purple in varying proportions. The samples of the isolated dyes, colored solutions and dyed silk and wool fibers demonstrate this.

In order to compare the strength of the red dyes obtained in the processes described they were compared with a sample of orcein as supplied by Merck & Co. This orcein was insoluble in water, chloroform, petroleum benzin and benzene. In alcohol it gave a carmine red solution and its solubility in alcohol was increased by the addition of a small amount of ammonia. With methyl alcohol it gave a carmine red solution, with acetone a scarlet, and with amyl alcohol a deep pink. With ether it yielded a pale yellow solution; this filtered off, gave with ammonia a violet, and when acidified with hydrochloric acid was changed to a pink lilac color. It was noticed that on adding more ether, this at first remained

---

[20] Ber. d. deutsch. chem. Ges. 7, page 247; 8, page 1649.

colorless but gradually became yellow as if some change was taking place in the presence of that solvent.

Solutions of each of these red dyes were prepared by using .050 gm. of the dye, 5 cc. ammonia water and sufficient diluted alcohol to make 100 cc. The Merck's sample was taken as the standard and for comparison 1 cc. of its solution was diluted to 100 cc. with distilled water. The results were as follows:

Merck's Orcein	Solution, clear dark purple.	1 to 100 cc. Standard.
A—Red by Process A, not purified beyond alcoholic extraction.	Solution, clear, lighter red-purple.	5cc. to 100 cc.
B—Purified red by acid extraction	Solution, clear, purple.	2.25 cc. to 100 cc.
C—Perseo Red	Solution, clear, deep purple.	3 cc. to 100 cc.
D—Orcein by Zulkowski and Peters' method	Solution, clear, deep purple.	.8 cc. to 100 cc. Solution more blue as if trace of litmus present.

On acidifying dilutions of these solutions the red produced was similar to a litmus red, this was somewhat less marked in solution A. Aromatic Elixir colored by these lacked the attractive brightness of cudbear coloring. It was concluded that orcein must have a limited field of usefulness in pharmacy and that it could not displace cudbear with satisfaction.

EXTRACT OF CUDBEAR.

Desiring to obtain a preparation that would represent all of the colorings present in cudbear, extracts were made. Preliminary experiments showed the necessity of washing the cudbear with cold water to remove salts before extraction, if non-hygroscopic and powdered extracts were to be expected, and in these experiments this was always a preparatory act. Alcohol, acetic acid, ammonia water U. S. P., and a mixture of ammonia water 1, water 3, were all used as menstruums, as well as the acid-alcoholic hot extraction previously referred to. It was found that the resulting extracts could be dried and powdered but that they were not freely soluble in alcohol or water, but that with each complete solution could only be effected by the addition of ammonia.

For the comparison of these extracts solutions were made by the following formula: Extract .5 gm., Ammonia Water 5 cc., Diluted Alcohol sufficient to make 100 cc. The tabulated statement exhibits the results. Efforts to compare these with the Arny and Raubenheimer Standard Solutions were not satisfactory, and comparison was made by using the dilution of the solution of the alcohol extract as a standard.

Menstruum.	Yield.	Character of Solution.	Amount Required to Match Standard.
Alcohol	8.3%	Solution complete, sediment very little.	1 cc. to 200 cc. Standard.
Acetic Acid	11.2%	Poorly soluble and solution not completely effected.	8 cc.
Ammonia Water	13%	Solution complete.	3 cc.
Ammonia Water 1, Water 3	20%	Solution nearly complete.	2.5 cc.
HCl and Alcohol	16%	Solution nearly complete.	4 cc.

Aromatic elixir colored by any of these solutions was distinctly purple but the red coloring was readily produced by neutralizing with citric acid. The use of an extract of cudbear would very materially reduce the variability in color of preparations in which it was used and it would also be available for the preparation of a more uniform tincture. Acetic acid extract is ruled out on account of its poor solubility and lack of strength. On the score of economy ammonia water extraction appeals but on the basis of strength and reliability alcoholic extraction is to be preferred.

THE DRUG MARKET.

HARRY B. FRENCH.

Senna Leaves.—The United States government is refusing admittance into the United States of what is known as Alexandria Senna Siftings. This is supposed to be the small leaves sifted out in obtaining whole leaf and half leaf garbled. These siftings are very often of good quality, but contain a large portion of sand and other foreign matter. We understand that the Government's limit of foreign matter and succeeded in reducing the percentage of extraneous matter to 9 per was sifted by us. The result was that we eliminated about 25 per cent. of foreign matter and succeeded in reducing the percentage of extradeous matter to 9 per cent. ash. This necessarily makes the price higher to the buyer, but he secures a better article. Ash insoluble in hydrochloric acid less than 1 per cent.

Opium.—Some time ago, we bought in Smyrna, dried opium of high test. This was sold to us as 22 per cent. On arrival we had it carefully tested and had this test corroborated by a prominent chemist in the city and the gum also is tested, at our request, by one of the very large manufacturing chemists in the city. The average result obtained was that the gum tested 20 per cent. U. S. P. Sample was also tested, as a favor to us, by a very prominent pharmaceutical house in the west, and they made the following very interesting report to us:

"Report on Sample of Dried Opium from Smith, Kline & French Co.
Laboratory No. C-3892.

"It is well known that there are several sources of error in the U. S. P. Opium assay, and also that other methods are not free from similar sources of error. One of the most fruitful sources of error is the difficulty of completely extracting the Opium and this varies with different samples of Opium, some being much more easily extracted than others. As the morphine is determined by the crystallizing out of a solution, a certain amount will be retained in the mother liquors and this amount will also vary with the character of the Opium. Another source of error is found in the impurities which may be weighed with the Opium, and here again the purity of the morphine is influenced by the character of the Opium. The above facts must be borne in mind by the comparing assays made upon any sample of Opium.

"In order to determine as accurately as possible the morphine content of this Opium, we have made 15 assays; 6 by the U. S. P. method and 9 by other methods. Our results may be summarized as follows:

"Adhering closely to the U. S. P. method, we have found an average morphine content of 20.2 per cent. Applying to these results corrections for the solubility