# Section on Practical Pharmacy and Dispensing

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## A UNIFORM EXTRACT OF CUDBEAR.

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After the excellent work done on cudbear during the past year by Raubenheimer, Gardner (Druggists Circular 55-1911-518) and especially by Beringer (Journ. A. Ph. A. 1912, p. 820), further reports on this coloring agent would seem at first glance scarcely necessary. But inasmuch as the writer's interest in cudbear is chiefly as referee on the subject for the National Formulary Committee, and especially as the findings of the previous investigators did not lead to a product suitable for the Formulary, the experience of the writer may be worth citing.

As has been elsewhere stated (American Druggist 59-1912-49), the Committee on National Formulary, at a conference held in Boston last August, did not adopt any of the several suggested schemes of standardizing tincture of cudbear by means of colored fluid and requested the sub-committee charged with this particular phase of the work of revision to take up the problem of preparing extracts of uniform tinctorial power.

At the last meeting of this Association, two such extracts were suggested, one alcoholic, the other made with acetone, and the writer has already reported his findings (Practical Druggist, April, 1912, p. 24), on such extracts from four samples of cudbear.

He showed that the alcoholic extracts contained appreciable quantities of the sodium chloride, which is a usual admixture of commercial cudbear, and the strongest of the eleven extracts prepared from the four samples by different means of extraction had five times more tinctorial power than had the weakest. The acetone extracts, suggested by Mr. Gardner, were more uniform. Four extracts from the four samples of cudbear were prepared and while the color of a 1 to 1,500 dilution of the strongest was matched by a dilution of 1 to 1,000 of the weakest, the other two extracts showed similar tinctorial power in dilutions of 1 to 13,000 and 1 to 14,000 respectively. This shows that these acetone extracts are more uniform in color than are those made from alcohol, but the weakest, having only two-thirds the color strength of the strongest, made the practicability of the acetone extracts problematic.

As extraction of cudbear with chloroform in the writer's laboratory showed that that solvent did not remove the purple-red pigment but did extract the

mahogany colored dyes, the plan of extraction of cudbear, first with chloroform and then with acetone, was tried and that with much success.

### THE "A. C. A." EXTRACTS.

In the experiments reported in the Practical Druggist, of the alcoholic extracts prepared, four were from four different samples of cudbear, made by extracting 100 grams of the coloring agent with cold (U. S. P.) alcohol until 1000 cc. of percolate were obtained, and after recovery of most of the alcohol by distillation, the residue was evaporated on a steam radiator to constant weight.

By this means, four dry extracts were obtained, the yield from the four samples of cudber being 12.7, 15.1, 18.3 and 12.4 percent. respectively. As mentioned above, these four extracts varied greatly in tinctorial power; the four in dilutions of 1 to 10,000 matching orcein dilutions of 1 to 120,000, 1 to 300,000, 1 to 100,000 and 1 to 160,000 respectively.

Of these alcoholic extracts, the sample from drug No. 1 was used up on fruitless experiments, but 10 grams of each of the extracts, Nos. 2, 3 and 4, were macerated to exhaustion with chloroform and then extracted with acetone. The chloroform extract was of a mahogany-brown tint, turning more or less purplish with ammonia. The acetone dissolved only a part of the residue, the acetone-insoluble part consisting largely of crystals of sodium chloride. The three resulting extracts made by successive use of alcohol, chloroform and acetone will hereafter, in this paper, for the sake of brevity, be called "A. C. A." extracts; ten grams of the three alcoholic extracts yielding respectively 1.42 gm., 1.65 gm., and 1.31 gm. of "A. C. A." extracts Nos. 2, 3 and 4.

### THE "C. A." EXTRACTS.

It is plain that the above described "A. C. A." extracts were produced by a cumbersome process and the next step was to see whether initial percolation with alcohol was necessary; so samples of cudbear Nos. 1, 2 and 3 (sample No. 4 having been used up) were directly percolated, first with chloroform and then with acetone. In each case, 100 grams of the dry cudbear were loosely packed in a narrow percolator, fitted with receiving bottle and glass tubes so as to constitute a volatile liquid percolating apparatus, and the sample was percolated to exhaustion with chloroform and then with acetone, the latter solvent being poured directly on the drained drug without the need of removal from percolator and repacking after drying. Of course, the first liquid dropping from the percolator after adding the acetone is the chloroform remaining in the drug, but this can be easily separated as chloroformic extract, inasmuch as the acetone percolate so soon as it reaches the bottom of the percolator, colors the pledget of cotton found there as straining medium, an intense crimson, that is a marked contrast to the practically colorless final portion of the chloroformic percolate.

Both solvents were recovered from their percolates by distillation, and the thin acetonic extracts were dried by "scaling." After 24 hours, the scales were dry enough to scrape from the plate and were then dried in air to constant weight. The figures given below as to yield relate to the fully dried extract, and as, of

course, some of the extract adhered to the scaling plates, the yield was somewhat more than here reported.

The following tabulation gives the data of manufacture:

"C. A." EXTRACTS FROM 100 GM. CUDBEAR.

| Sample No. | Chloroform Figures | | | Acetone Figures | | | Yield Ext. (in gms.) |
|---|---|---|---|---|---|---|---|
| | cc. Used | cc. Percolate | cc. Distillate | cc. Used | cc. Percolate | cc. Distillate | |
| 1 | 500. | 450. | 340. | 450. | 395. | 345. | 3.10 |
| 2 | 200. | 185. | 170. | 350. | 327. | 305. | 3.11 |
| 3 | 300. | 280. | 250. | 300. | 212. | 185. | 2.59 |

From the foregoing, it will be seen that 3.11 gm. "C. A." extract No. 1, was obtained at the cost of 100 gm. cudbear, 160 cc. chloroform and 45 cc. acetone; that 3.10 gm. extract No. 2 was obtained from 100 gm. cudbear with a waste of 30 cc. chloroform and 45 cc. acetone; and that 2.59 gm. "C. A." extract No. 3 meant using 100 gm. cudbear, 50 cc. chloroform and 115 cc. acetone. This means that the finished extract will be rather expensive, but when it is realized that to color a gallon of alkaline antiseptic solution will require one, or at most, two grains of the extract, the initial cost acquires less significance.

### PHARMACY OF THE "A. C. A." AND THE "C. A." EXTRACTS.

The finished extracts are reddish-brown granules or scales with a greenish lustre and are very slightly hygroscopic. They do not readily dissolve in water, but are instantly soluble in water containing ammonia, and are very soluble in alcohol. At the beginning of the experiments, ammoniated aqueous solutions were prepared and these on evaporation yielded ammoniated extracts which were instantly soluble in water, but as such extracts were found to lose solubility with aging and consequent loss of ammonia, the use of an alcoholic tincture was found to be a better procedure. Experience showing that there was likelihood of precipitation of some of the color when this alcoholic tincture was diluted with water, a trace of ammonia was added, when the resulting product became freely miscible with water.

So latterly a tincture consisting of the extract, 1 gram; 10 percent. ammonia, 2 cc.; and alcohol to make 1000 cc., was employed.

### COLORIMETRIC COMPARISON OF EXTRACTS.

While dilutions of the alcoholic percolates of cudbear matched dilutions of commercial orcein as has been pointed out both by Mr. Beringer and the writer, the pure purple-red pigment of cudbear and likewise the acetone extracts, have a shade quite different from orcein, which therefore cannot be satisfactorily employed as a standard for matching.

Merely as starting point, however, the writer will say that even as he has previously reported that a 1 to 40,000 dilution of orcein roughly matched a 1 to 10,000 of straight acetone extract from cudbear, so he will now report that a freshly prepared 1 to 4,000 dilution of the same orcein roughly matched a 1 to 30,000 dilution of "A. C. A." extract.

Experiments proved that the tints of the dilutions varied not merely as to

whether they were acid or alkaline, but also according to the quantity of ammonia present, and as disregard of degree of alkalinity made the first matchings futile, in those reported below all dilutions were of uniform alkalinity, each being started from 1 cc. of a tincture consisting of the extract (or orcein) 1.0 gm., 10 percent. ammonia, 2 cc., and alcohol to make 1000 cc. In order to avoid variation in ammonia strength, enough of the alkaline menstruum was prepared at one time to make all of the tinctures used at that time.

Finding that attempts to match with orcein were futile, there were prepared 1 to 40,000 dilutions of the six "A. C. A." and "C. A." extracts which were on hand. These, when fresh, so closely simulated each other that a separate set of 1 to 50,000 dilutions were prepared and the twelve fluids, placed in two-ounce tall Blakes, were submitted as unknowns to three observers, whose reports as to color sequence, with darkest first, are given below:

MATCHING "A. C. A." AND "C. A." EXTRACTS.

| Observer I | | Observer II | | Observer III | |
|---|---|---|---|---|---|
| "A. C. A." No. 2 | 1–40,000 | "A. C. A." No. 2 | 1–40,000 | "A. C. A." No. 2 | 1–40,000 |
| "C. A." No. 3 | | "A. C. A." No. 4 | | "C. A." No. 2 | |
| "C. A." No. 1 | | "C. A." No. 1 | | "A. C. A." No. 3 | |
| "A. C. A." No. 4 | | "A. C. A." No. 3 | | "A. C. A." No. 2 | 1-50,000 |
| "C. A." No. 2 | | "A. C. A." No. 2 | 1–50,000 | "A. C. A." No. 4 | 1–40,000 |
| "A. C. A." No. 3 | | "C. A." No. 2 | 1–40,000 | "C. A." No. 1 | |
| "A. C. A." No. 4 | 1–50,000 | "C. A." No. 3 | | "C. A." No. 3 | |
| "A. C. A." No. 2 | | "A. C. A." No. 4 | | "A. C. A." No. 4 | |
| "C. A." No. 1 | | "C. A." No. 2 | | "C. A." No. 1 | |
| "A. C. A." No. 3 | | "C. A." No. 1 | 1–50,000 | "C. A." No. 2 | 1–50,000 |
| "C. A." No. 2 | | "C. A." No. 3 | | "C. A." No. 3 | |
| "C. A." No. 3 | | "A. C. A." No. 3 | | "A. C. A." No. 3 | |

These results are so at variance as to seem worthless at first glance, but careful study shows that they strikingly prove how close is the tinctorial value of the six extracts. In the first place, note that, with the exception of one sample, all of the 1 to 40,000 dilutions were clearly distinguishable from the 1 to 50,000 dilutions, and while two observers placed the "A. C. A." extract No. 2, 1 to 50,000 among the 1 to 40,000 dilutions, the other observer placed it as the second lightest of the 1 to 50,000 dilutions.

As to order of sequence reported by the three observers, let it be understood that all three agreed that the color of the 1 to 50,000 dilutions on one hand and of the 1 to 40,000 on the other (with the one exception cited above) were so close that discernment of difference was scarcely short of guesswork, hence the writer feels justified in employing the adjective "uniform" for the chloroform-acetone extracts which he has prepared.

## CONCLUSIONS.

In the writer's hands, uniform cudbear extracts have been prepared by percolating the drug, first with chloroform to remove the brown pigment, and then with acetone; the acetone percolate being distilled and the thin extract thus obtained dried by "scaling."

This extract is soluble in water containing ammonia and in alcohol, and a faintly ammoniacal alcoholic tincture is freely miscible with water.

The tinctorial power of this extract is approximately three times that of a straight acetonic extract and about 300 times that of an average sample of tincture of cudbear, N. F.

As to uniformity, six samples of these extracts in a dilution of 1 to 40,000 were practically identical in tint and in intensity.

Of the six extracts just mentioned, three were prepared by making an alcoholic extract, removing the brown pigment from this by maceration with chloroform and extracting the residue with acetone; the acetonic solution being then distilled and the residue "scaled." This first step—alcoholic extraction—is, however, superfluous.

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## THE RED COLORING PRINCIPLE OF CUDBEAR.

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At the 1911 meeting of the A. Ph. A. held at Boston, a preliminary paper was read and discussed by Alexander Gardner and Otto Raubenheimer in reference to Cudbear. At that time the active principle was extracted by percolating the drug with acetone and evaporating the colate to a soft extract. This process while a step forward in the right direction was afterward abandoned owing to the amount of wax extracted which made the mass undryable.

After considerable experimenting by the author, a cheap process was obtained whereby the cudbear was packed firmly in a percolator and percolated with purified petroleum ether until entirely free from wax (which requires about 2500 cc. to 1000 gm. of drug) after which the drug is subjected to desiccation.

The drug is then repacked and percolated with acetone (which will require 2500 cc. acetone for thorough exhaustion). The colate is then placed in a still and the acetone recovered, or it can be evaporated spontaneously, after which the resulting mass is placed in a porcelain capsule and heated to 210 F. for thirty minutes. The mass is then pulverized and placed in a sulphuric acid desiccator for three days during which time it will lose about 25% of its weight.

This extractive I have designated as Persionin.

Persionin is a black lustrous powder with an aromatic odor, soluble in alcohol, glycerin, chloroform, ether, and hydroalcoholic liquids, but is only sparingly soluble in water.

The following has been the yield of 5 samples of drug.

| | |
|---|---|
| First sample | 6.5% of persionin |
| Second sample | 7 % of persionin |
| Third sample | 6 % of persionin |
| Fourth sample | 5 % of persionin |
| Fifth sample | 5.5% of persionin |

Each sample of persionin was tested by dissolving 1:100 in alcohol and glycer-