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With the author's compts.

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ON THE USE OF ALCOHOL AS A TEST FOR THE PURITY OF CROTON OIL.

BY

ROBERT WARINGTON, F.R.S., F.C.S.

The College of Physicians of Edinburgh in their Pharmacopœia of 1839, under the article "Croton Oil," contained in the Materia Medica, gave the following directions for testing its purity:—"When agitated with its own volume of pure alcohol and gently heated, it separates on standing, without having undergone *any apparent diminution*." The alcohol is ordered to be prepared from rectified spirit by well-burnt lime, and the density should not exceed ·796. This test has been transcribed *verbatim* into various works on Materia Medica, dispensatories, etc., and is repeated in the Pharmaceutical Journal for July, 1844, vol. iv. p. 47, and December, 1849, vol. ix. p. 296, in answer to correspondents. In the latter volume, however, at a later date, May, 1850, vol. ix. p. 499, a very valuable paper, by the late Dr. Pereira, was published on the subject, entitled, "On the Alcohol Test of the Purity of Castor and Croton Oils, by Jonathan Pereira, M.D., F.R.S." As it is only with the experiments and deductions concerning croton oil that we have to deal, I shall only allude to those parts of the paper which relate to it, and that as briefly as the nature of the subject will admit.

"Experiment 2.—Eight volumes of pale or amber-coloured East India croton oil were mixed with eight volumes of alcohol, specific gravity ·796, and gently heated. In two days a separation had taken place, *the oil now measured* $8\frac{3}{4}$ *volumes*, while the alcohol measured only $7\frac{1}{4}$ volumes (or 10 volumes oil + 10 volumes alcohol = 10·94 oil + 9·06 alcohol). In this case *the croton oil had taken up three-quarters of a volume of alcohol*." Dr. Pereira considers that these fluids exert a mutual solvent action on each other, similar to that of ether and water. This mutual action, however, he states, "is not uniform, but varies with the samples of oil. At first," he says, "I was inclined to ascribe this variation to differences of purity in the several samples of oil examined, but I am now convinced this is not the case, and that they depend on other circumstances."

"Experiment 6.—One volume of dark-coloured English-expressed croton oil was mixed with one volume of alcohol, sp. gr. ·796, by shaking, without any additional heat, a uniform transparent mixture was obtained; and no separation took place on standing for several weeks." Upon which Dr. Pereira naturally asks, "On what does this difference depend? Does it arise from

differences in the qualities of the seeds pressed, or from differences in the mode of preparing the oil?" He then, after acknowledging himself indebted to Mr. Redwood for his first information of these facts, quotes the test of the Edinburgh Pharmacopœia, and adds, "I have never been able to verify this statement;" and then repeats the results of experiment 6, and proceeds, "Mr. Redwood has verified the same fact with various samples of genuine croton oil," "and he finds that no subsequent separation takes place unless the mixture be subjected to *artificial cold;*" "in that case, the oil is found to have slightly increased in bulk, and the alcohol to have suffered a corresponding diminution of volume. I presume, however, that the statement of the Edinburgh College is intended to apply to the amber-coloured East India croton oil," and alludes to the results of experiment 2.

Dr. Pereira then mentions "a very interesting and important fact," that "croton oil enables other fixed oils to dissolve in alcohol;" and gives an illustration in "Experiment 17.—Two volumes of English expressed croton oil, one volume of olive oil, and three volumes of alcohol, were mixed together. By shaking, a homogeneous mixture was obtained." He then states that he considers "these various facts to be best explained by supposing that *croton oil contains some principle which confers the power of dissolving in alcohol*, and that this principle does not exist in all samples in the same proportional quantity. and hence their unequal solubility in alcohol." If "*the quantity of this solvent principle in croton seeds increases the longer the seeds are kept, we should have a ready explanation of the greater solubility of croton oil expressed in England from seeds brought from India*, and which are often musty, *than of those oils expressed in India from fresh seeds.*"

Such, then, was the extent of our knowledge on this subject in 1850.

In January, 1864, the British Pharmacopœia was published, and in the Materia Medica, under the head of "Oleum Crotonis. The oil expressed from seeds in England," we find as follows: "Test.—Agitated with its own volume of alcohol, and gently heated, it forms a clear solution, from which *about three-fourths* of the oil separate on cooling." This test has been *severely criticized*, and in rather *strong terms*, in the numbers of the Pharmaceutical Journal for February and April, 1864, vol. v. 2nd ser. pp. 363 and 485. In the first of these, in a paper entitled "Explanatory and Critical Notes on the British Pharmacopœia," we read, "This test is about *true* as regards *East Indian croton oil*, but *it is not true* with *English croton oil*, which is *wholly and readily soluble in alcohol*, and the solution thus formed is permanent at ordinary temperatures." In the second, under Lecture II., "On the Organic Materia Medica of the British Pharmacopœia," delivered before the Pharmaceutical Society of Great Britain, on the 23rd March, 1864, we read, "this is *a mistake*, the *framers of the Pharmacopœia having given the test for East India croton oil instead of that for English oil;* hence the test *is true* as regards the former, but *is not correct as regards the latter, or officinal oil, which is wholly and readily soluble in alcohol, and the solution thus formed is permanent at ordinary temperatures.*"

Now I presume that these statements, from their general context, are derived from the results published by Dr. Pereira in 1850. But if it is so, how is it that they are *not concordant with those results?* In Dr. Pereira we read "Experiment 2.—Eight volumes of East India croton oil and eight volumes of alcohol (sp. gr. ·796) gave 8·75 volumes of oil, or ten of oil gave 10·94, being *an increase* of 0·75 volume, or nearly one-tenth." But the British Pharmacopœia states that ten volumes of English-expressed croton oil and ten volumes of alcohol gave about 7·5 volumes of oil, or *a decrease* of 2½ volumes, or nearly one-fourth. Is this "*about true as regards East Indian croton oil*"? Is this "*a mistake*"? Have "*the framers of the Pharmacopœia given the test for East Indian croton oil*"? The *mistake*, I believe, lies with the *critic*, as

must be evident. Such statements should surely have been carefully examined into *before they were put in print*. But I think I have said enough to remedy the error. It is also to be regretted that the experiments conducted on English expressed croton oil of 1850 had not been repeated on genuine samples of oil, expressed from seed in England in 1863, before such strong assertions as to their truth were published.

It may be asked, and very properly, how does this subject interest me? and how come I to take it up? The case stands thus :—In the month of *November*, 1863, at the time the sheets of the British Pharmacopœia were passing through the press, Dr. Frederick Farre, the London editor, requested me to try the test for the purity of croton oil given by the Edinburgh College in 1850, before introducing it into the text of the forthcoming volume. This was done with an oil taken from our own stock, and the result published in January, 1864, in the Pharmacopœia. This croton oil had been purchased in July, 1863, of Messrs. Horner, who, it is well known, press their own seed in London. The volume of oil which separated may have been stated a trifle *lower* than what it should have been, owing to the graduations at that part of the tube employed not being perfectly accurate. It will be seen, however, that this error was only of small amount, and does not affect the general statement.

On finding the published test, deduced from this experiment, so warmly criticized before the Pharmaceutical Society by one of their own professors, and the *truth* of my result so strongly questioned, I lost no time in repeating the trial, in order to satisfy my own mind on the subject. This has led me to the conclusion that the use of alcohol as a test for the purity of croton oil was really of no value, and not to be relied on in any way. Between the buyer and seller this becomes a matter of importance, and, as such, I considered it worthy of publication. The sample of oil first tried was also purchased from Messrs. Horner, in May, 1864 ; the experiments having been commenced in June. For the purpose of more easy comparison, the volume of oil taken in each case is estimated at ten measures, and I have noted against Dr. Pereira's experiments above the results calculated on the same quantity.

Experiment 1.—Ten volumes of English-pressed croton oil (Messrs. Horner's) and ten volumes of alcohol were mixed, and agitated together ; but, on standing, they soon separated. They were again shaken, and gently warmed ; a perfectly clear solution was obtained, which was set aside, and, in the course of a few hours, had separated into two layers,—the under, or oily one, indicating 9·5 volumes ; the upper, or alcoholic one, measuring 10·5 volumes. The alcohol had become of an ordinary sherry tint, from the solution of some part of the oil.

About this time a parcel of foreign croton oil was notified on the drug lists for sale, of which Mr. Quincey very kindly forwarded me a sample, accompanied also by one of croton oil expressed from seed in this country about fourteen years since. The sample of imported oil was marked "ex Earl of Auckland v. Rotterdam in transit from Batavia."

Experiment 2.—Ten volumes of imported oil were mixed, as before, with ten volumes of alcohol, and briskly agitated. It soon separated, and was then again shaken and gently warmed ; perfect solution followed, and the tube was set aside. In a few hours the contents had separated into two layers, the oil measuring 11·5 volumes, and the alcohol 8·5 ; also coloured, from solution of part of the oil. This result shows a slight increase on that obtained by Dr. Pereira from East Indian croton oil, which was, from experiment No. 2, 10·94 volumes of oil, after separation.

Experiment 3.—Ten volumes of the old English-expressed oil were mixed with ten volumes of alcohol, as before, only as they seemed to unite immediately no agitation was required ; the mixture was very turbid, but exhibited no signs

of separation. On being warmed, it became transparent and remained permanently dissolved. Here then was a case corresponding exactly with the results published by Dr. Pereira in experiment 6. This old oil was very thick, and when the cold weather commenced became slightly crystallized.

In consequence of this result, I procured a sample of croton oil from Messrs. Hodgkinson, Tonge, and Co., and also another specimen of the imported oil. Experiment 4.—Ten volumes of croton oil (Messrs. Hodgkinson, Tonge, & Co.) + ten volumes of alcohol were gently mixed, and then agitated briskly ; separation soon occurred; the mixture was then warmed, when it formed a clear solution, which, by standing a few hours, separated into 9 volumes of oil and 11 of alcohol, the latter being much coloured, as in experiment 1.

Experiment 5.—Ten volumes of imported oil (specimen No. 2) + ten volumes of alcohol treated as before, yielded the same results as experiment 2.

In consequence of the alcohol in all these experiments becoming nearly as dark-coloured as the oil itself, the whole were put aside in a bottle for future experiment. When the result of experiment 3 was poured in, to my great surprise, the results from experiments Nos. 1 and 2 instantly formed a clear solution, and this also occurred on the addition of the separated materials from numbers 4 and 5. So that we have here the presence of 10 volumes of old oil causing 40 volumes of croton oil (composed of 20 volumes of English-expressed, and 20 volumes of imported oil) which would not dissolve in alcohol, to enter into perfect solution, and this without any application of warmth. I shall have occasion to refer to this again presently.

From these results, I was induced to try the solvent action of rectified spirit upon some of the specimens of croton oil. Experiment 6.—Ten volumes of English-expressed oil + ten volumes of rectified spirit, sp. gr. 838, were mixed as before, and well shaken together, but without solution ; the mixture warmed, but still no evidence of solubility. Mechanical admixture only took place, and this was followed by rapid subsidence of the oil.

Experiment 7.—Ten volumes of the English-expressed, fourteen-years-old oil, + ten volumes of rectified spirit, were mixed together and did not separate ; though turbid, the solution appeared to be perfect on the following morning, however, it was found that it had divided into two strata.

I have mentioned that these experiments were commenced in June, and the temperature of the air at that time was seldom below 70° Fahr. day or night. On the night of this last experiment, however, it was observed that the thermometer had fallen a few degrees lower. For the moment the separation of the oil was not attributed to the influence of this slight diminution of temperature, and the experiment was therefore repeated exactly as before; no solution, however, could be obtained by simple admixture, and when this was effected by a gentle heat, separation took place in a few hours by standing It was then found that as long as the temperature of the room was above 70°, the oil remained permanently dissolved, but that as soon as the thermometer had sunk three or four degrees lower, separation rapidly took place. So also with the mixed results of experiments 1, 2, 3, 4 and 5, as long as the temperature was at 68°, or above that, so long the solution was perfect ; but below that point, namely at 66°, separation gradually occurred. In consequence of these interferences from the effects of a few degrees differences of heat, I resolved to repeat these experiments when the temperature of the atmosphere was lower and more equable.

November, 1864, Experiment 9.—Ten volumes of English-expressed croton oil (from Messrs. Hodgkinson and Tonge) + ten volumes of alcohol gave by agitation an emulsion which separated by standing into 8·3 measures of oil + 11·7 of alcohol. It was again agitated and warmed ; it readily dissolved, but in a few hours separated into 8·2 volumes of oil and 11·8 of alcohol. The temperature of the air was about 50°.

Experiment 10.—The imported oil from Batavia (No. 1) gave by cold admixture 10·2 oil + 9·8 alcohol; by warmth and subsequent deposit, 10·1 oil + 9·9 alcohol.

Experiment 11.—Imported oil (No. 2 sample) gave by agitation without heat 10·2 oil + 9·8 alcohol; after heating and separation, 10·1 oil + 9·9 alcohol, being the same as experiment 10 on No. 1.

Experiment 12.—The specimen of old oil from Mr. Quincey yielded by agitation an opalescent or milky solution, which did not exhibit any signs of separation.

Experiment 13.—The English expressed oil from Messrs. Horner, by cold admixture and standing gave 9 of oil + 11 alcohol; after solution by warmth and repose 8·9 oil + 11·1 alcohol. The temperature in this case was about 60°.

I then made a few experiments with alcohol of ·794 sp. gr., with the following results:—

Experiment 14.—The imported oil from Batavia gave, by agitation, without heat, 9·3 volumes oil + 10·7 alcohol. After solution by warmth and subsequent deposit 9·4 oil + 10·6 alcohol. Temperature 56°.

Experiment 15.—Horner's English expressed oil, by cold agitation, yielded 8·8 of oil + 11·2 alcohol. After dissolving by heat and standing, 8·7 oil + 11·3 alcohol.

Experiment 16.—The imported oil was again tried, but increasing the volumes acted upon to double their previous quantity, when it gave by the cold operation 9·9 of oil + 10·1 of alcohol; after solution by heat and separation, 9·9 oil + 10·1 alcohol. Temperature 58°.

The results, from the experiments Nos. 14 and 16, were placed in the same bottle, and it was found that the oil entered into perfect solution at 75° Fahr. At 70° the solution became opalescent, but without any separation. But at 67° a complete deposition of the oil took place.

What conclusions now can we deduce from these results? My own opinion is that freshly expressed croton oil, or rather, I should say, *oil* expressed from *fresh seeds*, either abroad or in this country, does not dissolve in alcohol having a specific gravity from ·794 to ·796, to a greater extent than twenty per cent. at the temperature of 50°; but that if croton oil has undergone a chemical change, such as resinification or oxidation by time and exposure to the air, as in the old oil of the above experiments, or has been freshly expressed from seeds which have become changed in the same manner, then the oil is dissolved freely by the alcohol, as shown above and in the experiments of Dr. Pereira, which I consider therefore must have been made with croton oil, freshly expressed it is true, but from seeds which had undergone a chemical change; and this accords with his own deductions from his experiments. At the same time I cannot but consider that a *test* which is open to so many weighty objections, both from the influence of small fluctuations of temperature, and for indicating the purity of a material liable to such marked differences from the effects of such natural and in some cases inevitable chemical changes, is perfectly useless as a reliable indication of purity.