Papers Presented to Local Branches

THE OFFICIAL TESTS FOR CREOSOTE.

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The tests of the U. S. Pharmacopœia (VIII) for Creosote are indefinite and unsatisfactory.

The therapeutically active ingredients are chiefly the ethers guaiacol (b.p. 200° C.) and creosol (b.p. 219° C.) with the alcohols phenol (b.p. 182° C. B. P.), paracreosol (b.p. 203° C.), dimethyl-guaiacol (b.p. 230° C.) and propyl-guaiacol (b.p. 241° C.), (Food and Drugs, E. J. Parry, 1911, 454). Guaiacol and creosol are closely related, chemically, the former being methyl catecholate (C_6H_4 (OCH_3OH)), and the latter, methyl homocatecholate ($C_6H_3CH_3$ (OCH_3OH)).

Allen states (Commercial Organic Analysis, A. H. Allen (1900), Vol. II, Part II, 279) that "Phenol is present in genuine wood-tar creosote in very small quantity, the creosols in somewhat larger, and the xylenols in sensible proportions; but the two chief constituents are guaiacol and creosol. In Rhenish creosote, guaiacol predominates, but a sample of Morson's creosote from 'Stockholm tar,' examined by the author, boiled at 217° C., and consisted chefly of creosol." He writes (p. 285), that the range of boiling point from 200 to 220° C. "admits creosol to an equality with guaiacol as a legitimate and valuable constituent of creosote, which would appear to be justifiable both from analogy and from what is positively known of the therapeutic action of creosol."

There are considerable differences of opinion regarding the percentage of guaiacol in creosote. Some years ago it was believed to be 60 per cent. or more, but if this ever was the case, there has been a marked reduction in recent years.

Thus, Behal and Choay, in 1894 (Compt. rend. 119, 116; Abst. J. S. C. 1, 1894, 1087, 1187), obtained from beechwood creosote (two samples), *respectively*, 39 and 39 per cent. of monophenols, 19.7 and 26.5 per cent. of guaiacol, and 40 and 32.1 per cent. of crésosols and homologues.

In 1899, Kebler (Amer. Journ. Pharm. 1899, 409) found the proportion of guaiacol in commercial wood creosote to range from *nil* to 16 per cent.

In 1900, Allen wrote (p. 283) "in consequence of the large demand of recent years for guaiacol and its preparations, much of the wood creosote now sold has been deprived of its guaiacol, so that it is now rare to find specimens containing even 20 per cent. of that constituent," and Parry (Foods and Drugs, 1911, 455) states that "guaiacol is present to the extent of about 15 to 25 per cent."

The chief tests of the Pharmacopœia (VIII) for Creosote are the gravity (s.g. (corrected) 1.078 at 25° C.), and the boiling point ("when distilled most of it comes over between 200 and 220° C.").

*Read before the Scientific Section of the Philadelphia Branch.

While guaiacol boils at 200 to 205° C., creosol at 219° C. and the monophenols at less than 200° C. (the boiling point of phenol is 182° C. (B. P.)—188° C. (U. S. P.)), it is apparently possible (1) to distill off the low-boiling phenols and reserve, (2) to distill off all or a part of the guaiacol and (3) to add the reserved low-boiling monophenols to the high-boiling creosol and obtain a product that will comport with the U. S. P. standards.

In this way creosote can be deguaiacolized, and a product worth about $2.40 a pound can be obtained from one worth about 75 cents a pound, and the residue can be sold for creosote at 75 cents.

The Pharmacopœia seeks to prevent such a practice by requiring that when creosote is distilled "most of it" (a most indefinite statement) comes over between 200 and 220° C., evidently assuming that if the product contains much phenol it will boil at a lower boiling point than 200° C. As a matter of fact, this is not the case. Kebler has shown (Amer. Journ. Pharm., 1899, 410) that the fraction of creosote coming over between 200 and 210° C. may contain a goodly per cent. of phenol having a boiling point of 20° below the lowest boiling point, and the same fraction may contain more than one-third its weight of creosol, a body having the boiling point of 219° C.

Experiments made by H. M. Sechler in the Analytical Laboratory of the Smith, Kline & French Company, show that when phenol is added to creosote or guaiacol, the mixture does not boil at 188° C. (the boiling point of phenol is "not higher than 188° C."), but a number of degrees higher, depending upon the percentage added. Doubtless some of the lower-boiling liquid is vaporized by the heat, but the boiling point of the mixture is higher than that of the lower-boiling liquid added.

The results obtained were:

Creosote B. P.	208.5° C.
Phenol B. P.	188 ° C.
Creosote 75% / Phenol 25% B. P.	198.5° C.
Guaiacol B. P.	204.5° C.
Guaiacol 75% / Phenol 25% B. P.	197.5° C.

Five samples of Creosote marketed by American manufacturers and guaranteed under the Food and Drugs Act, have been examined by M. Becker in the Analytical Laboratory of Smith, Kline & French Co. The percentages of distillate obtained were by volume. The specific gravity of each sample at 25° C. was 1.080.

No. 1 vaporized at 198° C. and gave 8 per cent. of distillate below 200° C.; between 200 and 215° C. it yielded 80 per cent., and between 200 and 220° C., 84 per cent.

No. 2 vaporized at 198° C. and gave 28 per cent. of distillate below 200° C.; between 200 and 215° C. it yielded 60 per cent., and between 200 and 220° C., 64 per cent.

No. 3 vaporized at 195° C. and gave 36 per cent. of distillate below 200° C.; between 200 and 215° C. it yielded 58 per cent., and between 200 and 220° C., 62 per cent.

No. 4 vaporized at 197° C. and gave 24 per cent. of distillate below 200° C.; between 200 and 215° C. it yielded 64 per cent., and between 200 and 220° C., 68 per cent.

No. 5 vaporized at 198° C. and gave 8 per cent. of distillate below 200° C.; between 200 and 215° C. it yielded 80 per cent., and between 200 and 220° C., 84 per cent.

A sample of Morson's English creosote was examined, also, and found to have the specific gravity of 1.083 at 25° C. It vaporized at 203° C. and gave 80 per cent. of distillate between 203° and 215° C., and 94 per cent. between 203° and 220° C.

Parry (Food and Drugs, 1911, 455) claims that "a good creosote should have a specific gravity of at least that required by the British Pharmacopœia, preferably a little higher—up to 1.085. 1.085 at 15.5° C. (B. P. temperature; about equals 1.079 at 25° C., U. S. P. temperature, J. W. E.) On fractionation, three typical samples gave the following results with which pure samples will approximately correspond":

	Sp. Gr.	Guaiacol Percent	Under 200° C Percent	200-205° C Percent	205-210° C Percent	210-215° C Percent	215-220° C Percent
1	1.0815	21.5	6	39	22	25	6
2	1.0820	19.8	7.5	40	20	23	7
3	1.0800	23	5	35	24	22	10

Parry's experiments show that from 81 to 86 per cent. of English creosote distils between 200 and 215° C., and 6 to 10 per cent. between 215 and 220° C.; or 90 to 92 per cent. between 200 and 220° C.

Pure guaiacol was formerly described as a liquid, but has been obtained by Behal and Choay (Comp. rend. 116 (1893) 197) as a white solid liquefying at 28.5° to 33° C.

The specific gravity of liquid guaiacol at 15° C. is from 1.143 to 1.149 (Commercial Organic Analysis, Allen, Vol. II, Part II, 273).

The specific gravity of creosol at 13° C. is 1.0894 (Watt's Dictionary of Chemistry, 1894, 271).

The specific gravity of the phenols of creosote is probably much lower than that of guaiacol or creosol.

Creosote varies greatly in its percentages of guaiacol, creosol and monophenols. In therapeutic properties, it is analogous to phenol, being antiseptic, anesthetic and antipyretic, but it is believed to be more powerful in action. Creosote depends for its activity not only upon its guaiacol and creosol, which together are present in the larger proportions, but also, upon its monophenols, which Behal and Choay (previously quoted) found to the extent of 39 per cent., these (in creosote) distilling between 200 and 220° C.

Since "Creosote is more efficient than either of its principal constituents, guaiacol or creosol, even if given in proportionate dose" (Pharmacology and Therapeutics, Reynold Webb Wilcox, 1905, 598), its activity can *not* depend upon guaiacol or creosol, or both; it must depend also upon its monophenols. While guaiacol resembles creosote in its general action, it is much more powerful in reducing temperature and much less active as a germicide (U. S. D. 19 Edt., 603).

Hence, it would appear that the guaiacol-content or the creosol-content of cre-

osote, or both, are not indicative of therapeutic strength, and that the best procedure, apparently, for the Pharmacopœia, would be to eliminate the phrase "most of it" in the paragraph "when distilled most of it comes over between 200 and 220° C." and to require that, when distilled between 200 and 220° C., *a certain specified percentage of distillate (by volume) shall be obtained,* probably between 80 and 90 per cent., as indicated by the experiments of Parry and Becker.

It might be desirable, also, to raise the official specific gravity of creosote slightly, so as to ensure the presence of more guaiacol. The higher the gravity the greater the percentage of guaiacol, since guaiacol has the highest gravity of the several principles of creosote. The U. S. P. (VIII) gravity (corrected) of 1.078 at 25° C. is about 1.085 at 15.5° C. (the B. P. standard is not below 1.079) and this is lower than the gravity of either guaiacol (1.143-1.149 at 15° C.) or creosol (1.0894 at 13° C.). As has been shown (Am. Journ. Pharm., L. F. Kebler, 1899, 411), a gravity of 1.070 at 15° C. can be easily met by a creosote that does not contain any guaiacol. Parry recommends a gravity of 1.085 at 15.5° C. or about 1.079 at 25° C., which latter is practically the same as the present (corrected) U. S. P. gravity of 1.078 at 25° C.

ADULTERATION OF DRUGS.*

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The Food and Drugs Act of June 30, 1906, was enacted primarily for the purpose of preventing the manufacture, sale or transportation of adulterated, or misbranded, or poisonous, or deleterious foods, drugs, medicines and liquors. I would emphasize the words *adulterated, poisonous* and *deleterious drugs,* as they are in line with what I have to say this evening and because they have an important bearing on the other topics on the program, viz., the "Richardson amendment."

The Food and Drugs Act includes under the term *drug* all medicines and preparations recognized in the United States Pharmacopœia and National Formulary, for internal and external use, and any substance or mixture of substances intended to be used for the cure, mitigation or prevention of disease, of either man or other animals. This little word *drug* with its four letters is fraught with a mighty meaning. By the provisions of this law it embraces within its scope not only all the products enumerated in the U. S. P. and the National Formulary, which your association publishes, but every substance described in the most comprehensive dispensatory or dictionary of medicine, every true patent medicine and every popularly so-called *patent medicine,* every nostrum; all manner of "dope" if you please. Indeed it seems that we may catalogue here almost everything mineral and vegetable, and some animal, that God has created and that man, aided and abetted at times by the devil, has devised or fabricated. The surf and weeds of

*Read before the Denver Branch.