

with the results shown in Table III. Still others now being prepared will be studied later. Since the amount of free acid in the emulsions studied is small (p_H 5.8) it is doubtful how much any free formic acid present contributes to the anthelmintic effect. Perhaps renewed analytical investigation of oxygenated α -pinene and oxygenated limonene will give a clue to the identity of these very powerfully antiascaridic substances.

SUMMARY.

1. Hydrogen peroxide is very toxic to *Ascaris lumbricoides*. The relation of this observation to the anthelmintic activity of ascaridole has been discussed.

2. By passing oxygen or air over α -pinene, turpentine or *d*-limonene products are formed of pronounced toxicity to *Ascaris lumbricoides*. The toxic substances in these products are probably not peroxides.

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PHYSICAL PROPERTIES OF NEOARSPHENAMINE POWDER.*

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Very little has been written concerning the physical characteristics of neoarsphenamine powder. The United States Public Health Service specifications (1) for neoarsphenamine state that "Stability shall be determined by exposing the ampuled product to a temperature of 56° C. for a period of at least 24 hours, during which time it should show no marked change in color, consistency, or solubility." This statement does not, however, describe the various changes which can occur during the "heat-testing" of neoarsphenamines. The following discussion is based on a large number of observations made during the testing of a variety of neoarsphenamines all of which were sealed in evacuated ampuls.

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Although nearsphenamine is usually described as a yellow, free-flowing powder, there are several different types of powder.

- (a) A powder consisting of coarse, sandy particles which show no tendency to cling together when an ampul of the product is rotated slowly.
- (b) A very finely divided, fluffy type of powder whose particles cling together.
- (c) A powder containing a mixture of both fluffy and coarse particles with noticeable differences in color existing between the particles of different size.
- (d) A powder which is finely divided and which consists of small, sandy or hard particles, not of soft, fluffy ones.

All of these different types of powders have been found in commercial samples of nearsphenamine.

It is apparent that the differences between the several types of powder are due to variations in the physical characteristics of the individual particles such as size, shape, and hardness or porosity, and need not have any relation to the chemical or biological properties of the product. Since nearsphenamine is a complex product which is produced by precipitation, it is not unexpected that the physical properties may be varied rather extensively without altering the chemical or biological properties. The Public Health Service specification quoted above relates to changes in the color, consistency, and solubility of the powder. It is agreed that if chemical decomposition does occur during the heat test one might expect to find changes in the color, consistency, and solubility of the powder. However, if two powders which are chemically identical and chemically stable on heat test are different in physical properties, it would be possible for changes to occur in the particles which would be observed as color or consistency change and these two changes would not then be indicative of chemical sensitivity or instability. Any such purely physical changes should not, however, be accompanied by differences between solutions of the original and of the same material after heat test. We have been interested in the magnitude and character of the powder changes which are associated only with the physical characteristics of the powder and in the mechanism whereby these changes occur.

We will first mention the nature of the changes which have been noted and which are believed to be only physical; the consistency changes will be considered first. A free flowing powder may change to one whose particles show a distinct tendency to cling together. Also a dry looking powder may, after heating, show a greatly increased tendency to adhere to the wall of the ampul in which it is packaged. One further change sometimes noted is that a dry powder may develop a wet appearance after heating. Usually the heat-tested ampul is removed from the oven, allowed to cool for a short time, and compared with an unheated ampul. Very often, when some such comparison shows a difference, this difference will decrease greatly if the heat-tested ampul is allowed to stand at room temperature for 24 hrs. before comparison with an unheated ampul, *i. e.*, the powder gradually reverts to its original physical condition. If the consistency change taking place during heat test is only temporary, reversion will occur slowly in the sealed ampul, but by opening the ampul the powder can be returned to its original consistency almost instantly. These phenomena are very pronounced if the ampul, immediately after removal from the oven, is rotated so that the powder rolls around in the warm ampul. The powder may stick to the walls and appear to be

wet, but if the ampul is now opened the wet, sticky powder changes rapidly to its original dry, free-flowing condition. Reversions of this type are in themselves indicative of the fact that the consistency change was only physical, and this belief is supported by the clarity and color of a solution of the heat-tested powder.

A suggested explanation of the above findings is based on the fact that neoarsphenamines contain a small amount of volatile matter which may be water or some solvent used in the precipitation. When the highly evacuated ampul containing the powder is kept in the oven, these traces of liquid are volatilized and exist in the space above the powder.¹ The behavior of this volatile matter when the ampul is removed from the oven affects the consistency of the powder. Immediately after removal from the oven the glass ampul starts to cool and does so faster than the powder inside; therefore instead of passing back into the powder the vapor starts to condense on the ampul as well as on the powder particles. If the condensation on the glass is extensive a thin film of liquid will coat the ampul wall and if the ampul is rotated the particles become wetted by the liquid film and become wet and sticky in appearance. If on the other hand the ampul is removed from the oven very carefully so as not to agitate the powder and if the ampul is allowed to stand at room temperature, the liquid film which initially deposits on the glass starts to pass back into the powder; neoarsphenamine is very hygroscopic and therefore as the film of liquid gradually evaporates from the glass it is reabsorbed by the powder. We suggest therefore that in the absence of chemical decomposition, the consistency change in neoarsphenamine powder as a result of heat test is a function of the traces of volatile matter in neoarsphenamine and the manner in which it is reabsorbed by the powder.

Color change of powder is sometimes difficult to evaluate correctly because changes in the character of the particles which are observed as consistency changes can produce apparent color changes. Thus, it is known that two surfaces may have exactly the same shade of color but they will appear to be different if one is smooth and the other rough. Therefore if the powder changes in consistency, an apparent color change of powder is not unexpected. Also, if the vapor which is being reabsorbed by the heat-tested powder is all or partly water, a surface darkening of the particles would be expected because when these traces of water come in contact with the particles there would be an infinitesimal but still detectable "gumming" of particles on the surface. In so far as these color changes are associated with consistency changes, they should lessen when the ampul is handled, after heat test, in such a way that the consistency change disappears. Such is the case; however, there are also color changes of powder which do not disappear during the consistency reversion, but which nevertheless are not related to chemical change. A powder may have darkened permanently after heat test, but when its solution is compared with that made by dissolving an ampul which has not been heated, the two solutions may be identical in color. We conclude, therefore, that both the temporary color change which may be observed in conjunction with the consistency change and the more permanent one are related to the physical properties of the powder.

¹ If one is interested in observing the liquid which volatilized during the heat testing, the ampuls may be placed in a vertical position with the tip upward in the heat test oven using a temperature slightly above 56° C. At the conclusion of the test, liquid will be observed in the tip of the ampul.

The variable extent to which these consistency and color changes occur and the extent and rate of reversion are due or at least intimately related to the original character of the individual particles of which the powder is composed.

We wish to re-emphasize the fact that all discussion in this paper relates only to changes in powders which do not undergo chemical changes during heat test and the object has been to direct attention to and explain certain minor changes observable in tests used to control neoarsphenamine.

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DRUG EXTRACTION. I. A STUDY OF VARIOUS MENSTRUA FROM THE STANDPOINT OF SWELLING EFFECTS, PENETRATION AND EXTRACTION.

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(Continued from page 984, October Journal.)

PENETRATION OF VARIOUS SOLVENTS.

The penetration of liquids through cells is one of the fundamental factors to be considered in drug extraction. Since botanists have been more interested in living tissues, very little has previously been done on the permeability of dried tissues, such as drugs.

Penetration of Various Solvents into Chestnut Wood.—In connection with the tests of swelling on blocks of chestnut wood (see Table X) the rates of penetration of the solvents were determined by weighing the blocks at various intervals, the increase in weight indicating the amount of solvent which entered the block. There is a loss of soluble constituents from the blocks, but this does not introduce a serious error in the case of chestnut wood. For weighing, the blocks were removed from the liquid and the excess liquid on the surface removed by blotting with filter paper. The results are stated on a percentage basis, taking the original weight of the blocks as 100. Each result represents the average of three blocks.

The results in Table XVIII show the rate of penetration and the weight of liquid imbibed in 384 hours by blocks of chestnut wood. The rate of penetration is indicated by the slope of the curves (see graphs) and the time of attainment of equilibrium and from Table XIX. Water shows the most rapid rate of penetration, and a greater weight of water is absorbed. Alcohol also penetrates rapidly, but the weight imbibed is less than the weight of carbitol, ethylene glycol, dioxan and diethylene glycol. Propylene glycol and glycerin show the lowest rate of penetration and are imbibed to a much smaller extent than the other liquids (see Graph 8).

Of the binary mixtures of water, alcohol and glycerin, it is seen that a mixture of equal volumes of alcohol and water shows as fast a rate of penetration as does