

REFERENCES.

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THE DEPARTMENT OF MONOBROMATED CAMPHOR IN REFERENCE
TO COMPRESSED MEDICINAL TABLETS.*

BY GEORGE E. ÉWE.

Monobromated Camphor is "permanent in the air. . . . Melts at 76° C. and sublimates at a slightly higher temperature "according to the U. S. P. VIII." The U. S. P. IX also stated that Monobromated Camphor is "permanent in the air," but in addition, directed that it be preserved in well-closed containers, protected from light. In general, the literature does not emphasize the fact that this substance is definitely volatile; but in compressed medicinal tablet manufacturing practice it evidences a certain degree of volatility which warrants its consideration as a volatile substance.

Striking evidence of the volatile nature of this substance will be afforded by exposing a grain of the powdered substance to the air of the laboratory in a beaker covered with muslin, under which circumstances the monobromated camphor will have completely disappeared after several months. Two grains of the powdered substance when exposed to the air of the laboratory in a 100-cc. beaker covered with a single sheet of filter paper tied on with string required 7 months for complete volatilization. When 2 grains of powdered monobromated camphor were scattered on a 90-mm. filter paper with turned up edges and the paper so charged allowed to remain in a desiccator over sulphuric acid, a period of 2 months and 3 weeks was required for complete volatilization of the substance. About 2 Gm. of powdered monobromated camphor spread on a watch glass lost 0.7% in weight after 48 hours in a calcium chloride desiccator, 0.3% in the following 48 hours and exactly the same in 2 subsequent periods of 48 hours each. In an oven at 40-45° C. a 2-Gm. sample of the powdered substance lost 2.4% of its weight in 12 hours. At 50-55° C. a 2-Gm. sample lost 5.7% in weight in 7 hours.

A large number of various complex tablet granulations have been observed which suffered losses ranging from 1.3% to as much as 43% of their monobromated camphor content when subjected to drying operations on a manufacturing scale at practical degrees of elevated temperature, thereby necessitating adjustment of their content of this substance before compression into tablets. The windows of a room in which a tablet granulation containing this substance was being dried have been observed actually "frosted" with monobromated camphor when only a moderately excessive heat had been inadvertently applied.

Tablets containing monobromated camphor have been observed which became encrusted with glistening crystals of this substance after some time; although not to such a degree as to render the tablets unsightly. Apparently, the crystals were occasioned by volatilization of a portion of the monobromated camphor which subsequently re-deposited upon the outer surface of the tablets. Two such lots of tablets were assayed before and after brushing with a stiff camel's hair pencil with

* Scientific Section, A. P. H. A., Baltimore meeting, 1930.

the object of dislodging the adherent crystals of monobromated camphor, the assays indicating that the encrustation of crystals represented 1.9 and 1.8%, respectively, of the total monobromated camphor content of the tablets. These experiments point out the possible effect of attrition in tending to lower the monobromated camphor content of tablets encrusted with this substance.

Since this substance is frequently employed in medicinal tablets and shows a certain degree of volatility which is manifested even at room temperature the effect of this tendency to volatilize, upon the content of this ingredient in compressed medicinal tablets, deserves consideration. Various batches of compressed compound medicinal tablets made to contain 0.5 grain of monobromated camphor along with several other medicinal ingredients when stored in cork-stoppered, flint-glass bottles in a dark closet for 1 year were moderately encrusted with glistening crystals of monobromated camphor at the end of the storage period and showed losses of from 3 to 9% of their content of monobromated camphor in that length of time. One sample from a partially-filled container showed a loss of 9.8%. On the average this type of tablet was found to lose around 5% of its monobromated camphor content in one year's storage under normal conditions, due to volatilization and to loss of crystals of monobromated camphor from the slight encrustation through unavoidable attrition.

While the loss of this substance which may be sustained by tablets when kept with reasonable care would probably be of little therapeutic significance, yet where the tablets are subjected to unsatisfactory conditions, such as exposure to direct sunlight, storage in an excessively warm location, undue attrition or exposure to air currents through neglecting to replace the stopper of the container, the loss may become serious.

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A STUDY OF THE DARKENING OF COD LIVER OIL IN THE PRESENCE OF IRON.*

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When poultry cod liver oil is handled in iron drums, the oil frequently darkens upon aging, and in order to study this change an extensive series of observation and analytical experiments was set up so as to include (a) the condition of the oil and (b) the contact with the iron surfaces. A typical sample of market poultry oil was used; *firstly*, in its original condition; *secondly*, after clarification through ordinary filter paper; *thirdly*, after drying the clarified oil, and *fourthly*, after alkali refining and drying the clarified oil. Each of these four types of oil was stored under four conditions: (a) without the presence of iron; (b) in contact with iron so that iron surface is 11.6 sq. cm. per 100 cc. of oil; (c) as in (b) except that the surface exposed is 116 sq. cm. per 100 cc. of oil, and (d) as in (b) except that part of the iron surface is above the level of the oil—in (b) and (c) the iron was completely immersed in the oil. The sheet iron used in this work was pickled prior to use. The results of this study are presented in the following table:

* Scientific Section, A. Ph. A., Baltimore meeting 1930.—No discussion.