

3. The sum of the buffer capacities of the dehydrated alcohol and the re-extraction tinctures is essentially the same as the buffer capacity of the 80 per cent alcohol tincture.

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## SIGNIFICANCE OF STEARIN CONTENT OF COD LIVER OIL.\*

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Stearin is a normal constituent of the oil obtained upon rendering cod livers with steam in the manufacture of cod liver oil. Stearin congeals to a solid at only a moderately low temperature at which the other constituents of the oil remain quite fluid and it is the general practice to remove more or less of the stearin during the process of refining the oil by chilling the oil and filtering off the hardened stearin.

The object of removing this stearin is to produce a cod liver oil which will not become cloudy or thick from separation of stearin when the oil is subjected to practical low temperatures.

Removal of the stearin from cod liver oil has, in general, no significant effect upon the vitamin A potency of the oil. Crude cod liver oil and the refined oil and stearin all possess relatively high vitamin A potency, the refined oil sometimes having the higher potency of the three substances, although usually there is no significant difference between the potency of the crude cod liver oil and the refined oil made from it.

Prof. E. Poulsson of Oslo, Norway, in a private communication to the Tailby-Nason Co., writes on this subject, the following being a translation by S. Hammer, an employee of the Tailby-Nason Co.:

"Minute quantities of stearin present in refined cod liver oil have no influence on the digestive organs. Minute quantities of stearin present in cod liver oil do not lower the vitamin content in the oil. It has been shown by research work both here, and in other laboratories, that the separated stearin contains the same quantities of vitamins as the liquid oil. In earlier times, the refrigeration of cod liver oil was almost always done by exposing containers of cod liver oil to the cold in the winter. At present, as far as I know, refrigerating plants are in use, and the temperature of the oil varies between zero and 4 below zero Centigrade. This is sufficient for all practical uses; at a lower temperature, the oil will undoubtedly be cloudy, but we presume that oil exported from this country, very seldom is exposed to a lower temperature. I do not know of any literature bearing on the above questions. The above information is built partly on our own research work, partly on what I have read in different journals, and partly on my own experience (in regard to temperature), from producers."

\* Scientific Section, A. PH. A., Toronto meeting, 1932.

There is no uniformity of opinion regarding the temperature at which the stearin should be removed from cod liver oil.

Thorpe's "Dictionary of Applied Chemistry," in referring to the physical characteristics of an oil (olive) intended for ingestion, states that "oils intended for table use, which deposit 'stearine' in winter, must be freed from such solid fats." The British Pharmacopœia requires solid fat to be separated from cod liver oil by chilling of the oil at about  $-5^{\circ}$  C. ( $23^{\circ}$  F.), followed by filtration. The U. S. Dispensatory states "in some establishments this (stearin) is removed (from cod liver oil) by chilling to  $-10^{\circ}$  C. ( $14^{\circ}$  F.) and expression . . . . ."

The usual refining process does not entirely deplete the oil of stearin and consequently cod liver oil becomes cloudy or congeals if cooled below the temperature at which the chilling and filtration were conducted in the refining process. Commercial refining practices also vary widely in different establishments as regards temperature at which the stearin is removed and, consequently, the effect of an identical low temperature on the products of these establishments varies widely. For instance, when perfectly clear cod liver oils of various brands were kept at an identical low temperature some remained clear, some showed a mere trace of precipitate of stearin, some showed a heavy precipitate of stearin and others became almost solid from precipitated stearin.

The effects of low temperatures upon various brands of cod liver oil on the market are shown in the table below. The table indicates the effect of an identical temperature upon various brands and the effects of different temperatures on the same brand. In making these comparisons the oils were kept in bottles in air at the specified temperature for several hours and the results then recorded.

| Sample No. | 20° F.<br>(-7° C.) | 18° F.<br>(-8° C.) | 16° F.<br>(-9° C.) | 14° F.<br>(-10° C.) | 10° F.<br>(-12° C.) |
|------------|--------------------|--------------------|--------------------|---------------------|---------------------|
| 1          | C                  | C                  | P                  | T                   |                     |
| 2          | C                  | C                  | P                  | T                   |                     |
| 3          | C                  | P                  | T                  |                     |                     |
| 4          | C                  | P                  | T                  |                     |                     |
| 5          | C                  | C                  | P                  | P                   | T                   |
| 6          | C                  | C                  | P                  | P                   | P                   |
| 7          | C                  | C                  | T                  |                     |                     |
| 8          | C                  | H                  | P                  | T                   |                     |
| 9          | C                  | H                  | P                  | T                   |                     |
| 10         | C                  | H                  | P                  | T                   |                     |
| 11         | C                  | C                  | P                  | P                   | P                   |
| 12         | C                  | C                  | C                  | C                   | C                   |
| 13         | C                  | P                  | T                  |                     |                     |
| 14         | C                  | P                  | T                  |                     |                     |
| 15         | C                  | P                  | T                  |                     |                     |
| 16         | C                  | C                  | H                  | H                   | H                   |
| 17         | C                  | C                  | C                  | C                   | C                   |
| 18         | C                  | T                  |                    |                     |                     |
| 19         | C                  | T                  |                    |                     |                     |
| 20         | C                  | T                  |                    |                     |                     |
| 21         | C                  | T                  |                    |                     |                     |
| 22         | C                  | T                  |                    |                     |                     |

C=clear. H=hazy or cloudy. P=ppt. of stearin. T=thick or congealed by stearin.

It will be noted that all of the oils remained clear at  $20^{\circ}$  F. ( $-7^{\circ}$  C.) which

appears to be a sufficiently low temperature to insure preservation of the oil and which is much lower than the temperature at which it is administered.

There is no unanimity of opinion regarding the temperature to which it should be possible to cool cod liver oil without causing separation of stearin. The "U. S. P." does not refer to this subject. The British Pharmacopoeia states that no solid fat should separate when cod liver oil is exposed for 3 hours to a temperature of 0° C. (32° F.). Caspari's "Treatise on Pharmacy" also states that this oil should not deposit solid fat when cooled to 0° C. (32° F.).

While cod liver oil from which sufficient stearin has been removed to allow the oil to remain clear at about 0° C. (32° F.) would seem to answer all practical requirements, producers invariably refine this oil so as to withstand much lower temperatures without clouding.

One of the objections occasionally made to taking oily medicaments is the "oily" feeling in the mouth and throat caused mainly by the viscosity of the oil. Consequently, the more viscous the oil at a given temperature, the more objectionable from this standpoint. Since the stearin of cod liver oil causes thickening of this oil at excessively low temperatures it becomes of interest to ascertain the probable effect of the stearin content upon the viscosity of cod liver oil at temperatures at which it is likely to be taken. Assuming that the degree of haziness, precipitation or thickening shown by cod liver oil upon strong cooling is a rough measure of the stearin content, viscosity determinations were made on the samples marked 12, 5, 8 and 15 in the preceding table, the stearin content being apparently progressively greater in the order the numbers are here set down; the samples covering practically the full range of cold effects reported in the above table. The viscosity tests were made at room temperature (25° C.) and at refrigerator temperature (10° C.) since these are approximately the temperatures at which the oil is ordinarily kept and administered.

| Oil No. | U. S. P. IX Liq. Petrolatum Viscosity Test. |        |
|---------|---|--------|
|         | 25° C.                                      | 10° C. |
| 12      | 5.64  | 8.43   |
| 5       | 5.32  | 7.85   |
| 8       | 5.64  | 8.00   |
| 15      | 5.80  | 8.14   |

Examination of the results in this table indicate that there is likely no significant relation between the apparent stearin content of these oils and their viscosity either at room or refrigerator temperature, for the oils do not become significantly more viscous as the stearin content progressively rises. However, there is undoubtedly a decided relation between the stearin content and viscosity of these oils at much lower temperatures. The viscosities of numerous medicinal cod liver oils from various sources were not found to vary significantly at room temperature but all showed greatly increased viscosity at refrigerator temperature to substantially the same degree as shown in the preceding table. As a consequence, where it is desired to minimize the influence of viscosity upon the taking of cod liver oil it is well to direct that the dose be taken from a small bottle of the oil kept at room temperature, the main supply being preserved in the refrigerator or other cool place.

Initially clear cod liver oil which has become cloudy or even solid from low temperatures regains its original clarity when the temperature of the oil is allowed

to rise spontaneously to somewhat below room temperature, there being no necessity to apply strong heating measures, such as placing the container in an oven or in hot water. Cod liver oil apparently suffers no damage from this alternate "freezing" and "thawing," but when cloudy, precipitated or thickened or congealed by cold the product is less sightly and, consequently, should not be exhibited for sale purposes if it should happen to have been allowed to get into this condition.

While the ability of a cod liver oil to remain clear at extremely low temperatures is of value as one of the points of pharmaceutical elegance, proper consideration must also be accorded to other important characteristics such as vitamin potency, palatability, attractiveness of color, inoffensiveness of odor, freedom from rancidity and excessive acidity and peroxides, absence of bleaching or other chemical agents, uniformity of potency and physical characteristics and stability.

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## A COMPARATIVE STUDY OF THE COMMERCIAL VARIETIES OF MILD SILVER-PROTEIN, U. S. P. X.\*

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Preparations of Mild Silver-Protein as found commercially may be grouped as follows: (A) Mild Silver-Protein, U. S. P. X, (B) Proprietary brands of Mild Silver-Protein U. S. P., (C) Proprietary brands of related substances containing silver in colloidal form. Mild Silver-Protein, U. S. P. X, is defined as follows: Silver rendered colloidal by the presence of or combination with protein. It contains not less than 19 per cent and not more than 25 per cent of silver (Ag).

Group (A) preparations are usually labeled as follows: Mild Silver-Protein, U. S. P. X, containing not less than 19 per cent and not more than 25 per cent of silver. Group (B) preparations are generally labeled as follows: . . . . , A brand of Mild Silver-Protein U. S. P. X, containing from 19 per cent to 23 per cent (or 19 to 25 per cent) of silver in colloidal form. Group (C) preparations are usually labeled with a coined name, and no statement is made concerning their composition.

For the purpose of this study the following preparations were selected, Group (A), Mild Silver-Protein, U. S. P. Group (B) Silver Nucleinate, Silvol and Solar-gentum. Group (C) Argyrol, Lunargen and Silver Nucleinate.

In this study the author makes no claims concerning the comparative therapeutic value of these preparations. The work includes the description and physical properties of these substances together with identity tests and assays for silver.

### COMPARISON OF DESCRIPTION AND PHYSICAL PROPERTIES.

*Mild Silver-Protein, U. S. P.*—Dark brown or almost black shining scales or granules. It is odorless, and slightly hygroscopic. It is soluble in water, but almost insoluble in alcohol, chloroform and ether.

*Silver Nucleinate, Mild Silver-Protein, U. S. P.*—Brownish black to black shining scales. It is odorless, hygroscopic in moist air and efflorescent in dry air. It is soluble in water, but insoluble in alcohol, chloroform and ether.

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