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FAT-SOLUBLE VITAMIN CONCENTRATION

Loran Old Buxton, East Orange, N. J., assignor to
National Oil Products Company, Harrison, N. J.,
a corporation of New Jersey

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This invention relates to the preparation of fat-soluble vitamin concentrates and more particularly to the preparation of concentrates of vitamins A and D.

In preparing concentrates of fat-soluble vitamins at the present time, the fatty material containing these vitamins is usually saponified and the soaps which are formed are extracted with an organic solvent which is a solvent for the unsaponifiable material, but a non-solvent for the soaps, and the solvent solution of the unsaponifiable material then separated from the soaps. On evaporation of the solvent from the solvent solution, a concentrate of the unsaponifiable material is obtained. This concentrate contains the major portion of all the fat-soluble vitamins which were originally present in the fatty material. However, it also contains undesirable taste and odor constituents which were either present in the fatty material originally or which had been formed during the saponification process. Various amines and oxygenated bodies present in the oil are deleteriously affected by alkali; although these bodies are not so objectionable in their original form, the alkali tends to convert them into substances having undesirable tastes and odors, which substances are then concentrated along with the vitamins and other unsaponifiable matter when the soaps are extracted with the solvent. In addition to concentrating various constituents having undesirable tastes and odors, the saponification process also tends to concentrate and fix various color bodies which are in the fatty material, thus producing concentrates which have undesirable dark colors. Furthermore the saponification destroys substantially all of the natural antioxidants contained in the oil.

It is the object of this invention to provide an improved process for concentrating the unsaponifiable material in fats and oils.

A further object of this invention is to provide improved concentrates of fat-soluble vitamins.

A specific object of the invention is to provide improved concentrates of vitamins A and D prepared from oils of marine origin.

Another object of the invention is to provide light-colored concentrates of vitamins A and D which are substantially without odor or taste.

Still another object of the invention is to efficiently utilize the natural antioxidants contained in fat-soluble vitamin-containing oils.

Other objects of the invention will in part be obvious and will in part appear hereinafter.

The above and other objects of the invention may be realized by contacting a fat-soluble vitamin-containing oil with a solvent which is miscible with fatty materials at temperatures above room temperature and partially immiscible therewith at temperatures below room temperature, separating the solvent solution of a highly potent

vitamin extract from the remainder of the oil, saponifying the oil which has been separated from the solvent solution of the highly potent vitamin extract, and recovering the unsaponifiable material from the saponified mass. This unsaponifiable material constitutes a highly potent vitamin concentrate which is light-colored and substantially free of all undesirable tastes and odors. The process of the invention is preferably carried out by contacting a fat-soluble vitamin-containing marine oil with such a solvent at a temperature such that at least the major portion of the oil is miscible with the solvent and then cooling the mixture, preferably to below 0° C., whereby a substantial portion of the oil separates from the solution. The soluble fraction extracted from the oil has a much higher vitamin A and D potency than the portion which is insoluble in the solvent, and it contains a very large percentage of the natural antioxidants of the original oil. However, this fraction, which is extracted from the oil by the solvent, contains concentrated therein in addition to the fat-soluble vitamins and the natural antioxidants various constituents which have an undesirable taste and odor, also a major portion of the color bodies originally present in the oil. The residual oil, which remains after the solvent extraction, is a light-colored, pleasant-tasting oil which is not as potent as the original oil, but still contains a relatively large percentage of the original vitamins depending upon the number of extractions. This residual portion of the oil which remains after having been extracted with solvent in accordance with the above described process is completely saponified, and the unsaponifiable matter then separated from the resulting soaps in any suitable manner. Light-colored concentrates of the unsaponifiable material originally present in the oil which are substantially without taste or odor will be obtained. These concentrates are highly potent in fat-soluble vitamins A and D.

The process of the invention is particularly applicable to the treatment of vitamin-containing oils of marine origin, since concentrates which are produced from such oils by conventional saponification processes are notorious for their undesirable tastes and odors and dark colors. Apparently the solvent extraction of the oil removes therefrom not only all, or substantially all, of the substances which themselves have undesirable tastes or odors, but also those substances, e. g. amines and oxygenated bodies which undergo undesirable changes when acted upon by an alkali since the concentrates obtained by recovering the unsaponifiable material from the saponified mass are substantially free of all undesirable odors and tastes. As the solvent extraction also removes a large proportion of the color bodies from the oil, the concentrate, obtained from the

residual oil by saponification thereof and extraction of the unsaponifiable matter, is much lighter in color than concentrates produced by conventional methods, as well as being substantially without taste and odor. Therefore, it is now possible to produce not only highly stable fractions of vitamin-containing oils which are much more potent than the original oils, but also to produce highly potent, light-colored vitamin concentrates which are substantially without taste or odor. Thus, two highly valuable products are obtained, each of which is much more valuable than the original oil. It has been mentioned that the fraction of the oil which is extracted by the solvent contains the major portion of the color bodies of the original oil, as well as the undesirable taste and odor constituents. For some purposes, such constituents may not be too objectionable and these fractions which are so extracted may be used as such for various preparations. However, if it is desired to provide pleasant-tasting, light colored products from these fractions, they may be refined by means of activated carbon in accordance with my process described and claimed in copending application, Serial No. 227,599, filed August 30, 1938, which has issued as Patent No. 2,306,776.

In accordance with the process of the invention any fat-soluble vitamin A and D containing marine oil may be used, examples of which include, inter alia, cod liver oil, pollack liver oil, shark liver oil, tuna liver oil, ling cod liver oil, mackerel liver oil, sole liver oil, dog fish liver oil, sword fish liver oil, halibut liver oil, seal liver oil, whale liver oil, sardine oil, salmon oil and pilchard oil.

The solvents which are employed in the process of the invention are those characterized by being miscible with fatty materials at temperatures above room temperature and partially immiscible therewith at temperatures below room temperature. The solvent employed in accordance with the invention may be selected from a large number of aliphatic solvents found to be useful as a result of extensive experimentation; the choice of the solvent will depend to some extent upon the properties of the oil to be treated, as will become more evident from the detailed description hereinafter given. Results have indicated that the solvents preferably employed are members of well recognized chemical classes; it has also been found that the number of carbon atoms in the solvent to be used is a particularly important factor in determining the availability thereof for use in the practice of this invention. The following table sets forth the classes of solvents which have been found to be particularly useful in the practice of this invention:

Table

1. Aliphatic and alicyclic monohydroxy alcohols containing from 3 to 6 carbon atoms.
2. Esters formed by the reaction of aliphatic and alicyclic alcohols with aliphatic monocarboxylic acids, said esters containing not more than 8 carbon atoms.
3. Aliphatic and alicyclic aldehydes containing not more than 6 carbon atoms.
4. Aliphatic ketones containing not more than 6 carbon atoms.

Solvents falling in the classes above listed are all liquid aliphatic organic compounds having the properties of being miscible with fatty oils at temperatures above room temperature, i. e. 20°

to 25° C., and partially immiscible therewith at temperatures below room temperature, and it has been found that solvents falling within this class of compounds may be used in the practice of this invention. In addition it will be noted that the preferred solvents possess relatively low freezing points.

In order to more fully illustrate the nature of the solvents which may be employed, a partial list thereof is herewith given; it is to be understood, however, that this list is not intended to be complete, but is merely illustrative of the solvents which may be employed. Thus it has been found that the following solvents may be used: n-propyl alcohol, isopropyl alcohol, isopropylamine, n-butyl alcohol, n-amyl alcohol, isoamyl alcohol, secondary amyl alcohol, furfuryl alcohol, allyl alcohol, diacetone alcohol, acetyl methyl carbinol, β -hydroxy ethyl acetate, methyl formate, ethyl formate, ethyl acetate, methyl acetate, isopropyl acetate, glycol diformate, glycol diacetate, methyl levulinate, ethyl levulinate, methyl aceto acetate, ethyl aceto acetate, methyl furoate, vinyl acetate, furfural, propionaldehyde, crotonaldehyde, acetone, methyl ethyl ketone, acetyl acetone, propylene chlorhydrin, and acetic anhydride. Mixtures of these solvents may also be used. It will be noted that all these solvents belong to that class of aliphatic organic compounds which have the properties of being miscible with fatty oils at temperatures above room temperature and partially immiscible therewith at temperatures below room temperature; furthermore, it will be noted that the majority of these solvents have relatively low freezing points.

Occasionally it may be found that certain of the solvents hereinabove mentioned may be too miscible with some of the oils which may be treated by this invention to effect a separation of a solvent solution of a potent vitamin fraction therefrom; thus, for example, acetone is too miscible with some fat-soluble vitamin-containing oils to accomplish the purposes of this invention. However, this condition may be easily corrected by diluting the solvent either with a small amount of water or with a liquid aliphatic organic solvent relatively immiscible with fatty oils. In general it may be said that the effect of diluting any of the above solvents with water will be to render the solvents more immiscible with fatty oils, so that if difficulty is encountered in effecting proper separation of the potent extracts from the vitamin-containing oils, this difficulty may generally be overcome by the addition of a small amount of water to the solvent.

The solvents preferably employed in the practice of the invention are the aliphatic alcohols containing from 3 to 6 carbon atoms; of these solvents isopropanol and diacetone alcohol have proved to be the most successful. The presence of the hydroxyl group seems to impart to these solvents properties which make them particularly useful for present purposes.

In carrying out the solvent extraction of the fatty material, the fatty material to be treated is first mixed with the solvent to be employed. The relative portion of solvent to oil may vary widely. However, it is preferred in most cases to employ a ratio of at least one part of solvent for each part of oil. If it is desired that the fractions which are extracted be highly potent, it is preferred that a mixture containing between about 2% and about 25% of oil be employed. However, if the principal reason for solvent extracting the

oil is only to provide a residue which is free of undesirable constituents, the amount of solvent which is employed need not be and preferably is not as great as when it is desired to produce highly potent extracted fractions. Also, in case it is desired to produce principally a desirable residual oil, the number of extractions which are to be carried out need not be as great as when it is desired to produce highly potent vitamin fractions in addition to the desirable residual oil. For example, in the latter case, it is preferred that from 3 to 5 extractions be made, whereas in the former case 1 or 2 extractions may frequently be sufficient. The solvent and the oil are preferably contacted with each other at a temperature substantially above room temperature, especially when it is desired to extract highly potent vitamin fractions. After the oil and the solvent have been thoroughly contacted with each other, the mixture is then cooled to a temperature substantially below room temperature, e. g., 0° C. or lower. At this temperature it will be found that the mixture will separate into two layers; one layer consisting chiefly of that portion of the original oil which is insoluble in the solvent at a low temperature. This fraction usually has a considerably lighter color than the original oil and has lost substantially all of the characteristic taste and odor possessed by the original oil. It is this fraction of the oil which is subsequently saponified, and the unsaponified material therein recovered to produce the concentrate of the present invention. The solvent layer will contain a potent vitamin fraction which may be recovered by removal of the solvent therefrom and used for any desired purpose. This solvent fraction will also contain the majority of the antioxidants and the color bodies of the original oil and the undesirable taste and odor constituents which were therein, and it appears to contain those constituents of the oil which although they themselves do not have such objectionable tastes and odors, are converted into substances having undesirable tastes and odors when they are acted upon by alkali. When treating a vitamin-containing oil, it is preferred to carry out the mixing of the oil and the solvent under an inert gas atmosphere in order to minimize any oxidation of the vitamins A and/or D.

The solvent extraction step of the process of the invention may also be carried out, if desired, by continuously contacting a fat-soluble vitamin-containing oil with one of the above solvents at a relatively low temperature, e. g., below 0° C.; this method of operation effects a continuous extraction of a highly potent vitamin fraction from the oil leaving a residual oil which is highly suitable for the production of vitamin concentrates in accordance with the process of the invention.

The residual portion of the oil which is insoluble in the solvent at the low temperature is saponified by any suitable process and the unsaponified material recovered therefrom in any suitable manner, e. g., solvent extraction, etc. Preferably the saponification of the residual oil and the recovery of the unsaponified matter therefrom is accomplished in accordance with the process of copending application, Serial No. 333,114, of Buxton and Simons, filed May 3, 1940, which has issued as Pat. No. 2,318,748 or by the process of copending application, Serial No. 350,166, of Buxton and Colman, filed August 2, 1940, which has issued as Patent No. 2,318,749.

In accordance with the process of Serial No. 333,114, the residual oil is admixed with a lesser

quantity of a water-immiscible organic solvent, such as a hydrocarbon or halogenated hydrocarbon solvent, e. g., ethylene dichloride, trichloroethylene, methylene chloride, heptane, cyclohexane, etc., and sufficient alkali added to react completely with the saponifiable portion of the oil. The mass is then stirred to form a heavy super-solvented emulsion, which emulsion is then allowed to stand for several hours to insure complete saponification. The mass is then heated and stirred gently and an additional quantity of solvent then added thereto. In the course of this treatment, the saponification is carried to completion, the emulsion will break and the soap particles flocculate and separate from the solvent solution of the unsaponifiable matter. The moisture content of the soap is preferably adjusted so that it will contain about 22% to 26%. This adjustment may be effected before, during or subsequent to addition of further quantities of solvent. The soap will either rise to the top or sink to the bottom of the solution depending upon the relative specific gravity of the solvent and the soap. The solvent solution of the unsaponified material containing the vitamins may then be readily separated from the soap and the unsaponified material recovered therefrom by any suitable means, e. g., vacuum distillation. This process is highly efficient and will recover from 90 to 100% of all the vitamins A and/or D originally present in the oil treated.

In accordance with the process of application, Serial No. 350,166, the saponification of the residual oil is carried out either in the presence or the absence of such a solvent as is employed in Serial No. 333,114, while controlling the saponification so as to obtain a soap having a moisture content of less than 20%. Such a soap will be soluble in hydrocarbon or halogenated hydrocarbon solvents of the aforementioned type. If the saponification is not carried out in the presence of such a solvent, the soap, after the saponification, is then dissolved in such a solvent. The soap-solvent mass is then cooled to room temperature and sufficient water added to adjust the moisture content of the soap to above 20%, preferably to about 24% to 26%, whereby the soap is precipitated out in a granular form. The solvent solution of the unsaponifiable material will now be free of soap, and the soap and solvent solution may readily be separated. The unsaponifiable fraction containing the vitamins is then recovered from the solvent solution thereof by any suitable means, preferably by distilling the solvent off under reduced pressure and/or in the presence of an inert atmosphere such as nitrogen.

In any case, however, regardless of the manner in which the oil is saponified and the unsaponifiable fraction recovered therefrom, the concentrate of the vitamins which is obtained will be light-colored and substantially without taste or odor. Concentrates of fat-soluble vitamins which are so prepared may be used for fortification of other vitamin-containing oils, for the preparation of other various vitamin-containing products, for the production of vitamin capsules, etc.

For a fuller understanding of the nature and objects of the invention, reference should be had to the following examples which are given merely to further illustrate the invention and are not to be construed in a limiting sense, all parts given being by weight.

Example I

500 parts of crude shark liver oil containing 103,000 U. S. P. units of vitamin A per gram and possessing a distinct fishy taste and odor were mixed with 2000 parts of 99% isopropanol in the presence of N₂ gas and the mixture warmed to 31° C. to dissolve the oil. The oil solvent solution was then cooled gradually to about -25° C. After about 48 hours the upper solvent layer was decanted from the insoluble solidified oil layer and then filtered. The solidified oil fraction was reextracted as above and the solvent layer filtered. The two filtered isopropanol extracts were combined and the solvent removed by distillation under reduced pressure in the presence of N₂ gas. The recovered vitamin A ester concentrate contained 262,000 U. S. P. units of vitamin A per gram and possessed a strong characteristic fishy and slight concentrate taste and odor. Stability tests on this product indicated that essentially all the natural antioxidants present in the original crude oil were concentrated in this fraction. The oil fraction insoluble in the isopropanol was freed of solvent and was found to contain 82,500 U. S. P. units of vitamin A per gram (72% of the vitamin present in the original crude oil) and was substantially without taste and odor.

100 parts of the isopropanol insoluble oil fraction containing 82,500 U. S. P. units of vitamin A per gram and possessing substantially no fishy taste or odor were mixed with 50 parts of ethylene dichloride and 3 parts of 99% isopropanol. While stirring in the presence of N₂ gas, sufficient 45.5% aqueous KOH (45 grams) (15% in excess of the stoichiometrical quantity) to completely saponify the oil was added and the stirring continued for about 15 minutes. The thick soap-mass was then insulated and left to stand at room temperature over-night. The mass was then heated in the presence of N₂ gas to about 60° C. for 30 minutes. 400 parts of ethylene dichloride and sufficient water to bring the moisture content of the soap up to about 24% were then added. After cooling the solvent soap-mass to room temperature the stirring was stopped and the mass allowed to stand for about 30 minutes. The lower solvent layer was then removed and the soap-mass extracted six more times with fresh batches of ethylene dichloride. The combined solvent extracts were filtered and the solvent evaporated under reduced pressure in the presence of gaseous nitrogen. The recovered vitamin A alcohol concentrate was light golden in color, devoid of the usual characteristic bitter concentrate taste and odor and contained substantially all the vitamin A present in the original isopropanol insoluble oil fraction.

Example II

100 parts of crude Bluefin tuna liver oil containing 73,000 U. S. P. units of vitamin A and 20,000 U. S. P. units of vitamin D per gram were mixed with 400 parts of 97% aqueous acetone in the presence of N₂ gas. On heating, all the oil dissolved at about 43° C. The solvent-oil solution was then cooled gradually to about -18° C. and filtered. The insoluble solidified oil fraction was reextracted as above and the solvent layer filtered. The two filtered solvent extracts were combined and the solvent removed by distillation under reduced pressure in the presence of N₂ gas. The recovered ester concentrate contained 121,000 U. S. P. units of vitamin A per gram and possessed a strong fishy and slight bitter taste

and odor. The solvent insoluble oil fraction was freed of solvent and found to contain 58,200 U. S. P. units of vitamin A per gram and was entirely devoid of fishiness. 65% of the vitamin A originally present in the crude oil remained in this solvent insoluble oil fraction.

100 parts of the acetone (97%) insoluble oil fraction containing 58,200 U. S. P. units of vitamin A per gram and exhibiting little, or no, fishiness were completely saponified and the unsaponifiable fraction recovered essentially as described in Example I. The recovered vitamin A and D concentrate was a light golden orange color, devoid of the usual characteristic bitter concentrate taste and odor and contained essentially all the vitamin A and D present in the original acetone insoluble oil fraction.

Example III

100 parts of crude shark liver oil containing 157,000 U. S. P. units of vitamin A per gram and characterized by a dark red color and a strong fishy taste and odor were mixed with 400 parts of 99% isopropanol in the presence of N₂ gas and the mixture warmed to 33° C. to dissolve the oil. The solvent-oil solution was then cooled gradually to -18° C. After 36 hours the upper-solvent layer was decanted from the lower solidified oil layer and filtered. The solvent insoluble oil fraction was reextracted as above and the solvent layer removed and filtered. The combined filtered extracts were then freed of solvent as in the previous examples. The recovered vitamin A ester concentrate contained 288,000 U. S. P. units of vitamin A per gram and contained dissolved therein most of the taste and odor constituents associated with the original crude shark liver oil. The solvent insoluble oil fraction was freed of solvent and found to contain 133,000 U. S. P. units of vitamin A per gram and was completely devoid of the original fishy and slight bitter taste and odor associated with the crude oil. Approximately 70% of the vitamin A present in the original crude oil was still present in this fraction.

75 parts of the isopropanol insoluble oil fraction containing 133,000 U. S. P. units of vitamin A per gram and entirely devoid of fishiness and bitterness were mixed with 2.5 parts of 99% isopropanol in the presence of N₂ gas. While stirring, sufficient 45% aqueous KOH (33.0 parts) to completely saponify the oil were added and the stirring continued for 3 minutes. The solid soap mass (temperature 48° C.) was insulated and allowed to stand for 12 hours. 300 parts of ethylene dichloride were added and the mixture heated to about 70° C. for 30 minutes while stirring in the presence of N₂ gas. The water content of the soap was then increased to about 24% and the solvent-soap mixture cooled to room temperature and the stirring ceased. After about 30 minutes the lower solvent layer was removed and another fresh batch of ethylene dichloride added. A total of six extractions were conducted in the same manner. The combined solvent extracts were filtered and the solvent removed by distillation under reduced pressure in the presence of N₂ gas. The recovered vitamin A alcohol concentrate was light in color and free from the usual characteristic bitter concentrate taste and odor. Substantially all the vitamin A present in the original isopropanol insoluble oil fraction was concentrated in this vitamin A alcohol fraction.

From the above description, it may readily be

seen that the process of my invention provides means for obtaining several highly valuable products, each of which is much more valuable than the original material. Although the process is particularly applicable for producing concentrates of fat-soluble vitamins, it is also quite applicable for preparing concentrates of the unsaponifiable material contained in other fats and oils which are relatively high in various sterols, etc.

Since certain changes may be made in carrying out the above process without departing from the scope of the invention, it is intended that all matter contained in the above description shall be interpreted as illustrative and not in a limiting sense.

Having described my invention what I claim as new and desire to secure by Letters Patent is:

1. A process of producing an improved fat-soluble vitamin concentrate, which comprises contacting a fat-soluble vitamin-containing marine oil with a solvent selected from the group consisting of aliphatic and alicyclic monohydroxy alcohols containing from 3 to 6 carbon atoms, esters formed by the reaction of aliphatic and alicyclic alcohols with aliphatic monocarboxylic acids, said esters containing not more than 8 carbon atoms, aliphatic and alicyclic aldehydes containing not more than 6 carbon atoms and aliphatic ketones containing not more than 6 carbon atoms, heating the mass to dissolve at least a major portion of the oil in the solvent, cooling the mass to a temperature within the range of 0° C. to -70° C. whereby layers are formed, separating the solvent-insoluble fraction from the mass, saponifying said insoluble fraction and recovering the unsaponified matter therefrom.

2. A process of producing an improved fat-soluble vitamin concentrate, which comprises contacting a fat-soluble vitamin-containing marine oil with a solvent selected from the group consisting of aliphatic and alicyclic monohydroxy

alcohols containing from 3 to 6 carbon atoms, heating the mass to dissolve at least a major portion of the oil in the solution, cooling the mass to a temperature within the range of 0° C. to -70° C. whereby layers are formed, separating the solvent-insoluble fraction from the mass, saponifying said insoluble fraction and recovering the unsaponified matter therefrom.

3. A process of producing an improved fat-soluble vitamin concentrate, which comprises contacting a fat-soluble vitamin-containing marine oil with isopropanol, heating the mixture to dissolve at least a major portion of the oil in the isopropanol, cooling the mass to a temperature within the range of 0° C. to -70° C. whereby layers are formed, separating the isopropanol-insoluble fraction from the mass, saponifying said insoluble fraction and recovering the unsaponified matter therefrom.

4. A process of producing an improved fat-soluble vitamin concentrate, which comprises contacting a fat-soluble vitamin-containing marine oil with diacetone alcohol, heating the mixture to dissolve at least a major portion of the oil in the diacetone alcohol, cooling the mass to a temperature within the range of 0° C. to -70° C. whereby layers are formed, separating the diacetone alcohol-insoluble fraction from the mass, saponifying said insoluble fraction and recovering the unsaponified matter therefrom.

5. A process of producing an improved fat-soluble vitamin concentrate, which comprises contacting a fat-soluble vitamin-containing marine oil with aqueous acetone, heating the mixture to dissolve at least a major portion of the oil in the aqueous acetone, cooling the mass to a temperature within the range of 0° C. to -70° C. whereby layers are formed, separating the aqueous acetone-insoluble fraction from the mass, saponifying said insoluble fraction and recovering the unsaponified matter therefrom.

LORAN OID BUXTON.