

ALIEN PROPERTY CUSTODIAN

PROCESS FOR THE PREPARATION OF FATS AND OILS WHICH ARE SUITABLE FOR INJECTION

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This invention relates to a process for the preparation of fats and oils which are suitable for injection.

For the purpose of incorporating therapeutical remedies into the body by way of injection, dis- 5
persions, or solutions, or emulsions with an agent are used, which consist of refined fats and oils. More particularly raw fats and oils are concerned in this regard, which are purified by way of re- 10
fining methods, for instance a method with a caustic lye of soda. Crude oils and fats in the condition, in which they are obtained from the fatty or oily raw materials, are not suitable for purposes of injection, because the accessory sub- 15
stances contained therein would bring about phenomena of necrosis and encapsulations of fat at the place of injection, or even a fat embolus. Refined sesame oil, or olive oil are, for instance, frequently used as oil solvents for therapeutical 20
remedies.

As long as it was only a question of preparing a dispersing agent or a solvent, which is most readily assimilated by the body, and is without any biologicotherapeutical effects of its own, it was sufficient to prepare neutral fatty agents perfectly 25
free of accessory substances, and as pure and colourless as possible, from the raw fats and oils in accordance with the well-known refining processes. If, however, the end aimed at was to pre- 30
serve the biologically efficient substances or the agents enhancing the assimilative capacity of the oils or fats, other manufacturing methods had to be found, because by the processes of purification hitherto used these valuable agents were either 35
destroyed or removed.

The resorption of fats and oils is favourably influenced by the phosphatides. If it is thus intended to use the fats and oils as solvents, as dispersing agents or emulsifiers for therapeutical 40
preparations, it is advisable not to expel from them those accessory substances, which are contained in them and expedite their assimilative force, as was done hitherto by the processes of re- 45
fining and bleaching, but to take care that as great a fraction of them, as feasible, is preserved.

In the event that in view of the biological effect of their accessory substances the oils or fats are themselves intended to play the part of a remedial agent, it will also not be possible any longer to 50
prepare injectable and assimilative fats and oils under those methods of purification, as are already known, e. g. refining with alkaline substances, because these processes result in a considerable destruction and removal of the biologi- 55

cally important admixtures from the raw fats and oils.

When raw fats and oils are purified, frequently a destruction of those accessory substances con- 5
tained in them, as are of biological and therapeutical importance, will take place, which destruction is either due to the prolonged heating period at a raised temperature, when air is ad- 10
mitted at the same time, or to the refining agents, such as alkaline substances, acids, solvents. In addition, thereto the neutral fatty substance is, moreover, attacked during this refining action to a degree, which must not be underrated. As far 15
as a refining process with alkaline substances is concerned, the therapeutically important accessory substances of the fats and oils are, moreover, adsorbed and absorbed by the stock of soap, and thus separated, the great losses in neutral fat 20
sustained in consequence of this refining process must also be considered, said losses being of particular importance, of the fats and oils concerned are valuable and efficient under biological and therapeutical aspects.

It has now been found—and this is the main ob- 25
ject of the present invention—that fats and oils, which are suitable for injection and readily absorbed, can be prepared in a simple manner by heating the raw fats and oils having a biologico-therapeutical effect of their own, or not, in the 30
presence of an indifferent gas,—exposing them, if desirable, only to an instantaneous heating effect,—and subsequently cooling them.

By way of this simple treatment the raw fats and oils, either containing substances of their 35
own, or not, which are biologico-therapeutically efficient, are rendered suitable for purposes of injection, i. e. they are deprived of any irritative effect, and will neither bring about an irritated condition, nor any effect resulting in a shock, as 40
has been established by several hundreds of injection tests on men and animals.

In order to carry the process into practice, the type of apparatus used for instantaneous heating (Pasteurization) of milk is particularly suitable. Under the new process the substances detrimental 45
to injection are removed in an extremely un hurtful manner, and without any considerable detrimental influence upon the other ballast substances,—whether with or without a biological or therapeutical effect—which are important with 50
regard to resorption. The oils and fats obtained under the process show an increase in effect of the therapeutical remedies dispersed, dissolved or emulsified in them which increase seems to be due 55
to an improved resorption, or to an influence ex-

exercised upon the admixed therapeutical agents by the accessory substances, which further continues to be incorporated in the oils or fats. If biologicco-therapeutically efficient crude oils are treated under this process, the finished products are not only readily assimilated by the human body, but also prove to possess a practically unaltered biological effect.

Biologicco-therapeutically efficient accessory substances of raw fats and oils are, for instance, the accessory substances contained in germ oils, in particular the vitamin-B-complex (α, β, γ -tocopherole, and the protective agents), vitamin A and vitamin D in their active condition, and in particular vitamin F of the liver oils. The new process implies the advantage that no special refining substances are to be used, and moreover this process shows the surprising effect that those biologically and therapeutically efficient accessory substances, which are thermolabile, are not detrimentally affected to any considerable degree. Furthermore due to the effect of the heat just those parts of the accessory substances contained in the raw fats and oils are precipitated, which would cause troubles in case of injection.

If particularly thermolabile accessory substances displaying biologicco-therapeutical effects, are present in the fats and oils, as, for instance, in the case of oestrogenous substances, it is advisable to carry out the heating action not only in the presence of an indifferent gas, but preferably in vacuo, or at a pressure above atmospheric, with an addition of small quantities of water or steam. In this manner it will be possible to refine the fats and oils at considerably lower temperatures. In this regard water and steam act as heat equalizing factors, as indifferent protective substances and as dishydrogenising agents.

In the refinement of raw fats and oils possessing a biologicco-therapeutical effect of their own, it ought to have been expected that the method of heating them would perfectly fail. At any rate, however, it could not be expected that the thermolabile accessory substances, which display a biologicco-therapeutical effect, would not suffer any important loss in efficiency by the treatment with heat within the meaning of the new process.

Finally, it is to be considered that the stability, and in consequence thereof the storing capacity of the fats and oils is improved by the process under the present invention, both from the biological point of view and under the aspects of chemistry of fatty substances. It is a well known fact that the processes obtaining in oils and fats which grow rancid, are of an extremely intricate nature, and that with regard to these processes according to recent considerations a particularly great importance is to be attributed to the fatty peroxydes, which are formed, if stored fats and oils are exposed to the air, and that they bring about a so-called secondary oxydation of the neutral fatty matter within the meaning of a formation of fat aldehydes. If the fats and oils are treated under the new process, a reduction, for instance, of the vitamin E effect by the fatty peroxides is thereby prevented.

The process even permits to purify in such a way fats and oils, e. g. the highly unsaturated fats and oils of the types of wood oil, or of pitica oil, which up till now were considered to be toxicant and therefore unserviceable for purposes of injection, that new therapeutical effects are imparted to them, which were hitherto unknown.

The finished products obtained under the new process cannot only be used separated for purposes of dispersion, dissolution and emulsification, but also in combination with other efficient substances, and, if desirable, together with other neutral bodies.

As the raw fats and oils possessing a biologicco-therapeutical effect of their own, or not, frequently contain a great quantity of fatty acids in the free state, which exercise a disagreeable effect of irritation upon the skin at the place of injection, the primary substances and final products of the process can be esterified under the already known methods with glycerines or other multiple alcohols, e. g. sorbite, mannite, xylitone, or with other compounds with hydroxyl groups capable of esterification, whereby perfectly neutral final products are formed which can be injected and are readily assimilated.

The particularly important separation of the mucilaginous deposits from the treated fats and oils by filtration, in order to arrive at perfectly clear filtrates which later on will not separate any sediment, cannot be satisfactorily brought about by means of the hitherto known filtration methods and filtering devices, e. g. filter presses, suction filters with straining cloth, filter installations with vacuum cells. Therefore fats and oils, though refined under the new process, but purified in accordance with the hitherto known filtering methods, will not any longer, after having been stored for a prolonged period, during which they were exposed to varying external factors, e. g. variations in temperature, come up to the high demands made with regard to their purity and sedimentation upon fats and oils, which can be injected and are readily assimilated. This is not probably due to the fact that small traces of humidity still remaining in the finished product will probably bring about a precipitation of the phosphatides and sterines still existing in the fats and oils which have been treated, in particular in cases where water or vapor have been used, which precipitation will be particularly troublesome in the ampullae filled with the final product.

As a further development of this invention, it has now been found that these difficulties can be obviated by the use of a hygroscopic filtering matter possessing an active surface, e. g. dried sawdust. For this purpose sawdust of pine wood, fir wood, or larch wood, or mixture of same, are particularly well suitable. The filtration of fats and oils by means of sawdust, which is already known in itself, has most probably not yet been used for the preparation of injectable and readily assimilated fats and oils with, or without, biologicco-therapeutical effects of their own, because it had been assumed that the finished article would be made impure by particles of sawdust or wood powder, or that resinous substances and wood meal would enter the preparation to be used for purposes of injection. It was, however, found that not only this danger does not actually exist, but that, on the contrary by the use of sawdust a novel filtering effect is brought about, which exercises an advantageous influence upon the final product, which can be used for injection and is readily assimilated.

In order to filter the oils and fats, it is preferable to use two or more filters which are arranged one above the other in such a way that the process of filtration in one of the filters is performed in downward direction, whereas the passage through the lower one, with the aid of the hydro-

static pressure of the roughly filtered fats and oils takes place from bottom to top, i. e. with the use of counter-flow, wherefore small particles of sawdust or other dust after a preliminary period of operation of the filtering plant cannot be further carried along together with the filtrate, and moreover an intimate contact between the sawdust and the material to be filtered is rendered possible for purposes of dehydration, for drying, adsorption and absorption of the easily dischargeable ballast substances. The velocity of flow can be controlled by means of a cock inserted between the first and the second filtering vessels, and by the admission cock of the store tank. As a matter of course the number order, and arrangement of the pre-filtering and re-filtering devices can be varied at direction, though it has also been found to be preferable that the re-filtering device with its direction of flow from bottom to top is placed at the end of the series of filters.

It is, however, also possible to prepare fats and oils with or without a biologico-therapeutical effect of their own, which are highly serviceable, can be injected and are readily assimilated by the body, if the asbestos filters customary for "clarifying" are used, which have a sterilizing effect. i. e. are able to retain microbes, or still better, so-called F-K filters, e. g. those manufactured by the Seitz-Werke at Kreuznach, Germany, are used, or if the material used for the reaction, is not filtered, but freed of both the deposit and water in a purifying centrifuge, i. e. an Ultra-centrifuge or a high-efficiency centrifuge.

Examples

(1.) 100 kg of raw, cold-pressed wheat germ oil, which by its nature contains oestrogenic substances of the type of the follicle hormone, and shows vitamin-E contents corresponding to a biological effect of 50 Pacini-Linn units per g and a Lea figure of 50, are in a glass-enameled conical vessel, which under any circumstances must be free of iron and copper, heated to 110 centigrades for about 10 minutes upon permanent strong agitation with an admixture of 1% of water, and upon blowing through nitrogen gas. An indifferent gas is blown through further upon slow cooling, whereafter a settling period of about 2 to 3 days follows: In the course of this time in the treated oil a flaky sediment is deposited, which together with a portion of the water previously admixed is collected at the bottom of the vessel. The oil is separated from the sediment in such a way that the oil is tapped with a siphon and passed through filtering layers of dried sawdust, as described above. The finished product thus prepared is perfectly clear, and will also continue to be free of substances resulting in turbidity, even if stored for a prolonged period at varying temperatures. Its vitamin-E contents have been left unaltered, as compared with those ascertained in the case of the primary material, the Lea figure was considerably reduced by the treatment, and now only amounts to 3 units.

The clear wheat germ oil can be directly filled into ampullae. In tests with animals it will continue to show the originally existing effect causing oestrus, which most probably is due to the oestrogenic substances.

(2.) 100 kg of raw wood oil are upon careful stirring quickly heated in an aluminium vessel up to 160 centigrades upon blowing through nitrogen gas, whereupon it is cooled down just as quickly to about 0° by means of an intense tubular cooling device operated with cooling brine. Thereby a fine, flaky deposit is formed, which mainly consists of mucilage, in particular albuminous substances. A sterile oil suitable for injection and capable of ready assimilation is obtained, if the separated final product is filtered through a so-called "Seitz" filter with F-K filtering substances suitable for purposes of sterilization. By intramuscular injection of the highly unsaturated, purified wood oil quite novel therapeutical effects can be brought about, among others an intense influence upon the metabolism of fatty substances and hydrocarbons in the living.

(3.) 100 kg of raw gingill oil (sesame-oil) having an acidity figure of 0.63 are, upon blowing through carbonic acid gas, heated for two hours up to 220°, and 130 g of glycerine are upon stirring gradually admixed thereto for the purpose of esterification. Thereupon the mixture is quickly cooled down to zero, as described in example 2, and filtered through a filtering device filled with sawdust. The clear gingill oil thus obtained has an acidity figure of 0, and is particularly well adapted to dispersion or dissolution of any therapeutical remedies whatsoever.

(3.) 100 kg of raw halibut liver-oil with vitamin-A contents of 2500 I. U. per g, and vitamin-D contents of 1500 I. U. per g are heated for 1 to 3 minutes in a current of carbon dioxide up to 160 centigrades in an instantaneous heating device, e. g. of the "Tödt" type, as it is used for the pasteurization of milk (cf. Ullmann, "Enzyklopädie der technischen Chemie," Vol. 4, 2nd edition, p. 557 of 1931) and then, after having been cooled to 5 centigrades below zero point by a highest efficiency centrifuge of the "Padberg" type. The resulting substance is suitable for injection, and is to a high degree freed of "liver-oil stearin" with not much altered vitamin-A and vitamin-B contents, which oil will not be turbidified later on.

It is intended to make such oils suitable for purposes of injection under the new process, as are of acid character by their nature and contain vitamin susceptible to be impaired by heat and atmospheric oxygen, it is possible to treat these oils with aqueous monovalent alcohols in order to remove the free fatty acids, as practically only the free fatty acids are dissolved by the aqueous alcohol and thus eliminated from the oil, whereas the biologically efficient agents are almost insoluble in it.

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