



Edition: BP 2025 (Ph. Eur. 11.6 update)

Omega-3-Acid Ethyl Esters 60



General Notices

(Ph. Eur. monograph 2063)

Action and use

Lipid-regulating drug.

Ph Eur

DEFINITION

Ethyl esters of *alpha*-linolenic acid (C18:3 n-3), moroctic acid (C18:4 n-3), eicosatetraenoic acid (C20:4 n-3), timnodonic (eicosapentaenoic) acid (C20:5 n-3; EPA), heneicosapentaenoic acid (C21:5 n-3), clupanodonic acid (C22:5 n-3) and cervonic (docosahexaenoic) acid (C22:6 n-3; DHA). Omega-3-acid ethyl esters 60 are obtained by transesterification of the body oil obtained from fish of families such as *Engraulidae*, *Carangidae*, *Clupeidae*, *Osmeridae*, *Salmonidae* and *Scombridae* or from animals of the class *Cephalopoda* and subsequent physico-chemical purification processes, including molecular distillation. The minimum content of total omega-3-acid ethyl esters and the minimum content of the omega-3-acids EPA and DHA ethyl esters are indicated in Table 2063.-1.

Table 2063.-1

Total omega-3-acid ethyl esters	EPA and DHA ethyl esters	EPA ethyl esters	DHA ethyl esters
Minimum content (per cent)			
65	50	25	20
60	50	-	40
55	50	40	-

A suitable antioxidant may be added.

PRODUCTION

The content of dioxins and dioxin-like PCBs (polychlorinated biphenyls) is controlled using methods and limits in accordance with the requirements set in the European Union or other applicable regulations.

CHARACTERS

Appearance

Light yellow liquid.

Slight fish-like odour.

Solubility

Practically insoluble in water, very soluble in acetone, in ethanol (96 per cent), in heptane and in methanol.

IDENTIFICATION

A. Examine the chromatograms obtained in the assay for EPA and DHA ethyl esters.

Results The peaks due to eicosapentaenoic acid ethyl ester and docosahexaenoic acid ethyl ester in the chromatogram obtained with test solution (b) are similar in retention time to the corresponding peaks in the chromatograms obtained with reference solutions (a_1) and (a_2).

B. It complies with the limits of the assay for total omega-3-acid ethyl esters.

TESTS

Absorbance (2.2.25)

Maximum 0.60 at 233 nm.

Dilute 0.300 g to 50.0 mL with [trimethylpentane R](#). Dilute 2.0 mL of the solution to 50.0 mL with [trimethylpentane R](#).

Acid value (2.5.1)

Maximum 2.0, determined on 10 g in 50 mL of the prescribed mixture of solvents.

Anisidine value (2.5.36)

Maximum 20.0.

Peroxide value (2.5.5, Method A)

Maximum 10.0.

Oligomers and partial glycerides

Size-exclusion chromatography ([2.2.30](#)).

Test solution Dilute 50.0 mg of the substance to be examined to 10.0 mL with [tetrahydrofuran R](#).

Reference solution Dissolve 50 mg of [monodocosahexaenoin R](#), 30 mg of [didocosahexaenoin R](#) and 20 mg of [tridocosahexaenoin R](#) in [tetrahydrofuran R](#) and dilute to 100.0 mL with the same solvent.

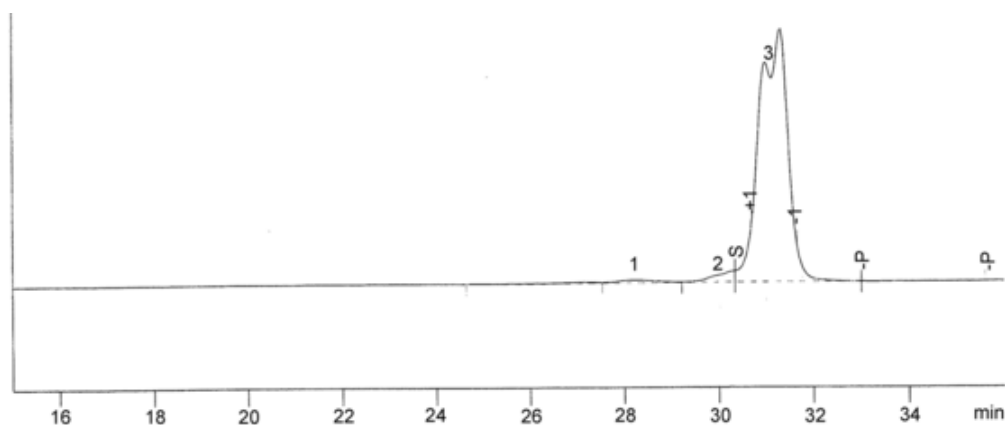
Column 3 columns to be connected in series:

- size: $l = 0.3$ m, $\varnothing = 7.8$ mm;
- stationary phase: [styrene-divinylbenzene copolymer R](#) (5 μ m) with the following pore sizes:
 - column 1: 50 nm;
 - column 2: 10 nm;
 - column 3: 5 nm;
- connection sequence: injector – column 1 – column 2 – column 3 – detector.

Mobile phase [tetrahydrofuran R](#).

Flow rate 0.8 mL/min.

Detection Differential refractometer.

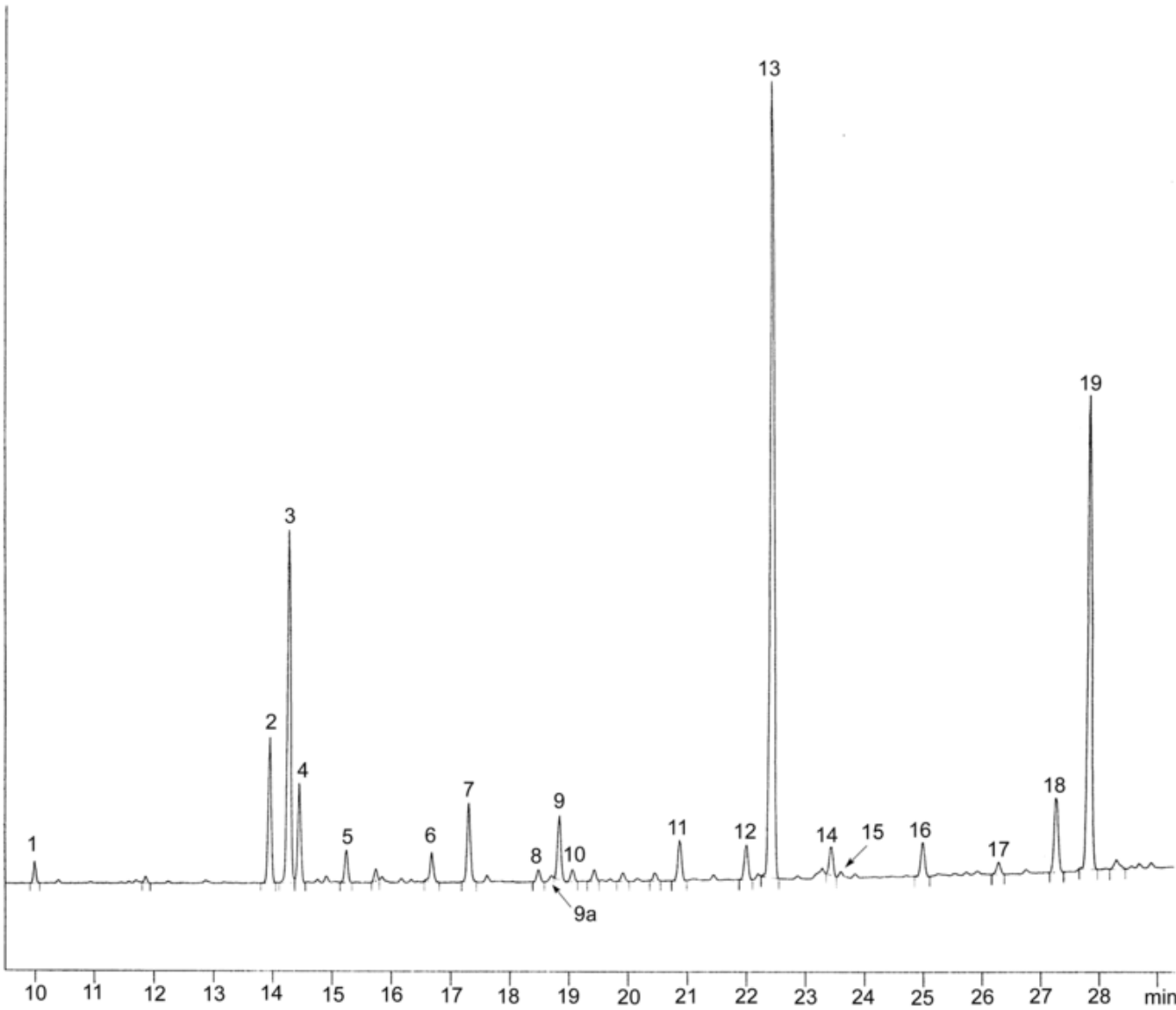


1. oligomers

2. monoglycerides

3. fatty acid ethyl esters

Figure 2063.-1. – Chromatogram for the test for oligomers and partial glycerides in omega-3-acid ethyl esters 60



- | | | | | | | |
|----------|--------------|--------------|----------------|----------------|---------------|---------------|
| 1. C16:0 | 4. C18:1 n-7 | 7. C18:4 n-3 | 9a. C20:1 n-11 | 12. C20:4 n-3 | 15. C22:1 n-9 | 18. C22:5 n-3 |
| 2. C18:0 | 5. C18:2 n-6 | 8. C20:0 | 10. C20:1 n-7 | 13. EPA | 16. C21:5 n-3 | 19. DHA |
| 3. C18:1 | 6. C18:3 n-3 | 9. C20:1 n-9 | 11. C20:4 n-6 | 14. C22:1 n-11 | 17. C22:5 n-6 | |

Figure 2063.-2. – *Chromatogram for the assays of omega-3-acid ethyl esters 60*

Injection 40 µL.

System suitability Reference solution:

- *elution order*: tridocosahexaenoin, didocosahexaenoin, monodocosahexaenoin;
- *resolution*: minimum 2.0 between the peaks due to didocosahexaenoin and monodocosahexaenoin; minimum 1.0 between the peaks due to tridocosahexaenoin and didocosahexaenoin.

Calculate the percentage content of oligomers plus partial glycerides using the following expression:

$$\frac{\text{sum of the areas of all the peaks in the chromatogram}}{A} \times 100$$

A = sum of the areas of all the peaks in the chromatogram;

B = sum of the areas of the peaks with a retention time less than the retention time of the peaks due to ethyl esters.

The ethyl ester peaks, which may be present in the form of an unresolved double peak, are identified as the major peaks in the chromatogram (see Figure 2063.-1).

Limit:

— *sum of oligomers and partial glycerides*: maximum 7.0 per cent.

ASSAY

EPA and DHA ethyl esters ([2.4.29](#))

For identification of the peaks, see Figure 2063.-2.

Total omega-3-acid ethyl esters ([2.4.29](#))

See Figure 2063.-2.

STORAGE

Under an inert gas, in an airtight container, protected from light.

LABELLING

The label states:

- the content of total omega-3-acid ethyl esters;
- the content of EPA ethyl ester and DHA ethyl ester.

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