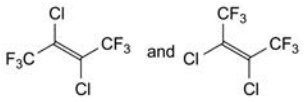
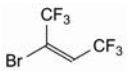
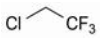


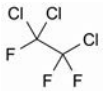
C. (*EZ*)-2,3-dichloro-1,1,1,4,4,4-hexafluorobut-2-ene (*cis* and *trans*),



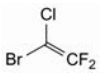
D. (*E*)-2-bromo-1,1,1,4,4,4-hexafluorobut-2-ene,



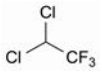
E. 2-chloro-1,1,1-trifluoroethane,



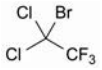
F. 1,1,2-trichloro-1,2,2-trifluoroethane,



G. 1-bromo-1-chloro-2,2-difluoroethene,



H. 2,2-dichloro-1,1,1-trifluoroethane,



I. 1-bromo-1,1-dichloro-2,2,2-trifluoroethane,

J. 1,2-dichloro-1,1-difluoroethane.

01/2020:0462

HARD FAT

Adeps solidus

DEFINITION

Mixture of triglycerides, diglycerides and monoglycerides, which may be obtained either by esterification of hydrogenated fatty acids of vegetable origin with glycerol or by interesterification of hydrogenated vegetable oils.

Each type of hard fat is characterised by its melting point, its hydroxyl value and its saponification value.

It does not contain additives.

CHARACTERS

Appearance: white or almost white, waxy, brittle mass.

Solubility: practically insoluble in water, slightly soluble in anhydrous ethanol and in methylene chloride.

When heated to 50 °C it melts, giving a colourless or slightly yellowish liquid.

IDENTIFICATION

A. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 1.0 g of the substance to be examined in *methylene chloride R* and dilute to 10 mL with the same solvent.

Plate: *TLC silica gel G plate R.*

Mobile phase: *ether R*, *methylene chloride R* (10:90 *V/V*).

Application: 2 µL.

Development: over 3/4 of the plate.

Drying: in air.

Detection: expose to iodine vapour until the spots appear and examine in daylight.

Results: the chromatogram shows a spot due to triglycerides with an R_F value of about 0.7 (R_{st} 1) and may show spots due to 1,3-diglycerides (R_{st} 0.6), to 1,2-diglycerides (R_{st} 0.4) and to 1-monoglycerides (R_{st} 0.07). For substances with a low hydroxyl value, the spots due to monoglycerides and diglycerides may be faint or absent. In this case, the test for hydroxyl value (see Tests) is also carried out to confirm identification.

B. Soya bean lecithin, macrogol cetostearyl ether and polysorbate 65. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 1.0 g of the substance to be examined in *methylene chloride R* and dilute to 10 mL with the same solvent.

Reference solution (a). Dissolve 0.100 g of *soya bean lecithin R* in *methylene chloride R* and dilute to 10 mL with the same solvent.

Reference solution (b). Dissolve 0.100 g of *macrogol cetostearyl ether R* in *methylene chloride R* and dilute to 10 mL with the same solvent.

Reference solution (c). Dissolve 0.100 g of *polysorbate 65 R* in *methylene chloride R* and dilute to 10 mL with the same solvent.

Plates: *TLC silica gel G plate R* (2 plates).

Mobile phase: *water R*, *methanol R*, *methylene chloride R* (4:25:65 *V/V/V*).

Plate 1

Application: 4 µL of the test solution and reference solution (a).

Development: over 3/4 of the plate.

Drying: in air.

Detection: expose to iodine vapour until the spots appear and examine in daylight.

Results:

– the chromatogram obtained with the test solution shows no spots corresponding to those of soya bean lecithin (R_F = about 0.3 and 0.5) in the chromatogram obtained with reference solution (a);

– the chromatogram obtained with the test solution shows a spot due to triglycerides with an R_F value of about 1.0.

Plate 2

Application: 4 µL of the test solution and reference solutions (b) and (c).

Development: over 3/4 of the plate.

Drying: in air.

Detection: spray with *potassium iodobismuthate solution R4* and examine in daylight.

Results:

– the chromatogram obtained with the test solution shows no orange spot corresponding to that of macrogol cetostearyl ether (R_F = about 0.85) in the chromatogram obtained with reference solution (b);

– the chromatogram obtained with the test solution shows no orange spot corresponding to that of polysorbate 65 (R_F = about 1.0) in the chromatogram obtained with reference solution (c).

C. Beeswax. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 1.0 g of the substance to be examined in *methylene chloride R* and dilute to 8 mL with the same solvent.

Reference solution. Dissolve 0.100 g of *white beeswax R* in *methylene chloride R* and dilute to 8 mL with the same solvent.

Plate: *TLC silica gel G plate R.*

Mobile phase: *ethyl acetate R*, *cyclohexane R* (10:90 *V/V*).

Application: 10 µL.

Development: over 3/4 of the plate.

Drying: in air.

Detection: spray with a freshly prepared 100 g/L solution of *phosphomolybdic acid R* in *ethanol (96 per cent) R* and heat at 120 °C for 3 min; examine in daylight.

Results: the chromatogram obtained with the test solution shows no black spot corresponding to that of white beeswax (R_F = about 0.9) in the chromatogram obtained with the reference solution.

TESTS

Alkaline impurities. Melt 10.00 g and while maintaining the temperature at about 50 °C, dissolve the melted mass in 40.0 mL of *ethanol (96 per cent) R*, mix and add 0.05 mL of *bromophenol blue solution R*. Not more than 0.75 mL of *0.01 M hydrochloric acid* is required to change the colour of the indicator to yellow.

Melting point (*2.2.15*): 30 °C to 45 °C, and within 2 °C of the nominal value.

Introduce the melted substance into a capillary tube and allow to stand at a temperature below 10 °C for 24 h.

Acid value (*2.5.1*): maximum 0.5.

Melt 5.0 g and dissolve in 20 mL of the prescribed mixture of solvents.

Hydroxyl value (*2.5.3, Method A*): maximum 50, and within 5 units of the nominal value; maximum 5 if the nominal value is less than 5.

Iodine value (*2.5.4, Method A*): maximum 3.0.

Peroxide value (*2.5.5, Method A*): maximum 3.0.

Saponification value (*2.5.6*): 210 to 260, and within 5 per cent of the nominal value, determined on 2.0 g.

Sulfated ash (*2.4.14*): maximum 0.2 per cent.

Heat a silica crucible to redness for 30 min, allow to cool in a desiccator and weigh. Evenly distribute 1.0 g in the crucible and weigh. Dry at 100-105 °C for 1 h and ignite in a muffle furnace at 600 ± 25 °C until the substance is thoroughly charred. Carry out the test for sulfated ash (*2.4.14*) on the residue obtained, starting from "Moisten the substance to be examined...".

STORAGE

Protected from light, at a temperature at least 5 °C below the nominal melting point.

LABELLING

The label states:

- the nominal melting point;
- the nominal hydroxyl value;
- the nominal saponification value.

FUNCTIONALITY-RELATED CHARACTERISTICS

This section provides information on characteristics that are recognised as being relevant control parameters for one or more functions of the substance when used as an excipient (see chapter 5.15). Some of the characteristics described in the Functionality-related characteristics section may also be present in the mandatory part of the monograph since they also represent mandatory quality criteria. In such cases, a cross-reference to the tests described in the mandatory part is included in the Functionality-related characteristics section. Control of the characteristics can contribute to the quality of a medicinal product by improving the consistency of the manufacturing process and the performance of the medicinal product during use. Where control methods are cited, they are recognised as being suitable for the purpose, but other methods can also be used. Wherever results for a particular characteristic are reported, the control method must be indicated.

The following characteristics may be relevant for hard fat used as basis for solid dosage forms.

Melting point (see Tests).

Hydroxyl value (see Tests).

Saponification value (see Tests).

01/2020:2731

HARD FAT WITH ADDITIVES

Adeps solidus cum additamentis

DEFINITION

Mixture of triglycerides, diglycerides and monoglycerides, which may be obtained either by esterification of hydrogenated fatty acids of vegetable origin with glycerol or by interesterification of hydrogenated vegetable oils.

Each type of hard fat with additives is characterised by its melting point, its hydroxyl value and its saponification value.

It contains additives such as lecithin, surfactants, beeswax or a mixture thereof.

CHARACTERS

Appearance: white or pale yellow, waxy, brittle mass.

Solubility: practically insoluble in water, slightly soluble in anhydrous ethanol and in methylene chloride.

When heated to 50 °C it melts, giving a colourless or slightly yellowish liquid.

IDENTIFICATION

A. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 1.0 g of the substance to be examined in *methylene chloride R* and dilute to 10 mL with the same solvent.

Plate: *TLC silica gel G plate R.*

Mobile phase: *ether R*, *methylene chloride R* (10:90 *V/V*).

Application: 2 µL.

Development: over 3/4 of the plate.

Drying: in air.

Detection: expose to iodine vapour until the spots appear and examine in daylight.

Results: the chromatogram shows a spot due to triglycerides with an R_F value of about 0.7 (R_{st} 1) and may show spots due to 1,3-diglycerides (R_{st} 0.6), to 1,2-diglycerides (R_{st} 0.4) and to 1-monoglycerides (R_{st} 0.07). For substances with a low hydroxyl value, the spots due to monoglycerides and diglycerides may be faint or absent. In this case, the test for hydroxyl value (see Tests) is also carried out to confirm identification.

B. Soya bean lecithin, macrogol cetostearyl ether and polysorbate 65. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 1.0 g of the substance to be examined in *methylene chloride R* and dilute to 10 mL with the same solvent.

Reference solution (a). Dissolve 0.100 g of *soya bean lecithin R* in *methylene chloride R* and dilute to 10 mL with the same solvent.