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1. Preface

In accordance with the recommendations of the WHO Expert Committee on Specifications for Pharmaceutical Preparations contained in its 28th and 29th reports¹, an entirely new section will be introduced into the 3rd edition of the International Pharmacopoeia. This will be devoted to excipients and other substances used in formulations of dosage forms, collectively termed "pharmaceutical aids"². It is anticipated that some 100 such monographs will be included in volume 4, priority being given to materials that are generally available in both developed and developing countries.

¹WHO TRS 681 and 704, respectively.

²The terms agreed by the members of the WHO Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations.

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The document contains 43 draft monographs prepared and reviewed in consultation with the initial group of collaborating specialists. The draft has been widely circulated for comments (panel members, specialists, institutions, etc.) A dozen returns have been received, and most comments have been incorporated. One group of monographs has been significantly amended on the basis of comments received and therefore require special attention. It has been decided that a separate text will deal with the general requirements for microbiological purity. A limit test to determine fluorides and the hydroxyl value will be prepared as well. The graphic formulas will be added at the time of printing.

Suggestions were forwarded to enlarge the rubric "Category". While some of these were accepted, an attempt was made to keep this text in line with corresponding monographs in world leading compendia. General notes and methods of analysis included in previous volumes of the third edition remain applicable.

We gratefully acknowledge the collaboration that we have already received from many experts around the world in the earlier development of these drafts.

2. Monographs

2.1 List of draft monographs

Acidum aceticum
Acidum alginicum
Acidum citricum
Adeps lanae, Adeps lanae cum aqua
Alcohol benzylicus
Alcohol cetylicus
Alcohol cetylstearylicus
Alcoholum
Aluminii magnesii silicas
Bentonitum
Benzalkonii chloridum
Benzylis hydroxybenzoas
Butylhydroxyanisolum
Butylhydroxytoluenum
Calcii hydrogenophosphas
Calcii phosphas
Calcii stearas
Calcii sulfas
Cellacefatum
Cellulosum microcrystallinum
Cera carnauba
Cetrimidum
Chlorobutanolum
Chlorocresolum
Ethanolum
Ethylcellulosum
Ethylis hydroxybenzoas
Gelatina
Glyceroli monostearas
Glycerolum
Glycerolum 85 % m/m
Gummi arabicum

Hydroxypropylcellulosum
Lactosum
Methylcellulosum
Methylis hydroxybenzoas
Oleum arachidis
Paraffinum album, Paraffinum flavum
Paraffinum durum
Phenylhydrargyri nitras
2-Propanolum
Propyleneglycolum
Propylis hydroxybenzoas

2.2 Significantly amended monographs

ACIDUM ACETICUM

Acetic acid

This monograph covers 3 concentrations, namely glacial acetic acid, acetic acid and dilute acetic acid.

Molecular formula. Glacial acetic acid, $C_2H_4O_2$.

Relative molecular mass. Glacial acetic acid, 60.05.

Graphic formula. Glacial acetic acid, CH_3COOH .

Chemical name. Acetic acid; CAS Reg. No. 64-19-7.

Description. Clear, colourless liquids. Glacial acetic acid may occur as a translucent, crystalline mass at a temperature below 15 °C; odour, characteristic and pungent.

Miscibility. Miscible with water, ethanol (~750 g/l)TS and with glycerol R.

Category. Acidifying agent.

Storage. Acetic acid should be kept in a tightly closed container.

Additional information. Glacial acetic acid is flammable and should be handled with care. Congealing point, about 15 °C.

Relative densities d_{20}^{20} = 1.050 for glacial acetic acid,
= 1.041 for acetic acid and
= 1.005 for dilute acetic acid.

REQUIREMENTS

General requirement

Glacial acetic acid contains not less than 99.0 % m/m and not more than 100.5 % m/m of $C_2H_4O_2$.

Acetic acid contains not less than 32.5 % m/m and not more than 33.5 % m/m of $C_2H_4O_2$.

Dilute acetic acid contains not less than 5.7 % m/m and not more than 6.3 % m/m of $C_2H_4O_2$.

Identity tests

A. Strongly acid, when diluted.

B. Transfer to a test-tube either 0.1 ml of glacial acetic acid to be tested with 1 ml of water, or take 1 ml of acetic acid or of dilute acetic acid to be tested, to each add 1 ml of ethanol (~750 g/l)TS and 1 ml of sulfuric acid (~1760 g/l)TS. and heat the mixture to boiling; ethyl acetate, perceptible by its odour (proceed with caution) is produced.

C. Either dilute 0.3 ml of glacial acetic acid to be tested with 3 ml of water, or 1 ml of acetic acid to be tested with 2 ml of water, or take 3 ml of dilute acetic acid to be tested, and neutralize each of them with ammonia (~100 g/l)TS. Then add 0.5 ml of lanthanum nitrate (30 g/l)TS, 0.1 ml of iodine TS and 0.05 ml of ammonia (~100 g/l)TS. Heat the mixture carefully to boiling and allow to stand; a dark blue colour appears.

Heavy metals. Take the following volumes of the solutions to be tested: either 3.5 ml of glacial acetic acid, 10 ml of acetic acid or 20 ml of dilute acetic acid.

Evaporate each of them to dryness on a water-bath. To each residue add 1.5 ml of hydrochloric acid (0.1 mol/l)VS, warm gently to dissolve and determine the heavy metals content as described under "Limit test for heavy metals", according to Method A (vol.1, p.119); glacial acetic acid, not more than 6 µg/g, acetic acid, not more than 2 µg/g; dilute acetic acid, not more than 1 µg/g.

Chlorides. Take 3.5 ml and proceed with the test as described under "Limit test for chlorides" (vol. 1, p. 116) (keep the remaining solution for the limit test for sulfates); the chloride content is not more than 70 µg/g.

Sulfates. Take 2 ml and proceed as described under "Limit test for sulfates" (vol. 1, p. 116); the sulfate content is not more than 0.24 mg/g.

Non-volatile residue. Evaporate a volume of known weight (not less than 10 g) to dryness on a water-bath and dry at 105 °C; any residue weighs not more than 0.1 mg/g.

Readily oxidizable substances. Either dilute 5 ml of glacial acetic acid with 10 ml of water and use 5 ml, together with 20 ml of water, or use 5 ml of acetic acid together with 20 ml of water, or use 25 ml of dilute acetic acid. Add 0.2 ml of potassium permanganate (0.02 mol/l)VS, and allow to stand for 30 seconds; the colour is not entirely discharged.

Assay. To about 2 g, accurately weighed, of glacial acetic acid and 50 ml of water, or 5 g of acetic acid and 50 ml of water, or 20 g of dilute acetic acid and 30 ml of water add 3 drops of phenolphthalein/ethanol TS and titrate with carbonate-free sodium hydroxide (1 mol/l)VS. Repeat the operation without the liquid being examined and make any necessary corrections. Each ml of carbonate-free sodium hydroxide (1 mol/l)VS is equivalent to 60.05 mg of C₂H₄O₂.

ALCOHOLUM

Alcohol

Description. A clear, colourless and mobile liquid; odour, characteristic.

Miscibility. Miscible with water, chloroform R, ether R and glycerol R.

Category. Solvent, antiseptic.

Storage. Alcohol should be kept in a well-closed container, and stored whenever possible at a temperature between 8 and 15 °C.

Labelling. The designation on the container should state the content of alcohol in % v/v.

Additional information. Different concentrations of alcohol are prepared from alcohol 96 % v/v and water at about 20 °C.

Note: Contraction of volume and rise in temperature occur when mixing alcohol with water.

Alcohol		Approximate relative density	ml of alcohol 96 % v/v to be diluted to 1000 ml with water
% v/v	g/l	d_{20}^{20}	
90	701.4	0.8304	934
80	625.3	0.8610	831
70	561.8	0.8872	727
60	488.0	0.9109	623
50	404.6	0.9320	519
45	341.3	0.9412	468
25	209.0	0.9699	259
20	163.8	0.9754	207

REQUIREMENTS

General requirement. Alcohol is a mixture of ethanol and water. It contains not less than 98.0 % and not more than 102.0 % of the declared content of ethanol (C₂H₆O).

Identity tests

A. Mix 0.25 ml in a small beaker with 1 ml of potassium permanganate (10 g/l)TS and 0.50 ml of sulfuric acid (0.5 mol/l)VS and cover the beaker immediately with a filter-paper moistened with a solution recently prepared by dissolving 0.1 g of sodium nitroprusside R and 0.5 g of piperazine hydrate R in 5 ml of water; an intense blue colour is produced on the filter-paper, the colour fading after a few minutes.

B. Mix a few drops with 1 ml of sulfuric acid (~1760 g/l)TS and a few drops of potassium dichromate (100 g/l)TS; a green colour is developed and an odour of acetaldehyde is perceptible.

Relative density. According to the labelled concentration, relate to the value stated under additional information.

Non-volatile residue. Place 100 ml in a porcelain dish and heat on a water-bath until volatilized, dry the residue at 105 °C for 1 hour and weigh; not more than 5 mg.

Water-insoluble substances. Dilute with an equal volume of water; the mixture is clear and after cooling to 10 °C it remains clear for 30 minutes.

Acidity. Add 20 ml of carbon-dioxide-free water R and 3 drops of phenolphthalein/ethanol TS to 20 ml of the test solution; no colour develops. Titrate with carbonate free sodium hydroxide (0.02 mol/l)VS; not more than 0.5 ml is required to obtain the midpoint of the indicator (pink).

Aldehydes and other foreign organic substances. Place 20 ml in a glass-stoppered cylinder that has been thoroughly cleaned with hydrochloric acid, then rinsed with water and the solution to be tested. Cool the contents to about 15 °C, and add, by means of a carefully cleaned pipette, 0.10 ml of potassium permanganate (0.02 mol/l)VS, noting accurately the time of addition. Mix at once by inverting the stoppered cylinder, and allow to stand at 15 °C for 5 minutes; the pink colour does not entirely disappear.

Fusel oil and allied impurities. Allow 25 ml to evaporate spontaneously from a porcelain dish, carefully protected from dust, until the surface of the dish is barely moist; no foreign odour is perceptible, and on the addition of a few drops of sulfuric acid (~1760 g/l)TS, no red or brown colour is produced.

Methanol. To 1 drop add 1 drop of water, 1 drop of phosphoric acid (~105 g/l)TS and 2 drops of potassium permanganate (25 g/l)TS. Mix, allow to stand for 1 minute, and add, drop by drop, sodium metabisulfite (50 g/l) TS until the permanganate colour is discharged. If a brown colour remains add 1 drop of phosphoric acid (~105 g/l)TS. To the colourless solution add 5 ml of freshly prepared chromotropic acid TS, and heat on a water-bath at 60 °C for 10 minutes; no violet colour appears.

Benzene. Record an absorption spectrum in a 1-cm layer against water between 220 nm and 350 nm. The absorbance is not more than 0.30 at 220 nm, 0.18 at 230 nm, 0.08 at 240 nm, and 0.02 at 270 to 350 nm. A curve drawn through these points is smooth.

GELATINA

Gelatin

Composition. Gelatin is a purified protein obtained either by the partial acid hydrolysis (type A), or by the partial alkali hydrolysis (type B) of animal collagen. It can exist as a mixture of both types.

Description. Faintly yellow to amber coloured sheets, flakes, granules or a powder; practically odourless; in solution it has a slight, characteristic bouillon-like odour.

Solubility. Practically insoluble in most organic solvents. In cold water it swells and softens, absorbing water 5 - 10 times its own mass. After swelling, soluble in hot water, acetic acid (~300 g/l)TS and in a hot mixture of glycerol R and water.

Category. Coating agent, encapsulating agent, suspending agent, tablet binder.

Storage. Gelatin should be kept in a well-closed container.

Additional information. These specifications do not necessarily apply to gelatin for parenteral use or other particular application. Attention should be paid to the microbiological quality since gelatin is of natural origin.

REQUIREMENTS

Identity tests

A. Dissolve about 1 g in carbon-dioxide-free water R, heat to about 55 °C and dilute to 100 ml with the same solvent. Keep the solution at this temperature throughout the following test. To 2 ml add 0.05 ml of copper(II) sulfate (160 g/l)TS, mix and add 0.5 ml of sodium hydroxide (~80 g/l)TS; a violet colour is produced.

B. Transfer 0.5 g to a test-tube, add 10 ml of water and allow to stand for 10 minutes. Heat at 60 °C for 15 minutes and keep the tube in a vertical position at 0 °C for 6 hours. Invert the tube; the content does not immediately flow out.

C. Dissolve 1.0 g in 100 ml of hot water. Place aliquots of 5 ml into 6 separate test-tubes and add 5 ml of a buffer to each tube, using buffers of pH 4.0, 5.0, 6.0, 7.0, 8.0 and 9.0 (citrate buffer, pH 4.0, TS or phosphate buffer, pH 4.0, TS or phthalate buffer, pH 4.0 TS; acetate buffer, pH 5.0, TS; phosphate/citrate buffer, pH 6.0, TS or acetate buffer, pH 6.0, TS; phosphate buffer, pH 7.0 TS; phosphate buffer, pH 8.0, TS or buffer borate, pH 8.0, TS; buffer borate, pH 9.0, TS). Cool the test-tubes and allow them to stand at 4 °C for 24 hours; the type of gelatin is recognized by the resulting opalescence - a maximum opalescence appearing at pH 5.0 indicates to gelatin type B, while a maximum opalescence between pH 7.0 and pH 9.0 indicates to gelatin type A.

Heavy metals. Use 1.0 g for the preparation of the test solution as described under "Limit test for heavy meetalas", Procedure 3 (vol. 1, p.118); determine the heavy metals content according the Method A (vol. 1, p. 119); not more than 10 µg/g.

Odour and water-insoluble substances. Dissolve 1 g in 40 ml of hot water; no disagreeable odour is perceptible. View the solution in a layer of 2 cm thickness; it is only slightly opalescent.

Sulfated ash. Use about 2 g; not more than 30 mg/g.

Loss on drying. Weigh 10 g and dry to constant weight at 105 °C; it loses not more than 0.15 g/g.

Sulfur dioxide. Dissolve 20 g in 150 ml of hot water using a round bottom flask with a long neck. Add 5 ml of phosphoric acid (~1440 g/l)TS and 1 g of sodium hydrogen carbonate R, and at once connect the flask to a condenser. (Note. Excessive foaming can be reduced by adding a few drops of an antifoaming agent). Distil 50 ml, receiving the distillate under the surface of 50 ml of iodine (0.05 mol/l)VS. Acidify the distillate with a few drops of hydrochloric acid (~70 g/l)TS, add 2 ml of barium chloride (50 g/l)TS, and heat on a steam bath until the liquid is nearly colourless. Filter the precipitate of barium sulfate, if any, wash, ignite and weigh. Make any necessary corrections determining a reagent blank; not more than 109.3 mg of barium sulfate, corresponding to not more than 1.5 mg/g of sulfur dioxide.

GLYCEROLUM

Glycerol

Molecular formula. $C_3H_8O_3$

Relative molecular mass. 92.09

Graphic formula.

Chemical name. 1,2,3-Propanetriol; CAS Reg. No. 56-81-5.

Other name. Glycerin.

Description. A clear, colourless or almost colourless, syrupy liquid; odourless.

Miscibility. Miscible with water and ethanol (~750 g/l)TS; slightly miscible with acetone R; practically immiscible with ether R and chloroform R.

Category. Solvent, humectant.

Storage. Glycerol should be kept in a tightly closed container.

Additional information. Glycerol is hygroscopic.

REQUIREMENTS

General requirement. Glycerol contains not less than 95.0 % and not more than 101.0 % of $C_3H_8O_3$, calculated with reference to the anhydrous substance.

Identity tests

A. Impregnate a piece of filter-paper with alkaline potassio-mercuric iodide TS; place it over a test-tube containing 1 ml of the liquid to be tested with 2 g of potassium bisulfate R and heat; the paper turns black.

B. Mix 2 g with 10 ml of water and add 1 drop of phenolphthalein/ethanol TS; the solution remains colourless. Add 1 drop of methyl red ethanol TS; the colour changes to yellow.

C. Mix 1 ml with 0.5 ml of nitric acid (~1000 g/l)TS and superimpose with 0.5 ml of potassium dichromate (100 g/l)TS; a blue ring is produced at the interface of the two liquids. Allow to stand for 10 minutes; the blue colour does not diffuse into the lower layer.

Refractive index. $n_D^{20} = 1.470-1.475.$

Relative density. $d_{20}^{20} = 1.258-1.263.$

Heavy metals. Use 1.0 g for the preparation of the test solution as described under "Limit test for heavy metals", Procedure 1 (vol.1, p. 118); determine the heavy metals content according to Method A (vol. 1, p. 119); not more than 5 µg/g.

Chlorides. Use 7 g in a mixture of 2 ml of nitric acid (~130 g/l)TS and 20 ml of water, and proceed as described under "Limit test for chlorides" (vol. 1, p. 116), using 0.20 ml of the standard opalescence solution; the chloride content is not more than 10 µg/g.

Sulfates. Use 30 ml and proceed as described under "Limit test for sulfates" (vol. 1, p. 116), diluting the standard turbidity solution 50 times; the sulfate content is not more than 20 µg/g.

Clarity and colour of solution. Mix 25 g with sufficient water to produce 50 ml; the solution is clear. Dilute 10 ml of this solution to 25 ml with water; the solution is colourless.

Chlorinated compounds. Place about 5 g, accurately weighed, in a dry round-bottomed 100-ml flask, add 15 ml of morpholine R, and connect to a suitable reflux condenser. Reflux gently for 3 hours. Rinse the condenser with 10 ml of water, receiving the washings in the flask, and cautiously acidify with nitric acid (~1000 g/l)TS. Transfer the solution to a suitable comparison tube, add 0.50 ml of silver nitrate (0.1 mol/l)VS, dilute with water to exactly 50 ml, and mix thoroughly; the turbidity is not greater than that produced in a solution similarly prepared, but omitting the refluxing, to which 0.20 ml of hydrochloric acid (0.02 mol/l)VS has been added (30 µg of Cl/g).

Acidity. Mix 50 ml of carbon-dioxide-free water R and add 0.5 ml of phenolphthalein/ethanol TS; the solution is colourless. Titrate with carbonate-free sodium hydroxide (0.1 mol/l)VS; not more than 0.2 ml is required to obtain a pink colour. (Keep the solution for the test of fatty acids and esters.)

Fatty acids and esters. To the solution remaining from the test for acidity add 5 ml of carbonate-free sodium hydroxide (0.5 mol/l)VS, boil the mixture for 5 minutes, cool, add phenolphthalein/ethanol TS, and titrate with hydrochloric acid (0.5 mol/l)VS. Repeat the operation without the substance being tested. Not more than 1 ml of carbonate-free sodium hydroxide (0.5 mol/l)VS is consumed.

Aldehydes and reducing substances. Transfer 5 ml of the solution to be tested to a glass-stoppered flask, mix with 10 ml of water and 1 ml of fuchsin/sulfurous acid TS. Allow the mixture to stand in the dark for 1 hour; the colour of the solution does not exceed that of a solution of potassium permanganate (0.0002 mol/l)VS.

Sulfated ash. Not more than 0.1 mg/g.

Water. Determine as described under "Determination of water by the Karl Fischer method", Method A (vol. 1, p. 135), using about 1.5 g of the substance; the water content is not more than 20 mg/g.

Assay. Transfer about 0.4 g, accurately weighed, to a 600-ml beaker, dilute with 50 ml of water, add bromothymol blue/ethanol TS and acidify with sulfuric acid (0.1 mol/l)VS to a green or greenish yellow colour. Neutralize with sodium hydroxide (0.05 mol/l)VS to a definite blue endpoint, free from green colour. Prepare a reagent blank containing 50 ml of water, and neutralize in the same manner. Pipette 50 ml of sodium metaperiodate TS into each beaker, mix by swirling gently, cover with a watch glass, and allow to stand for 30 minutes at room temperature (not exceeding 35 °C). Dilute each solution with water to about 300 ml and titrate with sodium hydroxide (0.1 mol/l)VS to pH 8.1 ± 0.1 for the substance being examined and pH 6.5 ± 0.1 for the blank, using a pH-meter. Make any necessary corrections for the blank. Each ml of sodium hydroxide (0.1 mol/l)VS is equivalent to 9.210 mg of C₃H₈O₃.

GLYCEROLUM 85 % M/M

Glycerol 85 % m/m

Composition. Glycerol 85 % m/m is a mixture of glycerol and water.

Other name. Dilute glycerol.

Description. A clear, colourless or almost colourless, syrupy liquid; odourless.

Miscibility. Miscible with water and ethanol (~750 g/l)TS; slightly miscible with acetone R; practically immiscible with ether R and chloroform R.

Category. Solvent, humectant.

Storage. Glycerol 85 % m/m should be kept in a tightly closed container.

Additional information. Glycerol 85 % m/m is hygroscopic.

REQUIREMENTS

General requirement. Glycerol 85 % m/m contains not less than 83.5 % m/m and not more than 88.5 % m/m of $C_3H_8O_3$, calculated with reference to the anhydrous substance.

Identity tests

A. Impregnate a piece of filter-paper with alkaline potassio-mercuric iodide TS; place it over a test-tube containing 1 ml of the liquid to be tested with 2 g of potassium bisulfate R and heat; the paper turns black.

B. Mix 2 g with 10 ml of water and add 1 drop of phenolphthalein/ethanol TS; the solution remains colourless. Add 1 drop of methyl red/ethanol TS; the colour changes to yellow.

C. Mix 1 ml with 0.5 ml of nitric acid (~1000 g/l)TS and superimpose with 0.5 ml of potassium dichromate (100 g/l)TS; a blue ring is produced at the interface of the two liquids. Allow to stand for 10 minutes; the blue colour does not diffuse into the lower layer.

Refractive index. $n_D^{20} = 1.499-1.455$.

Relative density. $d_{20}^{20} = 1.219-1.230$.

Heavy metals. Use 1.0 g for the preparation of the test solution as described under "Limit test for heavy metals", Procedure 1 (vol. 1, p. 118); determine the heavy metals content according to Method A (vol. 1, p. 119); not more than 5 µg/g.

Chlorides. Use 7 g in a mixture of 2 ml of nitric acid (~130 g/l)TS and 20 ml of water, and proceed as described under "Limit test for chlorides" (vol. 1, p. 116), using 0.20 ml of the standard opalescence solution; the chloride content is not more than 10 µg/g.

Sulfates. Use 30 ml and proceed as described under "Limit test for sulfates" (vol. 1, p. 116), diluting the standard turbidity solution 50 times; the sulfate content is not more than 20 µg/g.

Clarity and colour of solution. Mix 25 g with sufficient water to produce 50 ml; the solution is clear. Dilute 10 ml of this solution to 25 ml with water; the solution is colourless.

Chlorinated compounds. Place about 5 g, accurately weighed, in a dry round-bottomed 100-ml flask, add 15 ml of morpholine R, and connect to a suitable reflux condenser. Reflux gently for 3 hours. Rinse the condenser with 10 ml of water, receiving the washings in the flask, and cautiously acidify with nitric acid (~1000 g/l)TS. Transfer the solution to a suitable comparison tube, add 0.50 ml of silver nitrate (0.1 mol/l)VS, dilute with water to exactly 50 ml, and mix thoroughly; the turbidity is not greater than that produced in a solution similarly prepared, but omitting the refluxing, to which 0.20 ml of hydrochloric acid (0.02 mol/l)VS has been added (30 µg of Cl/g).

Acidity. Mix 50 g with 50 ml of carbon-dioxide-free water R and add 0.5 ml of phenolphthalein/ethanol TS; the solution is colourless. Titrate with carbonate-free sodium hydroxide (0.1 mol/l)VS; not more than 0.2 ml is required to obtain a pink colour. (Keep the solution for the test of fatty acids and esters.)

Fatty acids and esters. To the solution remaining from the test for acidity add 5 ml of carbonate-free sodium hydroxide (0.5 mol/l)VS, boil the mixture for 5 minutes, cool, add phenolphthalein/ethanol TS, and titrate with hydrochloric acid (0.5 mol/l)VS. Repeat the operation without the substance being tested. Not more than 1 ml of carbonate-free sodium hydroxide (0.5 mol/l)VS is consumed.

Aldehydes and reducing substances. Transfer 5 ml of the solution to be tested to a glass-stoppered flask, mix with 10 ml of water and 1 ml of fuchsin/sulfurous acid TS. Allow the mixture to stand in the dark for 1 hour; the colour of the solution does not exceed that of a solution of potassium permanganate (0.0002 mol/l)VS.

Sulfated ash. Not more than 0.1 mg/g.

Water. Determine as described under "Determination of water by the Karl Fischer method", Method A (vol. 1, p. 135), using about 0.2 g of the substance; the water content is not less than 0.12 g/g and not more than 0.15 g/g.

Assay. Transfer about 0.4 g, accurately weighed, to a 600-ml beaker, dilute with 50 ml of water, add bromothymol blue/ethanol TS and acidify with sulfuric acid (0.1 mol/l)VS to a green or greenish yellow colour. Neutralize with sodium hydroxide (0.05 mol/l)VS to a definite blue endpoint, free from green colour. Prepare a reagent blank containing 50 ml of water, and neutralize in the same manner. Pipette 50 ml of sodium metaperiodate TS into each beaker, mix by swirling gently, cover with a watch glass, and allow to stand for 30 minutes at room temperature (not exceeding 35 °C). Dilute each solution with water to about 300 ml and titrate with sodium hydroxide (0.1 mol/l)VS to pH 8.1 ± 0.1 for the substance being examined and pH 6.5 ± 0.1 for the blank, using a pH-meter. Make any necessary corrections for the blank. Each ml of sodium hydroxide (0.1 mol/l)VS is equivalent to 9.210 mg of C₃H₈O₃.

PHENYLHYDRARGYRI NITRAS

Phenylmercuric nitrate

Composition. Phenylmercuric nitrate is an equimolecular compound of phenylmercuric nitrate and phenylmercuric hydroxide.

Molecular formula. $C_6H_5HgNO_3, C_6H_5HgOH$

Relative molecular mass. 634.4

Chemical name. (Nitrate-O)phenylmercury; nitratophenylmercury; CAS Reg. No. 55-68-5.

Description. White, lustrous plates or a white, crystalline powder; odourless.

Solubility. Very slightly soluble in water; slightly soluble in ethanol (~750 g/l)TS; soluble in glycerol R and in fixed oils.

Category. Antimicrobial preservative.

Storage. Phenylmercuric nitrate should be kept in a tightly closed container, protected from light.

Additional information. Phenylmercuric nitrate is affected by light. It melts at about 188 °C with decomposition.

REQUIREMENTS

General requirement. Phenylmercuric nitrate contains not less than 98.0 % and not more than 101.0 % of $C_{12}H_{11}Hg_2NO_4$, calculated with reference to the dried substance.

Identity tests

A. To 10 ml of a saturated solution add 2 drops of sodium sulfide TS; a white precipitate is produced. Boil the mixture and allow to stand; the precipitate becomes black.

B. Heat 0.5 g with 0.5 g of zinc R powder, 0.5 g of reduced iron R and 5 ml of sodium hydroxide (~200 g/l)TS. Place a piece of red moistened litmus paper R over the vapours; the colour of the paper changes to blue.

C. To 10 ml of a saturated solution add 1 ml of hydrochloric acid (~70 g/l)TS and heat to boiling; a white precipitate is produced. Filter, to 5 ml of the filtrate add 2 ml of ferrous sulfate (15 g/l)TS; it yields reaction A described under "General identification tests" as characteristic of nitrates (vol. 1, p.114).

Mercuric salts and heavy metals. Heat 0.10 g with 15 ml of water, cool, filter and add 0.1 ml of sodium sulfide TS to the filtrate; the resulting precipitate shows no immediate colour.

Residue on ignition. Not more than 5.0 mg/g.

Loss on drying. Dry to constant weight at 105 °C; not more than 10 mg/g.

Acidity. To a 0.2 mg/ml solution add 3 drops of bromocresol green/ethanol TS; the solution is neutral (green).

Assay. Transfer about 0.2 g, accurately weighed, to a conical flask, and dissolve in 90 ml of water and 10 ml of nitric acid (~1000 g/l)TS. Add 2 ml of ferric ammonium sulfate (45 g/l)TS and titrate with ammonium thiocyanate (0.05 mol/l)VS. Each ml of ammonium thiocyanate (0.05 mol/l)VS is equivalent to 0.01586 g of $C_{12}H_{11}Hg_2NO_4$.

2.3 Draft Monographs

ACIDUM ALGINICUM

Alginic acid

Composition. Alginic acid is a polyuronic acid composed of residues of D-mannuronic and L-guluronic acids and is obtained chiefly from algae belonging to the Phaeophyceae, mainly species of Laminaria.

Description. A white to yellowish white, fibrous powder; almost odourless.

Solubility. Slightly soluble in water; practically insoluble in most organic solvents; soluble in solutions of alkali hydroxides.

Category. Tablet binder and disintegrant, viscosity-increasing agent, release-rate modifier.

Storage. Alginic acid should be kept in a well-closed container.

Additional information. Alginic acid has an equivalent weight of about 240. Attention should be paid to the microbiological quality since Alginic acid is of natural origin.

REQUIREMENTS

Identity tests

- A. Dissolve 30 mg in 5 ml of sodium hydroxide (0.1 mol/l)VS and add 1 ml of calcium chloride (55 g/l)TS; a voluminous, gelatinous precipitate is formed.
- B. Dissolve 30 mg in 5 ml of sodium hydroxide (0.1 mol/l)VS and add 1 ml of sulfuric acid (~570 g/l)TS; a heavy, gelatinous precipitate is formed.
- C. To about 5 mg in a test-tube add 5 ml of water and 1 ml of a freshly prepared solution of 1,3-naphthalenediol R containing 1 g in 100 ml of ethanol (~750 g/l)TS. Heat the mixture to boiling, boil gently for 3 minutes and cool to about 15 °C. Transfer the contents of the test-tube to a 30-ml separator with the aid of 5 ml of water and extract with 15 ml of diisopropyl ether R. For the blank repeat the procedure without the test substance. The diisopropyl ether extract from the test substance exhibits a deeper purple colour than that from the blank.

Heavy metals. For the preparation of the test solution ignite carefully in a crucible 1.0 g with 2 ml of nitric acid (~1000 g/l)TS and 5 drops of sulfuric acid (~1760 g/l)TS until white vapours evolve, then ignite completely. Cool, add 2 ml of hydrochloric acid (~420 g/l)TS and evaporate slowly on a water-bath until dry. To the residue add 1 drop of hydrochloric acid (~420 g/l)TS and 10 ml of water, then add sufficient ammonia (~260 g/l)TS to render the solution slightly alkaline, adjust the pH to 3-4

with acetic acid (~60 g/l)TS and dilute to 40 ml with water. Determine the heavy metals content as described under "Limit test for heavy metals", according to Method A (vol.1, p.119); not more than 40 µg/g.

Ash. Carry out the procedure as described under "Determination of ash" (vol.1, p.161); not more than 40 mg/g.

Loss on drying. Dry to constant weight at 105 °C; it loses not more than 0.18 g/g.

pH-value. Disperse 3 g in 100 ml of water, pH 1.5-3.5.

Acid value (vol.1, p.140). Suspend about 1 g, accurately weighed, in a mixture of 50 ml of water and 30 ml of calcium acetate (0.25 mol/l)VS. Shake thoroughly, allow to stand for 1 hour and titrate with sodium hydroxide (0.1 mol/l)VS, using phenolphthalein/ethanol TS as indicator. Repeat the performance without the substance to be examined and make any necessary corrections. Proceed with the calculation as given in "Determination of acid value" (vol. 1, p.140), using the number of ml of sodium hydroxide (0.1 mol/l)VS required as (a) and with reference to the dried substance; not less than 230.

ACIDUM CITRICUM

Citric acid

Citric acid, anhydrous
Citric acid monohydrate

Molecular formula. $C_6H_8O_7$ (anhydrous); $C_6H_8O_7 \cdot H_2O$ (monohydrate).

Relative molecular mass. 192.1 (anhydrous); 210.1 (monohydrate).

Graphic formula.

Chemical name. 2-Hydroxy-1,2,3-propanetricarboxylic acid;

CAS Reg. No. 77-92-9.

2-Hydroxy-1,2,3-propanetricarboxylic acid monohydrate;

CAS Reg. No. 5949-29-1.

Description. Colourless crystals or a white, crystalline powder; odourless or practically odourless.

Solubility. Very soluble in water; freely soluble in ethanol (~750 g/l)TS; sparingly soluble in ether R; practically insoluble in chloroform R.

Category. Acidifying agent, buffer component.

Storage. Citric acid should be kept in a well-closed container.

Labelling. The designation on the container of Citric acid should state whether the substance is the monohydrate or is in the anhydrous form.

Additional information. Citric acid effloresces in dry air.

REQUIREMENTS

General requirement. Citric acid contains not less than 99.5 % and not more than 101.0 % of $C_6H_8O_7$, calculated with reference to the anhydrous substance.

Identity tests A 20 mg/ml solution yields the reactions described under "General identification tests" as characteristic of citrates (vol. 1, p. 113).

Heavy metals. Use 1.0 g for the preparation of the test solution as described under "Limit test for heavy metals", Procedure 1 (vol. 1, p. 118); determine the heavy metals content according to Method A (vol.1, p. 119); not more than 10 $\mu\text{g/g}$.

Barium. Dissolve 1.0 g in 7.8 ml of sodium hydroxide (~80 g/l)TS and dilute to 10 ml with water. Acidify half of this solution with sulfuric acid (~100 g/l)TS and allow to stand for at least 1 hour; the solution remains clear when compared with the untreated solution.

Oxalates. Dissolve 1.0 g in 10 ml of water, neutralize with ammonia (~100 g/l)TS add 0.35 ml of hydrochloric acid (2 mol/l)VS, cool, and add 2.0 ml of calcium chloride (55 g/l)TS; no turbidity is produced.

Sulfates. Dissolve 0.10 g in 10 ml of water, add 1.0 ml of barium chloride (50 g/l)TS to which 1 drop of hydrochloric acid (~420 g/l)TS has been added; no turbidity is produced.

Water. Determine as described under "Determination of water by the Karl Fischer Method", Method A (vol.1, p. 135).

For the anhydrous form use about 1 g of the substance; the water content is not more than 10 mg/g.

For the monohydrate use about 0.15 g of the substance; the water content is not less than 75 mg/g and not more than 90 mg/g.

Sulfated ash. Not more than 1.0 mg/g.

Assay. Dissolve about 1.5 g, accurately weighed, in 50 ml of carbon-dioxide-free water R and titrate with carbonate-free sodium hydroxide (1 mol/l)VS, using phenolphthalein/ethanol TS as indicator. Repeat the operation without the substance being examined and make any necessary corrections. Each ml of carbonate-free sodium hydroxide (1 mol/l)VS is equivalent to 64.03 mg of $C_6H_8O_7$.

ADEPS LANAE ADEPS LANAE CUM AQUA

Wool fat
Hydrous wool fat

Composition. Wool fat is a purified fat-like material obtained from the raw wool of sheep (*Ovis aries* Linné).
Hydrous wool fat is a mixture of 75 % m/m of wool fat and 25 % m/m of water.

Other name. Anhydrous Lanolin, Lanolin. (In certain countries the name lanolin is used to describe a formulation containing wool fat, water and liquid paraffin).

Description. Wool fat is a brown-yellow, unctuous substance. Hydrous Wool fat is a yellowish white, unctuous substance. Odour, characteristic.

Solubility. Practically insoluble in water; soluble in chloroform R and ether R; slightly soluble in boiling ethanol (~750 g/l)TS.

Category. Ointment bases.

Storage. Wool fat should be kept in a well-closed container, at a temperature not exceeding 25 °C.

Additional information. Melted wool fat gives a clear or almost clear yellow liquid.

On heating of hydrous wool fat it separates at first into two layers, then water is driven off and the warm transparent residue forms, after cooling, a yellowish, tenacious, soft mass.

Melting point (Vol. 1, p. 23) for wool fat and hydrous wool fat after drying (use the residue obtained under wool fat content), 36-44 °C.

REQUIREMENTS

Identity tests

A. Dissolve 0.5 g in 5 ml of chloroform R, add 1 ml of acetic anhydride R and 0.1 ml of sulfuric acid (~1760 g/l)TS; a green colour is produced.

B. Dissolve 0.5 g in 5 ml of chloroform R and carefully superimpose 5 ml of sulfuric acid (~1760 g/l)TS; a bright, brown-red ring is gradually formed at the contact between the two liquids.

Melting range. For wool fat and hydrous wool fat after drying (use the residue obtained under wool fat content), 36-44 °C.

Acid value (vol.1, p.140). Wool fat, not more than 1.0; hydrous wool fat, not more than 0.8.

Saponification value (vol. 1, p. 139). Reflux for 4 hours; wool fat, 90-105; hydrous wool fat, 67-79.

Sulfated ash. Wool fat, not more than 1.5 mg/g; hydrous wool fat, not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at 105 °C for 1 hour; wool fat loses not more than 5.0 mg/g; hydrous wool fat loses not more than 0.32 g/g.

Wool fat content. Heat 30 g of hydrous Wool fat to constant weight on a water-bath, stirring continuously and weigh; the residue weighs between 21.8 g and 23.3 g (72.5-77.5 % m/m) (keep the residue for the melting range, the tests for water-absorption capacity and paraffins).

Water-absorption capacity. Place 10 g of Wool fat or hydrous Wool fat after drying (use the residue obtained under wool fat content) in a mortar. Using a burette add water in portions of 0.2-0.5 ml stirring vigorously after each addition to incorporate the water, until visible droplets separate and cannot be absorbed; not less than 20 ml of water is absorbed.

Water-soluble acid and alkaline substances. Melt 5.0 g of Wool fat or 6.7 g of hydrous Wool fat on a water-bath, add 75 ml of water heated to 90-95 °C and shake vigorously for 2 minutes. Cool and filter through a filter-paper previously moistened with water. To 60 ml of the filtrates that may show some

cloudiness (keep the remaining filtrates for the tests of water-soluble oxidizable substances and ammonia), add 0.25 ml of bromothymol blue/ethanol TS; not more than 0.2 ml of hydrochloric acid (0.02 mol/l)VS or 0.15 ml of sodium hydroxide (0.02 mol/l)VS is required to change the colour of the indicator (blue-yellow).

Water-soluble oxidizable substances. To 10 ml of the filtrates retained in the test for water-soluble acid and alkaline substances add 1 ml of sulfuric acid (~100 g/l)TS and 0.1 ml of potassium permanganate (0.02 mol/l)VS, and allow to stand for 10 minutes; the colour is not completely discharged.

Paraffins. To 40 ml of dehydrated ethanol R add 0.5 g of wool fat or hydrous wool fat after drying (use the residue obtained under wool fat content) and boil; the solution is clear or not more than opalescent.

Ammonia. To 5 ml of the filtrates obtained in the test for water-soluble acid and alkaline substances add 0.5 ml of sodium hydroxide (1 mol/l)VS and boil; the vapours do not turn red litmus paper R to blue.

ALCOHOL BENZYLICUS

Benzyl alcohol

Molecular formula. C_7H_8O

Relative molecular mass. 108.1

Graphic formula.

Chemical name. Benzenemethanol; CAS Reg. No. 100-51-6.

Description. A clear, colourless oily liquid; odour, slightly aromatic.

Solubility. Soluble in water; miscible with ethanol (~750 g/l)TS, chloroform R, ether R, fatty and essential oils.

Category. Antimicrobial preservative.

Storage. Benzyl alcohol should be kept in a tightly-closed container, protected from light.

Additional information. Benzyl alcohol is affected by air and light, and should be prevented from exposure to excessive heat.

REQUIREMENTS

Identity test

Add 2-3 drops to 5 ml of potassium permanganate (25 g/l) TS, and acidify with 1 ml of sulfuric acid (~100 g/l)TS; an odour of benzaldehyde is perceptible.

Refractive index. $n_D^{20} = 1.538 - 1.541.$

Relative density. $d_{20}^{20} = 1.043 - 1.050.$

Clarity of solution. Shake 2 ml with 60 ml of water; the solution is clear.

Sulfated ash. Evaporate 10 ml from a porcelain crucible and ignite to constant weight; not more than 0.05 mg/g.

Acidity. To 10 ml add 10 ml of ethanol (~750 g/l)TS and 1 ml of phenolphthalein/ethanol TS; not more than 1 ml of carbonate-free sodium hydroxide (0.1 mol/l)VS is required to obtain the midpoint of the indicator (pink).

Peroxide value. Not more than 5.

Chlorinated compounds. Mix 2.0 g with 50 ml of amyl alcohol R using a dry flask, add in small quantities 3 g of sodium R (Note: proceed with caution), connect the flask to a reflux condenser, warm gently until the evolution of hydrogen ceases, and boil gently for 1 hour. Cool the liquid to a little below 100 °C, add 50 ml of water, 5 ml of silver nitrate (0.1 mol/l)VS and 20 ml of nitric acid (~1000 g/l)TS. Titrate the excess of silver nitrate with ammonium thiocyanate (0.1 mol/l)VS, using ferric ammonium sulfate (45 g/l)TS as indicator. Repeat the operations without the substance being examined. The difference between the titrations does not exceed 0.3 ml.

Aldehydes. Transfer 20 ml to a 250-ml conical flask containing 5 ml of a solution containing 3.5 g of hydroxylamine hydrochloride R in 100 ml of ethanol (~600 g/l)TS, add 50 ml of ethanol (~600 g/l)TS and mix. Allow to stand for 10 minutes, add 1 ml of bromophenol blue/ethanol TS, and titrate with sodium hydroxide (0.1 mol/l)VS to a light green endpoint. Repeat the operation without the substance being examined and make any necessary corrections. The net volume of sodium hydroxide (0.1 mol/l)VS consumed does not exceed 4.0 ml, corresponding to 2.0 mg/g of benzaldehyde. Benzyl alcohol used for parenteral administration does not consume more than 1.0 ml, corresponding to 0.5 mg/g of benzaldehyde.

ALCOHOL CETYLICUS

Cetyl alcohol

Composition. Cetyl alcohol is a mixture of solid alcohols consisting chiefly of 1-hexadecanol (C₁₆H₃₄O).

Description. Unctuous, colourless flakes or a white, crystalline mass; odour, faint and characteristic.

Solubility. Practically insoluble in water; soluble in ethanol (~750 g/l)TS and ether R.

Category. Emulsifying agent; stiffening agent.

Storage. Cetyl alcohol should be kept in a well-closed container.

REQUIREMENTS

Melting range. 46-51 °C.

Acid value (vol.1, p.140). Not more than 2.

Saponification value (vol.1, p.139). Not more than 2.

Iodine value (vol.1, p.137). Not more than 3.

Hydroxyl value. Place about 2 g, accurately weighed, in a glass-stoppered 250-ml flask, add 2 ml of pyridine R and 10 ml of toluene R. To this mixture add 10.0 ml of a solution of acetyl chloride prepared by adding 10 ml of acetyl chloride R to 90 ml of toluene R. Insert the stopper in the flask, and heat in a water-bath at about 65 °C for 20 minutes. Add 25 ml of water, stopper the flask, and shake vigorously for several minutes to decompose the excess acetyl chloride. Titrate while shaking the flask vigorously throughout the titration in order to maintain the contents in an emulsified condition with carbonate-free sodium hydroxide (1 mol/l)VS using 0.5 ml of phenolphthalein/ethanol TS as indicator to a permanent pink endpoint. Repeat the operations without the substance being tested. Multiply the difference between the two titrations of ml of carbonate-free sodium hydroxide (1 mol/l)/VS by 56.1 and divide it by the weight used in g of the substance being examined; 218-238.

Paraffin. Dissolve 0.5 g in 20 ml of neutralized ethanol TS by warming; the solution is clear and not more intensely coloured than standard colour solution Bn2.

Sulfated ash. Not more than 1.0 mg/g.

ALCOHOL CETYLSTEARYLICUS

Cetostearyl alcohol

Composition. Cetostearyl alcohol is a mixture of solid aliphatic alcohols consisting chiefly of cetyl alcohol and stearyl alcohol.

Description. A white or yellowish white unctuous mass, or almost white flakes or granules; odour, characteristic and faint.

Solubility. Practically insoluble in water; soluble in ethanol (~750 g/l)TS, ether R and chloroform R.

Category. Retarding agent, stiffening agent.

Storage. Cetostearyl alcohol should be kept in a well-closed container, protected from light.

REQUIREMENTS

Melting range. 43 - 53 °C.

Acid value (vol.1, p.140). Not more than 2.

Saponification value (vol.1, p.139). Not more than 2.

Iodine value (vol.1, p.137). Not more than 4.

Hydroxyl value. Place about 2 g, accurately weighed, in a glass-stoppered 250-ml flask, add 2 ml of pyridine R and 10 ml of toluene R. To this mixture add 10.0 ml of a solution of acetyl chloride prepared by adding 10 ml of acetyl chloride R to 90 ml of toluene R. Insert the stopper in the flask, and heat in a water-bath at about 65 °C for 20 minutes. Add 25 ml of water, stopper the flask, and shake vigorously for several minutes to decompose the excess acetyl chloride. Titrate while shaking the flask vigorously throughout the titration in order to maintain the contents in an emulsified condition with carbonate-free sodium hydroxide (1 mol/l)VS using 0.5 ml of

phenolphthalein/ethanol TS as indicator to a permanent pink endpoint. Repeat the operations without the substance being tested. Multiply the difference between the two titrations of ml of carbonate-free sodium hydroxide (1 mol/l)VS by 56.1 and divide it by the weight used in g of the substance being examined; 208 - 228.

Paraffin. Dissolve 0.5 g in 20 ml of neutralized ethanol TS by warming; the solution is clear and not more intensely coloured than standard colour solution Bn2.

Sulfated ash. Not more than 1.0 mg/g.

ALUMINII MAGNESII SILICAS

Aluminium magnesium silicate

Composition. Aluminium magnesium silicate is a natural, colloidal hydrated aluminium magnesium silicate, a saponite, freed from gritty particles.

Description. A creamy white or greyish white powder or flakes; odourless or almost odourless.

Solubility. Practically insoluble in water and most organic solvents; when added to water it swells to form a colloidal suspension.

Category. Suspending agent; viscosity-increasing agent.

Storage. Aluminium magnesium silicate should be kept in a well-closed container.

Additional information. Several types of aluminium magnesium silicate occur, of which the powder or flakes vary in shape and size.

REQUIREMENTS

Identity tests

A. In a metal crucible fuse 1 g with 2 g of anhydrous sodium carbonate R. Add hot water to the residue, filter, and acidify the filtrate with hydrochloric acid (~420 g/l)TS. Evaporate to dryness and keep this residue for test B. Add 5 ml of hydrochloric acid (~70 g/l)TS and 10 ml of water to the residue remaining on the filter, and filter. To the filtrate add 2 ml of ammonia (~100 g/l)TS; a gelatinous, white precipitate is produced. Centrifuge (keep the precipitate for test C); neutralize 2 ml of the supernatant liquid, add 0.2 ml of titan yellow TS and 0.5 ml of sodium hydroxide (0.1 mol/l)VS; a bright red turbidity is formed which gradually settles to give a bright red precipitate.

B. Heat the residue obtained after evaporation in test A with a mixture of 10 mg of calcium fluoride R and a few drops of sulfuric acid (~1760 g/l)TS; a gas is evolved which in contact with water gives a white precipitate.

C. Dissolve the precipitate kept from test A after centrifugation in 2 ml of hydrochloric acid (~70 g/l)TS, and add 0.5 ml of thioacetamide TS; no precipitate develops. Add drop by drop sodium hydroxide (~80 g/l)TS; a gelatinous, white precipitate appears that redissolves on addition of further sodium hydroxide. Slowly add ammonium chloride (100 g/l)TS; the gelatinous, white precipitate reappears.

Heavy metals. Shake 1 g with 5 ml of hydrochloric acid (~70 g/l)TS for 5 minutes and centrifuge. Dilute the supernatant liquid to 10 ml with water, adjust the pH and determine the heavy metals content as described under "Limit test for heavy metals", according to method A (vol. 1, p. 119); not more than 40 µg/g.

Acid-insoluble impurities. To 1 g add 25 ml of hydrochloric acid (~70 g/l)TS and shake for 5 minutes. Filter through a tared sintered glass filter, wash the residue with water, dry to constant weight at 105 °C, and weigh; the residue weighs not more than 20 mg/g.

Alkalinity. Suspend 1.0 g in 50 ml of water and titrate with hydrochloric acid (0.1 mol/l)VS until a pH of 4 is reached; not more than 10 ml of hydrochloric acid (0.1 mol/l)VS is required.

BENTONITUM

Bentonite

Composition. Bentonite is a natural, colloidal, hydrated aluminium silicate. CAS Reg. No. 1302-78-9.

Description. A very fine, homogeneous, greyish white to cream-coloured powder; odourless.

Solubility. Practically insoluble in water and most organic solvents; when added to water swells to approximately twelve times its volume.

Category. Suspending agent.

Storage. Bentonite should be kept in a tightly closed container.

Additional information. Bentonite may also contain calcium, magnesium and iron. Attention should be paid to the microbiological quality since Bentonite is of natural origin.

REQUIREMENTS

Identity tests

A. In a metal crucible fuse 0.5 g with 0.4 g of anhydrous sodium carbonate R. Add hot water to the residue, filter, and acidify the filtrate with hydrochloric acid (~420 g/l)TS. Evaporate to dryness and keep this residue for test B. Add a few drops of hydrochloric acid (~420 g/l)TS to the residue remaining on the filter, dilute to 5 ml with water, and filter. To 2 ml of the filtrate add 2 ml of ammonium chloride (100 g/l)TS and 2 ml of ammonia (~100 g/l)TS; a gelatinous, white precipitate is produced which is soluble in hydrochloric acid (~420 g/l)TS, acetic acid (~300 g/l)TS and in sodium hydroxide (~80 g/l)TS, but insoluble in ammonia (~260 g/l)TS.

B. Heat the residue obtained after evaporation in test A with a mixture of 10 mg of calcium fluoride R and a few drops of sulfuric acid (~1760 g/l)TS; a gas is evolved which in contact with water gives a white precipitate.

Loss on drying. Dry to constant weight at 105 °C; it loses not less than 50 mg/g and not more than 150 mg/g.

Alkalinity. Shake 2.0 g with 100 ml of carbon-dioxide-free water R for 5 minutes using a stoppered flask. To 5 ml of the suspension add 0.10 ml of thymolphthalein/ethanol TS; a bluish colour is produced. Not more than 0.1 ml of hydrochloric acid (0.1 mol/l)VS is required to decolorize the test solution within 5 minutes.

Sedimentation volume. Mix 6 g with 0.3 g of freshly calcined light magnesium oxide R and add progressively 200 ml of water. Shake for 1 hour, place 100 ml of the suspension in a graduated cylinder and allow to stand for 24 hours; the supernatant liquid is not greater than 2 ml.

Swelling power. To 100 ml of sodium lauril sulfate (10 g/l)TS contained in a glass-stoppered cylinder of 100-ml capacity add 2 g in twenty portions at intervals of 2 minutes. Allow each portion to settle before adding the next. Allow to stand for 2 hours; the apparent volume of the sediment at the bottom of the cylinder is not less than 22 ml.

Fineness of powder. Triturate 2 g in a mortar with 20 ml of water. Allow to swell, disperse evenly with a pestle, and dilute with water to 100 ml. Pour the suspension through a sieve with the nominal aperture size of 75 μ m (sieve No. 75), and wash the sieve thoroughly with water; no grit is felt when the fingers are rubbed over the wire mesh of the sieve.

BENZALKONII CHLORIDUM

Benzalkonium chloride

Composition. Benzalkonium chloride is a mixture of alkylbenzyltrimethylammonium chlorides, the alkyl groups having chain lengths of C₈ to C₁₈.

Chemical name. Alkyldimethyl(phenylmethyl)ammonium chloride; alkylbenzyltrimethylammonium chloride; CAS Reg. No. 8001-54-4.

Description. A white or yellowish white powder, thick gel or gelatinous pieces; odourless or a slight aromatic odour.

Solubility. Very soluble in water and ethanol (~750 g/l)TS; freely soluble in acetone R; practically insoluble in ether R.

Category. Antimicrobial preservative, surfactant.

Storage. Benzalkonium chloride should be kept in a tightly closed container, protected from light.

Additional information. Benzalkonium chloride is hygroscopic.

REQUIREMENTS

General requirement. Benzalkonium chloride contains not less than 95.0 % and not more than the equivalent of 104.0 % of alkylbenzyltrimethylammonium chlorides, calculated as C₂₂H₄₀ClN (relative molecular mass 354.0) with reference to the anhydrous substance.

Identity tests

A. A solution of 0.1 g in 100 ml of water foames strongly when shaken.

B. To 5 ml of sodium hydroxide (~80 g/l)TS add 0.1 ml of bromophenol blue TS and 5 ml of chloroform R and shake; the chloroform layer is colourless. Prepare a solution of the substance to be tested containing 10 mg per ml of carbon-dioxide-free water R, and add 0.1 ml to the solution above and shake; the chloroform layer becomes blue.

C. A solution of 10 mg/ml in a mixture of equal volumes of water and ethanol (~750 g/l)TS yields reaction A described under "General identification tests" as characteristic of chlorides (vol 1, p.113).

Sulfated ash. Not more than 20 mg/g.

Water. Determine as described under "Determination of water by the Karl Fischer Method", Method A (vol. 1, p. 135), using about 0.1 g of the substance; the water content is not more than 150 mg/g.

Ammonium compounds. Dissolve 0.1 g in 5 ml of water, add 3 ml of sodium hydroxide (1 mol/l)VS and heat to boiling. Place a moistened piece of red litmus paper R over the solution; no change to blue is observed.

Assay. Dissolve about 2 g, accurately weighed, in water and dilute to 100 ml with the same solvent. Transfer 25.0 ml to a separating funnel, add 25 ml of chloroform R, 10 ml of sodium hydroxide (0.1 mol/l)VS and 10.0 ml of a freshly prepared solution of potassium iodide R containing 50 mg per ml. Shake well, allow to separate and discard the chloroform layer. Shake the aqueous layer with three quantities, each of 10 ml, of chloroform R and discard the chloroform layers. To the aqueous layer add 40 ml of hydrochloric acid (~420 g/l)TS, allow to cool and titrate with potassium iodate (0.05 mol/l)VS until the deep brown colour is discharged. Add 2 ml of chloroform R and continue the titration, shaking vigorously, until the chloroform layer no longer changes colour. Carry out a blank titration on a mixture of 10.0 ml of the freshly prepared potassium iodide solution (see above), 20 ml of water and 40 ml of hydrochloric acid (~420 g/l)TS and make any necessary corrections. Each ml of potassium iodate (0.05 mol/l)VS is equivalent to 35.4 mg of $C_{22}H_{40}ClN$.

BENZYLIS HYDROXYBENZOAS

Benzyl hydroxybenzoate

Molecular formula. $C_{14}H_{12}O_3$

Relative molecular mass. 228.3

Graphic formula.

Chemical name. 4-Hydroxybenzoate; CAS Reg. No. 94-18-8.

Description. A white to creamy white, crystalline powder; odourless or almost odourless.

Solubility. Practically insoluble in water; soluble in ethanol (~750 g/l)TS, ether R and in solutions of alkali hydroxides.

Category. Antimicrobial preservative.

Storage. Benzyl hydroxybenzoate should be kept in a well-closed container.

REQUIREMENTS

General requirement. Benzyl hydroxybenzoate contains not less than 99.0 % and not more than 101.0 % of $C_{14}H_{12}O_3$.

Identity tests

A. The absorption spectrum of a 10 µg/ml solution in ethanol (~750 g/l)TS, when observed between 230 nm and 350 nm, exhibits a maximum at about 260 nm; the absorbance of a 1-cm layer at this wavelength is about 0.76.

B. Dissolve 0.1 g in 2 ml of ethanol (~750 g/l)TS, boil, and add 0.5 ml of mercury/nitric acid TS; a precipitate gradually separates and the supernatant liquid becomes red.

C. Melting temperature, about 112 °C.

Sulfated ash. Not more than 1.0 mg/g.

Acidity. Dissolve 0.20 g in 10 ml of ethanol (~375 g/l)TS previously neutralized to methyl red/ethanol TS. Titrate with sodium hydroxide (0.1 mol/l)VS, using methyl red/ethanol TS as indicator; not more than 0.1 ml of sodium hydroxide (0.1 mol/l)VS is required to obtain the midpoint of the indicator (orange).

Assay. To about 0.12 g, accurately weighed, add 20 ml of sodium hydroxide (~80 g/l)TS, and boil gently under reflux for 30 minutes. Cool, and extract with three quantities, each of 20 ml, of dichloroethane R. Wash the combined extracts with 20 ml of sodium hydroxide (0.1 mol/l)VS and add the washings to the main aqueous phase, discarding the organic phase. To the aqueous solution add 25 ml of potassium bromate (0.0333 mol/l)VS, 6 ml of potassium bromide (100 g/l)TS and 10 ml of hydrochloric acid (~420 g/l)TS and immediately stopper the flask. Shake for 15 minutes and allow to stand for 15 minutes. Add 25 ml of potassium iodide (100 g/l)TS and shake vigorously. Titrate the liberated iodine with sodium thiosulfate (0.1 mol/l)VS using starch TS as indicator, added towards the end of the titration. Repeat the operation without the substance being examined and make any necessary corrections. Each ml of potassium bromate (0.0333 mol/l)VS is equivalent to 7.608 mg of $C_{14}H_{12}O_3$.

BUTYLHYDROXYANISOLUM

Butylated hydroxyanisole

Composition. Butylated hydroxyanisole contains a variable amount of 3-tert-butyl-4-methoxyphenol.

Molecular formula. $C_{11}H_{16}O_2$

Relative molecular mass. 180.3

Chemical name. 2-tert-Butyl-4-methoxyphenol;
(1,1-dimethylethyl)-4-methoxyphenol; CAS Reg. No. 25013-16-5.

Other name. BHA.

Description. A white or almost white, crystalline powder or a yellowish white solid; odour, faint and characteristic.

Solubility. Practically insoluble in water and propylene glycol R; freely soluble in ethanol (~750 g/l)TS, chloroform R, ether R and arachis oil R; soluble in solutions of alkali hydroxides.

Category. Antioxidant.

Storage. Butylated hydroxyanisole should be kept in a well-closed container, protected from light.

REQUIREMENTS

Identity tests

A. Dissolve 0.1 g in 10 ml of ethanol (~750 g/l)TS, add 4 ml of sodium tetraborate (10 g/l)TS and 1 ml of 2,6-dichloroquinone chlorimide/ethanol TS; a blue colour is produced (distinction from butylated hydroxytoluene).

B. Dissolve a few crystals in 10 ml of ethanol (~750 g/l)TS and add 0.1 ml of potassium ferricyanide (10 g/l)TS and 0.5 ml of ferric ammonium sulfate TS2; a green to blue colour is produced.

Solution in methanol. A solution of 1.0 g in 10 ml of methanol R is clear and not more intensely coloured than standard colour solution Yw3 when compared as described under "Colour of liquids" (vol. 1, p. 50).

Sulfated ash. Not more than 1.0 mg/g.

Hydroquinone. Carry out the test as described under "Thin-layer chromatography" (vol.1, p. 83), using silica gel R1 as the coating substance and a mixture of 4 volumes of chloroform R and 1 volume of ethyl acetate R as the mobile phase. Apply separately to the plate 3 µl of each of 2 solutions in ether R containing (A) 50 mg of the test substance per ml and (B) 0.10 mg of hydroquinone R per ml. After removing the plate from the chromatographic chamber, allow it to dry in air for a few minutes, spray with phosphomolybdic acid/ethanol TS, and while still damp expose it to the vapours of ammonia (~260 g/l)TS. Examine the chromatogram in daylight as soon as the yellow background has disappeared. The spot obtained with solution B is more intense than any spot, corresponding in position and appearance, obtained with solution A.

3-tert-Butyl-4-methoxyphenol. Carry out the test as described under "Thin-layer chromatography" (vol.1, p. 83), using silica gel R1 as the coating substance and chloroform R as the mobile phase. Apply separately to the plate 2 µl of each of 3 solutions in ether R containing (A) 25 mg of the test substance per ml, (B) 2.5 mg of the test substance per ml and (C) 0.125 mg of the test substance per ml. After removing the plate from the chromatographic chamber, allow it to dry in air, spray it with ferric chloride/potassium ferricyanide TS and examine the chromatogram in daylight. The blue-violet spot at R_f ~0.35 obtained with solution A is not more intense than the spot, corresponding in position and appearance, obtained with solution B. Any other spot obtained with solution A, is not more intense than the spot obtained with solution C.

BUTYLHYDROXYTOLUENUM

Butylated hydroxytoluene

Molecular formula. $C_{15}H_{24}O$

Relative molecular mass. 220.4

Graphic formula.

Chemical name. 2,6-Bis(1,1-dimethylethyl)-4-methylphenol; 2,6-di-tert-butyl-p-cresol; CAS Reg. No. 128-37-0.

Other name. BHT.

Description. Colourless crystals or a white or almost white, crystalline powder; odour, faint and characteristic.

Solubility. Practically insoluble in water; freely soluble in ethanol (~750 g/l)TS, acetone R, chloroform R, ether R and arachis oil R.

Category. Antioxidant.

Storage. Butylated hydroxytoluene should be kept in a well-closed container, protected from light.

REQUIREMENTS

Identity tests

A. Dissolve 0.1 g in 10 ml of ethanol (~750 g/l)TS, add 4 ml of sodium tetraborate (10 g/l)TS and a few crystals of 2,6-dichloroquinone chlorimide R; not more than a faint blue colour is produced (distinction from butylated hydroxyanisole).

B. Dissolve 10 mg in 2 ml of ethanol (~750 g/l)TS. Add 1 ml of testosterone propionate/ethanol (1 g/l)TS and 2 ml of sodium hydroxide (~80 g/l)TS. Warm in a water-bath at 80 °C for 10 minutes, and allow to cool; a blue colour is produced.

Congealing temperature. Not lower than 69.2 °C.

Sulfated ash. Not more than 1.0 mg/g.

Acid value (vol.1, p.140). Not more than 0.05.

CALCII HYDROGENOPHOSPHAS

Calcium hydrogen phosphate

Calcium hydrogen phosphate, anhydrous
Calcium hydrogen phosphate dihydrate

Molecular formula. $CaHPO_4$ (anhydrous); $CaHPO_4 \cdot 2H_2O$ (dihydrate).

Relative molecular mass. 136.1 (anhydrous); 172.1 (dihydrate).

Graphic formula.

Chemical name. Phosphoric acid, calcium salt (1:1); CAS Reg. No. 7757-93-9 (anhydrous).
Phosphoric acid, calcium salt (1:1), dihydrate; CAS Reg. No. 7789-77-7 (dihydrate).

Other name. Dibasic calcium phosphate.

Description. A white, or almost white powder; odourless.

Solubility. Practically insoluble in cold water and ethanol (~750 g/l)TS; soluble in dilute acids.

Category. Tablet diluent.

Storage. Calcium hydrogen phosphate should be kept in a well-closed container.

Labelling. The designation on the container of Calcium hydrogen phosphate should state whether the substance is the dihydrate or is in the anhydrous form.

REQUIREMENTS

General requirement. Calcium hydrogen phosphate contains not less than 30.9 % and not more than 31.7 % of calcium, Ca, calculated with reference to the ignited substance.

Identity tests

A. To 0.2 g add a mixture of 10 ml of hydrochloric acid (~70 g/l)TS, 10 ml of water, and heat to dissolve. To 10 ml of this solution add 2.5 ml of ammonia (~100 g/l)TS (keep the remaining solution for test B); it yields reaction A described under "General identification tests" as characteristic of calcium (vol. 1, p. 112).

B. Acidify the remaining solution from test A with nitric acid (~130 g/l)TS; it yields reaction A described under "General identifications tests" as characteristic of orthophosphates (vol. 1, p. 114).

Heavy metals. For the preparation of the test solution use 1.0 g dissolved in 10 ml of hydrochloric acid (~70 g/l)TS, filter if necessary, and add ammonia (~100 g/l)TS until a precipitate is formed. Add just sufficient hydrochloric acid (~70 g/l)TS to dissolve the precipitate and determine the heavy metals content as described under "Limit test for heavy metals", according to method A (vol. 1, p. 119); not more than 40 µg/g.

Arsenic. Use a solution of 1.0 g in 35 ml of hydrochloric acid (~70 g/l)TS and proceed as described under "Limit test for arsenic" (vol. 1, p. 122); the arsenic content is not more than 3 µg/g.

Barium. Dissolve 1.25 g in 10 ml of hydrochloric acid (~70 g/l)TS, filter if necessary, and add ammonia (~100 g/l)TS until a precipitate is formed. Add just sufficient hydrochloric acid (~70 g/l)TS to dissolve the precipitate and dilute with water to 25 ml. Place 2 portions, each of 10 ml, into two separate matched tubes. To 1 portion add 0.5 ml of sulfuric acid (~100 g/l)TS, and to the other 0.5 ml of water; the solutions remain equally clear when viewed after 15 minutes.

Carbonates. To 1.0 g add 5 ml of carbon-dioxide-free water R and 2 ml of hydrochloric acid (~420 g/l)TS and shake; no effervescence is produced.

Chlorides. Dissolve 0.10 g in a mixture of 2 ml of nitric acid (~130 g/l)TS and 20 ml of water, and proceed as described under "Limit test for chlorides" (vol.1, p.116); the chloride content is not more than 2.5 mg/g.

Fluorides. 0.5 g complies with the "Limit test for fluorides".

Sulfates. Dissolve 0.10 g in 5 ml of hydrochloric acid (~70 g/l)TS, and proceed as described under "Limit test for sulfates" (vol.1, p.116); the sulfate content is not more than 5 mg/g.

Acid-insoluble substances. To 5 g add a mixture of 40 ml of water and 10 ml of hydrochloric acid (~420 g/l)TS, heat until no more dissolves and dilute to 100 ml with water. Filter any residue, wash with hot water until the washing is free of chlorides, dry the residue at 105 °C for 1 hour and weigh; not more than 2 mg/g.

Loss on ignition. Ignite 1.0 g to constant weight between at 800 and 825 °C. The anhydrous form loses not less than 66 mg/g and not more than 85 mg/g. The dihydrate loses not less than 0.245 g/g and not more than 0.265 g/g.

Assay. To about 0.2 g, accurately weighed, add a mixture of 1 ml of hydrochloric acid (~420 g/l)TS and 5 ml of water, use gentle heat to dissolve and add 125 ml of water. Proceed with the titration as described under "Complexometric titrations" for calcium (vol. 1, p. 128). Each ml of disodium edetate (0.05 mol/l)VS is equivalent to 2.004 mg of Ca.

CALCII PHOSPHAS

Calcium phosphate

Composition. Calcium phosphate is a mixture consisting chiefly of $\text{Ca}_3(\text{PO}_4)_2$ together with CaHPO_4 .

Other name. Tribasic calcium phosphate.

Description. A white, amorphous powder; odourless or almost odourless.

Solubility. Practically insoluble in water and ethanol (~750 g/l)TS; soluble in hydrochloric acid (~70 g/l)TS and nitric acid (~130 g/l)TS.

Category. Adsorbent, tablet diluent, calcium supplement.

Storage. Calcium phosphate should be kept in a well-closed container.

Additional information. At relative humidities between about 15 and 65 %, the equilibrium moisture contents at 25 °C are about 2 %, but at relative humidities above about 75 %, it absorbs small additional amounts of moisture.

REQUIREMENTS

General requirement. Calcium phosphate contains not less than 34.0 % and not more than 40.0 % of calcium Ca, calculated with reference to the ignited substance.

Identity tests

A. Dissolve 0.05 g in 1.0 ml of hydrochloric acid (~70 g/l)TS by gentle warming, add 4 ml of water and 0.5 g of sodium acetate R. It yields reaction A described under "General identification tests" as characteristic of calcium (vol.1, p.112).

B. To 0.5 g add 2.0 ml of nitric acid (~130 g/l)TS and heat gently. This solution yields reaction A described under "General identification tests" as characteristic of orthophosphates (vol.1, p.114).

Heavy metals. For the preparation of the test solution use 1.0 g dissolved in 10 ml of hydrochloric acid (~70 g/l)TS heat to boiling, cool, dilute to 40 ml with water and mix. Determine the heavy metals content as described under "Limit test for heavy metals", according to Method A (vol.1, p.119); not more than 30 µg/g.

Arsenic. Use a solution of 3.3 g in 35 ml of hydrochloric acid (~70 g/l)TS, heat to dissolve and proceed as described under "Limit test for arsenic" (vol.1, p.122); the arsenic content is not more than 3 µg/g.

Barium. Mix 0.5 g with 10 ml of water, heat, add, drop by drop, hydrochloric acid (~420 g/l)TS until solution is effected, and then 2 drops of the acid in excess. Filter, and add to the filtrate 1.0 ml of potassium sulfate (0.1 g/l)TS; no turbidity appears within 15 minutes.

Carbonates. Suspend 5 g in 30 ml of carbon-dioxide-free water R and add slowly 10 ml of hydrochloric acid (~70 g/l)TS; not more than a slight effervescence is observed. (Keep the solution for the test on acid-insoluble substances).

Chlorides. Dissolve 0.20 g in a mixture of 2 ml of nitric acid (~130 g/l)TS and 20 ml of water, and proceed as described under "Limit test for chlorides" (vol.1, p.116); the chloride content is not more than 1.4 mg/g.

Fluorides. 4.0 g complies with the "Limit test for fluorides"; not more than 50 µg/g.

Sulfates. Dissolve 0.10 g in 5 ml of hydrochloric acid (~70 g/l)TS, and proceed as described under "Limit test for sulfates" (vol.1, p.116); the sulfate content is not more than 8 mg/g.

Acid-insoluble substances. Filter the solution prepared in the test for carbonates, wash the residue with water and dry to constant weight at 105 °C; the residue weighs not more than 15 mg (0.3 %).

Loss on ignition. Ignite 1.0 g to constant weight at 800 °C for 30 minutes; it loses not more than 80 mg/g.

Assay. To about 0.15 g, accurately weighed, add a mixture of 5 ml of hydrochloric acid (~420 g/l)TS and 3 ml of water, use gentle heat to dissolve and add 125 ml of water. Proceed with the titration as described under "Complexometric titrations" for calcium (vol.1, p.128). Each ml of disodium edetate (0.05 mol/l)VS is equivalent to 2.004 mg of Ca.

CALCII STEARAS

Calcium stearate

Composition. Calcium stearate consists of calcium salts of variable proportions mainly of stearic acid and palmitic acid; CAS Reg. No. 1592-23-0.

Description. A fine, white to yellowish white, bulky powder; odour, slight, characteristic.

Solubility. Practically insoluble in water, ethanol (~750 g/l)TS, acetone R and ether R.

Category. Tablet lubricant.

Storage. Calcium stearate should be kept in a well-closed container.

Additional information. The degree of lubrication depends on the particle form and size of the material.

REQUIREMENTS

General requirement. Calcium stearate contains not less than 9.0 % and not more than 10.5 % of CaO, calculated with reference to the dried substance.

Identity tests

A. Heat 1 g with a mixture of 25 ml of water and 5 ml of hydrochloric acid (~420 g/l)TS; fatty acids are liberated and float as an oil on the surface of the liquid. The aqueous layer yields the reactions described under "General identification tests" as characteristic of calcium (vol. 1, p. 112).

B. Mix 25 g with 200 ml of hot water, add 60 ml of sulfuric acid (~100 g/l)TS and heat the mixture until the separated fatty acid layer is clear. Wash the fatty acids with boiling water until free from sulfates, transfer them to a beaker, warm on a water-bath until the water separates and the fatty acids are clear. Allow to cool, pour off the water layer, melt the acids and filter into a dry beaker. Dry at 105 °C for 20 minutes; congealing temperature, not lower than 54 °C.

Loss on drying. Dry to constant weight at 105 °C, using 2-hours increments of heating; not more than 40 mg/g.

Assay. To about 1.2 g, accurately weighed, add 50 ml of hydrochloric acid (0.1 mol/l)VS, heat to boiling for 10 minutes, or until the separated fatty acid layer is clear, adding water, if necessary, to maintain the original volume. Cool, filter, and wash the filter and the flask thoroughly with water until the washing is free from acid when tested with litmus paper R. Neutralize the filtrate with sodium hydroxide (1 mol/l)VS against litmus paper R and proceed with the titration as described under "Complexometric titrations" for calcium (vol. 1, p. 128). Each ml of disodium edetate (0.05 mol/l)VS is equivalent to 2.804 mg of CaO.

CALCII SULFAS

Calcium sulfate

Molecular formula. $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ (dihydrate).

Relative molecular mass. 172.2 (dihydrate).

Graphic formula.

Chemical name. Sulfuric acid, calcium salt (1:1), dihydrate; CAS Reg. No. 10101-41-4.

Description. A fine, white to almost white powder; odourless or almost odourless.

Solubility. Slightly soluble in water; more soluble in dilute mineral acids; practically insoluble in most organic solvents.

Category. Capsule diluent, tablet diluent.

Storage. Calcium sulfate should be kept in a well-closed container.

REQUIREMENTS

General requirement. Calcium sulfate contains not less than 98.0 % and not more than 101.0 % of CaSO_4 , calculated with reference to the dried substance.

Identity tests

Dissolve 1.0 g in 20 ml of a solution prepared by mixing equal volumes of water and hydrochloric acid (~420 g/l)TS. Heat to boiling for 2 minutes, cool and filter if necessary. Use this solution for the following tests.

A. The solution yields the reactions described under "General identification tests" as characteristic of calcium (vol. 1, p. 112).

B. The solution yields the reactions described under "General identification tests" as characteristic of sulfates (vol. 1, p. 115).

Heavy metals. To 1.0 g add 10 ml of water and 20 ml of hydrochloric acid (~70 g/l)TS, heat to boiling until dissolved, cool and adjust the pH as described under "Limit test for heavy metals", Procedure 1 (vol. 1, p. 118); determine the heavy metals content according to method A (vol. 1, p. 119); not more than 20 µg/g.

Clarity of solution. Dissolve 1.0 g in a mixture of 45 ml of water and 5 ml of hydrochloric acid (~420 g/l)TS heating to 50 °C for 5 minutes; the solution is clear.

Loss on drying. Dry to constant weight at a temperature not lower than 250 °C; it loses not less than 190 mg/g and not more than 230 mg/g.

pH value. Slurry 20 g with 80 ml of carbon-dioxide-free water R, allow to settle and filter, 6.0 - 7.6.

Assay. To about 0.3 g, accurately weighed, add a mixture of 100 ml of water and 6 ml of hydrochloric acid (~70 g/l)TS, heat to boiling until dissolved and allow to cool. Proceed with the titration as described under "Complexometric titrations" for calcium (vol. 1, p. 128). Each ml of disodium edetate (0.05 mol/l)VS is equivalent to 6.807 mg of CaSO_4 .

CELLACEFATUM

Cellacefate

Composition. Cellacefate is composed of a partial mixture of acetate and hydrogen phthalate esters of cellulose. CAS Reg. No. 9004-38-0.

Other names. Cellulose acetate phthalate; cellacephate.

Description. A white, free flowing powder or colourless flakes; odourless or with faint odour of acetic acid.

Solubility. Practically insoluble in water and ethanol (~750 g/l)TS; freely soluble in acetone R; soluble in dioxan R. It dissolves in dilute solutions of alkali.

Category. Tablet coating agent (enteric), capsule coating agent.

Storage. Cellacefate should be kept in a well-closed container, and stored in a cool place; the container should be brought to room temperature before opening to avoid moisture from condensation to settle onto powder.

Additional information. Cellacefate is hygroscopic.

REQUIREMENTS

General requirement. Cellacefate contains not less than 30.0 % and not more than 40.0 % of phthalyl groups ($\text{C}_8\text{H}_5\text{O}_3$, relative molecular mass = 149.1) and not less than 17.0 % and not more than 26.0 % of acetyl groups ($\text{C}_2\text{H}_3\text{O}$, relative molecular mass = 43.05), both calculated with reference to the anhydrous substance.

Identity tests

A. To 10 mg add 1.0 ml of ethanol (~750 g/l)TS and about 1 ml of sulfuric acid (~1760 g/l)TS, and warm; ethyl acetate, perceptible by its odour (proceed with caution) is produced.

B. Transfer 10 mg to a small test tube, add 10 mg of resorcinol R, about 0.5 ml of sulfuric acid (~1760 g/l)TS and mix. Heat in a liquid bath at 160 °C for 3 minutes. Cool and pour the solution into a mixture of 25 ml of sodium hydroxide (1 mol/l)VS and 200 ml of water; the solution shows a vivid green fluorescence.

C. Dissolve about 0.1 g in 1.0 ml of acetone R and pour onto a clear glass plate; a glossy, clear film is deposited as the acetone evaporates.

Free acid. Shake 1.0 g of finely powdered material with 100 ml of carbon-dioxide-free water R for 5 minutes and filter. Wash the flask and the

filter with two quantities, each of 10 ml, of carbon-dioxide-free water R. Combine the filtrate and washings, add 0.1 ml of phenolphthalein/ethanol TS and titrate with carbonate-free sodium hydroxide (0.1 mol/l)VS until a faint pink colour is obtained. Repeat the procedure without the substance being tested. Each ml of carbonate-free sodium hydroxide (0.1 mol/l)VS is equivalent to 8.306 mg of phthalic acid. Not more than 60 mg/g (6.0 %) is found, calculated as phthalic acid, with reference to the anhydrous substance.

Sulfated ash. Not more than 1.0 mg/g.

Water. Determine as described under "Determination of water by the Karl Fischer method", Method A (vol.1, p. 135), using about 0.5 g of the substance and 20 ml of a mixture of equal volumes of dehydrated methanol R and chloroform R; the water content is not more than 50 mg/g, (5.0 %).

Assay

A. Phthalyl groups. Dissolve about 0.4 g, accurately weighed, in 20 ml of ethylene glycol monomethyl ether R previously neutralized to 0.1 ml of phenolphthalein/ethanol TS. Titrate with carbonate-free sodium hydroxide (0.1 mol/l)VS until a faint pink colour is obtained. Calculate the content of phthalyl groups in %: $(149n/(100-a)m) - 1.795S$, where n is the number of ml of carbonate-free sodium hydroxide (0.1 mol/l)VS used, a is the content of water in %, m is the mass of substance in g examined, and S is the content of free acid in %.

B. Acetyl groups. To 0.10 g add 25.0 ml of carbonate-free sodium hydroxide (0.1 mol/l)VS and heat on a water-bath under a reflux condenser for 30 minutes. Cool, add 0.1 ml of phenolphthalein/ethanol TS and titrate with hydrochloric acid (0.1 mol/l)VS until the colour is discharged. Repeat the procedure without the substance being tested. Calculate the content of acetyl groups in %: $(43(n_2-n_1)/(100-a)m) - (0.578P + 0.518S)$, where n_2 is the number of ml of hydrochloric acid (0.1 mol/l)VS used for the blank, n_1 is the number of ml of hydrochloric acid (0.1 mol/l)VS used for the substance, a is the content of water in %, m is the mass of substance in g examined, P is the content of phthalyl groups in %, and S is the content of free acid in %.

CELLULOSUM MICROCRYSTALLINUM

Microcrystalline cellulose

Composition. Microcrystalline cellulose is partially depolymerized cellulose and prepared from alpha cellulose. CAS Reg. No. 9004-34-6.

Description. A white or almost white, fine crystalline or granular powder; odourless.

Solubility. Practically insoluble in water and most organic solvents; slightly soluble in diluted solutions of sodium hydroxide.

Category. Adsorbent, capsule diluent, tablet diluent, suspending agent.

Storage. Microcrystalline cellulose should be kept in a well-closed container.

Additional information. Microcrystalline cellulose is usually defined by its particle size which ranges between 20 and 150 μ m.

REQUIREMENTSIdentity tests

A. Sieve 20 g for 5 minutes on an air-jet sieve equipped with a screen having a nominal aperture of 38 μ m. If more than 1.0 g is retained on the screen, mix 30 g with 270 ml of water; otherwise, mix 45 g with 255 ml of water. Perform the mixing in a high-speed blender (18 000 rpm) for 5 minutes. Transfer 100 ml of the mixture to a 100 ml graduated cylinder and allow to stand for 3 hours; a white, opaque, bubble-free dispersion is obtained without any supernatant liquid.

B. Dissolve 0.05 g in 10 ml of copper tetramine hydroxide TS; it dissolves completely without any residue. Add 5 ml of ethanol (~750 g/l)TS; a precipitate is produced.

Heavy metals. To 1.0 g add 4 ml of magnesium sulfate/sulfuric acid TS, mix and heat cautiously to dryness on a water-bath. Progressively heat to ignition, not exceeding a temperature of 800 °C, and continue to heat until a white to greyish residue is obtained. Moisten the residue with 1 drop of hydrochloric acid (~250 g/l)TS and continue as described under "Limit test for heavy metals", Procedure 3 (vol. 1, p. 118); determine the heavy metals content according to method A (vol. 1, p. 119); not more than 10 μ g/g.

Water-soluble substances. Shake 5.0 g with 80 ml of water for 10 minutes. Filter into a tared dish, evaporate to dryness on a water-bath, dry at 105 °C for 1 hour and weigh; the residue weighs not more than 2.0 mg/g.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry for 5 hours at 105 °C; it loses not more than 60 mg/g.

pH value. Shake 2.0 g with 100 ml of carbon-dioxide-free water R for 5 minutes; pH of the supernatant liquid, 5.0 - 7.5.

Organic impurities. Place about 10 mg on a watch-glass and add 0.05 ml of a freshly prepared solution of 0.1 g of phloroglucinol R in 5 ml of hydrochloric acid (~420 g/l)TS; no red colour appears.

Starch and dextrans. Shake 0.1 g with 5 ml of water and add 0.2 ml of iodine (0.05 mol/l)VS; no blue or red-brown colour is produced.

CERA CARNAUBA

Carnauba wax

Composition. Carnauba wax is obtained from the leaves of Copernicia cerifera Mart. (Fam. Palmae); CAS Reg. No. 8015-86-9.

Description. Pale yellow to light brown or yellow greyish moderately coarse powder, flakes or irregular lumps of hard, brittle wax; odour, characteristic and free from rancidity.

Solubility. Practically insoluble in water; soluble in warm chloroform R and toluene R; slightly soluble in boiling ethanol (~750 g/l)TS.

Category. Tablet coating agent, polishing agent for coated tablets.

Storage. Carnauba wax should be kept in a well-closed container.

REQUIREMENTS

Melting range. 78 - 85 °C.

Ash. Weigh 2 g and use an open porcelain or platinum dish. Heat over a flame; it volatilizes without emitting an acrid odour. Ignite; the residue weighs not more than 2.5 mg/g.

Acid value (vol.1, p.140). Use about 3 g; not more than 8.

Saponification value (vol.1, p.139). Use about 3 g, accurately weighed, add 25 ml of xylene R and dissolve by warming. To this solution add 50 ml of ethanol (~750 g/l)TS and proceed with the determination of saponification (vol. 1, p.139). Attach a reflux condenser and heat for 2 hours; 75 - 95.

Iodine value (vol.1, p.137). 5 - 14.

CETRIMIDUM

Cetrimide

Composition. Cetrimide is a mixture consisting chiefly of tetradecyltrimethylammonium bromide together with smaller amounts of dodecyltrimethylammonium bromide and hexadecyltrimethylammonium bromide.

Description. A white or almost white, voluminous, free-flowing powder; odour, slight and characteristic.

Solubility. Freely soluble in water, ethanol (~750 g/l)TS and chloroform R; practically insoluble in ether R.

Category. Antimicrobial preservative.

Storage. Cetrimide should be stored in a well-closed container.

REQUIREMENTS

General requirement. Cetrimide contains not less than 96.0 % and not more than 101.0 % of alkyltrimethylammonium bromides, calculated as $C_{17}H_{38}BrN$ (relative molecular mass = 336.4) and with reference to the dried substance.

Identity tests

A. Dissolve 5 mg in 5 ml of phosphate buffer, pH 8.0, TS. Dip a strip of methyl green/iodomercurate paper R into the solution. Prepare in a similar manner a blank solution without the substance being tested. After 5 minutes withdraw the strip of paper from the tube; the solution to be tested shows a more intense greenish blue colour than the blank solution.

B. Dissolve 0.20 g in 10 ml of carbon-dioxide-free water R and shake; it froths copiously (keep the solution for test C).

C. The solution prepared above yields reaction A described under "General identification tests" as characteristic of bromides (vol.1, p. 112).

Amines and amine salts. Dissolve 5.0 g in 30 ml of a mixture of 1 volume of hydrochloric acid (1 mol/l)VS and 99 volumes of methanol R and add 100 ml of 2-propanol R. Pass a stream of nitrogen R slowly through the solution. Gradually add 15.0 ml of tetrabutylammonium hydroxide (0.1 mol/l)VS and record

the potentiometric titration curve. If the curve shows two points of inflexion, the volume of titrant added between the two points is not greater than 2.0 ml.

Sulfated ash. Not more than 5.0 mg/g.

Loss on drying. Dry to constant weight at 105 °C for 2 hours; it loses not more than 20 mg/g.

Acidity or alkalinity. Dissolve 1.0 g in 50 ml of carbon-dioxide-free water R and add 0.1 ml of bromocresol purple/ethanol TS; not more than 0.1 ml of hydrochloric acid (0.1 mol/l)VS or 0.1 ml of sodium hydroxide (0.1 mol/l)VS is required to obtain the midpoint of the indicator (grey).

Assay. Dissolve about 2 g, accurately weighed, in 100 ml of water. Transfer 25 ml to a separating funnel, add 25 ml of chloroform R, 10 ml of sodium hydroxide (0.1 mol/l)VS and 10.0 ml of a freshly prepared solution containing 5.0 g of potassium iodide R in 100 ml of water. Shake well, allow to separate and discard the chloroform layer. Shake the aqueous layer with three quantities, each of 10 ml, of chloroform R, and discard the chloroform layers. Add 40 ml of hydrochloric acid (~420 g/l)TS, allow to cool and titrate with potassium iodate (0.05 mol/l)VS until the deep brown colour is almost discharged. Add 2 ml of chloroform R and continue the titration, shaking vigorously, until the colour of the chloroform layer no longer changes. Carry out a blank titration on a mixture of 10.0 ml of the freshly prepared solution of potassium iodide (see above), 20 ml of water and 40 ml of hydrochloric acid (~420 g/l)TS. Each ml of potassium iodate (0.05 mol/l)VS is equivalent to 33.64 mg of $C_{17}H_{38}BrN$.

CHLOROBUTANOLUM

Chlorobutanol
Chlorobutanol, anhydrous
Chlorobutanol hemihydrate

Molecular formula. $C_4H_7Cl_3O$ (anhydrous); $C_4H_7Cl_3O, 1/2H_2O$ (hemihydrate).

Relative molecular mass. 177.5 (anhydrous); 186.5 (hemihydrate).

Graphic formula.

Chemical name. 1,1,1-Trichloro-2-methyl-2-propanol; CAS Reg. No. 57-15-8 (anhydrous).

1,1,1-Trichloro-2-methyl-2-propanol hemihydrate; CAS Reg. No. 6001-64-5 (hemihydrate).

Description. Colourless crystals or a white, crystalline powder; odour, characteristic, camphoraceous.

Solubility. Slightly soluble in water; very soluble in ethanol (~750 g/l)TS and ether R; freely soluble in chloroform R; soluble in glycerol R.

Category. Antimicrobial preservative.

Storage. Chlorobutanol should be kept in a tightly closed container, and stored in a cool place.

Labelling. The designation on the containers of Chlorobutanol should state whether the substance is the hemihydrate or is in the anhydrous form.

Additional information. Anhydrous Chlorobutanol melts at about 95 °C and Chlorobutanol hemihydrate melts at about 77 °C both determined without previous drying.

REQUIREMENTS

General requirement. Chlorobutanol contains not less than 98.0 % and not more than 101.0 % of $C_4H_7Cl_3O$, calculated with reference to the anhydrous substance.

Identity tests

A. Shake 20 mg with 3 ml of sodium hydroxide (1 mol/l)VS, add 5 ml of water, then slowly, add 2 ml of iodine TS; iodoform, perceptible by its odour, is produced and a yellowish precipitate is formed.

B. To 20 mg add 1 ml of pyridine R and 2 ml of sodium hydroxide (~400 g/l)TS. Heat in a water-bath and shake. Allow to stand; the pyridine layer becomes red.

Solution in ethanol. A solution of 5 g in 10 ml of ethanol (~750 g/l)TS is not more opalescent than opalescence standard TS2 and not more intensely coloured than standard colour solution Yw3 when compared as described in "Colour of liquids" (vol.1, p.50).

Sulfated ash. Not more than 1.0 mg/g.

Water. Determine as described under "Determination of water by the Karl Fischer method", method A (vol. 1, p. 135). For the anhydrous form use about 2 g of the substance; the water content is not more than 10 mg/g. For the hemihydrate use about 0.3 g of the substance; the water content is not less than 45 mg/g and not more than 60 mg/g.

Acidity. Dissolve 2.0 g in 20 ml of ethanol (~750 g/l)TS and titrate with sodium hydroxide (0.01 mol/l)VS, using 0.1 ml of bromothymol blue/ethanol TS as indicator; not more than 1.0 ml is required to produce a blue colour.

Assay. Dissolve about 0.1 g, accurately weighed, in 20 ml of ethanol (~750 g/l)TS, add 10 ml of sodium hydroxide (~80 g/l)TS, heat in a water-bath for 5 minutes and cool. Add 20 ml of nitric acid (~130 g/l)TS, 25.0 ml of silver nitrate (0.1 mol/l)VS and 2 ml of dibutyl phthalate R, and shake vigorously. Add 2 ml of ferric ammonium sulfate (45 g/l)TS and titrate with ammonium thiocyanate (0.1 mol/l)VS until an orange colour is obtained. Repeat the operation without the substance being examined and make any necessary corrections. Each ml of silver nitrate (0.1 mol/l)VS is equivalent to 5.916 mg of $C_4H_7Cl_3O$.

CHLOROCRESOLUM

Chlorocresol

Molecular formula. C_7H_7ClO

Relative molecular mass. 142.6

Graphic formula.

Chemical name. 4-Chloro-3-methylphenol; CAS Reg. No. 59-50-7.

Description. Colourless or almost colourless crystals or a white, crystalline powder; odour, characteristic.

Solubility. Slightly soluble in water; very soluble in ethanol (~750 g/l)TS; freely soluble in ether R, fatty oils and sodium hydroxide (~80 g/l)TS.

Category. Antimicrobial preservative.

Storage. Chlorocresol should be kept in a well-closed container, protected from light.

REQUIREMENTS

General requirement. Chlorocresol contains not less than 98.0 % and not more than 101.0 % of C_7H_7ClO .

Identity tests

A. Shake 0.5 g, finely powdered, with 10 ml of carbon-dioxide-free water R for 2 minutes and filter. Add 0.1 ml of ferric chloride (25 g/l)TS; a bluish colour is produced.

B. Mix 0.05 g with 0.5 g of anhydrous sodium carbonate R and ignite strongly. Cool, add a mixture of 5 ml of water and 5 ml of nitric acid (~130 g/l)TS to the residue and filter. Add 1.0 ml of silver nitrate (0.1 mol/l)VS to the filtrate; a white precipitate is produced.

Melting range. 64 - 67 °C.

Non-volatile residue. Place about 2 g, accurately weighed, in a porcelain dish and heat on a water-bath until volatilized. Dry the residue at 105 °C and weigh; not more than 1.0 mg/g.

Assay. Place about 0.07 g, accurately weighed, in a ground-glass stoppered flask and dissolve in 30 ml of glacial acetic acid R. Add 25.0 ml of potassium bromate (0.0167 mol/l)VS, a solution composed of 3 g of potassium bromide R dissolved in 20 ml of water, and 10 ml of hydrochloric acid (~420 g/l)TS. Allow to stand protected from light for 15 minutes. Add 1 g of potassium iodide R and 100 ml of water. Titrate with sodium thiosulfate (0.1 mol/l)VS shaking vigorously and using starch TS as indicator added towards the end of the titration. Repeat the operation without the substance being examined and make any necessary corrections. Each ml of potassium bromate (0.0167 mol/l)VS is equivalent to 3.565 mg of C_7H_7ClO .

ETHANOLUM

Ethanol

Molecular formula. C_2H_6O

Relative molecular mass. 46.07

Graphic formula. C_2H_5OH

Chemical name. Ethyl alcohol; CAS Reg. No. 64-17-5.

Other name. Absolute alcohol, dehydrated alcohol.

Description. A clear, colourless and mobile liquid; odour, characteristic.

Miscibility. Miscible with water, chloroform R and ether R.

Category. Solvent, antiseptic.

Storage. Ethanol should be kept in a well-closed container, and stored whenever possible at a temperature between 8 and 15 °C.

Additional information. Ethanol is flammable, burning with a blue smokeless flame. Hygroscopic. Boiling point, about 79 °C.

REQUIREMENTS

General requirement. Ethanol contains not less than 98.8 % v/v and not more than 100.0 % v/v, corresponding to not less than 98.1 % m/m and not more than 100.0 % m/m of C₂H₆O.

Identity tests

A. Mix 0.25 ml in a small beaker with 1 ml of potassium permanganate (10 g/l)TS and 0.50 ml of sulfuric acid (0.5 mol/l)VS and cover the beaker immediately with a filter-paper moistened with a solution recently prepared by dissolving 0.1 g of sodium nitroprusside R and 0.5 g of piperazine hydrate R in 5 ml of water; an intense blue colour is produced on the filter-paper, the colour fading after a few minutes.

B. Mix a few drops with 1 ml of sulfuric acid (~1760 g/l)TS and a few drops of potassium dichromate (100 g/l)TS; a green colour is developed and an odour of acetaldehyde is perceptible.

Relative density. $d_{20}^{20} = 0.7904-0.7935$.

Non-volatile residue. Place 100 ml in a porcelain dish and heat on a water-bath until volatilized, dry the residue at 105 °C for 1 hour and weigh; not more than 5 mg.

Water-insoluble substances. Dilute with an equal volume of water; the mixture is clear and after cooling to 10 °C it remains clear for 30 minutes.

Acidity. Add 20 ml of carbon-dioxide-free water R and 3 drops of phenolphthalein/ethanol TS to 20 ml of the test solution; no colour develops. Titrate with carbonate-free sodium hydroxide (0.02 mol/l)VS; not more than 0.5 ml is required to obtain the midpoint of the indicator (pink).

Aldehydes and other foreign organic substances. Place 20 ml in a glass-stoppered cylinder that has been thoroughly cleaned with hydrochloric acid, then rinsed with water and the solution to be tested. Cool the contents to about 15 °C, and add, by means of a carefully cleaned pipette, 0.10 ml of potassium permanganate (0.02 mol/l)VS, noting accurately the time of addition. Mix at once by inverting the stoppered cylinder, and allow to stand at 15 °C for 5 minutes; the pink colour does not entirely disappear.

Fusel oil and allied impurities. Allow 25 ml to evaporate spontaneously from a porcelain dish, carefully protected from dust, until the surface of the dish is barely moist; no foreign odour is perceptible, and on the addition of a few drops of sulfuric acid (~1760 g/l)TS, no red or brown colour is produced.

Methanol. To 1 drop add 1 drop of water, 1 drop of phosphoric acid (~105 g/l)TS and 2 drops of potassium permanganate (25 g/l)TS. Mix, allow to stand for 1 minute, and add, drop by drop, sodium metabisulfite (50 g/l)TS until the permanganate colour is discharged. If a brown colour remains add 1 drop of phosphoric acid (~105 g/l)TS. To the colourless solution add 5 ml of freshly prepared chromotropic acid TS, and heat on a water-bath at 60 °C for 10 minutes; no violet colour appears.

Benzene. Record an absorption spectrum of the test solution in a 1-cm layer against water between 220 nm and 350 nm. The absorbance is not more than 0.30 at 220 nm, 0.18 at 230 nm, 0.08 at 240 nm, and 0.02 at 270 to 350 nm. A curve drawn through these points is smooth.

ETHYLCELLULOSUM

Ethylcellulose

Composition. Ethylcellulose is an ethyl ether of cellulose; CAS Reg. No. 9004-57-3.

Description. A free-flowing, white to light tan powder.

Solubility. Practically insoluble in water, glycerol R and propylene glycol R. When containing less than 46.5 % of ethoxy groups it is freely soluble in tetrahydrofuran R and chloroform R. When containing not less than 46.5 % of ethoxy groups it is freely soluble in ethanol (~750 g/l)TS, methanol R, toluene R and ethyl acetate R.

Category. Film-coating agent, tablet binder.

Storage. Ethylcellulose should be kept in a well-closed container.

Labelling. The designation on the container of Ethylcellulose should state its viscosity.

Additional information. The viscosity of Ethylcellulose should be indicated on the label.

REQUIREMENTS

General requirement. Ethylcellulose contains not less than 44.0 % and not more than 51.0 % of ethoxy (-OC₂H₅) groups.

Identity tests

A. Dissolve 5 g in 95 g of a mixture of 80 parts of toluene R and 20 parts of ethanol (~750 g/l)TS, by weight; a clear, stable, slightly yellow solution results.

B. Pour a few ml of the above solution onto a glass plate and allow the solvent to evaporate; a thin, though continuous, clear film is formed. Remove the film from the plate; it is flammable.

Heavy metals. Use 0.5 g for the preparation of the test solution as described under "Limit test for heavy metals", Procedure 3 (vol.1, p.118); determine the heavy metals content according to method A (vol.1, p.119); not more than 40 µg/g.

Sulfated ash. Not more than 4.0 mg/g.

Loss on drying. Dry at 105 °C for 2 hours; it loses not more than 30 mg/g.

Assay. Carry out the assay as described under "Determination of Methoxyl" (vol.1, p.136), using about 0.05 g, previously dried and accurately weighed. Each ml of sodium thiosulfate (0.1 mol/l)VS is equivalent to 0.7510 mg of (-OC₂H₅).

ETHYLIS HYDROXYBENZOAS

Ethyl hydroxybenzoate

Molecular formula. C₉H₁₀O₃

Relative molecular mass. 166.2

Graphic formula.

Chemical name. 4-Hydroxybenzoic acid ethyl ester; ethyl p-hydroxybenzoate;
CAS Reg. No. 120-47-8.

Other name. Ethylparaben.

Description. Small colourless crystals or a white, crystalline powder; odourless or almost odourless.

Solubility. Very slightly soluble in water; sparingly soluble in boiling water; freely soluble in ethanol (~750 g/l)TS and ether R.

Category. Antimicrobial preservative.

Storage. Ethyl hydroxybenzoate should be kept in a well-closed container.

Additional information. Ethyl hydroxybenzoate is normally used in combination with other hydroxybenzoates.

REQUIREMENTS

General requirement. Ethyl hydroxybenzoate contains not less than 99.0 % and not more than 101.0 % of C₉H₁₀O₃, calculated with reference to the dried substance.

Identity tests

A. See the test below under "Melting range".

B. To 0.5 g add 5 ml of sodium hydroxide (~80 g/l)TS, and heat in a water-bath for 5 minutes. After cooling, add 6 ml of sulfuric acid (~190 g/l)TS, collect the precipitate on a filter, wash thoroughly with a small amount of water and dry over silica gel, desiccant, R. Melting temperature, about 214 °C.

Melting range. 115-118 °C.

Sulfated ash. 1.0 mg/g.

Loss on drying. Dry at 80 °C under reduced pressure (not exceeding 0.6 kPa or about 5 mm of mercury) for 2 hours; it loses not more than 5.0 mg/g.

Acidity. Dissolve 0.2 g in 5 ml of ethanol (~750 g/l)TS, add 5 ml of carbon dioxide free water R and titrate with sodium hydroxide (0.1 mol/l)VS, using 0.1 ml of bromocresol green/ethanol TS as indicator; not more than 0.1 ml is required to obtain the midpoint of the indicator (green).

Assay. Place about 80 mg, accurately weighed, in a ground-glass-stoppered flask, add 25 ml of sodium hydroxide (~80 g/l)TS and boil gently under a reflux condenser for 30 minutes. Allow to cool, add 25.0 ml of potassium bromate (0.0333 mol/l)VS, 5.0 ml of potassium bromide (125 g/l)TS and 40 ml of glacial acetic acid R. Cool in ice-water and add 10 ml of hydrochloric acid (~420 g/l)TS. Stopper the flask immediately and allow to stand for 15 minutes. Add 30 ml of potassium iodide (80 g/l)TS, close the flask and mix. Titrate with sodium thiosulfate (0.1 mol/l)VS, using 2 ml of starch TS as indicator, added towards the end of the titration. Repeat the operation without the substance being examined and make any necessary corrections. The volume of potassium bromate (0.0333 mol/l)VS used is equivalent to half the volume for the titration. Each ml of potassium bromate (0.0333 mol/l)VS is equivalent to 5.540 mg of $C_9H_{10}O_3$.

GLYCEROLI MONOSTEARAS

Glyceryl monostearate

Composition. Glyceryl monostearate is a mixture of mono-, di- and tri-glycerides of stearic and palmitic acids.

Chemical name. Octadecanoic acid, monoester with 1,2,3-propanetriol; monostearin; CAS Reg. No. 31566-31-1.

Description. A white or yellowish white, hard waxy mass or unctuous powder or flakes; odourless or slight, agreeable fatty odour.

Solubility. Practically insoluble in water; freely soluble in chloroform R; soluble in ether R, benzene R and in ethanol (~750 g/l)TS at 60 °C.

Category. Emulsifying agent, ointment base.

Storage. Glyceryl monostearate should be kept in a tightly closed container, protected from light.

Additional information. Glyceryl monostearate may contain a suitable antioxidant. Self-emulsifying glyceryl monostearate contains additional emulsifying agents.

REQUIREMENTS

General requirement. Glyceryl monostearate contains not less than 35.0 % of monoglycerides, calculated as $C_{20}H_{40}O_4$, and not more than 6.0 % of free glycerol.

Identity tests

- A. Melting temperature, not lower than 55 °C.
- B. Dip a strip of filter-paper in a freshly prepared solution containing 9.5 ml of sodium nitroprusside (8.5 g/l)TS and 0.5 ml of piperidine R. Place the moistened filter-paper into the evolving vapours over the mouth of the test-tube containing 1 g of the substance to be tested and heat with 2 ml of phosphoric acid (~1440 g/l)TS; a strong blue colour is developed on the paper.
- C. Heat 2.5 with 40 ml of potassium hydroxide/ethanol TS1 on a water-bath under reflux for 30 minutes. Add 30 ml of water, evaporate the ethanol, acidify the hot mixture with 15 ml of hydrochloric acid (~70 g/l)TS, cool and shake with 50 ml of ether R. Wash the ether layer with three quantities, each of a mixture of 5 ml of sodium chloride (400 g/l)TS and 5 ml of water, dry the ether layer over anhydrous sodium sulfate R and filter. Evaporate the filtrate and dry the residue under reduced pressure at room temperature. Melt the residue, introduce it into capillary tubes and allow to stand for 24 hours in a well-closed container. Melting temperature, not lower than 53 °C.

Acid value (vol.1, p.140). Not more than 6.0.

Saponification value (vol.1, p.139). 155-177.

Iodine value (vol.1, p.137). Not more than 3.

Sulfated ash. Not more than 1.0 mg/g.

Assay. Transfer about 0.4 g, accurately weighed, to a glass-stoppered separating funnel, and dissolve in 50 ml of chloroform R, Cool, if necessary, add 25 ml of water and shake vigorously for 1 minute. Allow the layers to separate. If an emulsion is formed add a few drops of glacial acetic acid R. Carry out the extraction three more times using 25 ml, 20 ml and 20 ml of water, respectively. Collect the chloroform extracts to be used in the assay for monoglycerides. Filter the aqueous layers through a filter-paper moistened with water, wash the filter with two quantities, each of 5 ml, of water and dilute the combined filtrates and washings to 100 ml with water. Use this solution for the assay for free glycerol.

A. Free glycerol. Place 50 ml of the aqueous solution prepared above in a 500-ml ground-glass stoppered conical flask, add 25.0 ml of periodic acetic acid TS, and shake cautiously. Allow to stand at a temperature between 25 and 30 °C for 30 minutes. Add 100 ml of water and 25 ml of potassium iodide (80 g/l)TS. Titrate with sodium thiosulfate (0.1 mol/l)VS using 1 ml of starch TS as indicator added towards the end of the titration. Repeat the operation without the substance being examined and make any necessary corrections. Each ml of sodium thiosulfate (0.1 mol/l)VS is equivalent to 2.3 mg of glycerol.

B. Monoglycerides. Filter the combined chloroform extracts prepared above through a plug of cotton-wool. Wash the separating funnel and the filter with three quantities, each of 5 ml, of chloroform R, dilute the filtrate to 100.0 ml with chloroform R. Carry out the assay as described for free glycerol using 50 ml of the chloroform solution. Each ml of sodium thiosulfate (0.1 mol/l)VS is equivalent to 17.2 mg of monoglycerides, calculated as $C_{20}H_{40}O_4$.

GUMMI ARABICUM

Acacia

Composition. Acacia is the air-hardened, gummy exudate from the stem and branches of Acacia senegal (L.) Willdenow or other species of Acacia of African origin; it contains polymers of salts of arabic acid.

Description. Odourless; tasteless and mucilaginous.

Solubility. Very slowly soluble in twice its weight of water, leaving only a very small residue of vegetable particles; practically insoluble in ethanol (~750 g/l)TS and ether R.

Category. Emulsifying agent, suspending agent; encapsulating agent.

Storage. Acacia should be kept in a well-closed container.

Additional information. Attention should be paid to the microbiological purity of Acacia since it is of natural origin.

REQUIREMENTS

Macroscopical examination. Spheroidal, oval or reniform pieces, the diameter varying from about 1-3 cm, white, yellowish-white, yellow or pale amber, sometimes with a pinkish tint, translucent or somewhat opaque, friable, frequently with a cracked surface, easily broken into transparent angular fragments with a glassy appearance and occasionally iridescent. Acacia also occurs as thin, white to yellowish white flakes, powder or fine granules.

Microscopical examination. The flakes appears as colourless striated fragments, the powder presents angular, irregular, colourless, bright fragments with only traces of starch or vegetable tissues visible. No stratified membrane is apparent. The granules appear as colourless, glassy, irregular angular fragments up to 100 µm in thickness, some of which exhibit parallel linear streaks.

Identity tests

Note: All tests are performed with powdered material.

A. Dissolve 1.0 g in 2.0 ml of water, add 2.0 ml of ethanol (~750 g/l)TS and shake; a white, gelatinous mucilage is formed which becomes fluid on adding 10 ml of water.

B. Dissolve 0.20 g in 10 ml of water and add 4 drops of lead subacetate TS; a flocculent or curdy, white precipitate is formed immediately.

Starch and dextrin. Dissolve 1.0 g in 10 ml of water, boil and cool, then add 0.10 ml of iodine (0.05 mol/l)VS; no blue or reddish-brown colour is produced.

Sucrose and fructose. Dissolve 0.3 g in 5 ml of water, add 0.10 g of resorcinol R and 2.0 ml of hydrochloric acid (~420 g/l)TS. Heat on a water-bath for 1 minute. No yellow or pink colour develops.

Tannin. Dissolve 1.0 g in 10 ml of water and add 0.20 ml of ferric chloride (65 g/l)TS; a gelatinous precipitate is formed, but neither the precipitate nor the liquid shows a dark blue colour.

Solubility in water and acidity. Dissolve 1.0 g in 2.0 ml of water; the solution flows readily and is acid when tested with pH-indicator paper R.

Insoluble matter. To 5 g add 100 ml of water and 15 ml of hydrochloric acid (~70 g/l)TS, boil gently for 15 minutes, shaking frequently, filter while hot through a tared sintered glass crucible, wash the residue with hot water, dry at 105 °C for 1 hour and weigh; the residue weighs not more than 50 mg (1 %).

Sulfated ash. Not more than 50 mg/g.

Loss on drying. Dry to constant weight at 105 °C; it loses not more than 0.15 g/g.

HYDROXYPROPYLCELLULOSUM

Hydroxypropylcellulose

Composition. Hydroxypropylcellulose is a cellulose having some of the hydroxyl groups in the form of the 2-hydroxypropyl ether.

Description. A white or yellowish white powder; odourless.

Solubility. Soluble in cold water, chloroform R, ethanol (~750 g/l)TS, methanol R and propylene glycol R giving colloidal solutions; practically insoluble in hot water.

Category. Film coating agent, tablet binder.

Storage. Hydroxypropylcellulose should be kept in a well-closed container.

Labelling. The designation on the container of Hydroxypropylcellulose should state its viscosity.

Additional information. Hydroxypropylcellulose is hygroscopic after drying. The viscosity of Hydroxypropylcellulose should be indicated on the label.

REQUIREMENTS

Identity tests

- A. While stirring add 1.0 g of the dried test substance to 50 ml of carbon-dioxide-free water R heated to 90 °C. Allow to cool, dilute to 100 ml with carbon-dioxide-free water R and stir until dissolution is complete (keep this solution for identity test B). Heat 10 ml on a water-bath while stirring; at a temperature above 40 °C the solution becomes cloudy or a flocculent precipitate is formed, and on cooling the solution becomes clear again.
- B. Place 1 ml of the above solution onto a glass plate and allow to evaporate; a thin film is formed.
- C. Dissolve without heating 0.2 g in 15 ml of sulfuric acid (~1125 g/l)TS. Pour the solution with stirring into 100 ml of ice water, and dilute to 250 ml with ice water. In a test-tube, mix thoroughly while cooling in ice water 1 ml of the solution with 8 ml of sulfuric acid (~1760 g/l)TS, added drop by drop. Heat in a water-bath for exactly 3 minutes and immediately cool in ice water. While cold, carefully add 0.6 ml of triketohydrindene/sodium metabisulfite TS and mix well. Allow to stand at 25 °C for 100 minutes; a pink colour is produced immediately and it becomes violet.

Heavy metals. The 1.0 g for the preparation of the test solution as described under "Limit test for heavy metals", Procedure 3 (vol.1, p.118); determine the heavy metals content according to Method A (vol.1, p. 119); not more than 20 µg/g.

Sulfated ash. Not more than 5.0 mg/g.

Loss on drying. Dry to constant weight at 105 °C; it loses not more than 70 mg/g.

LACTOSUM

Lactose

Lactose, anhydrous
Lactose monohydrate

Molecular formula. $C_{12}H_{22}O_{11}$ (anhydrous);
 $C_{12}H_{22}O_{11}.H_2O$ (monohydrate).

Relative molecular mass. 342.3 (anhydrous); 360.3 (monohydrate).

Graphic formula.

Chemical name. 4-O-β-D-Galactopyranosyl-D-glucose; CAS Reg. No. 63-42-3.
4-O-β-D-Galactopyranosyl-D-glucose monohydrate; CAS Reg. No. 64044-51-5.

Description. A white or almost white, crystalline powder; odourless.

Solubility. Freely but slowly soluble in water; very slightly soluble in ethanol (~750 g/l)TS; practically insoluble in chloroform R and ether R.

Category. Capsule diluent, tablet diluent.

Storage. Lactose should be kept in a well-closed container.

Labelling. The designation on the container of Lactose should state whether the substance is the monohydrate or is in the anhydrous form.

REQUIREMENTS

Identity tests

A. Dissolve 0.1 g in 10 ml of water, add 3 ml of potassio-cupric tartrate TS and heat; a red precipitate is formed.

B. Dissolve 0.25 g in 5 ml of water, add 5 ml of ammonia (~260 g/l)TS and heat in a water-bath at 80 °C for 10 minutes; a red colour develops.

C. Dissolve 20 mg in 5 ml of water, add 0.2 ml of methylamine hydrochloride (20 g/l)TS and heat to boiling for 30 seconds. Add 0.2 ml of sodium hydroxide (~200 g/l)TS; the initial yellow colour of the resulting solution turns to red.

Specific optical rotation. Dissolve 10 g in 80 ml of water, heating to 50 °C. Allow to cool and add 0.2 ml of ammonia (~100 g/l)TS. Allow to stand for 30 minutes and dilute to 100 ml with water. Measure the rotation at 20 °C and calculate with reference to the anhydrous substance;

$$[\alpha]_{20}^D = +54.4 \text{ to } +55.9 \text{ }^\circ.$$

Heavy metals. Use 1.0 g for the preparation of the test solution, add 1 ml of hydrochloric acid (0.1 mol/l)VS and proceed as described under "Limit test for heavy metals", Procedure 1, (vol.1, p. 118); determine the heavy metals content according to Method A (vol. 1, p.119); not more than 5 µg/g.

Starch. Dissolve 1.5 g in 10 ml of boiling water. Cool, and add 1 drop of iodine (0.05 mol/l)VS; no blue colour is produced.

Clarity and colour of solution. A solution of 3.0 g in 10 ml of boiling water is clear, colourless or nearly colourless and odourless.

Ethanol-soluble substances. Add 10 g of finely powdered test substance to 40 ml of ethanol (~750 g/l)TS and shake for 10 minutes. Filter, evaporate 10 ml of the filtrate to dryness, and dry the residue at 100 °C for 10 minutes and weigh; not more than 20 mg.

Sulfated ash. Not more than 1.0 mg/g.

Water. Determine as described under "Determination of water by the Karl Fischer Method", Method A (vol.1, p.135).

For the anhydrous form use about 2.0 g of the substance; the water content is not more than 10 mg/g.

For the monohydrate use about 0.5 g of the substance; the water content is not less than 45 mg/g and not more than 55 mg/g.

Acidity or alkalinity. Dissolve 6.0 g by boiling in 25 ml of carbon-dioxide-free water R, cool and add 0.3 ml of phenolphthalein/ethanol TS; the solution is colourless. Not more than 0.4 ml of carbonate free sodium hydroxide (0.1 mol/l)VS is required to obtain the midpoint of the indicator (pink).

METHYLCELLULOSUM

Methylcellulose

Composition. Methylcellulose is a methyl ether of cellulose;
CAS Reg. No. 9004-67-5.

Description. A white, yellowish white or greyish white powder or a loose cotton-like, fibrous material; odourless.

Solubility. Practically insoluble in hot water, it swells in cold water and produces a clear to opalescent, viscous, colloidal suspension; practically insoluble in ethanol (~750 g/l)TS, ether R, chloroform R and acetone R; soluble in glacial acetic acid R and in a mixture of equal volumes of ethanol (~750 g/l)TS and chloroform R.

Category. Emulsifying agent, suspending agent, viscosity-increasing agent, coating agent.

Storage. Methylcellulose should be kept in a well-closed container.

Labelling. The designation on the container of Methylcellulose should state its viscosity.

Additional information. Methylcellulose is hygroscopic after drying. Aqueous suspensions are neutral to litmus R. The viscosity of Methylcellulose should be indicated on the label.

REQUIREMENTS

General requirement. Methylcellulose contains not less than 26.0 % and not more than 32.0 % of methoxy (-OCH₃) groups.

Identity tests

A. While stirring add 1.0 g of the dried test substance to 50 ml of carbon-dioxide-free water R heated to 90 °C. Allow to cool, dilute to 100 ml with carbon-dioxide-free water R and stir until dissolution is complete. (Keep this solution for identity test B). Heat 10 ml in a water-bath while stirring; at a temperature above 50 °C the solution becomes cloudy or a flocculent precipitate is formed, and on cooling the solution becomes clear again.

B. Place 1 ml of the above solution onto a glass plate and allow to evaporate; a thin film is formed.

C. Dissolve without heating 0.2 g in 15 ml of sulfuric acid (~1125 g/l)TS. Pour the solution with stirring into 100 ml of ice water, and dilute to 250 ml with ice water. In a test-tube, mix thoroughly while cooling in ice water 1 ml of the solution with 8 ml of sulfuric acid (~1760 g/l)TS, added drop by drop. Heat in a water-bath for exactly 3 minutes and immediately cool in ice water. While cold, carefully add 0.6 ml of triketohydrindene/sodium metabisulfite TS and mix well. Allow to stand at 25 °C for 100 minutes; a pink colour is produced immediately and does not become violet.

Heavy metals. Use 1.0 g for the preparation of the test solution as described under "Limit test for heavy metals", Procedure 3 (vol.1, p.118); determine the heavy metals content according to Method A (vol.1, p.119); not more than 20 µg/g.

Sulfated ash. Not more than 10 mg/g.

Loss on drying. Dry to constant weight at 105 °C; it loses not more than 100 mg/g.

Assay. Carry out the assay as described under "Determination of Methoxyl" (vol.1, p.136), using about 0.05 g, previously dried and accurately weighed. Each ml of sodium thiosulfate (0.1 mol/l)VS is equivalent to 0.5172 mg of (-OCH₃).

METHYLIS HYDROXYBENZOAS

Methyl hydroxybenzoate

Molecular formula. C₈H₈O₃

Relative molecular mass. 152.2

Graphic formula.

Chemical name. 4-Hydroxybenzoic acid methyl ester; methyl *p*-hydroxybenzoate;
CAS Reg. No. 99-76-3.

Other name. Methylparaben.

Description. Colourless crystals or a white, crystalline powder; odourless or almost odourless.

Solubility. Very slightly soluble in water; soluble in boiling water; freely soluble in ethanol (~750 g/l)TS and ether R.

Category. Antimicrobial preservative.

Storage. Methyl hydroxybenzoate should be kept in a well-closed container.

Additional information. Methyl hydroxybenzoate is normally used in combination with other hydroxybenzoates.

REQUIREMENTS

General requirement. Methyl hydroxybenzoate contains not less than 99.0 % and not more than 101.0 % of $C_9H_8O_3$, calculated with reference to the dried substance.

Identity tests

A. See the test below under "Melting range".

B. To 0.5 g add 5 ml of sodium hydroxide (~80 g/l)TS, and heat in a water-bath for 5 minutes. After cooling, add 6 ml of sulfuric acid (~190 g/l)TS, collect the precipitate on a filter, wash thoroughly with a small amount of water and dry over silica gel, desiccant, R. Melting temperature, about 214 °C.

Melting range. 125-128 °C.

Sulfated ash. 1.0 mg/g.

Loss on drying. Dry at 80 °C under reduced pressure (not exceeding 0.6 kPa or about 5 mm of mercury) for 2 hours; it loses not more than 5.0 mg/g.

Acidity. Dissolve 0.2 g in 5 ml of ethanol (~750 g/l)TS, add 5 ml of carbon-dioxide-free water R and titrate with sodium hydroxide (0.1 mol/l)VS, using 0.1 ml of bromocresol green/ethanol TS as indicator; not more than 0.1 ml is required to obtain the midpoint of the indicator (green).

Assay. Place about 80 mg, accurately weighed, in a ground-glass-stoppered flask, add 25 ml of sodium hydroxide (~80 g/l)TS and boil gently under a reflux condenser for 30 minutes. Allow to cool, add 25.0 ml of potassium bromate (0.0333 mol/l)VS, 5.0 ml of potassium bromide (125 g/l)TS and 40 ml of glacial acetic acid R. Cool in ice-water and add 10 ml of hydrochloric acid (~420 g/l)TS. Stopper the flask immediately and allow to stand for 15 minutes. Add 30 ml of potassium iodide (80 g/l)TS, close the flask and mix. Titrate with sodium thiosulfate (0.1 mol/l)VS, using 2 ml of starch TS as indicator, added towards the end of the titration. Repeat the operation without the substance being examined and make any necessary corrections. The volume of potassium bromate (0.0333 mol/l)VS used is equivalent to half the volume for the titration. Each ml of potassium bromate (0.0333 mol/l)VS is equivalent to 5.073 mg of $C_9H_8O_3$.

OLEUM ARACHIDIS

Arachis oil

Composition. Arachis oil is the refined fixed oil obtained from the seed kernels of Arachis hypogaea L.

Other name. Peanut oil.

Description. A clear, yellowish viscous liquid; odourless or with a very faint nutlike odour.

Miscibility. Very slightly miscible in ethanol (~750 g/l)TS; miscible with chloroform R, ether R and light petroleum R.

Category. Oleaginous vehicle, solvent.

Storage. Arachis oil should be kept in a well-filled and well-closed container, protected from light, and stored in a cool place.

Additional information. The quality of the material described is not suitable for parenteral administration.

REQUIREMENTSIdentity tests

To 0.5 ml add 10 ml of potassium hydroxide/ethanol TS1 and heat in a water-bath at 80 °C for 15 minutes, shaking intermittently. Allow to stand for 1 hour; a gelatinous cloudiness appears that adheres to the walls of the tube.

Refractive index. $n_D^{20} = 1.468 - 1.472.$

Relative density. $d_{20}^{20} = 0.912 - 0.920.$

Acid value (vol.1, p.140). Not more than 0.6.

Saponification value (vol.1, p.139). 185-195.

Iodine value (vol.1, p.137). 83-103.

Unsaponifiable matter (vol.1, p.139). Not more than 15 mg/g.

Peroxide value (vol.1, p.138). Not more than 5.0.

PARAFFINUM ALBUM
PARAFFINUM FLAVUM

White soft paraffin
Yellow soft paraffin

Composition. White and yellow soft paraffins are purified mixtures of semisolid hydrocarbons obtained from petroleum. White soft paraffin is bleached. A suitable stabilizer may be contained to prevent oil separation.

Other names. White petrolatum, yellow petrolatum; vaselinum album, vaselinum flavum.

Description. A white or a pale yellow to yellow, respectively, soft mass, unctuous to the touch; odourless.

Solubility. Practically insoluble in water and ethanol (~750 g/l)TS; soluble in chloroform R, ether R and in most fixed and volatile oils.

Category. Ointment bases.

Storage. White and yellow soft paraffins should be kept in a well-closed container.

Additional information. In a thin layer or when melted both paraffins show a slight fluorescence. Melting point, within 38-60 C°.

REQUIREMENTS

Identity tests

A. Melt 2 g and as soon as a homogenous phase is obtained add 2 ml of water and 0.2 ml of iodine (0.1 mol/l)VS. Heat until two liquid phases are obtained, shake and cool; the upper solid phase is pinkish violet.

B. Heat a small portion of the test substance; it ignites with a luminous flame and deposits carbon.

Sulfated ash. Not more than 1.0 mg/g.

Alkalinity. To 35 g add 100 ml of boiling water, cover the beaker, and heat to boiling, while stirring, for 5 minutes. Allow the phases to separate, transfer the aqueous layer to a suitable dish, wash the paraffin with two portions each of 50 ml of boiling water and adding them to the dish. Add 1 drop of phenolphthalein/ethanol TS and boil; no pink colour appears (keep this solution for the test of acidity).

Acidity. To the solution obtained in the test for alkalinity add 0.1 ml of methyl orange/ethanol TS; no red or pink colour is produced.

Organic acid. To 20 g add 100 ml of a mixture of equal volumes of neutralized ethanol TS and water, mix thoroughly and heat to boiling. Add 1 ml of phenolphthalein/ethanol TS and titrate rapidly with carbonate-free sodium hydroxide (0.1 mol/l)VS to a sharp pink endpoint, the colour change being observed in the ethanol-water layer; not more than 400 µl of carbonate-free sodium hydroxide (0.1 mol/l)VS is required.

Fixed oils, fats and rosin. Digest 10 g with 50 ml of sodium hydroxide (~200 g/l)TS at 100 °C for 30 minutes. Separate the aqueous layer and acidify with sulfuric acid (~570 g/l)TS; no oily or solid matter is observed.

Ultraviolet absorption. Dissolve 50 mg in 100 ml of 2,2,4-trimethylpentane R. Measure the absorbance of a 1-cm layer at 290 nm.
White soft paraffin = not greater than 0.5.
Yellow soft paraffin = not greater than 0.75.

PARAFFINUM DURUM

Hard paraffin

Composition. Hard paraffin is a purified mixture of solid hydrocarbons obtained from petroleum.

Description. A colourless or a white mass showing a crystalline structure, slightly unctuous to the touch; odourless.

Solubility. Practically insoluble in water and ethanol (~750 g/l)TS; freely soluble in chloroform R and ether R.

Category. Ointment base component, viscosity-increasing agent.

Storage. Hard paraffin should be kept in a well-closed container.

Additional information. Congealing point, within 47-65 °C.

REQUIREMENTS

Identity tests

A. Melt 2 g and as soon as a homogenous phase is obtained add 2 ml of water and 0.2 ml of iodine (0.1 mol/l)VS. Heat until two liquid phases are obtained, shake and cool; the upper solid phase is pinkish violet.

B. Heat a small portion of the test substance; it ignites with a luminous flame and deposits carbon.

Sulfated ash. Not more than 1.0 mg/g.

Acidity or alkalinity. Boil 5 g with 10 ml of ethanol (~710 g/l)TS previously neutralized to litmus TS, cool and add a few drops of litmus TS; the solution is neutral (violet).

2-PROPANOLUM

2-Propanol

Molecular formula. C₃H₈O

Relative molecular mass. 60.10

Graphic formula.

Chemical name. 2-Propanol; isopropyl alcohol; CAS Reg. No. 67-63-0.

Description. A clear, colourless mobile liquid; odour, characteristic.

Miscibility. Miscible with water, ethanol (~750 g/l)TS, ether R and chloroform R.

Category. Solvent, antiseptic.

Storage. 2-Propanol should be kept in a tightly closed container, in a cool place.

Additional information. 2-Propanol is volatile and flammable. Boiling range, 81-83 °C.

REQUIREMENTS

Identity tests

A. Mix 1 ml with 9 ml of water. To 1 ml of this solution add 2 ml of mercuric sulfate TS and heat to boiling; a white to yellowish white precipitate is produced.

B. Heat gently 1 ml with 3 ml of potassium dichromate (100 g/l)TS and 1 ml of sulfuric acid (~1760 g/l)TS; acetone, perceptible by its odour is evolved.

Refractive index. $n_D^{20} = 1.376-1.378.$

Relative density. $d_{20}^{20} = 0.783-0.787.$

Nonvolatile residue. Evaporate 50 ml to dryness on a water bath, heat at 105 °C for 1 hour and weigh; not more than 2.5 mg (0.005 %).

Acidity. To 50 ml add 100 ml of carbon-dioxide-free water R, 2 drops of phenolphthalein/ethanol TS and titrate with carbonate-free sodium hydroxide (0.02 mol/l)VS to a pink colour that persists for 30 seconds; not more than 0.70 ml of carbonate-free sodium hydroxide (0.02 mol/l)VS is required.

Aldehydes and ketones. Using a comparison tube mix 25 ml with 25 ml of water and 50 ml of hydroxylamine hydrochloride TS, allow to stand for 5 minutes, titrate with sodium hydroxide (0.1 mol/l)VS until the colour matches that of 50 ml of hydroxylamine hydrochloride TS placed in a similar tube and viewed down the axis; not more than 2.0 ml of sodium hydroxide (0.1 mol/l)VS is required.

PROPYLENEGLYCOLUM

Propylene glycol

Molecular formula. $C_3H_8O_2$

Relative molecular mass. 76.09

Graphic formula.

Chemical name. 1,2-Propanediol; CAS Reg. No. 57-55-6.

Description. A clear, colourless, viscous liquid; odourless.

Miscibility. Miscible with water, ethanol (~750 g/l)TS and chloroform R.

Category. Solvent, humectant.

Storage. Propylene glycol should be kept in a tightly closed container.

Additional information. Propylene glycol is hygroscopic. Boiling range, it distills completely between 185 and 189 °C.

REQUIREMENTSIdentity test

Place 0.5 ml of a 0.1 mg/ml solution in ice to cool, add 5 ml of a cooled mixture of 10 ml of water and 90 ml of sulfuric acid (~1760 g/l)TS. Heat on a water-bath at 70 °C for 10 minutes, cool and add 0.2 ml of triketohydrindene/sodium metabisulfite TS; a violet colour slowly appears.

Refractive index. $n_D^{20} = 1.431-1.433.$

Relative density. $d_{20}^{20} = 1.035-1.040.$

Heavy metals. Use 4 ml for the preparation of the test solution as described under "Limit test for heavy metals", Procedure 1 (vol. 1, p. 118); determine the heavy metals content according to Method A (vol. 1, p. 119); not more than 5 µg/g.

Clarity and colour of solution. The liquid to be tested is clear and colourless.

Sulfated ash. Use 50 g; the residue weighs not more than 5 mg (0.1 mg/g).

Water. Determine as described under "Determination of water by the Karl Fischer method", Method A (vol. 1, p. 135), using about 5 g of the substance; the water content is not more than 2.0 mg/g.

Acidity. To 10 ml add 40 ml of water and 0.1 ml of bromothymol blue/ethanol TS; the solution is greenish yellow. Titrate with sodium hydroxide (0.1 mol/l)VS; not more than 0.05 ml is required to obtain the midpoint of the indicator (blue).

Oxidizing substances. To 10 ml add 5 ml of water, 2 ml of potassium iodide (80 g/l)TS and 2 ml of sulfuric acid (~100 g/l)TS, and allow to stand in a stoppered vessel protected from light for 15 minutes. Titrate with sodium thiosulfate (0.05 mol/l)VS, using starch TS as indicator; not more than 0.2 ml of sodium thiosulfate (0.05 mol/l)VS is required.

Reducing substances. To 1 ml add 1 ml of ammonia (~100 g/l)TS and heat in a water-bath at 60 °C for 5 minutes; the solution is yellow. Immediately add 0.15 ml of silver nitrate (0.1 mol/l)VS and allow to stand for 5 minutes; the solution remains unchanged.

PROPYLIS HYDROXYBENZOAS

Propyl hydroxybenzoate

Molecular formula. $C_{10}H_{12}O_3$

Relative molecular mass. 180.2

Graphic formula.

Chemical name. 4-Hydroxybenzoic acid propyl ester; propyl p-hydroxybenzoate;
CAS Reg. No. 94-13-3.

Other name. Propylparaben.

Description. Colourless crystals or a white, crystalline powder; odourless or with a faintly aromatic odour.

Solubility. Very slightly soluble in water; slightly soluble in boiling water; freely soluble in ethanol (~750 g/l)TS and ether R.

Category. Antimicrobial preservative.

Storage. Propyl hydroxybenzoate should be kept in a well-closed container.

Additional information. Propyl hydroxybenzoate is normally used in combination with other hydroxybenzoates.

REQUIREMENTS

General requirement. Propyl hydroxybenzoate contains not less than 99.0 % and not more than 101.0 % of $C_{10}H_{12}O_3$, calculated with reference to the dried substance.

Identity tests

A. See the test below under "Melting range".

B. To 0.5 g add 5 ml of sodium hydroxide (~80 g/l)TS and heat in a water-bath for 5 minutes. After cooling, add 6 ml of sulfuric acid (~190 g/l)TS, collect the precipitate on a filter, wash thoroughly with a small amount of water and dry over silica gel, desiccant, R. Melting temperature, about 214 °C.

Melting range. 96-99 °C.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry at 80 °C under reduced pressure (not exceeding 0.6 kPa or about 5 mm of mercury) for 2 hours; it loses not more than 5.0 mg/g.

Acidity. Dissolve 0.2 g in 5 ml of ethanol (~750 g/l)TS, add 5 ml of carbon-dioxide-free water R and titrate with sodium hydroxide (0.1 mol/l)VS, using 0.1 ml of bromocresol green/ethanol TS as indicator; not more than 0.1 ml is required to obtain the midpoint of the indicator (green).

Assay. Place about 80 mg, accurately weighed, in a ground-glass-stoppered flask, add 25 ml of sodium hydroxide (~80 g/l)TS and boil gently under a reflux condenser for 30 minutes. Allow to cool, add 25.0 ml of potassium bromate (0.0333 mol/l)VS, 5.0 ml of potassium bromide (125 g/l)TS and 40 ml of glacial acetic acid R. Cool in ice-water and add 10 ml of hydrochloric acid (~420 g/l)TS. Stopper the flask immediately and allow to stand for 15 minutes. Add 30 ml of potassium iodide (80 g/l)TS, close the flask and mix. Titrate with sodium thiosulfate (0.1 mol/l)VS, using 2 ml of starch TS as indicator, added towards the end of the titration. Repeat the operation without the substance being examined and make any necessary corrections. The volume of potassium bromate (0.0333 mol/l)VS used is equivalent to half the volume for the titration. Each ml of potassium bromate (0.0333 mol/l)VS is equivalent to 6.007 mg of $C_{10}H_{12}O_3$.

REAGENTSAcetate buffer, pH 6.0, TS.

Procedure. Dissolve 100 g of ammonium acetate R in 300 ml of water. Add 4.1 ml of glacial acetic acid R and adjust the pH to 6.0 using either ammonia (~260 g/l)TS or acetic acid (~300 g/l)TS, and dilute with sufficient water to produce 500 ml.

Ammonium thiocyanate (0.05 mol/l)VS. Ammonium thiocyanate R, dissolved in water to contain 3.806 g of NH_4SCN in 1000 ml.

Method of standardization. Ascertain the exact concentration of the solution following the method described under ammonium thiocyanate (0.1 mol/l)VS.

Arachis oil R. Use arachis oil as described in the monograph, page 50.

Bromophenol blue TS.

Procedure. Dissolve 50 mg of bromophenol blue R with gentle heating in 3.73 ml of sodium hydroxide (0.02 mol/l)VS and dilute to 100 ml with water.

Calcium acetate (0.25 mol/l)VS. Calcium acetate R, dissolved in water to contain 44.04 g of $\text{Ca}(\text{C}_2\text{H}_3\text{O}_2)_2 \cdot \text{H}_2\text{O}$ in 1000 ml.

Calcium fluoride. CaF_2 .

Description. A white powder.

Solubility. Practically insoluble in water; slightly soluble in diluted acids.

Chromotropic acid TS.

Procedure. Dissolve 5 mg of chromotropic acid sodium salt R in 10 ml of a mixture of 9 ml of sulfuric acid (~1760 g/l)TS and 4 ml of water.

Chromotropic acid sodium salt R. $\text{C}_{10}\text{H}_6\text{Na}_2\text{O}_8\text{S}_2$ (SRIP, 1963, p. 69).

Citrate buffer, pH 4.0, TS.

Procedure. Dissolve 10.5 g of citric acid R in about 100 ml of water, add 100 ml of sodium hydroxide (1 mol/l)VS and dilute with sufficient water to produce 500 ml. Dilute 100 ml of hydrochloric acid (0.1 mol/l)VS with the solution prepared above to produce 250 ml.

Copper tetramine hydroxide TS.

Procedure. Dissolve 34.5 g of copper(II) sulfate R in 100 ml of water. Stir and add, drop by drop, ammonia (~260 g/l)TS until the precipitate formed has completely dissolved. Keep the temperature below 20 °C and add slowly, while stirring, 30 ml of sodium hydroxide (~400 g/l)TS. Filter the precipitate through a sintered glass filter (porosity 16 - 40 μm), wash with water until the filtrate is clear. Add 200 ml of ammonia (~260 g/l)TS to the precipitate, stir and filter.

Diisopropyl ether R. Isopropyl ether, $[(\text{CH}_3)_2\text{CH}]_2\text{O}$.

Description. A colourless liquid; odour, characteristic.

Boiling point. About 68 °C.

Note: It is highly flammable.

Fuchsin/sulfurous acid TS.

Procedure. Dissolve 0.10 g of fuchsin, basic R in 50 ml of water under gentle heating. To the cooled solution add 20 ml of sodium metabisulfite (50 g/l)TS and 1 ml of hydrochloric acid (~420 g/l)TS. Dilute to 100 ml with water, mix and allow to stand in the dark for 2 hours. The liquid should be colourless; it should not be used for more than 24 hours.

Hydroxylamine hydrochloride TS

Procedure. Dissolve 1 g of hydroxylamine hydrochloride R in 50 ml of water and add 50 ml of ethanol (~750 g/l)TS, 1 ml of bromophenol blue/ethanol TS and sodium hydroxide (0.1 mol/l)VS, until the solution becomes green.

Iron, reduced R. Fe (SRIP, 1963. p. 102).

Lead subacetate TS. Contains not less than 16.7 % (m/m) and not more than 17.4 % (m/m) of Pb in a form corresponding approximately to the formula $C_8H_{14}O_{10}Pb_3$.

Procedure. Dissolve 40.0 g of lead acetate R in 90 ml of carbon-dioxide free water R. Adjust the pH to 7.5 with sodium hydroxide (~400 g/l)TS. Centrifuge and use the clear supernatant solution.

Storage. Lead subacetate TS should be stored in a well-closed container.

Mercuric iodide R. HgI_2 .

Description. A heavy, crystalline scarlat-red powder; odourless.

Solubility. Slightly soluble in water and chloroform R; sparingly soluble in ethanol (~750 g/l)TS, acetone R and ether R; soluble in solutions containing an excess of potassium iodide R.

Storage. Mercuric iodide R should be stored protected from light.

Methylamine hydrochloride R. CH_5N, HCl .

Description. Deliquescent tetragonal tablets.

Solubility. Soluble in water and dehydrated ethanol R; practically insoluble in chloroform R, acetone R, ether R and ethyl acetate R.

Melting point. About 228 °C.

Methylamine hydrochloride (20 g/l)TS. A solution of methylamine hydrochloride R containing about 20 g of CH_5N, HCl per litre.

Methyl green R. 4-[[4-(Dimethylamino)phenyl][4-(dimethyliminio)cyclohexa-2,5-dien-1-ylidene]methyl}-NNN-trimethylbenzenaminium dichloride;

C.I. No. 42585; $C_{26}H_{33}Cl_2N_3$.

Description. A green powder.

Solubility. Soluble in water, soluble in sulfuric acid (~1760 g/l)TS giving a yellow solution and turning green on dilution.

Methyl green/iodomercurate paper R.

Procedure. Immerse strips of suitable filter paper in a solution of 4 g of methyl green R in 100 ml of water and allow to dry in air. Then dip the strips for 1 hour into a mixture composed of 14 g of potassium iodide R and 20 g of mercuric iodide R in 100 ml of water. Wash the strips with water until the washings are practically colourless and allow to dry in air.

Storage. Methyl green/iodomercurate paper R should be stored protected from light.

Morpholine R. Tetrahydro-1,4-oxazine. C_4H_9NO (SRIP, 1963, p. 121).

1,3-Naphthalenediol R. Naphthoresorcinol, $C_{10}H_8O_2$.

Description. Colourless crystals.

Solubility. Freely soluble in water, ethanol (~750 g/l)TS and ether R.

Melting temperature. About 124 °C.

Periodic acetic acid TS.

Procedure. Dissolve 0.446 g of sodium metaperiodate R in 2.5 ml of sulfuric acid (~570 g/l)TS and dilute to 100 ml with glacial acetic acid R.

Phloroglucinol R. Benzene 1,3,5-triol, $C_6H_3(OH)_3 \cdot 2H_2O$.

Description. White or pale cream coloured crystals.

Melting point. About 220 °C.

Phosphate buffer, pH 4.0, TS.

Procedure. Dissolve 5.04 g of disodium hydrogen phosphate R and 3.01 g of potassium dihydrogen phosphate R in sufficient water to produce 1000 ml and adjust the pH to 4.0 with glacial acetic acid R.

Phosphomolybdic acid/ethanol TS.

Procedure. Dissolve 5 g of phosphomolybdic acid R in sufficient dehydrated ethanol R to produce 100 ml.

Phthalate buffer, pH 4.0, TS.

Procedure. Dissolve 2.042 g of potassium hydrogen phthalate R in 50 ml of water, add 0.40 ml of sodium hydroxide (0.2 mol/l)VS, and dilute with sufficient water to produce 200 ml.

Piperazine hydrate R. $C_4H_{10}N_2 \cdot 6H_2O$.

Description. Colourless glossy, deliquescent crystals.

Melting point. 44 °C.

Potassium bisulfate R. $KHSO_4$ (SRIP, 1963, p. 146).

Potassium bromate (0.0333 mol/l)VS. Potassium bromate R, dissolved in water to contain 5.562 g of $KBrO_3$ in 1000 ml.

Potassium bromide (125 g/l)TS. A solution of potassium bromide R containing about 125 g of KBr per litre.

Potassium permanganate (0.0002 mol/l)VS. Potassium permanganate R, dissolved in water to contain 31.61 mg of $KMnO_4$ in 1000 ml.

Method of standardization. Ascertain the exact concentration of the solution following the method described under potassium permanganate (0.02 mol/l)VS, volume 1, p. 201.

Potassium sulfate (0.1 g/l)TS. A solution of potassium sulfate R containing about 0.1 g of K_2SO_4 per litre.

Sodium lauril sulfate R.

Composition. A mixture of sodium alkyl sulfates, consisting mainly of sodium dodecyl sulfates, $C_{12}H_{25}NaO_4S$.

Description. A white or pale yellow powder, crystals or flakes; odour, faint, but characteristic.

Solubility. Very soluble in water giving an opalescent solution; partly soluble in ethanol (~750 g/l)TS.

Sodium lauril sulfate (10 g/l)TS. A solution of sodium lauril sulfate R containing about 10 g of $C_{12}H_{25}NaO_4S$ per litre.

Sodium metabisulfite (50 g/l)TS. A solution of sodium metabisulfite R containing about 50 g of $Na_2O_5S_2$ per litre.

Sodium metaperiodate TS.

Procedure. Dissolve 60 g of sodium metaperiodate R in sufficient water containing 120 ml of sulfuric acid (0.05 mol/l)VS and dilute to 1000 ml with water. Do not heat to dissolve the periodate. If the solution is not clear, filter through a sintered-glass filter. Store the solution in a glass-stoppered, light-resistant container.

Suitability test. Pipette 10 ml into a 250-ml volumetric flask, dilute to volume with water and mix. To about 550 mg of glycerol to be tested dissolved in 50 ml of water add, using a pipette, 50 ml of the sodium metaperiodate TS. For a blank, transfer 50 ml of the sodium metaperiodate TS to a flask containing 50 ml of water. Allow the solutions to stand for 30 minutes, then to each add 5 ml of hydrochloric acid (~420 g/l)TS and 10 ml of potassium iodide (80 g/l)TS, and swirl to dissolve. Allow to stand for 5 minutes, add 100 ml of water and titrate with sodium thiosulfate (0.1 mol/l)VS, shaking continuously and adding 3 ml of starch TS as the endpoint is approached. The ratio of the volume of sodium thiosulfate (0.1 mol/l)VS between the two titrations should be from 0.750 to 0.765.

Sulfuric acid (~1125 g/l)TS. Sulfuric acid (~1760 g/l)TS, diluted with water to contain about 1125 g of H₂SO₄ per litre; $d \sim 1.61$.

Testosterone propionate R. C₂₂H₃₂O₃. Use testosterone propionate as described in the monograph in volume 2, p.263.

Testosterone propionate/ethanol TS.

Procedure. Dissolve 10 mg of testosterone propionate R in sufficient ethanol (~750 g/l)TS to produce 10 ml.

Thioacetamide, R. C₂H₅NS.

Note: Thioacetamide R is toxic.

Description. Colourless crystals or a white, crystalline powder; odour, faint of hydrogen sulfide.

Solubility. Freely soluble in water and ethanol (~750 g/l)TS.

Melting point. About 113 °C.

Thioacetamide, alkaline, TS.

Procedure. Dissolve 0.4g of thioacetamide R in 10 ml of water. Immediately before use add 0.2 ml of this solution to 1 ml of a mixture of 15 ml of sodium hydroxide (1 mol/l)VS, 5 ml of water and 20 ml of glycerol R. Heat on a water-bath for 20 seconds.

Triketohydrindene/sodium metabisulfite TS.

Procedure. Dissolve 3 g of triketohydrindene hydrate R in 100 ml of a solution composed of 4.55 g of sodium metabisulfite R in 100 ml of water.

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