EUROPEAN PHARMACOPOEIA

SUPPLEMENT TO VOLUME III 1977

COUNCIL OF EUROPE

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Published under the direction of the

COUNCIL OF EUROPE (PARTIAL AGREEMENT)

in accordance with the Convention on the Elaboration of a European Pharmacopoeia

(European Treaty Series No. 50)

Printed and published by
MAISONNEUVE S.A.
57 - Sainte-Ruffine - France
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The present Supplement contains certain amendments to Volumes I, II and III of the European Pharmacopoeia (English edition) and additions to Volume III. It has the same official status as the volumes already published.

CONTENTS

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AMENDMENTS TO VOLUME I

REAGENTS

Page 131. — Insert after the reagent " Aluminium potassium sulphate ":

" **Aminohippuric acid** — $C_9H_{10}N_2O_3$ (MW 194·2), 4-Aminohippuric acid.

A white or almost white powder, sparingly soluble in water, soluble in alcohol, very slightly soluble in chloroform and in ether.

mp: 206° to 209°.

Aminohippuric acid reagent Dissolve 3 g of phthalic acid R and 0·3 g of aminohippuric acid R in alcohol R and dilute to 100 ml with the same solvent. "

Page 137. — Insert after the reagent " Antimony trichloride solution ":

" **Arabinose** — $C_5H_{10}O_5$ (MW 150·1). L-(+)-Arabinose.

A white, crystalline powder, freely soluble in water.

$[\alpha]_D^{20}$: + 103° to + 105°, determined on a 5·0 per cent w/v solution. "

Page 137. — Insert after the reagent " Atropine sulphate ":

" **Barium carbonate** — $BaCO_3$ (MW 197·3).

A white powder or friable masses, practically insoluble in water. "

Page 142. — Insert after the reagent " Calcein mixed triturate ":

" **Calcium carbonate**

Complies with the requirements prescribed in the monograph on Calcii carbonas (Vol. I, page 269). "

Page 149. — **Cresol red solution**

Test for sensitivity. Replace the last sentence by " Not more than 0·15 ml of 0·02N hydrochloric acid is required to change the colour to yellow. "

Replace the colour change by:

" Colour change: pH 7·0 (yellow) to pH 8·6 (red). "

Page 151. — **Diethylphenylenediamine sulphate**

Replace the molecular formula and weight by:

" $C_{10}H_{18}N_2O_4S$ (MW 262·3) ".

Replace the last line by:
" It melts at about 185° (Vol. I, page 73), with decomposition. "

Page 153. — **Dimethyl yellow**

Thin-layer chromatography. Replace the text by the following:

" On a layer of silicagel G R apply 10 µl of a 0·01 per cent w/v solution in methylene chloride R and develop with the same solvent. The chromatogram shows only one spot ".

Page 159. — Insert after the reagent " Fuchsin, decolourised solution ":

" **Galactose** — $C_6H_{12}O_6$ (MW 180·2). D-(+)-Galactose.

A white, crystalline powder, freely soluble in water.

$[\alpha]_D^{20}$: + 79° to + 81°, determined on a 10·0 per cent w/v solution. "

Page 161. — **Holmium perchlorate solution**

Replace " 1·4N perchloric acid " by:

" a solution of perchloric acid R containing 14·1 per cent w/v of $HClO_4$. "

Page 162. — **Hydrochloric acid R1**

In the first line delete " (about 7M) ".

Page 164. — **Indophenol blue**

Thin-layer chromatography. Replace the text by the following:

" On a layer of silicagel G R apply 10 µl of a 0·01 per cent w/v solution in methylene chloride R and develop with the same solvent. The chromatogram shows only one spot. A stain may, however, remain at the starting point. "

Page 164. — Insert after the reagent " **Iodine** ".

" **Iodine 0·000 2N** Dilute 2·0 ml of **0·01N iodine** to 100·0 ml with water.

Prepare immediately before use. "

Page 167. — **Lead acetate cotton**

Replace the first sentence by:

" Immerse absorbent cotton in a mixture of 10 volumes of lead acetate solution R and 1 volume of dilute acetic acid R. "

Page 167. — **Lead acetate paper**

Replace the first sentence by:

" Immerse white filter paper weighing about 80 g per m^2 in a mixture of 10 volumes of lead acetate solution R and 1 volume of dilute acetic acid R. "

Page 167. — **Lead subacetate solution**

Replace the text by the following:

" Dissolve 40·0 g of lead acetate R in 90 ml of carbon dioxide-free water R. Adjust the pH to 7·5 (Vol. I, page 63) with strong sodium hydroxide solution R. Centrifuge and use the clear, supernatant solution. The solution remains clear when stored in a well-closed container. "

Page 170. — **Mercuric nitrate solution**

Change the title to: " Nitric acid solution of mercury ".

Replace the last sentence by:

" The reagent may be stored for not more than 2 months, protected from light ".

Page 172. — **Methylene blue**

Replace the text by the following:

" **Methylene blue** — $C_{16}H_{18}ClN_3S$ (MW 319·9). Tetramethylthionine chloride. Colour Index No. 52 015; Schultz No. 1 038.

A dark green or bronze, crystalline powder, freely soluble in water, soluble in alcohol. It occurs in different hydrated forms and may contain up to 22 per cent of water. "

Page 178. — **Osmium tetroxide**

Add at the end of the text:

" *Caution. The fumes are corrosive to the eyes, the mucous membranes and the skin* ".

Page 184. — **Potassium hydroxide, alcoholic solution**

Add at the end of the text:

" Prepare immediately before use. "

Page 184. — **Potassium hydroxide, alcoholic solution, free from carbonate**

Add at the end of the text:

" Prepare immediately before use. "

Page 188. — Insert after the reagent " Resorcinol ":

" **Rhamnose** — $C_6H_{12}O_5, H_2O$ (MW 182·2). L-(+)-Rhamnose.

A white, crystalline powder, freely soluble in water, $[\alpha]_D^{20}$: + 7·8° to + 8·3°, determined on a 5·0 per cent, w/v solution. "

Page 199. — **Sudan red G**

Thin-layer chromatography. Replace the text by the following:

" On a layer of silicagel G R apply 10 µl of a 0·01 per cent w/v solution in methylene chloride R and develop with the same solvent. The chromatogram shows only one spot. "

STANDARD SOLUTIONS FOR LIMIT TESTS

Page 209. — **Arsenic standard solution (10 ppm As)**

Replace the text by the following:

" Dilute to 100 times its volume with water a solution prepared by dissolving a quantity of arsenious anhydride R equivalent to 1·320 g of As_2O_3 in 20 ml of dilute sodium hydroxide solution R and diluting to 1 000·0 ml with water. "

BUFFER SOLUTIONS

Page 212. — **Buffer solution pH 3·5**

Replace the text by the following:

" Dissolve 5·0 g of ammonium acetate R in 5 ml of water and add 7·6 ml of hydrochloric acid R1. Check the pH (Vol. I, page 63) and adjust, if necessary, with dilute hydrochloric acid R or dilute ammonia R1. Dilute to 20·0 ml with water. "

MONOGRAPHS

ACACIAE GUMMI

Page 234. — IDENTIFICATION REACTIONS. Add the following:

" F. Examine by thin-layer chromatography (Vol. I, page 88), using kieselguhr G R as the coating substance. Use a 1·6 per cent w/v solution of sodium dihydrogen phosphate R instead of water for preparing the slurry.

Test solution Heat 1 g of powdered drug under a reflux condenser for 90 minutes on a water bath with 25 ml of a 4 per cent w/v solution of sulphuric acid R. Neutralise 10 ml of the solution with about 2 g of barium carbonate R, shaking for about 90 minutes, and filter. Dilute 1 ml of the filtrate with 9 ml of methanol R and centrifuge.

Reference solution Dissolve 10 mg of galactose R, 10 mg of dextrose R, 10 mg of arabinose R and 10 mg of rhamnose R in 1 ml of water and dilute to 10 ml with methanol R.

Apply separately 5 µl of each solution in bands 15 mm long and not more than 3 mm wide. Develop over a path of 10 cm using a mixture of 40 volumes of *n*-butanol R, 50 volumes of acetone R and 10 volumes of a 1·6 per cent w/v solution of sodium dihydrogen phosphate R. Dry the plate for a few minutes in a current of warm air and again develop with the same mobile phase over a path of 15 cm. Dry the plate for 10 minutes in an oven at 110°, spray with aminohippuric acid reagent R and again heat for 10 minutes at 110°. The chromatogram obtained with the reference solution shows four clearly separated, coloured zones, of galactose (yellowish-brown), dextrose (yellowish-brown), arabinose (reddish-brown) and rhamnose (yellow) in order of increasing Rf values.

The chromatogram obtained with the test solution shows three zones corresponding to galactose, arabinose and rhamnose. The zone corresponding to dextrose is absent. No other zones are visible, particularly in the upper part of the chromatogram. "

CALCII AMINOSALICYLAS

Page 266. — Delete the monograph.

Page 297. — Replace the monograph HYDROGENII PEROXIDUM by the two following monographs:

HYDROGENII PEROXIDUM 30 PER CENTUM

Hydrogen Peroxide Solution (30 per cent)

Hydrogen peroxide solution (30 per cent) contains not less than 29·0 per cent w/w and not more than 31·0 per cent w/w of H_2O_2 (MW 34·02). A suitable preservative may be added.

CHARACTERS

A colourless, almost odourless liquid.

IDENTIFICATION

A. Cautiously make the solution alkaline. It decomposes with vigorous effervescence.

B. Mix 1 drop with 2 ml of dilute sulphuric acid R, 2 ml of ether R, and 1 drop of potassium chromate solution R and shake. The ether layer is coloured deep blue.

TESTS

Acidity Dilute 10 ml with 100 ml of water and add 5 drops of methyl red solution R. Not less than 0·05 ml and not more than 0·5 ml of 0·1N sodium hydroxide is required to change the colour of the solution.

Organic preservatives Shake 20 ml with 10 ml of chloroform R and then with two quantities, each of 5 ml, of chloroform R. Evaporate the combined chloroform extracts under reduced pressure at a temperature below 25°, and dry in a desiccator. Any residue weighs not more than 10 mg.

Non-volatile substances Allow 25 ml to decompose in a platinum dish, cooling if necessary. Evaporate the decomposed solution on a water bath and dry in an oven at 100° to 105°. Any residue weighs not more than 50 mg.

ASSAY

Dilute about 1·00 g, accurately weighed, to 100·0 ml with water. To 10·0 ml of this solution, add a cold mixture of 2·5 ml of sulphuric acid R and 20 ml of water. Titrate with 0·1N potassium permanganate.

1 ml of 0·1N potassium permanganate is equivalent to 1·701 mg of H_2O_2.

STORAGE

Store protected from light; if the solution does not contain a stabiliser, store at a temperature below 15°.

LABELLING

If the solution contains a stabiliser, the label states that it is stabilised.

CAUTION

Hydrogen peroxide solution (30 per cent) decomposes vigorously in contact with oxidisable organic matter and with certain metals and if allowed to become alkaline.

HYDROGENII PEROXIDUM 27 PER CENTUM

Hydrogen Peroxide Solution (27 per cent)

Hydrogen peroxide solution (27 per cent) contains not less than 26·0 per cent w/w and not more than 28·0 per cent w/w of H_2O_2 (MW 34·02). A suitable preservative may be added.

CHARACTERS

A colourless, almost odourless liquid.

IDENTIFICATION

It complies with the identification tests given in the monograph on Hydrogenii Peroxidum 30 Per Centum (Suppl. to Vol. III, page 10).

TESTS

It complies with the tests given in the monograph on Hydrogenii Peroxidum 30 Per Centum (Suppl. to Vol. III, page 10).

ASSAY

Carry out the assay prescribed in the monograph on Hydrogenii Peroxidum 30 Per Centum (Suppl. to Vol. III, page 11).

1 ml of 0·1N potassium permanganate is equivalent to 1·701 mg of H_2O_2.

STORAGE

Store protected from light; if the solution does not contain a stabiliser, store at a temperature below 15°.

LABELLING

If the solution contains a stabiliser, the label states that it is stabilised.

CAUTION

See the monograph on Hydrogenii Peroxidum 30 Per Centum (Suppl. to Vol. III, page 11).

HYDROGENII PEROXIDUM DILUTUM

Page 299. — TESTS. **Barium** Delete the test.

STORAGE. Replace the text by the following:

" Store protected from light; if the solution does not contain a stabiliser, store at a temperature below 15°. It should not be stored for long periods. "