Pharmaceutical literature, pharmacopoeias

Pharmaceutical Propaedeutics

Institute of Pharmaceutical Technology and Biopharmacy

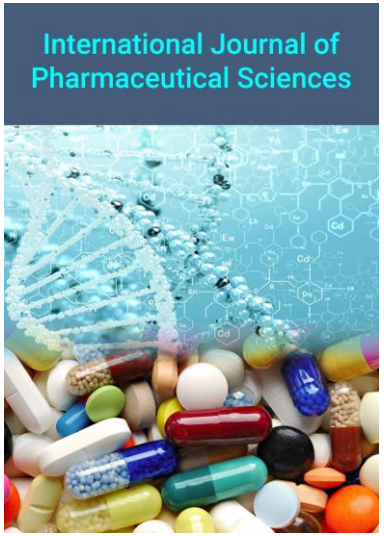
Pharmaceutical literatures

- ***Professional books***
  - encyclopedias
  - other books
  - journals

- ***Official books***
  - Pharmacopoeias
  - National Formularies
    - (Formulae Normales FoNo 7th Edition)

Journals


nature
FIVE HUBS OF ASIAN SCIENCE
Research and investment in Hong Kong, Malaysia, Singapore, South Korea and Taiwan
COMPLEX PROCESS
THE ROCKY ROAD TO MARS
CAUSE AND EFFECT


International Journal of Pharmaceutical Sciences


Oncogene
Epigenetic cancer therapy
nature publishing group


Science
AAAS
ILLUMINATING
THE BRAIN
Examining gene expression, development, and disease

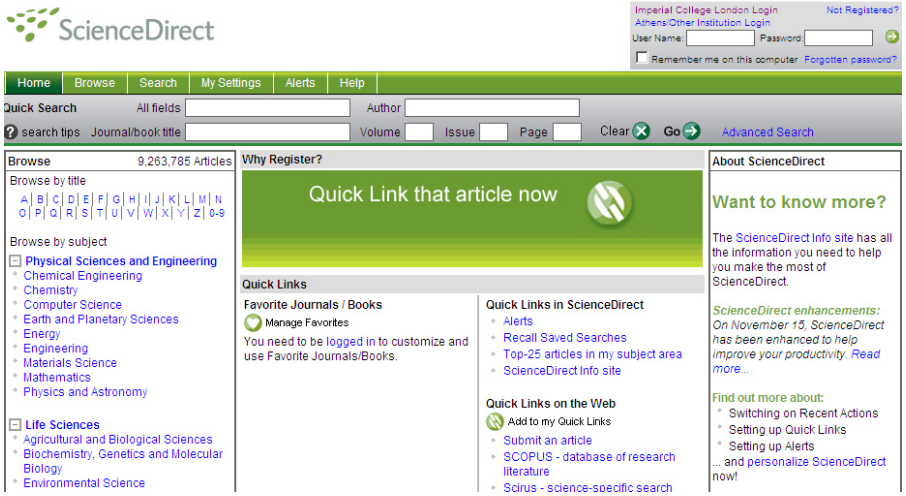
Literature in foreign languages

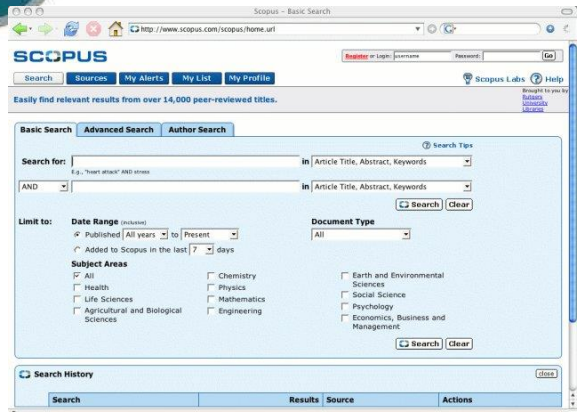
- Subscription: Pharmazeutische Industrie
  - scientific aspects are dominated

- Pharmaceutical Technology
  - marketing aspects are dominated
  - Free of charge, registered
- Science
- Nature

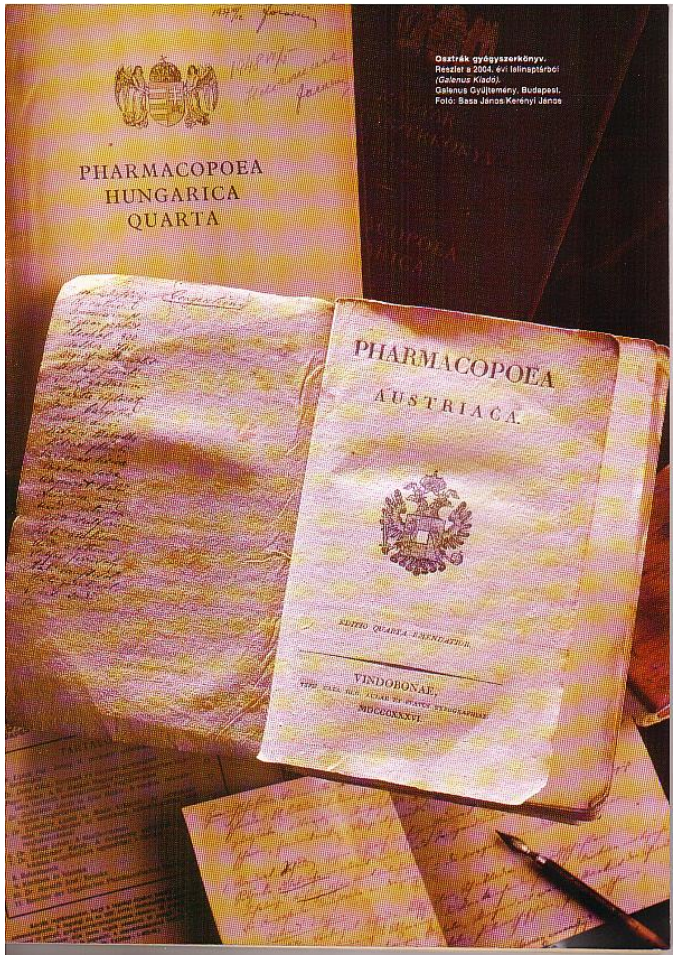
Searching journals

- Science Direct
- PubMed
- Scopus





Pharmacopoeias



Osztrák gyógyszerkönyv.
Részlet a 2004. évi lelinsplsrbci
(Galenus Kiadó).
Galenus Gyűjtemény, Budapest.
Fotó: Bass János.Kerényi János

Pharmacopoeia

- **Ebers papyrus** has been written around BC. 1600, which is found by a german Egyptologist, Georg Ebers in Théba in 1873.
- *Antidotarium Mesue* – Bagdad - XI. century
- *Antidoratium - Nicolaus prépos* in XII. century
- *Dynameron - Myrepsus Nicolaus prescription collection dealing with effects of medications* – in XIII. century

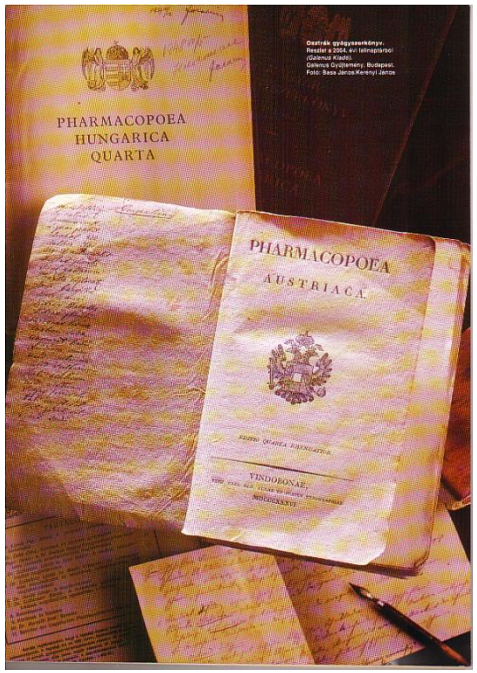
Antidotarium Nicolai

- Ancestor of our Pharmacopoeias has been created in about 1220-1250 in Salerno
- Pharmaceutics as an independent activity
- Written by medical teacher, who called himself to Nicolaus
- 142 is chosen from more than thousand ones
  - **leaflets are integrated,**
  - **compounds**
  - **their quantities are listed**.
- prescriptions are standardized – more systematic

Antecedent of Hungarian Pharmacopoeias

- **Aim of standardization and integration of pharmaceutical distribution**

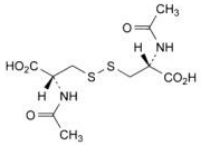
- **Hungarian Pharmacopoeias in the past**
  - ❖ **Dispensatorium Vienense**
  - ❖ **Pharmacopaea Austriaco-provincialis**
  - ❖ **Pharmacopaea Austraca**
  - ❖ **Taxa pharmaceutica Posoniensis**



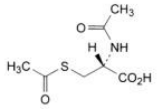
Most significant information of Hungarian Pharmacopoeia

	Year of publication	General editor	Number of monographs	Pages
I.	1871	Than Károly	510	581
II.	1888	Than Károly	516	716
III.	1909	Bókay Árpád	537	430
IV.	1934	Vámossy Zoltán	564	435
V.	1954	Schulek Elemér	819	1627
VI.	1967	Schulek Elemér, Végh Antal	815	1526
VII.	1986	Végh Antal	705	2206
VIII.	2004	Paál Tamás	>2000	> 4530

Monograph of acetylsalicylic acid



C. *N,N'*-diacetyl-L-cystine,

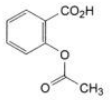


D. *N,S*-diacetyl-L-cysteine.

01/2005:0309

ACETYLSALICYLIC ACID

Acidum acetylsalicylicum



$C_9H_8O_4$ M_r 180.2

DEFINITION

Acetylsalicylic acid contains not less than 99.5 per cent and not more than the equivalent of 101.0 per cent of 2-(acetyloxy)benzoic acid, calculated with reference to the dried substance.

CHARACTERS

A white, crystalline powder or colourless crystals, slightly soluble in water, freely soluble in alcohol.

It melts at about 143 °C (instantaneous method).

IDENTIFICATION

First identification: A, B.

Second identification: B, C, D.

A. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *acetylsalicylic acid CRS*.

B. To 0.2 g add 4 ml of *dilute sodium hydroxide solution R* and boil for 3 min. Cool and add 5 ml of *dilute sulphuric acid R*. A crystalline precipitate is formed. Filter, wash the precipitate and dry at 100 °C to 105 °C. The melting point (*2.2.14*) is 156 °C to 161 °C.

C. In a test tube mix 0.1 g with 0.5 g of *calcium hydroxide R*. Heat the mixture and expose to the fumes produced a piece of filter paper impregnated with 0.05 ml of *nitrobenzaldehyde solution R*. A greenish-blue or greenish-yellow colour develops on the paper. Moisten the paper with *dilute hydrochloric acid R*. The colour becomes blue.

D. Dissolve with heating about 20 mg of the precipitate obtained in identification test B in 10 ml of *water R* and cool. The solution gives reaction (a) of salicylates (*2.3.1*).

TESTS

Appearance of solution. Dissolve 1.0 g in 9 ml of *alcohol R*. The solution is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Related substances. Examine by liquid chromatography (*2.2.29*). *Prepare the solutions immediately before use.*

Test solution. Dissolve 0.10 g of the substance to be examined in *acetonitrile for chromatography R* and dilute to 10.0 ml with the same solvent.

Reference solution (a). Dissolve 50.0 mg of *salicylic acid R* in the mobile phase and dilute to 50.0 ml with the mobile phase. Dilute 1.0 ml of this solution to 100.0 ml with the mobile phase.

Reference solution (b). Dissolve 10.0 mg of *salicylic acid R* in the mobile phase and dilute to 10.0 ml with the mobile phase. To 1.0 ml of this solution add 0.2 ml of the test solution and dilute to 100.0 ml with the mobile phase.

The chromatographic procedure may be carried out using:

– a stainless steel column 0.25 m long and 4.6 mm in internal diameter packed with *octadecylsilyl silica gel for chromatography R* (5 µm),

– as mobile phase at a flow rate of 1 ml/min a mixture of 2 volumes of *phosphoric acid R*, 400 volumes of *acetonitrile for chromatography R* and 600 volumes of *water R*,

– as detector a spectrophotometer set at 237 nm.

Inject 10 µl of each solution. Continue the chromatography of the test solution for seven times the retention time of acetylsalicylic acid. The test is not valid unless in the chromatogram obtained with reference solution (b), the resolution between the two principal peaks is at least 6.0.

In the chromatogram obtained with the test solution the area of any peak, apart from the principal peak, is not greater than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent); the sum of the areas of all the peaks is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.25 per cent). Disregard any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a).

Heavy metals (*2.4.8*). Dissolve 1.0 g in 12 ml of *acetone R* and dilute to 20 ml with *water R*. 12 ml of this solution complies with limit test B for heavy metals (20 ppm). Prepare the standard using lead standard solution (1 ppm Pb) obtained by diluting *lead standard solution (100 ppm Pb) R* with a mixture of 6 volumes of *water R* and 9 volumes of *acetone R*.

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.000 g by drying *in vacuo*.

Sulphated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

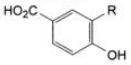
In a flask with a ground-glass stopper, dissolve 1.000 g in 10 ml of *alcohol R*. Add 50.0 ml of *0.5 M sodium hydroxide*. Close the flask and allow to stand for 1 h. Using 0.2 ml of *phenolphthalein solution R* as indicator, titrate with *0.5 M hydrochloric acid*. Carry out a blank titration.

1 ml of *0.5 M sodium hydroxide* is equivalent to 45.04 mg of $C_9H_8O_4$.

STORAGE

Store in an airtight container.

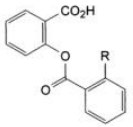
IMPURITIES



A. R = H: 4-hydroxybenzoic acid,

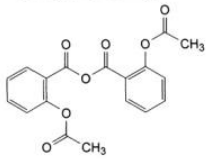
B. R = CO_2H: 4-hydroxybenzene-1,3-dicarboxylic acid (4-hydroxyisophthalic acid),

C. salicylic acid,



D. R = O-CO-CH_3: 2-[[2-(acetyloxy)benzoyl]oxy]benzoic acid (acetylsalicylsalicylic acid),

E. R = OH: 2-[(2-hydroxybenzoyl)oxy]benzoic acid (salicylsalicylic acid),

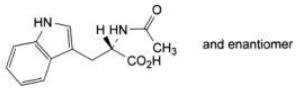


F. 2-(acetyloxy)benzoic anhydride (acetylsalicylic anhydride).

01/2005:1383

N-ACETYLTRYPTOPHAN

N-Acetyltryptophanum



and enantiomer

$C_{13}H_{14}N_2O_3$ M_r 246.3

DEFINITION

N-Acetyltryptophan contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of (*RS*)-2-acetylamino-3-(1*H*-indol-3-yl)propanoic acid, calculated with reference to the dried substance.

PRODUCTION

Tryptophan used for the production of *N*-acetyltryptophan complies with the test for 1,1'-ethylidenebistryptophan and other related substances in the monograph on *Tryptophan (1272)*.

CHARACTERS

A white or almost white, crystalline powder, or colourless crystals, slightly soluble in water, very soluble in alcohol. It dissolves in dilute solutions of alkali hydroxides.

It melts at about 205 °C.

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D, E.

A. It complies with the test for optical rotation (see Tests).

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *N-acetyltryptophan CRS*.

C. Examine by thin-layer chromatography (*2.2.27*), using a *TLC silica gel F_{254} plate R*.

Test solution. Dissolve 50 mg of the substance to be examined in 0.2 ml of *concentrated ammonia R* and dilute to 10 ml with *water R*.

Reference solution (a). Dissolve 50 mg of *N-acetyltryptophan CRS* in 0.2 ml of *concentrated ammonia R* and dilute to 10 ml with *water R*.

Reference solution (b). Dissolve 10 mg of *tryptophan R* in the test solution and dilute to 2 ml with the same solution.

Apply to the plate 2 µl of each solution. Develop over a path of 10 cm using a mixture of 25 volumes of *glacial acetic acid R*, 25 volumes of *water R* and 50 volumes of *butanol R*. Dry the plate in an oven at 100-105 °C for 15 min and examine in ultraviolet light at 254 nm. The principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a). The test is not valid unless the chromatogram obtained with reference solution (b) shows two clearly separated spots.

D. Dissolve about 2 mg in 2 ml of *water R*. Add 2 ml of *dimethylaminobenzaldehyde solution R6*. Heat on a water-bath. A blue or greenish-blue colour develops.

E. It gives the reaction of acetyl (*2.3.1*). Proceed as described for substances hydrolysable only with difficulty.

TESTS

Appearance of solution. Dissolve 1.0 g in a 40 g/l solution of *sodium hydroxide R* and dilute to 100 ml with the same alkaline solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution Y_7 or GY_7 (*2.2.2, Method II*).

Optical rotation (*2.2.7*). Dissolve 2.50 g in a 40 g/l solution of *sodium hydroxide R* and dilute to 25.0 ml with the same alkaline solution. The angle of optical rotation is − 0.1° to + 0.1°.

Related substances. Examine by liquid chromatography (*2.2.29*).

Buffer solution pH 2.3. Dissolve 3.90 g of *sodium dihydrogen phosphate R* in 1000 ml of *water R*. Add about 700 ml of a 2.9 g/l solution of *phosphoric acid R* and adjust the pH to 2.3 with the same acidic solution.

Prepare the solutions immediately before use.

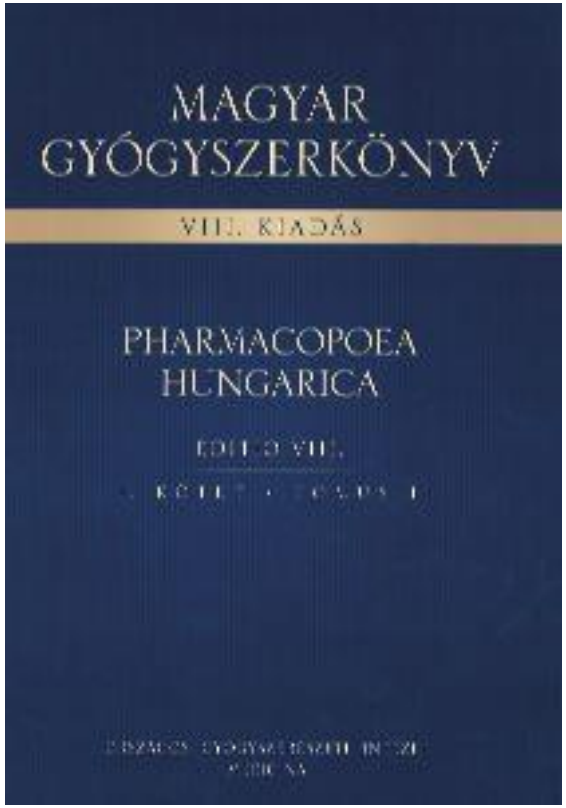
Test solution. Dissolve 0.10 g of the substance to be examined in a mixture of 50 volumes of *acetonitrile R* and 50 volumes of *water R* and dilute to 20.0 ml with the same mixture of solvents.

Reference solution (a). Dilute 1.0 ml of the test solution to 100.0 ml with a mixture of 10 volumes of *acetonitrile R* and 90 volumes of *water R*.

Reference solution (b). Dissolve 1.0 mg of *1,1'-ethylidenebis(tryptophan) CRS* in a mixture of 10 volumes of *acetonitrile R* and 90 volumes of *water R* and dilute to 100.0 ml with the same mixture of solvents.

Reference solution (c). To 4.0 ml of reference solution (a), add 20.0 ml of reference solution (b) and dilute to 100.0 ml with a mixture of 10 volumes of *acetonitrile R* and 90 volumes of *water R*.

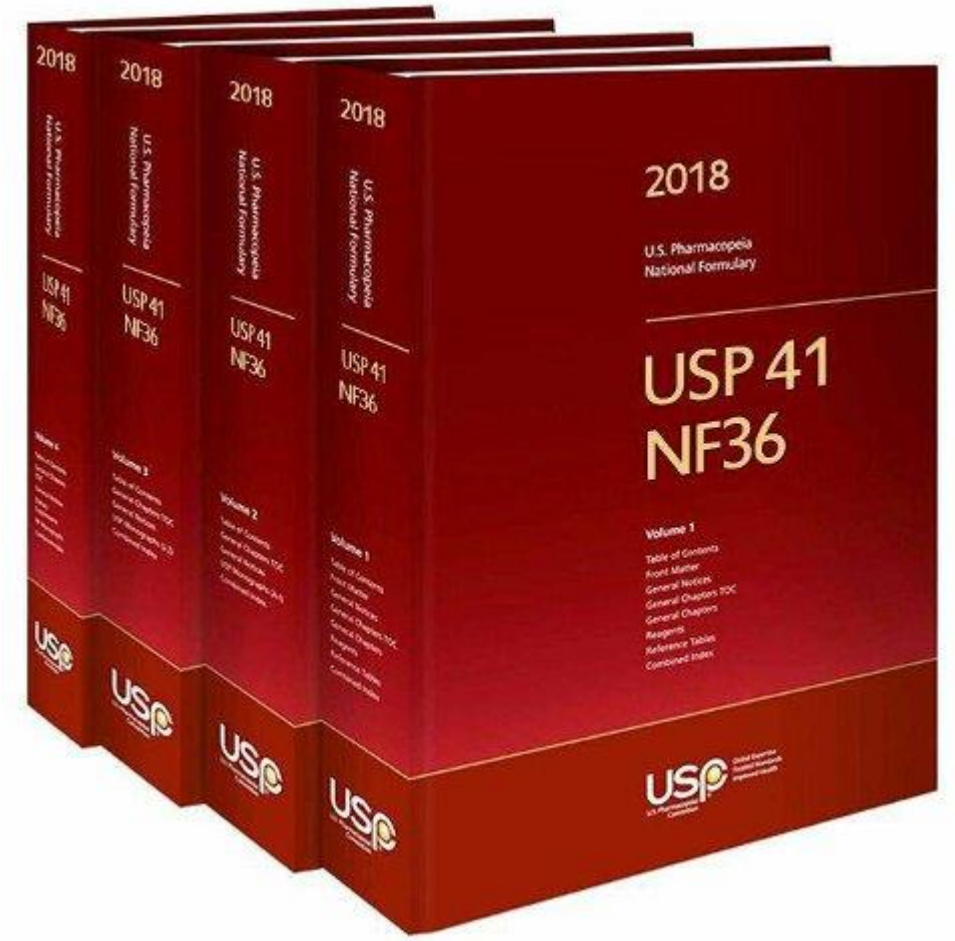
- ***Pharmacopoeias contain:***
  - Manufacture
  - Monograph description,
  - Examination, control,
  - Qualification of medicine
- ***Official publication*** regulated and modified by laws and regulations according to government
- Containing general rules related to quality and evaluations of medicines
- Valid, official publication for
  - manufacturers,
  - wholesalers,
  - physicians, pharmacists.



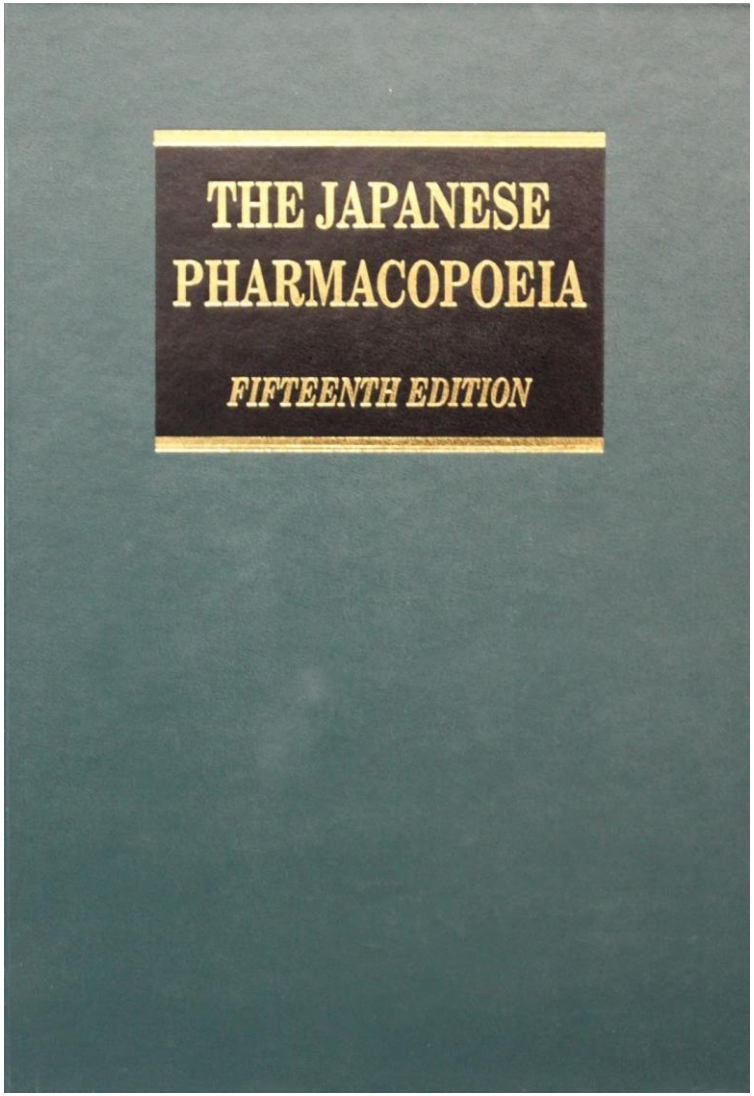
Contents of volumes

- **General information**
- **Monographs**
  - herbal,
  - animal drugs,
  - basic preparations
  - bandages,
  - vaccines
- **Examinations**
- **Charts, tables**

United States Pharmacopoeia (1820)



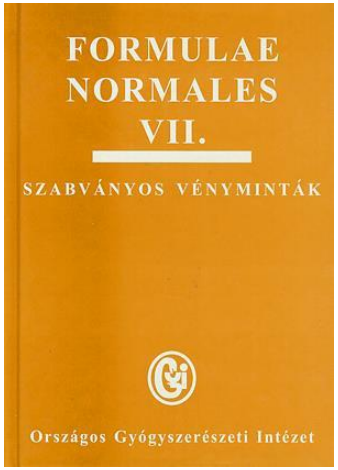
Japanese Pharmacopoeia (1886)



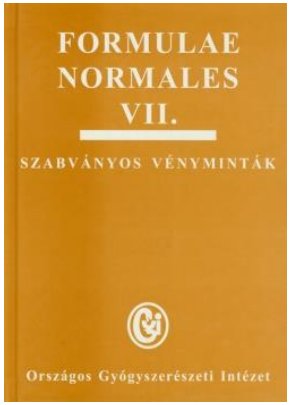
Formularies

- **Unofficial formularies:**
  - ❖ **Unknown pharmacy practitioners' notes**

- **Official formularies :**
  - ❖ **Formulae Normales (Hungary)**
    - **- physician's edition**
    - **- pharmacist's edition**



FoNo VII.



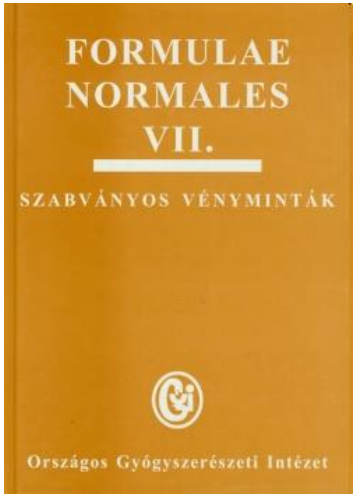
Formula(e) Normale(s)

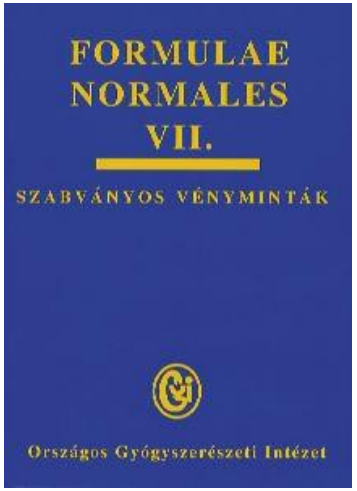
(translation: standard catalog of prescription samples)

- Prescription samples prescribed frequently (standard preparations)
- Can be prescribed according to their official name
- Standardized and unified in Hungary

Formulae Normales

- General rules of contemporaneous preparation, compounding





- ***Official publication*** regulated and modified by laws and regulations according to government

- Valid, official publication for
  - manufacturers,
  - wholesalers,
  - physicians, pharmacists.

Formulae Normales VII

Solutio sulfurata pro balneo

Rp.

Calcii oxydati

grammata triginta (g 30,0)

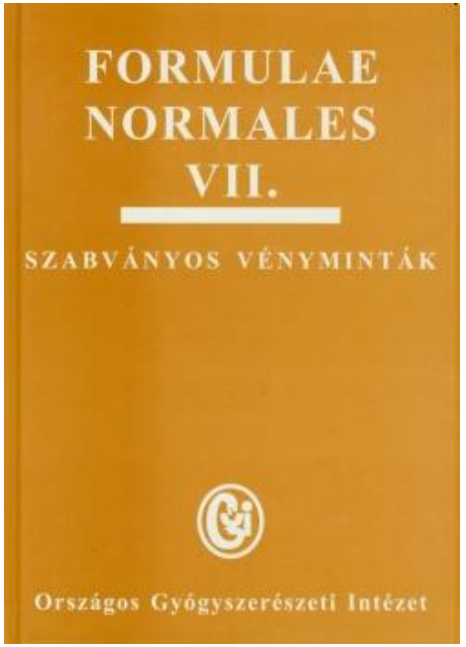
Sulfuris praecipitati

grammata sexaginta (g 60,0)

Aquae destillatae

ad grammata quingenti (ad g 500,0)

D.S.: 1 bottle (100g) for a bathtube water



This preparation was official in FoNo VI. edition, before FoNo VI, it was included in Pharmacopoeia called as Solutio calcii sulfurati.

FoNo VII.

- ***Content of pharmacist's edition:***
  - ***General knowledge***
  - ***Technological direction*** for preparation process of medication of standard catalog (description of general preparation of dosage forms and tools/ equipment)

    Preparation guideline in the case of incompatibility
  - ***Prescription samples***
  - ***Basic preparations (bases)***
  - ***Application modes*** of pharmaceutical forms
  - ***Synonim names*** of basic materials (names are according to European Pharmacopoeia)

Dosage forms from Pharmacopoeias

	I	II	III	IV	V	VI	VII	VIII
Diluendum (aromatic water)	+	+	+	+	+	+		
emulsion	+	+	+	+	+	+	+	*
pharmaceutical wines	+	+	+	+	+			
paints	+	+	+					
decocts and infusions	+	+	+	+	+	+	+	
tinctures	+	+	+	+	+	+	+	+

Dosage forms from Pharmacopoeias

	I	II	III	IV	V	VI	VII	VIII
extractions	+	+	+	+	+	+	*	*
solutions	+	+	+	+	+	+	+	+
eye drops					+	+	+	+
eye wash liquids					+	+	+	*
syrups	+	+	+	+	+	+	+	*
suspensions			+	+	+	+	+	*

Dosage forms from Pharmacopoeias

	I	II	III	IV	V	VI	VII	VIII
gels							+	+
poultice								+
ointments	+	+	+	+	+	+	+	+
pastes							+	+
sampons								+
caoutchouc patches			+	+	+	+		

Dosage forms from Pharmacopoeias

	I	II	III	IV	V	VI	VII	VIII
granules						+	+	+
capsules			+	+	+	+	+	+
pastilles			+					+
powders			+	+	+	+	+	+
tablets			+	+	+	+	+	+
pilules	+	+	+	+	+	+	+	Ø

THANK YOU FOR ATTENTION !!!