

Medicinal Plants in the European Pharmacopoeia: Current Changes

PKZ Conference

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The European Pharmacopoeia (Ph.Eur.)

- Basis: Convention of the Elaboration of a European Pharmacopoeia (1964)
- Council of Europe
- European Directorate for the Quality of Medicines and Healthcare (EDQM), Strasbourg
- Ph.Eur. Commission and expert groups, e.g. 13A, 13B for phytochemistry



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Procedure for Preparation of Monographs

Ph.Eur. Work Programme*)

- Addition of new projects e.g. Cannabis liquid extract
- Revision of text and monographs, e.g. fennel
- Participation through EDQM HelpDesk



*) Source: EDQM Homepage, Ph.Eur.. Work Programme



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Procedure for Preparation of Monographs

- Preparation of a draft/ revision e.g., in Expert Groups 13 A/13 B by order of the Ph.Eur. Commission
- Consideration of the real conditions (origins, value-determining constituents)
- Development and review of analytical methods (e.g., by proficiency tests)
- Publication of a draft in PHARMEUROPA and consultation period
- Discussion of comments received in the expert group
- Adoption by the Ph.Eur. Commission
- Publication

Procedure for Preparation of Monographs

Ph.Eur.: where are we?

- 175th session of the Commission
March 2023 → Supplement 11.4
- 176th session of the Commission
June 2023 → Supplement 11.5
- 177th session of the Commission
November 2023 → Supplement 11.6
- 178th session of the Commission
March 2024 → Supplement 11.7

Published Monographs

175th Session of the Commission March 2023 → Supplement 11.4 published 1 October 2023 → implemented 1 April 2024

New Monographs

- Gumweed herb (*Grindeliae herba*): assay titration of diterpenic acids
- Rose flower (*Rosa gallica*, *R. x centifolia*, *R. x damascena*; tannin determination)

Revisions

- Green tea (*Camellia sinensis*): reagent fast blue salt B replaced by anisaldehyde; HPTLC
- Ribwort plantain (*Plantago lanceolata*) test for *Digitalis lanata* optimised; HPTLC introduced
- Shepherd's purse (*Capsella bursa-pastoris*, assay diosmin)

Published Monographs

176th Session of the Commission June 2023 → Supplement 11.5 published 1 January 2024 → implemented 1 July 2024

New Monographs

- Cannabis flower
- Cannabidiol
- *Rhodiola rosea*: min. 0.1% salidroside, min. 0.5% total rosavins (assay HPLC)
- Green bean pods (*Phaseoli fructus sine semine*): min. 0.06% of total flavonoids expressed as hyperoside

Revisions

- *Centaurii herba*: synonyms changed, illustration powdered herbal drug

Published Monographs

177. Session of the Commission November 2023 → Supplement 11.6 to be published 1 July 2024 → implemented 1 January 2025

New Monographs

- Sesame seed (*Sesamum indicum* syn. *S. officinale*)
- Hedge mustard (*Sisymbrium officinalis* herba)

Revisions

- Black cohosh (*Cimicifuga rhizoma*): Identification, especially differentiation adulteration / substitution
- Meadowsweet (*Filipendulae ulmariae* herba): Identification HPTLC, solvent without hexane
- Valerian dry aqueous extract / Valerian dry hydroalcoholic extract / Valerian root / Valerian root, cut / Valerian tincture: HPTLC, assay solvent adapted to Technical Guide

Published Monographs

178. Session of the Commission March 2024 → Supplement 11.7 to be published 1 October 2024 → implemented 1 April 2025:

New Monographs

- Eschscholtzia californica
- Cypress oil
- Grapevine leaf
- Walnut leaf
- Australian dodder seed
- Phyllanthus emblica fruit

Revisions

- Hop strobile
- Platycodon root
- Quillaia bark

Draft Monographs for Comment

Pharmeuropa

- Publication of draft monograph and further information
- Online and free of charge
- Access via EDQM website

Draft Monographs for Comment Pharmeuropa 36.1

- Liquorice root for flavouring purposes: HPLC column and flow rate modified
- Liquorice root: HPLC column and flow rate modified; illustration powdered herbal drug
- Cloves (*Caryophylli flos*): HPTLC introduced for identification
- Clove oil: HPTLC introduced for identification; chromatographic profile
- *Salviae sclareae aetheroleum*: chromatographic profile
- NEW: Cedar oil (*Cedrus atlantica*, *C. deodara*)
- **Comments invited by 31 March 2024**



Draft Monographs for Comment Pharmeuropa 36.2

- NEW: Myrti aetheroleum (*Myrtus communis* L.)

Calendula for homoeopathic preparations und Chamomilla for homoeopathic preparations

- Pilot study for the establishment of the HPTLC method for semi-quantitative determination (in case plants with non-toxic constituents; background: different traditions German HAB – Ph. Française)
- Comparison of the intensities of the spots of the test and reference solution (visually or using software)
- Same method as identification
- Arnica planta tota follows

Comments invited by 30 June 2024

Draft Monographs for Comment Pharmeuropa 36.3

- Psyllium seed (*Plantago afra*, *Plantago indica*):
Introduction of HPTLC for identification and differentiation from Ispaghula seed and husk (*Plantago ovata*)
- NEW Ribwort plantain liquid extract (*Plantago lanceolata*):
minimum 1.2 % of total *ortho*-diphenolic compounds expressed as acteoside; identification HPTLC; assay photometry
- ...

Comments invited by 30 September 2024

Industry's Requests for Revision: Examples

- BAH Proposal for General Monograph „Essential Oils“ (January 2022): Reference to „any relevant monograph“ may lead to misinterpretation, therefore : „...herbal drugs used for the production of essential oils may be substantially different from the definition of the respective herbal drug monograph“. Current state of discussion: Reference only in case applicable, clarification in Information Chapter on Essential Oils
- Bitter Fennel Oil/Anise Oil: Determination method for estragole planned by EDQM (in the context of a general discussion on the determination of toxic constituents in essential oils); TIMEFRAME?
- Sage leaf, cut: Proposal BAH June 2019 to lower the minimum content of essential oil to 8 mL/kg): *still under discussion (probably separate monograph for cut herbal drug)*

Specific Case: Bitter Fennel

- BAH Proposal 2023 to reduce the essential oil content in fennel fruit
- Reasons: stability of the essential oil in the cut herbal drug AND reduction of the estragole content
- Amendment to bitter fennel whole: Reduction of the essential oil content from at least 40 mL/kg to at least 30 mL/kg and reduction of the estragol content from 5% to max. 3.5%
- Application for bitter fennel, cut: Determination of the essential oil content with at least 20 mL/kg, the fenchone content with at least 10% and the estragol content with max. 3.5%
- Basis: Data from 50 batches 2013 – 2022

Specific Case: Bitter Fennel

- March 2022: Final HMPA Public Statement on herbal medicinal products containing estragole
- Background: Genotoxic effects of metabolic activation of estragole by CYP450 into a 1'-hydroxy derivative, which is converted by sulfo-transferases into a reactive 1'-sulfoxy compound that forms DNA adducts
- Conclusion HMPA: „ *the intake of estragole from HMPs in the general population should be **as low as possible**, which includes a short-time duration of use (maximum 14 days) and a discussion about the single / daily doses necessary for adults and adolescents according to the risk assessment relevant for the concerned HMP. **For example, to reach or come as close as possible to the guidance value of 0.05 mg/ person per day, the lowest dose should be consistently selected if ranges of single and daily doses are available from traditional use ...***”
- Pregnancy/lactation: 0.05 mg/day, children up to 11 years: 1,0 µg/kg b.w.

Specific Case: Bitter Fennel

- Application for reduction of the essential oil content in bitter fennel fruit currently on the Work Programme of the Ph.Eur.
- Outcome?



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Thank you for
your attention!
Dziękuję za
uwagę!

For any questions: steinhoff@pharmadeutschland.de