

Workshop Dissolution Testing

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HMPs containing comminuted herbal drugs

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Problem

For a variety of herbal drugs, Commission E (and ESCOP) monographs refer under „dosage“ to

„XYZ g of herbal drug; equivalent preparations“

This poses a problem where clinical data are available in the meantime for some preparations, mostly extracts, although a wide range of preparations has been used in the same tenor for a long time when the monograph was established.

Problem

- Especially where the clinically undocumented preparation contains the comminuted drug doubts have been raised as to whether the relevant substances would sufficiently dissolve

BfArM/Commission E approach

- Where therapeutically active substances are known, dissolution of these substances from different products may be compared.
- Where therapeutically active substances are not known, comparison of the dissolution of suitable marker substances from the crude drug preparation with the respective infusion or approved/sufficiently documented extract preparation can be acceptable.

"Erläuterungen zum Antrag auf Zulassung eines Arzneimittels beim Bundesinstitut für Arzneimittel und Medizinprodukte" , 3. Auflage, vom 31.10.1996 (BAnz. Nr. 44a vom 05.03.1997)"

Example 1 – Senna leaf

Commission E

Comminuted herb, powder or dried extracts for teas, decoctions, cold macerates, or elixirs.

20-30mg hydroxyanthracene derivatives daily, calculated as sennoside B

Product, Dosage

Senna Tea; 1.0-1.2g Senna leaf acc. to 30mg hydroxyanthracene derivatives calc. as sennoside B; Excipients (herbs) 0.4-0.6g

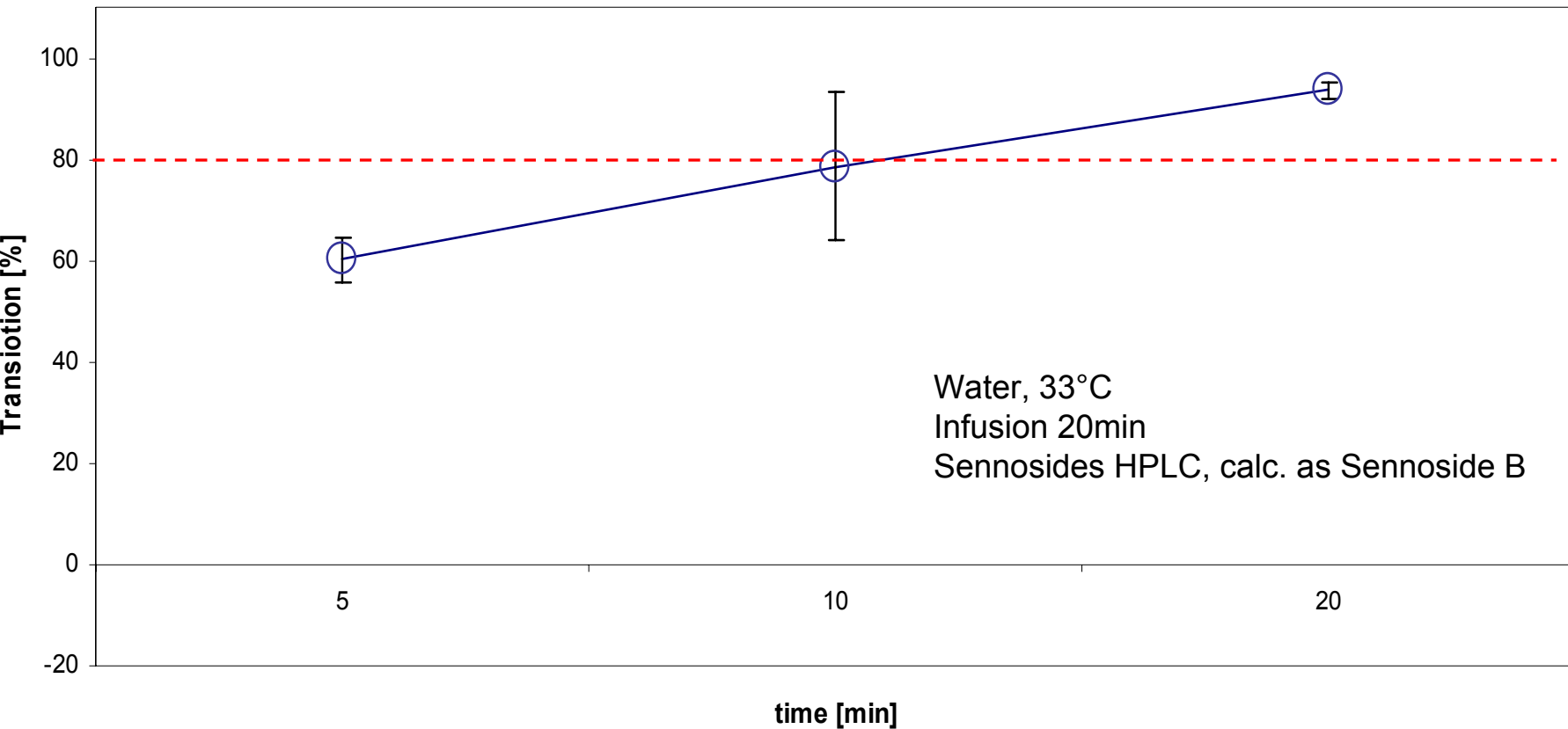
Proposed mode of administration

Infuse with cold or warm water for 20 min or administer directly with water

Are Sennosides sufficiently available from ingested leaf powder?

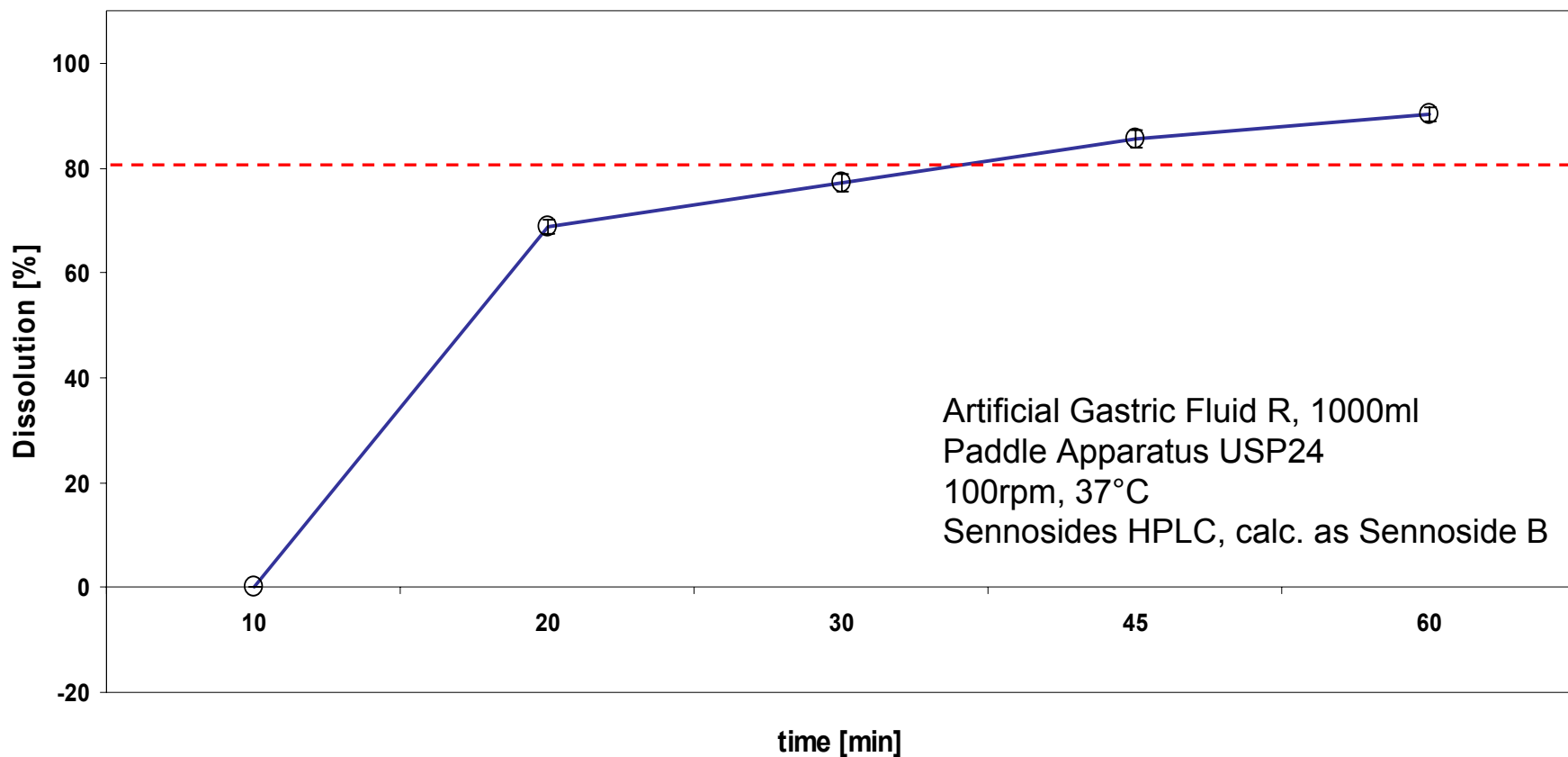
Example 1 – Senna leaf

Transition Rate of Sennosides into Senna leaf infusion



Example 1 – Senna leaf

Dissolution Profile of Sennosides from Senna leaf powder



Example 2 – Ginseng root

Commission E

Unless otherwise prescribed (daily)
1-2g of root; equivalent preparations

ESCOP

Adult daily dose: 0.5-2g of dried root;
equivalent preparations

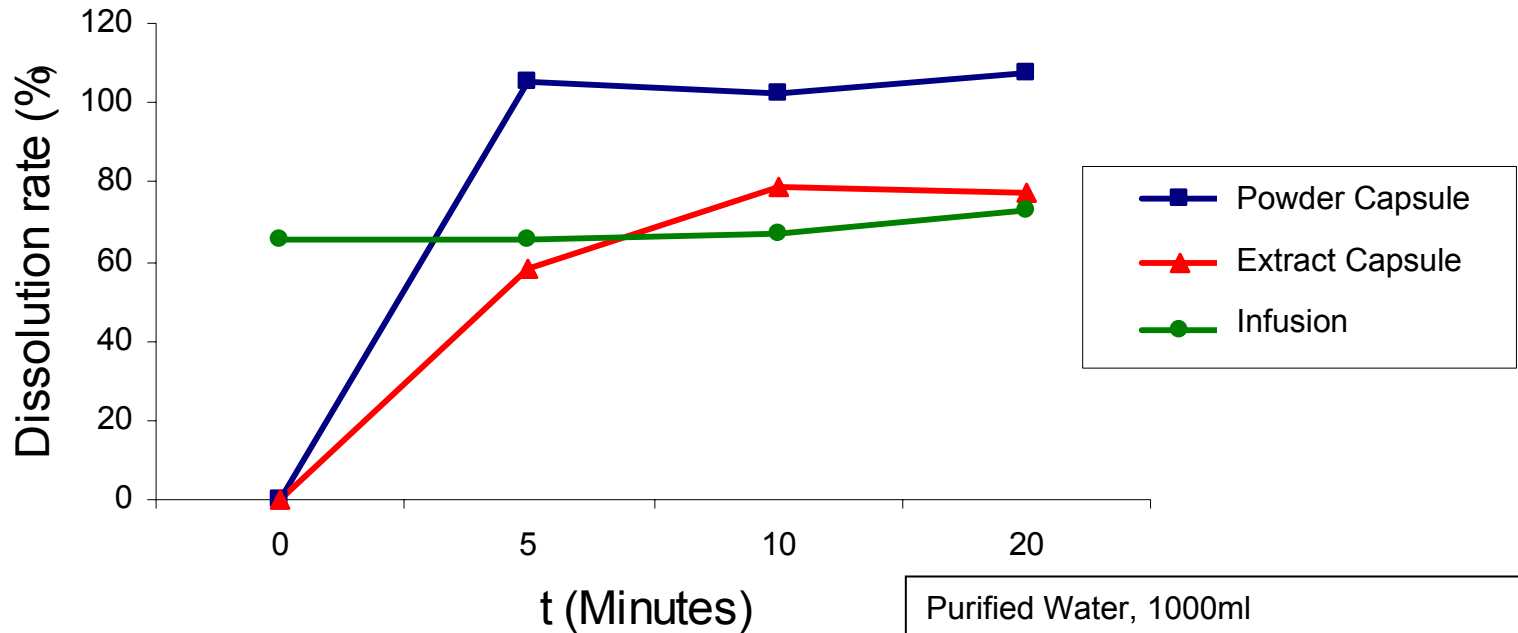
Product, Dosage

Ginseng root capsules;
350mg Ginseng root powder

Are Ginsenosides sufficiently available from Powder Capsules?

Example 2 – Ginseng root

Dissolution of Ginsenoside from Ginseng Powder, Ginseng Extract and transition rate of Ginsenosides in Ginseng infusion



Purified Water, 1000ml
 Paddle Apparatus DAB 1996
 120rpm, 37°C
 Ginsenosides Rg1, Re, Rf, Rb1,
 Rc, Rb2, Rd, calc. as Ginsenoside Rg1

Example 3 – *Lycopus europaeus*, Bugleweed

Commission E

Dosage lies between a daily dose of 1-2g of drug for teas and water-ethanol extracts equivalent of 20mg of drug.

Note: Each patient has his own individual optimal level of thyroid hormone. Only rough estimation of dosage is possible for thyroid disorders, in which age and weight must be considered

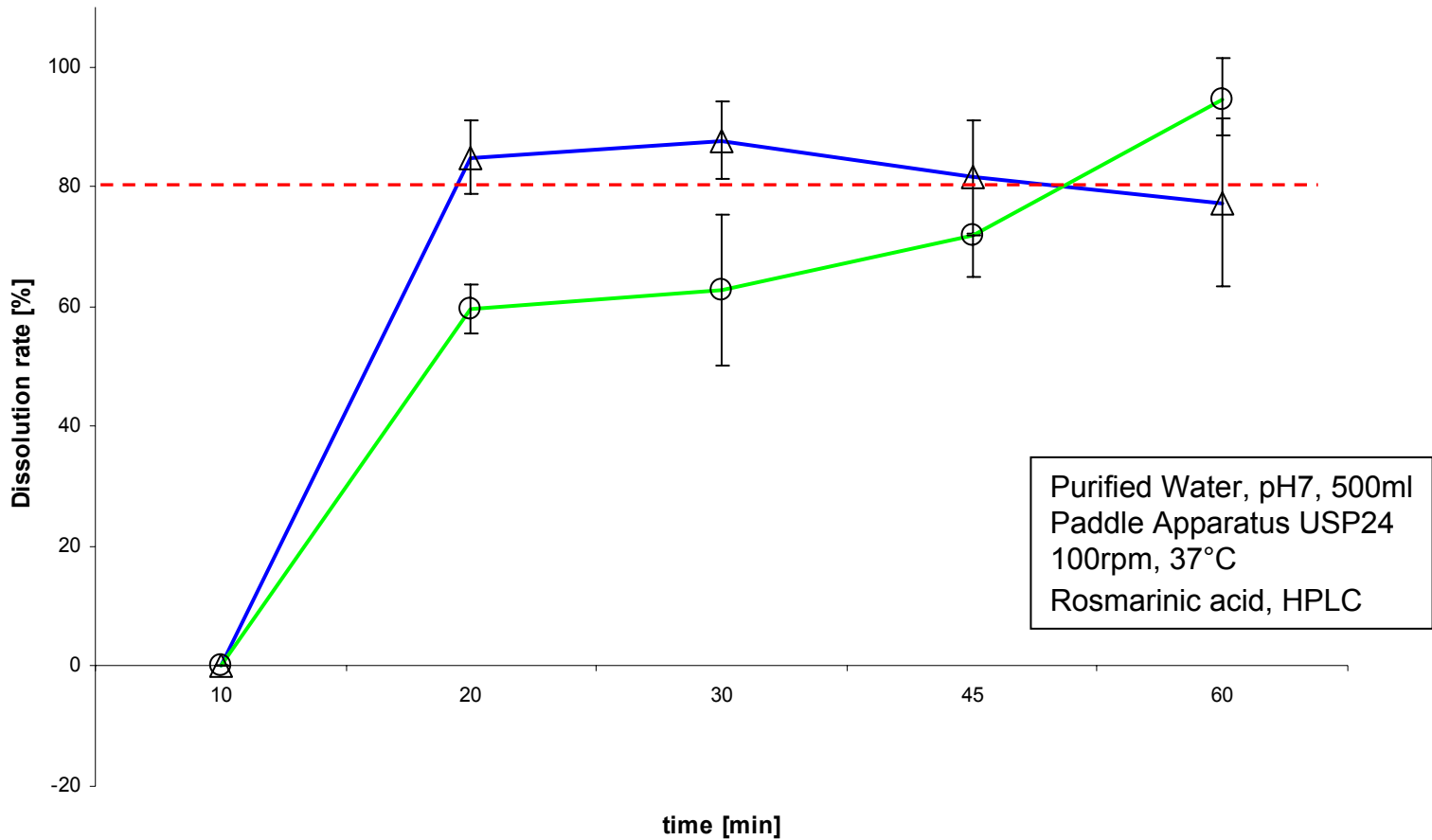
Product, Dosage

1 Tablet contains
Lycopi europaei herba 20mg

Are tablets with powdered herb equivalent to extract tablets?

Example 3 – *Lycopus europaeus*, Bugleweed

Dissolution of Rosmarinic acid from **Extract** and **Powder Tablets**



Conclusion

- In many cases secondary substances are at least equally soluble from the herbal matrix under simulated intestinal conditions as compared to extracts or a hot water infusion
- The extent and speed of dissolution from herbal matrices depends on particle size. Particle size must therefore be adequately specified and controlled.

Conclusion

- The examples show that administration of comminuted herbs may be reasonable in many cases.
- demonstration of high dissolution rates (>80%/45min) from the herbal matrix of therapeutically active substances should be acknowledged in WEU applications of herbal products with no sufficient direct clinical evidence.
- demonstration of high dissolution rates (>80%/45min) from the herbal matrix of markers assumedly contributing to efficacy may be suitable to add plausibility for the claimed indication in THMP procedures where other preparations of the same herbal drug are approved on WEU level.



Thank you