LECTURE 6

Standardisation and analysis of liquid dosage forms for oral use

Solutions, syrups, suspensions, emulsions and drops: physical stability, dosing accuracy, preservation and assay

Standardisation of Medicines and Raw Materials
Educational programme 6B10102 – Pharmacy · 4th year · Department of Fundamental Medicine, Al-Farabi Kazakh National University

OUTLINE

Lecture plan

1. Types of liquid oral preparations (Ph. Eur. 0672)
2. Specification and physicochemical tests
3. Specific tests for suspensions and emulsions
4. Dosing: uniformity and deliverable volume
5. Microbial quality and preservative efficacy
6. Assay of viscous liquids: sampling by mass

Liquid oral dosage forms

Oral solutions

Clear solutions of one or more active substances; most homogeneous form

Syrups

Sweet, viscous aqueous preparations; may contain sucrose at least 45% m/m

Oral suspensions

Solid particles dispersed in a liquid; may sediment but must redisperse

Oral emulsions

Oil-in-water dispersions; may separate but must reform on shaking

Oral drops

Small volumes measured with a dropper

Powders and granules for oral solutions or suspensions

Reconstituted before use; stable as dry form

TYPICAL SPECIFICATION

What we test in a liquid oral preparation

Test	Method / chapter	Purpose
Appearance, clarity, colour	2.2.1, 2.2.2	Detect precipitation, degradation
pH	Potentiometry 2.2.3	Stability, preservative activity, taste
Relative density	Pycnometer, densimeter 2.2.5	Conversion mass ↔ volume, filling control
Viscosity	Rotational viscometer 2.2.10	Dosing, physical stability of suspensions
Ethanol content	2.9.10	Tinctures, elixirs; labelled for safety
Identity and assay	HPLC, UV, titration	Active substances and preservatives
Related substances	HPLC	Degradation in solution
Uniformity / deliverable volume	2.9.27, 2.9.28	Dosing accuracy
Microbial quality	5.1.4, 2.6.12, 2.6.13	Patient safety

Suspensions and emulsions need extra tests

Suspensions

- **Redispersibility:** uniform after shaking for a defined time
- **Sedimentation volume:** F = Vu / V0; the closer to 1, the better
- **Particle size** by microscopy or laser diffraction
- **Crystal growth** and polymorphic changes on storage
- **Uniformity of dose** after shaking

Emulsions

- **Type of emulsion:** o/w or w/o (dilution, dye, conductivity tests)
- **Creaming:** reversible; cracking (coalescence) is irreversible
- **Droplet size** by microscopy or laser diffraction
- **Phase separation** after centrifugation or storage
- **Oxidation** of the oil phase (peroxide value)

Label: “Shake before use” is mandatory for suspensions and emulsions

PH. EUR. 2.9.27 AND 2.9.28

Accurate doses from multidose containers

20 doses

Uniformity of mass of delivered doses (2.9.27)
dosing device supplied with

≤ 2 > 10%

Deviation from the mean
not more than 2 doses deviate by more than 10%

0 > 20%

Maximum deviation
no dose deviates by more than 20%

≥ label

Deliverable volume (2.9.28)
contents that can be poured out are not less than the

Why it matters: the patient doses with a spoon, cup, syringe or dropper; errors with household spoons are common, so a calibrated measuring device is supplied

PH. EUR. 5.1.4 AND 5.1.8

Microbiological quality of non-sterile oral preparations

Preparation	TAMC, CFU/g or mL	TYMC, CFU/g or mL	Specified microorganism
Aqueous preparations for oral use	10^2	10^1	Absence of E. coli (1 g or 1 mL)
Non-aqueous preparations for oral use	10^3	10^2	Absence of E. coli (1 g or 1 mL)
Herbal teas used with boiling water (Ph. Eur. 5.1.8)	10^7	10^5	E. coli ≤ 10^3 CFU/g; no Salmonella in 25 g



Interpretation

- TAMC: total aerobic microbial count
- TYMC: total combined yeasts/moulds count
- 10^2 means the maximum acceptable count is 200
- Methods: 2.6.12 (enumeration), 2.6.13 (specified microorganisms)

Is the preservative strong enough?

Criteria for oral preparations

- **Bacteria:** ≥ 3 log reduction at 14 days, no increase at 28 days
- **Fungi:** ≥ 1 log reduction at 14 days, no increase at 28 days
- **Test organisms:** P. aeruginosa, S. aureus, E. coli, C. albicans, A. brasiliensis
- **Preservatives:** parabens, sodium benzoate, potassium sorbate
- **Result here:** criteria met

WORKED EXAMPLE

Assay of a syrup sampled by mass

1 Density	2 Sample by mass	3 Dilute and measure	4 Per dose	5 Compare
• Pycnometer: $\rho = (m_2 - m_0)/(m_1 - m_0) \times 0.99820$ • ρ = 1.1122 g/mL	• Viscous liquid: weigh 1.1203 g • $V = m/\rho$ = 1.0073 mL	• UV or HPLC vs reference standard • Found 24.49 mg	24.49 / 1.0073 × 5 = 121.6 mg per 5 mL	• Label 120 mg/5 mL → 101.3% • Limit 95.0–105.0% → complies

Why by mass? viscous syrups and suspensions cannot be measured accurately with a pipette; density converts the result to volume

Key take-aways

1. **Liquid oral forms** include solutions, syrups, suspensions, emulsions, drops and powders for reconstitution
2. **Physical tests** (pH, density, viscosity, redispersibility, droplet size) control stability
3. **Dosing:** 20 doses, ≤ 2 outside 10%, none outside 20% (2.9.27)
4. **Microbiology:** aqueous oral TAMC 10^2, TYMC 10^1, no E. coli; preservative efficacy per 5.1.3
5. **Viscous samples** are taken by mass and converted with density

SELF-CHECK

Control questions and literature

Questions

1. Name the types of liquid preparations for oral use.
2. Which tests show the physical stability of a suspension?
3. What is the difference between creaming and cracking of an emulsion?
4. Describe the test for uniformity of mass of delivered doses.
5. Give the microbial limits for aqueous oral preparations.
6. What are the criteria of preservative efficacy for oral preparations?
7. Why are viscous liquids sampled by mass?
8. Calculate mg per 5 mL: found 9.8 mg in 1.20 g of syrup, density 1.20 g/mL.

Sources

- Ph. Eur. 0672 Liquid preparations for oral use
- Ph. Eur. 2.9.27, 2.9.28, 5.1.3, 5.1.4
- Ph. Eur. 2.2.3, 2.2.5, 2.2.10, 2.9.10
- State Pharmacopoeia RK, Vol. 1