DEVELOPMENT OF A DENSITY MEASUREMENT PROTOCOL FOR INJECTABLE STERILE DRUGS : APPLICATION TO AMSACRINE IN A HOSPITAL PHARMACY

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BACKGROUND AND IMPORTANCE

Gravimetric Control (GC) is an in-and post-process control technique used for monitoring the preparation of sterile injectable drugs.

However, it requires precise data on the density of molecules, which are not always available in the summary of product characteristics (SPC) or from pharmaceutical laboratories.

AIM AND OBJECTIVES

The aim of our study is **to develop an accessible, accurate and reproducible density measurement protocol**, suitable for use in hospital pharmacy, using amsacrine* density measurement as an example.

** a cytotoxic agent used to induce remission in acute adult leukemia*

MATERIALS AND METHODS

1 BIBLIOGRAPHY

Measuring equipment prescribed in the monograph 2.2.5 « Relative density » of the European Pharmacopeia

- Density bottle
- Hydrostatic balance
- Hydrometer
- Digital density meter

The pycnometer (PYC) method was selected for its precision and suitability for hospital pharmacy

2 MATERIALS

A borosilicate glass pycnometer (type Gay-Lussac, Megal®)*

A precision balance (Sartorius QUINTIX®)

Standard solutions
- 0.9% NaCl (Fresenius®)
- 5% / 30% Dextrose (Fresenius®)
- Dichloromethane (DCM) / Methanol (MeOH) (Riedel-de Haën®)

Amsalyo® 75 mg
- reconstituted with 50 mL of water for injectable preparations

3 CALCULATION

The mass of the filled PYC (m) was measured after weighing the empty PYC (mo)

The PYC was filled with the test solution (standard solutions first, then amsacrine), ensuring no air bubbles

The density (d) of each sample solution was calculated by using the following formula :

$$d = \frac{\rho}{\rho_{ref}} = \frac{m - m_o}{m_{ref} - m_o}$$

* m_{ref} : mass of PYC + WFI

4 METHODS

1) Approximately 25 mL of solution / measurement

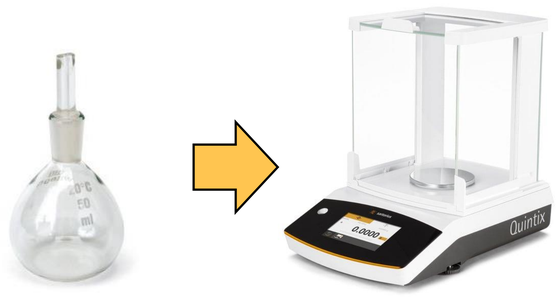
2) 3 distinct measurements at same temperature

3) Validation of our protocol by testing with standard solutions of known density

4) Determination of the density of the amsacrine solution**

**prepared under laminar flow hoods due to the cytotoxic risk.

RESULTS



Temperature : 20-21°C
n = 3
m_o = 33,3020 g
m_{ref} = 57,1184 g

(1) Table of calculated density of standard solutions vs their theoretical densities.

Standard solutions	Calculated mean density (g/mL)	Standard deviation (g/ml)	Theoretical density ** (g/ml)	Percentage deviation (%)
5% Dextrose	1.0189	0.0002	1.0175	0,1344
30% Dextrose	1.1127	0.0004	1.1260	-1,1793
0.9% NaCl	1.0063	0.0005	1.0053	0,1085
MeOH	0.7958	0.0001	0.7911	0,5979
DCM	1.3324	0.0011	1.3260	0,4807

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Validation of our protocol through the **concordance** between the calculated and theoretical results for standard solutions

Amsacrine
m : 57,133 g
ρ = 1,0059 g/mL

CONCLUSION – RELEVANCE

The density measurements for amsacrine solutions were in line with the excipient composition of Amsalyo® (lactic acid, WFI).
While the pycnometer technique is reliable and cost-effective, it is time-consuming and requires safety precautions.
An electronic densimeter offers faster measurements but at a higher cost.
Overall, our study has established a simple, reliable protocol for occasional measurements, exemplified by the determination of amsacrine density, suitable for use in a sterile drug production unit.

3PC-034

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