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INTRODUCTION

Photometric titration = classical titrimetry + photometric detection

- Aim: quantify the concentration of analyte in solution
- In contrast to manual titration using a burette, this technique has the advantage of being **automated**, **objective**, and ensure **traceability** of the assay

Objective: **Develop and validate a photometric titration method**

MATERIALS AND METHOD

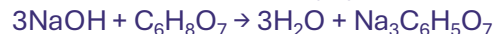
Materials:

- Automatic titrimer (Mettler Toledo T5) with the **DP5 phototrode**
- Sodium hydroxide solution (NaOH) standardised to 0.1 mol/L
- Color indicator: phenolphthalein



Method:

- Example of the acid-base assay of citric acid $C_6H_8O_7$ involving the reaction:

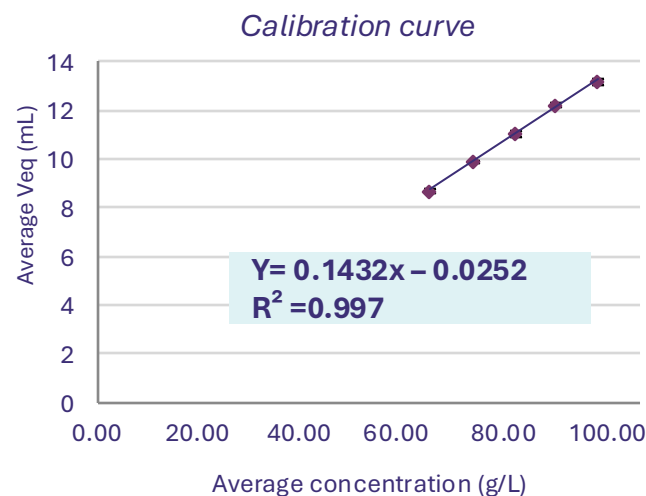


➡ **equivalence point was detected at 590 nm by the phototrode thanks to colour change of the indicator**

- Validity criteria^{1,2,3}:
 - **Linearity**: 5 calibration points with a coefficient of determination $R^2 > 0.995$
 - **Accuracy**: evaluated over 3 days with coefficients of variation (CV) and relative differences (RD) < 3 %
- Determination of the limit of quantification (LOQ)

RESULTS

- **Linearity:**



- **Accuracy:**

		day 1	day 2	day 3
80%	TC (g/L)	58.60	58.60	58.60
	AC (g/L)	59.27	59.47	59.40
	RD %	1.14	1.48	1.37
	CV %	0.20	0.19	0.19
100%	TC (g/L)	73.20	73.20	73.40
	AC (g/L)	74.60	74.60	74.25
	RD %	1.91	1.91	1.16
	CV %	0.27	0.27	0.56
120%	TC (g/L)	88.00	88.00	88.00
	AC (g/L)	89.00	89.00	88.30
	RD %	1.14	1.14	0.34
	CV %	0.78	0.22	0.00

TC: theoretical concentration
AC: average concentration

- **LOQ: 0.02 g/L**

DISCUSSION - CONCLUSION

Validation of the photometric titration

➡ Routine application

Photometric titration:

- **Robust, easy and fast**
- **Precision and traceability system** ➡ Well adapted to pharmaceutical controls

This validation protocol will be used to validate futures analytical methods using titrimetry, and paves the way for the automation of burette assays with color indicators

¹ Recommendations for titration methods validation, USP

² Validation of titration, a guideline for regulated laboratories, Mettler Toledo

³ Q2 R(1) Validation of analytical procedures, International Council for Harmonisation