

Comparing automated titrimetry method to manual titrimetry on samples from a production unit

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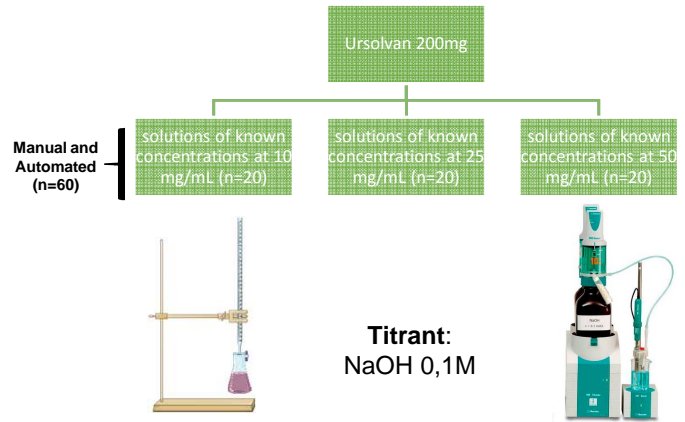
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Context :

The content control carried out after the production of the hospital preparation of Ursodeoxycholic Acid capsules is achieved by titrimetric assay. This method can be automated or manual. Although the manual method is widespread in preparation units, it has several drawbacks, including operator-dependent variability (eg at the end point reading) and time-consuming.

Objective: compare manual titrimetry, currently in use with an automated titration technique.

Materials and methods :



Titrant:
NaOH 0,1M

Manual titration technique:
colorimetric technique (addition of phenolphthalein)

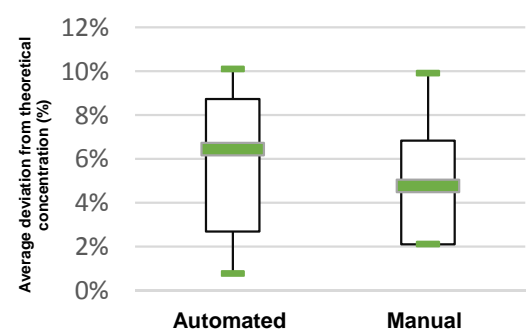
Automated titration technique:
titrator 905 Titrande Metrohm®

Parameters measured: Relative standard deviation (RSD), average deviation from theoretical concentration (EM), average handling time(D)

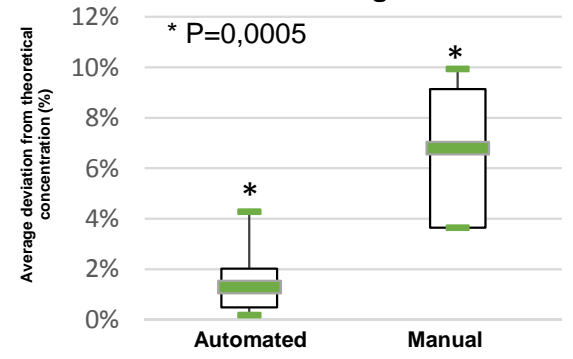
➤ Comparison by **Fisher Snedecor (RSD) + Wilcoxon test (EM + D)**

Results:

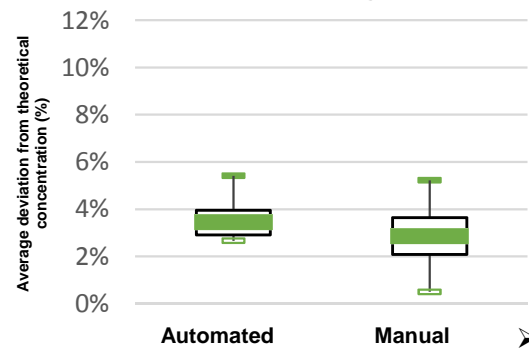
Solution at 10mg/mL



Solution at 25mg/mL



Solution at 50mg/mL



Solutions (mg/mL)	Daut vs Dman (min)	P value	RSDaut vs RSDman (%)	P value
10	8,04 vs 38,55	0,0001	6,062 vs 5,722	>0,05
25	8,36 vs 42	0,0001	1,721 vs 2,583	<0,05
50	8,25 vs 47,94	0,0001	0,863 vs 1,473	<0,05

RSDaut=Relative standard deviation automated, RSDman=Relative standard deviation manual, Daut= average handling time automated, Dman= average handling time manual

Total average deviation is dose-independent (p=0,0974)

Conclusion:

Analytical control by automated titration optimizes the capacity for hospital preparation analysis:

- **significant improvement in accuracy** (25 et 50mg/mL)
- **no significant difference** in EM between the two methods (10 et 50mg/mL).

In addition to being significantly faster, this technique requires little presence time of the operator.

Reproducibility tests by different operators will be needed to improve the robustness of the study. This apparatus could also be used within the unit for other dosages (e.g. aqueous boric acid, acetylsalicylic acid).