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Background

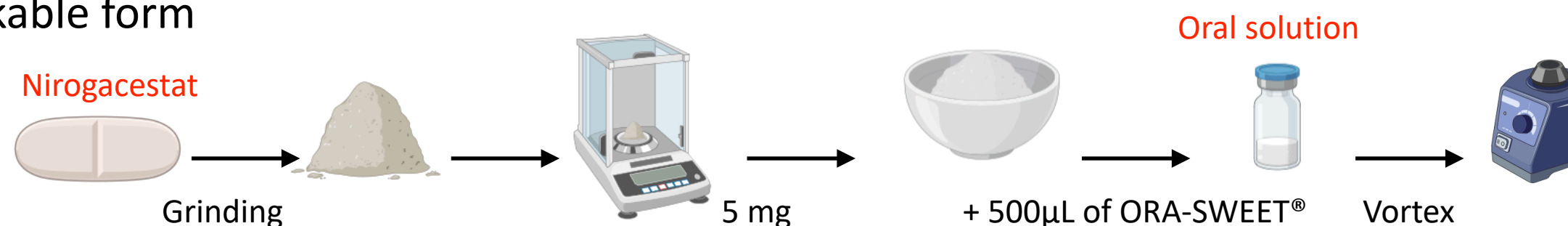
- **Desmoid tumors** : Benign, non-metastatic but painful soft tissue tumors.
- **Treatment** : Gamma secretase inhibitor, Nirogacestat.
- **Patient** : Good responder but major dose-dependent skin intolerance.
- **Tolerance induction** : Concentrated oral solution (C°) at 2 mg/mL.
- A **previous study** revealed, at **48 hours** : a **degradation** (difference of C° > 10% vs. theoretical C°).

Objectif

Capture the moment of Nirogacestat degradation in ORA-SWEET® by taking 3 samples : at **H0, H7, and H24**.

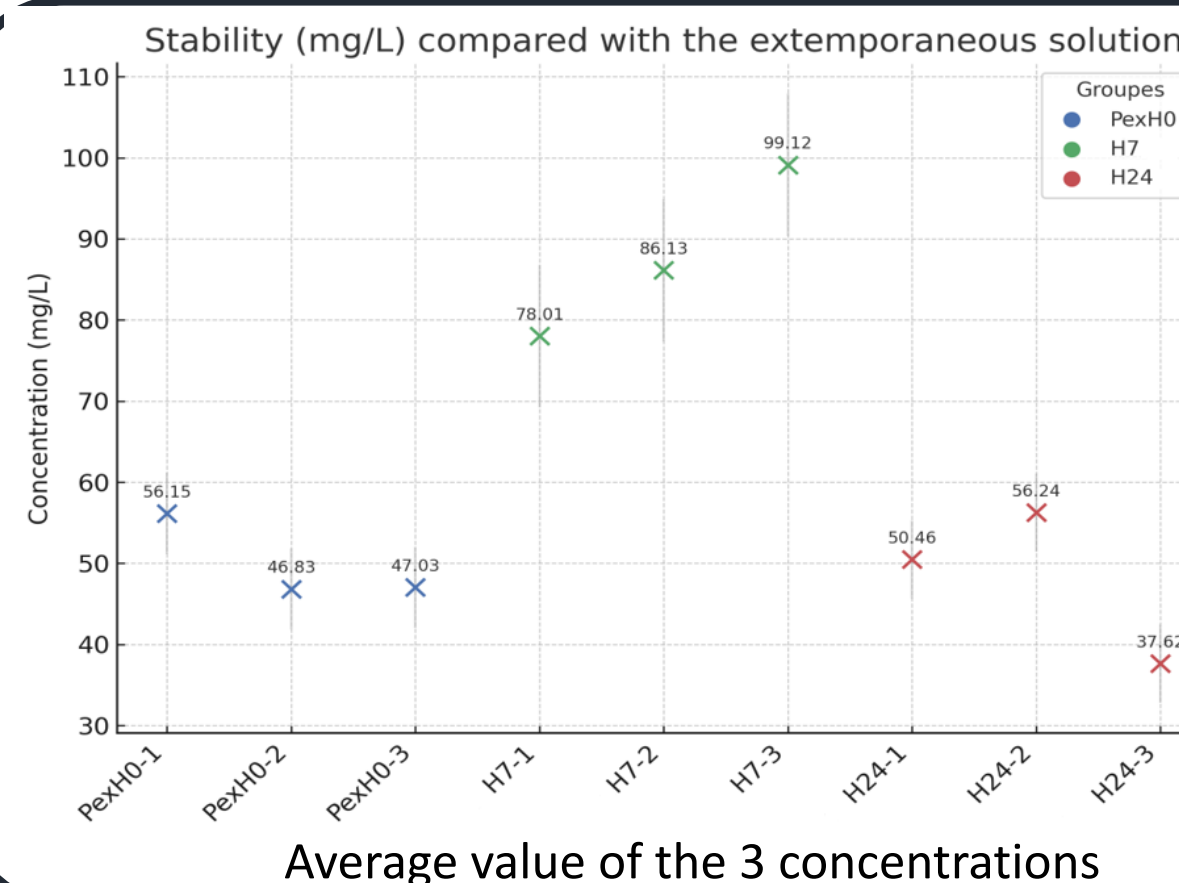
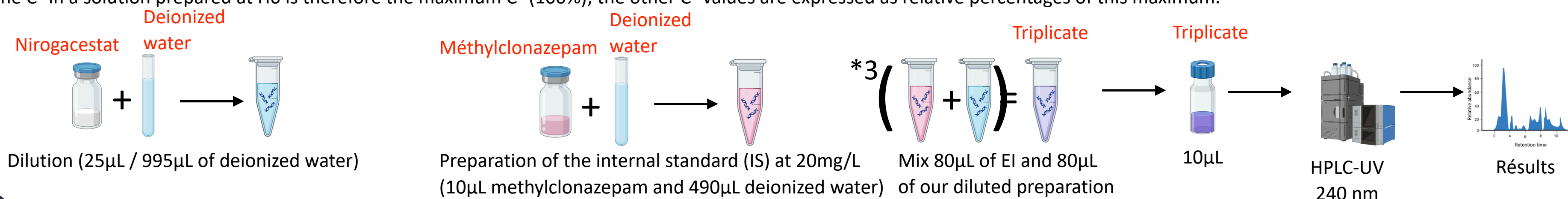
Materials and methods

1) Preparation of the drinkable form



2) Nirogacestat dosage

The C° in a solution prepared at H0 is therefore the maximum C° (100%); the other C° values are expressed as relative percentages of this maximum.



Results and discussion

Average temperature of triplicate extemporaneous solutions at 0h, 7h, and 24h

- **PexH0** = 50,353 mg/L
-> 100% Nirogacestat
- **PexH7** = 88,26 mg/L
-> 175% Nirogacestat
- **PexH24** = 48,373 mg/L
-> 96% Nirogacestat

The measured C° values **expressed** as a **percentage of Pex H0** (100% Nirogacestat).

At **H7**, the **+10%** threshold is **exceeded**. This could be explained by **insufficient equilibration time at room temperature** before preparation for injection into the chromatograph.

At **H24**, the threshold is **not exceeded**. The **equilibration time at room temperature** before injection was **optimal**, and the average concentration was as **expected**.

Conclusion

It is likely that the point at which our Nirogacestat 2 mg/mL preparation in ORA-SWEET® begins to **degrade significantly** is between **24 and 48 hours**.

However, this 24-hour **stability** remains **to be confirmed**.

If it is, this would allow: for tolerance induction, an **oral solution** to be prepared that can be used for **2 consecutive days**.