Optimization of a Novel Formulation for mAbdi2, a Biosimilar Monoclonal Antibody

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Purpose

Precision in formulation is key to the success of biosimilars, and our motivation stems from the desire to contribute to the advancement of therapeutic biologics through innovative and precise formulation strategies. This study aimed to optimize the formulation for mAbdi2, a promising biosimilar mAb, ensuring its stability and efficacy.

Objective

- To enhance the stability and efficacy of the drug product by optimizing the formulation composition
  - Evaluating the effects of different excipients and additives.
  - Determining the optimal pH and ionic strength levels.
  - Optimizing solubility and tonicity
- To characterize the shelf life and degradation profiles of the formulation.
  - Long-term stability studies under different storage conditions.
  - Freeze-Thaw stability studies.

Methods

The workflow for the development of the mAbdi2 non-infringing formulation, prepared for preliminary studies, is clearly presented in Figure 1.

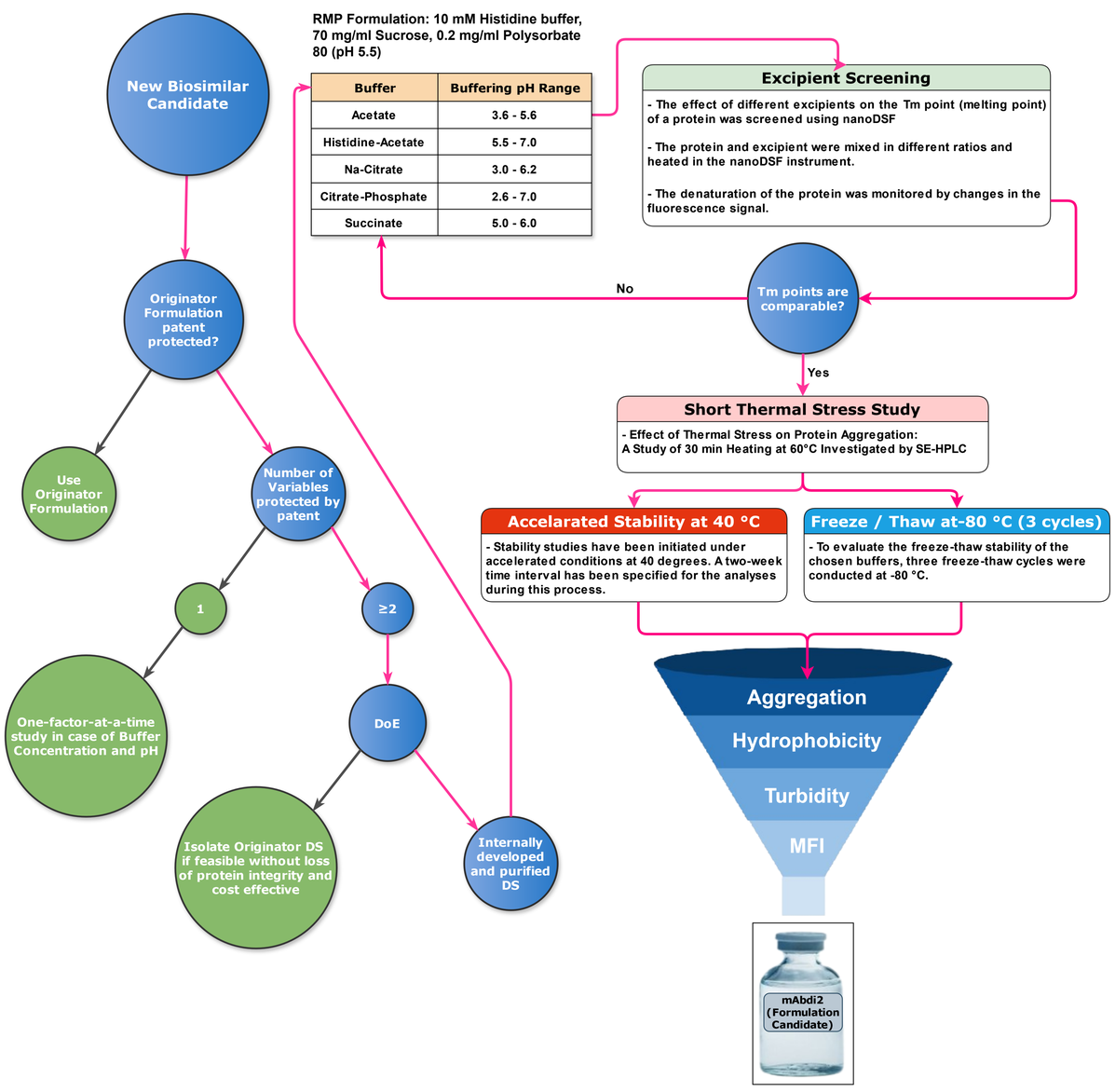


Figure 1: Decision Tree on Biosimilar Formulation Development Strategy

Note: The development-grade Drug Substance (DS) was utilized for excipient screening experiments.

Results

The results are presented sequentially based on the workflow outlined in the Methods section.

Note: You can scan the QR code for additional results.

A) Determination of Optimal pH for Each Buffer System Using NanoDSF

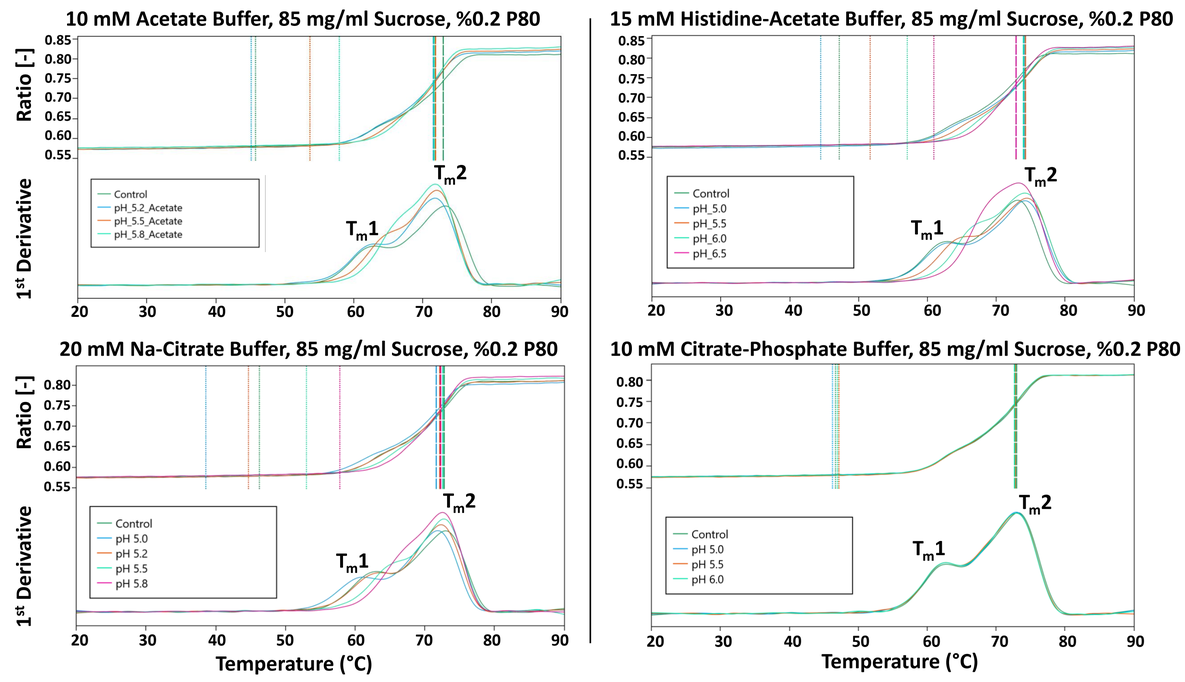


Figure 2: Thermal Transitions with Different Buffers and pH levels

B) Excipient Screening for the Selected pH and Buffer Using nanoDSF

Table 1: Screened excipient effects on mAbdi2 using nanoDSF

Excipients	15 mM Histidine-Acetate (pH 5.0)	20 mM Na-Citrate (pH 5.2)	8 mM Citrate-Phosphate (pH 5.5)	10 mM Acetate (pH 5.2)
Sucrose	+	+	+	+
Mannitol	+	+	+	+
Sorbitol	+	+	+	+
Glycine	+	+	-	+
Arginine	-	-	-	-
NaCl	-	-	-	-
Methionine	+/-	+/-	+/-	+/-
Polysorbate 80	+/-	+/-	+/-	+/-
Poloxamer 188	+/-	+/-	+/-	+/-

+ Stabilization; - Destabilization; +/- No effect

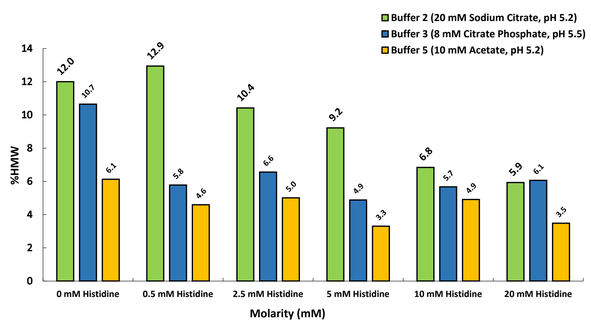


Figure 3: The impact of selected excipients on Aggregation

C) Thermal Stability (Two Weeks at 57.5°C) of Different Buffers with Selected Excipient

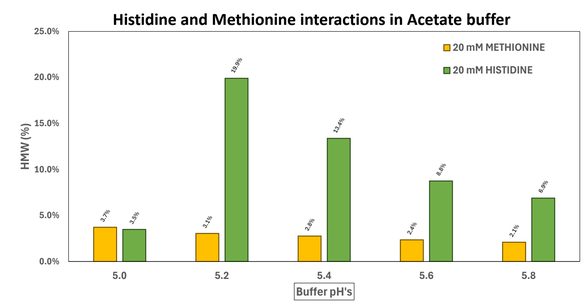
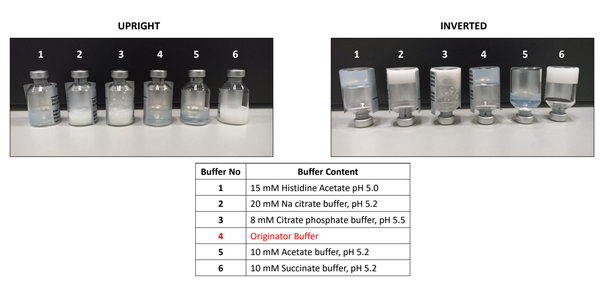


Figure 4: Histidine and Methionine Effects on Aggregation



Buffer No	Buffer Content
1	15 mM Histidine Acetate pH 5.0
2	20 mM Na citrate buffer, pH 5.2
3	8 mM Citrate phosphate buffer, pH 5.5
4	Originator Buffer
5	10 mM Acetate buffer, pH 5.2
6	10 mM Succinate buffer, pH 5.2

Figure 5: Acetate buffer showing less aggregates

Conclusions

- Acetate buffer + Methionine + Sucrose + Polysorbate 80 is selected for further studies.
- To achieve promising results for other buffers, additional excipient screening has been initiated, including compounds such as Glycine, Arginine, and others.
- No observable aggregation was noted after undergoing four cycles of freeze/thaw in all buffers.
- Also, acetate buffer turbidity comparable with originator buffer.

KEY REFERENCES

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MORE INFORMATION

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