J.T.Baker® Viral Inactivation Solution Ease of Use

OBJECTIVE

J.T.Baker® Viral Inactivation Solution (JTB VIS) is a readily biodegradable[1], ready-to-use, nonionic detergent-based solution for inactivation of adventitious viruses in biomanufacturing processes. JTB VIS can achieve ≥6.5 log reduction of viral inactivation independent of typical manufacturing temperatures ranging from 4°C to 24°C[2]. This solution is compatible with classical bioprocessing steps[3] and structurally diverse protein therapeutics[4]. Moreover, JTB VIS is removed through the subsequent chromatography steps and the residual detergent can be detected by a simple HPLC-based analytical method[5].

Triton X-100[6] has widely been used for viral inactivation, however, the substance group **2-[4-(2,4,4-trimethylpentan-2-yl)phenoxy]ethanol, which includes** Triton™ X-100, has been designated a "substance of very high concern" by the European Chemicals Agency's Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) regulations in Europe[7]. In contrast, the JTB VIS is a readily biodegradable, free of alkylphenols, and environment, health, and safety (EHS) compliant novel viral inactivation solution.

The use of detergents for viral inactivation can impose process challenges when used at commercial scale due to viscous material handling and potential for excessive foam generation, which can lead to pump cavitation, product loss, deviations, and adverse events on the manufacturing floor. To assess ease of use, JTB VIS viscosity was compared with other traditionally used detergents[8,9,10] and foam height generation was evaluated against Triton™ X-100 to determine whether JTB VIS may potentially create adverse foaming conditions during bioprocessing.

METHOD

To assess foaming characteristics, foam height determinations were conducted according to ASTM D1173, Standard Test Method for Foaming Properties of Surface-Active Agents[11]. All foam height measurements were evaluated at 25 °C (ambient temperature) using a Ross-Miles Foam Apparatus (VWR Cat# 14007-876) by Wilmad-Labglass. The foam height of JTB VIS and Triton X-100 was measured at 0.1% detergent concentration at time zero and after 5 minutes of hold.

RESULTS AND DISCUSSION

The foam height results at time zero and after 5 minutes of hold time are shown in Figure 1. The foam height generated by JTB VIS was about 10% and 15% lower at time zero and after 5 minutes of hold compared to Triton X-100, respectively. The foam dissipation rate was also quicker for JTB VIS at 6.7% per minute compared to Triton X-100 having a dissipation rate of 5.6% per minute. The foam dissipation rate was calculated as:

$$\text{Foam dissipation rate} = \frac{\text{Foam height at t=0 - Foam height at t=5 min}}{\text{time (5 min.)}}$$

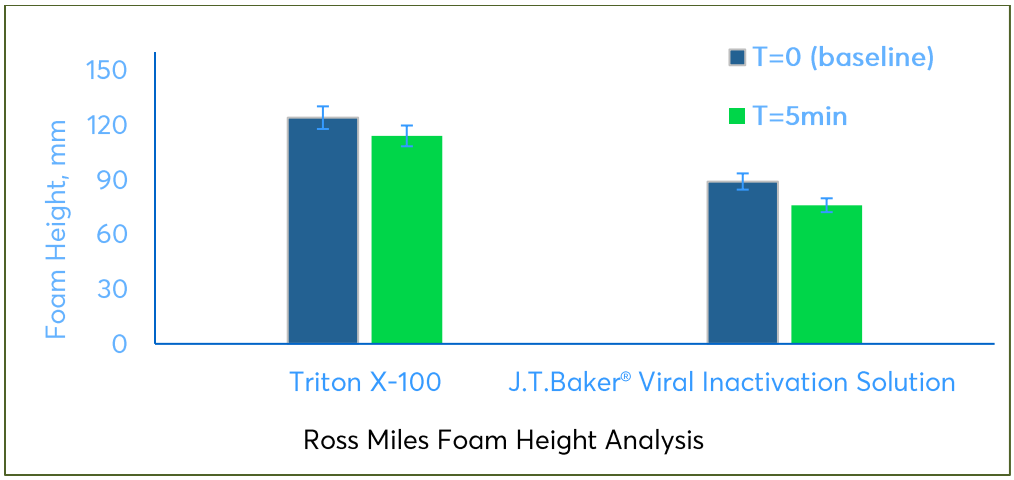

Fig. 1. Foam development assessed by Ross Miles foam height analysis at two time points.

The viscosity (25 °C) data of JTB VIS and other commonly used detergents for VI are summarized in the Table 1. Viscosity of JTB VIS was determined using Brookfield viscometer to measure viscosity at 25°C and was found to be almost hundred times lower compared to the other detergents. High viscosity of a detergent can cause complexity in material handling and inaccurate material quantification, which can lead to a deviation. In comparison, the lower viscosity of the ready-to-use JTB VIS provide benefits in safe and easier handling of material.

Table 1. Viscosity of typically used detergents for viral inactivation.

Reagent	Viscosity at 25 °C
JTB VIS	2-4 cPs
Triton™ X-100	240-270 cPs
Polysorbate 20	370-430 cPs
Polysorbate 80	300-500 cPs

CONCLUSION

Excessive foam generation can result in loss of protein and aggregate formation. Moreover, the foam formation may create manufacturing challenges related to fluid handling, product loss, vent filter wetting, and pressure issues. Ideally, solutions used for VI should be able to inactivate viruses with minimal foam generation. JTB VIS generate 15% less foam and dissipates quicker than Triton X-100. On the other hand, substantially lower viscosity enables safer, easier, and efficient material handling and transfer. Lower foam height generation and viscosity characteristics of JTB VIS made this solution unique for operational efficiency and ease of applications.

REFERENCES

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