

RAPID ASSESSMENT OF PRESERVATIVE PERFORMANCE USING BIOCALORIMETRY

INTRODUCTION

Preservative efficacy testing (PET) is widely used in the development of cosmetics, personal care, household, and pharmaceutical formulations. It is traditionally performed over 28 days by measuring the number of viable microorganisms recovered at defined time points. Although this provides quantitative log-reduction data, it requires repeated sampling, plating, incubation, and colony counting.

Isothermal microcalorimetry (IMC) offers a faster and more efficient approach by continuously monitoring microbial activity throughout the preservative challenge. Since microbial metabolism generates heat, changes in activity can be detected in real time without repeated sampling or plating. This enable rapid screening of multiple formulations, allowing strong, intermediate, and weak preservative responses to be identified early and promising candidates to be prioritized for compendial PET.

MEASUREMENT PRINCIPLE

The calScreener[®] (Fig. 1) system continuously measures the heat generated by microbial metabolism under controlled isothermal conditions. The heat-flow profile provides information on microbial activity over time.

Key parameters include:

- **Time to detection** – how quickly activity becomes measurable
- **Peak heat flow** – maximum metabolic activity
- **Duration and curve shape** – timing and persistence of activity
- **Total heat** – cumulative metabolic activity over a defined time window

Effective preservative activity is reflected by lower and/or shorter metabolic responses compared with an untreated or reference formulation (Fig. 2). Unlike discrete CFU measurements, biocalorimetry continuously captures changes in microbial activity throughout the experiment, including between conventional sampling points.



Figure 1. calScreener[®] system for rapid PET.

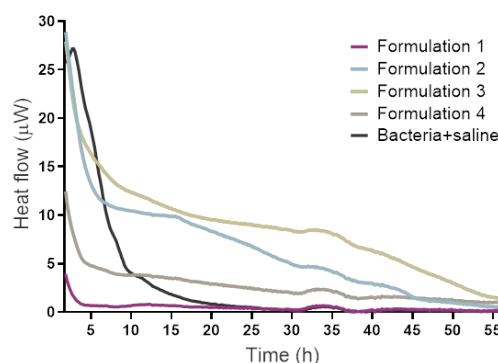


Figure 2. Representative heat-flow profiles over 120 h. Differences in amplitude, onset, duration, and curve shape illustrate how formulations can affect microbial metabolic activity.

WORKFLOW

- 1. Challenge:** Combine the test microorganism with each formulation and appropriate control.
- 2. Measurement preparation:** Transfer a defined volume into sealed measurement vials.
- 3. Continuous measurement:** Place the vials in the calScreener[®] and monitor heat production continuously.
- 4. Data analysis:** Compare heat-flow profiles and total heat between formulations.

Depending on the organism and formulation, meaningful differences can be detected within a few hours, enabling screening before conventional PET results are available.

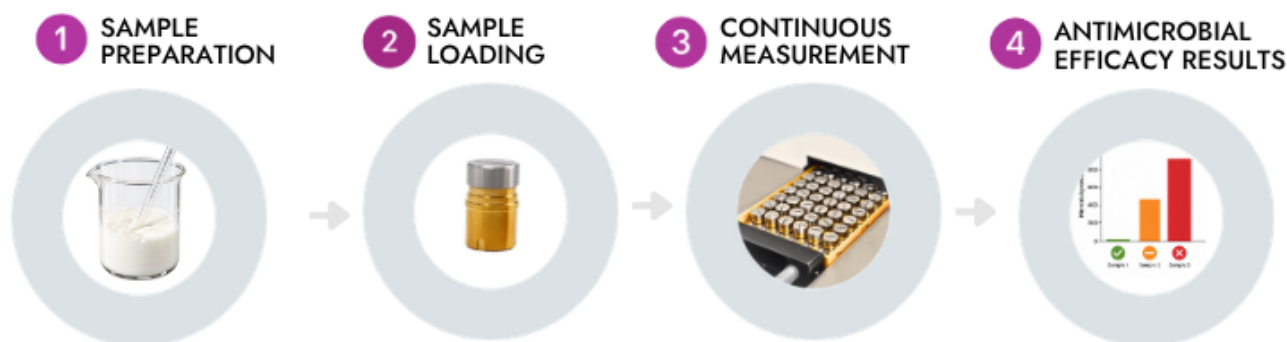


Figure 3. General workflow for assessing preservative performance using continuous microcalorimetry.

RAPID COMPARISON OF FORMULATIONS

A typical experiment includes untreated or reference control together with formulations containing different preservative systems, concentrations, or compositions. Test formulations can then be ranked according to their ability to reduce or delay microbial activity relative to the control. Early total heat can be calculated over predefined windows such as 0–5, 0–10, and 0–15 h.

Importantly, the different time windows demonstrate the speed of the approach. In the example shown, the same differences between formulations can already be identified using the first 5 h of data as with 10 or 15 h (Fig. 4). In other words, extending the measurement window does not change the overall interpretation, demonstrating that formulation performance can be distinguished

at a very early stage. This provides a major advantage for screening: results do not necessarily require a long measurement period to become informative.

TIMELINE COMPARISON

Biocalorimetry enables rapid screening and ranking of formulations, with conventional PET used for confirmatory testing.

Table 1. Comparison of conventional PET and calScreener biocalorimetry based system.

Conventional PET	Biocalorimetry
Sampling at predefined time points	Continuous monitoring
Repeated plating and incubation	No sampling or plating necessary
Colony counting required	Automated heat-flow measurement
Results become available after incubation and enumeration	Meaningful differences can be visible within hours
High hands-on workload	Lower hands-on workload

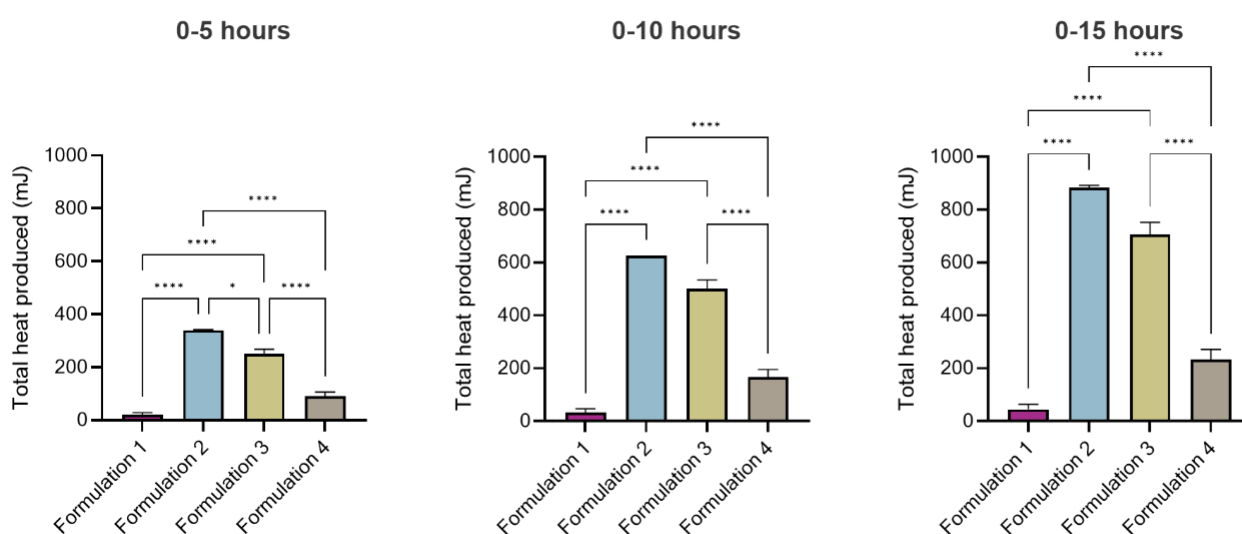


Figure 4. Total metabolic heat measured over different time windows. Lower total heat indicates lower cumulative microbial activity during the corresponding measurement period.

CONTINUOUS METABOLIC RESPONSE AND CFU COUNTS

The complete heat-flow profile provides information beyond a single endpoint. Differences in onset, amplitude, duration, and curve shape can reveal how strongly and how long a formulation suppresses microbial activity.

Microcalorimetry can be complemented by conventional viable-count measurements to establish formulation- and organism-specific relationships between metabolic activity and microbial survival.

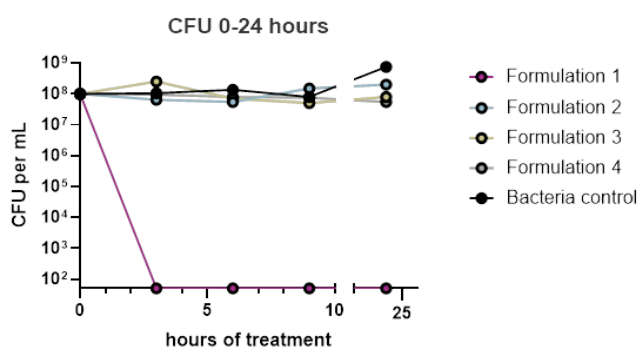


Figure 5. Example of CFU recovery over time for different formulations. CFU measurements can be compared with corresponding calorimetric responses.

CFU remains the conventional quantitative measure of microbial reduction, whereas biocalorimetry provides continuous information between sampling points. Because the relationship between heat production and viable-cell numbers is organism- and formulation-dependent, a standard curve should first be established to estimate viable cell-reductions from calorimetric data.

INTERPRETATION OF RESULTS

Lower and shorter calorimetric activity generally indicates stronger microbial suppression. Formulations can therefore be broadly categorized as:

Table 2. Interpretation of results.

Strong suppression	Intermediate suppression	Weak suppression
Little or no detectable metabolic activity	Delayed or reduced metabolic activity	Rapid onset of metabolic activity
Rapid return toward baseline	Measurable activity over a limited period	Sustained heat production
Low total heat	Moderate total heat	High total heat approaching the control response

This enables early identification of promising formulations and candidates that may require reformulation.

ACCELERATED SCREENING IN PRESERVATIVE DEVELOPMENT

Biocalorimetry provides a rapid screening tool to support formulation decisions before confirmatory PET.

A tiered workflow can be used: **Screen** → **Rank** → **Prioritize** → **Confirm**

Multiple formulations can first be screened by microcalorimetry. Candidates showing the desired preservative response can then be prioritized for confirmatory CFU-based PET, reducing the number of formulations subjected to more time-consuming testing. This can reduce repeated sampling, plating, colony counting, and associated hands-on work during early formulation development.

CONCLUSION

Continuous isothermal microcalorimetry provides a rapid, information-rich approach for assessing preservative performance. By continuously monitoring microbial metabolic activity, differences between formulations may be identified within a few hours.

In the example presented here, comparison of the 0–5, 0–10, and 0–15 h datasets shows that formulation ranking was already possible using the first 5 h of data, highlighting the speed of the technique.

Biocalorimetry therefore offers a practical way to screen multiple formulations, identify promising candidates earlier, and focus laboratory resources on the most relevant formulations before conducting full 28-day compendial PET.

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