Quantitation of Influenza HA from the MIMIX Vaccine Patch by VaxArray System

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Abstract

The MIMIX™ vaccine patch delivers a microarray of controlled release tips composed of a silk fibroin matrix, releasing entrapped influenza antigen into the skin over time. MIMIX delivery mimics natural infection kinetics to elicit an improved immune response compared to traditional bolus vaccine administration. MIMIX patches require a highly sensitive potency assay that can measure fractions of the total antigen loaded in the microneedles. The VaxArray® Platform delivers the necessary sensitivity which would not be feasible with the traditional SRID potency assay. The VaxArray Influenza HA Assay is a stability indicating immunoassay measuring the identity, integrity, and quantity of influenza vaccine in less than 1 hour and has been implemented for assessing HA potency of MIMIX microneedle patches.

Materials and Methods

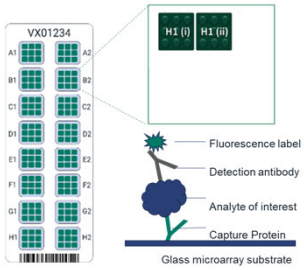


Figure 1: VaxArray Influenza H1 Assay

The VaxArray Influenza HA Assay is a slide-based multiplexed immuno-assay to determine the identity, integrity, and quantity of HA in a sample. Samples containing the analyte of interest are applied to the slide. Here, MIMIX devices are tested on the monovalent H1 assay. Multivalent and neuraminidase (NA) assays are also available.

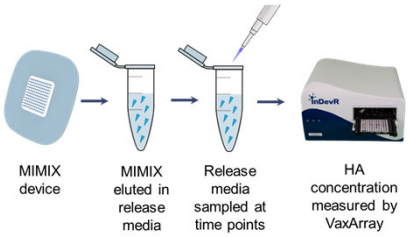


Figure 2: MIMIX in vitro potency assay

MIMIX patches containing influenza antigen are eluted into release medium. The release medium is sampled over time and the samples are analyzed for HA content on the VaxArray system.

Stability and Matrix Effect

The VaxArray system was assessed for its ability to differentiate between intact influenza antigen in MIMIX release media as compared to heat stressed antigen; as well as detecting antigen in the presence of excipient.

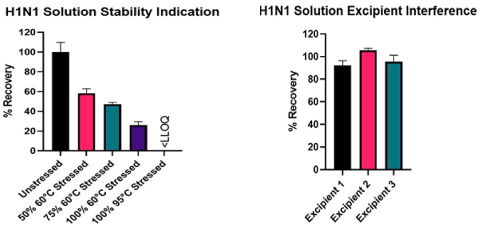


Figure 3: (Left) Antigen heat-stressed at 60°C for 24 hours and 95°C for 15 minutes in comparison to unstressed antigens. (Right) Antigen recovery in different excipients, detecting within 10% of expected values.

In Vitro Release Assessment

Antigen recovery from MIMIX patches was quantified under in vitro release conditions. The assay was also used to assess the H1N1 stability in solution over time.

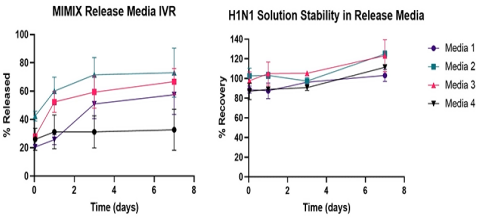


Figure 4. Comparison of antigen recovery in different release media. (Left) HA release from MIMIX over time. (Right) Stability of HA under in vitro release assay conditions over time. Medium 2 was selected for further assay development.

Formulation and Stability

The VaxArray HA Assay was implemented as a tool for screening MIMIX formulations for their antigen in vitro release profiles and to assess patch stability.

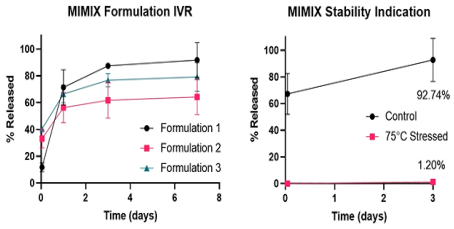
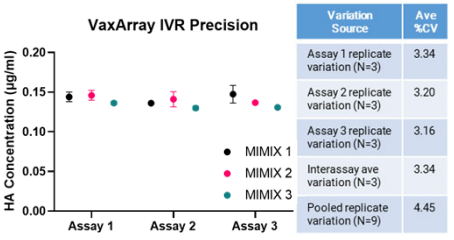


Figure 5: (Left) Formulation screening study of different MIMIX formulations for their release profiles. (Right) MIMIX patch stability study comparison between patches heat stressed at 75°C and control MIMIX patches stored at room temperature.

Assay Precision

With a defined formulation in hand, the HA concentration as released from MIMIX patches was evaluated for assay precision. Inter-assay and intra-assay precision were acceptable with <5% CV.



Variation Source	Ave %CV
Assay 1 replicate variation (N=3)	3.34
Assay 2 replicate variation (N=3)	3.20
Assay 3 replicate variation (N=3)	3.16
Interassay ave variation (N=3)	3.34
Pooled replicate variation (N=9)	4.45

Figure 6: Precision evaluation (intra-assay, inter-assay) of 3 MIMIX patches in 3 replicates per sample per assay

Conclusions

- Superior assay sensitivity established the VaxArray Platform as the preferred in vitro potency assessment for MIMIX patches.
- Stability-indicating use is supported by reduced heat-stressed recovery, and formulation excipients do not interfere with the assay results.
- Rapid formulation assessment enabled development of the target product profile as quantified through antigen release.
- The monovalent H1 assay measured the identity, integrity, and quantity of H1N1 released from the MIMIX microneedle patch.

Multivalent assays to simultaneously measure H1, H3, B/Victoria, and B/Yamagata in a quadrivalent flu vaccine could also be employed, along with multivalent assays for the neuraminidase (NA) component of microneedle influenza vaccines.

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