



TECHNICAL PAPER

ADVANCING ANTICOAGULANT DELIVERY WITH TRANSDERMALS

Enhancing patient compliance and steady-state therapeutic efficacy with weekly apixaban patches

INTRODUCING ARx

ARx is a trusted, full-service partner specializing in advanced drug delivery systems that enhance control of drug release, bioavailability, and patient experience. As pioneers in polymer science and alternative dosing strategies, we push the boundaries of therapeutic potential across oral, mucosal, and transdermal applications. Collaborating with pharmaceutical companies, we create patient-friendly solutions to deliver what's possible, one product at a time.

THE CHALLENGE

Eliquis® (apixaban), a direct factor Xa anticoagulant, is currently available as a twice-daily oral medication in 2.5 mg and 5 mg strengths. While effective, this dosing regimen can present compliance challenges due to its frequency. The oral form also causes fluctuating plasma levels. A weekly transdermal delivery system for apixaban could offer a more convenient, steady-state solution that minimizes the need for frequent dosing, reducing its variability.

THE METHOD

ARx developed a weekly transdermal patch (global patent application pending) for apixaban and conducted rigorous in vitro permeation studies. Franz diffusion cells with human cadaver skin (equipped with jackets for temperature control) were used to measure the skin permeation rate (flux) over time. They were analyzed via UPLC-UV for accurate drug concentration profiling. The lead formulation was tested with six different skin donors, producing 42 replicates to ensure reliable data.

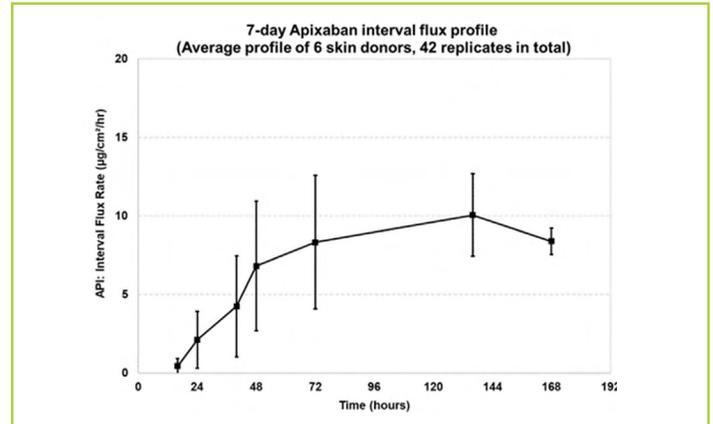
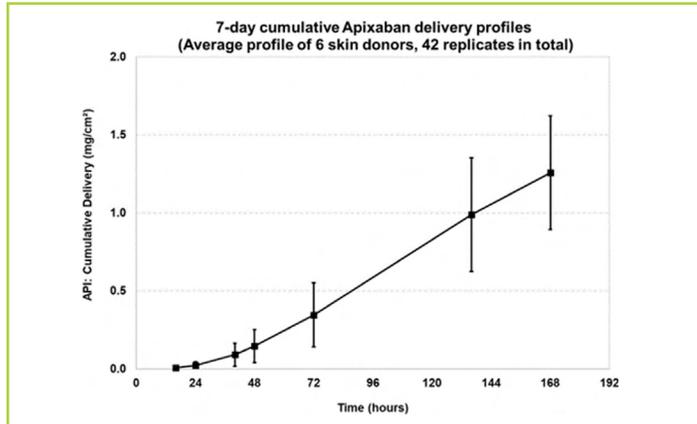
The following experimental parameters were kept throughout the studies:

- **Receiver Solution Replacement:** Franz cells were replenished after each sampling to ensure accurate concentration readings.
- **Permeation Analysis:** Drug concentration was monitored over time to establish cumulative and steady-state permeation profiles.
- **Stability Testing:** Preliminary stability studies confirmed consistent apixaban release profiles, reinforcing the patch's reliability in maintaining therapeutic delivery over time.
- **Skin Irritation Testing:** Rabbit skin studies showed a Primary Irritation Index (PII) of <1, indicating minimal immune response.



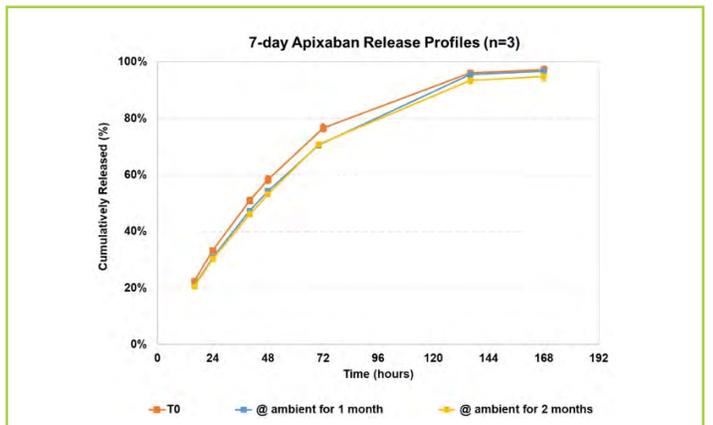
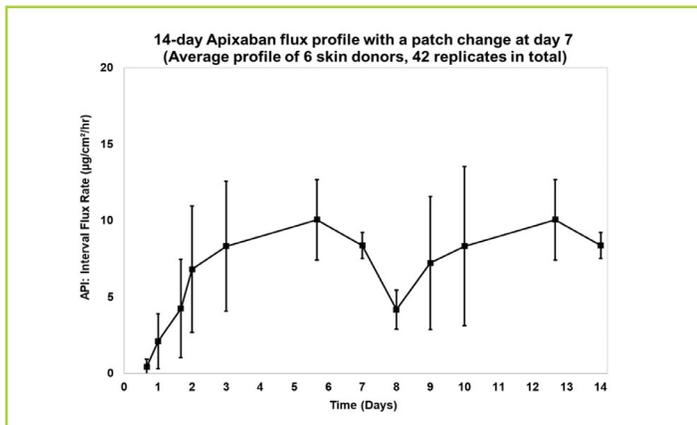
THE RESULTS

The apixaban transdermal patch achieved an average 7-day flux rate of 7.5 $\mu\text{g}/\text{cm}^2/\text{h}$, supporting a patch size of less than 40 cm^2 .



Trough flux analysis, simulating weekly patch changes, showed an average trough flux of 4.2 $\mu\text{g}/\text{cm}^2/\text{h}$, aligning with the minimum therapeutic plasma concentration (C_{min}) achievable through oral dosing (49.6 ng/ml).

Preliminary stability studies confirmed that the apixaban release profiles remained consistent, demonstrating the patch's ability to deliver drug therapy over time.



THE BENEFITS

The weekly apixaban transdermal patch offers significant advantages over traditional oral dosing. By simplifying dosing to just once a week, the patch improves patient compliance, making it easier for patients to maintain consistent therapy compared to the twice-daily tablets. The transdermal system also provides more stable plasma concentrations, avoiding the fluctuations seen with oral dosing.

Additionally, the patch bypasses the gastrointestinal tract, potentially reducing the risk of side effects like nausea and GI bleeding while avoiding first-pass metabolism to potentially increase bioavailability. In the event of adverse reactions, the patch can be removed immediately, halting drug administration and enhancing patient safety.

CONTACT

For more information about ARx's transdermal apixaban delivery system, **please contact:**

Megan Greth,
Director of Business Development and Sales
✉ mgreth@arglobal.com | ☎ (717) 818-4212

James Hoberg,
Director, Strategic Business
✉ jhoberg@arglobal.com | ☎ (717) 680-3823

Chad Harris,
Sr. Business Development Executive
✉ cdharris@arglobal.com | ☎ (717) 680-2750

Haider Cheema,
Senior Business Development Executive
✉ hcheema@arglobal.com | ☎ (717) 688-2879

