ImQuest BioSciences

ImQuest BioSciences, a leading provider of preclinical research services in infectious disease, cancer, biologics, immunology and formulation has a proven track record in providing the support required to effectively move compounds from the discovery phase through to preclinical IND-enabling studies for human clinical trials. Our senior management has over 35 years of combined experience both the commercial and industrial environments.

Unique Capabilities

Our expertise is deeply founded in core scientific capabilities in virology, microbiology, cell biology, molecular biology, cancer biology and assay development - ImQuest has the flexibility, resources and scientific creativity to speed drug development and effectively evaluate new and novel therapeutic products in a highly customized and consultative fashion.

Our Therapeutic Areas

- Infectious Disease
- Cancer
- Biologics
- Immunoassay
- Formulation
- Topical Microbicides

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With the increasing number of novel and specialized drug molecules being developed in the market, traditional delivery methods and standard formulations are becoming less effective in meeting the pharmaceutical demands of these new compounds. In addition, user compliance can have a significant effect on the success of a therapeutic intervention. Missed doses resulting from forgetfulness, or perceived inconvenience by the user, can have serious consequences on the overall therapeutic effect. Formulations that consider these facts are likely to prove advantageous to both the user and the manufacturer. Additionally, in combating disease in a worldwide market, varying cultural preferences will play a factor in product formulations. Formulations successful in one market may not be acceptable in other markets. This is particularly true in combating sexually transmitted diseases where sexual norms and preferences vary widely geographically and culturally. Traditional topical formulations used in the treatment of sexually-transmitted diseases have generally taken the form of gels and creams. Aside from the financial costs of applicators, container costs, bulk shipping costs, and the cost of manufacturing, these formulations have not been universally well-received due to concerns of messiness, leakage and concealment. It is this need for improved formulations in the prophylaxis of sexually transmitted diseases that the development of therapeutic patches and films is focused.

Polymeric Delivery using Films and Patches

Solid dosage forms such as polymeric films are one of the emerging technologies generating significant interest in drug delivery. Films are capable of addressing a wide range of drug delivery needs and can be formulated into a quick-dissolving dosage form to provide rapid topical delivery to the area of interest. Films can also be formulated into patches which can provide controlled release of drug over extended periods of time.

ImQuest BioSciences has the capabilities to formulate polymeric films and patches with a wide array of compositions and characteristics through either solvent casting or extrusion. Solvent casting is a low heat manufacturing process that can accommodate sensitive drug compounds. The active pharmaceutical ingredient (API) and excipients, present as a polymeric slurry, are spread and dried to manufacture the film or patch. Extrusion requires a more robust API and excipient recipe; however, extrusion technology is more readily available worldwide and may reduce the cost of manufacturing.

Film batches are formulated to meet the specific requirements of the API. The ability to generate small volume films allows an iterative approach to formulation optimization with minimal requirement for drug. Many attributes must be considered in the development of a successful film, such as physical size, strength, disintegration time, dissolution time, hygroscopy, content uniformity, stability, as well as specific attributes unique to the particular formulation. Presented below are two "case studies" of film-based formulations in development that highlight the capabilities of ImQuest BioSciences to develop and evaluate polymeric solid dosage forms for drug delivery and release as a formulation in a rapid, efficient and cost-effective manner.

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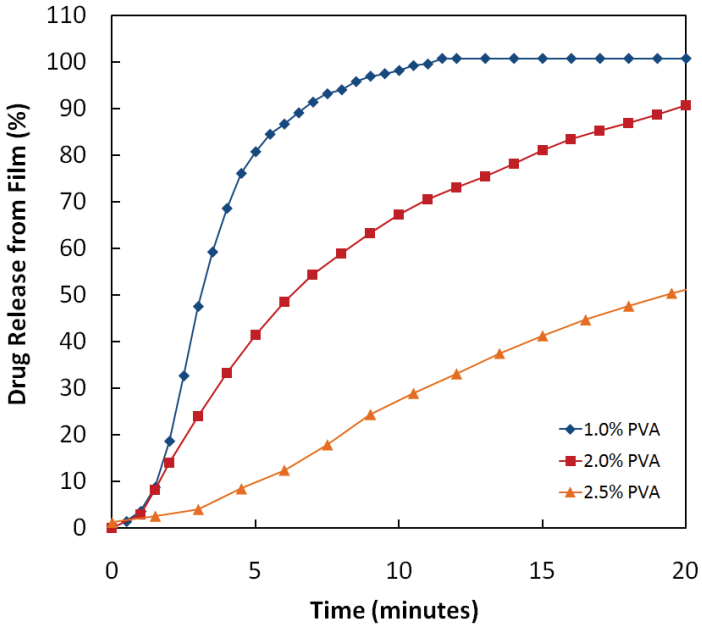
Rapid Topical Drug Delivery - Films

Quick-dissolving films have become an increasingly attractive method of user-controlled drug administration, and are most commonly experienced as over-the-counter films such as film breath strips. Polymeric films are water soluble solid delivery vehicles that quickly disintegrate and release drug upon the introduction of water to the surface. Therefore, films are not limited to oral administration and can be used to topically deliver drugs to any moist surface including vaginally or rectally, as in the prophylaxis of sexually transmitted diseases. Topically applied microbicide films, used as a prophylaxis for infection by HIV and other viruses, quickly deliver the drug to the areas of infection in a bolus dosage amount. Easily and inexpensively manufactured, films are capable of delivering a wide range of drug types from large macro-molecules to small molecule drugs. Additionally, the unique dosage form of films is easily concealable, essentially undetectable and its use does not disrupt normal activity which may increase product acceptability and compliance in the regions of world where therapeutic intervention is most needed.

Manufactured from excipients and materials approved for vaginal use, semi-transparent, flexible, smooth films can be used to deliver microbicides for protection from sexually transmitted diseases and complement vaginal rings and gels as a dosage form. The physical properties of the films are highly dependent upon the excipient composition and can be optimized to suite individual development needs. The films currently under development microbicide delivery have a tensile strength between 670 kg/m^2 and 5500 kg/m^2, a puncture strength between 0.75 kg and 4.0 kg and contain 1.25% (w/w) of anti-HIV compound. The films maintain a high degree of drug content uniformity with a coefficient of variability in the drug concentration of only 6% throughout the film. The films visually disintegrated within 10 minutes with a near complete release of drug from the film matrix. The delivery of drug is also highly dependent upon the specific composition of the film. For example, by increasing the amount of polyvinyl alcohol (PVA) in the film, the rate of release of drug from the film can be significantly altered, and subsequently controlled to individual requirements (Figure 1). The quick-dissolving vaginal microbicide films were evaluated for toxicity against normal vaginal flora

Figure 1



Lactobacillus and vaginal epithelia using *in vitro* cell-based assays and were found to be non-toxic. Drug incorporation into film formulation also did not change the activity of the anti-HIV compound as compared to solution-formulated drug. Additionally, with the near complete release of drug from this thin dosage form, films provide a more efficient method of drug delivery than vaginal gels allowing less drug per dose to be used to achieve the same level of protection. Finally, films have demonstrated no product or API degradation under regular and accelerated environmental conditions for 1 year when packaged into individual pouches and stored at either 30°C or 40 °C.

Controlled Drug Delivery - Patches

In contrast the rapid, bolus dosing achieved with thin films, the drug delivery characteristics of patches result in long-term controlled drug delivery. With conventional dosage forms, such as oral and parenteral, the release rate of drug results in a "peak and valley" profile where immediately after dosing there is a sharp increase in the plasma level of the drug followed by a drop to levels often below the therapeutic threshold. In many therapeutic interventions sustained exposure is viewed as more desirable than the cyclic exposure that results from bolus dosing, and methods to minimize fluctuation in drug plasma levels has led to the development of controlled drug delivery systems. Patches can be formulated to deliver sustained release of drug over extended period of time and can increase patient compliance. Patches are intended for external application, such as transdermal delivery, and as such are more robust than the topical films designed to be used internally. There are several patch designs, including adhesive – where the adhesive layer responsible for maintaining patch-skin contact is also responsible for drug release; reservoir – where a liquid layer separate from the backing and adhesive is responsible for drug release; vapor – where the adhesive also releases a vapor drug; and matrix – the most popular design where the drug solution or suspension is incorporated into patch polymer matrix, that can be tailored to drug of interest. While commercial success in transdermal patches has largely occurred in the therapeutic areas of hormone therapy and addiction treatment, patch-based formulations are in principle applicable to most therapeutic applications.

Patches can be formulated to deliver sustained release of drug over extended period of time

ImQuest is developing a transdermal patch to delivery an HIV therapeutic drug for extended period of time in a single dose. Formulated with a mixture of hydrophobic and hydrophilic polymers, matrix patches were manufactured in a casting method similar to topical films, resulting in a robust, smooth, translucent to opaque patch that can be cut to various sizes dependent upon the requirements. Similar to the topical films, the physio-chemical characteristics of the patches are dependent upon the composition of the patch. The release rate of drug is highly dependent upon the hydrophilic content of the patch where increased hydroscopicity typically increases the rate of drug release and patch flexibility, but reduces drug stability. Patches maintain a high drug content uniformity similar to thin films with a coefficient of variation in API concentration of 5% throughout the patch. Unlike thin films, which are designed to completely disintegrate to deliver drug, the patches release drug via transport through the patch polymer matrix resulting in a much slower release of drug. Data from four individual patches showed little variability in the release of drug

Figure 2

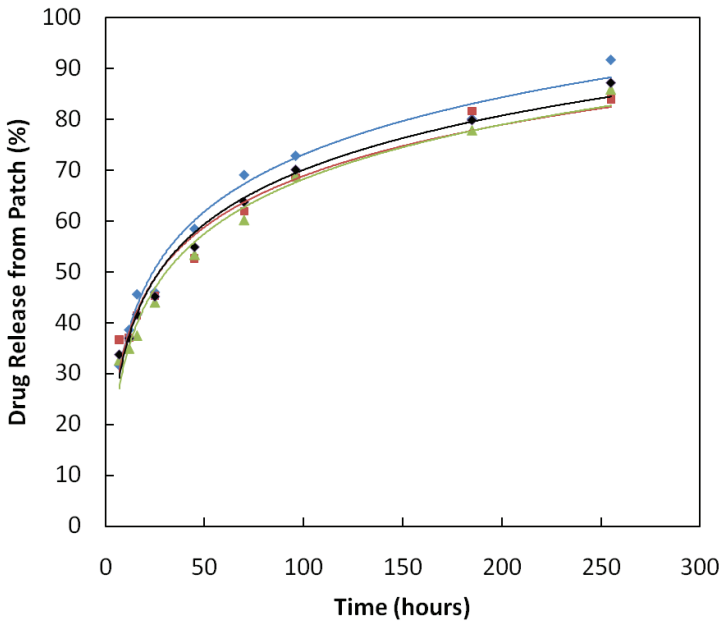


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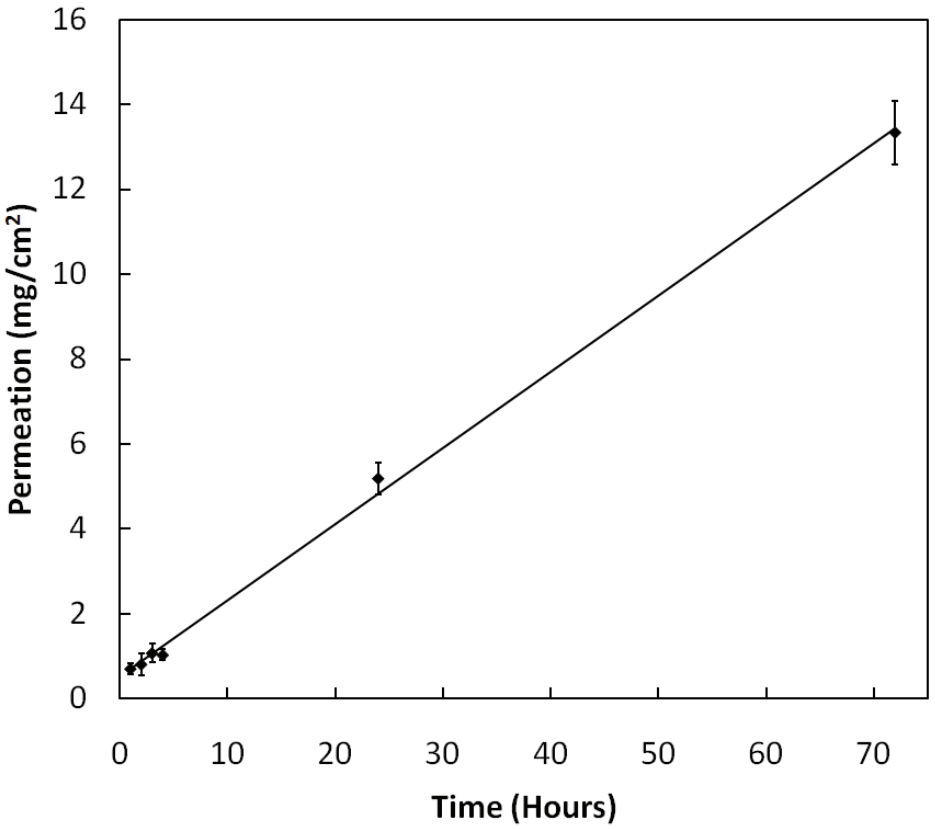
Figure 3



over ten days (Figure 2). Release from the patch is only the first stage of drug delivery; the second is the ability to deliver the drug though the skin. While the characteristics of the API are most important factors when considering skin transport, the patch is a necessary component in the analysis and provides the proper delivery platform for the API. *In vitro* skin membrane assays with the HIV therapeutic transdermal patches resulted in a controlled linear permeability profile of the drug through a surrogate epidermal membrane of 13.34 mg/cm^2 over 72 hours (Figure 3). As with thin film formulations, patches have not been observed to alter the stability or the efficacy of the drug delivered. Patches containing anti-HIV therapeutic demonstrated no product or API stability issues when packaged in individual pouches under various environmental conditions for over 3 months.

The ImQuest Advantage - Customization

In addition to traditional formulation science, ImQuest BioSciences has significant capabilities in developing novel formulation solutions for your product including polymeric films and patches and nanoparticle-based formulations that can be targeted to the therapeutic site. We understand our formulations and assays must reflect the uniqueness of each compound to fully realize the potential of the drug. We listen to your drug development and formulation needs and customize our strategies to fit your needs. Our iterative approach to formulation development coupled with our in-house drug development services can expedite the "discovery to clinic" progress of your drug product.