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# A Pharmacokinetic Study of Two Oxybutynin Formulations with Transient Heat Exposure

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## PURPOSE

Heat sources such as heating pads and electric blankets can potentially alter the drug delivery profile from formulations applied to the skin. Local application of heat has been shown to enhance cutaneous blood flow, skin permeability, and drug solubility followed by increased drug absorption. The purpose of the pharmacokinetic (PK) study was to evaluate the influence of elevated temperature on the transdermal delivery of oxybutynin from two formulations (Product A: Oxytrol® for Women transdermal delivery system, TDS (3.9 mg/24 hours) and Product B: Gelnique® transdermal gel, 10%). For product A, the effect of heat on transdermal permeation was evaluated after steady state was achieved and immediately after removal of TDS. For product B, the effect of heat was evaluated immediately after application and later in the wear duration.

## METHOD(S)

An open-label, four-way crossover clinical PK study in healthy volunteers using two oxybutynin products was performed. Heat was applied using a heating pad for 1.5 h, with the target skin temperature of 42 ± 2°C. Two separate study arms were completed for each product. The PK profiles in the absence of heat application were characterized (sessions I-product A and II-product B). For product A, heat was applied at 24 h (early heat) and at 30 h (late heat) post TDS application (session III). For product B, heat was applied at either 0 h (early heat) and 7 h (late heat) post gel application (session IV). Product A was removed at 30 h and product B was removed at 12 h post application during the respective study sessions. For product B, the skin surface area of gel application was covered with an occlusive backing film during sessions II and IV for the 1.5 h time period corresponding to heating pad application. Skin temperature was monitored using Novatemp® skin sensors series 400. Blood samples were drawn at pre-determined time points throughout the duration of the study. Serum samples were analyzed to determine oxybutynin concentrations using a validated LC-MS/MS method.

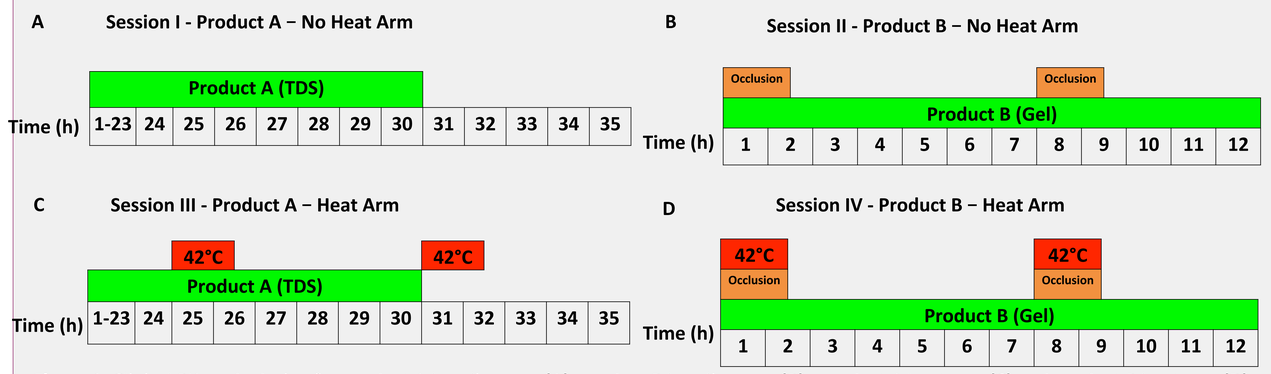


**Figure 1.** Clinical PK study design for product A baseline arm **(A)**, product B baseline arm **(B)** , product A heat arm **(C)** and product B heat arm **(D)**.

## RESULT(S)

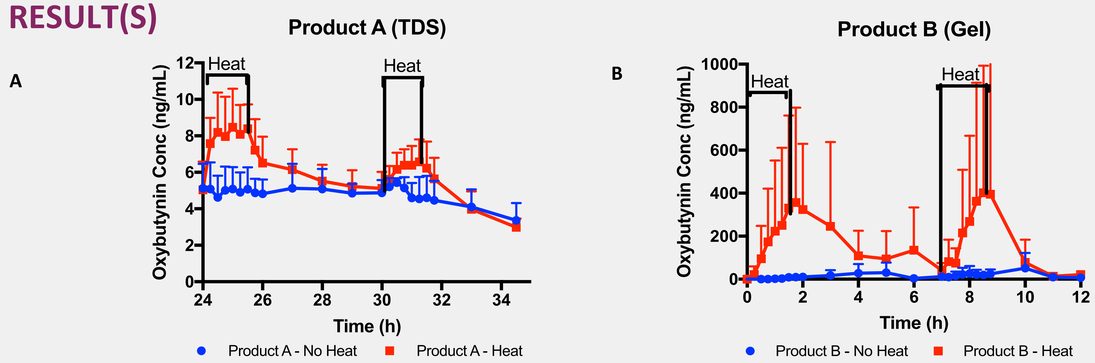


**Figure 2.** Serum oxybutynin concentrations obtained after applying product A **(A)** and product B **(B)** with and without transient heat exposure (B), n=3, mean ± SEM.

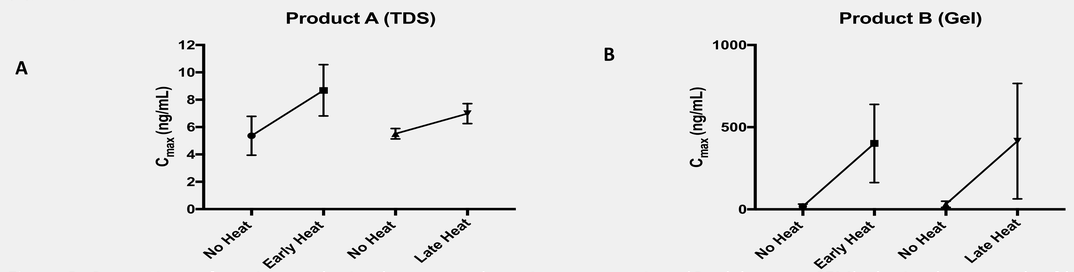


**Figure 3.** Comparison of maximum obtained serum oxybutynin concentrations ($C_{max}$) (mean ± SEM) obtained as a result of heat exposure with $C_{max}$ in the absence of heat application in baseline study arm for Product A **(A)** and Product B **(B)** .

## CONCLUSION(S)

- Based on data obtained from three subjects, when exposed to an elevated temperature *in vivo*, both products (Gel and TDS) exhibited an increase in the oxybutynin levels relative to its baseline levels at normal (32 ± 2°C) skin temperature conditions.
- The elevated oxybutynin levels did not return to baseline levels immediately after the external heat source was removed.
- The systemic oxybutynin levels were very high following heat exposure for product B. Hence the study design for product B (sessions II and IV) was modified to eliminate heat exposure.
- The purpose of the new study design is to evaluate the effect of occlusion on product B. The skin surface area of gel application will be covered with an occlusive backing film during the 3 h time period from 7 – 10 h for session 4. The PK profile in the absence of occlusion will be characterized during session 2.

## ACKNOWLEDGMENT

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