

BioFreeze Ingredient Ilex Increases Skin Blood Flow

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Background: BioFreeze gel is clinically utilized as a topical analgesic to relieve pain through gate-control theory. Our lab has previously demonstrated that illex, a skin conditioning component of BioFreeze, induces cutaneous vasodilation, likely through endothelium-derived hyperpolarizing factors. Menthol, which causes the cooling sensation of BioFreeze, did not alter skin blood flow (SkBF). However, this previous work covered the gels in heated water, which may alter vasoactivity. Purpose: The purpose of this experiment was to investigate whether or illex would increase SkBF without controlled skin temperature or contact of water with the gel. The aim of this double blind, placebo controlled study was to examine the separate and combined effects of menthol and illex on microvascular SkBF after topical application. Methods: On 4 separate days, 10 healthy young subjects (5 men, 5 women, age 23 ± 2 years) were treated with 1ml of either (1) menthol, (2) illex, (3)

placebo, or (4) BioFreeze gel applied to the ventral forearm. To prevent gel evaporation, the ventral forearm was covered with plastic wrap throughout the entirety of the experiment. Cutaneous blood flow, expressed as red blood cell flux, was measured using laser speckle contrast imaging. Data were collected for 15 minutes before gel application and until a 15 minute stable plateau in SkBF was obtained post gel application. Cutaneous vascular conductance (CVC) was calculated as red blood cell flux divided by mean arterial pressure to normalize for changes in blood pressure. Results: There was no significant change in CVC following the application of the menthol ($\Delta\text{CVC} -0.01 \pm 0.08$) or placebo ($\Delta\text{CVC} 0.09 \pm 0.174$) gels from baseline (both $p > 0.05$). CVC was increased significantly after the application of illex and BioFreeze gels (Ilex: $\Delta 2.428 \pm 0.325$; BioFreeze $\Delta -0.006 \pm 0.082$, both $p < 0.001$). Ilex and BioFreeze elicited significant vasodilation of the cutaneous microvasculature compared to placebo (both $p < 0.001$). Conclusions: These data suggest that it is possible for illex and Biofreeze to be effective outside of the research setting and provides proof of concept for further study of illex as a potential treatment for disease mechanisms such as peripheral neuropathy.