

# Enhancing Transdermal Delivery of Highly Lipophilic Drugs: *Insights from Cannabinoid-Based Cream Formulations*

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## PURPOSE

Morphine and its derivatives, including diamorphine (Heroin) and methadone, are extensively researched for topical analgesia in wound care. Despite their efficacy, the adverse effects and addiction potential have led to a search for safer alternatives. In response, this study pioneers the use of medical cannabinoids, namely Delta-9-tetrahydrocannabinol (THC) and Cannabidiol (CBD), in specially formulated creams for pain relief and wound healing. Focusing on conditions such as Pyoderma Gangrenosum, Acne Vulgaris, Atopic Dermatitis, Eczema, and rheumatic and musculoskeletal pain, our formulations are poised to offer a significant therapeutic advantage.

## METHODOLOGY

The Finite Dose In Vitro Permeation Test (IVPT) model was utilized to assess percutaneous absorption through human torso skin. Skin absorption kinetics were measured using six replicates from six donors over 48 hours, employing the Phoenix RDS Automated Diffusion system. Cannabinoid analysis was conducted via the Waters Xevo TQ-S Acquity UPLC-MS/MS system, incorporating deuterated standards for precision. Parameters analyzed included total absorption, penetration rates and extents, and distribution within the skin. Pre-study integrity checks of each skin section involved assessments of transepidermal electrical resistance (TEER) and transepidermal water loss (TEWL), ensuring the reliability of permeability data.

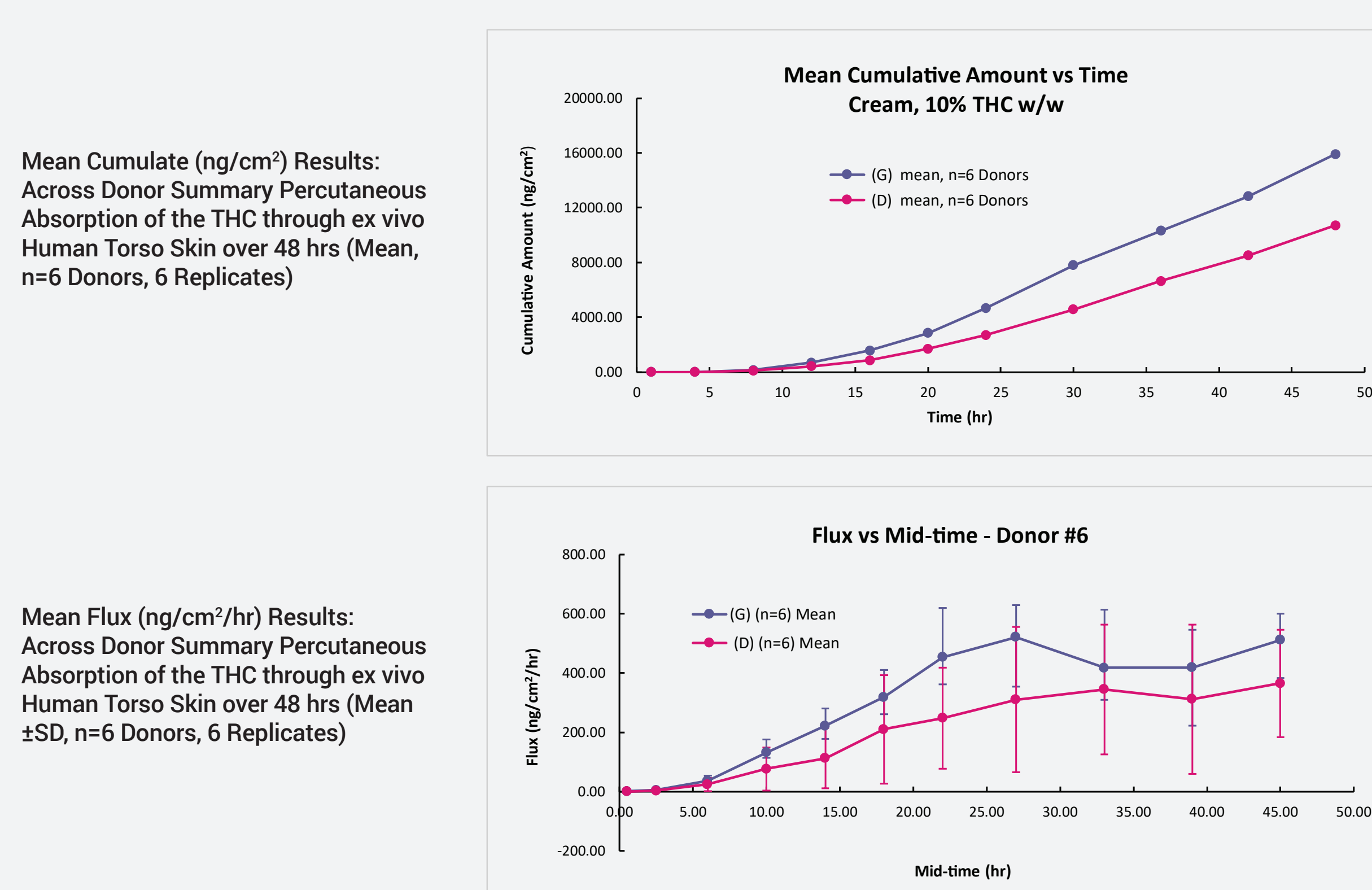
## RESULTS

The study highlights the challenges in delivering highly lipophilic cannabinoids across the skin, necessitating innovative carriers like nanocomposite polymeric multi-layered lipid vesicles and liposomes for improved bioavailability. Despite diverse technological foundations, the four formulations tested showed uniform effectiveness, particularly in sustained transdermal delivery. In vitro absorption data confirmed the transcutaneous feasibility of cannabinoids, with Delta-9-THC showing a peak delivery rate ( $J_{max}$ ) of 350-500 ng/cm<sup>2</sup>/hr.

## CONCLUSION

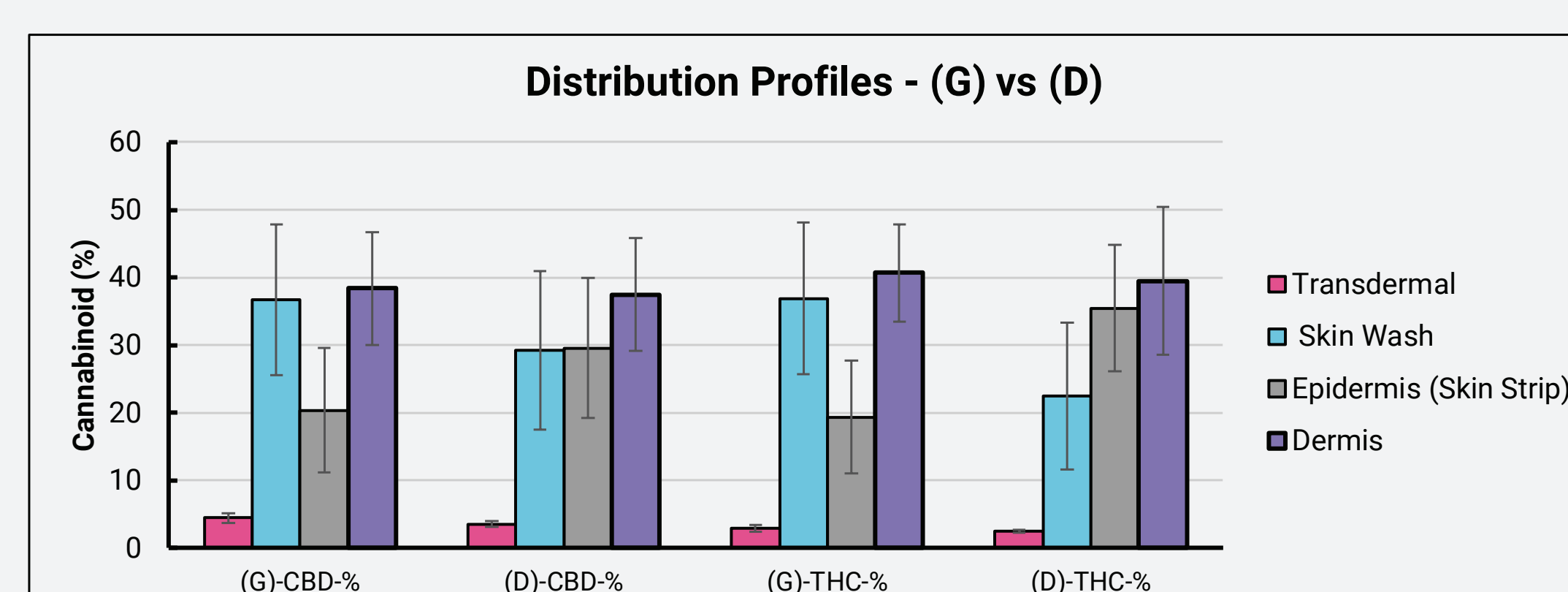
In vitro permeation studies proved invaluable for formulation optimization, mirroring in vivo results, and advancing the preclinical development process. This research marks a significant step towards the targeted delivery of lipophilic cannabinoids, encouraging further investigation into advanced topical delivery systems. The findings support the potential for routine evaluation of medical cannabis products, contributing significantly to therapeutic range determinations for conditions requiring potent drug delivery via the skin.

**Fig.** IVPT absorption profiles of Transdermal Cream Formulations (G) -third party and (D) -Diteba Inc. 10%-THC (w/w)



**Table.** Distribution profiles into the Skin layers of Transdermal Cream Formulations 5% THC, 5% CBD (w/w)

Item	THC, CBD Mean Value of Formulations (D) and (G)			
	(G)-CBD-%	(D)-CBD-%	(G)-THC-%	(D)-THC-%
Transdermal	4.5	3.6	3.0	2.5
Skin Wash	36.7	29.3	36.9	22.5
Epidermis (Skin Strip)	20.4	29.6	19.4	35.5
Dermis	38.4	37.5	40.7	39.5



## ABOUT DITEBA Inc.

Since 2005, Diteba Inc. has been a leader in IVRT/IVPT research, contributing to numerous successful ANDA submissions. Our commitment to advancing drug delivery technologies underscores our role in pioneering therapeutic innovations for pain management and inflammation.