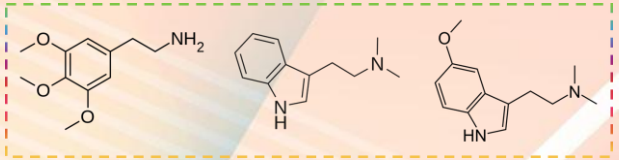
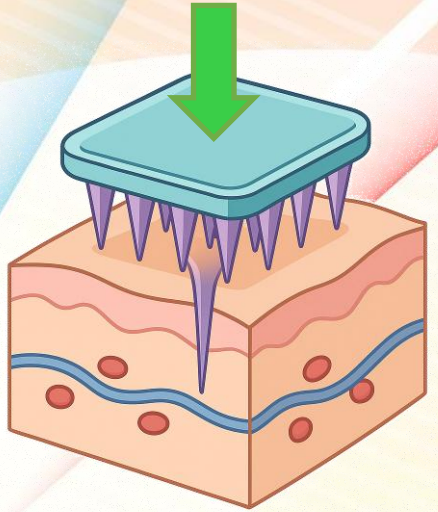
Pharmacokinetics and Skin Permeation of Psychedelic Drugs Delivered by Hydrogel-Forming Microneedles





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CRS 2025 ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
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NEXT-GENERATION DELIVERY INNOVATIONS

Sections

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Psychedelics

WHAT ARE PSYCHEDELIC DRUGS?

They've been used for a long time - more than 10,000 years.

They are substances that cause users to TO TRIP:

To hallucinate and feel an extreme sense of euphoria.

They alter users' thoughts and feelings, and awareness of their surroundings

Trips typically last about 6-12 hours

The most common psychedelics are:

LSD (acid) | Magic mushrooms | Ayahuasca (DMT) | Mescaline

PSYCHEDELICS ARE TYPICALLY DRANK IN LIQUIDS, EATEN, OR SMOKED

Psychedelics

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Prehistoric Era

Use of psychoactive plants in ritual and healing by Indigenous cultures (e.g., psilocybin mushrooms, ayahuasca).

1943

Synthesis and first self-experimentation of LSD by Albert Hofmann.

1950s–1960s

Clinical research for mental health (e.g., depression, alcoholism). Term "psychedelic" coined by Humphry Osmond (1957).

1971

UN Convention on Psychotropic Substances → Criminalisation and end of most clinical research.

1990s

"Psychedelic renaissance" begins. Multidisciplinary Association for Psychedelic Studies founded.

2006

Johns Hopkins publishes landmark study on psilocybin and mystical experiences

2020–Present

Renewed clinical trials for depression, PTSD, addiction. Increasing interest in microdosing and novel delivery route.

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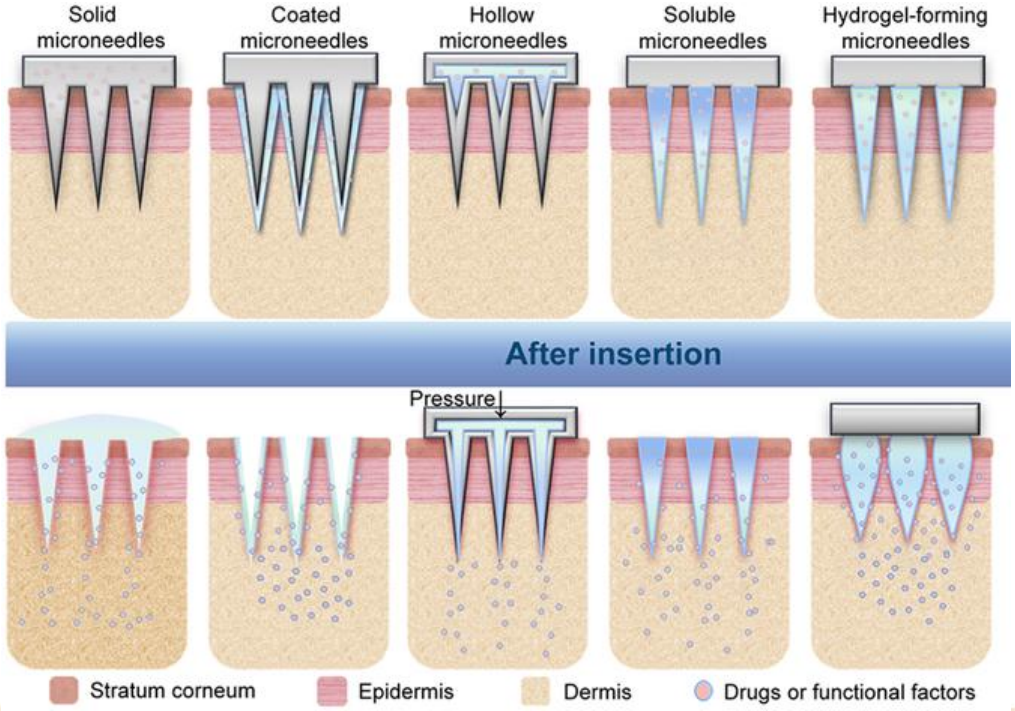
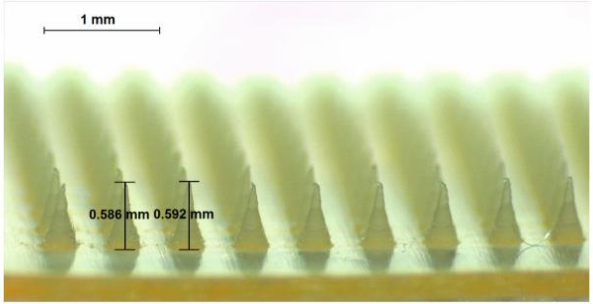
Microneedles





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Microneedles

Bypasses First-Pass Metabolism

- Avoids hepatic degradation, enhancing bioavailability

Minimally Invasive and Painless

- Microneedles penetrate only the stratum corneum, causing little to no pain or bleeding

Controlled and Sustained Release

- Enables precise dose control and prolonged therapeutic effect, ideal for microdosing.

Improved Patient Compliance

- Needle-free, patch-like systems are more acceptable for needle-phobic or chronically treated patients

Reduced Gastrointestinal Side Effects

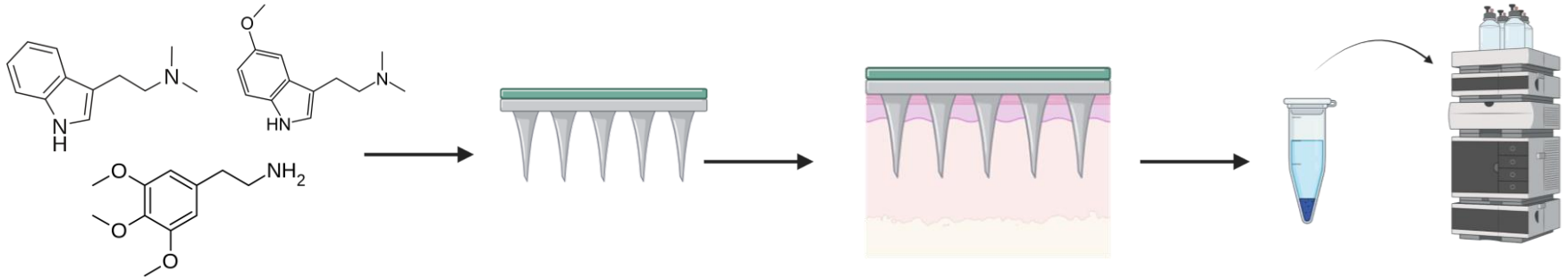
- Avoids irritation, nausea, or food-drug interactions common with oral drugs.

Stable for Sensitive Molecules

- Suitable for drugs that degrade in the stomach or intestines (e.g. peptides, some psychedelics).

Study Aim

The goal is to develop a formulation that is suitable for the transdermal administration of psychedelic compounds at microdose levels. In addition, evaluate the feasibility and therapeutic effectiveness of microneedle-assisted transdermal delivery of psychedelics *in vivo*.



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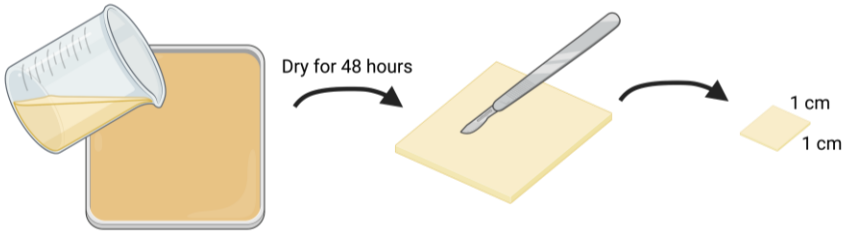
Preparation of hydrogel-forming films



Psychedelic Formulations	Drug (% w/w)	PVA 9-10 kDa (% w/w)	PVP 58 kDa (% w/w)	Glycerol (% w/w)	PEG 400 (% w/w)
DMT-F1	5	20	20	2.5	
DMT-F2	5	20	20		2.5
5-MeO-DMT-F1	2.5	20	20	2.5	
5-MeO-DMT-F2	2.5	20	20		2.5
MES-F1	5	20	20	2.5	
MES-F2	5	20	20		2.5

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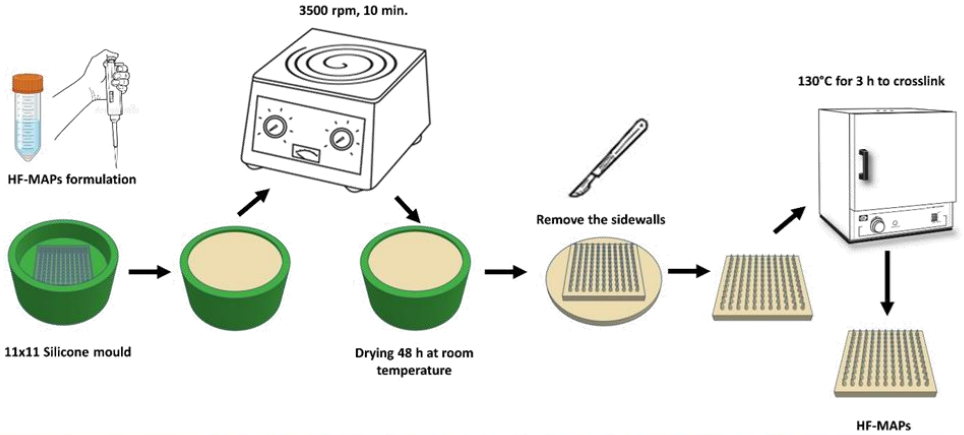
Preparation of hydrogel-forming microarray patches

Component	Concentration (w/w)	Drying condition	Crosslinking condition
PVA 85-124 kDa	15%		
PVP 58 kDa	10%	48 h, RT	3 h, 130 °C
Citric Acid	1.5%		



Characterisation

Results

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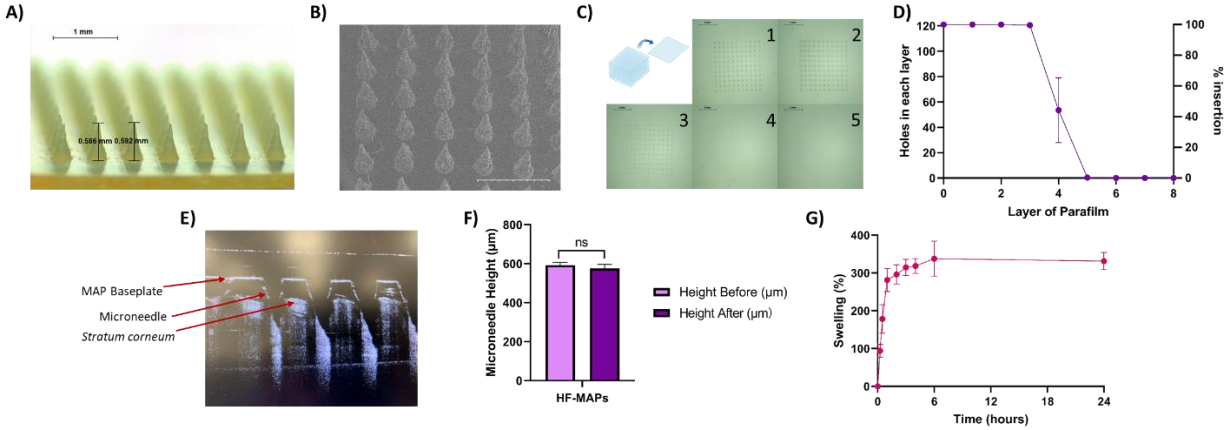

The mechanical characterisation of HF-MAPs are summarised in the figure above. **A)** Digital light microscope images of HF-MAPs (scale bar = 1 mm length). **B)** SEM images for HF-MAP. C) Digital light microscope images of the first five layers of Parafilm® M after the application of 32 N force for 30 s to HF-MAPs. **D)** Insertion depth for HF-MAPs in Parafilm® M layers and percentage of holes created in each layer® (Means ± SD, *n* = 3). **E)** Images of HF-MAPs inserted in full thickness stillborn porcine skin using OCT. **F)** Height reduction of HF-MAPs before and after their insertion (32 N force for 30 s) into eight layers of Parafilm® M. (Means + SD, *n* = 6). **G)** Swelling kinetics profile of hydrogel-forming films in PBS (pH 7.4). (Means ± SD, *n* = 3)

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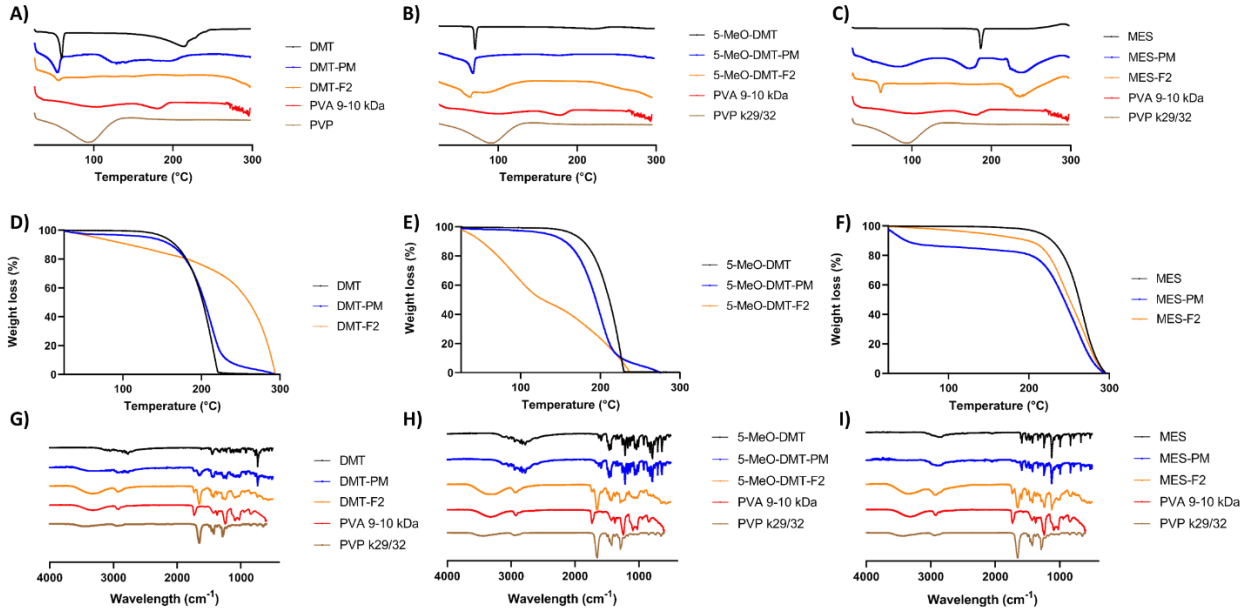
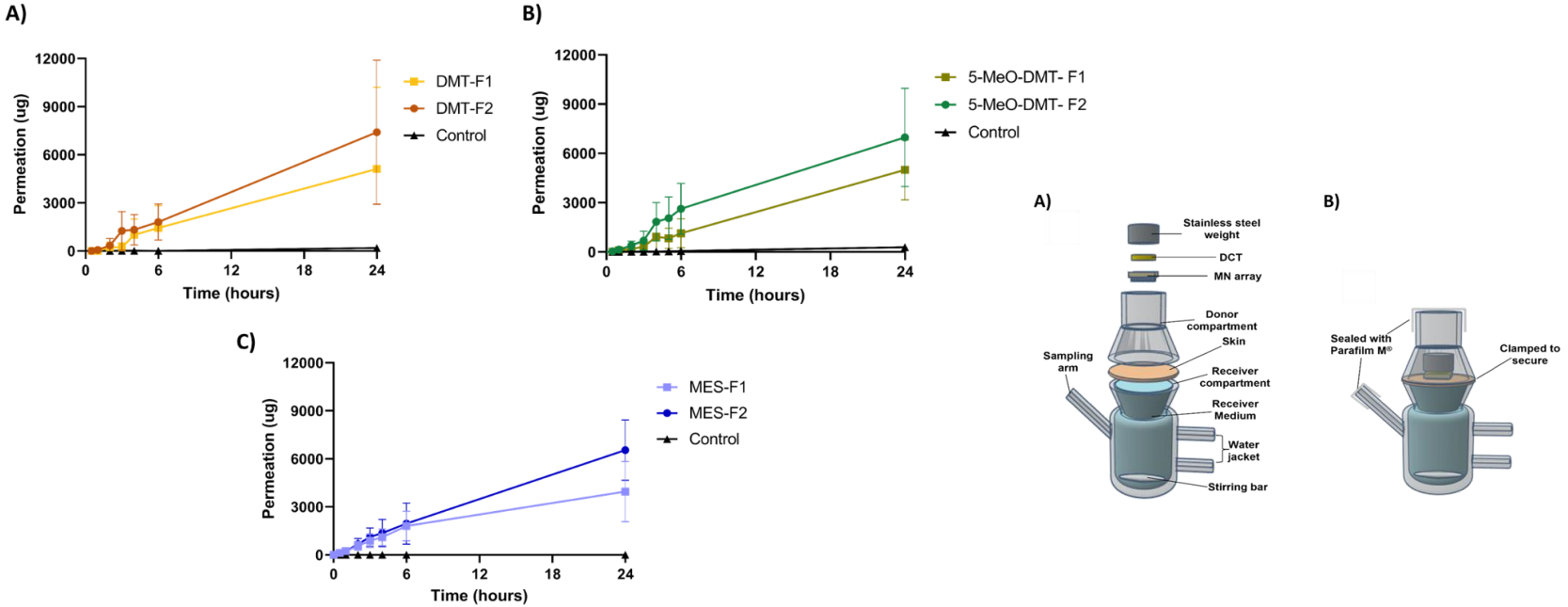
Reservoir DSC, TGA and FTIR analysis



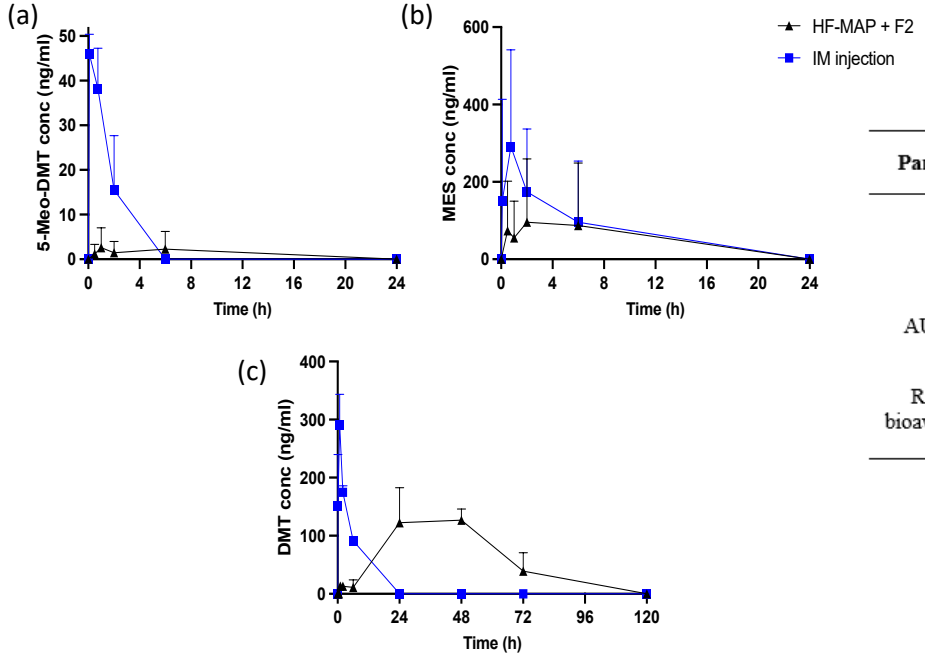
Representative DSC thermograms for psychedelic drugs, related polymers and physical mixtures (PMs) of **A)** DMT. **B)** 5-MeO-DMT. **C)** MES.
Representative TGA thermograms for psychedelic drugs, related polymers and physical mixtures (PMs) of **D)** DMT. **E)** 5-MeO-DMT. **F)** MES.
Representative FTIR spectra for psychedelic drugs, related polymers and physical mixtures (PMs) of **G)** DMT. **H)** 5-MeO-DMT. **I)** MES.

In vitro permeation study



In vitro permeation study using Franz cells setup for A) DMT-F1; DMT-F2 and control. B) 5-MeO-DMT-F1; 5-MeO- DMT-F2 and control. C) MES-F1; MES-F2 and control. Means ± SD $n = 3$.

Pharmacokinetic study



Parameter	Unit	5-Meo-DMT		Mescaline		DMT	
		IM	MAP	IM	MAP	IM	MAP
t_{max}	h	0.08	1	0.75	2	0.08	48
C_{max}	ng/mL	45.93 ± 4.44	4.46 ± 2.57	291.22 ± 250.01	95.52 ± 163.71	291.23 ± 52.14	126.89 ± 19.35
$AUC_{t0\text{-final}}$	ng/mL*h	94.60 ± 26.28	36.72 ± 31.13	1846 ± 1512	1527 ± 1278	1803 ± 53.25	7186 ± 1296
Relative bioavailability (F)	%		6.17 ± 4.36		10.07 ± 0.62		72.43 ± 10.97

Plasma profiles in Sprague Dawley rats following HF-MAP + F2 or IM administration for a) 5 Meo-DMT (Dose: HF-MAP + F2 = 11.70 mg/rat and IM = 2.10 mg), b) MES (Dose: HF-MAP + F2 = 15.63 mg/rat and IM = 1.96 mg/rat), c) DMT (Dose: HF-MAP + F2 = 12.18 mg/rat and IM = 2.22 mg/rat). Means + SD $n = 3$ for 0-24 h and $n = 6$ for 24-120 h

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Conclusions

- ✓ HF-MAPs (hydrogel-forming microarray patches) demonstrated effective microdosing potential for three psychedelic compounds: DMT, 5-MeO-DMT, and MES.
- ✓ In vivo pharmacokinetic analysis in Sprague Dawley rats confirmed the successful systemic absorption of all three psychedelics delivered via HF-MAPs.
- ✓ Notably, DMT delivered via HF-MAPs produced plasma levels comparable to intramuscular administration, supporting its viability for microdosing applications.
- ✓ This study provides the first experimental evidence of a minimally invasive, pain-free transdermal approach for psychedelic microdosing.

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Thank you very much for your attention ! ☺