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Abstract

There is a very high incidence of mental health problems throughout the world, Depression, Post Traumatic Stress Disorder (PTSD), traumas, Schizophrenia, etc. Psychedelics have been in history for a long time now, used by indigenous people for rituals, recreationally by the hippies because of the war ranging on and now, by scientific researchers for the investigation of psychedelic therapy for mental illness. Lysergic Acid Diethylamide (LSD) is a semi-synthetic compound first developed in 1938 by Dr. Albert Hofmann at the Sandoz pharmaceutical company. LSD quickly became recognized for its possible therapeutic effects. Using the therapeutic effects advantage then there have been various anecdotal reports suggesting that repeated use of very low doses of LSD, known as micro-dosing, improves mood and cognitive function.

Transdermal patches are designed to deliver active drugs across the skin into the systemic circulation in a sustained or controlled manner. Using this mechanism, a transdermal patch was designed that uses LSD as an active ingredient for drug therapy as treatment for mental illness with a controlled delivery of micro-doses.

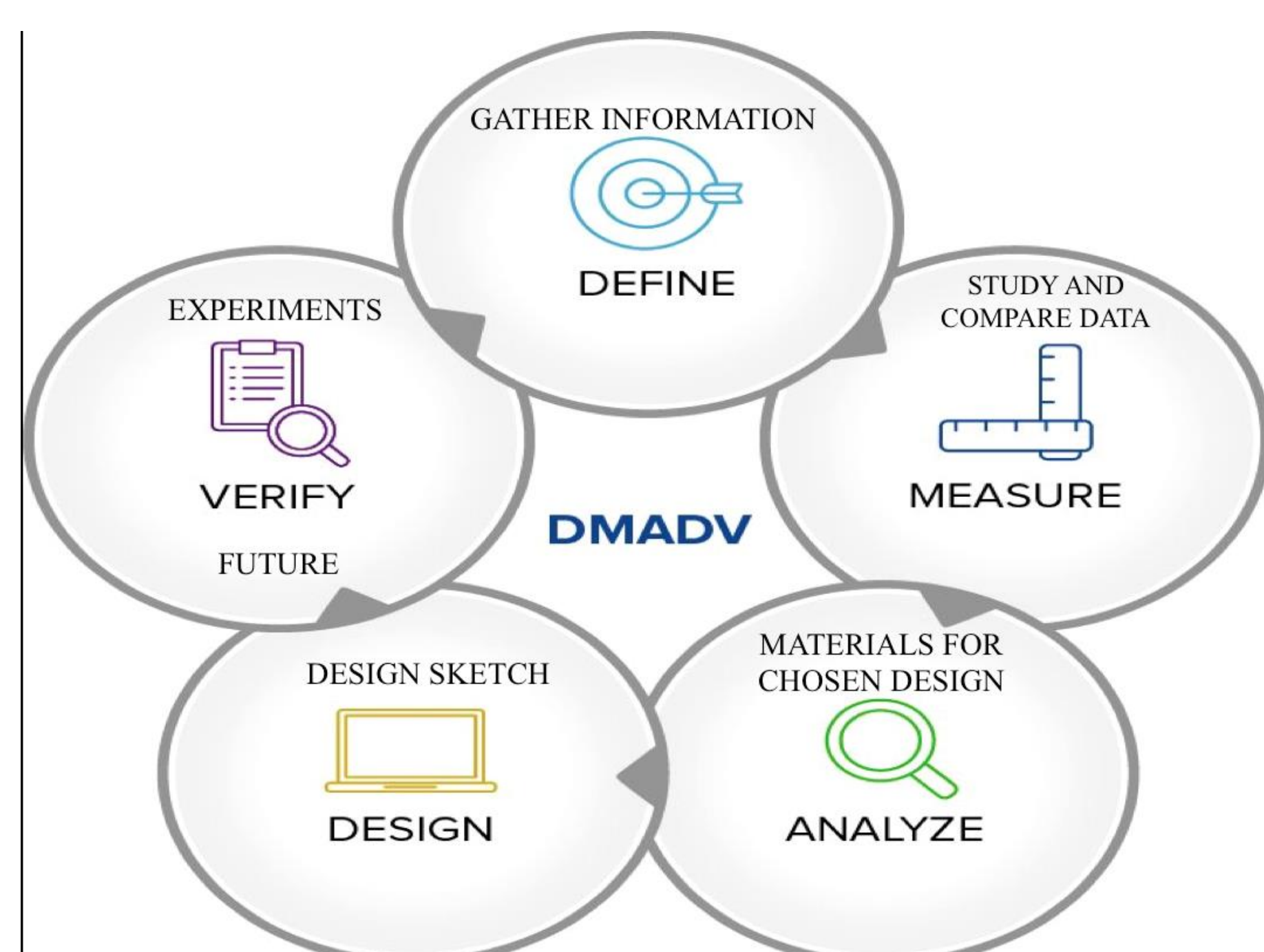
Introduction

Psychedelics have been in history for a long time now, used by indigenous people for rituals, recreationally by the hippies because of the war ranging on and now, by scientific researchers like The Multidisciplinary Association for Psychedelic Studies, for the investigation of psychedelic therapy for mental illness. LSD is a semi-synthetic compound first developed in 1938 by Dr. Albert Hofmann at the Sandoz pharmaceutical company in Basel, Switzerland. After Dr. Hofmann first discovered its effects in 1943, LSD quickly became recognized for its possible therapeutic effects. Transdermal patches are designed to deliver active drugs across the skin into the systemic circulation in a sustained or controlled manner. Using this mechanism, we want to design a transdermal patch that uses LSD as an active ingredient for mental illness drug therapy with a controlled delivery of micro-doses.

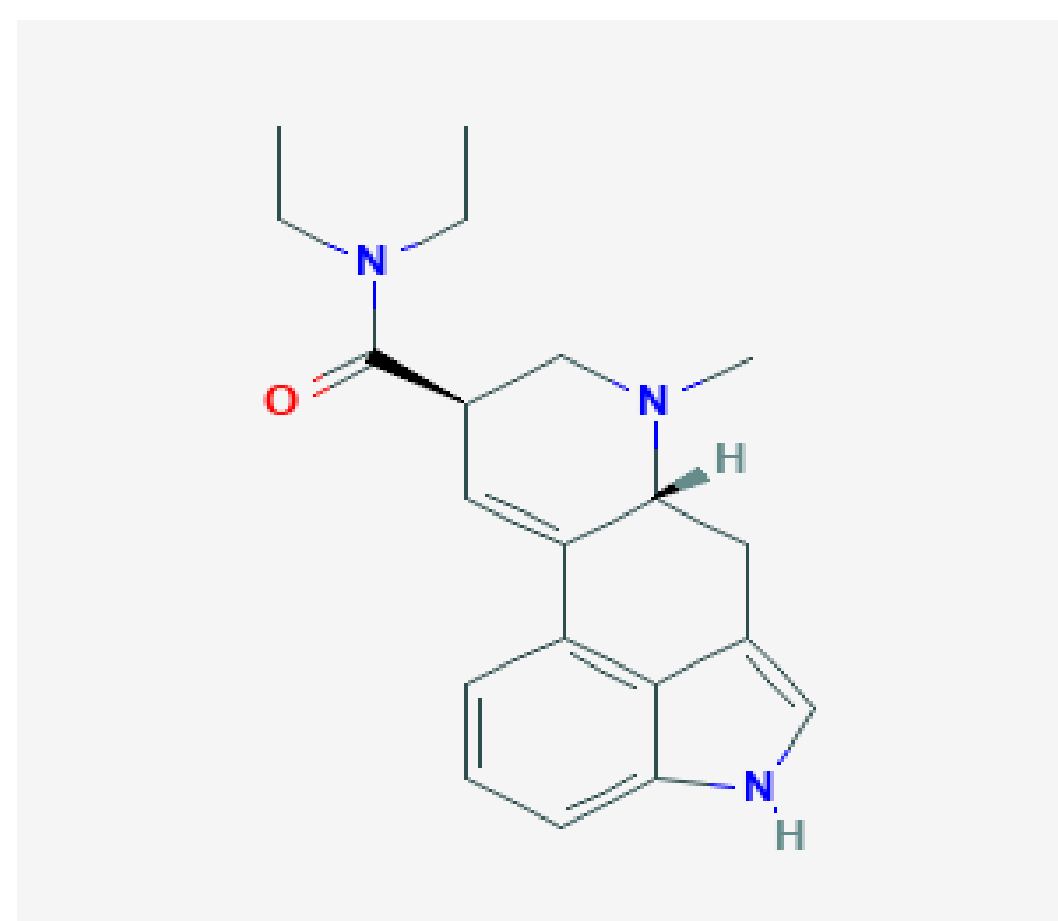
Objective

The main goal of this research is to design a transdermal patch using LSD micro-doses as active drug as mental illness therapy.

Methodology



Lysergic Acid Diethylamide (LSD)



Lysergic Acid Diethylamide or LSD is a synthetic amide of lysergic acid found in a fungus on grains called ergot. LSD has powerful mind-altering effects, usually called hallucinogenic or psychedelic, which is what makes it illegal and a Schedule I controlled substance in the United States and other countries.

LSD in Psychiatry

The experiential effects of LSD include positive aesthetic, psychological, and spiritual transformations. Aesthetically, the effects center on perceptual changes, especially to the visual field, which is intensely enhanced with greater mobility, colorfulness, transiency, luminosity, energy, swelling, vividness, and synesthesia. Psychologically, the effects of LSD include mood changes, particularly feelings of well-being and euphoria; a new and greater awareness of the world and of self; a deeper understanding of human relationships; a transcendence of time and space; and a sense of ineffability. Spiritually, the effects of LSD include a sense of rebirth; a sense of encounters with divinity; a sense of the world as sacred; and a sense of communion, unity, and non-duality.

LSD micro-doses in Psychiatry

Using the therapeutic effects advantage then there have been various anecdotal reports suggesting that repeated use of very low doses of lysergic acid diethylamide (LSD), known as micro-dosing, improves mood and cognitive function. In the study Acute subjective and behavioral effects of micro-doses of LSD in healthy human volunteers the effects of single very low doses of LSD (0-26 µg) on mood and behavior in healthy volunteers under double-blind conditions are examined. single microdoses of LSD produced orderly dose-related subjective effects in healthy volunteers, indicating that a threshold dose of 13 µg of LSD might be used safely in an investigation of repeated administrations.

Transdermal therapy and Patches

Controlled drug delivery systems offer numerous advantages over conventional dosage forms, including improved therapeutic effects, reduced toxicity, and increased patient compliance and convenience, it is a method of drug administration to the needs of a condition at hand so that the optimal amount of drug is used to cure or control the condition in a minimum time. A transdermal patch or skin patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. It has several components like liners, adherents, drug reservoirs, drug release membrane etc., which play a vital role in the release of the drug via skin.

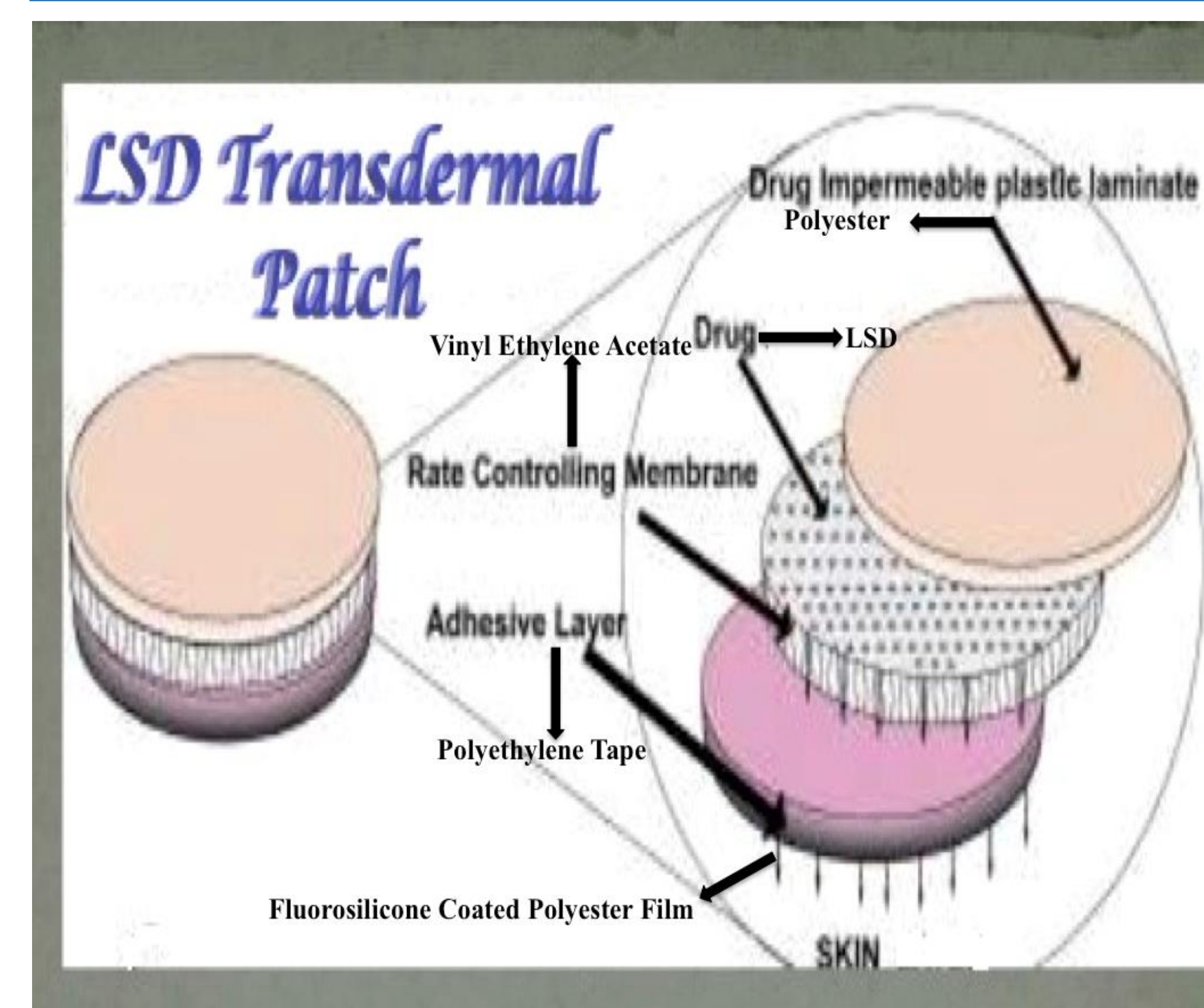
Property	Ideal Drug Properties	LSD Drug Properties
Molecular Weight	< 500 Daltons	323.4 g/mol(Daltons)
Lipophilic (Log P)	Log P ≥ 0	Log P = 3
Hydrophilic	pKa ≤ 7	pKa = 7.8
Half-life	Short	2.5 hours
Melting point	Low melting point	82.5 °C.
Dosage Form	Liquid, Solid, Semi-solid or gas	Liquid
Dose	Low doses	13 – 25 µg

Membrane permeation Controlled systems

the drug can be totally or partially encapsulated within the drug reservoir, its drug release surface is covered by a rate controlling polymeric membrane. The drug molecules are permitted to release only through the rate-controlling membrane having a specific permeability. In the drug reservoir compartment, the drug solids are either dispersed in a solid-polymer matrix or suspended in a viscous liquid medium to form a paste like suspension. A thin layer of adhesive polymer is applied to the external surface of the rate-controlling membrane to achieve an intimate contact of the transdermal system and the skin surface.

For the LSD Transdermal patch, the Membrane permeation Controlled system would be the ideal design. The DIA cannot be because we need the LSD drug to be secured inside the patch, out of contact from light to minimize degradation of the molecule, so it can't just be in an adhesive. The matrix diffusion controlled system, also does not work because we want LSD release to be at once not a slow release, because of the same reason of degradation, after a time it the drug won't have the same effect, same for micro-reservoirs. Therefore, the membrane permeation controlled system is the one chosen.

Design



Conclusions

Repeated use of very low doses of lysergic acid diethylamide (LSD), known as micro-dosing, improves mood and cognitive function. These therapeutic effects are consistent both with the known actions of LSD on serotonin receptors

Since LSD is so easily absorbed through the skin, a transdermal patch or skin patch was chosen. A transdermal patch or skin patch, which is a medicated adhesive patch that delivers a specific dose of medication through the skin and into the bloodstream, to cure or control a condition in a minimum time overcoming various side effects.

After evaluating LSD's drug properties to match for a transdermal patch, Membrane Permeation Controlled system was chosen as the mechanism for a transdermal patch. In this type, the drug can be totally or partially encapsulated within the drug reservoir, its drug release surface is only done through a rate controlling polymeric membrane.

Once the type of mechanism was chosen, the specific materials for each component of the transdermal patch was chosen. These components were liners, adhesives, drug reservoirs, drug release membrane etc., which play a vital role in the release of the drug via skin. The materials were chosen from real products from 3M manufacturer, leader in making transdermal patches.

After choosing material a first design was made and then after further evaluation a second one was made.

Future Work

Since resources for experimenting in real life are hard to obtain in general, and on top of that, it is expensive, but with the funding, experiments can be done. For this phase, it would be ideal to be able to assess the effectiveness of this transdermal patch based on dose, area, vehicle and device, as well as, quantify the rate of the time of absorption of Lysergic Acid Diethylamide micro-dose from the transdermal patch designed.

References

- National Center for Biotechnology Information. "PubChem Compound Summary for CID 5761, Lysergide" *PubChem*, <https://pubchem.ncbi.nlm.nih.gov/compound/Lysergide>.
- Aanstoos, Christopher M., PhD, "LSD". *Research Starters. Salem Press Encyclopedia of Health*, 2020, 2p. 93788071.
- Niemi, Robert. "LSD emerges". *Research Starters. Salem Press Encyclopedia*, 2019, 1p. 89311830.
- Mucke, Hermann A. M. "From Psychiatry to Flower Power and Back Again: The Amazing Story of Lysergic Acid Diethylamide." *Assay & Drug Development Technologies*; Jun/Jul2016, Vol. 14 Issue 5, p276-281, 6p.
- Dyck, Erika. "Psychedelic psychiatry: LSD from clinic to campus." Baltimore, Md. : *Johns Hopkins University Press*, c2008.
- Fuentes Juan José, Fonseca Francina, Elices Matilde, Farré Magí, Torrens Marta. "Therapeutic Use of LSD in Psychiatry: A Systematic Review of Randomized-Controlled Clinical Trials." *Frontiers in Psychiatry*, V.10, Pag. 943, 2020. <https://www.frontiersin.org/article/10.3389/fpsy.2019.00943>.
- Anya K Bershad , Scott T Schepers , Michael P Bremmer , Royce Lee , Harriet de Wit. "Acute subjective and behavioral effects of microdoses of LSD in healthy human volunteers." [PMC6814527](https://doi.org/10.1016/j.biopsy.2019.05.019) (available on 2020-11-15). DOI: [10.1016/j.biopsy.2019.05.019](https://doi.org/10.1016/j.biopsy.2019.05.019).
- Pastore MN, Shakya Pragati, Khwaja Sadiya. "Transdermal Patches." *Integral University*, Lucknow, U.P, India. <https://www.pharmatutor.org/articles/detail-information-on-transdermal-patches>.