Transdermal Drug Delivery

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Introduction

Objective:

- Formulate and compare three different nanoemulgel patches for transdermal delivery

Background:

What are nanoemulsions?

- Emulsions consisting of water, oil, and a surfactant
- Less than 100 nm in size with uniform size distribution

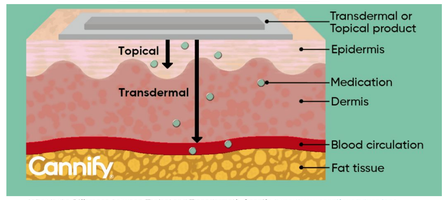
Components of emulsion/emulgel:

- Active Pharmaceutical Ingredient (API)
- Water and oil phases, where one is dispersed into the other
- Surfactant and cosurfactant to reduce surface tension
- Gelling agent to thicken and further stabilize emulgel

Factors under consideration:

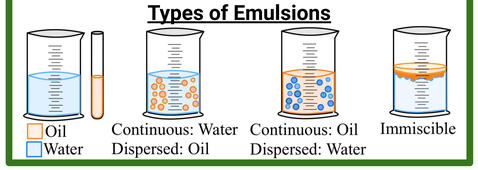
- Drug Hydrophobicity: affects API phase for formulation
- Phase Ratio: impacts stability and emulgel composition
- Separation time: determines stability through homogeneity
- Viscosity: higher values correlate to smaller particle sizes
- Particle size: less than 100 nm to penetrate the skin barrier

Cross-Section of skin



What Is the Difference between Topical and Transdermal?, Cannify, https://www.cannify.us/education/

Types of Emulsions



Theory

Transdermal Barrier:

- Stratum corneum → viable epidermis → dermis → blood circulation

Permeation:

- 1st phase (Administration phase) - application of patch on skin
- 2nd phase (Pharmaceutical phase) - patch releases drug into the skin
- 3rd phase (Pharmacokinetic phase) - after dissolution, body undergoes absorption, body distribution, and metabolism
- 4th phase (Pharmacodynamic phase) - drug interacts with receptors and enzymes

Advantages of Transdermal Drug Delivery:

- Allows for smoother consistent dosing, less side effects, and more efficient drug release
- Nanosized particles increase penetration of API

Oil-in-Water Emulsion

- Oil dispersed in continuous water phase; favorable with hydrophobic APIs

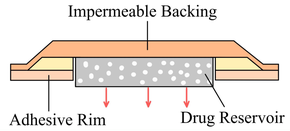
Water-in-Oil Emulsion

- Water dispersed in continuous oil phase; favorable with hydrophilic APIs

Ultrasonic Homogenizer

Branson SFX250 Sonifier, Cole-Palmer, https://www.coleparmer.com/i/branson-sfx250-sonifier

Delivery Patch System



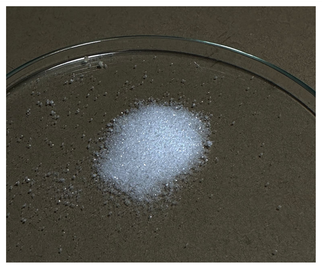
Methods

Emulsion Formulation:

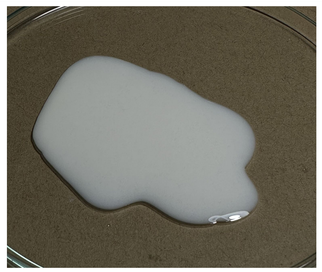
1. Oil and water phases were made separately with the model drug and surfactant added to their appropriate phases.
2. The dispersed phase was added dropwise to the continuous phase until homogenized.
3. The mixture was sheared using the Bamix hand mixer and Ultrasonic homogenizer to ensure nanosized and homogeneous particles.
4. Viscosity and particle size measurements were taken.
5. The samples were periodically monitored for separation to check the stability of each emulsion.

Gel and Patch Preparation:

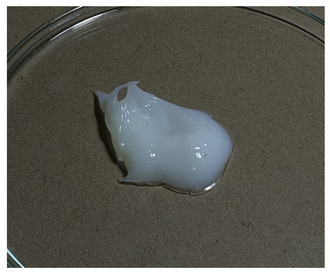
1. Sodium alginate (gelling agent) was added to the water phase prior to shearing until a desirable semi-solid gel matrix was formed.
2. Sodium alginate ratio was varied to produce the most desirable emulgel properties.
3. Emulgel was molded to fit appropriate size for the patch.
4. Patch was designed with an outside layer of impermeable backing, followed by the emulgel reservoir, adhesive, and liner.



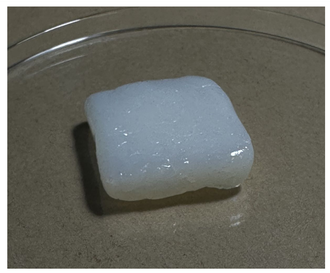
Appropriate oil and water phases added to form emulsion



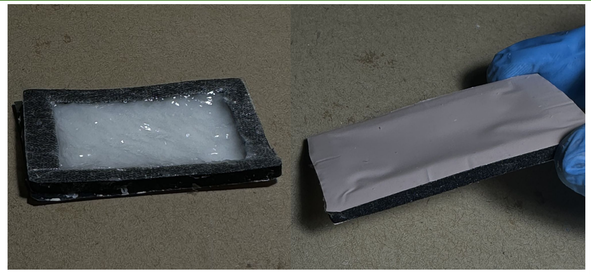
Ultrasonic homogenizer reduces particles to nanosized.



Gelling agent added to thicken material into semi-solid



Impermeable backing, adhesive rim, and liner surround the emulgel

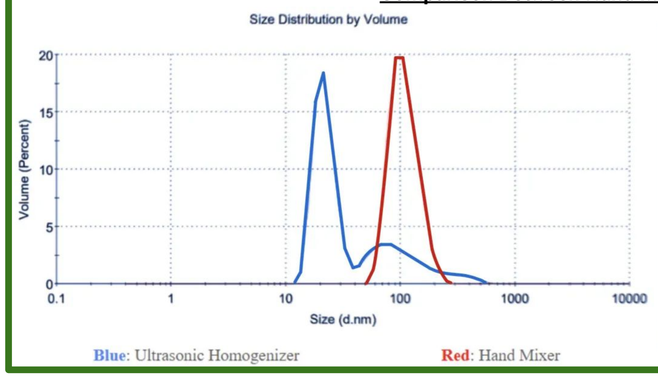


Active Pharmaceutical Ingredient | **Microemulsion** | **Nanoemulsion** | **Drug Emulgel Matrix** | **Final Transdermal Patch**

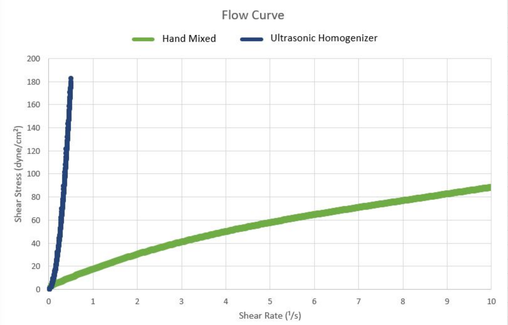
Formulation:

Drug:	Aspirin	Caffeine	Ibuprofen
Hydrophobicity	Hydrophilic	Hydrophilic	Hydrophobic
Phase Configuration	Water in Oil	Water in Oil	Oil in Water
Dispersed to Continuous Phase	42:58	42:58	16:84
Model Drug	Vitamin C	Caffeine	Benzoic Acid
Oil	40% Corn Oil	40% MCT Oil	4% MCT Oil
Surfactant	20% Tween 80	20% Tween 80	10% Tween 80
Cosurfactant	7% Ethanol	7% Ethanol	N/A
Gelling Agent	1% Sodium Alginate	1% Sodium Alginate	4% Sodium Alginate

Comparison Between Hand Mixing and Ultrasonic Homogenizing on Emulsions



The graph to the left compares the particle sizes of both the sonicating and hand mixing cases with respect to particle size. The use of the ultrasonic homogenizer reduced the particle size of the emulsion from micrometers to nanometers. This subsequently increased emulsion viscosity as shown on the right graph. The flow curve identifies the two emulsions as non-Newtonian fluids with the steeper line indicating higher viscosity for the ultrasonicated case.

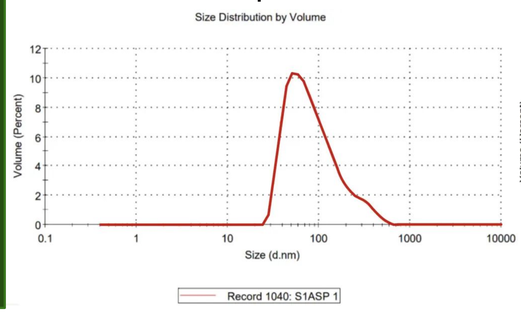


Drug Comparison

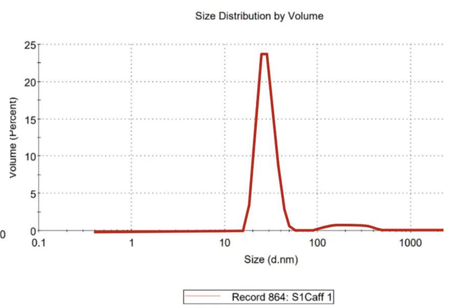
Drug:	Aspirin	Caffeine	Ibuprofen
Mixing Time	5 min shearing 2 min sonifying	5 min shearing 2 min sonifying	5 min shearing 7 min sonifying
Emulsion Consistency	Highly viscous	Highly viscous	Non-viscous
Emulgel Characteristics	Opaque (yellow hue)	Opaque (white hue)	More translucent (white hue)
Functional Groups	Carboxyl, Ester	Amine, Amide, Carbonyl	Benzene ring, Carboxyl

The graphs to the right display the particle sizes for the 3 different drugs that were tested. The peaks were all below 100 nm confirming that nanosized emulsions were formulated. The ibuprofen graph contains two peaks indicating that the emulsion wasn't as homogenous as the others. The mixing for aspirin and caffeine were more thorough, with caffeine having the most narrow size distribution.

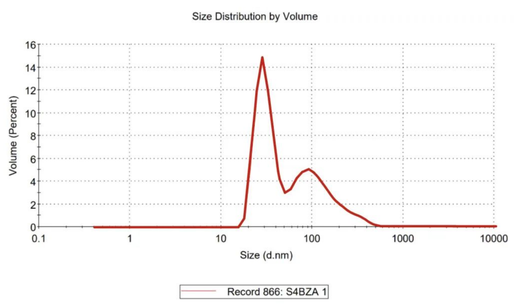
Aspirin



Caffeine



Ibuprofen



Conclusion

- Successfully formulated a nanoemulsion for three different drugs as o/w and w/o emulsions
- Created a semisolid gel matrix component for the emulgel reservoir in the transdermal patch

Future Work

- Dissolution testing to measure the API diffusion rate from the emulgel.
- Optimize effectiveness of transdermal patch dimensions and materials.
- Applying appropriate dosage within the patch

Acknowledgements

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