Multilayer Polymer Film Drug Delivery System to Treat Hypothyroidism

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Clinical Need

Critical Problem: Hypothyroidism is a condition in which the thyroid gland is unable secrete T3 and T4 hormones which regulate the Hypothalamic-Pituitary-Thyroid axis. It is diagnosed by the increased level of TSH and decreased level of T4 and T3 in the blood. If left untreated, Hypothyroidism can lead to heart disease, obesity, cold intolerance, neurological problems.

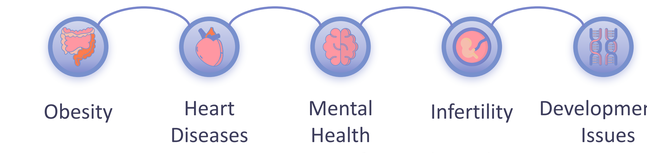


Figure 1: Symptoms of Hypothyroidism

Current Therapy Problems: There is currently only one form of treatment available for Hypothyroidism, which is a daily dose of Levothyroxine. This treatment has many obstacles associated with it, resulting in 35-60% of patients never being regulated.

Mission Statement

Thydaxa is working towards a new innovative way to help those with Hypothyroidism reach ideal TSH levels with convenience and comfort.

Market Analysis

Thyroid Disease Market Size	• 2.45 billion to 3.14 billion [3]
Number of Patients Affected	• 226 cases /100,000 individuals /year [4]
Added Cost to Hypothyroidism Patients	• $460 to $2555 per patient [3]

Final Specifications

Final Specifications	Target Value
Polymer Film (D x H)	35 mm x 2 mm
Steel microneedle sheet	4 cm x 4 cm
Levothyroxine (T4 drug)	1.6 mcg/kg/day
Silicone Sheet	6 cm x 6 cm
Skin Adhesive Sheet	8 cm x 8 cm
Product Lifespan	3-4 Days
Product Shelf Life	> 6 months

Projected Production Cost per Unit: $6 - 12

Acknowledgements

We would like to thank Dr. Brent Vernon for supporting our team in product development during Capstone Design and providing many valuable insights and suggestions throughout this time. We would also like to thank Dr. Campos and Dr. Gronski for their valuable insights as out clinical mentors which helped make a product that takes all users into account and accommodates their needs, Additionally, we would like to acknowledge our facilitators, Dr. Greger, Dr. Vernon, and Professor Sobrado for guiding us throughout the project and providing us with incredible information and connections. Lastly, we would like to recognize Ding Ding Zheng for guiding us as a team and furthering our success thus far.

Prototyping and Design

Figure 2: Model of multilayer L-Tyrosine infused super loaded polymer film.

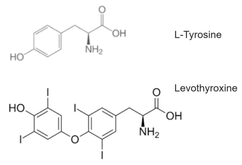


Figure 3: L-Tyrosine is a smaller molecule and diffuses more readily than Levothyroxine.

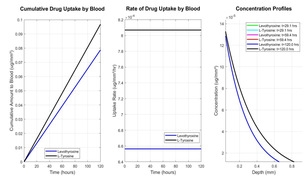
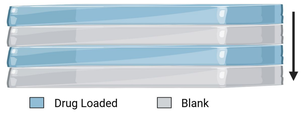
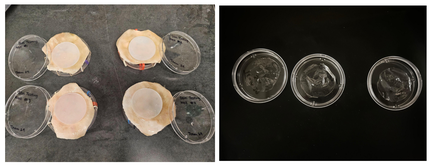


Figure 4: L-Tyrosine vs Levothyroxine uptake modeling over 5 days using analytical solution of Fick's Second Law of Diffusion.

Validation Data





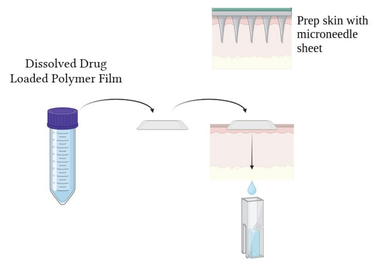


Figure 5: A hydrogel swell test was conducted first in order to determine the amount of water needed to keep the hydrogel above saturation when being administered into the skin. Once this was determined, the porcine skin was prepped with the microneedle sheet and and hydrogels were placed on the surface. These samples were all placed on petri dishes containing a 50 mL reservoir of water into which the drug was diffused. Concentration was measured in increments over the span of 4 days.

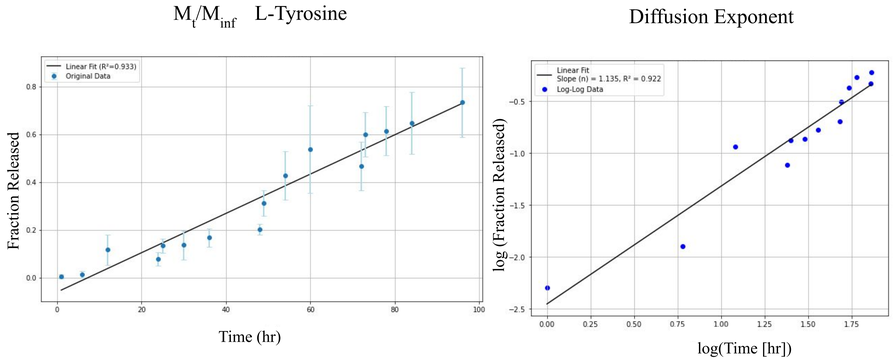
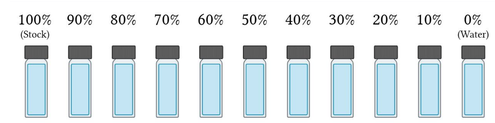


Figure 6: Mass of L-Tyrosine diffused through porcine skin over the span of four days taken 1, 6, 12, and 24 hours daily. Amount of drug diffused by fraction of total loaded drug is displayed on the left, while the log/log graph on the right is used to further analyze the diffusion exponent, giving information of the mechanism of release.

Standard Curve



%	Concentration (mg/mL)	Absorbance (nm)
0	0	0
10	0.04	0.234
20	0.08	0.508
30	0.12	0.726
40	0.16	0.981
50	0.2	1.228
60	0.24	1.392
70	0.28	1.699
80	0.32	1.909
90	0.36	2.112
100	0.4	2.285

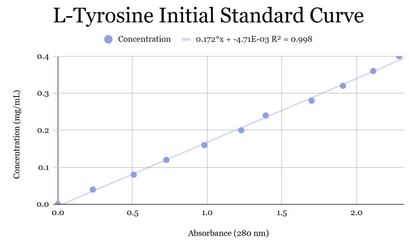


Figure 7: Shown is a standard curve generated prior to testing to show the relationship between concentration of the drug in water and absorbance recorded. Given the R^2 value of 0.998, there is indication that the data collected should show highly accurate results with consistent measurements taken.

Future Directions

Further Validation/ Verification → Feedback and Alterations → Design Changes → Regulatory Approval Strategy → Market

Regulatory Pathway:

This device will have to comply with the standard GP17-A31 to ensure lab safety and that proper guidelines are followed during manufacturing so that each patch is made consistent. As with all medical devices, ISO 13485 will establish a base for quality assurance throughout the manufacturing process. Additionally, ISO 10993 will assess biocompatibility, ISO 11607 will be the standard for sterilization, ISO 14971 for evaluating risk factor, 21 CFR Part 820 for quality system regulations by the FDA, USP 661.1 & 661.2 for chemical and physical safety requirements, and ISO 14644 if manufacturing takes place in a cleanroom to control contamination.

Intellectual Property

Based on prior art search, most individual components aren't patentable due to them pre-existing prior to our research, but combination of these components a thus far seems like unique intellectual property based on modeling and implementation of our device. This is mainly due to the focus in application we have chosen to go with, as there is little motivation in this field to find alternative methods for drug delivery.

Prior Art Search

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[8] Images created in https://BioRender.com