Biodegradable Mouthpiece for Metered-Dose Inhaler

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Problem Statement

Background

- Metered dose inhalers (MDIs) atomize drug solutions for delivery to a patient's airways to treat diseases and disorders like asthma or COPD.
- Plastic medical devices contribute significantly to plastic waste, with only 0.5% of all inhalers issued by the NHS being recycled properly[1].
- The industry as a whole is trying to move towards greener solutions for products, with efforts to phase out propellants that contribute to global warming. The primary propellant used in MDIs, HFC-134a, has a GWP 1430 times that of CO_2 [2].

Motivation

- Our clients Ms. Jenna Vande Hey and Dr. Beth Martin hope to contribute to the current environmental efforts to reduce waste.
- Easily disposable products increase accessibility for impoverished or inaccessible communities in need of treatment.

Goal

- Our goal is design and develop a sustainable alternative to traditional MDIs that contribute to global waste reduction efforts. We have explored various polymers and means of fabrication to arrive on this solution to the problem at hand.

Design Specifications

Performance Requirements:

- The inhaler must have a lifespan of at least 2-3 years prior to disposal and detrimental degradation.
- The inhaler must also be strong enough to withstand forces such as sitting on it or dropping it.
- Must be fully biodegradable, but not degrade fast enough to not function properly during shelf life.
- The inhaler must produce particles within the recognized effective range of 1 to 5 micrometers [3].

Safety:

- The inhaler must be safe for human use, including no immunocompromisation, or lung pollutants.
- The polymer being used should be FDA approved specifically by Medical Device Regulations of Class II devices[4].

Physical Properties:

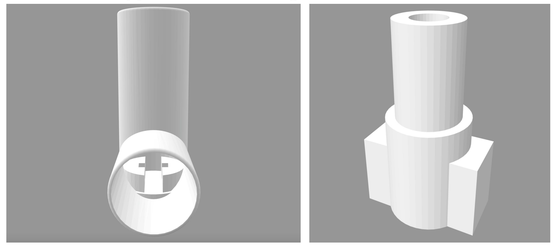
- The design of the inhaler must be similar to that of the current HDPE plastic inhalers to ensure ease of use.
- The full body of the inhaler should be 5-6 cm long, 2.5-3 cm wide, and around 2.5 cm in diameter, in order to stay similar to the original one.
- The weight should also be close to the current MDI inhaler around 10 grams.
- The diameter of the atomizing nozzle should be around 0.5 mm to produce particles of ideal size.

Optimal Product Cost

- If this inhaler is to be produced in bulk and not by 3D printing, it should cost <$1 to mass produce, as the prototypes were ~$0.50 to 3D print.

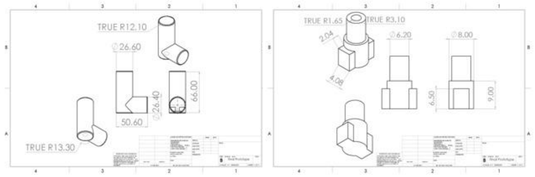
Final Design

Final Prototype for 3D Printing:



A) B)

Figure 2: Final prototype 3D models for the **A)** mouthpiece and **B)** actuator nozzle.



A) B)

Figure 3: Final prototype drawings for the **A)** mouthpiece and **B)** actuator nozzle.

Biodegradable Material: PLA/PHA Hybrid Filament

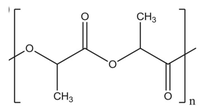


Figure 4: PLA/PHA Hybrid chemical structure.

Other Design Considerations and Details:

- Actuator Diameter = .56 millimeters (within the .14-.6 mm standard)
- No cyanoacrylate or glues used that are non-biodegradable
- Purely made with PLA/PHA Hybrid material

Testing Methods

Biofilm Degradation testing:

- Create Biofilm by mixing human saliva and water and fill up the compartment testing tray with the liquid.
- Weigh the initial mass and place testing cubes into trays in numerical order and by group.
- Record the mass after each week for two weeks total, being held at room temperature (23 C).
- Determine percentage of mass loss and rate of mass loss from data.

Stress Testing:

- Use the MTS machine with a proper 10 kN load cell to test the PLA/Hybrid cubes post degradation test and dry samples.
- Get stress-strain curves for each of the tests to compare the Young's Modulus for each sample.

Actuator Testing:

- Using the MDI propellant, spray the actuator on a petri dish from ~23 cm away.
- Put the petri dishes under microscope and use either 20x or 40x magnification to see the droplets clearly.
- Take pictures of the tests and a calibration slide to determine the diameters.
- Use ImageJ to sample 10 droplet sizes and then average those droplet sizes out for each test.

Testing Results

Biofilm Degradation Testing:

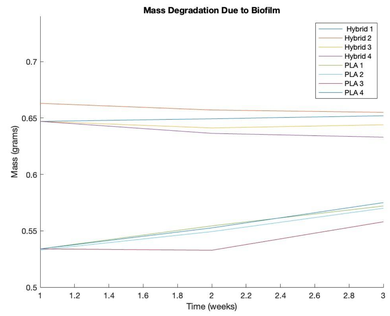
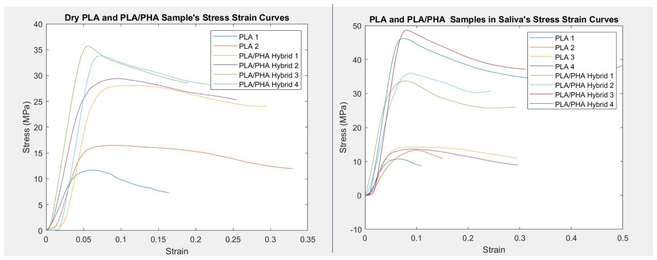


Figure 5: Shows the mass degradation of bioplastic PLA/PHA hybrid samples held in a salivary solution.

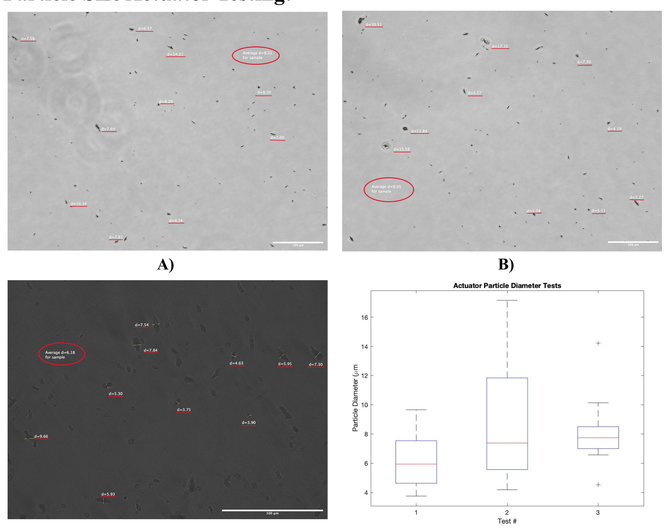
Stress Testing for PLA and PLA/PHA:



A) B)

Figure 6: Shows the mechanical properties of PLA and PLA/PHA hybrid samples held in **A)** dry and **B)** salivary conditions via stress strain curves.
*Note: dry samples PLA 1, saliva samples PLA 1 & 2, and all Hybrid 1 & 2 samples were stress tested under different grain boundary orientations

Particle Size Actuator Testing:



A) B) C) D)

Figure 7: Shows the diameter of multiple drug particles from three different sprays from **A)** 40x and **B)** & **C)** at 20x magnification. Box plot of particle diameter distributions across each test shown in **D)**.

Discussion

Degradation & Stress Testing:

- Both PLA and PLA/PHA hybrid samples were 3D printed at 20% infill, giving rise to negative space on the interior. This could explain the mass gain in the pure PLA tests, where the solution filled the interior space and hydrolysis of the polymer would not occur until 40 C [5].
- Under each testing condition, there are two significant groupings of data. Those of lesser ultimate strength (see Fig 5A; PLA 1, Hybrid 1 and 2, and Fig 5B; PLA 1 and 2, Hybrid 1 and 2) were tested with 3D printed layer faces perpendicular to the face of the platens, while those with greater ultimate strength (see remaining samples in Fig 5A-B) were oriented with printed layers parallel to the platens.
- The PLA/PHA hybrid samples in saliva solution had a higher ultimum strength and greater Young's Modulus than the control samples, while pure PLA in solution remained similar to the control.
- The gain of strength after immersion in saliva could be explained by the reversibility of the hydrolysis reaction. This effect has been seen previously in pure PLA immersed in water at 70 C for one day [6]. As the sample overall undergoes hydrolysis, some esterification likely also occurs between chemically separate 3D printed layers, leading to an increase in Young's Modulus and Ultimate Strength.
- PLA/PHA hybrid trended to having a higher young's modulus and stiffness versus PLA alone.
- On average, the PLA/PHA samples lost 0.0025 g/week while submerged in saliva solution. Three years of degradation at this rate would yield a percent loss of 59.91%.

Actuator Testing:

- The FDA recognizes that the optimum particle size for oral inhalation products is 1 to 5 micrometers [4]. Across 3 tests with a 3D printed PLA/PHA actuator, there were particles from the sample that fall within that range, but the average remains above. This is likely due to the size and precision limitations associated with drilling by hand.
- Uneven spray patterns due to the aforementioned drilling limitations may have led to the deviations across test images/petri dish location.

Future Work

Testing:

- Re-do biofilm degradation testing with higher infill PLA Samples.
- Perform the biodegradation tests longer for more accurate predictions of biodegradation rates.
- Maximize ImageJ/MATLAB analysis for particle size distribution.
- Add heat as a component for PLA and PLA/PHA hybrid degradation testing..

Design & Fabrication:

- Provide more aesthetic choices like color and finish.
- Alter shape of the mouthpiece to better conform to the average mouth shape.
- Utilize a smaller drill bit for drilling actuator's hole for droplets to be closer to the desired particle size.
- Create more designs for accommodating different medication canisters.
- Look into injection molding for potential mass production opportunities.

Miscellaneous

- SHARx Tank preparation in regards to the business aspects of the projects proposal.

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References

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