UNIVERSITY OF WISCONSIN – MADISON

Personalized Medication Disposal System

Department of Biomedical Engineering
BME 301

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Abstract

An increase in unwanted and unneeded prescription medication is becoming more commonplace since the rise of opioid prescription frequency. Frequently, patients will be prescribed more opioids than they need, and this presents a problem because they are lacking a reasonable way to legally dispose of these medications. This project was started in order to address the current need for a personalized at-home medication disposal system, which will aid in slowing the rising opioid abuse problem in Wisconsin. The proposed system would be easy to use and small enough to fit in an average household without issue. The system would also have to be effective at making the active ingredient of the prescription drug inert and inaccessible.

There are currently products on the market. One is a controlled substances sink that is intended for use in clinical settings. The other is a small baggy filled with activated charcoal that patients can dispose of their meds with. Our design team has worked to improve upon these current methods in terms of increased convenience and environmental friendliness. Various dissolution and absorbance tests were done using both hydrocodone and oxycodone. Through these tests, a method of use for our product was formulated. Additionally, dimensional analysis of prescription standard bottles allowed us to create a compatible design with the current drug delivery system. Our design consists of a modified pill bottle that contains a grinder in the cap to disperse the medication tablets. The pill bottle also comes with an inactivating absorbent clay that permanently adsorbs the active ingredient in controlled substances, and a hydrogel that slows reaction with the body if ingested. These two aspects are expected to be easy enough for the patient, while also reducing risk of these pills polluting the environment.

Introduction

Motivation

Federal health officials have starting taking note of a rise in overdose deaths from opioids, including heroin and prescription painkillers that lead to opioid abuse. A persistent upward trend of deaths in the U.S. have been caused by prescription opioids, which rose 2% in 2010 and accounted for 16,917 lives [1]. Another report found that 71.3% of pharmaceutical overdose deaths in 2013 involved opioid analgesics [2].

The recent national problem with opioid use, both prescription and non-prescription, has been paralleled in Wisconsin, partly because of the abundant supply of such drugs due to an increase in prescriptions. Table 1 demonstrates the frequency of opioid prescription relative to other controlled substances from 1/1/14 - 9/30/14. Hydrocodone/Acetaminophen and Oxycodone HCL combined for 28% of all controlled substances prescribed in the first half of 2014, and 55% of all controlled substance

Drug Name	Drug Class	Number of Rx	Percent of All Rx
Hydrocodone/Acetaminophen	Opioid	111,831	19.0
Dextroamphetamine/Amphetamine	Stimulant	55,432	9.4
Oxycodone HCL	Opioid	52,888	9.0
Lorazepam	Sedative	45,132	7.7
Clonazepam	Sedative	40,045	6.8
Zolpidem Tartrate	Tranquilizer	32,441	5.5
Alprazolam	Sedative	29,126	4.9
Methylphenidate HCL	Stimulant	27,696	4.7
Oxycodone HCL/Acetaminophen	Opioid	26,305	4.5
Morphine Sulfate	Opioid	21,600	3.7

Table 1: Top Ten Controlled Substances Dispensed in Dane County between 1/1/14 - 9/30/14. A controlled substance is generally a drug or chemical whose manufacture, possession, or use is regulated by the government. Opioids are highlighted red for emphasis. Source: Wisconsin Prescription Drug Monitoring Program (PDMP)

prescriptions were opioids. Since 2000, over 75% of opioid related deaths involved prescription drugs as opposed to "street" drugs such as heroin [3]. Heroin death rates have generally been lower, but recently heroin death rates have increased substantially [3]. A recent national report showed that there were 4,397 heroin deaths across the country in 2011, which was a 44% increase from 2010 [1]. This increase in death rates can be correlated to the increase in prescription opioid usage. Many people who exhibit opioid dependence report starting their opiate addiction with prescription pain medications [3]. Once the prescriptions run out, many new addicts must find other ways to acquire opioids, and often heroin becomes their drug of last resort. Because most prescription opioids are hard to come by, and heroin is

relatively abundant, opioid addiction becomes more affordable when using heroin. An 80 mg OxyContin can cost $60 to $100 a pill. In contrast, heroin costs about $45 to $60 for a multiple-dose supply [4]. For addicts, prescription opioids effectively become gateway drugs to more dangerous substances, and so many believe that the root of the problem comes from the over prescription of opioids as pain killers.

Current Methods

A substantial contribution to the opioid problem in Wisconsin comes from the dilemma around the storage and disposal of medications. Some patients have access to hundreds of pills over the course of a treatment schedule, and many prescriptions go unused [5]. If people throw them in the trash, give them to a friend, or leave them in their medicine cabinet, complications will often arise. The pills may make it to the street for resale, law enforcement may find them, or pets and wild animals may ingest the drugs.

The disposal dilemma extends to domains other than the household. Until recently, pharmacists and physicians could not legally take back pain medication due to liabilities [6]. Additionally it is environmentally harmful to dispose of pills in the trash or to flush them down a drain. The impact of birth control flushing on aquatic life has been devastating, and the impact of opioids in waterways is not yet known [7].

There are no official protocols in the U.S. for a safe and environmentally friendly opioid disposal method [8]. Ninety-seven percent of pharmacies have formal procedures in place to dispose of their own unused medication, but only 5% of them offer recommendations on disposal to their customers [8].

According to the World Health Organization, controlled substances must be destroyed under supervision of a pharmacist or the police depending on national regulations. Such substances must not be allowed into the public domain as they may be abused. They should either be rendered unusable, by encapsulation or inert-ization, or then dispersed among the municipal solid waste in a landfill, or incinerated [9].

FDA approved methods of medication disposal include: medicine take-back programs, mixing of medication with unpalatable substances, and flushing down a drain (in some cases) [10]. Flushing of potent opioids, such as the extended release hydrocodone tablet Zohydro ER, down a drain is recommended by the FDA because these drugs are considered to be high-risk drugs if unintentionally ingested [11]. The FDA's current stance on opioid disposal is focused on immediate safety of household and community residents, and less focused on environmental effects of disposal, or deactivation of the active ingredient inside the medication.

Medication Drop Box: Statewide disposal methods have also been undertaken. Many police stations now have a medication drop box with which to dispose of unused medication. Once collected, these drugs are then incinerated at a secure location [12]. This method, along with other take-back programs, is inconvenient and cumbersome to many, and virtually unknown to others.

Cactus Smart Sink: The Cactus Smart Sink is designed to dispose of medical wastes in a medical facility safely and easily. The smart sink is designed to dispose of solid medicines, liquid medicines, and medicinal patches. It disposes of liquids and solids by placing them into a key-locked compartment [13]. Although this product meets many of the criteria needed for an at-home product, as a team, it is has been decided that the Cactus Smart Sink is too expensive and too bulky for an at-home, personal basis

Medsaway: Medsaway is an in-home medication disposal system. The system involves a sealable plastic bag, lined with activated charcoal. When medicines and water are added to the pouch, the activated carbon attaches itself to the medicines, rendering them "inert." Upon further research, no concrete evidence could be found confirming the products viability to inactivate the drugs themselves. The only research performed, has been performed by the company and analyzed by the company [14].

Figure 1: Medication Drop box. These drop boxes provide a safe and secure method of disposal, but are inconvenient to use. Source: City of Racine homepage

Figure 2: Cactus Smart Sink The Cactus Smart Sink is a specific disposal system for certain medications. Source: Apothecary Products

Figure 3: Medsaway packaging. Medsaway medication disposal system uses activated charcoal to neutralize most medications. However, it has an unknown environmental impact. Source: Apothecary Products

In conclusion, we feel that the all on the market drug disposal systems do not meet criteria set by the client. All systems currently available are too expensive, unreliable, or not available on an at-home basis. From this, we conclude that there is still a need for an at-home medication disposal system.

Problem Statement

The number of prescriptions prescribed to patients continues to increase exponentially with each passing year. Dane county households with an excess of prescription and over the counter drugs have become commonplace, and both unintentional and intentional overdoses are increasing in frequency. Current methods of medication disposal are inconvenient and potentially dangerous, and so stockpiling medication or disposing of it in an environmentally harmful manner are a popular practice in dealing with excess medication.

A personalized medication disposal container has been proposed to physically or chemically deactivate medication through a safe and easy process, which will render it inert and environmentally safe to dispose of. A neutralizing method for opioids such as hydrocodone and oxycodone are of particular interest, as these are the most prescribed and most abused opiates.

Background

Physiology on Opioid Analgesia and Dependency

Opioids are an effective tool for modulation and attenuation of pain in both clinical and outpatient settings. The main mode of action for opioid analgesic drugs involves the interpretation and perception of pain by the patient. Acute pain is primarily transmitted by A-delta afferent nerves, and chronic pain is transmitted via unmyelinated C afferent nerves. These nerve endings can be found all over the body, and respond to chemical, mechanical, and thermal stimuli [31]. Upon activation of these nerve endings (nociceptors), an action potential is generated down the A-delta or C afferents towards the CNS. Upon reaching the central nervous system (CNS), the afferent nerves synapse with integrating nerves (interneurons) through various neurotransmitters, especially glutamate and substance P [31]. This integration occurs along the spinal cord and continues into the brain, eventually leading to the perception of pain by the CNS.

Pharmacological opioids affect the physiological pain pathway via descending pathways in the brain that transmit signals after pain stimulation. Opioids also modulate pain through multiple interconnecting nerve pathways that decrease frequency of transmission through the CNS [31]. Figure 4 shows a flow diagram of the pain pathway, and the common areas of action for pharmacological opioids. The neurotransmitter, GABA, inhibits descending pathway activity, which in turn causes ascending pathway (pain transmission) to proceed regularly.

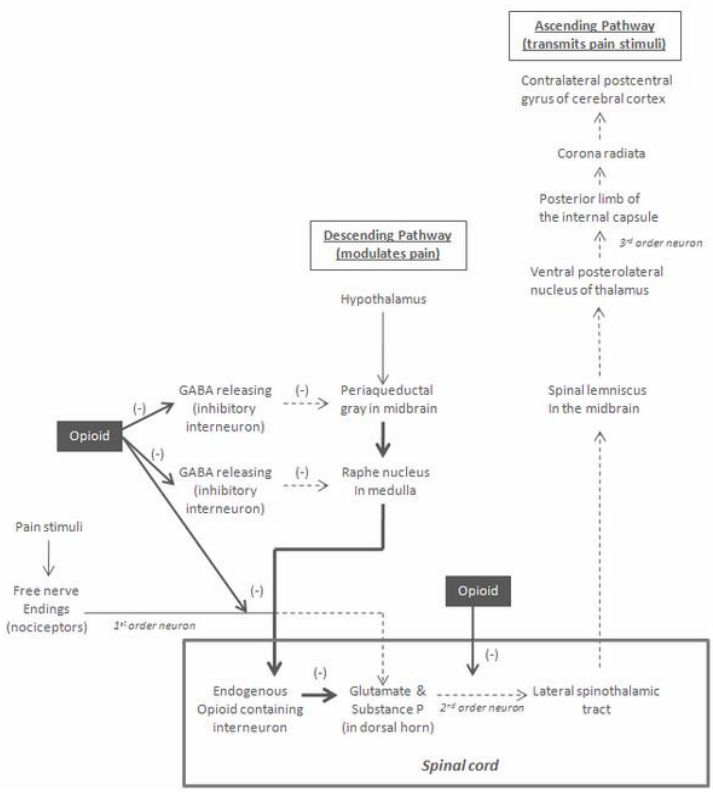


Figure 4: Opioid effects on the neural pain pathway. Opioids decrease pain transmission to the brain by causing activation of the descending nerve fibers. In addition, opioids directly inhibit afferent nerve transmission in the spinal cord. Source: Pharmacology Weekly, Inc, 2009.

Opioids bind to opioid receptors (delta, kappa, and mu) in the brain. Mu receptors are often found on the interneurons that regulate the pain pathway. When opioids bind to these receptors, the interneurons that inhibit endogenous opioids (endorphins) are themselves inhibited, resulting in increased endogenous opioid release [31]. Opioids also inhibit afferent pain sensing nerves. This leads to an overall lower frequency of action potential from the afferent neurons, leading to less pain stimuli that the CNS has to deal with. The overall effect of opioid action in the body is inhibition of pain transmission to the brain and a decrease in the perception and experience of pain by the patient [31].

Opioid dependency and abuse is commonly due to opioid induced tolerance, also known as pharmacodynamic tolerance [32]. Tolerance is thought to be due to a change in opioid receptor affinity. Opioid receptors are notoriously susceptible to desensitization and down regulation with prolonged exposure to pharmacological opioids [32]. Opioids normally bind to G-protein coupled receptors, leading to decreased excitability of affected neurons, through suppression of the ion channels necessary for depolarization of the cell membrane. Desensitization often occurs when the opioid receptor decouples with the G-protein, and binding of opioid no longer triggers G-protein activation [32]. Additionally, excessive internalization of opioid receptors following prolonged opioid exposure can result in lower density of receptors for the opioid ligand, which results in lower analgesic effects from the same dose of opioid [32].

Opioid withdrawal due to dependence is a major reason for opioid addiction and abuse. In addition to decreased analgesia due to tolerance, opioids have effects on other pathways in the body, and these mechanisms must also adjust in response to prolonged opioid use. For example, opioids are known to suppress noradrenaline (NA) levels in the brain. With repeated exposure to opioids, the neurons that release NA adjust to become more active to compensate for the near-constant opioid inhibition [33]. When opioids are not present to suppress NA activation, the neurons release too much NA, resulting in prolonged symptoms related to the sympathetic response, even without stimuli, which can be very traumatic for the patient [33]. The need to avoid opioid withdrawal is a common factor for people to continue taking opioids after their initial pain has subsided, eventually resulting in addiction and abuse.

Market Research

After analyzing the current competition for the proposed personal medication disposal system, an informal survey was constructed to gain more insight on how people currently dispose of excess medication and their knowledge of the Medication drop boxes around Dane county.

Of the 20 college students surveyed, 55% do not dispose of their excess medication. Furthermore, 75% have never heard of Medication drop boxes before, and 95% do not know where the closest one is located. When asked if they were willing to travel up to 5 miles to dispose of their medications in a drop boxes, 50% said they would.

The results of this survey demonstrate a clear need for a safe medication disposal solution that is convenient for the user, like the personal medication disposal system proposed by this project. The full survey is located in Appendix D.

Client Information

Dr. Philip Bain is an internist in Madison, Wisconsin and is affiliated with multiple hospitals in the area. He received his medical degree from University of Wisconsin School of Medicine and Public Health and has been in practice for 29 years, specializing in headaches and other pain management.

Product Design Specifications

The entire device is to be of the same diameter, or slightly larger diameter than a medication pill bottle of choice. Also, the entire grinding grind should be less than3.81cm tall. The product must be affordable for pharmacies or insurance providers. The product should cost no more than $5 to produce a single unit, with the deactivation packets included. In fact, we would like the device, and all ingredients to be distributed at the cost of the pharmacy or insurance providers. The device needs to be very simple to operate, with a procedure of disposal less than 10 steps in total. The device should be able to grind up at least five pills at a time without too much difficulty. It should also be able to store at least an entire prescription worth of opiates to be disposed of, i.e. 30 pills. After use, the product should be easily disposable in the trash in its entirety. The complete PDS can be found in Appendix A.

Preliminary Designs

Hydrogel Powder

The main idea behind the "hydrogel powder" concept is that the drug tablets would become incorporated into a new compound, and this compound would be rendered inert, effectively trapping the active ingredients inside. The hydrogel powder would contain one or more excipient agents, and one or more desiccating agents that would interact with the opioid in order to facilitate disposal. An excipient is a substance that is incorporated into the active ingredient of a medication. These excipients perform numerous functions, such as binders, disintegrates, and lubricants, which generally work together to facilitate controlled release and solubility of a drug [15]. The excipient will likely take the form of a hydrogel that will incorporate the drug into its matrix. A desiccant is a substance that dries its surrounding environment, commonly by adsorbing water. The desiccant will likely take the form of a fast-hardening plaster. These agents would ideally solidify over time to discourage the ingestion of the finished product, to aid in making the finished product inert to the environment, and to increase ease of disposal. The final chemical agent would likely have both hydrophilic and hydrophobic properties. The interaction between these compounds and the active ingredient would ideally be easy for the patient to use, since all they would have to do is pour the powder in with the medication and add water.

Many hydrophilic polymers were considered for the hydrogel. Hydrophilic polymer matrix systems are widely used in oral controlled drug delivery because of their flexibility to obtain a desirable drug release profile, cost effectiveness, and broad U.S. Food and Drug Administration acceptance [16].

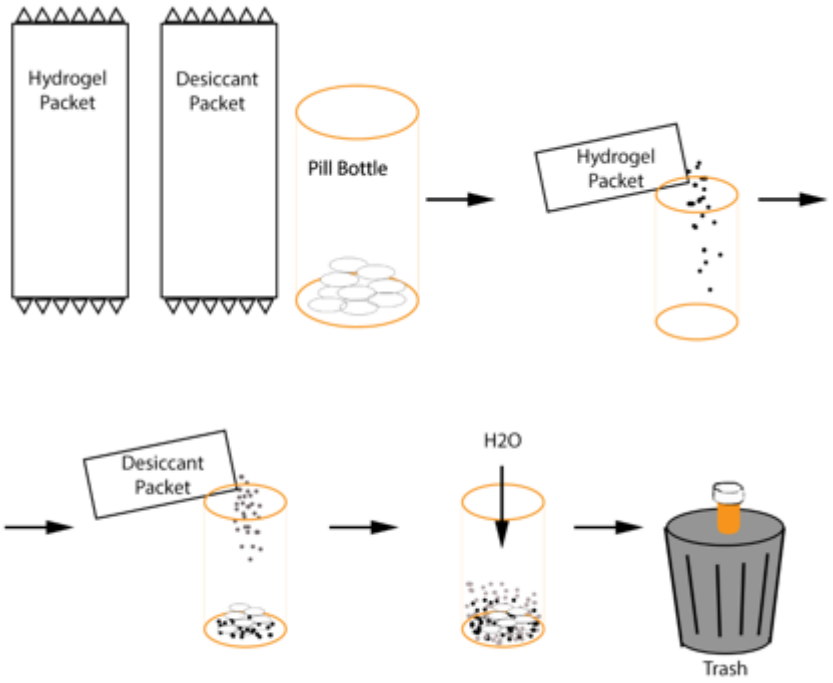


Figure 5: Hydrogel packet procedural outline. The patient would ideally only have to pour in a few tear-off type packets and add water in order to use such a design.

Figure 5 shows the theoretical process of the hydrogel powder design. Many hydrogels and desiccants were considered in the design process, most notably:

Polyethylene glycol (PEG): PEGylation is the act of covalently coupling a PEG structure to another larger molecule, for example, a therapeutic protein, which is then referred to as a PEGylated protein. It is coupled to hydrophobic molecules to produce non-ionic surfactants. When attached to various protein medications, polyethylene glycol allows a slowed clearance of the carried protein from the blood. This makes for a longer-acting medicinal effect and reduces toxicity, and allows longer dosing intervals. This type of material could be useful for the addition of antagonistic substances to the composite in the future.

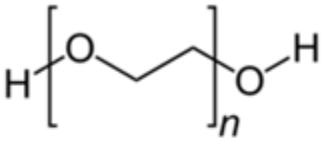


Figure 6: PEG.
PEGylation of our target drug May be an applicable design in Terms of aggregation.
Source: Wikipedia.

Sodium Bentonite: Sodium Bentonite expands when wet, absorbing several times its dry mass in water. It provides a self-sealing, low permeability barrier when interacting with a solvent [33]. Bentonite has previously been prescribed as a laxative. Sodium Bentonite is most notable in the medical field for its properties as a desiccant and absorbent substrate. Bentonite is a common substance for use in the protection of pharmaceutical products from moisture degradation. Sodium Bentonite adsorption is also a DEA recommended procedure for disposal of schedule II

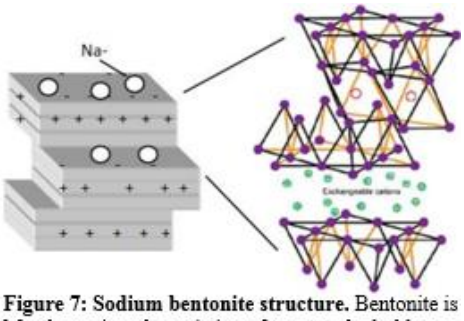


Figure 7: Sodium bentonite structure. Bentonite is Mostly a mineral consisting of two tetrahedral layers sandwiched around an octahedral layer. Interactions between Na^+ and interlayer cations forms a sheet-like structure indicative of a clay.
Source: CETCO, 2013.

controlled substances by pharmaceutical entities, and Bentonite complies with the FDA for contact with food and drugs [33].
More material considerations can be found in Appendix C.

UV Light

Hydrocodone and other medications are stored in a light resistant containers [25]. This suggests that hydrocodone may undergo some reaction with light. In fact, hydrocodone reacts with light that has a wavelength of less than 290 nm, which would include short length UV light [26]. It is possible that light of certain wavelengths could provide enough energy to allow electrons to move to a more excited state. Once in this excited state, the chemicals within these pharmaceuticals would more readily react with their environment. And it is due to such reactions that as of 1998, the FDA mandated that all pharmaceuticals must undergo photo stability testing [27]. Given this information a design was postulated that a UV light emitting device could be used to dispose of opiates in an at home setting.

This design was essentially a miniaturized tanning bed. It would be a small cylinder lined with UV light bulbs. The left over opiates could then be dumped into the container, the UV lights would be turned on, the cylinder would be closed, and the opiates would be left to sit. While basking in the UV light, the opiates would ideally lose most of their potency [28]. Then upon completion of the reaction, the drugs could hopefully just be thrown away, as the light should have rendered them relatively inert.

This design had the major advantage of being fairly safe. The only major safety concerns with the design is if someone were to look directly at the UV lights, or there was some kind of electrical short. Also in theory the design would be easy and fairly inexpensive to fabricate. It would simply be a matter of creating the containing and attaching light bulbs in parallel to a switch.

However, this design also has several drawbacks. For starters, each formulation of the opiate may have a different reaction to the light. These reactions could be relatively harmless or they could be fairly active. Likewise the reaction could give off unknown by-products. Furthermore, it is uncertain what the final product will be and how long the reaction will take. If one or more of the bulbs is going out, the reaction could take longer than recommended. Hence, a major issue with this design is a lack of certainty and a lack of control. Additionally finding bulbs that are fairly short, and produce light that has a wavelength of less than 290 nm is not an easy task.

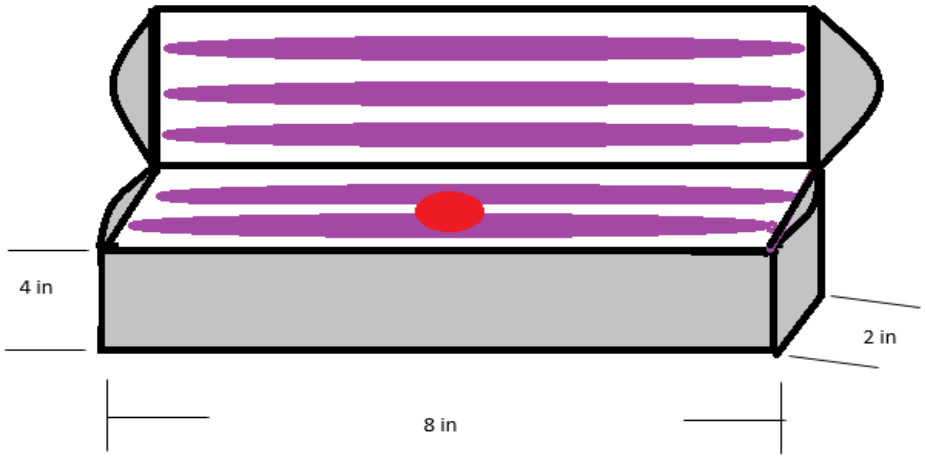


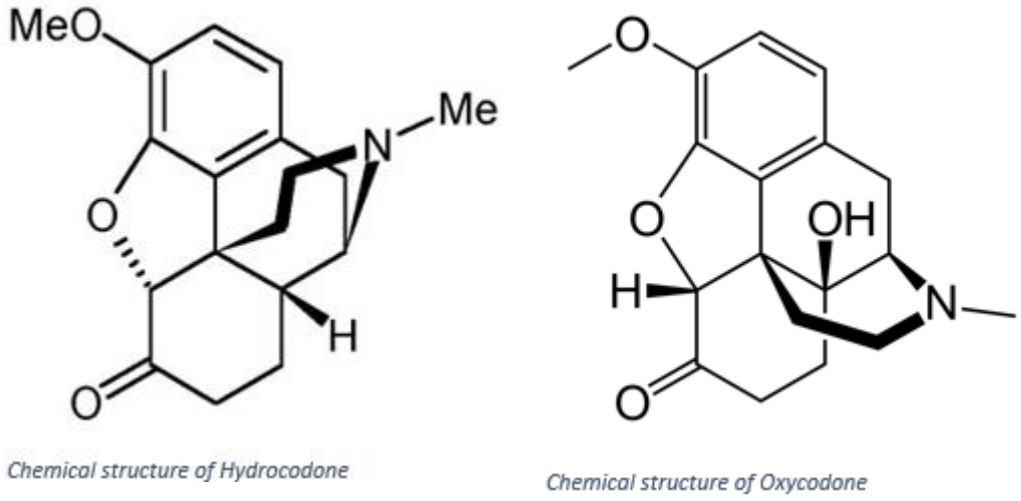
Figure 8: Preliminary design of UV Light bed for pill deactivation. This design is meant to mimic a typical tanning bed design, and would allow the user to put multiple pills in at a time, turn on the device, and let sit until the active ingredients are deactivated.

Bond Vibrational Frequency

Chemical bonds between atoms vibrate back and forth at specific frequencies. These specific vibrational frequencies within a molecule can be found using a wave generator [29]. It should be possible to create a bandwidth of frequencies matching those bond frequencies found. Theoretically, if we are able to produce this wave with a large enough amplitude, it should cause the bonds in the molecule to break apart from one another, thus rendering the molecule inert and unable to react with the human body.

Below are the molecular structures of hydrocodone and oxycodone. In order for these molecules to be broken down and activated in the human body, they must first undergo O-demethylation, N-demethylation, and 6-keto reduction. [30] If we are able to remove these groups of molecules, then the molecule will be ineffective in the human body.

The groups we are interested in are the R-OMe, R-C-N, and C=0. These bonds have wavelengths measuring 1210-1320 cm^{-1}, 1000-1250 cm^{-1}, and 1705-1720 cm^{-1} sequentially. Therefore, if we were to produce a wave with a bandwidth of frequencies matching those bond vibrational frequencies, the bonds should break [29]. Once these bonds are broken, the opiate (hydrocodone or oxycodone) should be rendered inert and unusable.



Chemical structure of Hydrocodone

Chemical structure of Oxycodone

Figure 9: Chemical Structure of common opioids. These opioids have very similar bonds and activate many of the same receptors.

This design would have the benefit of completely destroying the drugs, as the chemical bonds that make the effective would be broken. Once these bonds are broken, the specific medication should lose all of its potency. Thus making it impossible to overdose or abuse this medication.

However, it will involve a very sensitive reaction with an unknown energy release. Breaking bonds releases energy, and as such by breaking the bonds this design could pose a danger to the user. Additionally the creation of a device that could effectively match the wavelengths of a specific chemical bond would be incredibly time consuming and expensive to create. There would also be no guarantee that once the wave generator was removed from the pills that the broken bonds would just reform.

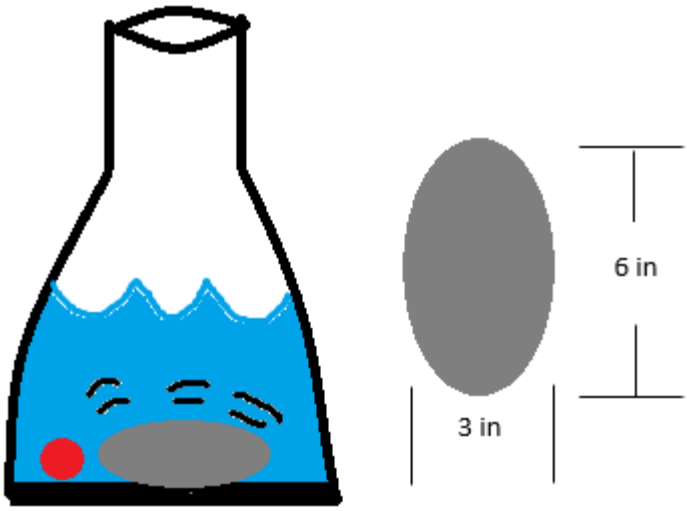


Figure 10: Preliminary design of bond vibrational frequency design. This design features a small, vibrating, pill-shaped object that vibrates at a predetermined frequency that will dismantle the bonds of the substance, leaving the medication inert.

Preliminary Design Evaluation

Design Criteria

An important consideration for this design is how inaccessible the drugs will be after the design has run its course. Inaccessibility could mean that there is simply no way to get at the drugs after implementation of the design, or it could imply that the drugs have been lost their therapeutic effect and no one could overdose off of the final product. This criteria is opposed by safety. As there are many ways to render a drug inaccessible, but not all of them are safe. The criteria of safety does not just pertain to the safety of the user. While safety of the user is still very important, safety should also consider the environmental impact of the design. A design that has an end product that would negatively affect the water table when thrown out is not a safe design, even if the process to get to the final product was safe and easy for the user.

Another key component to this design, is that is needs to appeal to people. People need to find it convenient to use this device. As such, two additional criteria would be cost and ease of use. People will not use a product that is ridiculously expensive, while their current methods of disposal have minimal fiscal cost. Likewise, if the design is far too complicated to use, then people won't use it. A substantial demographic of opioid prescriptions involves the elderly and disabled, and so the design must be minimally rigorous in use. Additionally, the design must be child-proof-able.

Finally it is important to consider the marketability and the manufacturability of the design. Ideally this design would go to market, and be used by many consumers. As such, the design cannot be too off-putting. Designs that seem too dangerous for a user to want to have in their home are considered very disadvantageous. Also, in order for this device to go to market it would need to be mass produced. Thus, the method in which the design is manufactured needs to be fairly simple.

Design Matrix

Design Matrix (Weight)	Hydrogel Powder		UV Light		Bond Vibrational Frequency	
Inaccessibility (25)	(4/5)	20	(4/5)	20	**(5/5)**	**25**
Safety (25)	(4/5)	20	**(5/5)**	**25**	(3/5)	15
Cost (20)	**(5/5)**	**20**	(3/5)	12	(2/5)	8
Ease of Use (15)	**(5/5)**	**15**	(4/5)	12	**(5/5)**	**15**
Marketability (10)	**(5/5)**	**10**	(4/5)	8	(4/5)	8
Manufacturability (5)	**(5/5)**	**5**	(4/5)	4	(2/5)	2
Total (100)	**90**		81		73	

Figure 11: Design Matrix The goal of the project is to create a device that renders opiates inaccessible and is safe for the user and environment. As such, those two categories had the most weight. Next was cost followed by ease of use. A design that is too expensive or difficult to use will not be used by consumers. This design should be used, as such a design that score well in those categories would encourage people to use it. Lastly, should the design go to market it will need to be marketable and easy to manufacture. Thus those two categories are also included, but are not weighed as heavily as they are not a major concern at this point.

From the design matrix it can be seen that, hydrogel powder won overall and won all the categories except inaccessibility and safety. This is because the hydrogel powder design would be cost-effective, as the individual components are not expensive, as well as easy to use, as it would just be a matter of mixing several packets together. Likewise, mixing to inert compounds together would not be off-putting for consumers, and the manufacturing process for this design would also be very easy. UV light, only won safety. This is because there are many unknowns that occur with the UV light reaction. However, UV light is fairly safe to use unless someone were to stare at it directly. Bond vibrational frequency won inaccessibility and ease of use. The device would simply obliterate the opiates, such that there was nothing left to access. Likewise it would be very easy to use.

Nonetheless, hydrogel powder won the design matrix. Predominantly because it renders the drugs fairly inaccessible and is fairly safe to use, in addition to meeting all the other criteria.

Proposed Budget

The client did not specify a budget range initially, but given the simplicity of our design and the inexpensive materials and processes needed to complete it, the overall costs for fabrication and testing should total to less than $200. Because the primary goal of this product would be to get people to use it, the team would like the final product to cost around $5 to produce.

Proposed Final Design

Since the Hydrogel Powder design ended up scoring the most points in the design matrix, the final design proposed by the team incorporates the method of trapping the active hydrocodone in a gel solution. The proposed final design is a "modified pill bottle" complete with a grinder attachment on the lid and the bottle serving as a reaction compartment for the hydrogel powder to be mixed with the grinded medication and water. The grinder lid is complete with an upper and lower portion, with the upper portion fitting snugly on top of the bottom portion, and the bottom portion screwing on to the bottle attachment to create a tight seal for the reaction and also creating a child-lock seal. Both portions of the grinder lid have pyramid-like spikes evenly distributed around them and spaced far enough apart to allow the average sized hydrocodone or oxycodone pill to fit inside. The upper portion of the grinder also comes with crushing spikes so as to crush the hydrocodone and oxycodone pills before the grinding to ensue. The bottom portion of the grinder features holding spikes in order to hold the pill in place for ideal crushing conditions. The bottom portion also has holes evenly distributed around the bottom surface that will allow the ground medication to fall through into the original pill bottle.

The intended use of this product would have the user place the unused pills in the bottom portion of the grinder one at a time, which will be screwed onto the reaction chamber, and place the top portion on top of the bottom portion, crushing the pill. Then, proceed to turn the top portion in a circular motion until all the medication is ground into a powder and in the bottom of the reaction chamber. Once the grinding is complete, the user can pore tap water into the reaction chamber, shake vigorously, and then let stand for a period of time. Next, the user should add the correct amount of kitty litter and PEG to the pill bottle to achieve a solid, not consumable to any meaningful effect product. Once complete, the user can dispose of the products in the trash. The grinder lid, pill bottle, kitty litter, and PEG are intended to be distributed with the user's opioid prescription at the pharmacy.

Pill Grinder Dimensions:

- Cap outer diameter: 37.67 mm
- Cap inner diameter: 35.40 mm
- Top cap height: 16.50 mm
- Top cap grinder spike length: 6.00 mm
- Top cap lid volume capacity: 5.5mL
- Bottom cap height: 10.10 mm
- Bottom inner cap diameter: 35.5 mm

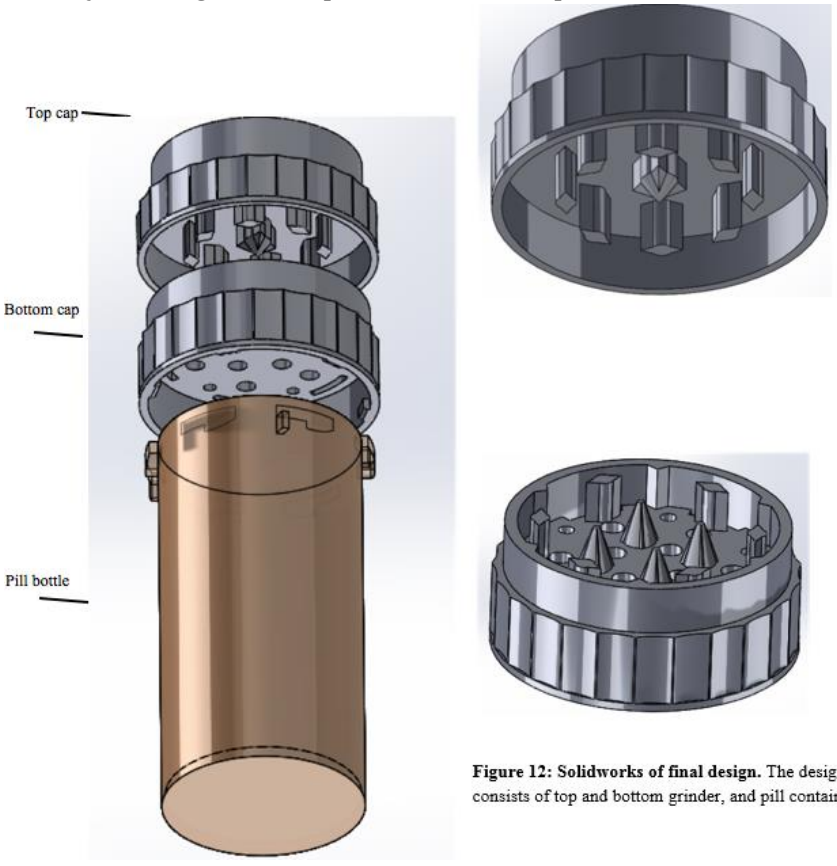


Figure 12: Solidworks of final design. The design consists of top and bottom grinder, and pill container.

- Bottom cap pore diameter: 4.00 mm
- Bottom cap spike length: 5.50 mm
- Distance between bottom cap crusher spikes: 7.50 mm
- Total Cap height: 26.50 mm

Fabrication/Development Process

Materials

Natural Poly(lactic acid) Filament: Natural Poly(lactic acid) Filament is the plastic used for the 3D printing done in the David Beebe Lab, which is where all the 3D printing of grinder designs was done for this project since the team was able to print multiple prototypes without cost. This material is also relatively inexpensive and is fairly similar to the type of plastic used in current pill bottle caps. The printing for the final design was 100% fill, while earlier prototypes were tested at 15% and 75%, but these were found to be too weak to crush the medication without breaking the grinder spikes.
PEG: Polyethylene glycol (PEG) was used in this design as a hydrogel substance meant to hinder the adsorption of the active ingredients of the controlled substances by the human body. The PEG also acts as a laxative, which would further discourage the consumption of the system's end products that contain the active ingredients. During testing, liquid PEG 300 was used under the recommendation of Dr. Edmond Elder.
Sodium Bentonite: Sodium Bentonite, more commonly known as kitty litter, was used as the desiccant in this system, since it is a relatively cheap substance that absorbs water well. The use of sodium bentonite is also in line with the recommended disposal procedure of several federal government agencies, and also acts to deter consumption of the system's end products.
Rubber: A rubber O-ring was used to further help child-lock the system, as another preventative measure to deter tampering with the controlled substances. The elastic deformation properties of rubber allow this structure to deform and compress to provide a tighter seal for the locking capabilities of the GrindCap to a pill bottle.

Methods

In order to proceed from design proposal to final prototype, our team needed to use good design practices that would ensure proper compatibility with the current method of drug delivery. The main finite element of our design was the two piece grinder cap. The team decided to 3D print the grinder cap because CNC milling the cap was very involved and prone to error. The 3D printing method was thought to be more reliable, and able to withstand the stresses of normal use.

Before we were able to proceed with 3D printing; however, we had to create a computer aided drawing(CAD) with the computer program SolidWorks. The SolidWorks was the primary tool for creating a compatible design. First, a standard pill bottle and cap were measured and dimensioned using a caliper. These dimensions were then used to replicate the standard pill bottle and cap on SolidWorks. Following the standardization process, a top cap piece was added with similar dimensions to the bottom piece. The bottom piece was then modified to tightly fit underneath the top cap. The two pieces of the grinder would now fit snugly onto one another, with a good degree of rotational freedom. At this point,

numerous grinder designs could be implemented in the space between the top and bottom cap. For our design, crusher and grinder spikes were added with radial symmetry on both the top and bottom cap. Finally, radially symmetric pores were added to the bottom cap floor, and ridges were added to the side for easier grip.

In order to 3D print our device, we used MakerBot software and a MakerBot 3d printer. In order to have a stable structure, both settings for rafts and supports must be selected in the 3d printer settings. Furthermore, a 100% fill capacity ought to be selected to ensure that the grinder does not break when grinding the pills. The pieces out to be oriented with spikes up to ensure their shape during printing. A resolution of .1 mm was used to create our 3d prints.

Finally, a working child lock needed to be properly fabricated. The bottom cap was modified to include small inward protruding teeth that would fit correctly into the child-lock teeth of the standard prescription bottle. Additionally, a custom O-ring was fabricated using a flat sheet of rubber. The ring was made by cutting out pre-measured concentric circles that corresponded to the bottom cap diameter.

The team did not explicitly design a method for preparation of PEG and sodium bentonite packets. The idea is to include these substances pre-packaged with a prescription, and these packages would be similar to mass produced condiment packages found in restaurants.

Final Prototype

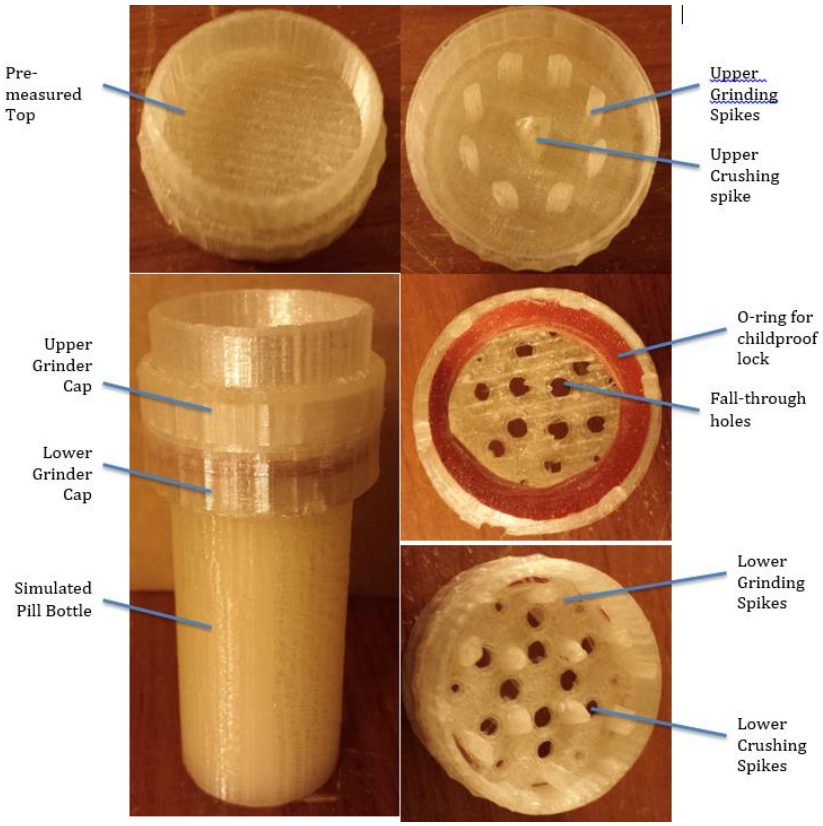


Figure 13: Final design 3D print of grinder with simulated pill bottle. The bottle and grinder are both designed for standardized use for prescription delivery.

The GrindCap System is designed to be an inexpensive, easy to use, and versatile drug disposal solution that is compatible with the current method of drug distribution.

The overall cost of production per unit is estimated to be around $1.50, even though the team designed it with zero expense. This estimate comes from totaling the materials and fabrication costs for the grinder, the PEG and sodium bentonite costs, as well other miscellaneous packaging and distributing costs. The low cost is one of the major benefits to this design, and may help it be adopted for use by pharmacies and drug distributors easily.

The GrindCap is also easy to use, as it comes with only a few small parts with little to no assembly required. Since the system comes with everything needed in the package, it will eliminate the need for the user to leave the house to purchase extra materials. The system also includes an easy to follow, 7 step procedure that requires little effort and can be completed in less than 20 minutes. The grinder portion is also designed so that the user can simply crush and grind the pills without exerting too much force.

The design is versatile in that the dimensions of the GrindCap can easily be modified based on the size of the pill bottle, and the size and composition of the pill being disposed of, allowing it to be applied for multiple different medications. The compatibility of the design with the current method of drug distribution is one of its most prominent strengths, as it will be relatively easy to adopt into current drug distribution methods, and it also acts to encourage the user to think more carefully about the importance of safely disposing of their controlled substances.

Testing and Results

In order to develop a method to dispose of hydrocodone and oxycodone safely in an at home setting, we needed to perform many crucial tests.

Grinder Performance Testing

For testing the functionality of the prototype, we used ibuprofen and altoids in order to make sure our grinder spikes were strong enough. Upon 3d printing the first design, we found that the grinding spikes were far too thin and fragile to even handle a chalky altoid. We improved on the design by adding a large base to each spike. With the addition of a large base area, the grinders were entirely able to grind up any ibuprofen and altoids we tested them with. We did not test the grinder with either hydrocodone or oxycodone tablets because we had a limited number of tablets and did not want to contaminate the pills with the ibuprofen remnants. Although the grinder design did not break, we feel that the herb grinder design is not ideal for pill crushing and grinding. The herb grinder design does not create a powdered pill, more so small chunks. We feel that having an ideal, powdered grinder will is important to dissolution rate into our solvent. Through testing, we've determined that how fine the pill is ground, is directly correlated to dissolution rate.

PEG per Pill Absorbance testing

In order to know the quantity of PEG or liquid in general that needs to be added per pill in order for the pill to be fully suspended in liquid. This test was performed with an ideally powder grinded hydrocodone and oxycodone tablets. As a result, we've determined that it takes 1 mL PEG in order to fully suspend one tablet of hydrocodone. This means that if a user were to dispose of their entire prescription of hydrocodone (30 tablets), 30 mL. of PEG must be added to fully suspend the pill in fluid.

As a result of our oxycodone absorbance testing, we found that it takes a total of 170 micro-liters of fluid to fully suspend an oxycodone tablet. This is because the oxycodone tablets are significantly smaller in size. This means that if a user were to try to dispose of their entire prescription (30 pills), it would require a total of 5.1 mL of PEG to fully suspend the prescription.

Figure 14: PEG in pill Absorbance Test. Both Hydrocodone and oxycodone were crushed, and then PEG was added drop-wise until pill was suspended.

Figure 15: PEG in Sodium Bentonite Absorbance Test. Sodium bentonite was weighed, then PEG was added drop-wise until bentonite was suspended.

PEG in Sodium Bentonite (Kitty Litter) Absorbance testing

We feel that the final product of our disposal method should result in a complete solid, no excess liquid; therefore, we needed to perform experiments testing how much PEG can be absorbed into kitty litter. As a result of this testing, we found that a total 1.1077 mL PEG can be absorbed into 1 gram of kitty litter. This results to 0.903 grams kitty litter required to dissolve 1 tablet of hydrocodone. Furthermore, a minimum of 0.153 grams of kitty litter are required per pill of oxycodone in order to have a fully solid product.

H_2O vs. PEG Dissolution Rate

In order to determine a recommended solvent type to dissolve your hydrocodone and oxycodone into for the fasted dissolution rate, we took samples of the quantity of our active ingredient dissolved into the solution at 15, 30, 45, 90, and 120 minute intervals. Unfortunately, no meaningful results could be determined from oxycodone testing because the HPLC machine procedure for oxycodone failed, this accounts for all testing of oxycodone.

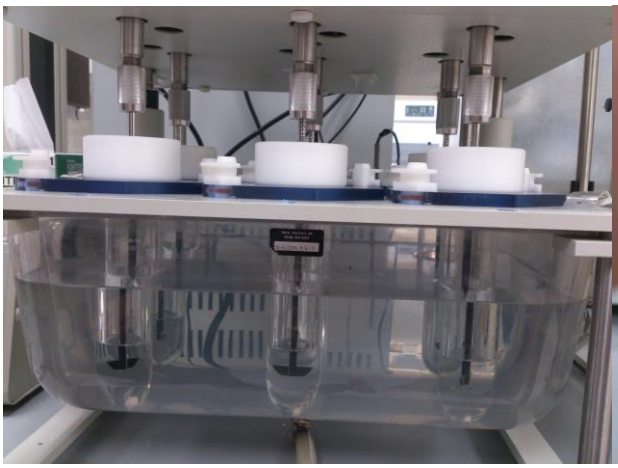


Figure 16: Stir bar method testing with whole pills used for HPLC testing

Figure 17: A fully dissolved, uncrushed oxycodone pill

Although Dr. Edmund Elder and the team cannot explain why results were unobtainable, simply by qualitative testing, we were able to see that oxycodone dissolved significantly faster into H_2O than PEG. Results of the hydrocodone testing show that H_2O is a significantly better solution to dissolve your hydrocodone into than PEG is. This can be concluded from the results of the following graph.

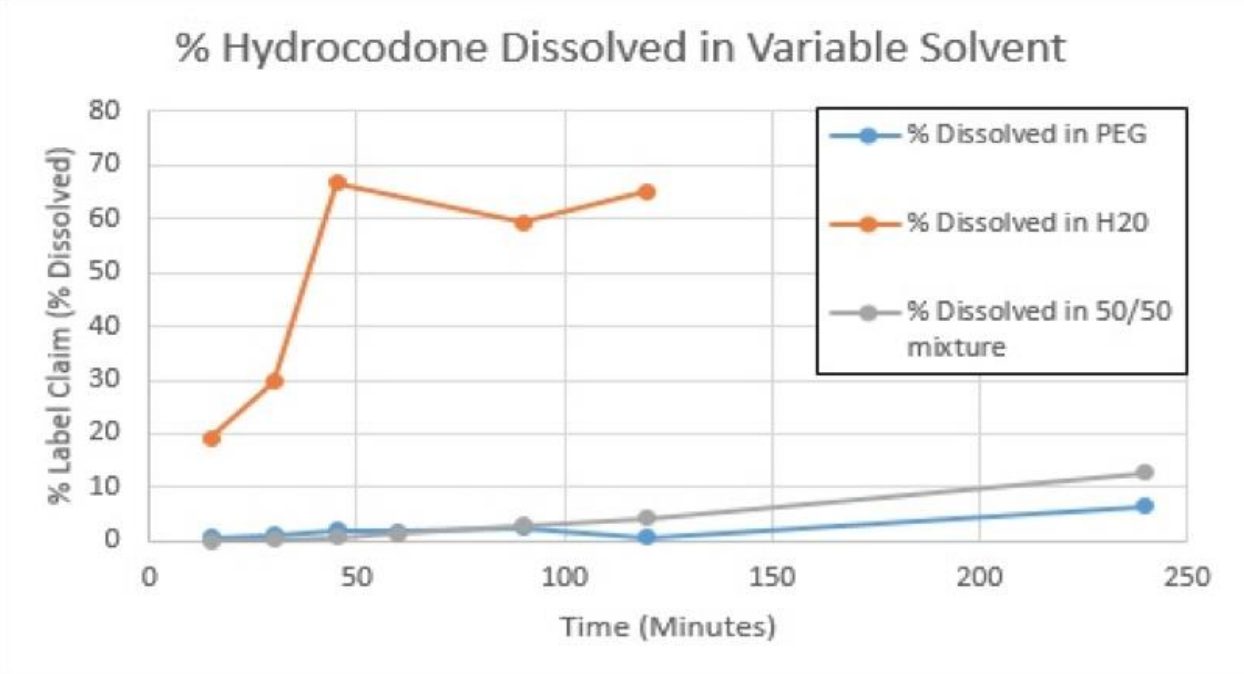


Figure 18: Hydrocodone Dissolution in Different Solvents. Testing shows that a whole pill dissolves into an H_20 solvent than PEG. This means that pills should first be dissolved into water first, then PEG should be added later to obtain drug nulling effects.

Agitation Method Dissolution Rate

In order to determine whether a stir bar system, tilting system, or simply vigorous shaking would be necessary to fully dissolve a pill into its solution. In order to accomplish this, we tested multiple

ideally ground powder tablets into both H_2O and PEG. The variable changing was the method of stirring. The three methods of stirring include a stir bar system, a rotator tilting system, and a vigorous shaking for 1 minute, then letting stand.

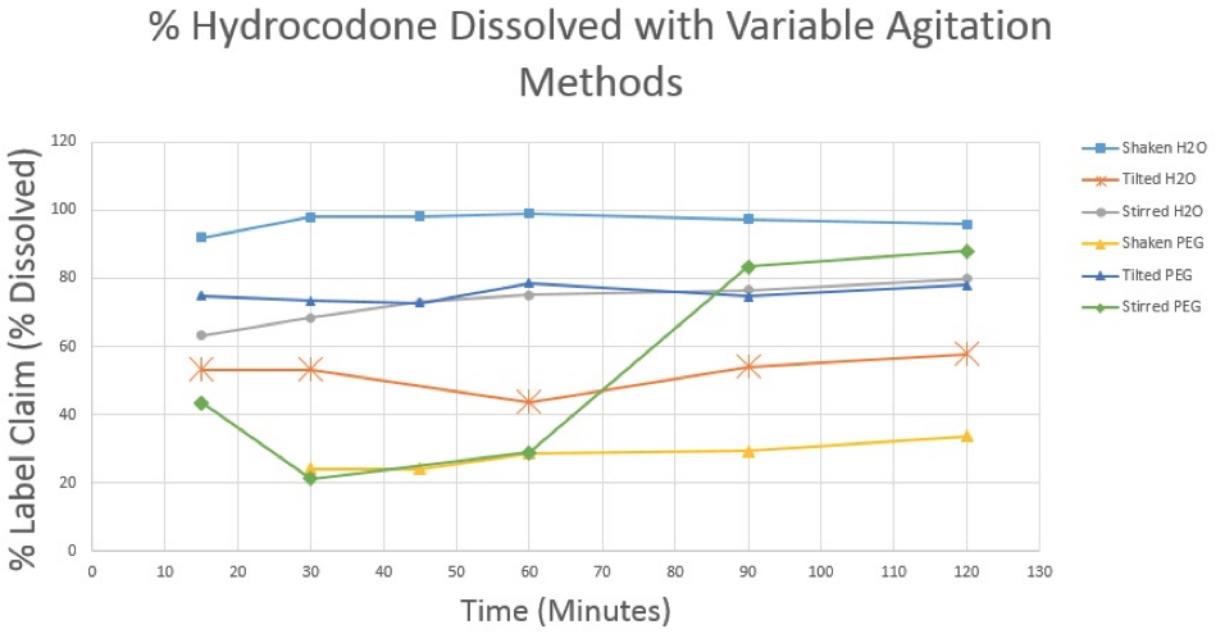


Figure 19: Hydrocodone Dissolution with Different Methods. Although testing does not appear to be conclusive, we feel that vigorous shaking for 1 minute followed by letting the mixture stand for fifteen minutes is a good method of use.

From the graph, we've determined that an at-home rotator or stir bar system is not necessary to fully dissolve hydrocodone into H_2O. Therefore, vigorous shaking for 1 minute with an ideally ground pill has been determined to be sufficient for a method of disposal.

Whole Pill vs. Ideally Ground Dissolution Testing

In order to determine if grinding the pill is truly a necessity, we performed both whole pill and ideally ground powder pill dissolution rates. From Figure 18 and Figure 19 it can be determined that that having an ideally ground pill is indeed a factor to dissolution rate. Figure 19 used ideally ground pills while Figure 18 used whole pills. From the graphs, it can be determined that ideally grounding your pill before dissolved indeed a major factor to dissolution rate. Therefore, we can conclude that ideally crushing a pill is a necessity to this method of disposal.

Discussion

Discussion of Testing

Using the results provided by the testing, the team was able to develop a recommended procedure for their device. The dissolution tests for both ground and whole pills reveal that water is a far better solvent for hydrocodone, than PEG. The results also show that shaking a ground hydrocodone pill in

water for 1 minute and then letting stand is the method of agitation which will yield the highest dissolution rate. Given this information and the saturation tests for hydrocodone and sodium bentonite the following procedure was devised:

1. Grind pills one at a time into bottle.
2. Add 1 mL water per hydrocodone pill.
3. Shake vigorously for 1 minute.
4. Let sit for 15 minutes.
5. Add one 27g sodium bentonite packet (per 30 pills).
6. Add one 15 mL PEG packet (per 30 pills).
7. Dispose of bottle in trash

PEG is still being added to the final mixture, despite its low dissolution rates, because it adds an additional level of protection. With PEG in the mixture even if the final product were consumed the person would be unlikely to receive the desired effect as PEG will cause the mixture to move through the digestive tract at an accelerated rate.

However, this current method is not as exact as it could be. Most of the data is based upon PEG, and since water is now what is being suggested more water saturation tests are needed. Meaning we need to find how much water would saturate sodium bentonite and hydrocodone tablets. Additionally, the tests focused on one pill to a certain amount of water and not 30 pills (as are suggested in the method). As such it would be beneficial to conduct dissolution and agitation tests using 30 hydrocodone pills. Finally, all the oxycodone results were inconclusive. It would be very beneficial to rerun those tests and attempt to get viable data. It would also be useful to just run some of these tests again. Each test conducted only has one run, and in order to be more thorough and ensure that our results were not just a fluke it is necessary to rerun many of our tests.

Doing additional trials for our testing would also help eliminate or minimize some of the sources of error. Many of these experiments were run simultaneously and as such certain time intervals were missed or taken late. Another source of error is that two of the tests using pre-ground pills, we did not filter the extracted samples. During these tests small particulates of hydrocodone could have been picked up and placed into the sample vials. These particles were then given an entire weekend to dissolve into the PEG/water which could skew the results.

Ethics

The major ethical concerns with our testing revolve around the fact that hydrocodone and oxycodone are schedule II controlled substances. This means that they cannot be moved from the location to which they are authorized, and individuals must be approved by the Department of Safety and Professional Services before they can access them. This is the only ethical course of action to pursue when testing these substances. While there are other methods of attaining these medications, they would not be considered ethical. This group conducted their tests under the supervision of Dr. Edmund Elder who is authorized to test hydrocodone and oxycodone. Additionally all tests using these substances were conducted in an authorized location and no samples ever left this location.

It is important that the final product of our process is neither toxic to human nor the environment. It is known that there are individuals who would attempt to abuse this substance, perhaps even after

undergoing our method of disposal. Therefore it is very important that the end result is not harmful to human beings in any way. Also the individual components of the design cannot be toxic. This means that if someone were to consume the sodium bentonite or PEG, they must not be harmed. It is possible that children could get to this product, as such it is important that it is not non-toxic to just adults but children as well. With the addition of being toxic, it also must not result in a dangerous chemical process. For example, if the pieces of our design resulted in a highly exothermic reaction that would be dangerous as the excessive heat could burn an individual. While not being harmful to human beings is important, it is also important to consider the environment. We recommend that the end result of this process is thrown out in the trash. To recommend this type of disposal knowing that the end result would have a negative effect on the water table or ecosystem would be unethical. Due to this, this design will still need a fair amount of environmental toxicity testing as to ensure that it is in no way harmful to the environment. Currently, throwing it in the trash is recommended as that is in line with FDA protocols. However, these protocols don't account for the addition of PEG.

Conclusion

Since many people aren't properly disposing of their unused medication, the rates for addiction and accidental overdoses on controlled substances such as hydrocodone and oxycodone have greatly increased. To decrease the amount of controlled substances with the potential to be abused, this design allows the user to render their leftover pills unusable by others by grinding them into a powder, dissolving them into water, solidifying the solution with sodium bentonite, and adding PEG to inhibit digestion. The team has concluded this to be the most effective method possible based on research, the results of the design matrix, and testing. The testing showed that water was the best solvent for dissolving hydrocodone and that ground pills dissolve faster than whole pills. Additionally the testing showed that shaking for one minute was the superior agitation method.

In retrospect, the herb grinder design that we implemented was not the best grinder design. A better alternative to look into would have been an actual pill grinder or perhaps something closer to a pepper grinder. The current grinder does not make a very fine powder and it leaves large chunks of material that does not fall through the holes. Whereas this would not be an issue with a pepper grinder design, even though such a design would be more difficult to fabricate. Also we would use a higher resolution 3D printer for our final design in the future. The 3D printer which was used was not accurate enough to get all the dimensions within a suitable error range and left behind a fair amount of scaffolding which had to be manually removed. A 3D printer with higher accuracy would allow for a grinder that fit more snuggly on the pill bottle. That being said, the current testing protocols worked well. Dissolution testing is probably the best method for testing how accurately a solvent would extract the active ingredients from the medication. However, it would be vital to have multiple trials for this.

Future Work

For future work, there is simply a lot more data that needs to be collected. The current method can only be guaranteed for one pill. There is no data for multiple pills at a time. As such when recommending our method we used a linear scale to approximate the amounts required, however, it is uncertain whether or not the process actually scales linearly. In general, more trials could be done of the tests that were already completed to ensure that the results were not a fluke, and the tests regarding oxycodone would need to be re-tested in an attempt to get tangible data. One more test that would provide

useful information would be saturation tests using water instead of PEG. This would give data on the amount of water that it takes to fully dissolve or encapsulate the medication and sodium bentonite. Another variable to investigate would be a different solvent. We only tested water and PEG. It is possible that there are superior solvents for this process that have yet to be investigated. These additional material tests could help ensure the functionality of the process.

Additional work would also include mechanical testing of the grinder, human toxicity testing, and environmental toxicity testing. Since many of the people using this device will be elderly it is important that the grinder itself is not too hard to turn. Tangible data on the force required for crushing a pill with the grinder would therefore be vital for ensuring that the device is user friendly for all ages. The toxicity testing is important for the ethical concerns discussed earlier. There is a very real chance of the end product being digested and there is a chance that a child may attempt to consume the individual components, as such it must be known that the end result is in no way toxic to humans. One of the components of the problem statement is that the end product must be environmentally friendly. It is also ethical to ensure that the end product does not have a negative impact on the ecosystem.

These future endeavors should lead to a more concrete final design and method. Once those are completed this design may be ready for the market.

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Appendix

PDS

Personalized Medication Disposal System

Product Design Specifications

Joseph Ulbrich, Evan Jellings, Alison Walter, Nick DiFranco

Function: When opiates like oxycodone or hydrocodone are prescribed to patients, often times they are not taken to completion by the user. If these drugs are not disposed of by the patient, the drugs can often times be stolen, abused, or misused by family and friends. Moreover, if the drugs are disposed of incorrectly, they present a threat to the quality of water in the water tables. A personalized medication disposal system to prevent the improper use of opiates is proposed. Currently, there are medication disposal systems available in hospitals and some police stations. There are also at-home, single use drug disposal packets available for purchase. Our goal is to design and develop a re-useable, at-home opiate disposal system that renders these drugs unusable and unrecoverable.

Client Requirements:

1. Render hydrocodone and oxycodone inert
2. Able to use in an "at home" setting
3. Nearly as convenient as dumping drugs down toilet/sink
4. Does not produce harmful by-products
5. Eco-friendly
6. Costs less than $5 to produce
7. Safe for use for the vast majority of persons (possibly those with severe arthritis are excluded)

1. Physical and Operational Characteristics:

a. Performance:

- Must completely neutralize/denature medication
- Drugs must be easily unrecoverable by physical or chemical means
- Drugs must be neutralized within a 48-hour time period

b. Safety:

- Safe for use by the vast majority of persons (possibly those with severe arthritis are excluded)
- No dangerously high temperatures, pHs, etc.
- Environmentally friendly

- Non-toxic
- Children-safe locking cap
- Directions for proper disposal must be included and be no more than 10 steps long

c. Accuracy and reliability:
- Must be able to render drugs inert and in an unrecoverable state

d. Life in service:
- The device needs to be able to dispose of a minimum of 30 pills without fail
- Able to take apart without risk to integrity
- Activated ingredient ought to be made available for purchase in bulk from store locations.

e. Shelf life:
- Should be able to sit on the shelf for a few years without breaking down or becoming ineffective

f. Operating environment:
- Homes, pharmacies, portable, etc.
- Able to be used practically anywhere with water access

g. Ergonomics:
- Easy to understand and use
- Sit flat on a level surface
- Not slippery
- Does not get too hot on exterior
- Smooth rotational movement

h. Size:
- The entire device should be the same diameter or slightly larger than pill bottle diameter
- The height of the device should not exceed 1.5 inches
- Small enough for at home, personal use

i. Weight:
- Less than 2.25 kg

j. Materials:
- Powder substance used to transform and render the medicine inert
- Grinder cap where pills will be placed for future grinding
- Pill bottle attachment with holes for medicine powder to fall through

- Measuring device attached to grinder cap for easy measuring of water.
- Containment unit
    - Original or designed plastic medication pill bottle

k. Aesthetics, Appearance, and Finish:
- Not overly complex
- Compact
- Not intimidating to use

2. Production Characteristics

a. Quantity:
- One, reusable if desired

b. Target Product Cost:
- Manufactured for less than $5
- Testing can cost ~$200

3. Miscellaneous

a. Standards and Specifications:
- Adhere to Federal and Dane County medication disposal regulations
- No illegal products/byproducts
- Federal DEA regulations do not permit controlled substances to be removed for disposal without special approval according to procedures established by regional DEA offices.
- Medical facilities must submit extensive record keeping for the disposal of controlled substances.
- Controlled substances can never be returned to the pharmacy for re-use.
- Controlled substances are more tightly regulated, and so must often be destroyed by a licensed pharmacist or nurse practitioner with another licensed medical staff person as witness.
- 17 states are silent on the specific process of destruction.

b. Customer:
- Usable in residential setting
- Easy enough for use by average person
- No components unsafe for use by average person
- Safe for standard household use

c. Patient-related concerns:
- All parts included must be safe for use by average person
- Must not create harmful products
- Outside does not exceed 37 degrees C or get less than -33 degrees C
- pH of potential chemicals in use/ by products 9-5 to prevent chemical burns

d. Competition:

- Cactus Smart Sink®
- Med Drop boxes at Police Stations
- Other patented personal medication disposal systems (Medsaway)

B. Testing Procedures

Opioids Needed:

- 12 Hydrocodone tablets: 5 mg hydrocodone, 325 mg acetaminophen, ovular shape
    - Weight: .4215 g
    - Dimensions:15mm L 7 mm W, 5 mm H
- 12 Oxycodone tablets: 5 mg oxycodone
    - Weight: .1241g
    - Dimensions: 6.46 mm Dia, 3.69 mm H

Test 1: Dissolution & HPLC Machine - Whole Pill

This tests how much of the active ingredients are extracted from the pill into the solution at given time intervals.

Materials:

- 50mL graduated cylinder
- 100 µL pipette
- dissolution machine
- HPLC sample vials
- Hydrocodone & oxycodone - 3 tablets of each (6 total)
    - Sample 1: 25 mL PEG, 25 mL water mixture + pill
    - Sample 2: 50 mL PEG + pill
    - Sample 3: 50mL H2O + pill
- Dissolution machine
    - Speed: 50 RPM
    - Bath temperature: 22.1 °C
    - Time: 15 min, 30 min, 45 min, 60 min, 90 min, 120 min, 240 min

Procedure:

1. Add solution and one pill to each test tube for the dissolution machine
2. Stagger samples by 1 minute
3. Stir continuously at 50 RPM
4. Pull 100 µL sample from each mixture at given time intervals
5. Place samples in HPLC sample vials
6. Run samples through HPLC

Observations:

- In PEG solution, pill floats, then sinks
- In mixture, pill sinks right away

Test 2: PEG absorbance

How much PEG is absorbed into a crushed tablet, based on visual observations.

Pills are crushed into powder, keep adding PEG until powder fully absorbs

Materials:

- 1 sample of each (hydrocodone & oxycodone)
- Mortar and pestle
- Petri dish
- PEG

Procedure:

1. Crush tablet into fine powder
2. Add powder to petri dish
3. Add PEG drop wise until the powder if fully absorbed by the PEG (qualitative)

Observations:

Hydrocodone

- PEG initially beads up on top of powder
- After mixing, PEG and hydrocodone have viscous, paste-like consistency

Results:

Hydrocodone

- 1 mL PEG until fully absorbed, with mixing

Oxycodone

- 170 µL PEG to one 5mg oxycodone tablet

Test 3: Sodium Bentonite & PEG absorbance

Tests the amount of PEG required to saturate approximately 0.5 g of sodium bentonite (cat litter).

Materials:

- 0.5 g sodium bentonite
- Mortar and pestle
- Petri dish
- PEG

Procedure:

1. Grind sodium bentonite into smaller granules (unless already in fine granules)
2. Weigh out 0.5g sodium bentonite

    a. actual weight: 0.5868g
3. Add PEG drop wise until sodium bentonite visually becomes saturated

Results:

- 650 microliter maximum of PEG
- 1.1077 mL/g

Test 4: Pre-ground Dissolution & HPLC Test

Tests how much of the active ingredient is extracted into the solution when the pills are already ground.

Materials:

- 50mL graduated cylinder
- 100 µL pipette
- dissolution machine
- HPLC sample vials
- Mortar and pestle
- Hydrocodone & oxycodone - 2 tablets of each (4 total)
    - Sample 2: 50 mL PEG + pill
    - Sample 3: 50mL H2O + pill
- Dissolution machine
    - Speed: 50 RPM
    - Bath temperature: 22.1 °C
    - Time: 15 min, 30 min, 45 min, 60 min, 90 min, 120 min

Procedure:

1. Grind tablet into fine powder
2. Add solution and powder (equivalent to one tablet) to each test tube for the dissolution machine
3. Stagger samples by 1 minute
4. Stir continuously at 50 RPM
5. Pull 100 µL sample from each mixture at given time intervals
6. Place samples in HPLC sample vials
7. Run samples through HPLC

Observations

- Hydrocodone and PEG forms a gel-type solution when mixed
- With water, both dissolved readily (separated from other solids well, not dissolution)

Test 5: Shaken for 1 min with ground pill Dissolution & HPLC

Materials:

- 100 μL pipette
- 4 test tubes
- HPLC Sample vials
- Mortar and pestle
- 50mL graduated cylinder
- PEG
- Water
- 2 oxycodone tablets
- 2 hydrocodone tablets

Procedure:

1. Grind one tablet to fine powder
2. Add powder and 50 mL water (or PEG) to test tube
3. Shake vial vigorously for 1 minute
4. Repeat steps 1 - 4 such that there are four samples
    a. Sample 1: hydrocodone + 50mL water
    b. Sample 2: hydrocodone + 50mL PEG
    c. Sample 3: oxycodone + 50mL water
    d. Sample 4: oxycodone + 50mL PEG
5. Pull 100 μL sample at: 15 min, 30 min, 45 min, 60 min, 90 min, 120 min
6. Place sample in HPLC vial

Observations

- Solution completely dissolved in all samples, cloudy liquid

Test 6: Rotating Pre-ground Samples Dissolution & HPLC

Materials:

- 1 LabQuake machine
- 100 μL pipette
- Filtered syringes
- 4 test tubes
- HPLC Sample vials
- Mortar and pestle
- 50mL graduated cylinder
- PEG
- Water
- 2 oxycodone tablets
- 2 hydrocodone tablets

Procedure:

1. Grind one tablet to fine powder
2. Add powder and 50 mL water (or PEG) to test tube
3. Put test tube in LabQuake

4. Repeat steps 1 - 4 such that there are four samples
    a. Sample 1: hydrocodone + 50mL water
    b. Sample 2: hydrocodone + 50mL PEG
    c. Sample 3: oxycodone + 50mL water
    d. Sample 4: oxycodone + 50mL PEG
5. Pull 100 µL sample at: 15 min, 30 min, 45 min, 60 min, 90 min, 120 min
6. Put sample into filtered syringe to remove excess solid
7. Place filtered sample in HPLC vial

HPLC Procedures:

High Performance Liquid Chromatography (HPLC) is a method for testing the dissolution rates of certain molecules in their solution when prepared at predetermined rates. The setup parameters for the HPLC machine vary based on the molecule being tested; the parameters for hydrocodone and oxycodone are summarized below.

	Hydrocodone	Oxycodone
Column	4.6 mm x 25 cm	2.1 mm x 250 mm
Column Temperature	50 C	50 C
Injection Volume	10 mcl	20 mcl
Flow Rate	3 ml/min	.3 ml/min
Detector	UV at 206 nm	UV at 210 nm
Mobile Phase	.005 M Na heptane sulfonate, methanol, phosphoric acid, trimethylamine (900:100:5:2) adjusted to pH 2.5 w/ NaOH	6.8 g/L monobasic potassium phosphate and acetonitrile (85:15) buffer with .2 mL triethylamine per L of buffer

HPLC tests require the user prepare an Assay Preparation: the solution being tested, and a Standard Preparation: a representation of the maximum peak area. To run the tests, a predetermined volume of each solution must be injected into the HPLC machine, and the peak areas of the Standard Preparation and the Assay Preparation must be recorded. Using the recorded peak areas, the concentration of the molecule in the undiluted samples can be determined from this equation:

$$\frac{MW\,disesquihydrate}{MW\,anhydrous} \times .1C \times \frac{ru}{rs}$$

$MW\,anhydrous$ = Anhydrous Molecular Weight

$MW\,disesquihydrate$ = Disesquihydrate Molecular Weight

C = Standard Preparation Concentration

r_s = Standard peak response

r_u = Assay peak response

For these tests, hydrocodone and oxycodone tablets were dissolved in either a PEG or water solution through several different methods in either a ‘whole pill’ or ‘ideally crushed’ state, creating multiple different conditions to measure varying dissolution rates. Samples from each of these different conditions were taken at time intervals ranging from 15 minutes to 240 minutes after preparation to determine how the dissolution rate varied over time for each.

Figure B1: **Tilting mechanism used for tilt method of testing**
The LabQuake machine constantly spun the samples around its axis.

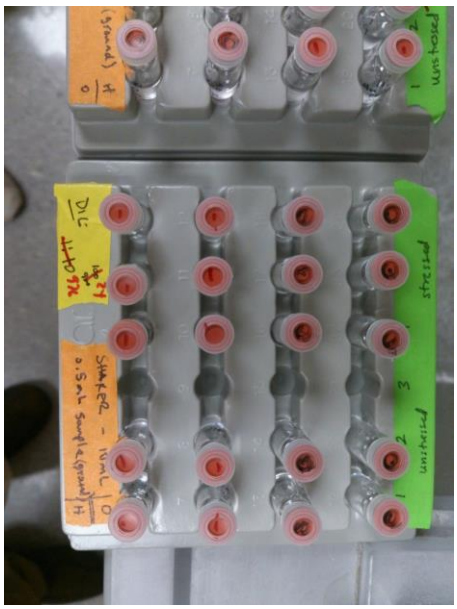


Figure B2: **Organization of samples**
Samples organized by stirring method and solvent

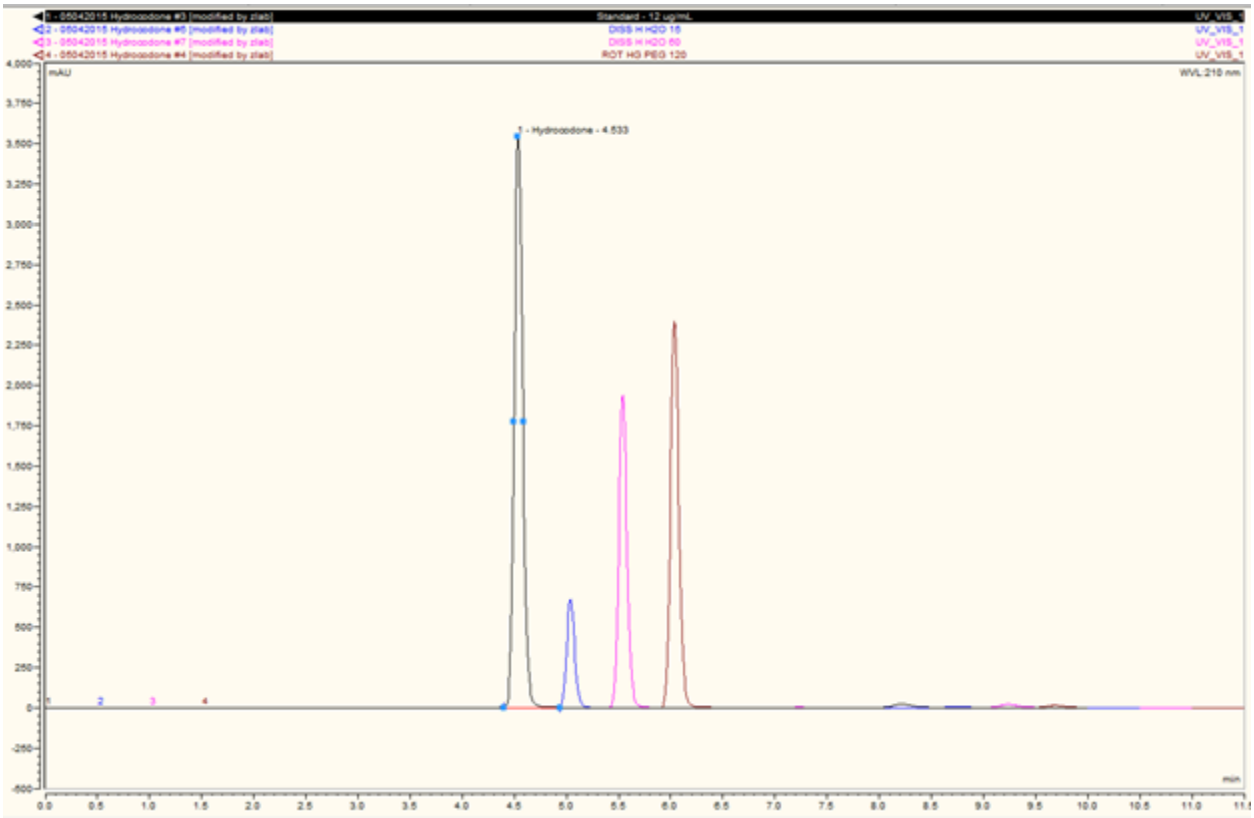
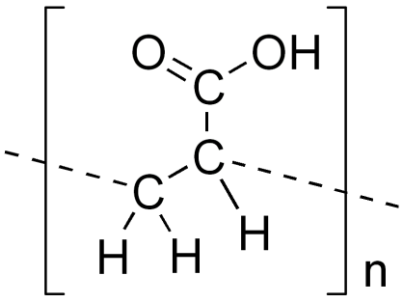
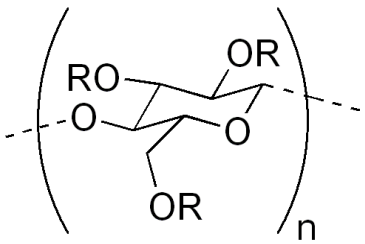


Figure B3: Chromatography overlays, with 5% time shift between, to facilitate visual interpretation.

C. Material Considerations

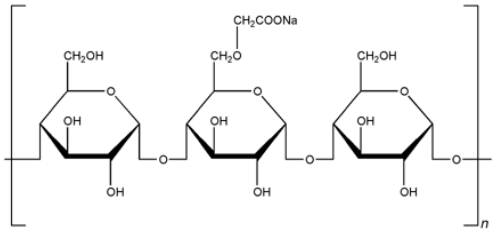


Poly(acrylic acid) (PAA): Polyacrylic acid contains a carboxyl group pendant chain, and so at non-acidic pH, this pendant chain will ionize. The resulting negative charge, accompanied by the macrostructure of the polymer, allows PAA to trap water at each pendant chain, resulting in swelling of the macromolecule complex. Materials with this property are known as polyelectrolytes. PAA is frequently used as thickening and suspension agents for petroleum recovery, pigment dispersion in paint, ion exchange resins (with cross-linking), and flocculating agents for particles suspended in water, and adhesives [17].

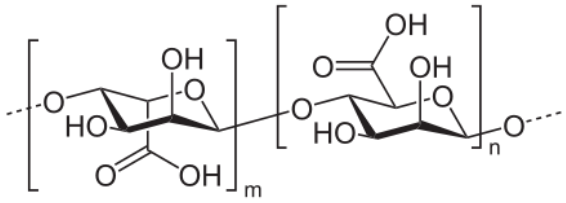


Hydroxypropyl methylcellulose (HPMC): HPMC is an inert, non-toxic polymer used as an excipient and controlled delivery component in oral medications. When combined with medication in water, HPMC will aggregate to form a suspended group, called a colloid [16]. Although HPMC is inert, it combusts when reacting with oxidizing agents. HPMC has been widely used to control the administration of a drug by delaying its release. HPMC is also used as a drug binder, which helps to dry and maintain structural support [18].

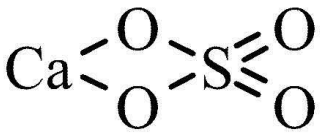
Sodium Starch Glycolate: Sodium Starch Glycolate falls under the category of superdisintegrants. The cross-linked starch glycolate is an anionic polymer that is produced by crosslinking and carboxymethylating potato starch [19]. Sodium Starch glycolate is used as a dissolution excipient for tablets and capsules. Because of its swelling properties in the presence of water, it is used as a disintegrant, suspending agent, and gelling agent [20].



Sodium Alginate: Alginate is a linear polysaccharide created from algae. Alginate gelling is mild enough to allow encapsulation of large biomaterials such as cells [21]. Mammalian cells do not interact with alginate through receptors, and alginate promotes very little protein adsorption, and subsequently very little cell adhesion. Alginate also makes a good base material to incorporate specific physical and chemical properties into the excipient substance. Alginate hydrogels are highly porous, allowing molecules to diffuse in and out of the matrix [21]. In addition to hydrogels, numerous desiccants were considered in the design process. Desiccants are widely used in food preservation, and are chemically inert. A few of them include:



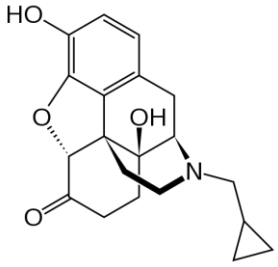
Calcium Sulfate: Calcium sulfate is a common lab chemical. In the anhydrous form it is used as a desiccant and coagulant. The hemihydrate and dihydrate form are known as Plaster of Paris and Gypsum respectively, and are used as plasters and thickening agents [22].



Cement Plaster: Cement plaster consists of sand, portland cement, and suitable plaster. When combined with water, a smooth paste is created, which hardens quickly. Cement plaster has the advantage of being strong, hard, quick-drying, and durable [23].

The hydrogel powder design also allows for increased flexibility in terms of what is included in the final compound. Specifically, there is a possibility that a substance that works to neutralize, degrade, or antagonize the active ingredient could be included, in order to further discourage ingestion of the finished product. One potentially viable antagonist is:

Naltrexone: Naltrexone is an opioid antagonist used in both opioid and alcohol dependence treatment. It mostly comes in a hydrochloride salt, Naltrexone hydrochloride. Naltrexone blocks opioid euphoric effects, thus helping patients overcome their addiction [24].



D. Survey

Be honest, we are looking for accurate results

Questions:

1. How have you disposed of excess medication in the past?
    a. Down a sink/toilet
    b. Into the garbage
    c. Medication drop box
    d. Did not dispose of

2. Do you know what a medication drop box is?
    a. Yes
    b. No

3. Do you know where your closest medication drop box is located?
    a. Yes
    b. No

4. Would you be willing to travel up to 5 miles to the closest medication drop box to dispose of excess medication?
    a. Yes
    b. No

E. Expenses

There were no recorded expenses for this project, therefore a table of the team's expenses does not exists.