Liquid Medication Delivery System

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Client: Engineering World Health

Abstract

In the developing world, AIDS has become a rampant problem, especially its transmission from mothers to newborn children. In order to combat the spread of AIDS, single doses of nevirapine, an anti-HIV drug, are given to infected pregnant mothers. This project seeks to design an inexpensive bottle-top dispenser for Viramune®, a brand of nevirapine. By consistently, easily, and efficiently measuring single doses of medication, the treatment will become more affordable; thus, more patients can be reached and the spread of disease will slow. The team designed a device that acts like a piston pump, incorporating two check valves and a syringe. A prototype was assembled and tested. Preliminary results suggest the device meets expectations.

Problem

Motivation and Background

AIDS kills 3.1 million people every year, over 80% of whom live in developing nations.[1] In the developed world, the progression of AIDS can be slowed significantly and held stagnant in a relatively nonthreatening state. However, the medications which effectively treat AIDS are quite expensive and thus not a practical solution for many parts of the world. Fortunately, a single 0.6 mL dose of nevirapine (sold commercially as Viramune®) administered at birth has been shown to effectively reduce HIV transmission from mother to child by nearly 50%.[2]

Well, if nevirapine is really so useful in these settings, why aren't all newborns of infected mothers treated at birth? Unfortunately, societies in many parts of the world are not set up with adequate access to healthcare. In many parts of Africa for example, a pregnant mother will only see a doctor once and give birth at a location relatively remote from any medical facility or pharmacy. Therefore, the mother must have an appropriate dose of medication that lasts from the visit to the doctor to the time she gives birth. A type of foil packet has been designed to help maintain the dose during this period, but a cheap way to measure the dose and dispense it into the packet is needed.[3]

Photo courtesy of Dr. Vivian Rexroad, PharmD.

http://www.healthcare-packaging.com/images/PATH.jpg

Figure 1: Top: Liquid nevirapine medicine bottle with oral syringe and cap currently used to deliver doses. Bottom: Foil packets used to contain doses of liquid nevirapine.

Client Requirements

- Liquid medication bottle-top dispenser
- Sterilely deliver fixed doses of liquid nevirapine into foil packages
- Dispense 0.6 mL (± 0.05 mL) of medicine (8% error margin)
- Accurately deliver 400 doses; operable for 6 months
- Seal medicine bottle and prevent contamination
- Cost ≤ $2.00 (USD)

Design

The device consists of two check valves in series, with a syringe inserted between them. It functions like a piston pump. When the syringe is pulled, it draws liquid from the medicine bottle, while a check valve prevents reverse airflow. When the syringe is pushed, a check valve prevents medication backflow, and the medication exits the dispenser into the foil packet[4].

The valves are diaphragm valves; they contain a flexible diaphragm which blocks reverse fluid flow. They were selected instead of ball valves, in which a spring-loaded ball blocks reverse fluid flow. Ball valves are more precise, because they are rigid and spring-loaded, but they are also more expensive. Diaphragm valves are cheap, so they were selected instead.

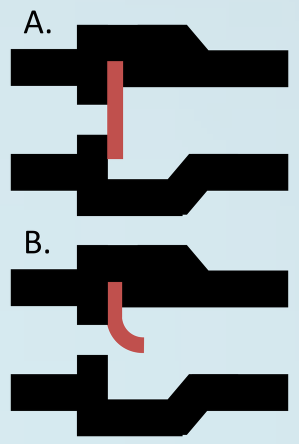
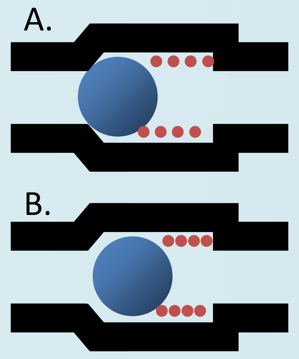


Figure 2: Diaphragm valve, closed in A, open in B.

The valves prevent fluid from flowing backwards, so the syringe must not overfill. A string connecting the syringe piston and chamber prevents this problem.

The tubing which connects the valves and the medicine bottle is rigid polypropylene. Its rigidity allows it to firmly support the valves and syringe, and allows it to be more easily glued to them. Polypropylene is also chemically inert, making it safe for use with the medication.



Adapted from Fronczak, F. (2009). Personal Communication.

Figure 3: Ball check valve, closed in A, open in B.

The upper tubing is flexible PVC, making its tip easy to reposition. A modified Airsoft BB narrows its exit spout, which helps to seal the dispenser and reduce the variability in the drip volume of the medication.

Figure 4: Prototype attached to a sample bottle with the same volume.

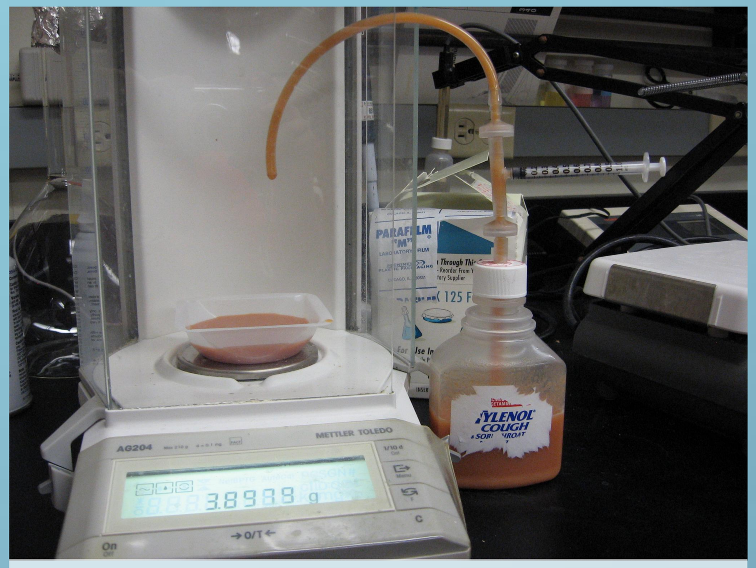


Figure 5: Prototype filled with testing fluid (cold tomato soup with milk).

Acknowledgements

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2. Guay LA, Musoke P, Fleming, T, et.al (1999) Intrapartum and Neonatal single-dose Nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET012 randomised trial Lancet 354:785-802.
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Testing

At the recommendation of Dr. Vivian Rexroad, a PharmD. at John's Hopkins University, we used cold (14.5 °C) Campbell's tomato soup made with milk as a substitute for nevirapine. We first found the mass of 0.6 mL of soup to be 0.6432 g with a standard deviation of ± 0.0148 g (n = 5). Using this mass, we determined that the syringe in the medication dispenser must be filled to the 0.7 mL mark to eject 0.6 mL of soup. We then wrote a procedure on how to operate the device, and each team member independently conducted ten trials. This demonstrates variation in operation by different users.

In Figure 6, the black line shows the actual mass of 0.6 mL and the red lines correspond to 8% error on the graph, the range within which the device must operate. The trial average was 0.6427 g (n = 50), slightly higher than the mass of 0.6 mL. The overall standard deviation was 0.0252 g. The average percent error was 0.082%, well within the required ± 8% error range.

Qualitatively, it was observed that constant speed and continuous motions result in the accurate volumes. Occasionally droplets would hang from the spout altering the expelled volume. To address this, a modified Airsoft BB was inserted into the spout to minimize dripping.

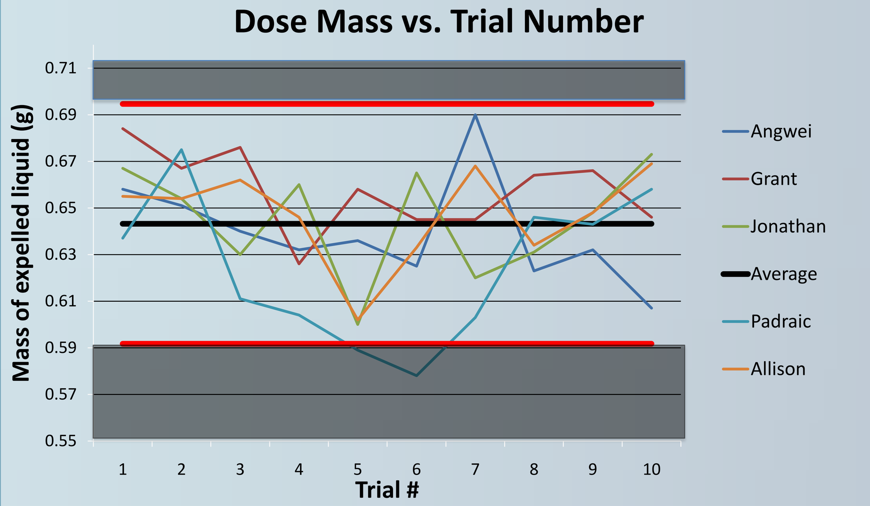

Figure 6: Testing results. Mass of dose was obtained for ten trials for each member and compared to the standard.

Cost Analysis

Quantity	Item	Price per unit	Sub-total
2	1/4" PP Liquid/Gas Check Valves	66.3¢	$1.33
1	Polypropylene Cap with Foamed PE Liner	5¢	$0.05
1	Precision-Glide, Tuberculin Syringe - 1 mL	22.11¢	$0.22
1 serving	Loctite Plastic Bonder	5.44¢	$0.05
23 cm	5/16" OD x 3/16" ID Polypropylene Tubing	0.984¢	$0.23
1	6 mm, 0.12 g Translucent Green Airsoft BB	0.240¢	$0.00
15 cm	Bonded Nylon #46 Thread	0.003¢	$0.00
1	Thumb Tack	0.935¢	$0.01
13.75 cm	1/4" OD x 0.170" ID Clear Vinyl Tubing	0.809¢	$0.11
		Total:	**$2.00**

Future Work

- Investigate manufacturing cost
- Use a more biocompatible glue to ensure complete patient safety
- Due to viscosity concerns, optimize medication volume for accurate dose delivery from foil packet
- Obtain nevirapine bottle from Boehringer Ingelheim to complete design
- Conduct reliability testing with both the medication and the foil packets