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Freeze-Dried Medication

The extent the freeze drying process is needed for human survival.

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Abstract

This essay looks into the topic of the Freeze-Drying process. The question is “To what extent is the freeze-drying process essential for human survival?” The essay starts off with an overview of the problems that could be caused without the lack of the process in the medical field. A detailed explanation of what the process is and how the process occurs is placed in the beginning so basic knowledge can be used throughout the essay. The essay then explains how important the process is for the survival of humans, essential for harvesting and keeping vaccines, a very impactful instrument for human survival, safe for a longer period of time. Examples of how the process helps in the real world today is used to come to the conclusion that the process is very essential for the survival of humans worldwide who can’t get treatment right away. Some of these examples include viruses that are very common amongst humans but treated with the help of medicine that is freeze-dried. This includes mostly the patients in third world countries that does not have the necessary tools and equipment to provide the vaccines within their own healthcare system. Without the freeze-drying process, many different viruses and infections near eradication could make a return and ultimately damage the lives of humans worldwide.

Introduction

In today’s world, there are many things that can cause harm to the human body. And for a minority of these things, humans have evolved to fight and become immune to some of these infections. But for the rest of them, humans have had to find solutions, or medications, to help the body kill off or get rid of the intruder. Although this seems like a great way to increase the survivability of humans, there are better ways of treating
illnesses than to use medication every time somebody gets sick. This is when other forms of medicine come into play, medicines that allow humans to use once or a few times in their lives. These medicines cause the body to become immune to the illness, the most common and well-known example is a vaccine.

The idea of vaccines or immunity was discovered by Edward Jenner in 1796. He found out that getting cowpox helped the body become immune to smallpox. This breakthrough in medicine has led to what all the different types of vaccines, and ultimately have saved millions and possibly billions of lives from life-threatening diseases (History). Even though we have developed many forms of medicine in our time, there are still many people around the world that do not have access to them. Medications are not all the same, most of them have to be treated differently, and because of this special precautions have to be taken into effect when processing medication. Some treatments cannot be left unused for a long period of time and can often be sensitive to many variables. If these variables are not taken into consideration, the medication can become useless, or even harmful to whoever consumes it. One way that medicine is preserved is by the process of freeze-drying, or lyophilization.

What is the process of Lyophilization?

The process of lyophilization is used to remove all the water from a frozen item using a process called sublimation. The process of sublimation is a transition from the solid state to the gaseous state without going through the liquid state (Lyophilization Info). In this case, ice is being turned into vapor without ever turning into a liquid. The reason why this is even possible is that you decrease the temperature of the product
while you are increasing the pressure. This causes the product to undergo the sublimation process. This is what lyophilization is, making the product undergo the sublimation process. This process has three main phases: the freezing phase, the primary drying phase, and the secondary drying phase. This process is used on a variety of different things, food and medications being the most common. Lyophilizing both food and medication will lengthen the longevity of the product, some more than others. Treatments today is one of the most important things, and increasing the longevity of these drugs will ultimately increase the longevity of humans.

The first phase of the freeze-drying process is the freezing phase. Usually, the ideal temperature for the freezing stage is around -40 °C. You slowly decrease the temperature of the freezer by 1 °C every minute and then hold in the freezer for 2 hours (Lyophilization Process Development). Crystals form when the products are frozen, but the rate of which the crystals all start to form can be random. For example, some solutions can start the process of crystallization around -40 °C, but every one of the solutions won’t form crystals at the exact time. In order for all of the products to undergo crystallization at the same time, you have to increase the temperature of the shelf the products are sitting on while the freezer’s temperature is decreasing (Lyophilization: Workshop for Formulation and Process Development).

The second phase is called primary drying. The goal of this phase is to remove the majority of the water that is in the product. "At the start of primary drying the product container, on average, 95% is water. At the end of primary drying, the amount of water remaining is on the order of 5% to 10 %" (Sterile Drug Products). One of the most
crucial things in this phase to watch out on is the critical temperature, or sometimes called the “collapse temperature” (Sterile Drug Products). The product has to be kept below this temperature or else the product has the chance to “collapse”. A product "collapses" when the products exceed the critical temperature but then goes back to the required temperature. This causes “the product to soften up to the extent that it no longer can support its own structure” (Lyophilization info). If the product collapses, then the product can no longer be used and has to be discarded. When the ice is removed from the product, the remaining solute has to form its own rigid structure. This is why it is essential that the product stays below the critical temperature and why the product is discarded if a collapse occurs (Sterile Drug Products).

The third phase of the process is called the secondary drying phase. In this phase, the water that is left over from the primary drying phase is taken out. Around 95% of the water is removed in the primary drying phase, and that 5% is usually taken care of during the secondary drying phase. The water is taken out of the product through the process of diffusion. During this phase, you can take out samples of products in order to see if they have been properly taken care of. Usually, they take out samples every 2-4 hours for around 10 hours during the phase. This is the phase of the process that you do not need to worry that much about. The risk of collapse is completely gone after the primary drying phase.

Why is the Freeze Drying Process so important?

The whole point of the process is to improve the stability of the formulation, both chemically and physically (Intro Workshop). When one refers to chemical stability, they are talking about things like the creation and even breaking of bonds in the solution.
One example of chemical stability is the time of the half-life. The half-life is the time required for half the solution to degrade (Intro to Workshop). When talking about physical stability, an example can be how proteins can unfold if they are left in a solution for too long or collapse of a solution. These are the things that the process counters and avoids. If a solution that goes to a medicine does not have a good chemical stability and the properties degrade, then the solution cannot be used. If you inject a person with a vaccine that has degraded, the vaccine will not be effective at all. That is why it is key to maintain the solution in a stage that will keep it from degrading quickly.

Some people usually like to overlook possible epidemics of infections, diseases, viruses etc. because they trust the advancement in technology and that medicine will be available if a certain outbreak would happen. Although there are some diseases that will kill humans if they are infected, there are much more that could just cause distress, discomfort, or just simply make life harder to handle. One example of an infection that could cause all these things to happen is an MRSA infection. An MRSA infection is actually very common. "Staphylococcus aureus, or "Staph" is a very common germ that about 1 out of every 3 people have on their skin or in their nose. This germ does not cause any problems for most people who have in on their skin. But sometimes it can cause serious infections such as skin or wound infections, pneumonia, or infections of the blood“(CDC). Staph doesn't do any major damage until it gets deep into your body and one of the easiest ways for these germs to get into your body is through a surgical wound.

An antibiotic is often given to treat these germs, so it doesn't risk the health of the patient. A common freeze-dried drug that treats these antibiotics is Vancomycin. This
drug is used to treat infections, and this is a possible drug hospital could use to kill off the Staph germs.

“Vancomycin reconstituted intravenous solutions are stable for 14 days at room temperature or refrigeration. Solutions diluted for administration in either D5W or NS are stable under refrigeration for 14 days or at room temperature for 7 days” (DIC).

Without refrigeration, the antibiotic can last only 7 days, and it can only last 14 days when refrigerated. This is when the antibiotic is reconstituted, after being freeze dried. Because of that short duration, it is necessary for this drug to be freeze dried.

This would cause problems for patients around the world. It would require less than 14 days for the manufacturer to ship the drug around the world before the potency wears off. Without this antibiotic, it would increase the risk of many patients falling to the MRSA infections. Since the Staph germs that cause the MRSA infections are so common, it could risk the health and even the lives of many patients around the world, especially from countries that are not as sanitary. The Vancomycin is not the only antibiotic that is required to be freeze-dried, and losing this process could take out many drugs off the market. The freeze-drying process is both essential to the economy and the health and wellness of many patients for different reasons.

What are the Advantages of Lyophilization?

There are many advantages of freeze-drying medications that need it. When a product is freeze-dried, it is in a dry, stable state. This makes it easier to transport than if the medication were to be a liquid. The drugs that are usually the most benefited from the freeze-drying process are the drugs that are very sensitive to the air (Intro). One of the
biggest advantages is the time it takes to reconstitute the medications. Reconstitution is the process of restoring the medication by adding a liquid to restore it to its liquid form. The powdered form of a drug will not be useful at all without having the liquid to reconstitute it, after reconstituting the drug, it is available after a certain amount of time to use. The solvent, or diluent, that is added to the powdered drug is not always the same. The solvent has to be different between different drugs. Another reason why the solvent has to be different is that of the patient. A common solvent used to reconstitute powdered drugs are sterile water and 0.9% sodium chloride. There are many people that can be allergic to sodium chloride so other solvents have to be used.

Also, as stated before, the process saves a large number of lives. It creates a possibility, a small chance to those who live around the world to receive the rightful treatment the same way people in wealthy countries like the United States do. There are many unfortunate individuals who cannot get the treatment they need around the world, treatments that most people take for granted. The measles vaccine is one most people overlook, the same with polio.

Disadvantages of Lyophilization

Although there are many advantages of freeze-drying medications, there are also some disadvantages. In every company, you have to spend money in order to make money. And in the case of companies that work specifically on freeze drying products, they have to spend a lot of money in order to create their merchandise. The equipment necessary to freeze dry products and materials are very powerful and require a lot of maintenance in order to keep them intact. This equipment can be very expensive and
there are numerous parts that go into building a machine capable of freeze-drying medicine. You have to have a refrigeration system that is strong enough to cool down its substances to the required temperature and remain that temperature for potentially hours. A vacuum system is also required and the condenser as well. All these different systems have to be running constantly which would require a lot of energy. The amount of electricity and power required to keep these machines going is huge and it impacts the environment drastically. The process of freeze-drying is by no means environmentally friendly but it is a necessity to keep the process going.

Without freeze drying medicine, at the same time that we are saving millions of people, we are also damaging the Earth. But if we stop the process, how many people could possibly be affected. Let's take a look at one of the most common vaccines people receive in the United States, the Polio vaccine. The polio vaccine was introduced in 1955 and was very common in the United States. For the majority of the people infected with the Polio virus, they received flu-like symptoms that lasted 1-10 days such as a fever, sore throat, headache etc.

There were rare cases where polio could lead to paralytic polio, the most serious form of the disease. "Paralytic polio has several types, based on the part of your body that's affected — your spinal cord (spinal polio), your brainstem (bulbar polio) or both (bulbospinal polio)". The symptoms represented normal polio until after a week. Then symptoms like loss of reflexes, severe muscle aches, and loose and floppy limbs happened (mayoclinic.org).

When the vaccine for polio was introduced, it saved many of lives. But truly how impactful is the vaccine today? Well in the United States, most people get their vaccines
when they are children. Between the ages of 2 months to 6 years, there are a total of four vaccines given to children to add their immunity to the poliovirus. Around the world, around 85% of infants receive at least 3 doses of the polio vaccine (source). So what would happen if we stopped the freeze-drying process? Polio is a virus that can be completely eradicated, it can only spread from human to human, and meaning if everybody is immune to the virus, a person that is infected cannot spread the virus anymore, leading to the eradication of the virus. Without the freeze drying process, the virus would go from near eradication to the spreading of it once more. It would spread to a small amount due to 99% of it being eradicated and all of the people already being immune to it. The virus would have to wait for the birth of a new generation for it to spread to the number of people it once infected.

What would happen if vaccines run short?

The shortage of vaccines could become a major problem if the freeze-drying process would to stop. There have been shortages of vaccines for different types of infections and illnesses, some more major than others. One of these shortages that happened over a decade ago was the shortage of the influenza vaccine in 2004-2005. Influenza is just the simple flu, and this is a very common issue in the United States. Due to the high population, especially in extremely dense places like New York City, Chicago, and Los Angeles, the simple flu can spread quickly from person to person. The CDC predicts that "millions of people get the flu every year, hundreds of thousands are hospitalized and tens of thousands of people die from flu-related causes every year" (https://www.cdc.gov/flu/protect/keyfacts.htm). Most people in the United States usually
like to overlook the flu as a minor illness that everybody gets, they do not realize that it could vary every season.

In 2004-2005, a company by the name of Chiron Corporation suffered a license suspension by the United Kingdom’s Medicines and Healthcare Products. This caused a major shortage of the influenza vaccine, as the corporation was supposed to supply around half the estimated 100 million doses required in the United States (NCBI). In this case, all it took was one license suspension from a corporation to create a shortage of over 50 million doses of the influenza vaccine. The whole situation got out of control. The government had to track every place that needed these doses, they needed to find the supply and demand of these doses, which included private health offices, clinics etc.

“The Veterans Health Administration (VHA) is the nation’s largest integrated health care system, and as of June 2005 operated approximately 157 medical centers, 862 community-based outpatient clinics, 134 nursing homes, and 337 other types of facilities and programs” (NCBI). With this large health care system, one can only imagine the amount of doses is demanded from this administration. In 2002, the Veterans Health Administration purchased around 1.58 million doses of the influenza vaccine. This number steadily grew and in 2005, they purchased 2.49 million doses. This shows the extra amount of demand that these vaccines had, but they didn’t have the supply to fulfill this demand. According to statistics, the Veterans Health Administration’s patients are usually older in age, sicker than regular patients from other administrations, and are usually poorer.

In order to find out how this shortage of influenza vaccines impacted their patients, the Veterans Health Administration Office of Quality and Performance
conducted a survey to its patients. They ended up surveying 218,775 patients between the months of October of 2004 and May of 2005, this was a typical period of the influenza vaccination. The patients were asked the question “Did you get a flu shot in September 2004 or later?” They had the responses “yes”, “no, and “I don't know”. If the patients were to answer “no”, then they would be asked why they were not able to be vaccinated.

The results that were received from this survey were interesting as you could see a major impact of the vaccine shortages in the age group of 54-65, but a marginal difference in change in the age group of 65+ years old. In 2002-2003, 48.3% of people from ages 50-64 were vaccinated in their local setting, while 38.0% had to travel to another location, and only 13.7% were not vaccinated. But if you skip forward two years when the shortage of vaccines occurred, the percentage of people vaccinated stayed around the same percentage, going from 48.3% in 2002-2003, to 47.0% in 2004-2005. The most interesting part is the large decrease of the people who went to another setting to get their vaccination and the large increase in people who did not get their vaccinations. During the years of 2002-2003, 38% of the patients went to a different setting to get their vaccinations done. 13.7% didn't get their vaccinations at all. Compare those to the patients from the years of 2004-2005, where the shortage of vaccinations occurred. Only 9% of people went to another setting for their vaccinations and 44% did not receive their vaccinations. That is a 29% decrease in the number of people who went to a new location and a 30.3% increase in people who did not receive their vaccinations at all.
Having 44% of a certain age group not get their vaccinations can be a major problem. With all the statistics about how sick and how serious the flu can get, a lot of people were put at risk of having possible hospitalized sicknesses because of the lack of supply. Surprisingly, for the age group of 60+, the percentage of people that were vaccinated went up. From this data collected by the Veterans Health Administration, we can conclude that the shortage of vaccines for influenza was more impactful towards the age group of 50-64 than the age group of 65+. “Our data suggest that VHA users aged 50–64 were most affected by the national influenza vaccine shortage, but the impact on VHA patients appears smaller than what was experienced outside VHA” (NCBI).

Pre-Cautions with Freeze Drying Medicine

One thing that is necessary when using medications is to keep it sterile and clean. Sterility is a bigger precaution that needs to be taken when dealing with injections or vaccines. Injections go directly into your body, and most times they can go directly into your bloodstream. If your needle or drug is not sterile or clean when you inject the drug inpatient that could pass many bacteria and other substances to get the patient extremely sick. When a patient gets inject directly into the bloodstream, the bacteria will never pass through the immune system, making it impossible for the patient’s body to fight it off. One issue that could happen is the use of one needle on multiple people. This is a very rare case of ever happening in the medical centers across first world countries but it is not as rare in poorer countries. There are cases of medical personnel using the same needle to treat patients in third world countries. One example would be the case that happened in South Sudan. Around May of 2017, 15 children died and over
32 others got sick in South Sudan due to unsanitary conditions when they were getting their measles vaccinations. The vaccines were not refrigerated, something that is required to keep the medication stable and safe to use. There was also a good amount of untrained personal injecting people during their vaccinations. Without the proper training on how to vaccinate somebody, it is completely possible for somebody to inject somebody incorrectly or make the needle unsanitary. It was also reported that the same needle was used on multiple people. The vaccination was for the measles virus, which is a problem in third world countries like South Sudan. Using the same needle can be an even bigger problem in countries like South Sudan because there is a risk that people getting injected can have another disease. When a syringe is used, it can carry many bacteria of the person who was injected with it. It is even worse if the person was carrying a disease because the disease could easily be transmitted to everybody else that gets injected with that needle. This might have been the case in South Sudan to the children. This is one example of how many possibilities a freeze-dried product can do but it still has to be treated correctly in order for the product to work. Freeze dried products have to be treated carefully in the making of the product, the shipping of the product, the storage, and the application of the product into its desired patient.

Conclusion

Looking at all the different types of the way the freeze-drying process could be used in the medical field, I believe that the process is crucial for human longevity. The process allows the potency of a certain drug to last way longer than if it were to remain
in its standard state. Because of this, it allows the medicine to be made and processes here in the United States and then be shipped over to around the world. The drugs were in a solid form makes the transportation and shipping process way easier, as you do not have to worry about spilling it over. The freeze-dried drugs are also was easier to maintain and is also easier to give it to a patient that needs it. It helps with sanitary conditions and the process itself is involved with many drugs that cure and protect us from dangerous infections and illnesses.
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