

## Temperature Management of Thermolabile Medicines: Transport Device Development

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**ABSTRACT:** This paper presents a study on the development of a temperature-controlled thermal refrigeration container to facilitate the transport of thermolabile drugs to remote places or places without access to medicines. Because of this, the project has as its problem the manufacture of a refrigerated thermos container with temperature control that can help the transportation of thermolabile drugs. Consequently, its objectives are: to study the materials and tools to complete such a task, as well as to design their operation through studies, and to utilize existing equipment from other operations. The methodology was modified as a polyurethane cooler, where we added a device to cool the container, a sensor for monitoring, and a power bank to power the refrigerators. The results obtained in the studies are valid, and we believe the project is viable, but we will only have concrete results after the prototype tests.

**KEYWORDS:** Thermolabile Medicines, Refrigeration, Temperature monitoring.

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### I. INTRODUCTION

The exposition of thermolabile drugs to adverse conditions recommended by the manufacturer may suffer a decrease in their potency, a reduction in their shelf life, and changes in their toxicity [1]. Also, improper packaging of thermolabile products can cause adverse effects in patients who use it [2]. The American Pharmacopoeia's MEDMARX medication error notification system recorded almost 1000 notifications involving errors associated with thermolabile drugs, most of the time due to incorrect transport, and therefore, the transport of these drugs requires special attention [3].

The main factors in maintaining the quality of the drugs are the temperature during storage and transport so that if not respected, they cause changes and the deterioration of the drugs [4]. The transport of thermolabile medicines is a significant step to reach the final consumer in the ideal condition of consumption, without changes in their formulas and having the effectiveness proposed by the manufacturer [3]. Acceptable transport practices are part of the quality assurance that attests that the transport process occurs within the appropriate quality standards for developing all stages of the transport of medicines [5]. This guarantee in transport does not always occur since the thermal packaging used for this function does not meet the conditions necessary to keep the medicine preserved [6]. To carry out transporting medicines, thermal packages, or refrigerated vehicles must be used, to guarantee the ideal conditions of transport [4].

The storage of drugs must be done in appropriate environments, according to the specific characteristics and conditions of conservation [1] and must be done based on each drug's requirements according to its manufacturers [3]. The storage of thermolabile medications requires a constant temperature of around 20 °C with  $\pm 2$  °C of variation, constant temperature measurements and records, and an alert system for possible defects in refrigeration equipment [4].

The transport of thermolabile medicines in places of difficult access becomes complicated because one of the factors that hinder locomotion is that the national roads are in critical condition, lacking adequate vehicles and inadequate containers [7]. The transport of thermolabile medicines occurs with polystyrene boxes, the medicine stored with ice, and the monitoring is done with laser thermometers or with an extension cable. It is an inadequate form, and without guarantee, we are often unable to guarantee that the medicine temperature remained in the range of 2 °C to 8 °C [8].

There is an apparent problem concerning the low conservation of thermolabile drugs and the difficulty in transporting them. With that said, it is justified to develop a device that can transport the thermolabile medicines

while maintaining their temperature so that the medicine does not lose its properties and to facilitate transportation in more remote places with difficult access to these medicines.

This paper is a study in which it contains the procedures for the theoretical realization of a cooling device to transport thermolabile medicines with automatic temperature adjustment.

## **II. LITERATURE REVIEW**

The storage of thermolabile medicines is temperature-sensitive products that must occur according to the pharmaceutical industry's temperature range. Many of the thermolabile drugs indicated for treating chronic diseases, such as diabetes, and cancers when a cold chain failure occurs, they may have their effectiveness impaired [9]. Most thermolabile is in the range of 2 °C to 8 °C, and if they do not occur at this temperature during transport or storage, they can have their cold chain destabilized, thus impairing its performance.

Thermolabile medications require a specific storage process, as they are sensitive to temperature action. Thus, for the correct storage of medicines and thermolabile products to occur, they must be stored in refrigerated equipment, with continuous temperature control, through maximum and minimum thermometers, adequately calibrated and qualified [10]. Storage of thermolabile medications requires a constant temperature in the range of 2 to 8 °C with  $\pm 2$  °C of variation, constant temperature measurements and records, and an alert system for possible defects in refrigeration equipment [9]. Temperature records must be kept at least during the product's validity period and available for possible evaluations [4].

The proper storage of thermolabile medicines maintains their integrity and efficiency during the entire storage period in which these medicines pass so that the environments dedicated to this are clean, dry and are adequate to the temperature standards and the medicines are distributed organized form and away from the floor, facilitating its cleaning and inspection [4-10]. Temperature mapping should also be carried out in these environments, in different seasons, to check the uniformity of temperature distribution in these locations and adjust the thermometers [4-10].

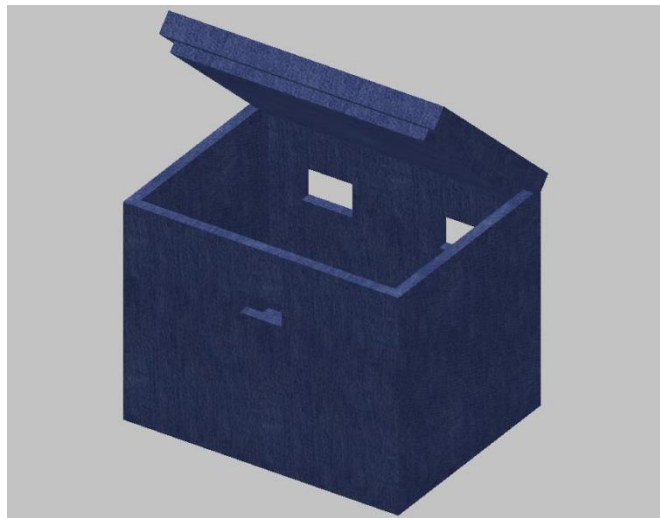
To guarantee the best transportation of the thermolabile medicines is necessary to make sure that the medicine transportation occurs in suitable thermal packages, and for that, the process of qualification and validation of thermal packages is carried out [11]. The qualification deals with a set of procedures to prove and register that a passive isothermal system works appropriately to achieve the expected results [8]. This process occurs in two stages, operational qualification, and performance qualification. Under extreme conditions, the operational qualification determines that an experimental packaging acts as expected, within parameters such as thermal mass, thermal box cubage, time, and temperature [4-8].

The performance qualification proves that thermal packaging designed according to acceptable transport practices' criteria observes the essential requirements. It is characterized by the sending of thermolabile products, through known routes, to determine if the packaging is being adequate and reproductive for the transportation of these products. This type of test must be performed twice a year, in winter and summer, evaluating the temperature records during the entire transport period [4]. Projects developed using 3D modeling software, simulation, and computational support are suitable for Assistive Technology (AT) [12] or improvements in hospital devices and devices to support people with disabilities [13-14].

## **III. MATERIALS AND METHODS**

The projection of a thermal box according to the packaging model for the transport of thermolabile medicines (Fig. 1) where the material of the box will be polyurethane, the thermal insulator will be the styrofoam or thermal blanket. For the cooling system, we will adapt the model for the cold element, because instead, we will use another cooling system where we will use the principle of the Peltier effect, using the Peltier tablets, therefore, in the box, there is an opening to just couple the cooling system. Cooling, and an opening in the front to place the thermometer display. The projected box has dimensions of 260 mm x 200 mm x 20 mm, which supports up to 5 L. However, the volume reduction with the cooling system will occupy a little of the box's internal space.

**Figure 1. Image of the 3D projection.**



In the cooling system's projection occurs the use of two Peltier, as we can point out that they are incredibly light. Peltier has precise temperature control, is completely silent, there is no vibration, requires less physical space than compression and absorption cycles, and require little maintenance, and to avoid overheating of the insert plates, heat sinks and fans occurs on both sides of the inserts (Fig. 2). To increase its efficiency, we will use thermal paste between the plates and the heatsinks to make the heat exchange easier. This system will be coupled to the upper rear part of the container, so that an air cycle can be generated inside the container, because as the cold air goes down, and the hot air goes up, they enter a cycle, thus improving the efficiency of the cooler.

**Figure 2. Refrigeration system image made by the Inventor.**



In the projections made in Inventor, the components and systems are not with the real dimensions since the projection is just a demonstration and assumption of what the real prototype will be necessary. A 12 Volts source will power the cooling system since this is the source recommended by the manufacturers, but we plan to add a battery. The transportation of the container occurs without needing any source of energy.

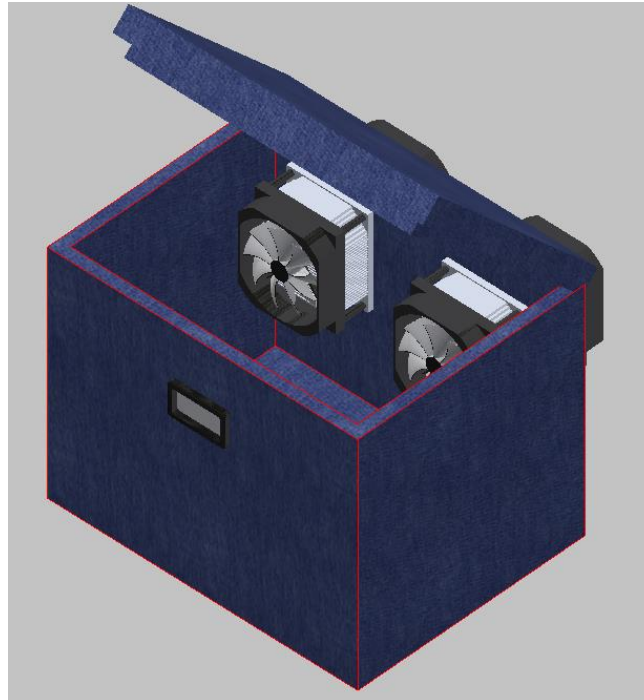
To choose the thermoelectric pads, research on the most used in refrigerators and containers with a similar purpose to ours occurs. They are sold in the market today, and the model Peltier Cell Tec1-12706 has dimensions of 40 mm x 40 mm x 4 mm, its temperature range varies between -30 C° to 70 C°, its weight is 30 g and its power consumption when in operation is 72 Watts.

For the choice of standard aluminum sinks, since our module has a consumption of approximately 70 Watts, and a fan for increasing heat dissipation. The chosen heatsinks were of the Heatsink model of the brand 3C Digital Electronic with 40 mm x 40 mm x 11 mm dimensions, where it will be glued together with the thermoelectric chip with a thermal paste to facilitate the heat exchange. The fans will also be 40 mm to facilitate fitting in the heatsinks.

Finally, we will add the monitoring system, which initially planned to install only a thermometer with an external sensor and a display to check the temperature from the outside of the container. Future an intelligent

temperature sensor that will take temperature measurements and transmit data for those responsible for monitoring the container for generating quality control reports on the conservation of thermolabile drugs, since this is a requirement for carrying out the task of transporting such drugs (Fig. 3).

**Figure 3. Final projection of the thermal box with cooling system.**



#### **IV. RESULTS**

The material defined by the group for the future manufacture of the box is polyurethane recommended for the manufacture of refrigeration coolers. It is a thermal insulator of excellent quality and follows the packaging model for the transport of thermolabile medicines. Recommended using some thermal insulator inside the packaging, which we define as Styrofoam or thermal blanket.

The cooling system of the thermal packaging defined was using the Peltier effect since there are many cases where the transport of these thermolabile drugs using dry ice or other refrigeration methods that are not very reliable. The tablet chosen by the group is of the model Peltier Cell Tec1-12706, which will also use heatsink of the model Heatsink of the brand 3C Digital Electronic.

For the monitoring system, the use of a monitoring sensor provided by the company SensorWeb defined, since this sensor emits temperature variation data to generate reports and thus be able to control and verify the quality of the medication preservation, which must be issued by the least during the validity of the drug to be stored.

#### **V. CONCLUSION**

After analyzing the results shows that it is still possible to proceed to realize the proposed product; however, losses of efficiency of the cooling system not considered due to lousy sealing or problems during the heat exchange, for example. As the tests start to occur, the results can become more realistic and valid. The research has not yet been completed, so the authors have the prospects of making the prototype, made with different types of thermal insulating materials, to improve it in the best possible way, as well as checking the efficiency of the refrigeration system and trying to improve it by increasing its effectiveness.

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