Study of drug degradation at Mars Desert Research Station

Martin Roumain
Université catholique de Louvain, Belgium
martin.roumain@uclouvain.be

Abstract

Medications degrade over time. Degradation of an active pharmaceutical ingredient (API) can result in reduced drug potency and increased toxicity due to degradation products formation. This degradation is accelerated by suboptimal storage conditions. Environmental factors of a Mars expedition such as microgravity, temperature variations and radiation may catalyze these drug alterations .

The use of medications during space missions is common. Pain relievers, antihistamines/decongestants and sleep aids are among the most used medicines in space . Medications used by astronauts aboard the International Space Station are resupplied before their expiration date. However, with an average medication shelf life of 1 or 2 years, this will not be possible for a long duration mission such as a Mars expedition.

With an expected duration of 6 to 7 months, a journey to Mars will most likely induce a significant drug degradation. It is then of paramount importance to study this accelerated degradation. A better understanding of this phenomenon will help to elaborate an especially space-designed packaging to ensure safety of acute and prolonged treatments to astronauts.

1 Objectives

There are two main objectives to this experiment. First, we want to show that it is actually possible to quantify active pharmaceutical ingredients in a rather small lab in the middle of the desert. Second, we want to quantify a potential degradation of such complex organic molecules by quantifying them throughout our stay at MDRS.

2 Procedures

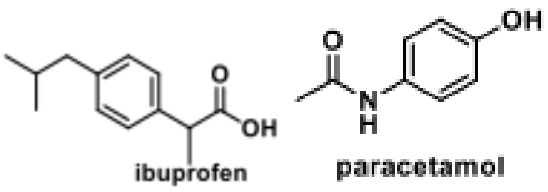
We want to quantify drug degradation throughout a Mars simulation. In order to do so, we will quantify API (active pharmaceutical ingredient) levels three times during our stay: on SOL1 (11th March 2017), SOL7 (17th March 2017), and SOL13 (23rd March 2017).

On SOL13, we will quantify samples stored in a plastic bag outside the base throughout the expedition. These organic molecules will undergo suboptimal storage conditions which will cause a forced degradation. We expect this degradation to be significant so that it provides us a positive control of drug degradation.

We will also quantify samples after the expedition and compare our results with samples left in Belgium. This will allow us to discriminate expedition-related and normal degradation. Each measurement will be done in triplicate to minimize errors.

A Mars expedition will last one year at least. It means that astronauts will need an enormous amount of medicines. We selected 4 different molecules among the most used medicines in space missions[1,2]:

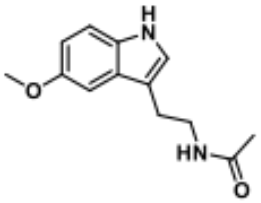
- Two painkillers and/or anti-inflammatory drugs commonly used in acute treatment of headaches and muscular pain: ibuprofen and paracetamol (known as acetaminophen in the US);



- One dietary supplement used as a treatment of

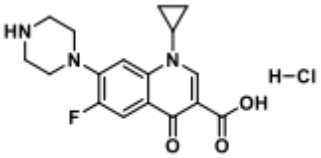
[1] Du B. et al., AAPS J., 2011;13(2):299-308
[2] Wotring V.E., AAPS J., 2016;18(1):210-6

sleep disorder: melatonin;



melatonin

- One antibiotic used to treat various bacterial infections: ciprofloxacin hydrochloride.



ciprofloxacin hydrochloride

These molecules will be analyzed using a spectrophotometric method. These dosage methods are based on the interaction between the molecule of interest and the light. The more a solution is concentrated, the more it absorbs light. After looking for the optimal wavelength of the beam (the wavelength where the absorbance is at its maximum), we will proceed to the measurements. The equation of Lambert-Beer connects the absorbance (A) of a solution to its concentration (c):

$$A_\lambda = \epsilon_\lambda \cdot l \cdot c$$

The molar attenuation coefficient ϵ and λ being unknown, we won't be able to directly use this equation. We will then construct a calibration curve. This calibration curve will link the absorbance and the concentration of our solution. We will construct it by measuring the absorbance of the solution on several concentrations. This is shown in Figure 1. We will then be able to connect the measured absorbance at MDRS to the solution's concentration.

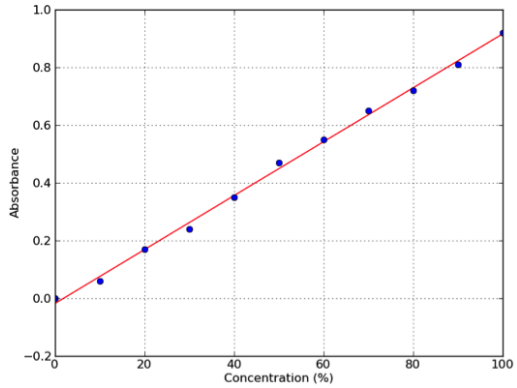


Figure 1: Absorbance of the solution on several concentrations.

2.1 Construction of the calibration curves

Ibuprofen and paracetamol As described in [3]:

- Prepare solutions of 10 μg/mL, 9.5 μg/mL, 9 μg/mL, 8 μg/mL, 5 μg/mL, 2.5 μg/mL and 0 μg/mL in sodium hydroxide 0.1 M.
- With the 10 μg/mL solution, look for the maximum absorbance within the 200-400 nm range.
- Measure the absorbance of the solutions at the optimal wavelength.

Melatonin As described in [4]:

- Prepare solutions of 20 μg/mL, 19 μg/mL, 18 μg/mL, 16 μg/mL, 10 μg/mL, 5 μg/mL and 0 μg/mL in hydrochloric acid 0.1 M.
- With the 20 μg/mL solution, look for the maximum absorbance within the 200-400 nm range.
- Measure the absorbance of the solutions at the optimal wavelength.

Ciprofloxacin hydrochloride As described in [5]:

- Prepare solutions of 10 μg/mL, 9.5 μg/mL, 9 μg/mL, 8 μg/mL, 5 μg/mL, 2.5 μg/mL and 0 μg/mL in hydrochloric acid 0.1 M.
- With the 10 μg/mL solution, look for the maximum absorbance within the 200-400 nm range.
- Measure the absorbance of the solutions at the optimal wavelength.

2.2 Sample quantification

Ibuprofen and paracetamol

- Dissolve 10 mg in sodium hydroxide 0.1 M, then adjust to 100 mL with the same solvent.
- Dilute 1 mL of this solution to 10 mL with the same solvent (final concentration = 10 μg/mL).
- Measure the absorbance of the solution at the optimal wavelength.

[3] Joshi R.S. et al., Der Pharmacia Sinica, 2011;2(3):164-71
[4] Uslu B. et al., Analytical Letters, 2002;35(14), 2305-17
[5] Hopkała H et al., Acta Pol Pharm, 2000;57(1):3-13

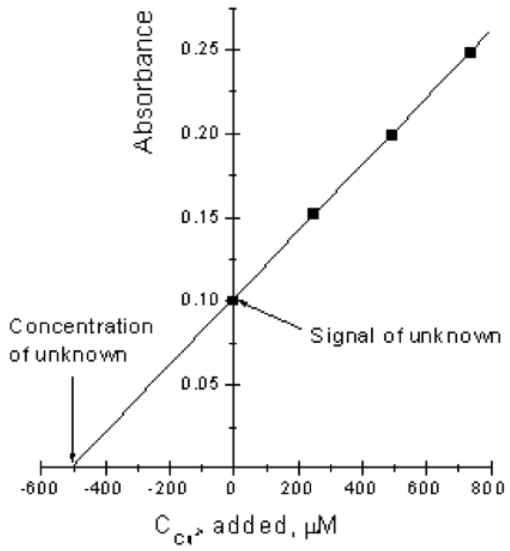


Figure 2: Determining the of amount of paracetamol.

We will also quantify paracetamol directly in tablets. The main reason is that the ratio

$$\frac{\text{active pharmaceutical ingredient mass}}{\text{total tablet mass}}$$

is high enough to quantify paracetamol by the standard addition method.

- Dissolve the equivalent of 10 mg paracetamol in sodium hydroxide 0.1 M, then adjust to 100 mL with the same solvent.
- Take 10 mL of this solution and put it in 6 different vials.
- Add 0 μg, 200 μg, 500 μg, 1000 μg, 1500 μg and 2000 μg of standard paracetamol in each vial.
- Dilute 1 mL of these solutions to 10 mL with the same solvent (final concentrations = 10 μg/mL, 12 μg/mL, 15 μg/mL, 20 μg/mL, 25 μg/mL, 30 μg/mL).
- Measure the absorbance of the solutions at the optimal wavelength.
- Graphically determine the amount of paracetamol in the tablet, as shown in Figure 2.

Melatonin

- Dissolve 20 mg in hydrochloric acid 0.1 M, then adjust to 100 mL with the same solvent.
- Dilute 1 mL of this solution to 10 mL with the same solvent (final concentration = 20 μg/mL).
- Measure the absorbance of the solution at the optimal wavelength.

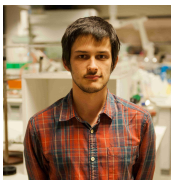
Ciprofloxacin hydrochloride

- Dissolve 20 mg in ethanol, then adjust to 100 mL with the same solvent.
- Dilute 1 mL of this solution and adjust to 10 mL with the same solvent (final concentration = 20 μg/mL).
- Measure the absorbance of the solution at the optimal wavelength.

3 Material

- 250 mg ibuprofen
- 250 mg paracetamol
- 500 mg melatonin
- 250 mg ciprofloxacin hydrochloride
- Paracetamol Sandoz 60×1 g
- 7 L sodium hydroxide 0.1M
- 3 L hydrochloric acid 0.1M
- 1 UV spectrophotometer
- 4 graduated flasks 10 mL
- 4 graduated flasks 100 mL
- 2 graduated cylinders 100 mL
- Distilled water for cleaning and dilutions
- 1 precision pipette (100-1000 μL) with adapted tips
- 1 precision balance
- 2 graduated pipettes 10 mL
- Some Pasteur pipettes
- 2 pipette bulbs for the Pasteur pipettes
- Some weighing paper
- 2 spatulas
- 2 pipette bulbs for graduated pipette 10 mL
- 1 mortal and 1 pestle
- 10 glass vials 30 mL
- 10 plastic vials 10 mL
- 1 metallic box

About the author



Martin recently graduated in pharmaceutical sciences at the Université catholique de Louvain. During his studies, he decided to work in a research group (Bioanalysis and Pharmacology of Bioactive Lipids research group) as a researcher student. His work consisted in analyzing biological samples such as cell cultures, blood, plasma or tissues, using a mass spectrometer. This formation brought him scientific rigor, communication skills and the ability to teamwork. He now works in the same group as a PhD student and teaching assistant. As a pharmacist, he has strong scientific knowledge, particularly in medical sciences, chemistry and biology. His multidisciplinary training makes him a good addition to the crew.