Shelf Life of Lidocaine

Rural Scholars 2017/2018
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“two-thirds of the time you’ll probably fail” - Scott Shaw
Lidocaine Background

- Lidocaine is a local anesthetic used to numb tissue
  - Ex) used to numb gums at the dentist office
- A buffer is added to resist major changes in the pH
  - The buffer used is NaHCO₃
  - Makes the solution less acidic, which is less painful for patient
- Why:
  - We chose this because all of us are going into dentistry or medical fields and lidocaine related to both of these
Societal Impacts

Cost efficiency for clinics that use lidocaine

- Know more about the shelf-life of normal + buffered lidocaine
  - Minimize waste
- Know which conditions maximize the shelf life of each solution
- Gain insight on why the efficiency of lidocaine injections changes between patients
Experimental Question

What factors affect the degradation of lidocaine?

- How fast does degradation occur under each factor?
- Which environment is most suitable to maximize the shelf life of lidocaine?
Experimental Plan

● Investigating degradation of buffered and unbuffered lidocaine
  ○ Concentration of lidocaine and epinephrine in solution have been shown to decrease significantly after one week

● Testing in presence of different factors
  ○ Light
  ○ Dark
  ○ Cold
  ○ Heat
  ○ Control groups

● Determine what environments affect how long buffered and unbuffered lidocaine lasts
Controls

Cold vs Heat

Dark vs Light
Expected Outcomes

- We predict that the solutions placed in the dark and cold will have the longest shelf life, as compared to those placed in heat or light, which should degrade faster.
Challenges

- Unfamiliar unit conversions
  - Medical units (mEq - milliequivalent units)
- Inexperience in lab devices
  - Infrared
  - NMR
  - Mass Spectrometry
- Time constraints
- Insolubility of lidocaine and buffer
  - NaHCO$_3$ needed more water to dissolve fully
  - Need to recheck calculations
  - 3 different solutions were made—all were insoluble
Solubility of Sodium Bicarbonate

- Sodium bicarbonate is a salt that is normally very dissolvable in water
- We used 4.2 grams NaHCO3 (8.4%)
- Prediction:
  - First we must dilute the Sodium Bicarbonate so it is 8.4% when mixed with water
  - This diluted version must then be added to the Lidocaine Epinephrine solution in a 1:10 ratio
    - 5 mL diluted Sodium Bicarbonate with 45 mL Lidocaine Epinephrine solution
- Changed experiment plan - did not work for us
Mechanisms

NMR - Nuclear Magnetic Resonance
- NMR is used to determine physical and chemical properties of molecules
  - Can show us where hydrogen groups or carbon groups are located in relation to each other
  - Shows the proton environment

IR Spectroscopy - Infrared Spectroscopy
- IR uses infrared light to determine the functional groups present in a molecule
  - Measured onto a graph of absorbance vs wavenumber
  - Each peak at a wavenumber range corresponds to different functional groups
- Helps us see structure of samples

Together we can use NMR and IR Spectroscopy to determine the structure of the lidocaine samples
Mass Spectrometry (MS)

- Sorts ions by mass-to-charge ratio
- Uses electromagnetic fields
- We use it to compare the weight of our standard solution of lidocaine to the samples of lidocaine that were sitting for 2 months
- We didn’t actually do this
Data

Obtained using IR, MS, and NMR
Spectra for IR Spectroscopy

IR Spectroscopy of Sodium Bicarbonate (buffer) and Lidocaine HCl w/ Epinephrine.

- IR spectrum has peaks representing amount of light transmitted & is used to determine functional groups in molecules.
- Carbon Dioxide and C=O bonds are the cause of some of the peaks.

Carboxylic Acid Group

C=O group

NMR Spectra for Standard Solution

Integral Intensity
Gives us the number of hydrogen atoms in each region of the molecule

3-(Trimethylsilyl)-1-propanesulfonic acid sodium salt
(Mol. Weight, 218.32)

Lidocaine HCl
We conducted NMR tests on two tubes of each of the different lidocaine sample in the different environments.
Quantitation: Internal Standard Method

\[ l.I_{ox} \propto n_{ox} \]
\[ l.I_{ox} \propto M_{ox} \]
\[ l.I_{ox} = K_s M_{ox} n_{ox} \frac{V_{gas}}{V_{tot}} \quad \ldots..[1] \]

\[ l.I_{ox} \] - Integrated intensity of a group of resonances due to the oxygenate
\[ K_s \] - Spectrometer constant
\[ n_{ox} \] - Number of protons generating the signal
\[ V_{gas} = 100\mu l \]
\[ V_{tot} = 600\mu l \]
\[ M_{ox} \] - Molar concentration of oxygenate

The integrated intensity ratio of the oxygenate to the internal standard is then:
\[ \frac{l.I_{ox}}{l.I_{DMO}} = \frac{K_s n_{ox} M_{ox} (V_{gas}/V_{tot})}{K_s n_{DMO} M_{DMO}} \quad \ldots..[2] \]

\[ M_{DMO} \] - Molar concentration of DMO in the NMR sample

Rearranging equation [2]

\[ M_{ox} = \frac{l.I_{ox}}{l.I_{DMO}} \frac{n_{DMO}}{n_{ox}} M_{DMO} \frac{V_{tot}}{V_{gas}} \quad \ldots..[3] \]
Nuclear Magnetic Resonance (NMR)

- Original concentration of Lidocaine was 85 mM = 0.085 M
Mass Spectrometry Data

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<th>Name</th>
<th>Sample Text</th>
<th>Type</th>
<th>Std. Conc</th>
<th>RT</th>
<th>Area</th>
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Results

● Never finished buffered solution
● Cold and dark samples degraded the most
  ○ Based on the data from NMR and MS
  ○ Final concentrations were the lowest
  ○ We don’t know why
● Coming back in the fall for more research