Extraction of Benzocaine from Hemorrhoid Cream

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Abstract

Americaine branded hemorrhoid ointment consists of the active ingredient, benzocaine, carried in polyethylene glycol. The aim of this experiment was to separate these two, with specific emphasis on extracting pure benzocaine. This was done through a solvent extraction using diethyl ether derived from engine starter fluid, decantations, and washing with water. The final yield of benzocaine was disappointingly low (2.79%) but the theory behind the extraction was proven to be on solid foundations. Further research and testing will be necessary to perfect the procedure.

1 Introduction

In the modern day, it may seem as though anything imaginable can be delivered straight to one's doorstep by a pitiably overworked and underpaid Amazon delivery driver within a week. Rarely do we encounter situations where we are forced to confront the fact that increasingly complex manufacturing processes are responsible for producing all of the luxuries we take for granted. Products do not come into existence for most, they simply are.

This question of how all our stuff is made is somewhat interesting, but it is answered daily by countless people, countless times. A TV show was even made about it. However, what good is knowing how things are made when one cannot feel a connection to the materials on a visceral, physical level? A short time spent Googling by someone with nothing better to do will yield fascinating factoids like how toothbrushes are made of a molded polypropylene or polyethylene handle and nylon bristles. But does that mean anything really? We understand toothbrushes not as a list of chemicals, but as a whole toothbrush. When it comes to its components, that it is made out of plastic is about the most specific description we could give it without relinquishing the inputs of our physical senses. Similarly, when one chugs a jar of mayonnaise, as one does, little thought is put into the ingredients that have been so masterfully blended together to create it. We do not taste mayonnaise as the product of its parts. We taste the indivisibly delicious flavor of mayonnaise. And so, having all the constituent parts of mayonnaise laid out to look at is a revelatory experience. Being able to pick up and inspect them gives one the deepest comprehension of mayonnaise that could ever be attained.

Enter hemorrhoid cream (Americaine Hemorrhoidal Ointment)

What is it? What does it do? How is it made? What's in it? These are all questions. However enthralling as the others may be, we are most concerned with figuring out what it is made of. It should be no surprise by now that the procedure chosen to answer this question involves stripping it down to its essence: benzocaine, a local anaesthetic, and two polyethylene glycol (PEG) variants, PEG 300 and PEG 3350.

The number contained within the name of each PEG type indicates its average molecular weight (g/mol). Each type requires a different separation method.To separate out the PEG 3350, a solvent extraction was found to be the simplest option. PEG 3350 is insoluble in diethyl ether, a common laboratory solvent, while benzocaine and PEG 300 are. By thoroughly mixing the hemorrhoid cream in diethyl ether, the benzocaine and PEG 300 should separate from the PEG 3350 to the diethyl ether. Afterwards, the PEG 300 and benzocaine can be separated with the techniques of decanting and washing with water as PEG 300 is soluble in water. This last step may be aided by the manipulation of PEG 300's viscosity with low temperature.

This experiment aims to be as easily reproducible as reasonably possible, as it is hoped that future generations will be able to gain a greater understanding of hemorrhoid cream by repeating this procedure. As such, great pains were taken to ensure that the requisite materials and equipment would be easy to acquire. The distillation of diethyl ether from engine starter fluid, while unnecessary should one have access to it already, is included in the procedure to increase its accessibility.

2 Materials

- Americaine Hemorrhoid Cream
- Engine Starter Fluid containing diethyl ether
- Simple Distillation Setup
- Assorted Glassware
- Hot Plate
- Stir Bar

3 Procedure

1. Process diethyl ether
   (a) Set up a simple distillation for the starter fluid.
   (b) Collect the distillate that formed at around 50°C.
   (c) Re-distill the distillate.
   (d) Repeat steps b-c until the distillate no longer possesses the scent of petroleum.
   (e) The distillate should now be sufficiently pure diethyl ether.

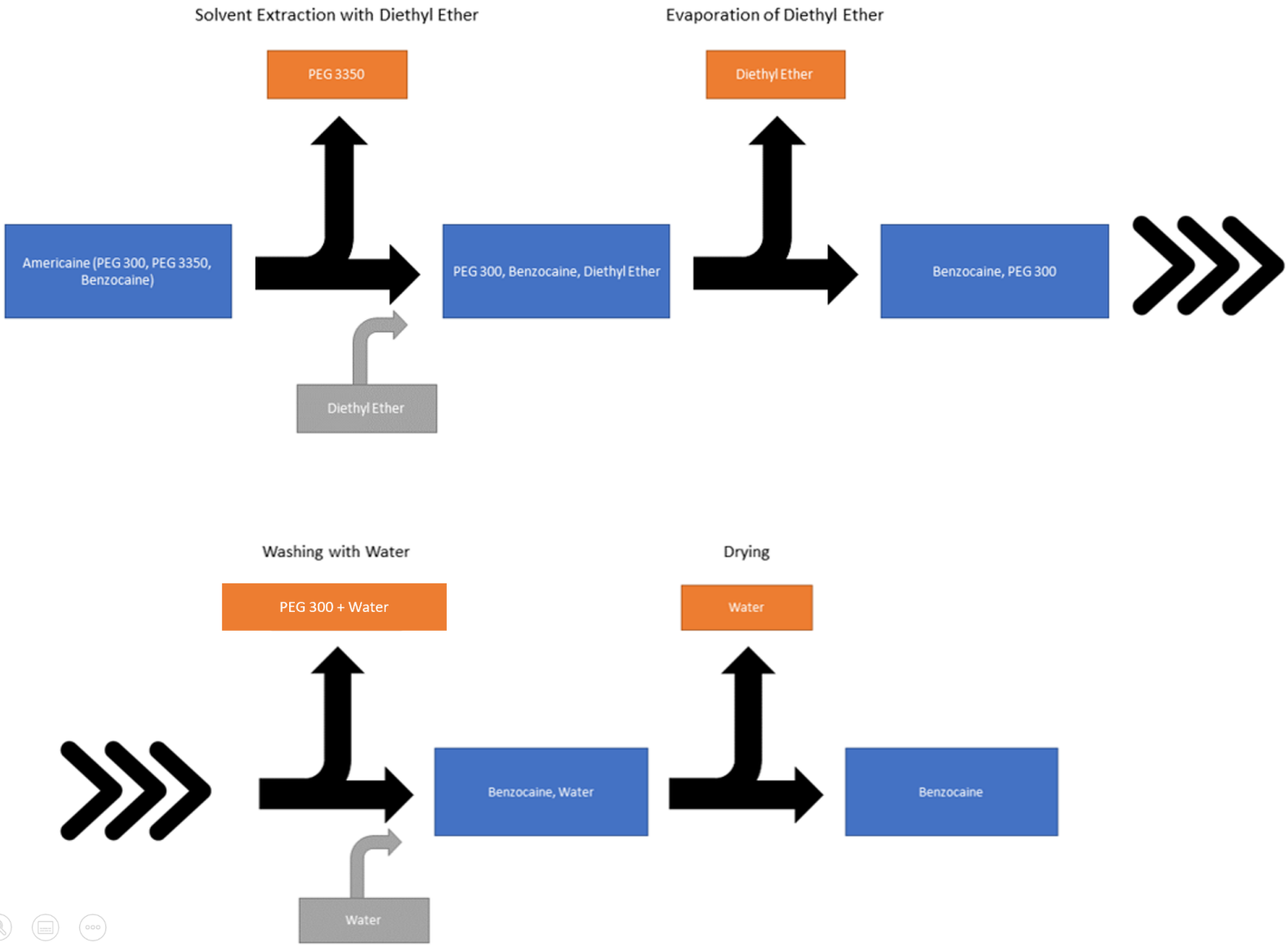
Solvent Extraction with Diethyl Ether
Evaporation of Diethyl Ether
PEG 3350
Diethyl Ether
Americaine (PEG 300, PEG 3350, Benzocaine)
PEG 300, Benzocaine, Diethyl Ether
Benzocaine, PEG 300
Diethyl Ether
Washing with Water
Drying
PEG 300 + Water
Water
Benzocaine, Water
Benzocaine
Water

Figure 1

2. Conduct separation. Refer to Figure 1 on the previous page for an overview.

   (a) Mix a small amount of Americaine Hemorrhoid Ointment with diethyl ether in a beaker using a stir bar, allowing benzocaine to dissolve in the ether. Figure 2 shows what this mixture's appearance is like.

Figure 2: A heterogeneous mixture of clear ether solution and insoluble PEG 3350, seen as opaque white solids.

   (b) Decant out the ether and wash the beaker out with more.

   (c) The decanted ether solution contains ether, benzocaine, and PEG 300. Store this in a flask and seal it to prevent the ether from permeating the other contents and walls of the freezer in the next step.

   (d) Keep the solution in a freezer overnight.

   (e) Decant the solution quickly while it is still cold, leaving behind as much PEG as possible. The PEG 300 and ether are both clear but the PEG 300 should be much more viscous at this point and should visibly lag behind the ether when poured (see Figure 3).

Figure 3: Droplets of the thicker PEG 300 can be seen sticking to the bottom of the beaker toward the left, apart from the ether solution to the right.

(f) Boil off most of the ether leaving behind a mixture of liquid PEG 300 and benzocaine in nearly supersaturated solution and decant again. Perform this step slowly on low heat and be careful not to boil off all the ether or the PEG 300 will degrade and turn yellow/brown (see Figure 4 for what it looks like when you mess up). Note, again, that PEG 300 is a clear liquid just like ether. Just because you have a small amount of clear liquid at the bottom of the beaker does not mean you still have ether left. You should end up with a waxy or powdery solid like in Figure 5.

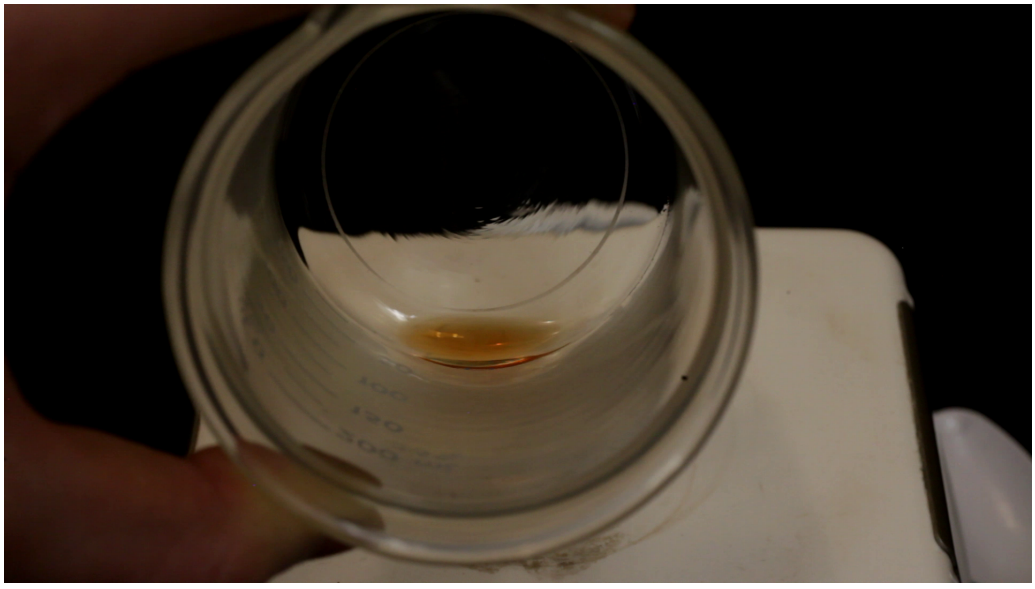

Figure 4: Overheated PEG 300

Figure 5: PEG 300 + benzocaine, the whiter and more powdery this mixture the better; the unwanted PEG 300 contributes to yellowing and waxiness.

(g) Wash the mixture with water to clean it up a bit. Benzocaine is very insoluble in water while PEG 300 dissolves readily.

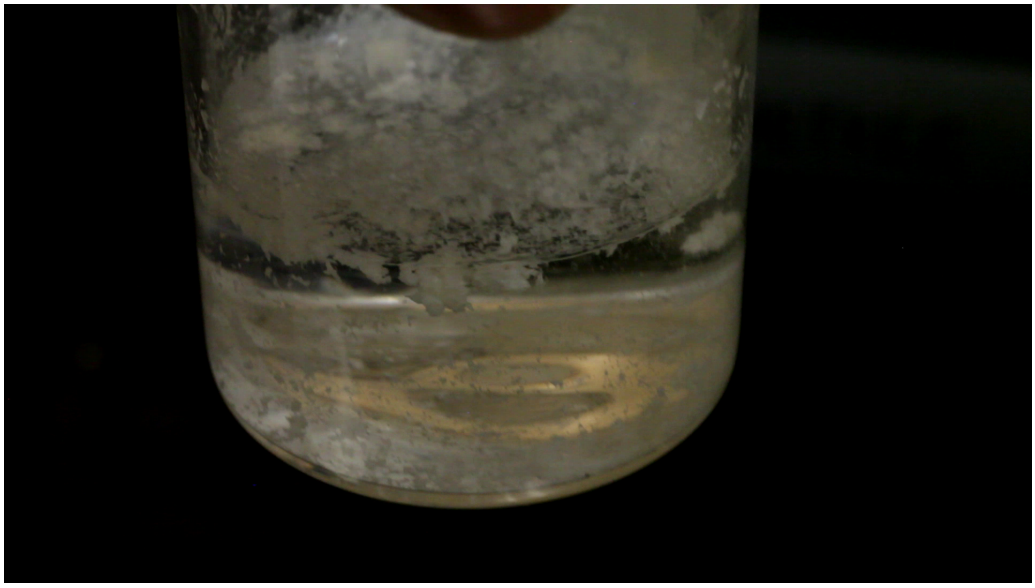

Figure 6: The substance in the beaker becomes noticeably whiter when mixed in water as PEG 300 gets drawn away from the benzocaine.

(h) Allow water to evaporate and gather the clean benzocaine. Your final product should look like Figure 7. Examples of less pure samples can be seen in Figure 8. To confirm the identity of the product, an unknowing test subject applied some of it to his lips. This can be seen in Figure 9.

Figure 7: Pure benzocaine is a fine white powder.

4 Results

$$\frac{2.56\,\text{g Benzocaine}}{55.83\,\text{g Americaine} \cdot 20\%\ \text{Theoretical Yield}} = 2.79\,\%\text{Yield} \tag{1}$$

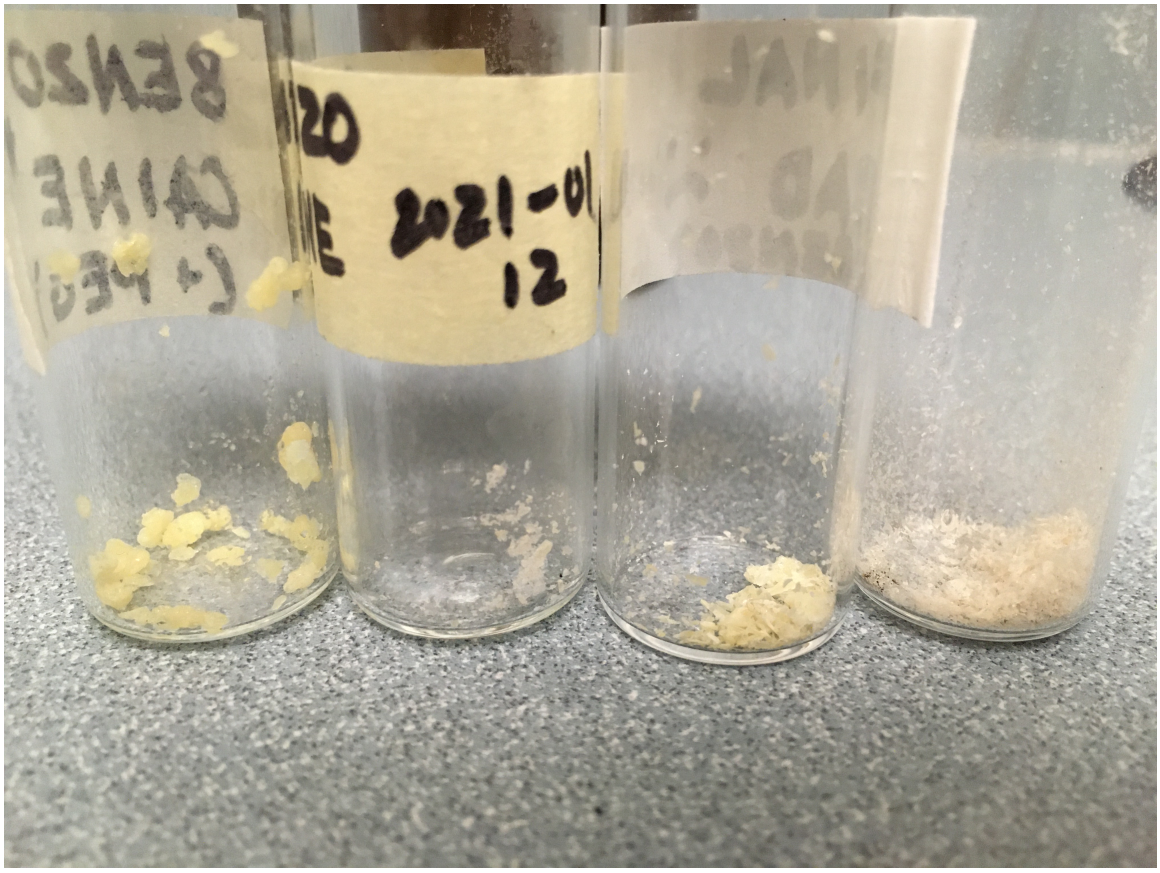

Figure 8: Results over the course of multiple experiments with various techniques. Evidently some samples are more pure than others.

Figure 9: A reluctant test subject topically applies our benzocaine to his lower lip to confirm its local anaesthetic effects. We have yet to find a volunteer to intravenously test the general anaesthetic effects of our benzocaine samples.

Yes, it numbs.

5 Discussion

In order to minimize the losses due to filtration, it was avoided. The washing step was somewhat effective, but time constraints prevented further exploration of the technique. Future experimentation will be necessary to investigate whether the washing step could be used more productively. Most of the losses can likely be attributed to the first step, as it did not seem that much of the benzocaine in the PEG passed over to the ether.

Each of the decantation and transfer between beakers cause non-negligible loss of benzocaine. These losses take the form of high-purity benzocaine residues left behind after the ether film evapourates (see Figures 10 and 11).

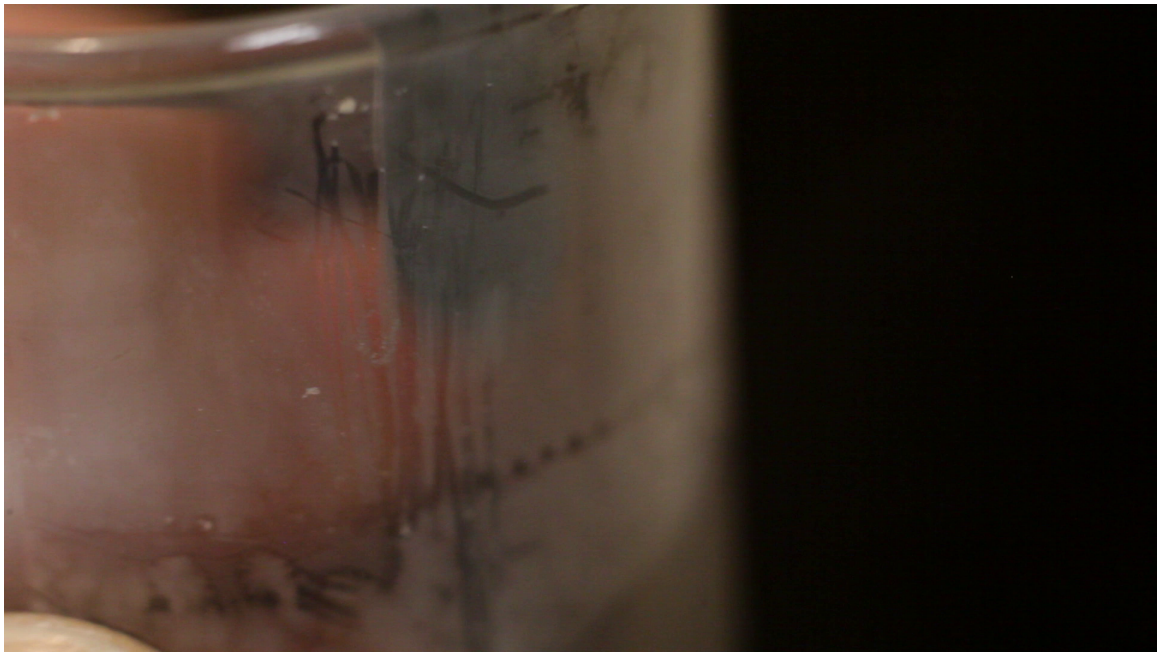

Figure 10: Benzocaine residue appears on anything that comes into contact with the ether solution.

Figure 11: This is especially noticeable on dark surfaces.

Due to the lack of a simple test for finding the purity of diethyl ether, the primary method of determining how the purity of the distilled ether was to use its scent, which is quite qualitative.

This could have potentially been a factor contributing to the low yield, as impurities in the ether could impact its ability to dissolve benzocaine and keep PEG separate. More research is required to perfect the diethyl ether acquisition step.

Based on the effect the final product had when orally tested on a researcher, it was determined that benzocaine was successfully extracted, though, a double-blinded experiment involving a control would be required to know for sure. Regardless, its purity was difficult to discern as tests like IR spectroscopy could not be done.

By far the most difficult part of the extraction is separating PEG 300 from benzocaine. PEG 300 is a clear sticky liquid at room temperature which makes it difficult to separate simply from benzocaine. PEG 300 is both insoluble in ether and significantly denser than it so separating them should not be difficult in theory. In practice, though, we found it virtually impossible to even distinguish between the two. To help separate them at this stage, we chose to use ether's very low freezing point and PEG 300's attainable freezing point of about -15C. If the mixture is brought below -15C, the PEG 300 should solidify, allowing easy filtration. However, in leaving the mixture of PEG 300 and benzocaine dissolved in ether in a chest freezer overnight, the PEG 300 only became very viscous. This likely had to do with the presence of unknown additives decreasing the freezing point of PEG 300. Still, most of the PEG 300 could be eliminated by pouring the ether solution into a new beaker before the cold PEG 300 could catch up.

We found that the remaining solution still contained significant amounts of PEG impurities that discoloured the benzocaine and gave it a distinctly waxy texture. To resolve this, we used water which PEG 300 readily forms intermolecular bonds with whereas benzocaine does not. This noticeably purified the benzocaine, but we found water generally quite difficult to work with due to its high boiling point compared to organic solvents like ether. Also, separating the powdery benzocaine from the PEG-laced water proved to be non-trivial, considering water's tendency to stick to everything. Even after this procedure, the benzocaine left was not as pure as that obtained by crystallization.

The purest samples of benzocaine were obtained from precisely the same phenomenon that caused our losses in transferring the ether between beakers. In fact, very pure, albeit small, samples could often be recovered by scraping the residue off used glassware. We found that highly pure benzocaine crystals would form in supersaturated solution with ether. This phenomenon often occurs unintentionally. For example, when pouring highly saturated ether solution from a beaker, the benzocaine will often leave solution and form along the wall of the beaker before reaching the spout (see Figure 13). The difficulty of using this technique is still in performing the mechanical separation of the ether solution from PEG 300 such that the benzocaine crystals do not form anywhere near PEG 300. We did not include this technique as part of our official procedure because we have yet to come up with a reliable way to perform it at scale.

Figure 12: A large yellow impurity can be seen toward the bottom left.

Figure 13: Beautiful benzocaine crystals forming at the bottom of a beaker indicate that the solution here is supersaturated with benzocaine.

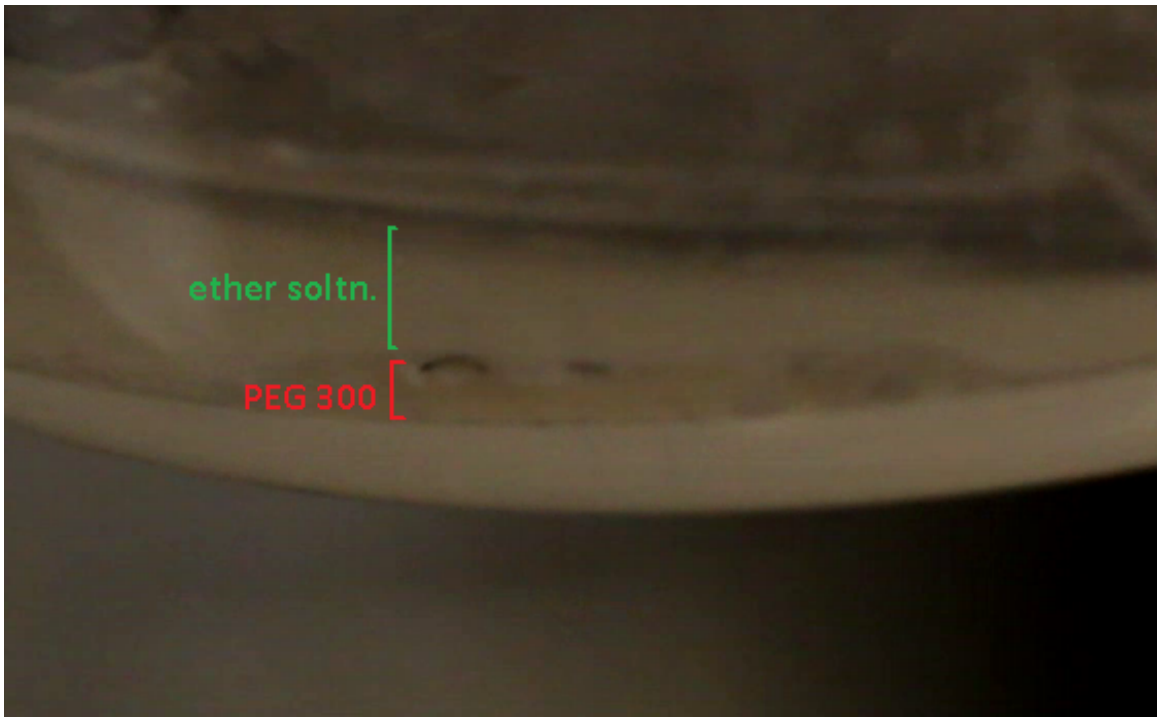

Figure 14: We were able to separate the PEG 300 and the ether into distinct layers here. More experimentation is necessary to discover an application for this technique.

6 Conclusion

The theory behind the separation of PEG from Benzocaine in Americaine through a solvent extraction appears to be sound, but more experimentation and tinkering with the fine details of the procedure are necessary to improve the abysmal benzocaine yield.

7 References and Further Reading

1. Solubilities table:

   drugfuture.com/Pharmacopoeia/USP32/pub/data/v32270/usp32nf27s0_m6h00100.html

2. Monographs:

   PEG: fao.org/fileadmin/user_upload/jecfa_additives/docs/Monograph1/Additive-316.pdf

   Benzocaine: who.int/medicines/publications/pharmacopoeia/Benzocaine.pdf?ua=1

3. Diethyl Ether Acquisition:

   sciencemadness.org/smwiki/index.php/Diethyl_ether