



Farmacología en el Espacio

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Pharmaceutical Development & Antibiotic Effectiveness
EVOLUTION FROM LABORATORY GROUND STUDIES TO
THE ADVENT OF A FLIGHT CAMPAIGN





Compound Derivatives Series - Synthesis & Evaluation of Antimicrobials in Space

Background

- Promoting scientific discovery through biomedical research
- Creation of synthesized compounds
- Testing in extreme environments
- Chalcones



Background

CHALCONES

Open chain flavonoids

Diet rich in flavonoids → low incidence of cancer

Found in:

Legumes, vegetables, fruit, tea, spice, other edible plants

Properties – Biological Value

- Antibacterial
- Antiviral
- Anti-fungal
- Anti-inflammatory
- Anti-tumor
- Antioxidant

There is a link between aromatase activity, adipose tissue, and breast tumors.

FIND A CURE



Vitamin E

Zinc

CHALCONES

“...natural elements have been found to have inhibiting effects on aromatase.”

AGENDA

PHASE I

PHASE II

PHASE III

PHASE IV

PHASE V

The Science: CD-SEAS*

Understanding the Environment

Flight Campaign: Mission Microgravity

Research & Development

Future Direction

PHASE I

THE SCIENCE CD-SEAS

Establish the Science, Measures, & Testing

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The Process

↓
Why?

Aromatic Rings w/electron withdrawing moieties not heavily studied

Research to date – only certain variations of chlorine substitution have been reported

OBJECTIVE

Expand on known reactivity

Research shows → anti-tumor activity of Chalcones can be improved w/EWG (Chloro) added to the aromatic ring.

What's Responsible for Activity?

Substituent Effect

Adding **Electron Withdrawing Groups**

Alpha, beta unsaturated functional group

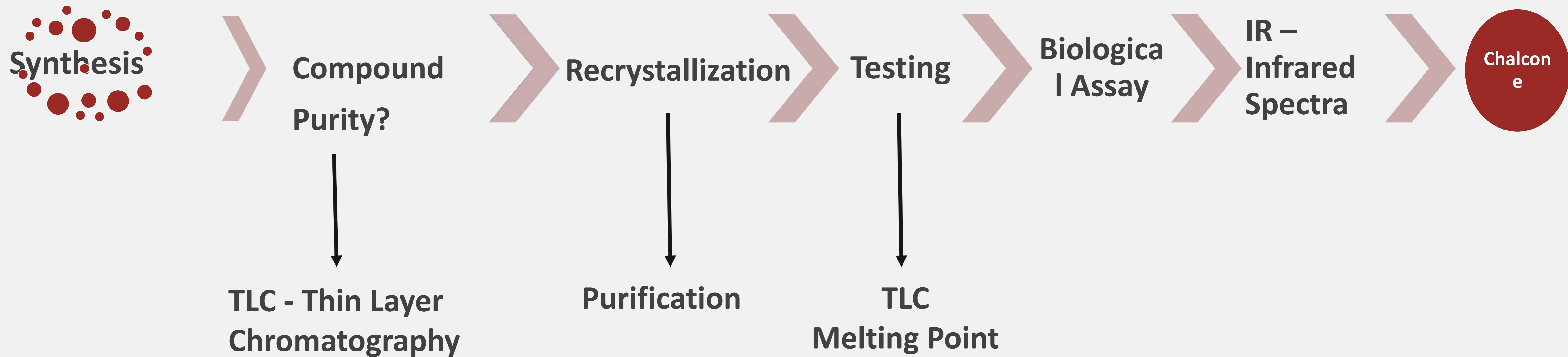
Responsible for antimicrobial activity against tested bacteria

Why Use a Halogen?

Chlorine

- Halogens possibly bind to a specific receptor
- Allows access to the B-carbon
- Facilitates conjugate addition

The Process



Biological Results → validated → highly reactive α,β -unsaturated ketone provides value against potentially pathogenic bacteria.

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Day 1, Exp 1 formation of Crude Product, Time Zero



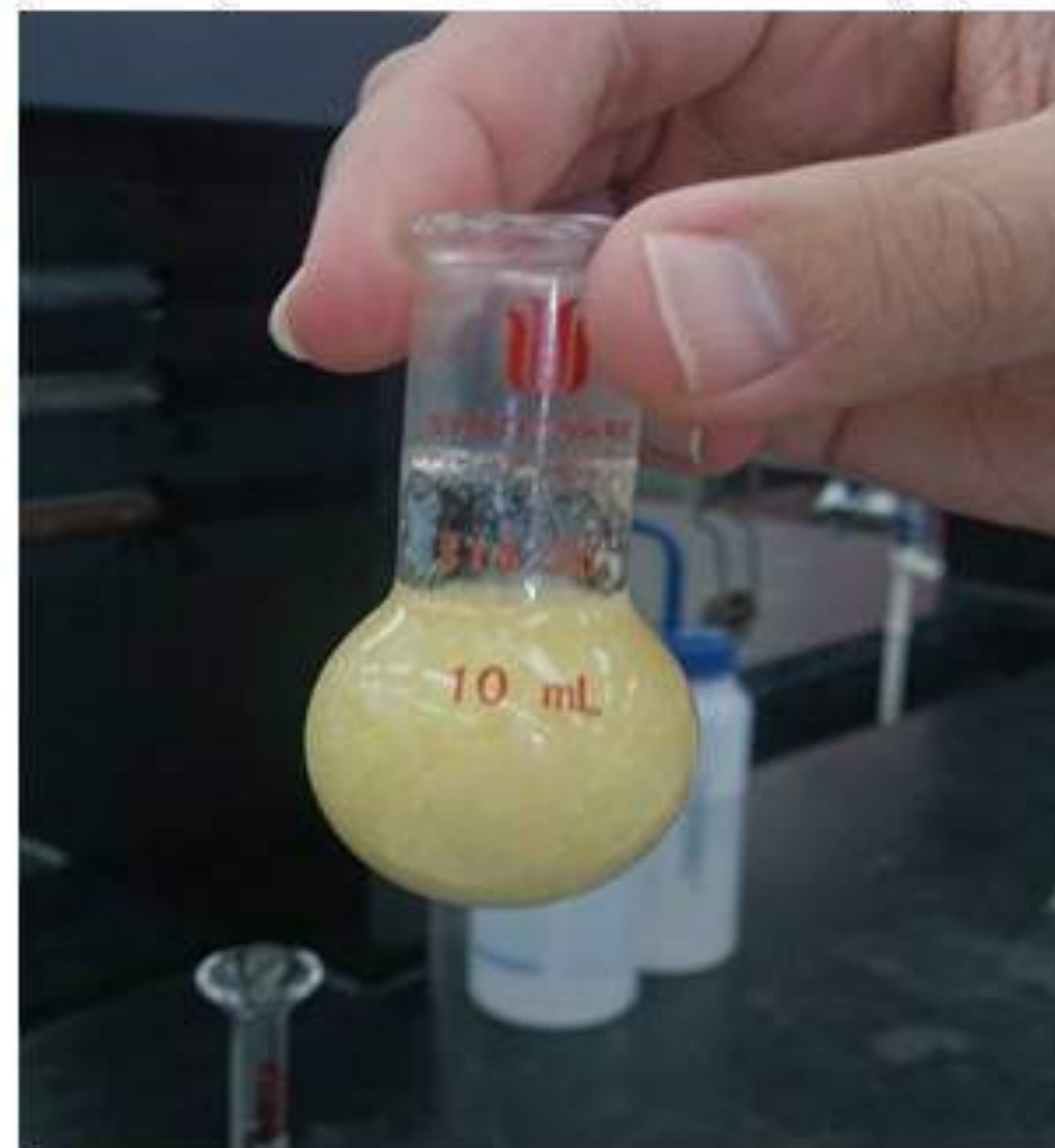
Crude Filtered Product
0.3506 grams

Day 2, Exp 1, Synthesized Crude Pdt, Time 16.5 hrs



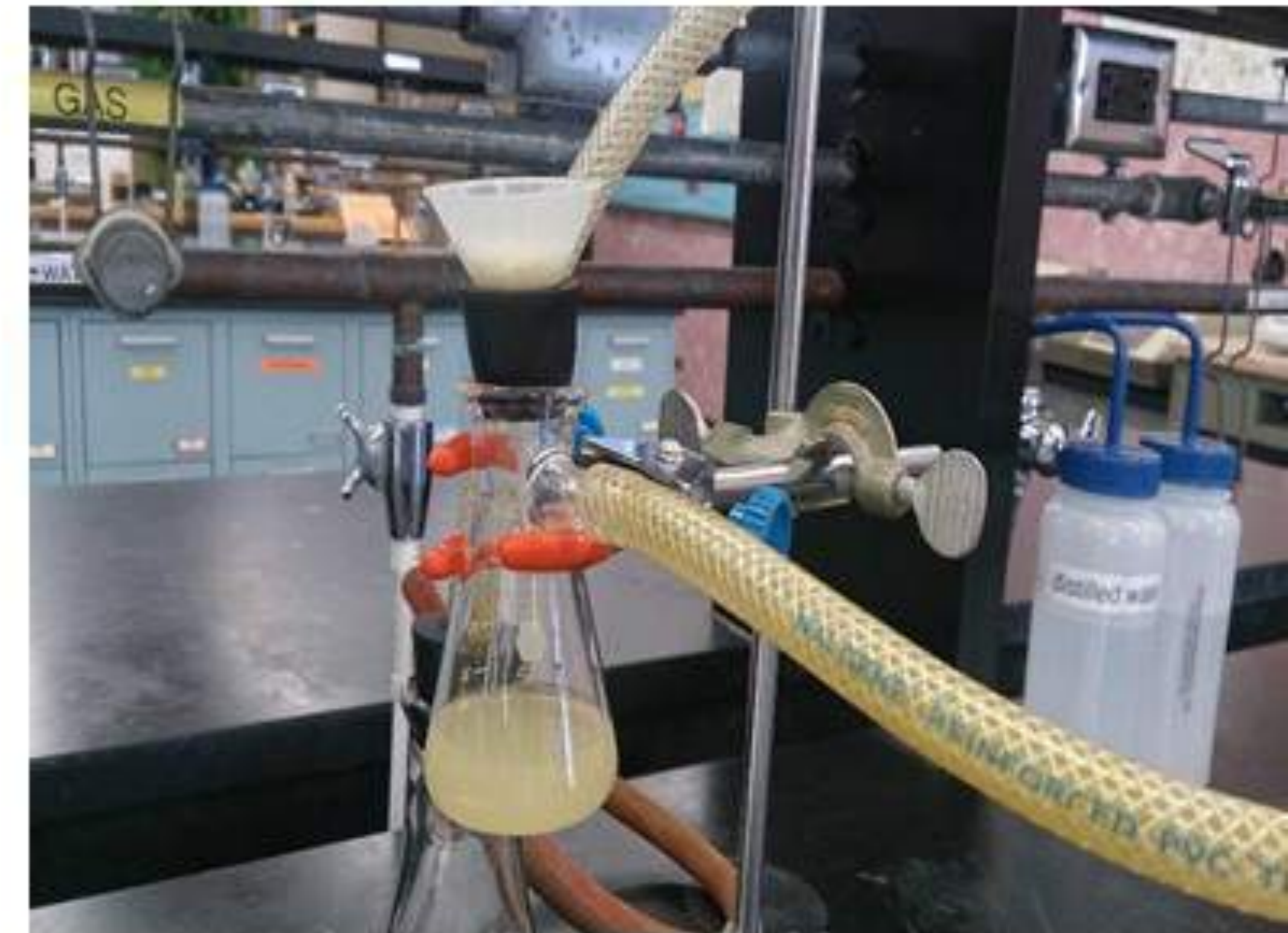
Crude Product & Filtrate

Day 2, Exp 1, after adding 2X 5ML Icebath water prior to filtration (color change)



TLC Plate in 10
EtOAc/Hex

Crude/Recrystallization Filtration Process



Day 1 & 2, TLC Plates showing incomplete product formation, column D still shows evidence to starting materials column A of 4-Methoxybenzaldehyde and column B of Acetophenone

Reacts with Base



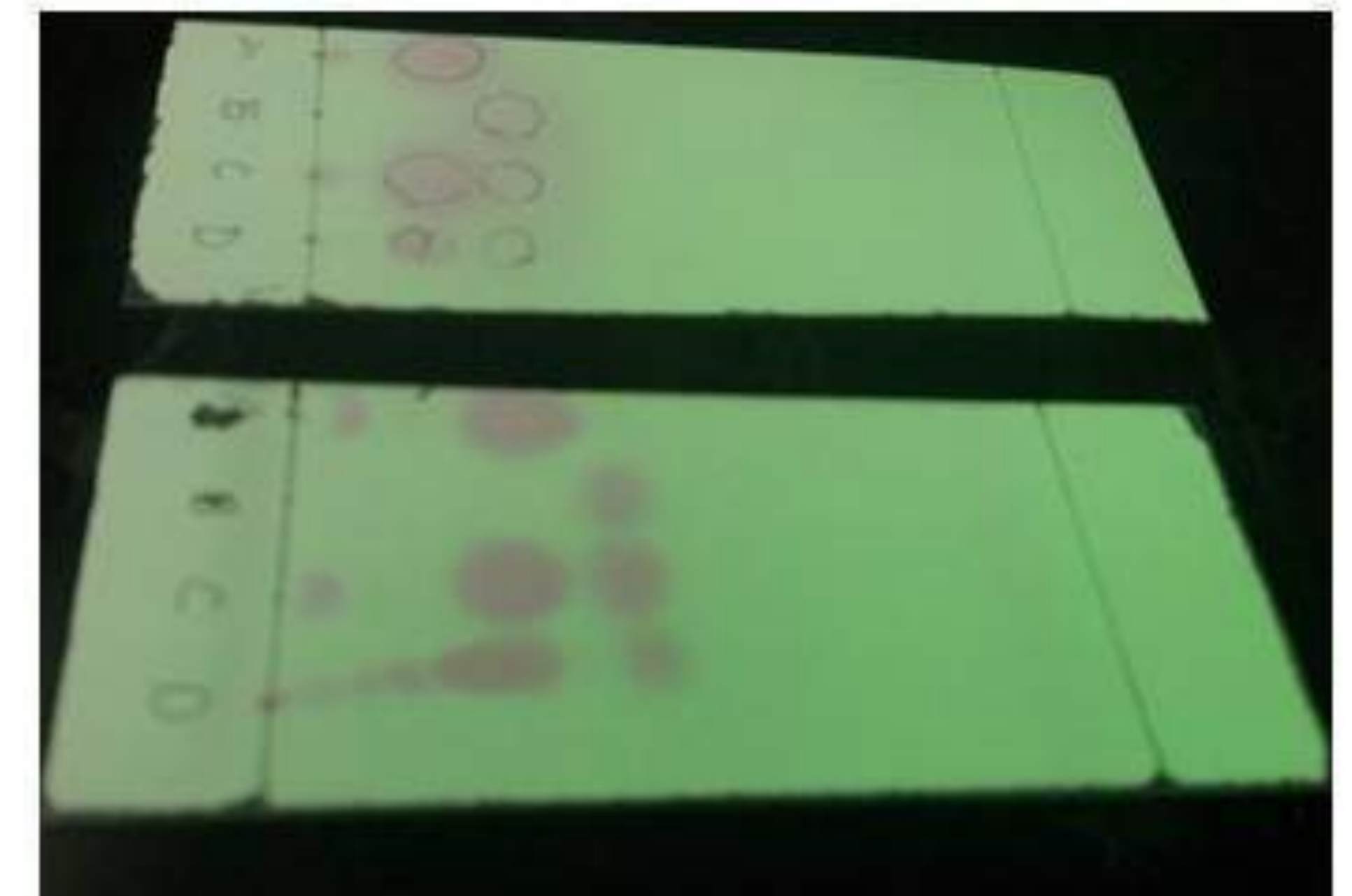
6/3/2014



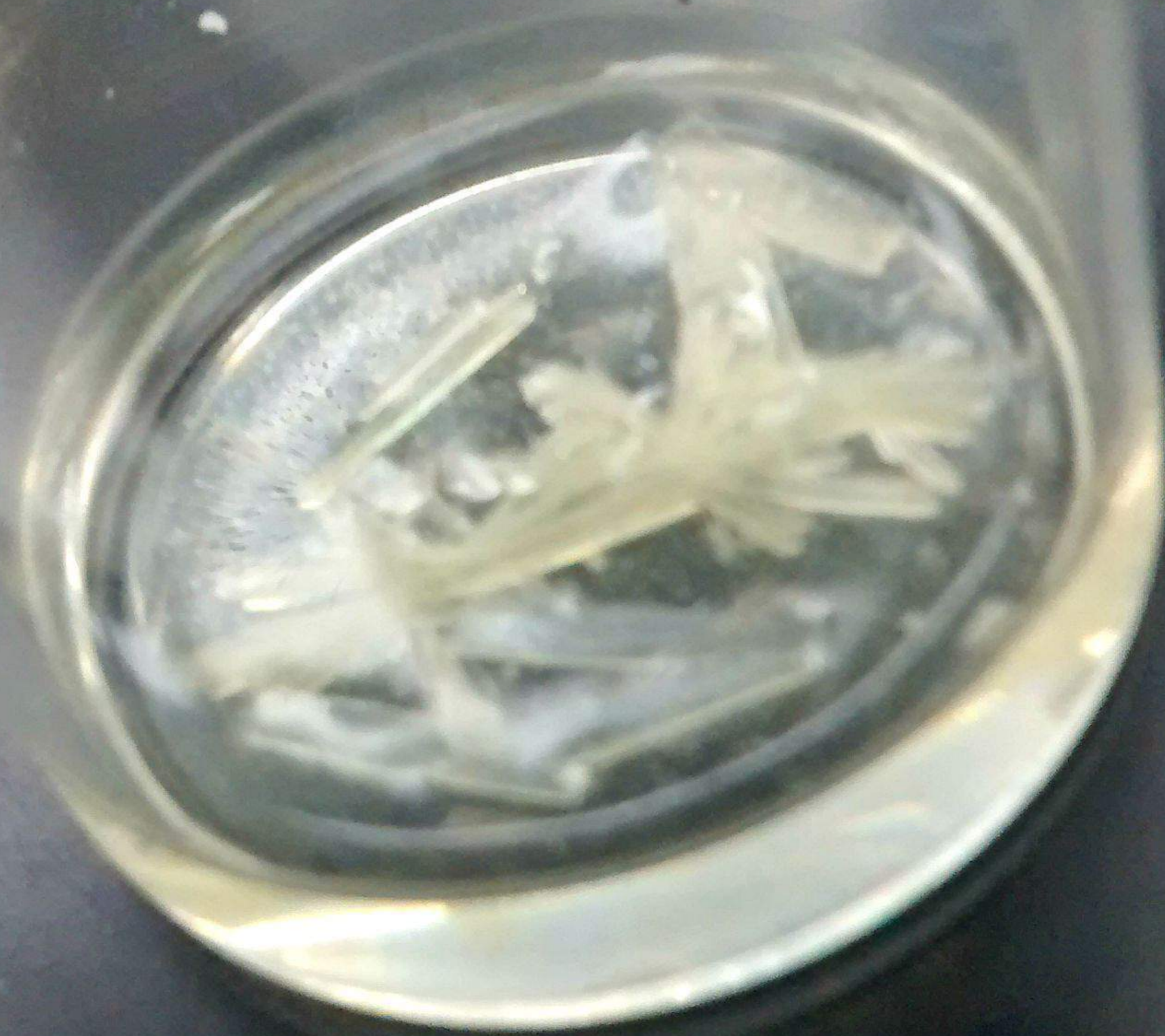
Synthesis & Antimicrobial Evaluation of
Chalcone Derivative



Synthesis, Recrystallization & Testing



**August 13, 2015 at 7:22 pm,
Chalcone Crystals forming.
Purification successful!**



CD-SEAS

Infrared Spectroscopy (IR)

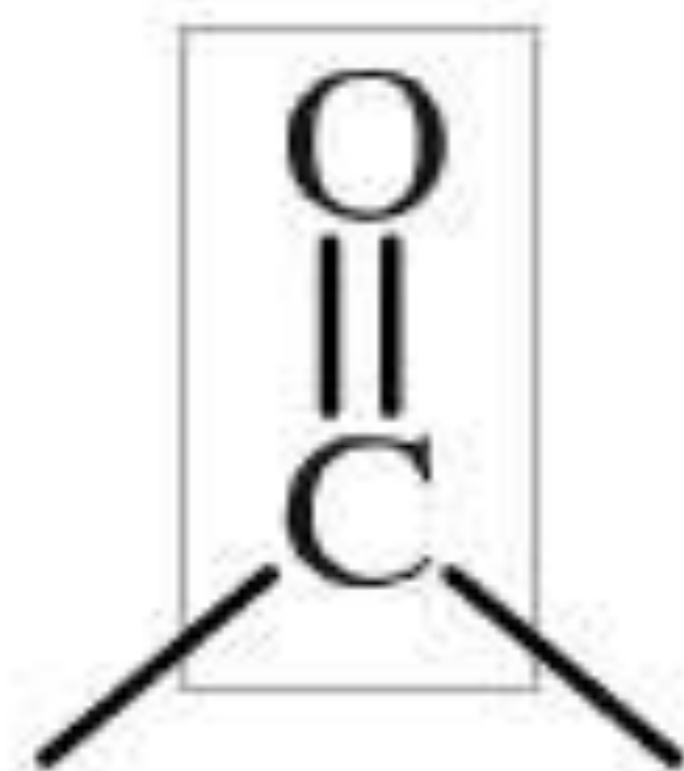
- Data about a compound's structure
- Absorbed by each of the 16 tested compounds
- Different bonds = Different Functional Groups

Functional Group

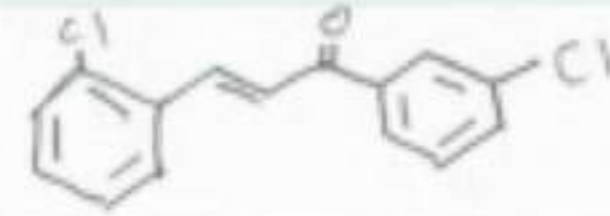
Carbonyl

1800-1650

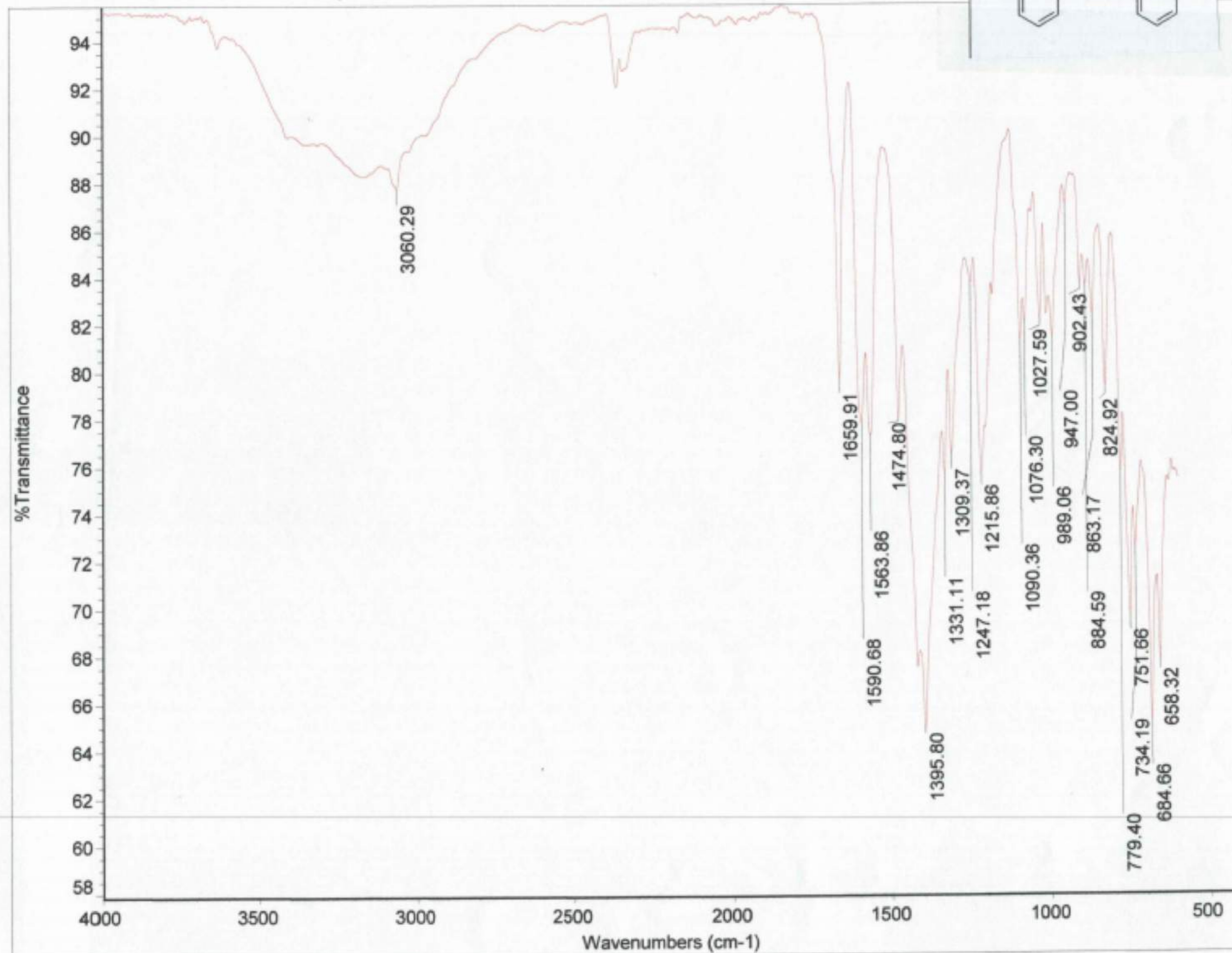
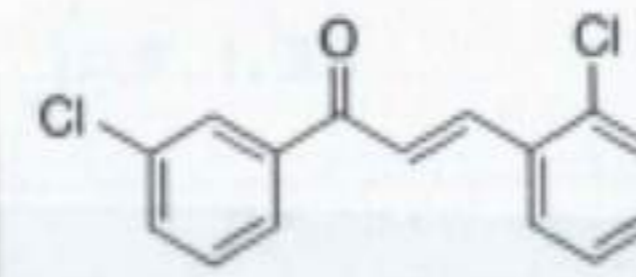
(often ~ 1700) cm^{-1}



Jan. 1.23



2,3'-dichlorochalcone



Bond Types

Csp³-H at 3060.26 cm^{-1}

C=O at 1659.91 cm^{-1}

Aromatic Rings:

1590.66 & 1563.86 cm^{-1}

Complex IR Spectra, 1450 – 600 cm^{-1} is the fingerprint region and is difficult to assign

Above 1450 cm^{-1} are the Functional Groups

*% Transmittance = Absorbance

Nuclear Magnetic Resonance (NMR)

- Details about the compound's structure
- Verifies the identity of the compound

How?

- Thru, intramolecular magnetic field surrounding an atom in the compounds varies the resonance frequency
- Resonant frequency, energy of absorption, and intensity of the signal = strength of magnetic field

Melting Point

2,2-dichlorochalcone

- 250 Degrees Celsius, color change from yellow powder to orange/red
- Higher than 250°C
- No melting (decomposition)

Pros & Cons

- High Melting Point → low volatility = a plus for safety operations in a flight campaign
- Difficulty in creating → sterically hindered





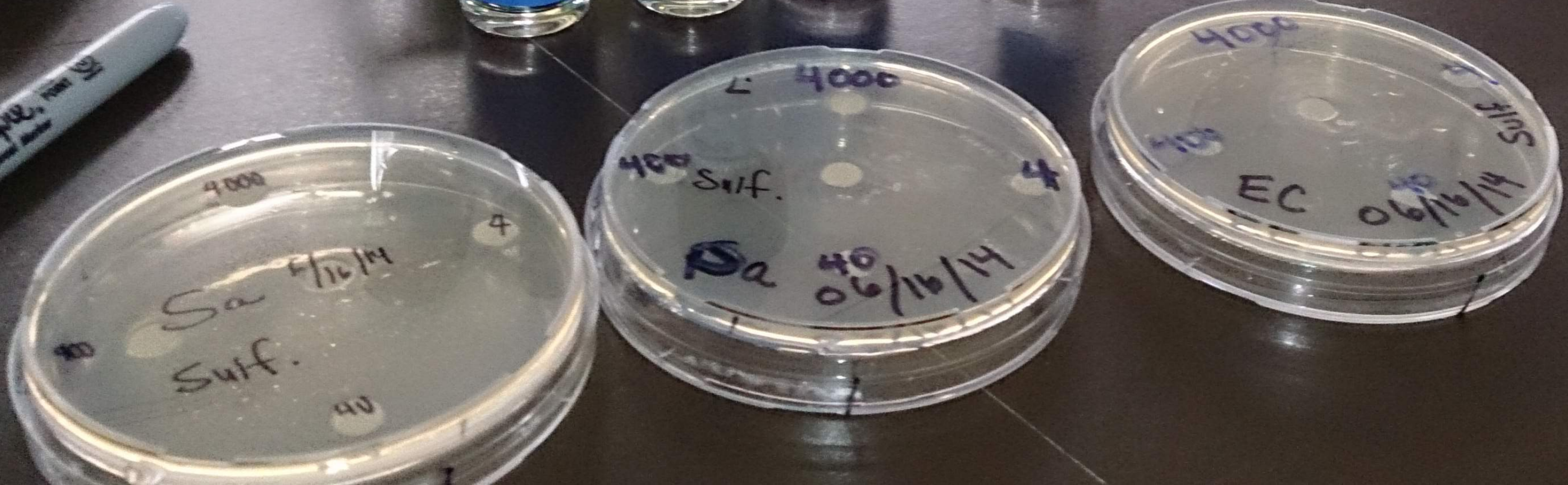
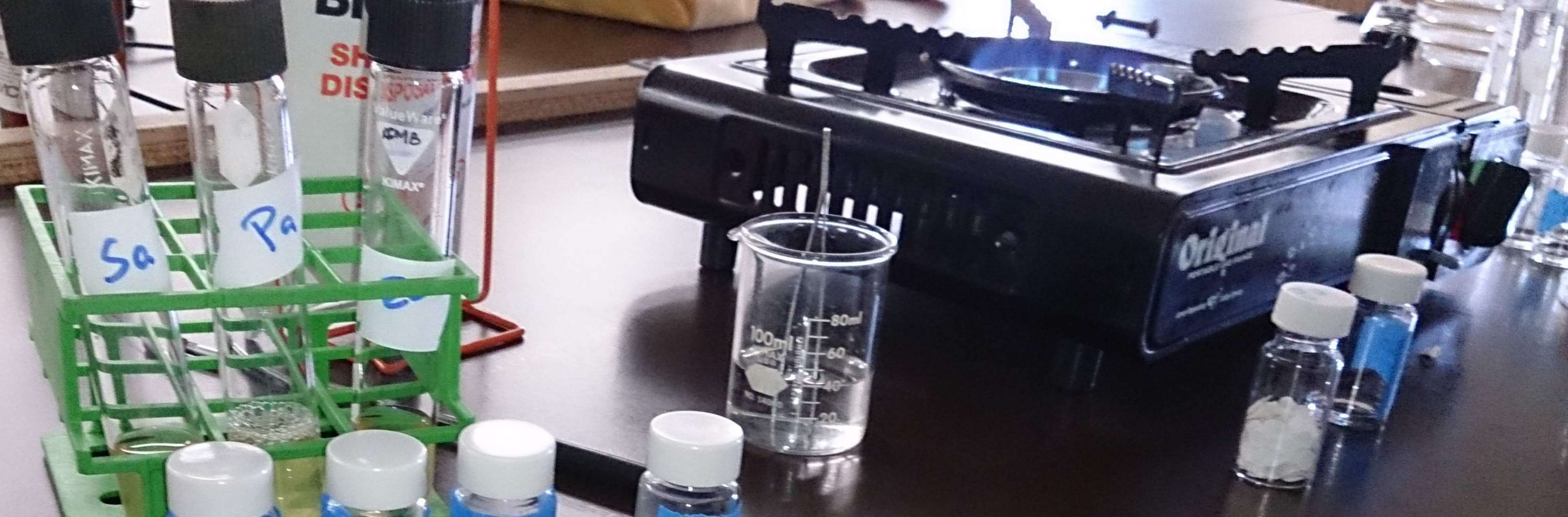
BIOLOGY

Purpose:

Testing synthesized compounds for antimicrobial effectiveness

- *Escherichia coli*
- *Staphylococcus aureus*
- *Pseudomonas aeruginosa*

Gram negative & Gram positive



Biologicals are done on the biologicals time.
Chemistry is done on the researchers time.

Ground Control Biological Results

Many of synthesized compounds = effective as Positive Control

**Negative Control: DMSO
-Positive Control: Sulfanilamide**

Synthesized chlorinated chalcones:

- **Prevalent antibacterial activity**
- **Potential to serve as new antimicrobial agents**
- **Effective against gram negative & gram positive bacteria**

Flight dynamics spanned 30 sec at 2g, 20 sec
0 g, 15 sec 2g, per each parabolic maneuver



Photo Credit: NRC, Ottawa, Canada

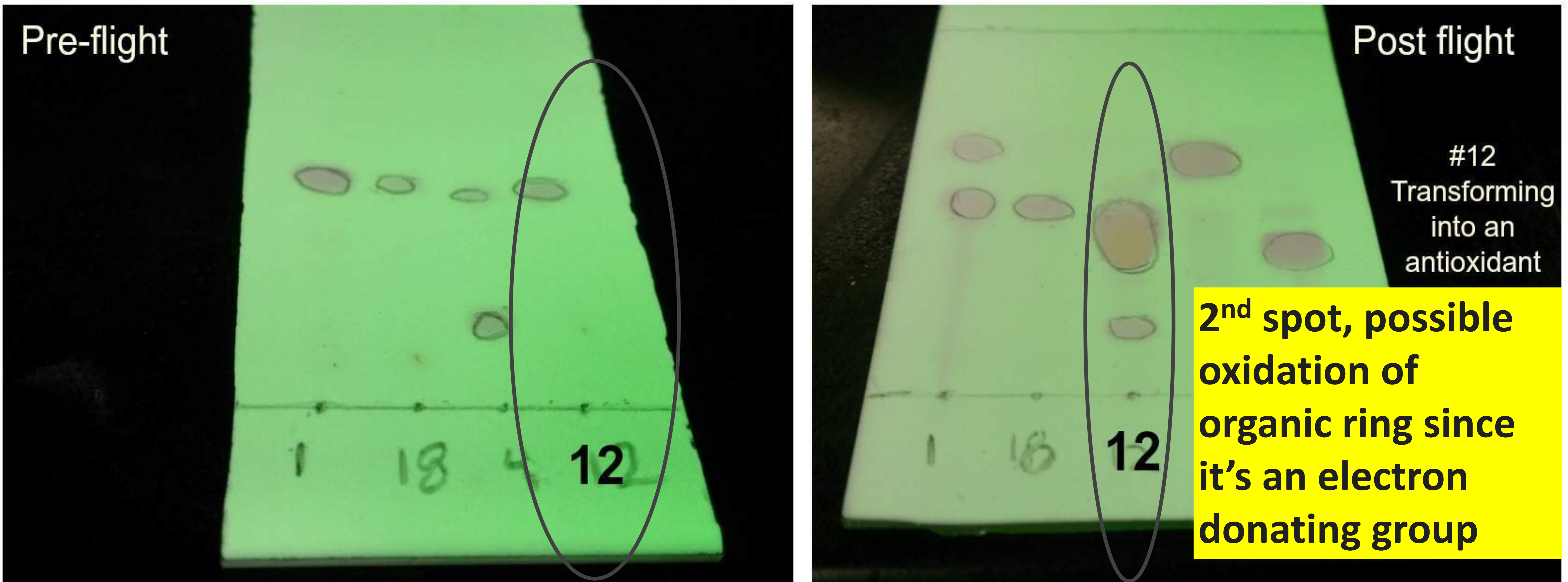


FLIGHT RESULTS

Disintegration Transformation Antioxidant

CD-SEAS
Mission
Microgravity

TLC



IR – showed a new carbonyl appearing post flight → compound's transformation indicative of an antioxidant (similar to Coenzyme Q10). Molecule will give up one or both electrons → act as antioxidant.

CHALLENGE #1

Long-term storage in spaceflight may have direct effects on decomposition of pharmaceuticals prior to expiration date.

SOLUTION

Advance state of the art → preservation stability is necessary.

Compound molecular breakdown – only isolated to this compound? NO

CHALLENGE #2

Acknowledge countermeasures against cancer

SOLUTION

- **Advance state of the art technology**
- **Sustain & preserve compounds w/anti-tumor effects**
- **Dual Applications = Medical advances on Earth & Support astronaut health**

- Phase IV

Research & Development



CD-SEAS
MISSION MICROGRAVITY

- **Additional Testing**
- **Compound Discovery**
- **Patent for a Composition of Matter**
- **Designing a Biomedical Device**

Phase
V

The
Future



Press Release

Citizens in Space Announces Payload Manifest for First Space Mission

DALLAS, Aug. 13, 2015 /PRNewswire/ -- Citizens in Space, a project of the United States Rocket Academy, has announced a list of 10 experiments selected for its first research mission on the XCOR Aerospace Lynx spacecraft. The experiment will be carried aboard the Lynx Cub Payload Carrier, an open-source payload carrier developed for the Lynx spacecraft by Citizens in Space. Experiments will be controlled in flight by a Citizens in Space science-mission-specialist astronaut.

The experiments announced today are:

**"...CD-SEAS of Honolulu, HI
Effectiveness of Anti-Microbial Coatings in Microgravity Conditions"**

10 experiments selected for 1st suborbital research mission. CD-SEAS selected for this manifest.

**Potential for harm is in what
you can't see → these compound may treat**

Bacterial Mutations

Antibiotic Resistance

**Extreme environment of G & short-term
microgravity → molecular decomposition in 3 of the compounds
flown.**



Photo Credit: <http://www.myscizzle.com/blog/>

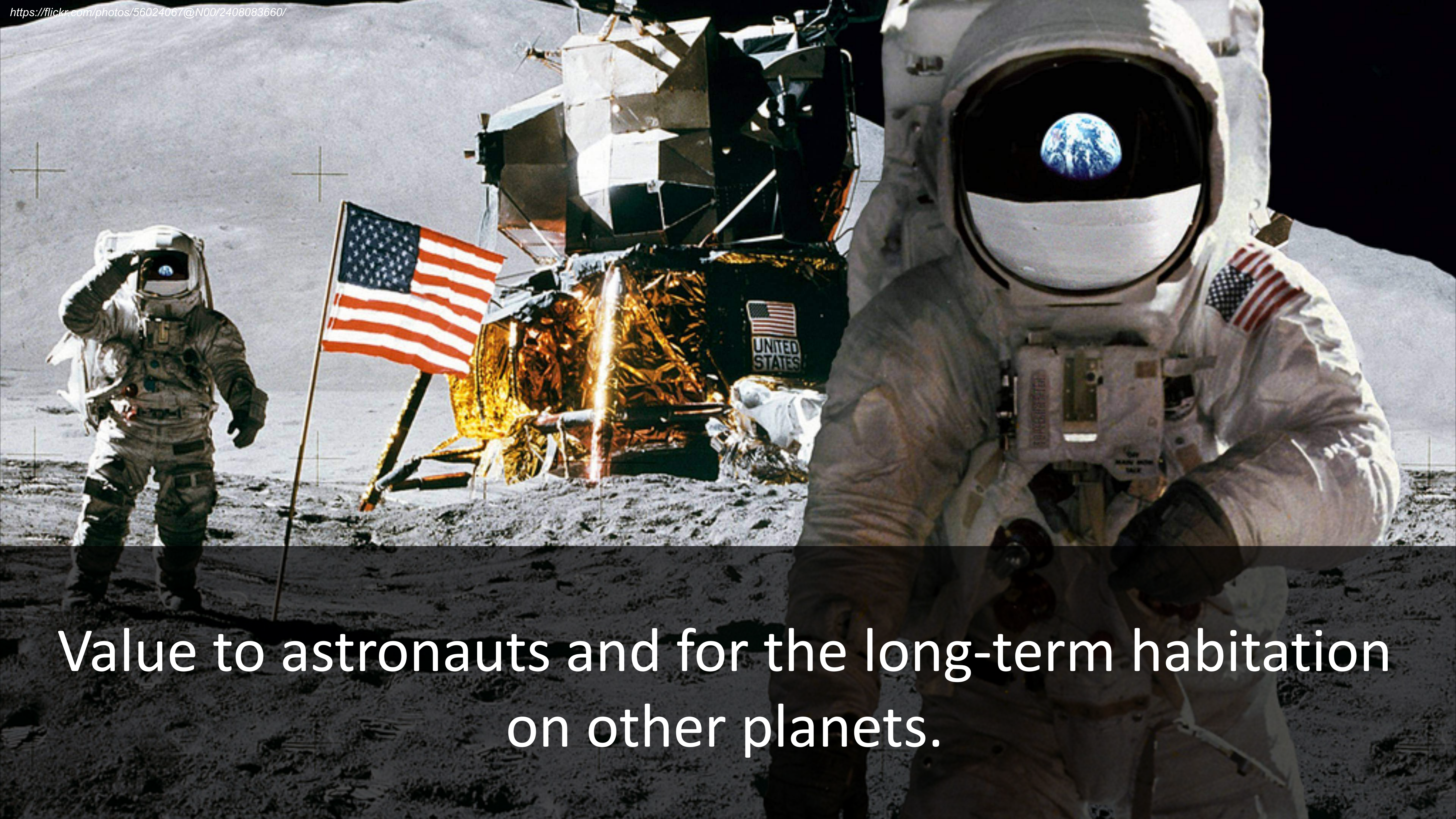
Goals:

Placement of this biomedical experiment on the International Space Station

Why?

- Ideal for the study of the compounds' in their exposure to an extreme environment.

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Value to astronauts and for the long-term habitation
on other planets.



Muchas Gracias

- *Universidad Nacional Autónoma de México (UNAM)
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- *Consejo Nacional de Ciencia y Tecnología



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