Synthesis of Renewable Micelles from Fatty Acids and Glucose

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Abstract

Synthesis of liposomes, or micelles, is an actively growing field of research, as these molecules serve various functions from surfactants to drug-delivery systems. Surfactants are amphiphilic molecules that work by disrupting surface tension. They are often used as detergents but can also work as efficient delivery systems for therapeutic drugs to targeted tissues. The majority of synthesized molecules on the market today are not derived from renewable sources, but from petrochemicals or other harmful substances. These compounds do not degrade naturally, resulting in chemical pollution. Renewable options have been produced, but the process is not yet cost- or time-efficient for manufacturers. This study aims to develop a procedure to produce micelles from natural and renewable sources such as isolated fatty acids and monosaccharides.

Keywords: liposomes, micelles, surfactants, drug delivery systems, renewable, natural products, enzymes.

Introduction

Literature suggests that utilizing natural molecules in combination with enzymes will allow for a new, simplified route in the biosynthesis of micelles.

- Isolate fatty acids from naturally occuring and readily available vegetable oils using *C. antarctica* lipase[9]
  - Vegetable oil: Literature precedence, diverse triglycerides[9]
  - Coconut oil: Unattempted reaction, favored fatty acid length for micelles[9]
  - Lipase: Breaks triglycerides into fatty acids and glycerol[9] **(Scheme 1)**
  - Oxidize glucose in Bromine water[7] **(Scheme 2)**

- Known synthesis pathway to gluconic acid but slow reaction rate[3]
  - Attempt to synthesize D-glucose into gluconic acid using Glucose oxidase with and without the addition of Catalase[1,3] **(Scheme 3)**
    - Catalase enzyme removes H_2O_2 to protect oxidase and facilitate reaction[1]
    - Oxidase: Facilitates oxidation of glucose[3,5]

- Once Gluconic Acid and fatty acids have been isolated then attachment can synthesize a micelle molecule[10]

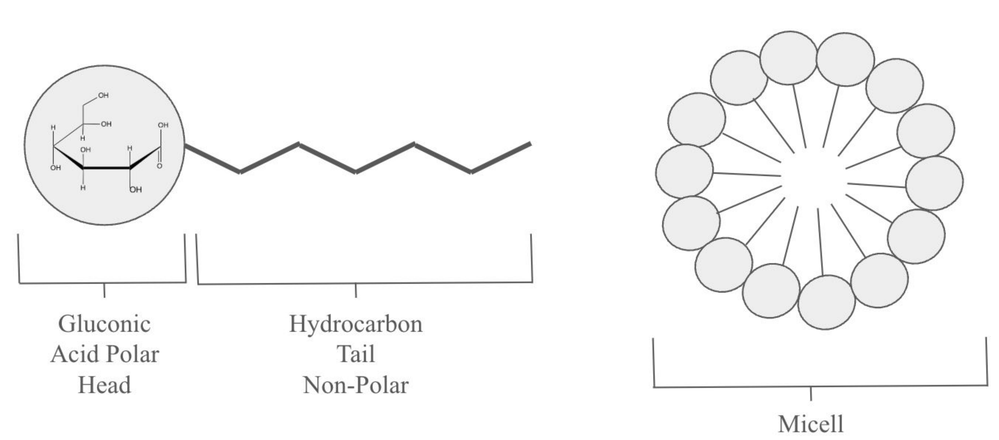


Figure 1. Amphiphilic Fatty Acid Sugar Ester for Micelle Assembly**.** The components of the micelle molecule being synthesised and a formed micelle.

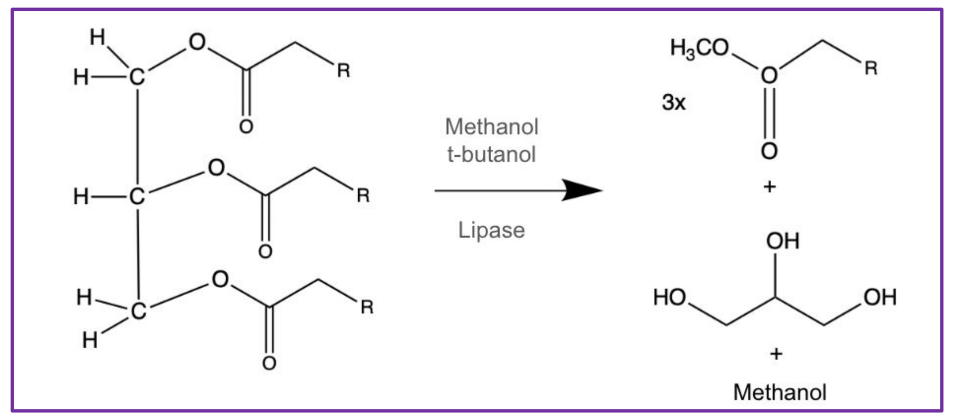
- Micelles can be formed depending on the environment the molecules are placed into, trapping drugs, metals, and more inside
  - Polar environments can lead to capsule formation
  - Surfactant molecules can be aggregated either by cationic, anionic, zwitterionic, or non-ionic groups[11]

- Micelles can be broken apart with external or internal signals, such as temperature, pH, ultrasound, or enzymes

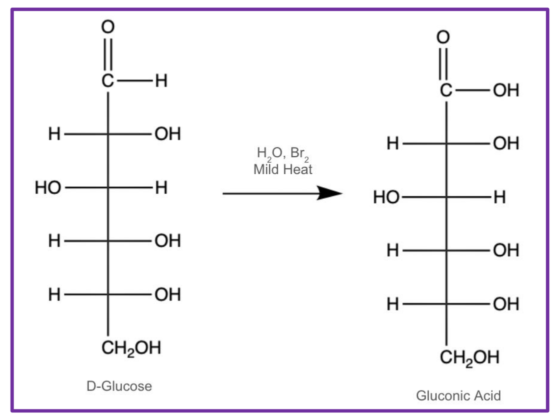
Methods

The isolation of fatty acid methyl esters from Coconut oil was accomplished using a *C. antarctica* lipase enzyme. Glucose oxidation was carried out using two different methods. The first method employed was the addition of bromine water while the second involved an enzyme, Glucose oxidase[1,3,5,7].

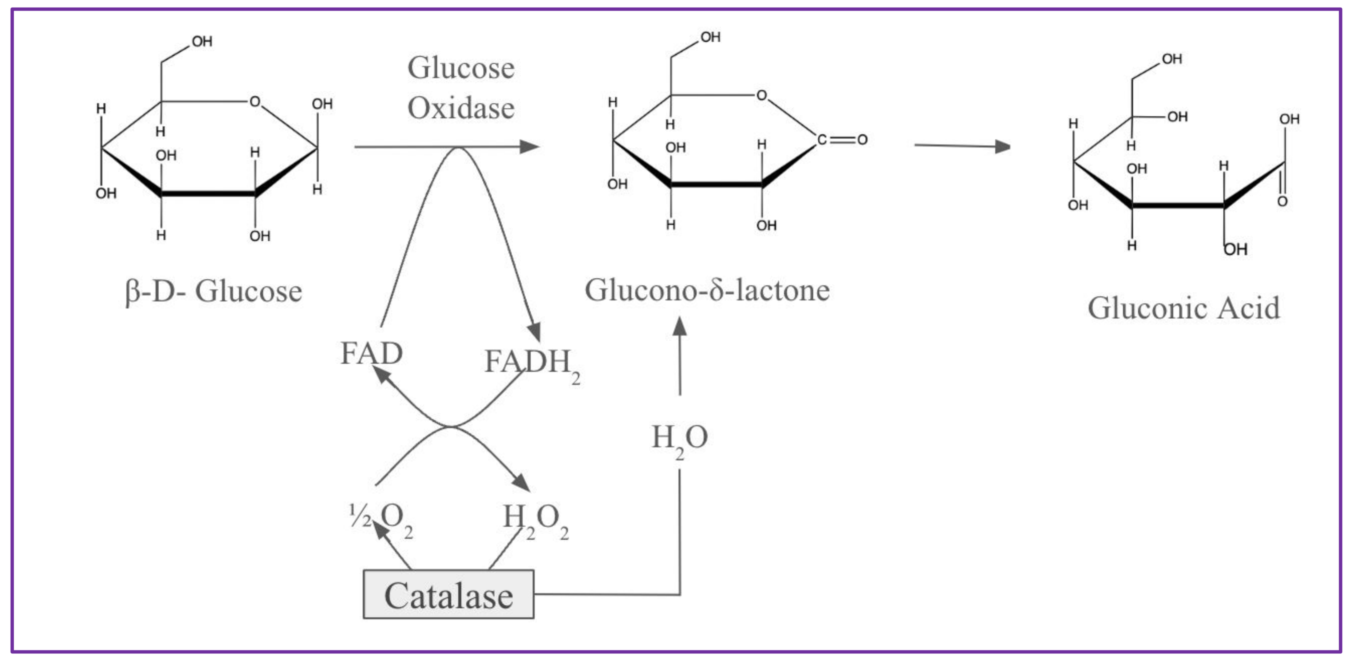
Scheme 1: Isolation of free fatty acid from triglyceride using lipase enzyme



Scheme 2: Formation of Gluconic Acid Using Bromine Water



Scheme 3: Reaction of D-glucose to gluconic acid in the presence of Glucose oxidase



Results

After reactions where completed ^{1}H NMR was run on the coconut oil product from lipase reaction. The Glucose oxidase reaction product was then run as a 13 hour ^{13}C NMR.

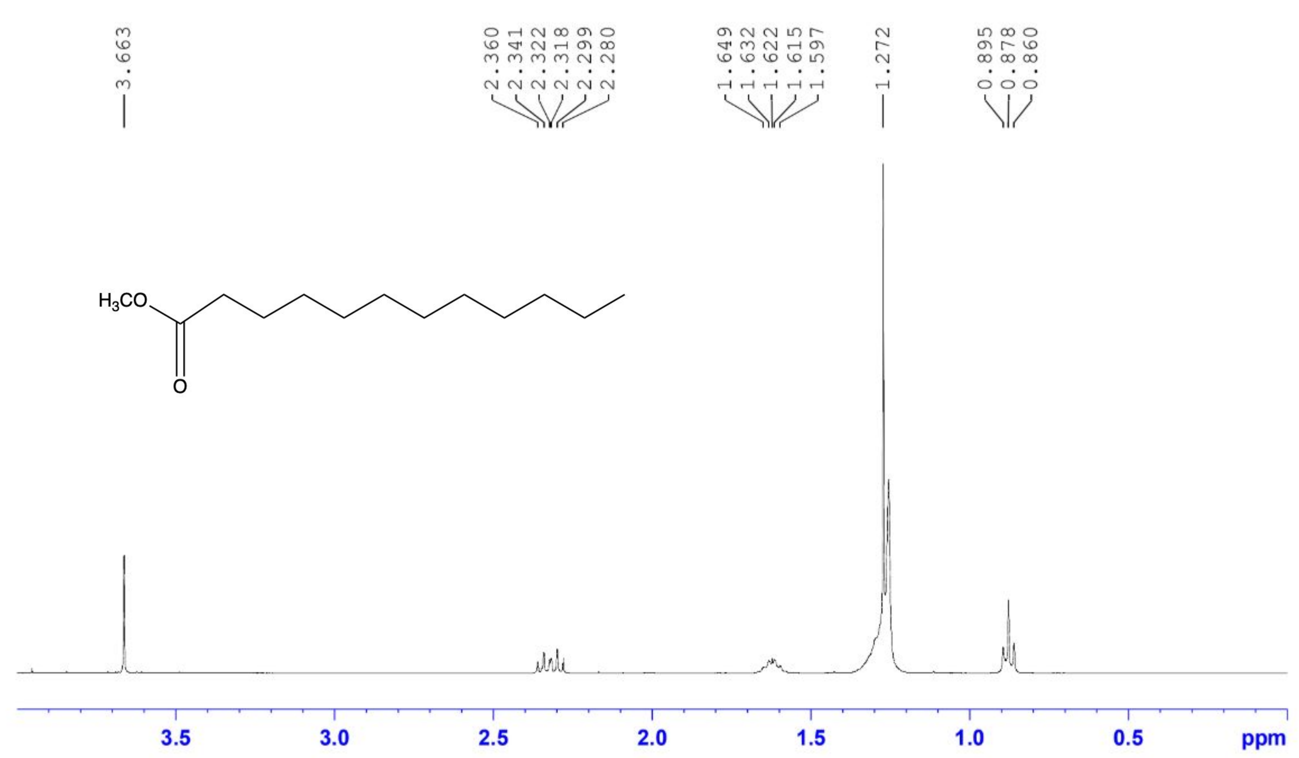


Figure 2. ^{1}H NMR of fatty acid methyl esters (FAMEs) isolated from coconut oil. The singlet at 1.272 ppm represents the methyl group on the end of the FAME near the carbonyl.

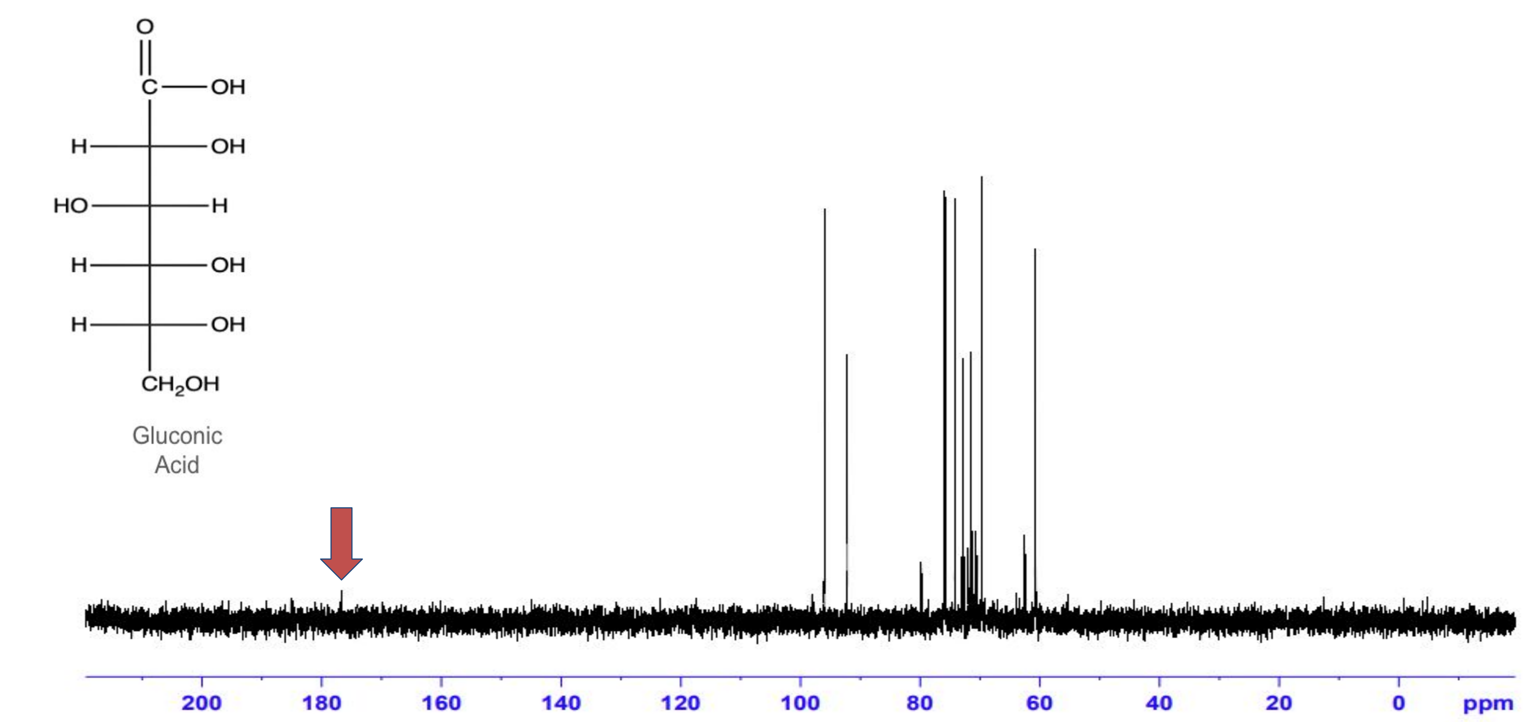


Figure 3. ^{13}C NMR of isolated gluconic acid from Glucose oxidase reaction. Arrow points to peak in 170 ppm region indicating Gluconic acid was made.

Conclusion

- Fatty acid methyl esters were synthesised from coconut oil via an enzymatic reaction with lipase as seen in **Figure 2** with the observation of an additional CH_3 peak (at 3.663) not seen in a triglyceride

- Gluconic acid was potentially synthesized via an enzymatic reaction **(Figure 3)**

- Enzymatic fatty acid sugar ester synthesis was unsuccessful
  - Reaction was not observed
  - Reaction was too viscous for workup

- Fatty acid sugar ester reaction requires further direction
  - Ligase
  - Decrease viscosity of reaction
  - Peptidyl transferase

Future Directions

- Micelles formed from fatty acid ester reaction could be used for drug delivery systems because micelles can increase drug solubility (10-500 times more soluble), reduce toxicity, prolonged circulation time (protecting short half-life drugs), enhance tissue penetration, and have targeting ability.[12]

- Micelles could also be used as a sugar-based detergent that would naturally degrade overtime providing alternative to petrochemical surfactants on the market

- This study will contribute to an ever-growing field of research for renewable vesicles and micelle from natural products.

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