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Sustainable Antibacterial and Antiviral Polyesters based on Succinic Acid, Mercaptosuccinic Acid, and Eugenol

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Sustainable Antibacterial and Antiviral Polyesters based on Succinic Acid, Mercaptosuccinic Acid, and Eugenol

by

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A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Science in Materials Science and Engineering

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Abstract

Synthetic polymers have become indispensable in modern life. However, the prevalent use of synthetic polymers has created major sustainability issues including petroleum resource depletion and overfilling of landfills. At the same time, antibiotic resistance and the spread of new viruses have driven a need for antimicrobial and antiviral materials. A sustainable way to make materials antibacterial or antiviral is to use essential oils. Eugenol is a commonly used essential oil for these purposes, but it has been found to cause tissue irritation on contact. When eugenol is covalently connected to the material, these effects of oil leaching can be avoided. By creating a poly(butylene succinate) based polymer containing eugenol, we made a potentially degradable polymer that could fulfill many uses. After a catalyst study, three different polymerization routes were investigated to obtain the target polymer. The obtained polymers are semi-crystalline and thermally stable up to 325°C. The addition of butylated hydroxytoluene in the reaction resulted in polymers with a higher degradation temperature. Even with low eugenol content, the polymers showed over 90% bacterial reduction and even moderate eugenol content produced a polymer that was semi-crystalline. Through characterization, we co-optimized antimicrobial and physical properties to develop a material for a variety of uses such as food or medical packaging and equipment.

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Abbreviations

^{13}C NMR – carbon-13 nuclear magnetic resonance
BHT or B – butylated hydroxytoluene
DMPA - 2,2-dimethoxy-2-phenylacetophenone
DSC - differential scanning calorimetry
EMEM – Eagle's Minimum Essential Medium
Eug*- eugenol
Eug diol – monomer obtained from Eug and N-(2-hydroxylethyl)-1,3-oxazolidine
GPC – gel permeation chromatography
^{1}H NMR- proton nuclear magnetic resonance
M_n – number average molecular weight
M_w – weight average molecular weight
MS or M* - mercaptosuccinic acid
MS-Eug – monomer obtained from thiol-ene reaction of MS with Eug
P. Aeruginosa – Pseudomonas aeruginosa
PBMS – poly(butylene mercapto succinate)
PBS - poly(butylene succinate)
PCL - poly(caprolactone)
PDI – polydispersity index
PHA - poly(hydroxyalkanoates)
PLA - poly(lactic acid)
S. aureus – Staphylococcus aureus
Triflate - trifluoromethanesulfonate
T_{dec} – decomposition temperature
T_g – glass transition temperature
TGA- thermogravimetric analysis
T_m – melting point temperature
VSV – vesicular stomatitis virus

*: used in labels of polymers described later in the Results section

Table of Contents

List of Figures

List of Schemes

List of Tables

Additional Equations

1. Introduction

1.1 Sustainable Polymers

Since the discovery of Bakelite in 1908, synthetic polymers, mostly plastics, have become ubiquitous materials. The prevalent use of these materials has created major sustainability issues. Many current commercial plastics are made of nonrenewable petroleum resources, and as these resources are depleted, the need for materials made of bio-based feedstock or another biomass is growing. Many predict that by 2050, the plastic industry will use 20% of the oil consumed annually.[1] The other major problem created by the use of plastics is the excessive amount that is being deposited into landfills or oceans. Synthetic polymers currently make up about 11% of the municipal solid waste stream by mass. [1] Degradable materials could help to minimize this accumulation.

Synthetic polymers provide many benefits and, when considering reducing their use, social and economic needs must also be considered. [1] When considering global sustainability in 1987, The UN World Commission on Environment and Development felt that it was important that society "meets the needs of the present without compromising the ability of future generations to meet their own needs." [2] While discontinuing the use of synthetic polymers could seem like the most environmentally friendly option, it would eliminate the many sustainable benefits of these materials, such as lightweight transportation, membranes for efficient water purification, and food packaging to prevent spoilage. [1] Banning the use of these materials could also prevent many communities from meeting their current needs.

Reducing the use of polymers entirely has proven to be a highly challenging task causing the emergence of renewable and sustainable polymers. Current renewable polymers have been synthesized from seed oils, carbohydrates, protein-based materials, and natural monomers through chemical and biocatalytic

processes. While traditional renewable polymers were made from natural sources and then modified, synthetic sustainable polymers are an inexpensive alternative and could offer new capabilities. These synthetic processes still have a lot of room for cost reduction. Due to the necessity for processing in aqueous environments, aqueous-based separation is necessary. Renewable materials have a greater growth rate than petrochemical-based materials. Some current bioplastics in production include poly(lactic acid) [PLA], poly(hydroxyalkanoates) [PHA], and poly(butylene succinate) [PBS].[3]

1.2 Antimicrobial Materials

Synthetic materials have recently seen a large growth in their use against bacteria and viruses. The presence of harmful microorganisms is growing due to antibiotic resistance. These microorganisms form biofilms on surfaces and account for nearly 80% of infections. Many microbes can survive on surfaces for days and current disinfectants have only a short duration of action and high environmental toxicity. There is a growing need for effective, long-term antibacterial and biofilm preventing materials. By using polymeric materials for this purpose, surfaces can be made antimicrobial and have reduced toxicity. Natural polymers, such as chitin, heparin, and polylysine, show some antimicrobial action, while synthetic polymers can be made antimicrobial with quaternary nitrogen groups, guanidine groups, halogens, or by mimicking natural peptides. [4]

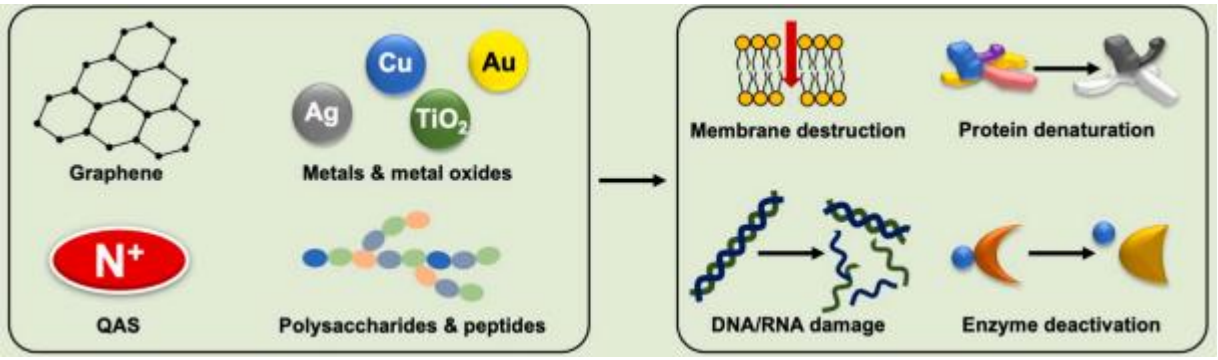


Figure 1. Antimicrobial materials and their main mechanism of microbial reduction[5]

An ideal antimicrobial material should be highly stable over a long period of time, easy and inexpensive to synthesize, and produce no toxic byproducts through decomposition. It is also ideal for a material to have broad-spectrum antimicrobial activity, be non-toxic and non-irritating, and be able to disinfect water by being water insoluble. There are many properties of a material that affect its antimicrobial activity. For most antibacterial agents, an acidic pH is ideal for maximum effect. Antimicrobial activity has been found to be parabolically dependent on molecular weight.[4] Positive charge density in the polymer creates better electrostatic interactions with the negatively charged cell walls of microbes. Properties such as alkyl chain length and polymer conformation contribute highly to the charge density of a polymer. Hydrophilicity is required for a polymer to show any antimicrobial behavior because hydrophobic polymers will not be able to interact with the microbes.[4]

The most common methods for evaluating antimicrobial properties are serial dilution tests and disc tests. Serial dilution tests are done by observing the visible microbial growth on a series of agar plates or broth containing dilutions of antimicrobial agents. Disc tests are performed by using different concentrations of antibiotic solutions in paper wells, cups, or discs placed over the surface of seeded agar plates containing a type of bacteria. Both test methods show how well an antimicrobial agent prevents the growth of microbes. Antimicrobial materials have a future in numerous applications, such as water filtration systems, fibers, food packaging, surgical industries, surfactants, detergents, and pharmaceuticals. Polymers and other materials are a promising future approach to reducing microbes by reducing drug-resistant bacteria in biofilms. [4]

1.3 Potential Uses of Antimicrobial Materials

Materials that are both biodegradable and antimicrobial could find countless uses in food and medical packaging and equipment. Bacterial and viral resistance would keep tools and equipment sterile and, since medical materials are often nonreusable, it would be beneficial for them to biodegrade. Infections are the most common cause of biomaterial implant failure in uses such as dental restorative implants or orthopedics.[6] Using intrinsically antibacterial materials would provide the biomaterial with some antimicrobial properties while not releasing bactericide components due to stabilization. Antibacterial materials can be incorporated into fibers, resins, and oils for use in meshes, gels, or ointments. The main challenge faced by intrinsically antibacterial materials is controlling the loss of stability in the body environment. [6]

Synthetic antimicrobial polymers are fairly new but have been found to be safe. Antimicrobial polymers prevent biofilm adhesion through antifouling and antimicrobial mechanisms. Biocidal polymers are nonvolatile, chemically stable, environmentally friendly, and durable. Some natural biocidal polymers exist such as chitosan, halamines, and polybiguanides. [7]

Bacterial resistance could help to keep food from spoiling and being wasted. It would also help to stop the spread of illnesses among people. Contamination can spread viruses or cause foodborne illnesses. The commercially available microbial resistant polymers include Novaron, Zeomic, Aglon, and Cleanaid. Synthetic or biobased plastics can be used for food contact surfaces or packaging while biopolymers (proteins, lipids, or polysaccharides) can be used to coat edible food products. [7]

1.4 Antiviral Polymers

The COVID-19 pandemic has created an increase in the need to prevent the spread of microorganisms. SARS-COV-2 is more contagious than other pathogens and has gone through multiple mutations, making preventative measures highly important. Direct human-to-human transmission is avoidable through physical distancing, wearing masks, and maintaining hygiene practices. Indirect contact uses inanimate

objects, such as telephones, light switches, and handrails, to spread the infection. Once a person touches a contaminated object the virus transfers to their hands and then their eyes, mouth, or nose. Covid-19 lives in the air and on surfaces for a few hours to days. Silver, copper, and titanium dioxide are current common antimicrobial agents used in the effort to end the pandemic. [7]

There is currently not enough research on effectively fighting viruses, and this is partially due to the fact that strategies against bacteria do not work against viruses. Due to viruses' small size and large diversity, they can be very challenging to control. The most effective strategies found have been to use physical and chemical approaches to block or deactivate viruses before they reach a host. Physical treatments include UV irradiation, heating, or desiccating, while chemical sanitations are done with strong acids, alkalis, oxidants, alcohols, or surfactants. Both of these methods are labor and material intensive and having intrinsically antiviral materials would reduce these. There are many current design ideas to create antiviral materials including extracting natural inhibitors from herbs or other plants, using antiviral metal nanoparticles (such as silver), using metal nanoparticles that generate heat or light (such as gold), using highly catalytic materials (like tungsten oxide), using bioinspired materials, or modulating surface porosity.[8]

There are two types of antiviral materials: active and passive. Active antiviral polymers have the benefits of having low density, high strength, high elasticity, good electrical insulation, and corrosion resistance. The most used active antiviral polymers are cationic polymers, such as polyethyleneimine. These polymers can not only deactivate viruses like influenza but also damage resistant water borne viruses. Cationic polymers are antiviral since most viruses are negatively charged and the positively charged polymer is able to promote removal through electrostatic adsorption. Passive materials do not possess antiviral properties but can be made antiviral through additive or external actions. TiO_2 or graphene oxide can be added to kill viruses or actions such as electric fields or alkaline environments can be used. The largest disadvantage to passive materials is that they can easily become contaminated again after

disinfection. Also, nanoparticles do not easily disperse in polymers and agglomeration reduces physical and chemical properties. Polymers do not currently make ideal antiviral materials because their antiviral property decreases over time due to low long-term stability and also the potential of unknown safety concerns.[8]

1.5 Eugenol

The emergence of new pathogens has created the need for new antimicrobial therapies. The biggest challenge is balancing effectivity and toxicity. Using natural essential oils as an antimicrobial agent can reduce the risk of toxicity. Essential oils are complex mixtures of low molecular weight compounds extracted from natural sources such as plants. Many essential oils have inherent antimicrobial activity caused by their different functional groups. The major challenge of adding an essential oil to a polymer is that it reduces the tensile strength of the material. Thymol, from thyme, is one of the most effective antimicrobial essential oils due to its water solubility while curcumin, from turmeric, and capsaicin, from chili peppers, also have beneficial properties such as wound healing and anti-inflammatory abilities. [7]

Eugenol is a well-known antimicrobial essential oil commonly used in dentistry as a root canal sealer. It is most commonly derived from clove oil, but can also be extracted from basil, cinnamon, and nutmeg. Eugenol inhibits the growth of a wide range of microbes including E. Coli, Penicillium Citrinium, and the human herpes virus. The release of eugenol from a material can cause tissue irritation and induce inflammation. However, covalently linking eugenol to a macromolecule can reduce the migration of eugenol into tissues. [7]

Like many essential oils, eugenol contains reactive and useful functional groups. The addition of eugenol to a material through polymerization rather than through blending reduces the risk of leaching, release of the smell, and discoloration in the material.

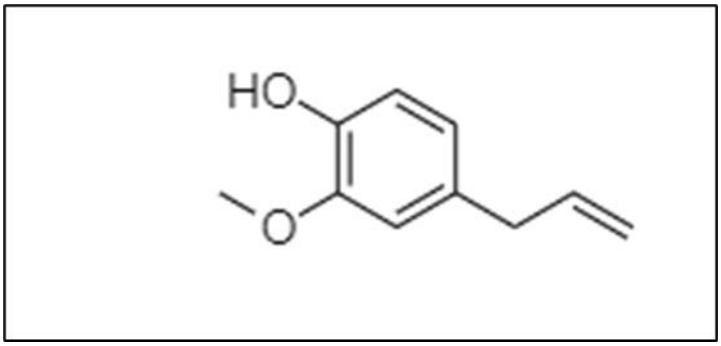


Figure 2. The chemical structure of eugenol

Eugenol contains three exterior functional groups off of its aromatic ring that can be used for reactions or to give eugenol its antimicrobial properties: allyl, hydroxyl, and methoxy groups. It is believed that the hydroxyl group on eugenol is able to penetrate the membrane of bacterial cells as well as inhibit protease and ATPase. The hydroxyl group has also been found to be responsible for helping eugenol prevent viral replication and infection. [9]

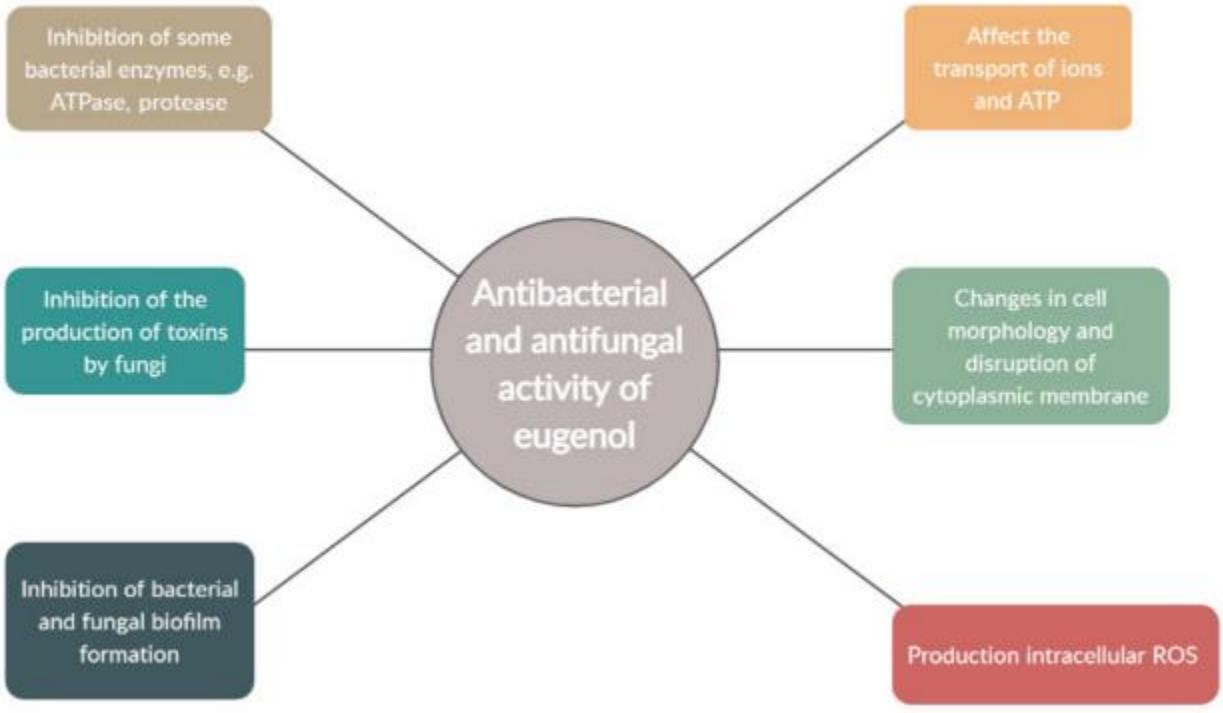


Figure 3. Antibacterial mechanisms of eugenol [9]

It was shown that when eugenol was copolymerized with ethylene by coordination polymerization the pendant aromatic methoxy and phenol groups created an antimicrobial effect. By comparing eugenol to fossil fuel based 4-penten-1-ol in copolymerization with ethylene, it was found that eugenol could perform superiorly to other monomers in many ways. Eugenol had a higher activity, was easier to incorporate into the polymer, and had less chain transfer than 4-penten-1-ol. Incorporating eugenol also made the polymer antibacterial. This polymer resulted in a 96% reduction of bacteria when the polymer contained only 6.8 mol% eugenol, compared to a poly(ethylene) control.[10]

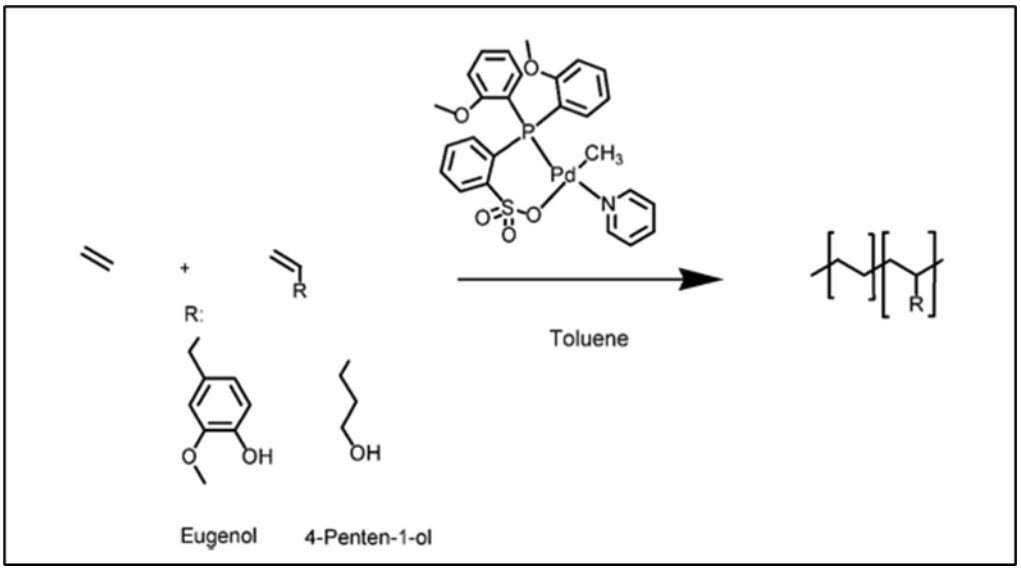
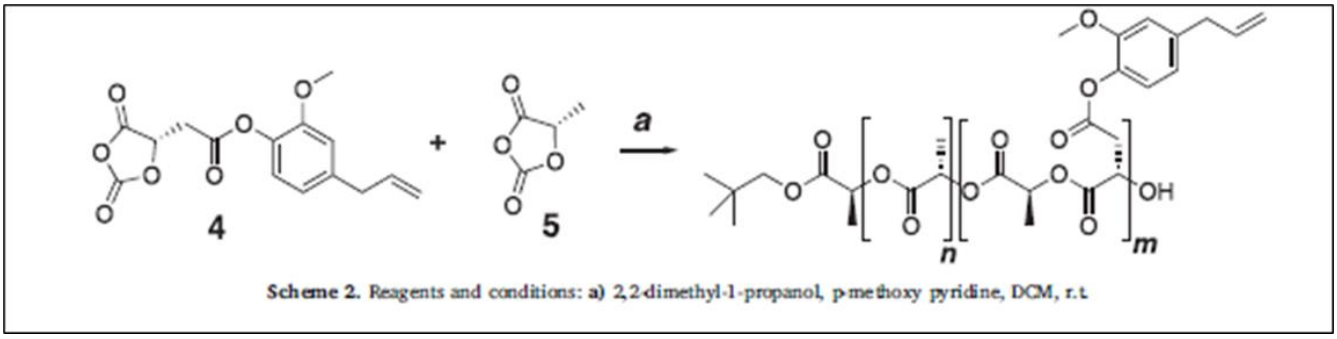


Figure 4. Polymerization of eugenol or 4-penten-1-ol with ethylene[10]

More recently it was published that a poly(lactic acid) based material containing a eugenol moiety for bioactive food packaging was created. This material was synthesized with o-carboxyanhydrides with eugenol attached through its hydroxyl group and only showed moderate antimicrobial activity when containing the highest eugenol concentration.[11] This polymer attached eugenol through its hydroxyl group, which limits its antimicrobial abilities.



Scheme 2. Reagents and conditions: a) 2,2-dimethyl-1-propanol, p-methoxy pyridine, DCM, r.t.

Figure 5. The reaction to create a poly(lactic acid) based material containing eugenol [11]

A polyester was synthesized using a eugenol-based diol and dodecanoic acid. This polymer had eugenol entirely in the main chain, leaving none of its functional groups pendant. While this polymer would be less likely to gain antimicrobial benefits from the eugenol, it was found that eugenol could produce a polymer with comparable mechanical properties to polymers produced with traditional petroleum-based monomers. [12]

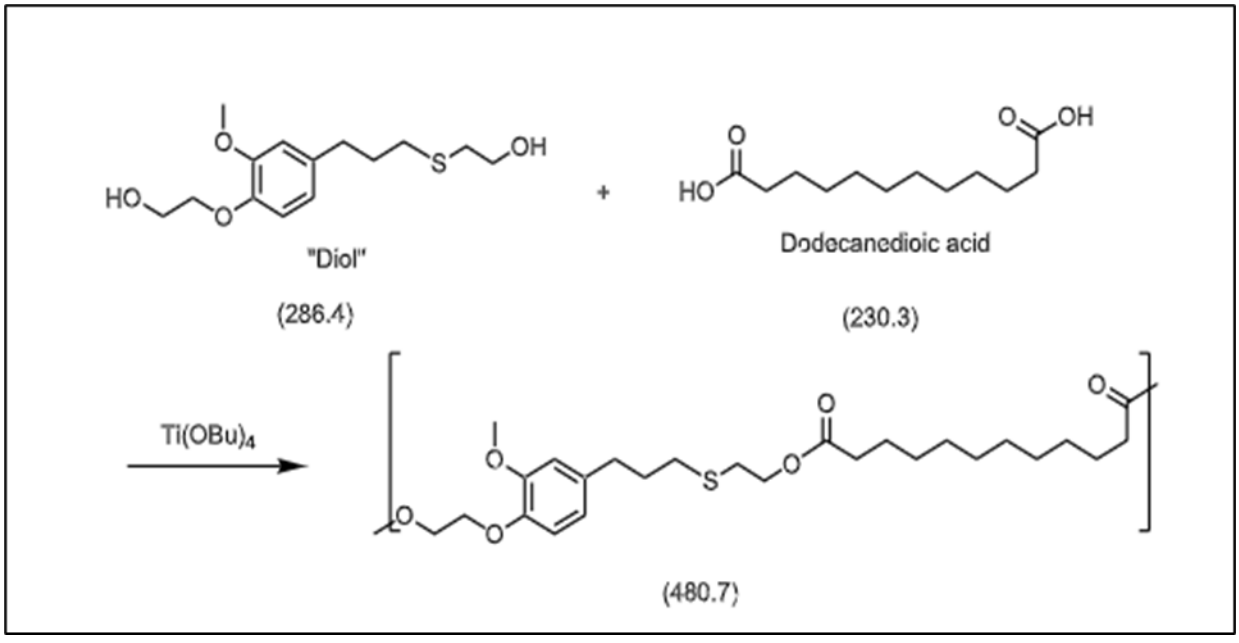


Figure 6. The reaction between the eugenol-based diol and dodecanoic acid.[12]

Dai et. Al. were able to synthesize eugenol bearing monomers made up of molar equivalents of eugenol, mercaptosuccinic acid, and using 1wt% DMPA as a photo catalyst. They were able to perform this reaction without using any solvent, making the reaction completely green as it also produced no volatile emissions. The reaction mixture was stirred and irradiated with UV at room temperature for 1 hour. [13]

1.6 Aliphatic Polyesters

Aliphatic polyesters are often used for biomaterials and biodegradable polymers. Polyesters contain hydrolyzable ester bonds and degrade into benign byproducts. Some commercially important examples include poly(lactic acid) [PLA], poly(caprolactone) [PCL], and poly(butylene succinate) [PBS]. PBS is one of the most important commercially available biodegradable polymers and has the potential to replace many conventional plastics due to its mechanical strength and applicable melting temperature. PBS is also biodegradable and potentially compostable.

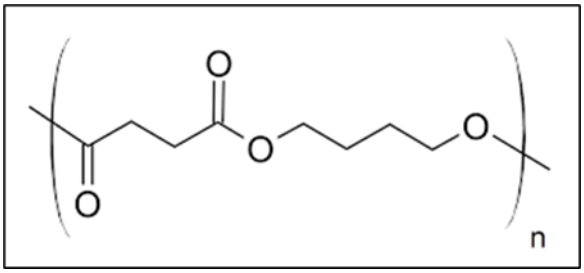


Figure 7. The chemical structure of poly(butylene succinate) [PBS]

PLA and PCL are prepared by ring-opening polymerization while PBS can be synthesized through Fischer esterification. Fischer esterification is the reaction of a diol with a diacid resulting in polyester formation and the condensation of water. Typically, a protonic acid is needed to catalyze the polymerization and the reaction is done in two stages. The first stage is done under elevated temperatures (about 180°C) and an inert gas (often Argon) to produce oligomers. The second stage is done under high vacuum (about 0.1 torr) and high temperatures (about 230°C) to produce high molecular weight polymers.

1.7 Lewis Acids as Polymerization Catalysts

Acid catalyzed reactions are the most common and studied reaction type. Nucleophilic reagents are reacted in the presence of acids as a catalyst. Lewis acids are electron pair acceptors. In order for a catalyst to be considered green, it must be able to be separated from the reaction mixture and recycled multiple times. This is more cost effective and productive than only using a catalyst once but also provides considerable waste reduction. Recycling is hard to achieve with a Lewis acid because the procedure for using a Lewis acid often requires a step to destroy the acid-base adduct between the catalyst and the product, which decomposes the catalyst. The most common Lewis acids used in polymerizations are zinc chloride ($ZnCl_2$), aluminum chloride ($AlCl_3$), and titanium tetrachloride ($TiCl_4$). Most Lewis acids are not suitable for catalysis because they are highly reactive with protic substances, such as water and alcohols. Due to this, Lewis acids cannot be used for dehydration polycondensation, where a small protic substance is produced. [14]

1.8 Metal Triflates

Metal triflates, or trifluoromethanesulfonates, are Lewis acids that don't react with protic compounds. They can be quantitatively recovered at the end of the reaction and only require catalytic quantities, allowing them to be considered green catalysts and be more cost effective. Metal triflates allow reactions to proceed under milder conditions allowing for the use of thermally unstable monomers. The first reported water stable Lewis acids were lanthanide triflates. Rare earth metal triflates were found to work as well as yttrium and scandium triflates. [15]

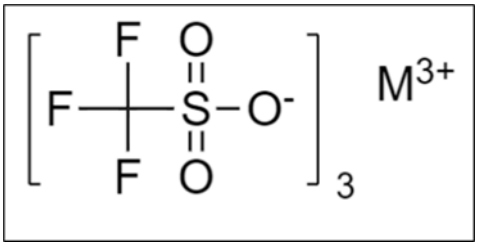


Figure 8. The general structure of a metal triflate

Scandium triflate is able to catalyze many types of reactions at low temperatures. It generally shows the highest activity of all metal triflates due to the small ionic radius of scandium causing high acidity. [15]

A group led by Takasu published, in 2003, their one step synthesis of substituted aliphatic polyesters using scandium triflate as a catalyst under milder conditions than normal. Their polymerization was done at significantly lower temperatures than was previously reported and yielded a white polymeric solid. After the polymerization, the catalyst was able to be recovered through reprecipitation and extraction with water. [16]

Initially, polymerization with a metal triflate catalyst was performed at 35°C for 124 hours. Takasu's group performed a catalyst study to find improved efficiency. Scandium triflate was compared to other scandium catalysts with stronger electron withdrawing ligands and to some rare-earth metal catalysts with strong ligands, as shown in Figure 7. Although scandium triflate was not found to be the most efficient, it did achieve the second highest conversion (second only to scandium nonafluorobutanesulfonate) and also produced polymers with the highest molecular weight. It was found that efficiency could be improved by adding mild amounts of heat, for example 80°C for 24 hours.[17]

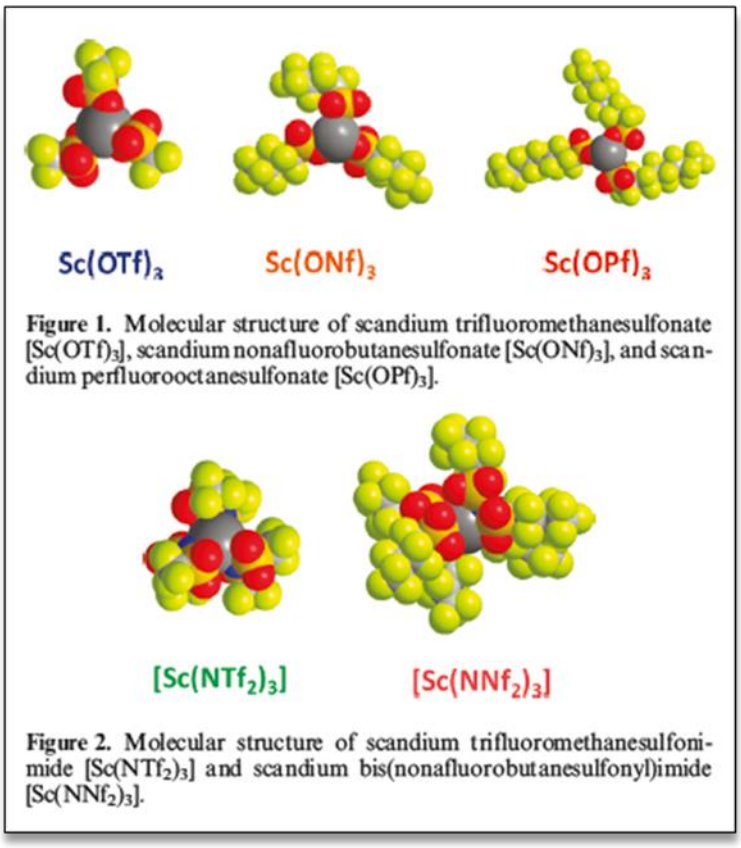


Figure 1. Molecular structure of scandium trifluoromethanesulfonate [$Sc(OTf)_3$], scandium nonafluorobutanesulfonate [$Sc(ONf)_3$], and scandium perfluorooctanesulfonate [$Sc(OPf)_3$].

Figure 2. Molecular structure of scandium trifluoromethanesulfonimide [$Sc(NTf_2)_3$] and scandium bis(nonafluorobutanesulfonyl)imide [$Sc(NNf_2)_3$].

Figure 9. Molecular structures of the compared metal triflates [17]

More recently, Takasu et al. created a polymer with pendant mercapto groups through ternary polycondensation of thiomalic acid, adipic acid, and 1,5-pentanediol at 80°C. These pendant groups allowed for a polymer-based hybrid material with various functionalities. Through low temperature polycondensation of dicarboxylic acid and diols, thermally unstable functional monomers could be used such as those containing double bonds, bromine, hydroxyl groups, and mercapto groups. [18]

Mercapto groups and other thermally unstable monomers cannot usually be used in conventional polyesterification. Traditionally, polyesterification is done at high heat, which encourages sulfur to crosslink. Sulfur crosslinking, also called sulfur vulcanization, was discovered by Charles Goodyear and Thomas Hancock. During crosslinking, sulfur forms three-dimensional networks and makes the

mechanical properties of a polymer superior. Vulcanization causes the formation of a strong and resilient rubber, which contrasts with the unvulcanized polymer which is an amorphous and putty-like material. Studies have suggested that vulcanization occurs due to homolytic cleavage of sulfur producing thiyl radicals which allows the process to happen at relatively low temperatures.[19] Using scandium triflate for catalysis allows polymerization to be performed at 80°C, which is still under the sulfur vulcanization temperature.

1.9 This Study

In this study, poly(butylene succinate) containing eugenol moieties will be synthesized in an attempt to create a potentially biodegradable, antibacterial, and antiviral polymer. The ideal amount of eugenol added will allow for the co-optimization of antimicrobial and physical properties of the polymer. After a catalyst study, three different strategies will be applied to incorporate eugenol into the polymer, as described in the results section. The obtained materials will then be characterized for their thermal, molecular weight, antibacterial, and antiviral properties in order to determine the optimal eugenol composition.

2. Experimental

2.1 Materials

The following materials were used for the synthesis of the polymers: succinic acid (Alfa Aesar, 99%), mercaptosuccinic acid (Alfa Aesar, 98%), 1,4-butanediol (Sigma Aldrich, 99%), butylated hydroxytoluene [BHT] (Aldrich, 99%), scandium trifluoromethanesulfonate (TCI, 98%), aluminum trifluoromethanesulfonate (Alfa Aesar), and bismuth trifluoromethanesulfonate (Alfa Aesar).

Adduct monomers were synthesized with mercaptosuccinic acid (Alfa Aesar, 98%), eugenol (TCI, 99%), 2,2-Dimethoxy-2-phenylacetophenone [DMPA] (Acros Organics, 99%), paraformaldehyde (Alfa Aesar, 98%), and diethanolamine (Acros Organics).

Post polymerization reactions were done with eugenol (TCI, 99%) and DMPA (Acros Organics, 99%).

2.2 Monomer Synthesis

2.2.1 Synthesis of the Mercaptosuccinic Acid- Eugenol Adduct (Route B)

A 100mL quartz flask was fitted with two 365nm UV lamps placed 10cm away and a 0.5in stir bar. This flask was purged with argon and basic vacuum. Equimolar amounts of mercaptosuccinic acid and eugenol were added to the flask followed by just enough methanol to dissolve the mixture. A catalytic amount of 2,2-dimethoxy-2-phenylacetophenone (DMPA) was added and the mixture was stirred and irradiated for 6 hours. NMR was used to confirm complete conversion.

2.2.2 Synthesis of Diol-Eugenol Adduct (Route C)

A 100mL three-neck flask was fitted with a condenser and an adapter with a thermometer. A magnetic stirrer was used as well as a silicon oil bath for heating. While stirring, paraformaldehyde, and diethanolamine were added in equimolar amounts and heated at 65°C for 2.5 hours. After, the flask was heated to 120°C to distill off water to form the oxazolidine intermediate. Eugenol was then added in an equimolar amount and the mixture was heated at 95°C for 8 hours.

2.3 General Synthesis of Polyesters

The polyesters based on different amounts of diol(s) and diacid(s) were synthesized in a 100mL three-neck flask using a mechanical overhead stirrer, a vacuum tight stirrer bearing, and a distillation trap. A silicon oil bath was used for heating. The polyesters were synthesized through a two-stage bulk polymerization above the melting temperatures of the monomers but below the vulcanization temperature of sulfur. The monomers were added to the flask and heated until uniform. When polymers were made with scandium triflate, the reactor was heated to 80°C under argon. Oligomers were obtained during the first stage by heating the monomers under an argon stream for 2 hours. During the second stage, vacuum was applied to achieve a reduced pressure of 0.1 torr for 20 hours. After cooling the product, chloroform was used to dissolve the polyester and stirred until fully dissolved. This solution was then crashed in a poor solvent for the polymer and filtered. For the PBMS, diethyl ether was used as a poor solvent, and for the eugenol containing polymers, methanol was used as a poor solvent. The resulting polyester was then vacuum dried at 30°C for 24 hours.

2.3.1 Modifications for the Catalyst Study

15mol% of mercaptosuccinic acid, 40 mol% of succinic acid, and 50 mol% of 1,4-butanediol were added to the flask. When aluminum and bismuth triflate were applied the polymerization had to be heated to 200°C to obtain a uniform mixture.

2.3.2 Modifications for Route C

Between 5-15 mol% of the previously made eugenol-diol, 45-35 mol% of 1,4-butanediol, and 50 mol% of succinic acid were added to the flask. This route then followed the general polyester synthesis.

2.4 Post Polymerization

2.4.1 Post Polymerization Modifications for Route A

A 50mL quartz flask was fitted with two 365nm UV lamps placed 10cm away, and a 0.5in stir bar. A silicon oil bath was used to heat the flask to 50°C. After this flask was purged with basic vacuum and argon, the previously made polyesters were added and dissolved in excess amounts of eugenol. If it was necessary to make the polymer stirrable, some chloroform was added as a solvent. Catalytic amounts of DMPA were added and the mixture was stirred and irradiated with UV for 6 hours or longer until the thiol-ene reaction could be confirmed by ^{1}H NMR.

2.6 Characterization

2.6.1 Nuclear Magnetic Resonance

^{1}H NMR and ^{13}CNMR spectra were recorded on a 500MHz Bruker Advance NMR spectrometer. All samples were dissolved in $CDCl_3$. The ^{1}H NMR spectra was measured with 32 scans with a 2s pulse delay while the ^{13}CNMR spectra were recorded with 5000 scans applying a 10s pulse delay.

2.6.2 Differential Scanning Calorimetry

Thermal transitions were studied with a Shimadzu DSC 60. Between 5 and 15 mg of the polymer were heated and cooled at 10°C/min from -50°C to 140°C. Three heating cycles were applied, and the reported transition temperatures are from the third cycle. T_g was measured as extrapolated onset temperature.

2.6.3 Thermal Gravimetric Analysis

The thermal stability of the polymers was determined with a TA instrument Q500 under nitrogen. Samples were heated at 5°C/min to 600°C.

2.6.4 Gel Permeation Chromatography

Measurements were made on a Shimadzu LC2030 GPC chromatograph. Chloroform was applied as mobile phase at 30°C at a 1.0mL/min flow rate. Polystyrene samples were used as standards. The samples and standards were dissolved in the mobile phase.

2.7 Antibacterial/ Antiviral Studies

2.7.1 Antibacterial

The antibacterial activity was evaluated through an agar slurry serial dilution method [20] using Pseudomonas aeruginosa ATCC 15422 (gram negative) bacteria. Cultures of bacteria were grown for 18 hours in TSB in a shaking incubator set to 30°C. Sterile soft agar, composed of 0.85% saline NaCl, 0.3% agar, and 100mL DI water, was then inoculated with the bacteria. Samples were prepared by dissolving a polyester into a small amount of chloroform and then casting this sample onto a 2.5 by 3.5 cm glass slide. Exactly 0.7mL of inoculated soft agar was pipetted onto the sample to create a layer about 1mm thick. The samples were then placed in an incubator for 24 hours at 30°C. After this contact time, samples were washed with 0.9% saline to remove the soft agar and the saline and agar were transferred to sterile tubes. This mixture was then used for a serial dilution and spread into tryptic soy agar. After 48hours of incubation at 30°C, the colony numbers were counted and recorded. Each assay was performed in duplicate, and results were expressed as colony forming units per mL (CFU/mL).

2.7.2 Antiviral

The antiviral activity of the polymers was evaluated by assessing the infectivity of vesicular stomatitis virus (VSV) cells following contact with the sample. Polymer samples were made into powders. After sterilizing the samples in ethanol, 1.5mL microfuge tubes were filled about 1/3 with polymer and 20µL virus. The samples were left to expose for 3 hours. After, samples were rinsed with EMEM media and placed on a shaker for 30 minutes to detach the viral particles from the sample and plate. The remaining viral particles were measured through a plaque assay.

3. Results and Discussion

3.1. Preliminary Studies

3.1.1 Catalyst Study

For the catalyst study 1,4-butanediol (50 mol%), succinic acid (35 mol%) and mercaptosuccinic acid (15 mol%) were polymerized, without eugenol. We compared scandium triflate to triflates containing cheaper, more stable metals: aluminum and bismuth. Aluminum is generally the cheapest metal triflate which would make it ideal if effective. Bismuth, while still more expensive than aluminum, is cheaper than scandium while also having comparable activity.

The polymer obtained with scandium triflate had fairly amorphous physical properties, which can be attributed to the mercaptosuccinic acid content incorporating more pendant groups. It was tough and rubbery but was able to dissolve in chloroform. Due to being amorphous, the polymer was unable to be crashed fully in diethyl ether because it formed a gel and could not be separated from the solvent. After evaporation, the polymer left behind was a brittle, off-white solid. Polymerization with scandium triflate resulted in a yield of 79.9%.

The polymer with the aluminum triflate showed signs of crosslinking such as being unable to dissolve in chloroform. This polymer was unable to be purified so the product likely contained unreacted monomers and byproducts. The product was tough, sticky, and off-white. Because it could not be purified, a reasonable yield could not be measured for this polymer.

The polymer with bismuth triflate was initially a bright yellow color and was a thick liquid. It was able to be dissolved in chloroform and crashed in diethyl ether. The resulting polymer was bright yellow and dough-like in texture. This bright color is likely caused by oxidation occurring during the polymerization. Later the polymer turned brown. This catalyst produced a yield of 59.3%.

The aluminum and bismuth catalysts did not produce comparable polymers to the scandium catalyst. The scandium catalyst produced a polymer more similar to commercial PBS, which is white and semi-crystalline. While the scandium catalyzed polymer was colorless and solid, the aluminum and bismuth polymers were soft or colored. These polymers were also less pure and had lower yields than the scandium catalyzed polymer.

When comparing the NMR spectra of the polymers, as shown in Figure 10, the aluminum catalyzed polymer does not show clean, resolved peaks. While the bismuth catalyzed polymer shows cleaner peaks, it shows lower conversion.

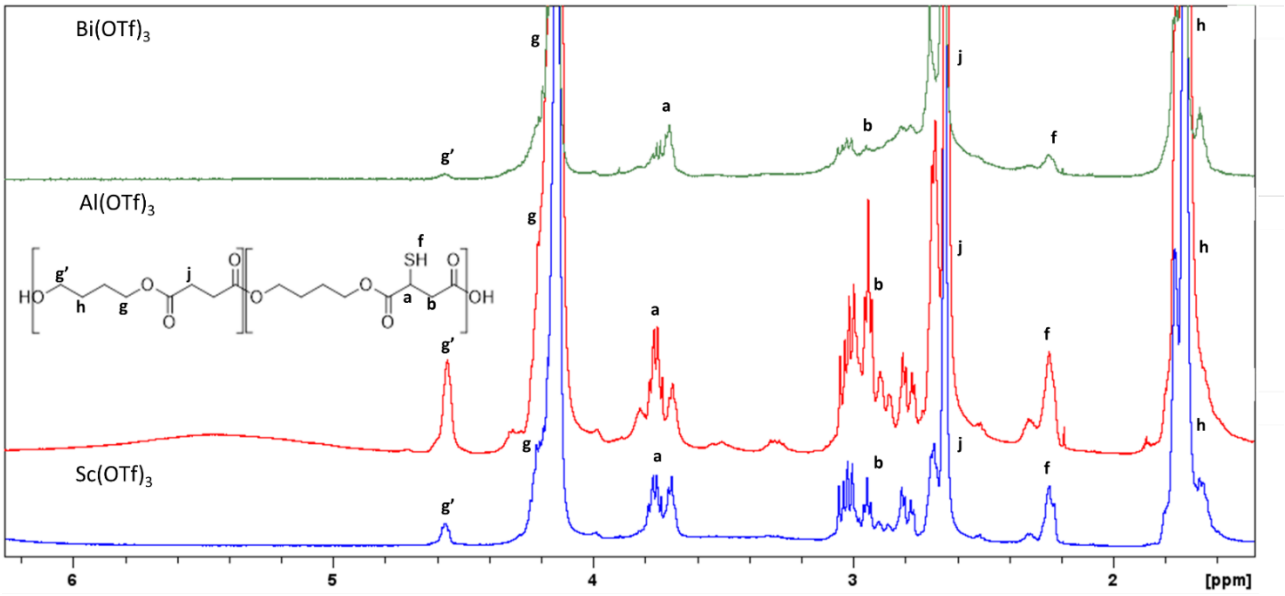
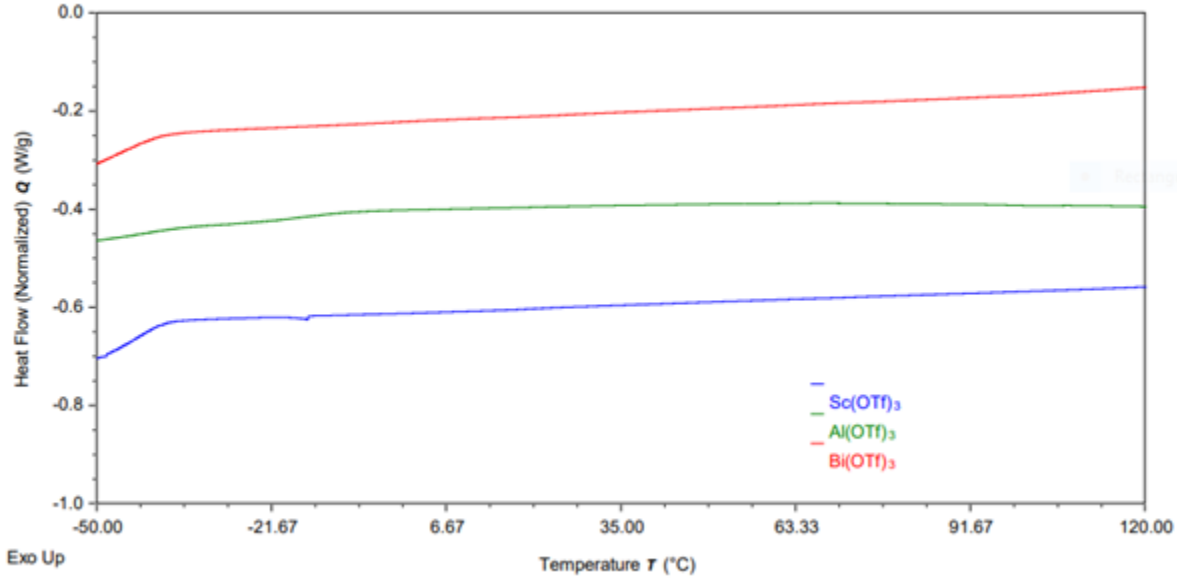


Figure 10. NMR comparison of the polymer PBMS produced with scandium, aluminum, and bismuth triflates.

Thermal analysis through DSC, seen in Figure 11, showed that all of the polymers were highly amorphous. All three had very low glass transition temperatures, below -30°C. This would not allow the polymers to behave like crystalline solids at room temperature.

(a)



(b)

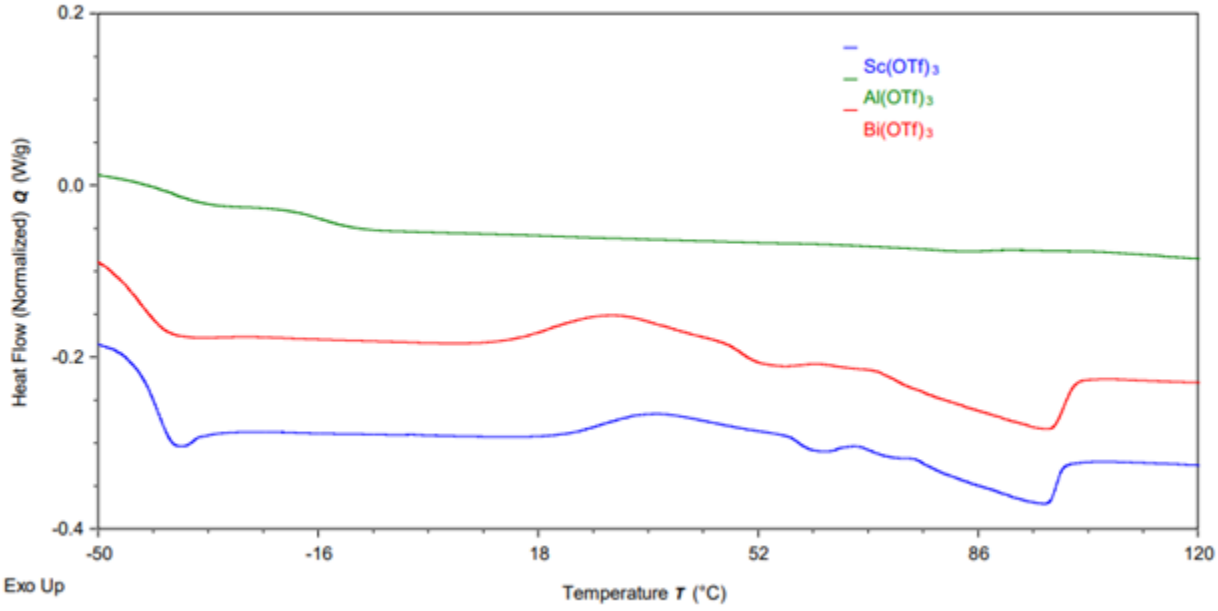


Figure 11. DSCs for PBMS made with the three catalysts, (a) cooling and (b) heating traces.

Analysis through TGA, seen in Figure 12, showed that the polymer made with bismuth triflate had a low decomposition temperature (less than 200°C). The aluminum-based polymer showed a high catalyst residue up to 700°C.

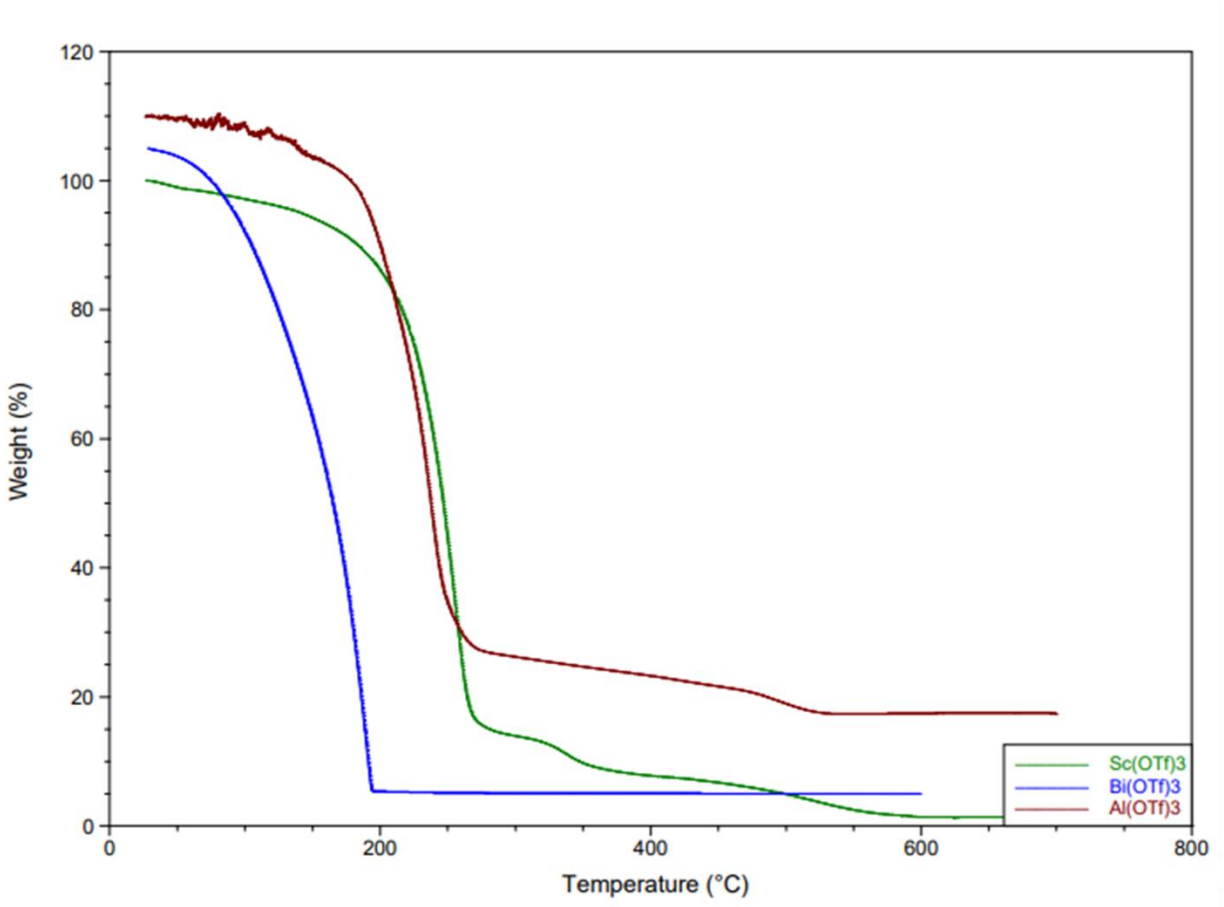


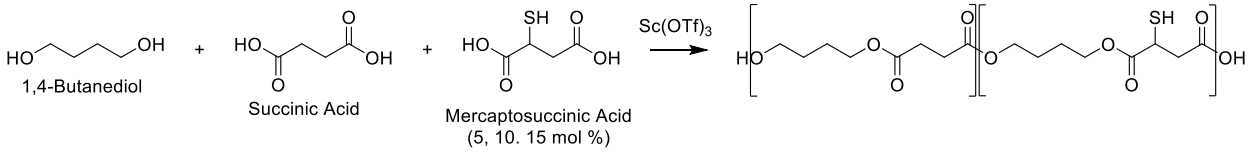
Figure 12. TGA curves comparing the three polymerization catalysts.

Because the aluminum or bismuth triflates would produce polymers with poor conversion and physical properties, we decided to only use the scandium triflate for catalysis for future polymerizations.

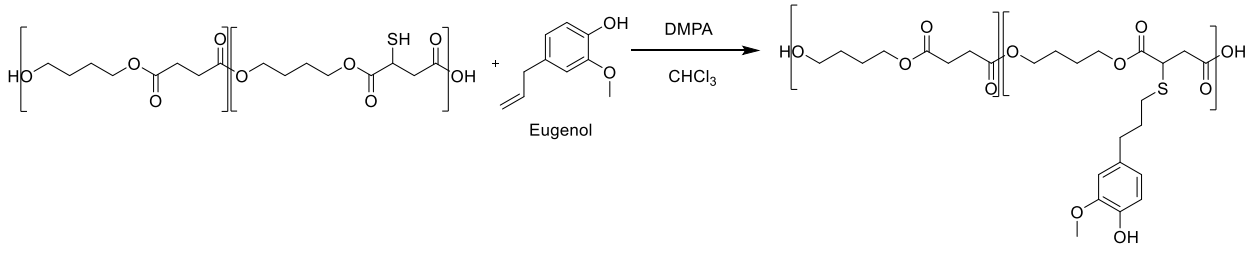
3.1.2 Route A

In Route A, as seen in Scheme 1, we developed a method to create a eugenol-containing PBS by first synthesizing a polymer containing pendant mercapto groups and then attaching eugenol through thiol-ene addition.

(a)



(b)



Scheme 1. (a) polymerization and (b) post-polymerization via Route A.

Thiol-ene reactions have a "click" nature because they are highly efficient and green.[21] This type of reaction has a growing use in materials applications, surface modifications, polymer modifications, and polymer synthesis. The versatility of this procedure comes from a weak hydrogen-sulfur bond that makes the reaction able to be initiated by many different precursor materials. Sulfur is highly reactive due to its high electron density so it can be used to modify many physical and chemical properties. Thiol-Michael Addition is considered green because it is often solventless and uses mild catalysts.[21]

We assumed that this method would be effective and efficient due to the high reactivity of sulfur. The largest challenge for this method would be avoiding cross-linking when synthesizing the initial polymer with pendant mercapto groups.

We were successfully able to synthesize polymers containing 5, 10, and 15 mol% mercaptosuccinic acid. ^{1}H NMR analysis of these polymers confirmed that each polymer contained roughly its target amount of mercaptosuccinic acid. However, the NMR spectra did not show clean or resolved peaks which suggests that side reactions may have occurred, as seen in Figure 13.

These polymers were then used in a thiol-ene reaction to attempt to connect eugenol at the pendant mercapto group. Initial attempts at this reaction using stoichiometric amounts of eugenol showed little to no conversion. The rigid polymer formed did not leave room for eugenol to be incorporated. Conversion was eventually achieved after reacting the polymer with 35 times the stoichiometric amount of eugenol. Distillation was tried to remove the excess eugenol, but the polymer quickly became hard and trapped the excess eugenol inside. It was decided that this method for producing a eugenol-containing PBS would not be efficient because we did not have an effective way to remove the remaining reactants.

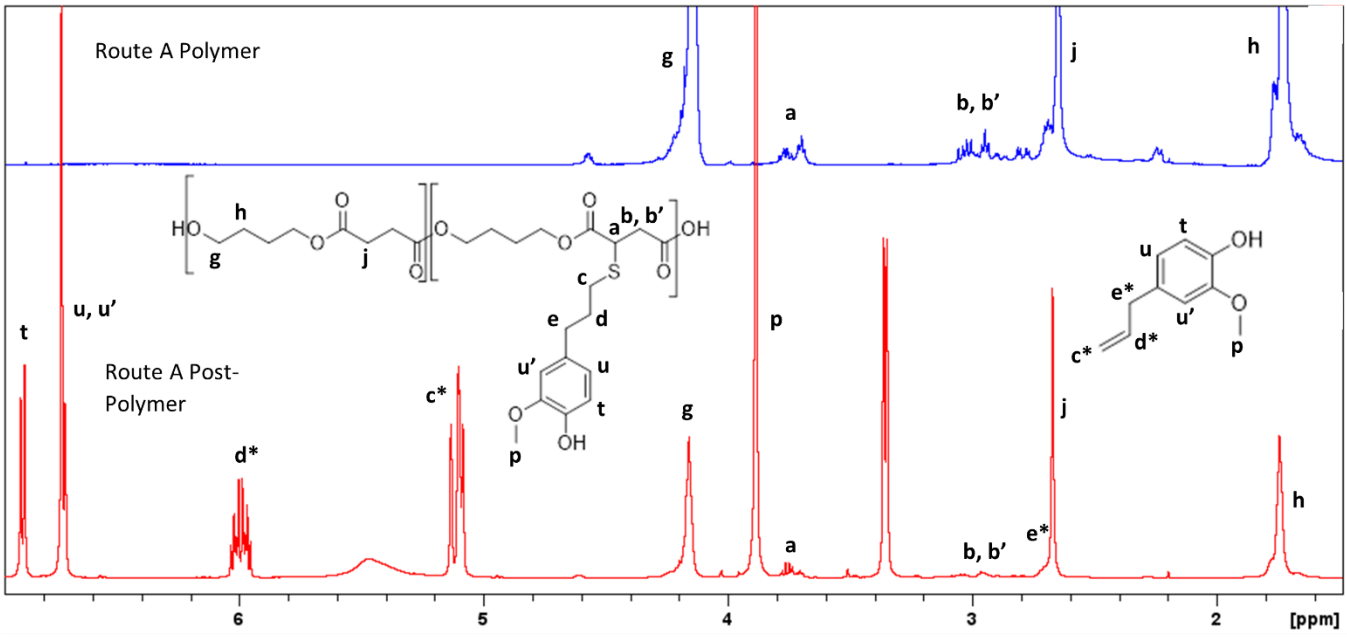
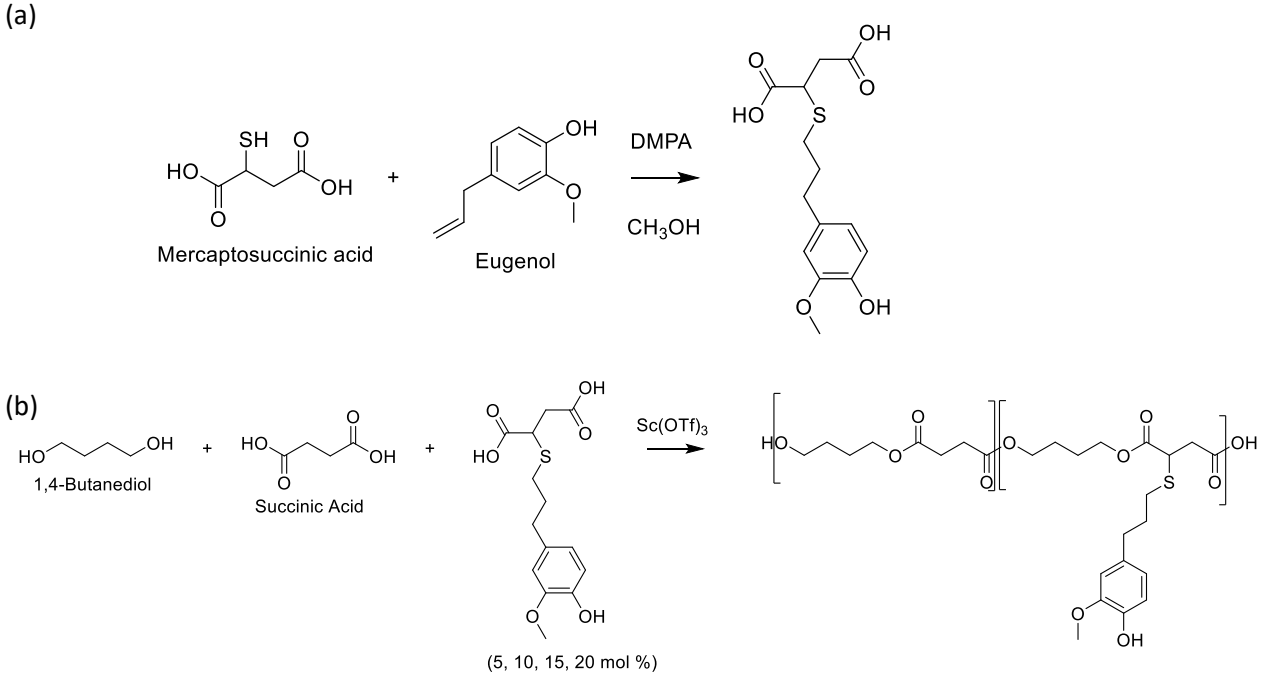


Figure 13. ^{1}H NMR spectra obtained of polymer and post-polymer using Route A

3.1.3 Route B

In Route B we first synthesized a monomer of the mercaptosuccinic acid with eugenol, and then applied this monomer in the polymerization with 1,4-butanediol and succinic acid, as seen in Scheme 2.



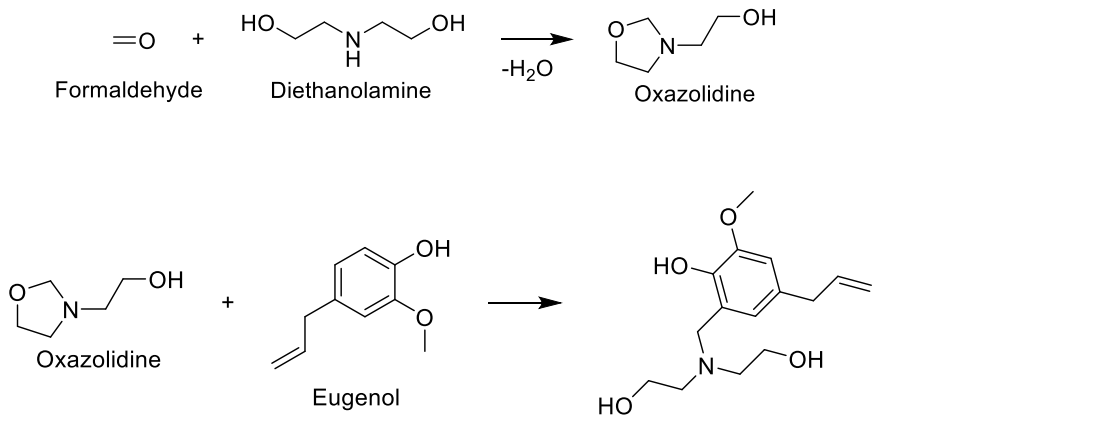
Scheme 2. (a) Monomer synthesis and (b) polymerization for Route B.

Because this turned out to be the most efficient route to obtain the desired polymer, we will discuss this route and the results in the subsequent section 3.2 in more detail.

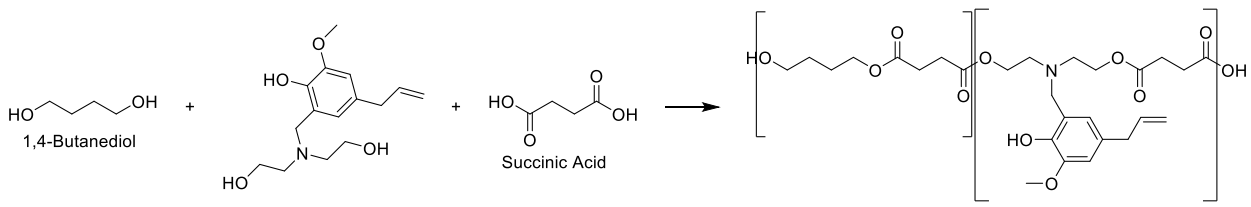
3.1.4 Route C

We planned to create the eugenol-based diol to use as a comonomer with 1,4-butanediol for polymerization with succinic acid, as seen in Scheme 3. Compared to our other attempted synthesis routes, this method would attach the eugenol to the diol instead of the acid. Because a mercapto group would not be needed to introduce eugenol to the polymer, the possibility of cross-linking could be avoided. Here, the Eugenol-diol (10 mol%), 1,4-butanediol (40 mol%), and succinic acid (50 mol%) were applied.

(a)



(b)



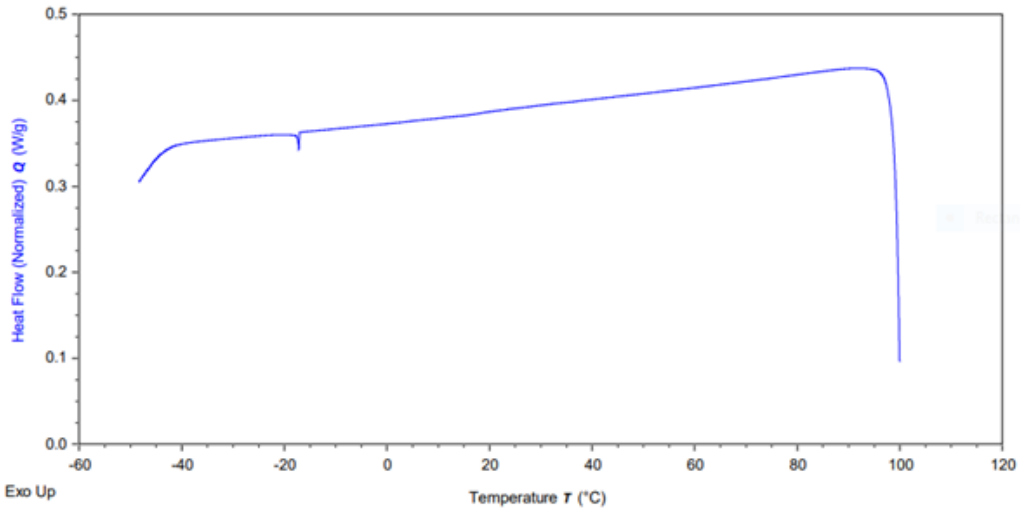
Scheme 3. (a) Monomer synthesis and (b) polymerization for Route C.

Mahajan et al. produced bio-based polyester polyols using eugenol and renewable diacids such as dimer, sebacic, succinic, and maleic acids.[22] This reaction created the conversion of renewable materials into valuable polymeric materials which is ideal for environmental and economic causes. Because only the ortho positions are available for substitution in eugenol, a Mannich reaction could be used to introduce dihydroxyl functionality allowing eugenol to be used as a good alternative to petroleum-based precursors.

The eugenol- diol adduct was able to be synthesized according to the original procedure but was found to be very impure. This monomer was distilled to remove excess eugenol before being used in polymerizations.

The resulting polymerization showed little conversion, the best yield being 49.69%. The DSC showed that the polymer was not uniform and also showed a low glass transition temperature (Figure 14) suggesting that the polymer was highly amorphous.

(a)



(b)

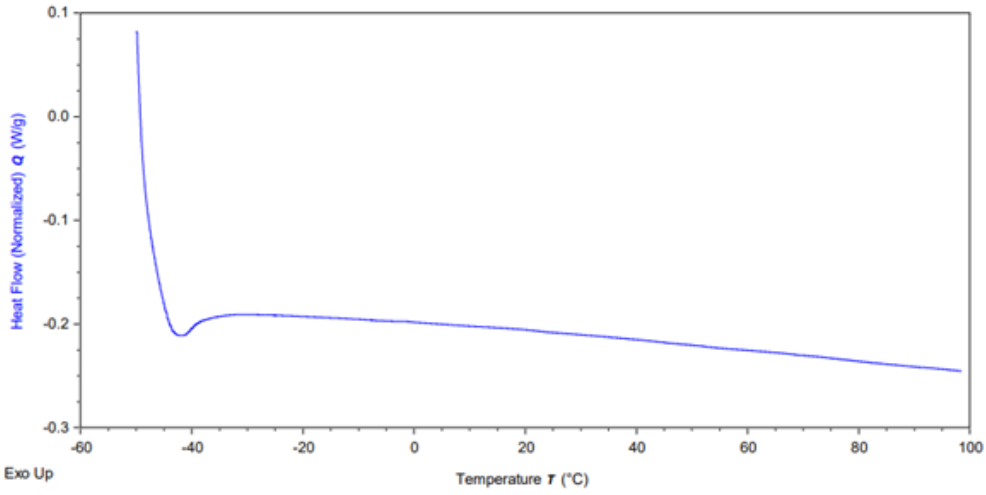


Figure 14. (a) cooling and (b) melting curves obtained through DSC of the Route C polymer

All attempts to make a solid polymer failed. We believe this polymer being so amorphous was due to a high flexibility of the pendant eugenol group between the single bonded oxygen atoms. ^{1}H NMR showed little incorporation of eugenol, seen in Figure 15.

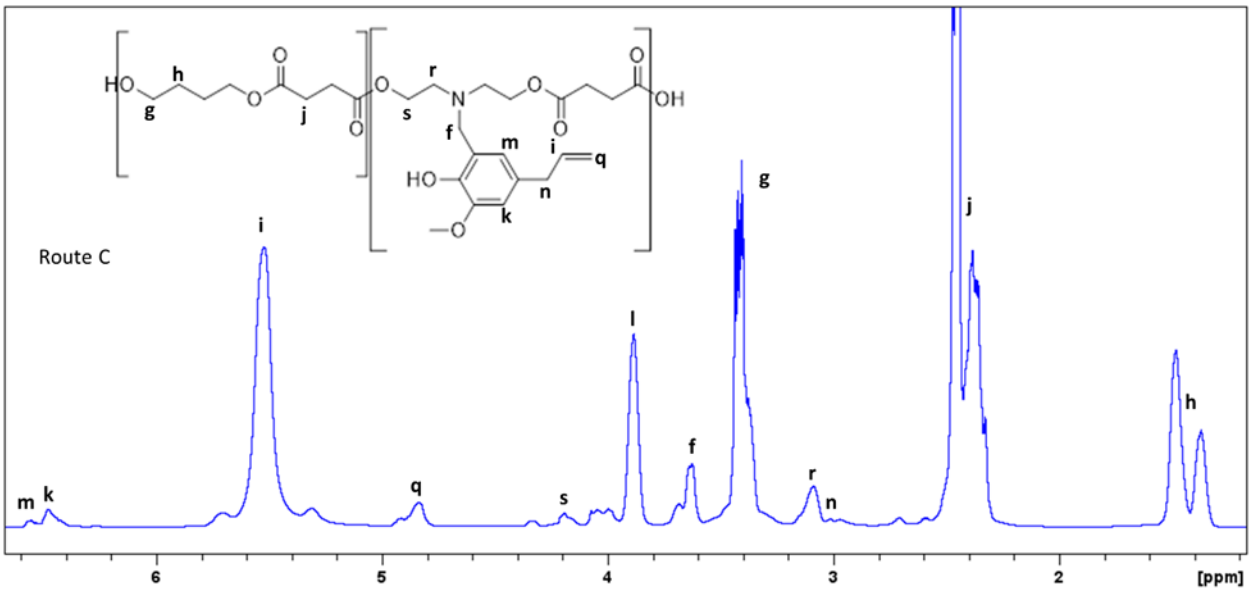
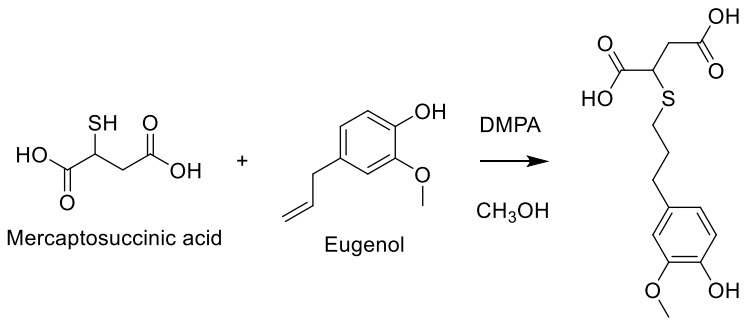


Figure 15. ^{1}H NMR spectra of Route C product

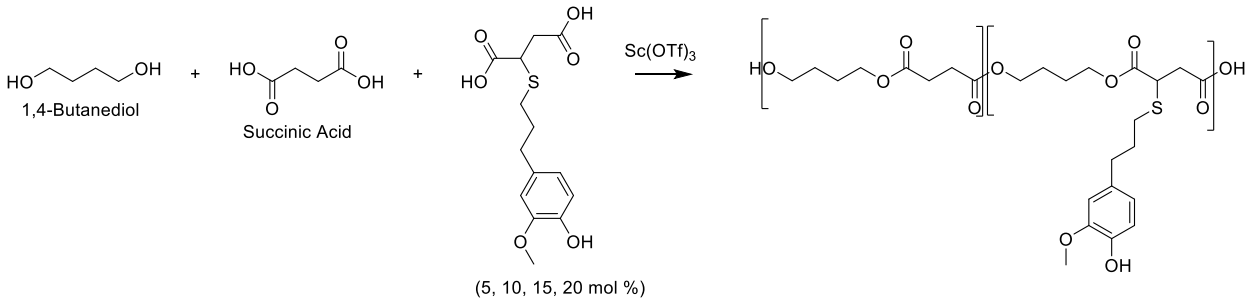
3.2 Main Results and Discussion on Route B

Scheme 2 shows the reactions applied for Route B.

(a)



(b)



Scheme 2. (b) Monomer synthesis and (b) polymerization for Route B.

3.2.1 Monomer Synthesis

We based the monomer synthesis on the method by Dai et al. however, no reaction occurred when following this protocol exactly.[11] Instead, methanol was used to dissolve the reagents to combine well, and no heat was needed for complete dissolution. After allowing the thiol-ene reaction to occur for 6 hours complete conversion was achieved. As seen in Figure 16, the peaks representing the protons on the allyl group of eugenol are no longer present. The solvent was removed through rotovap followed by vacuum drying. The resulting product was a tough white solid that was able to be used in future polymerizations.

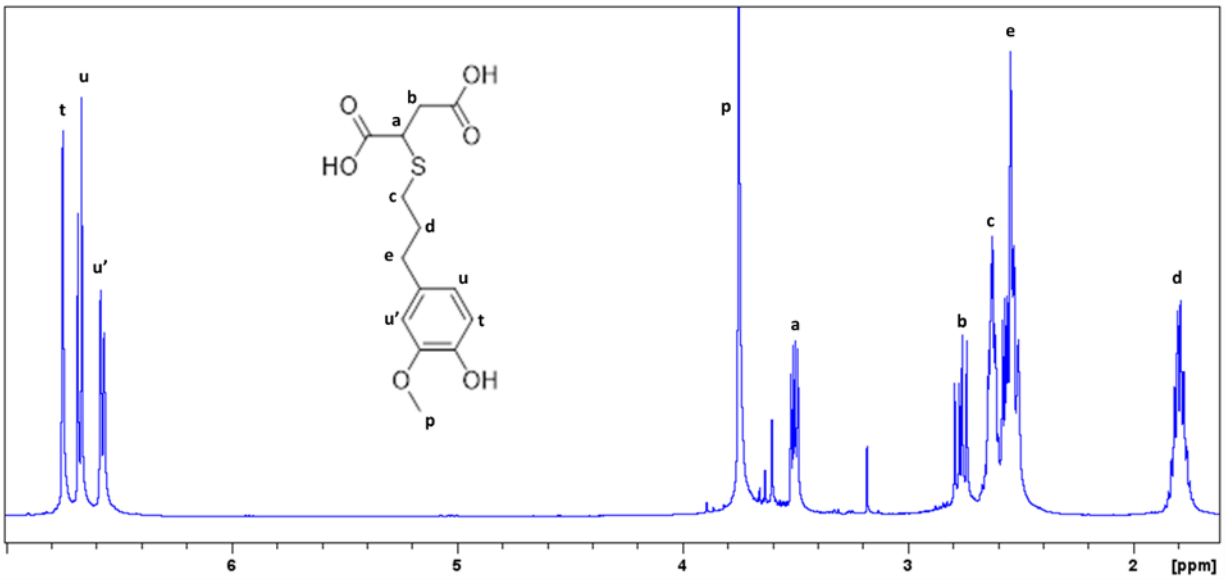


Figure 16. ^{1}H NMR of monomer made of mercaptosuccinic acid and eugenol

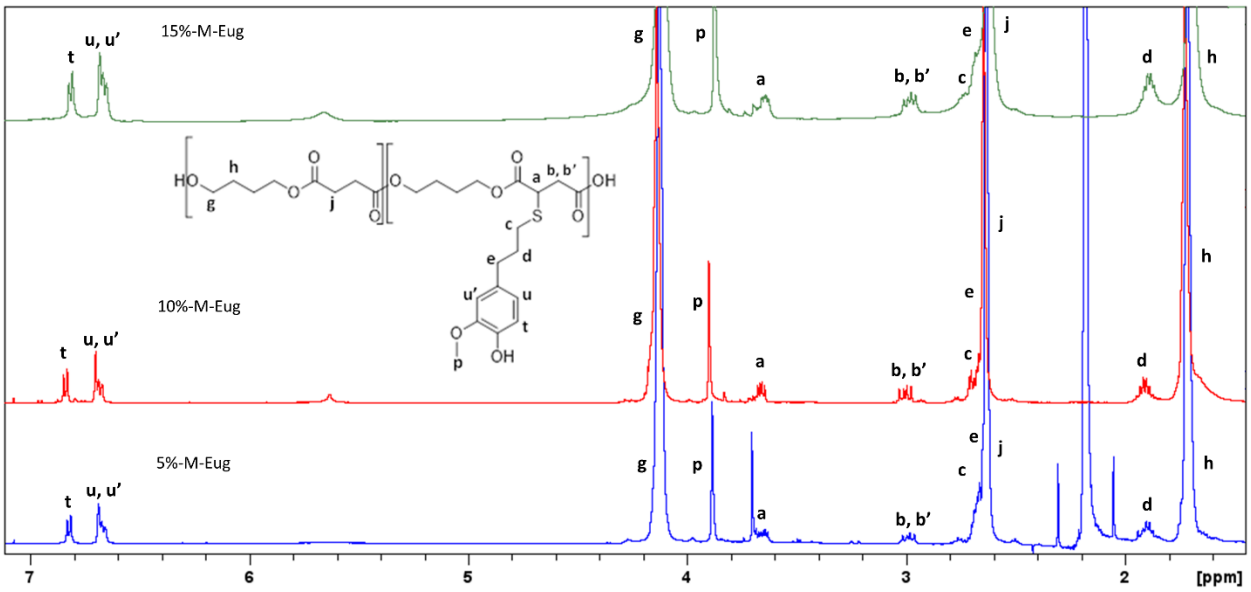
3.2.2 Polyester Synthesis

The polyesters were synthesized using scandium triflate as a catalyst. The resulting polymer was pink and tough and easily dissolved in chloroform. After crashing in methanol, the polyester became a white semi-crystalline powder which was then vacuum dried. In order to prevent vulcanization, we also ran a series with butylated hydroxytoluene (BHT), to scavenge radicals. The ^{1}H NMRs of these polymers showed clean, sharp peaks, as shown in Figure 17.

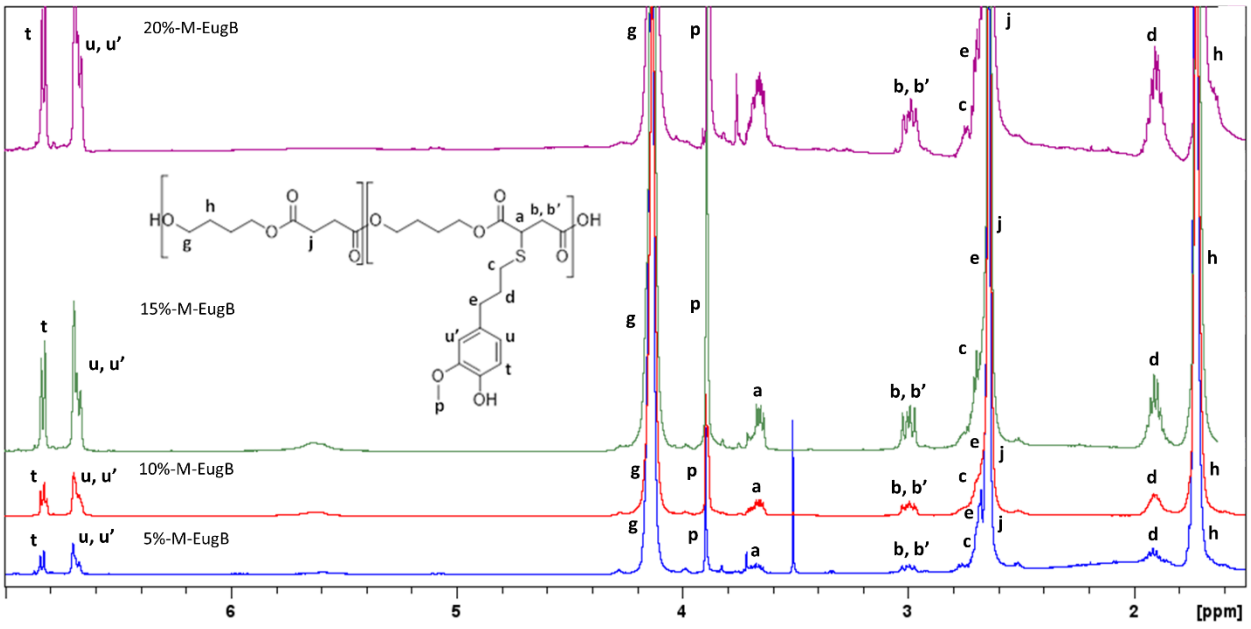
Table 1. Polymers made by Route B and a polymer formed with in-chain eugenol

0%-M-Eug	PBMS contains 0 mol% Eugenol
5%-M-Eug	PBMS based polymer containing 5 mol% Eugenol
10%-M-Eug	PBMS based polymer containing 10 mol% Eugenol
15%-M-Eug	PBMS based polymer containing 15 mol% Eugenol
5%-M-EugB	PBMS based polymer containing 5 mol% Eugenol and BHT as an antioxidant
10%-M-EugB	PBMS based polymer containing 10 mol% Eugenol and BHT as an antioxidant
15%-M-EugB	PBMS based polymer containing 15 mol% Eugenol and BHT as an antioxidant
20%-M-EugB	PBMS based polymer containing 20 mol% Eugenol and BHT as an antioxidant
In-Chain Eug	A polymer synthesized from a eugenol-based diol and dodecanoic acid. It has eugenol entirely in its main chain

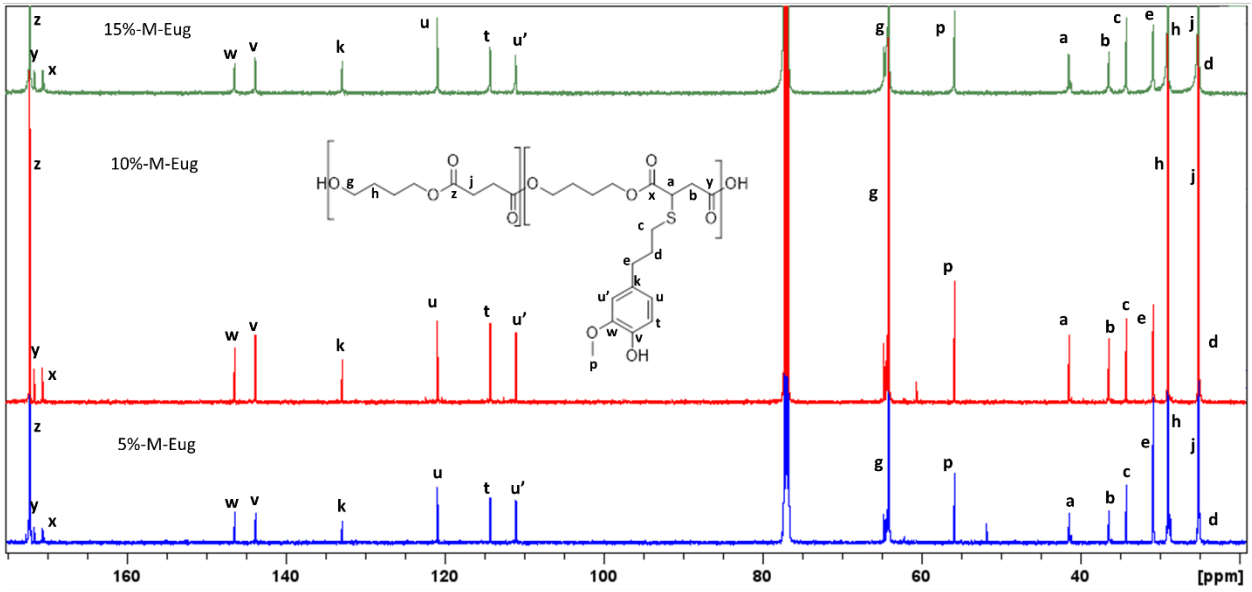
a)


15%-M-Eug
10%-M-Eug
5%-M-Eug
t
u, u'
g
p
a
b, b'
c
e
j
d
h
[ppm]

(b)


20%-M-EugB
15%-M-EugB
10%-M-EugB
5%-M-EugB
t
u, u'
g
p
a
b, b'
c
e
j
d
h
[ppm]

(c)



(d)

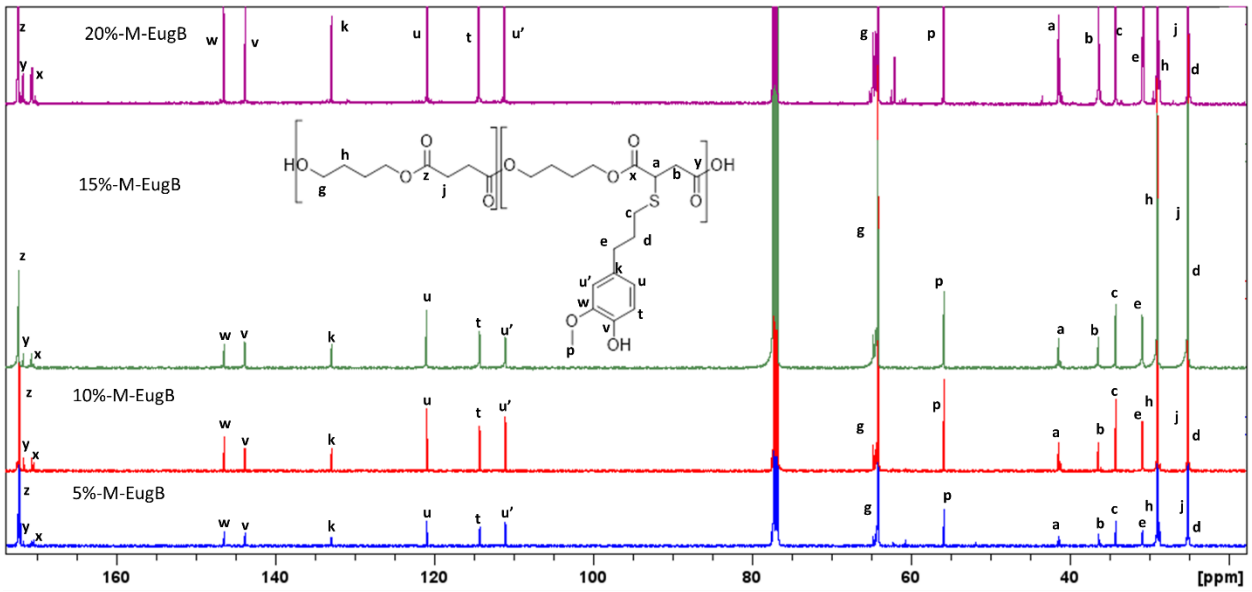


Figure 17. ^{1}H NMRs of polymers (a) without BHT and (b) with BHT and ^{13}C NMRs (c) without BHT and (d) with BHT

3.2.3 Yield Percentage and Eugenol Incorporation

The ideal yield for these polymers was around 73% but, high enough eugenol content appears to worsen the yield, as seen in Table 2.

Table 2. Polymer Yields and Eugenol Content

Polymer	Yield (%)	Eugenol Content (mol %)
0%-M-Eug	72.86	0
5%-M-Eug	69.76	4.81
10%-M-Eug	74.65	8.05
15%-M-Eug	52.4	11.28
5%-M-EugB	72.85	4.32
10%-M-EugB	72.85	8.56
15%-M-EugB	54.04	11.75
20%-M-EugB	N/A	17.58

The yield of the polymers remains around 73% until 15% eugenol is added to the polymers which causes a significant decrease in yield to around 53%. A reliable yield could not be measured for the 20% eugenol sample because this polymer was too amorphous to recrystallize and therefore could not be purified, as seen in Figure 18.

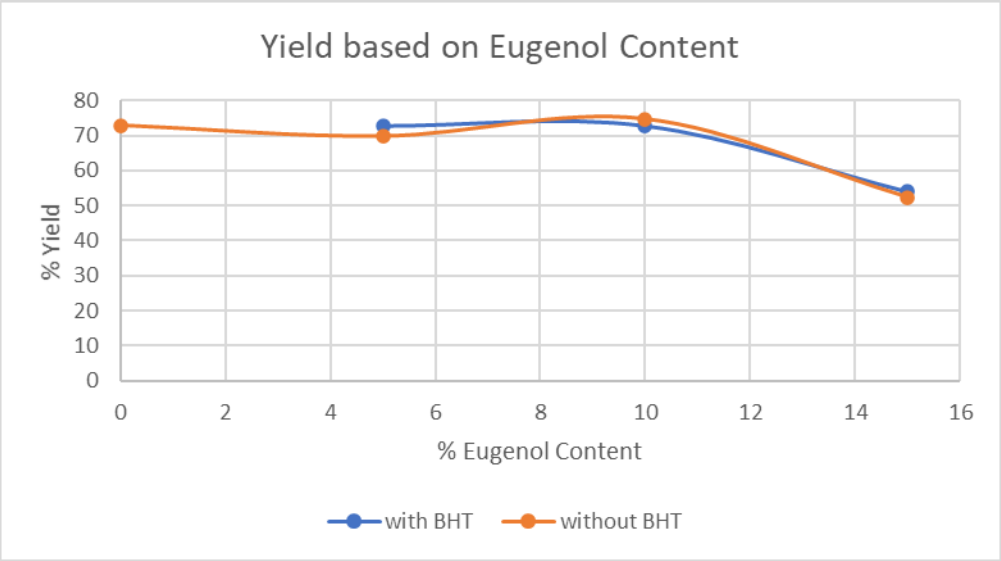
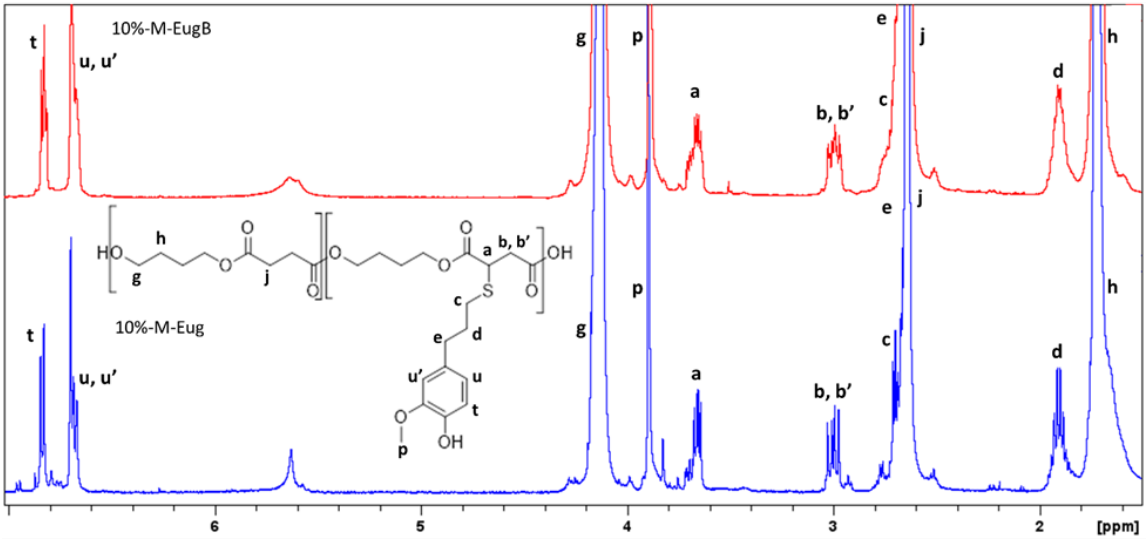


Figure 18. Percent yield compared to eugenol content

3.2.4 Effect of BHT

As seen in Figure 19, the addition of BHT made the ^{1}H NMR peaks less sharp and clear but did not make any noticeable differences in the ^{13}C NMR peaks or the structure of the resulting polymer.

(a)



(b)

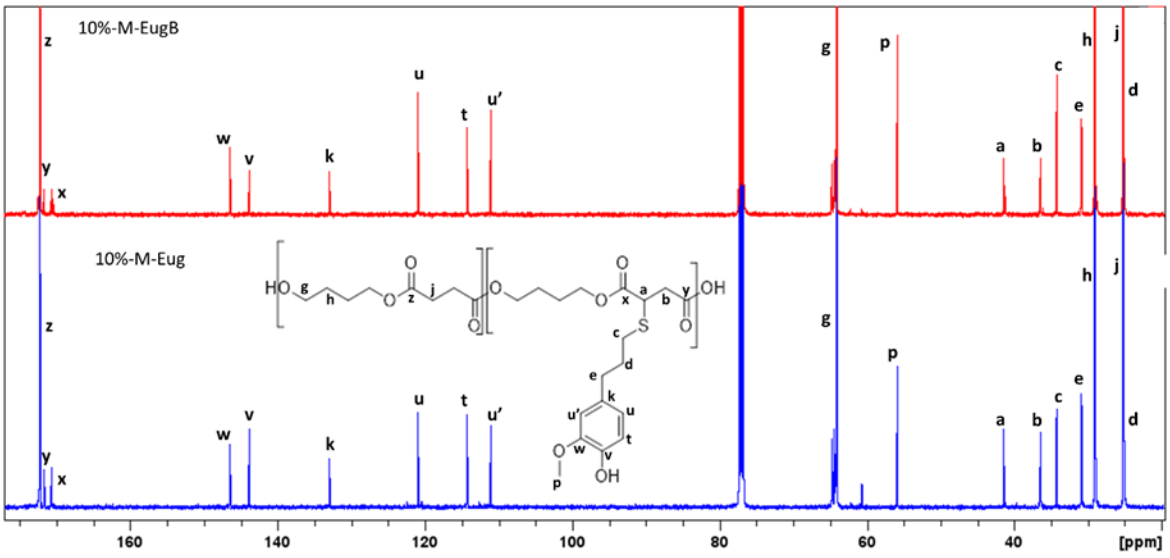
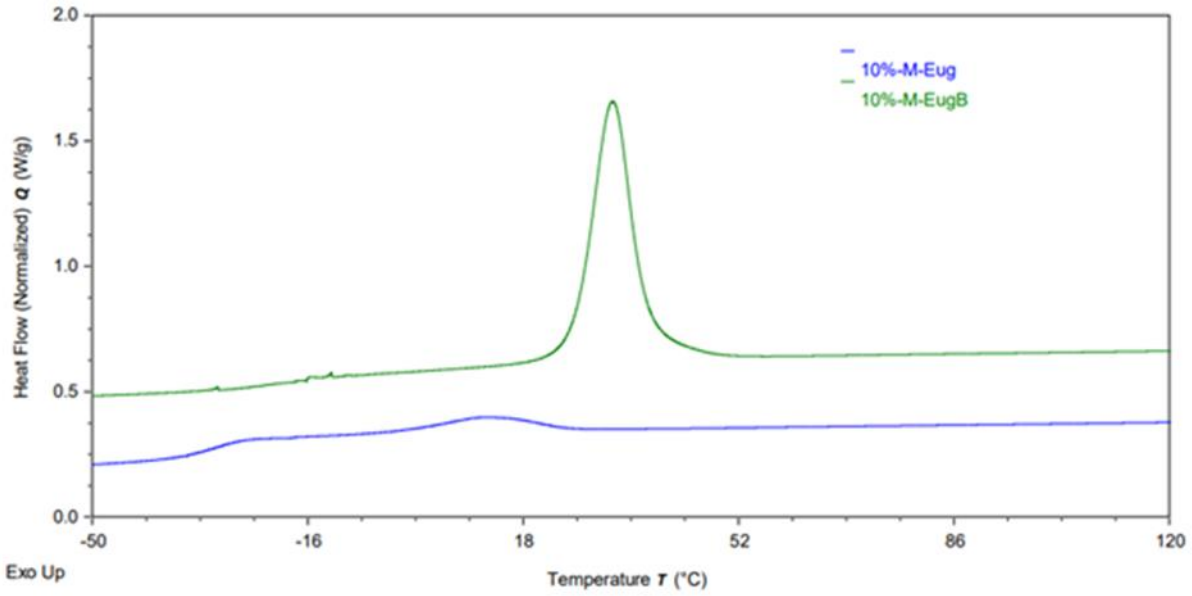


Figure 19. (a) ^{1}H NMR spectra and (b) ^{13}C NMR spectra of the polymers containing 10% eugenol

Adding BHT made the resulting polymer more brittle and created noticeable changes in the thermal properties of the material. The DSC curves seen in Figure 20 show that adding BHT increased the melting temperature of the polymer as well as its glass transition temperature.

(a)



(b)

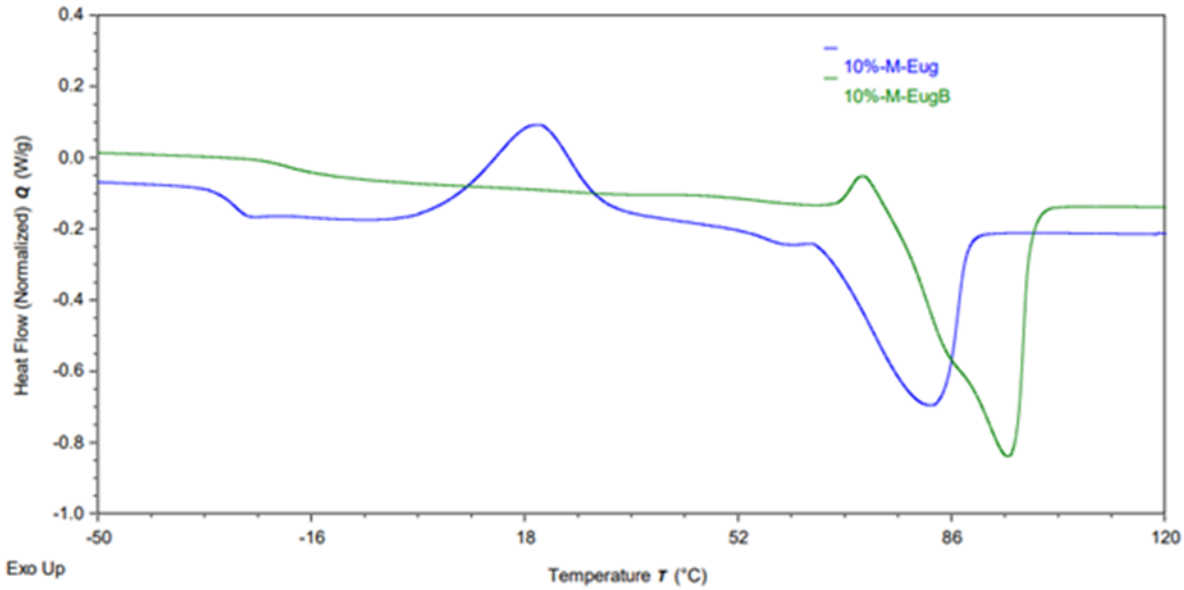


Figure 20. (a) Cooling and (b) melting curves from DSC for the 10% eugenol containing polymers with and without BHT

3.2.5. Eugenol Composition Determination

^{1}H NMR was used to determine the actual eugenol content of the polymers. As seen in Figure 21, by comparing the peak integration values and how many protons create each peak, we can determine what percent of the polymer is composed of eugenol compared to the other components.

$$n_{msa-eugenol} = \frac{(\frac{t}{1}+\frac{u}{2}+\frac{b,b'}{2}+\frac{p}{3}+\frac{d}{2})}{5} \qquad n_{1,4-butanediol} = \frac{(\frac{g}{4}+\frac{h}{4})}{2} \qquad n_{succinic\ acid} = n_{1,4-butanediol} - n_{msa-eugenol}$$

Here:

$$n_{msa-eugenol} = \frac{(\frac{0.014}{1}+\frac{0.021}{2}+\frac{0.013}{2}+\frac{0.037}{3}+\frac{0.026}{2})}{5} = 0.011 \qquad n_{1,4-butanediol} = \frac{(\frac{0.254}{4}+\frac{0.306}{4})}{2} = 0.07 \qquad n_{succinic\ acid} = 0.07 - 0.011 = 0.059$$

$$\%\ msa-eugenol = \frac{0.011}{(0.011+0.07+0.059)} \times 100 = 8.048\%$$

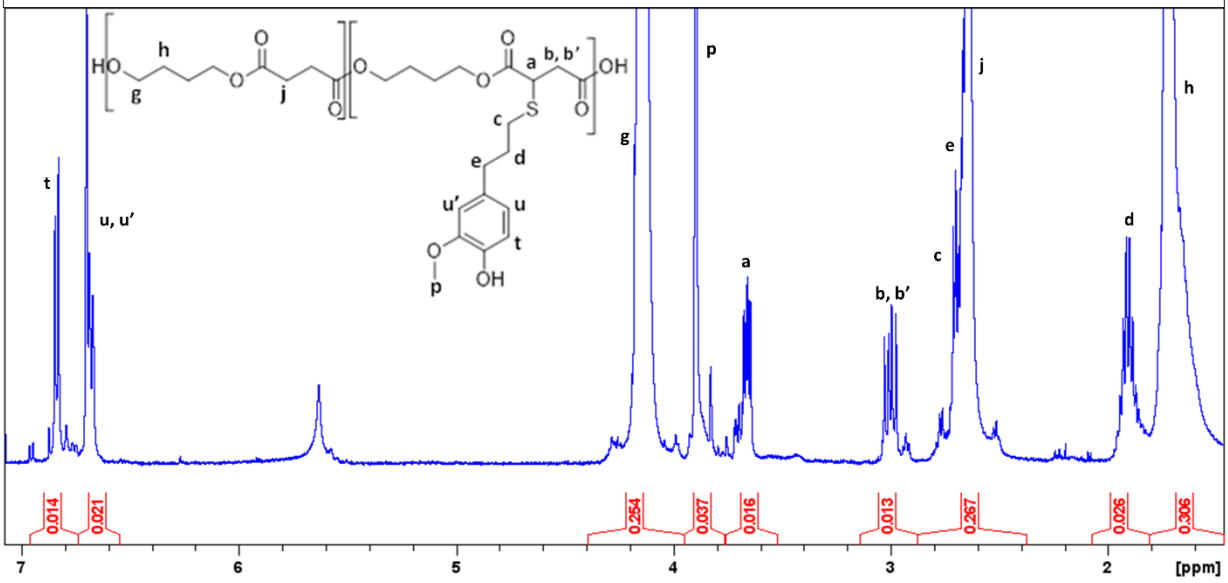


Figure 21. The process of eugenol composition determination through ^{1}H NMR

Comparing the added eugenol content and the measured eugenol content (Figure 22), we can see that these two factors are linearly related.

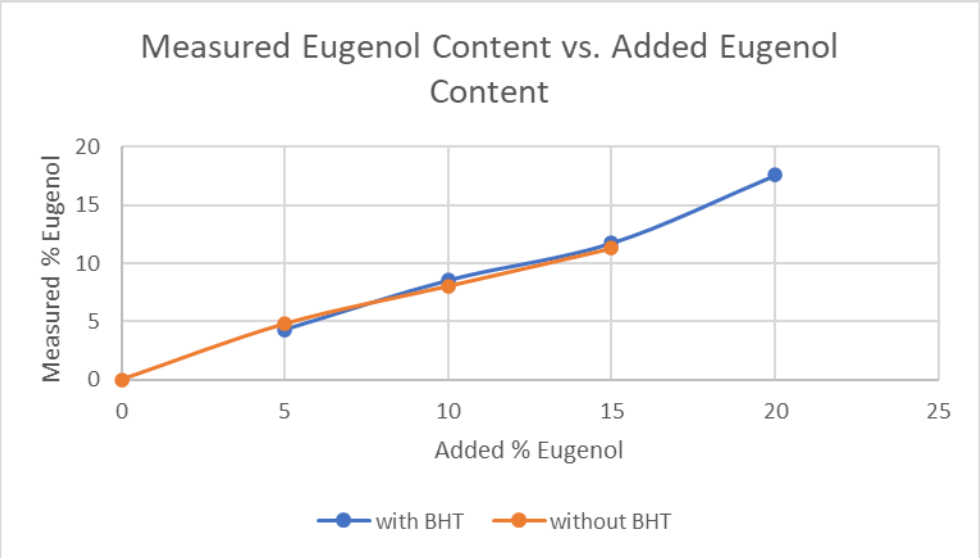


Figure 22. Comparison between the added and measured eugenol content

This means that the correlation between the two can be predicted and the target amount of eugenol in a polymer can be incorporated. Also, the amount of incorporated eugenol is only about 10% lower than the amount of eugenol offered in the feed, as seen in Table 3.

Table 3. Eugenol Content in the Polymerization Feeds and in the Obtained Polymers

Polymer	Eugenol Content in Feed (mol%)	Eugenol Content in Polymer (mol%)
PBS	0	0
0%-M-Eug	0	0
5%-M-Eug	5	4.81
10%-M-Eug	10	8.05
15%-M-Eug	15	11.28
5%-M-EugB	5	4.32
10%-M-EugB	10	8.56
15%-M-EugB	15	11.75
20%-M-EugB	20	17.58

3.2.6 Thermal Studies

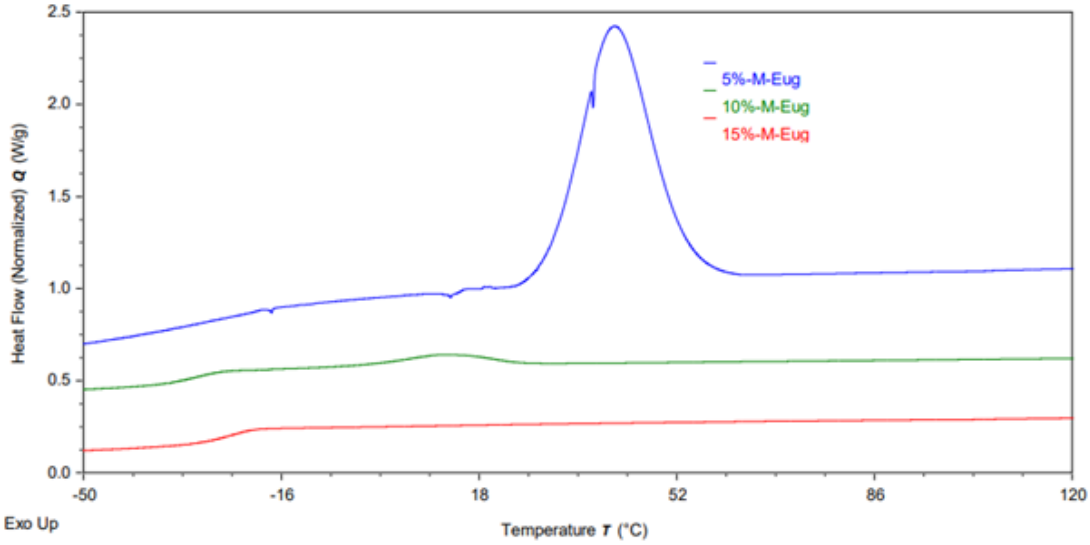
TGA and DSC were used to determine the thermal properties and transitions of the polymers. These transitions include melting points, glass transitions, and decomposition temperatures, as seen in Table 4.

Table 4. Thermal Properties

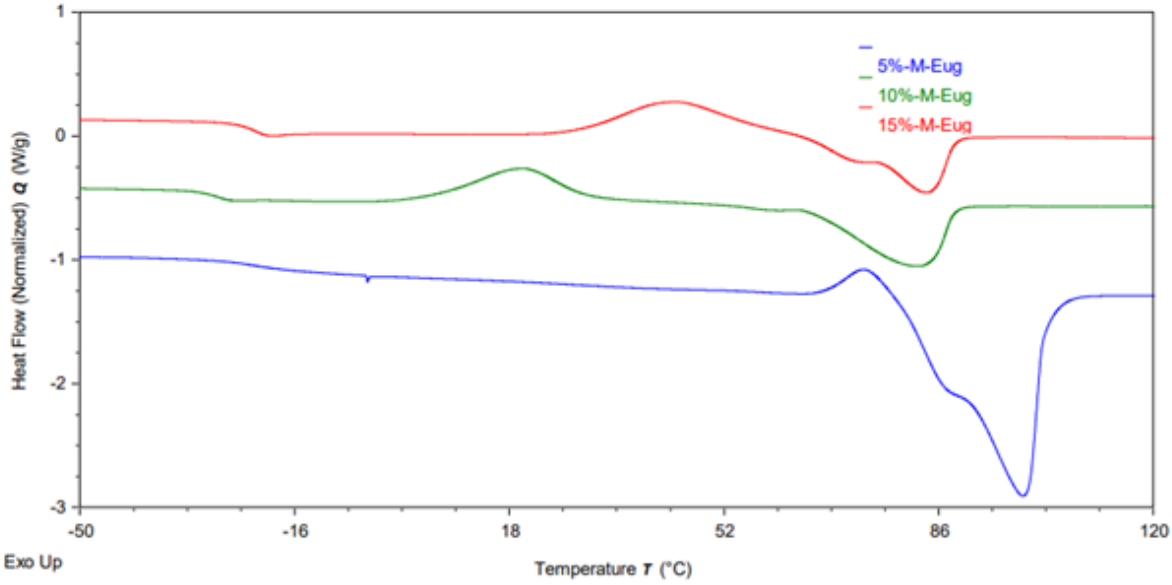
Polymer	Tg (°C)	Tm (°C)	Tdec (°C)
PBS	-38.34	114.01	N/A
0%-M-Eug	N/A	N/A	253.12
5%-M-Eug	-19.34	99.31	257.97
10%-M-Eug	-27.97	82.35	296.77
15%-M-Eug	-24.25	83.9	257.63
5%-M-EugB	N/A	96	316
10%-M-EugB	-18.8	94.97	335.25
15%-M-EugB	-24.9	75.6	329.79
20%-M-EugB	-32.82	N/A	281.78

In general, higher eugenol content lowers all of the thermal transitions, which was anticipated because more eugenol pendant groups made the polymer chains bulkier and more amorphous. As seen in Figure 23, the polymers with lower eugenol content have sharper melting peaks occurring at higher temperatures. Lower thermal transitions correlate with lower crystallinity which is also observed with higher eugenol content.

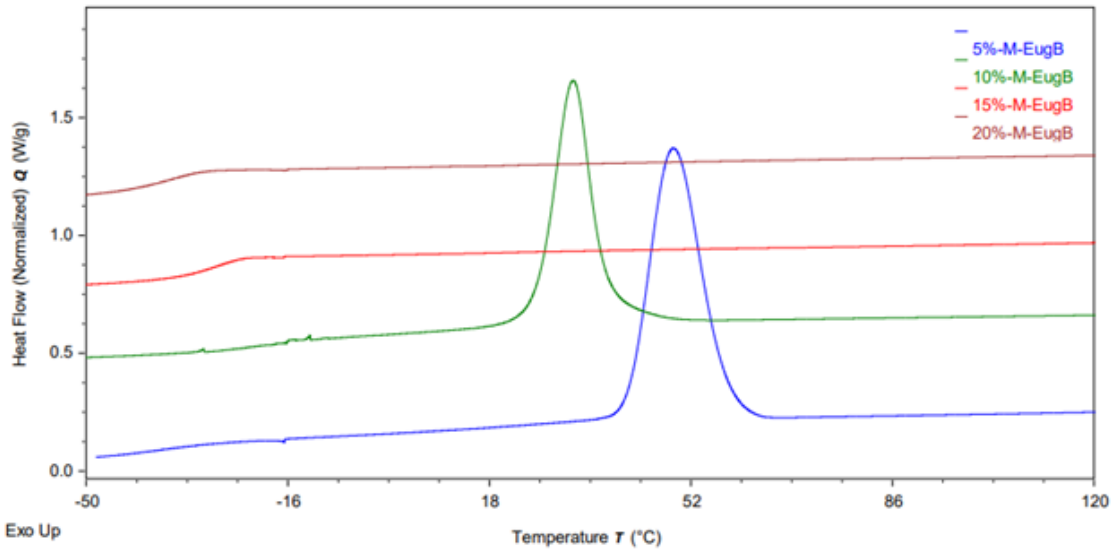
(a)


2.5
2.0
1.5
1.0
0.5
0.0
Heat Flow (Normalized) Q (W/g)
5%-M-Eug
10%-M-Eug
15%-M-Eug
-50
-16
18
52
86
120
Exo Up
Temperature T (°C)

(b)


1
0
-1
-2
-3
Heat Flow (Normalized) Q (W/g)
5%-M-Eug
10%-M-Eug
15%-M-Eug
-50
-16
18
52
86
120
Exo Up
Temperature T (°C)

(c)



(d)

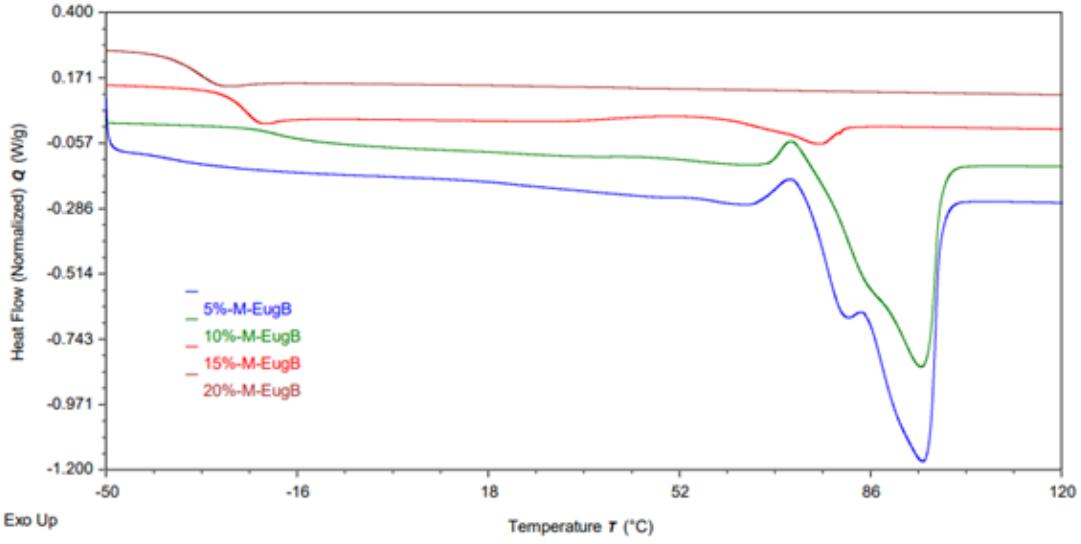
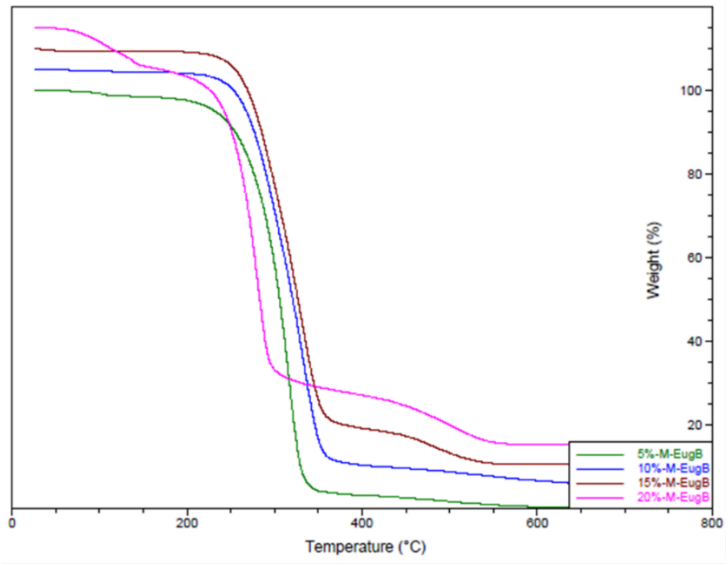


Figure 23. (a) Cooling and (b) melting curves for polymers without BHT and (C) cooling and (d) melting curves for polymers with BHT

Remarkably, the polymers containing up to 15 mol% eugenol have melting peaks and are semi-crystalline. This makes them useful for many target applications, for example packaging. As seen in Figure 24, all of the polymers have high decomposition temperatures, over 250°C.

(a)



(b)

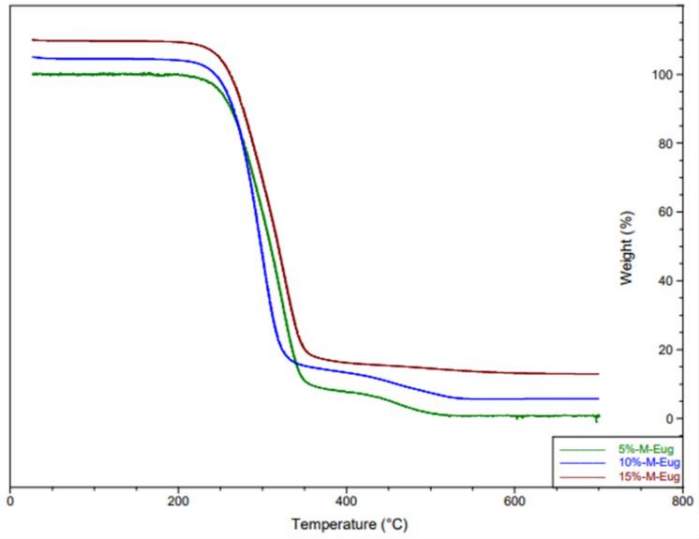


Figure 24. TGA curves for polymers (a) with BHT and (b) without BHT

3.2.7 Molecular Weight Studies

GPC was used to determine molecular weight properties including M_w, M_n, and PDI. All of these properties seem to be affected by eugenol content and by the addition of BHT. As seen in Table 5, the molecular weights of the polymers appear to be relatively low compared to most polyesters, even in the absence of eugenol. Low molecular weight could contribute to lower mechanical strength. Compared to Takasu et al., we applied slightly less catalyst and shorter polymerization times, which caused M_n to be about a third of what their group obtained.[14] The addition of BHT to the polymer caused a decrease in the molecular weight of the polymer but causes little change in the PDI of the polymers.

Table 5. Molecular Weight Properties

Polymer	Mw (g/mol)	Mn (g/mol)	PDI
PBS	3342	1057	3.16153
0%-M-Eug	5886	1356	4.34015
5%-M-Eug	6345	1767	3.59083
10%-M-Eug	11735	3593	3.26576
15%-M-Eug	5379	1938	2.7762
5%-M-EugB	5886	1356	4.34015
10%-M-EugB	5004	1325	3.77593
15%-M-EugB	4972	1401	3.54836
20%-M-EugB	6713	3221	2.08457

3.2.8 Antibacterial Properties

The antibacterial properties of the polymers generally follow the expected trends, where more eugenol correlates to a higher percent reduction, as seen in Table 6.

Table 6. Antibacterial Studies Using P. Aeruginosa

Polymer	Eugenol Content (mol%)	% Reduction
0%-M-Eug	0	89.46
5%-M-Eug	5	98.55
10%-M-Eug	10	96.66
15%-M-Eug	15	99.80
5%-M-EugB	5	99.89
10%-M-EugB	10	99.92
15%-M-EugB	15	93.89
20%-M-EugB	20	100.00

The different functional groups of eugenol contribute to its antibacterial function differently. While our 10 mol% eugenol containing polymer produced a 99.92% reduction in bacteria, the in-chain eugenol polymer, produced earlier by our group[12], which left no functional groups pendant, only produced a 22.09% reduction (Table 7). This confirms our theory that the phenol and methoxy function groups need to be accessible for eugenol to contribute antibacterial properties to a polymer. This corresponds well with previously found results from our group. [10]

Table 7. Antibacterial Studies Comparing Pendant versus In-Chain Eugenol

Polymer	Functional Group(s) Left Pendant	% Reduction
PBMS	Does not contain eugenol	89.46
In-Chain Eugenol	none	22.09
10%-M-EugB	phenol and methoxy	99.92

PBMS, which contains no eugenol, also showed high antibacterial action, though not as much as the eugenol bearing polymers. This is due to it containing free thiol groups which have been found to broaden a material's antibacterial activity against gram-negative activity.[23]

3.2.9 Initial Antiviral Tests

Preliminary antiviral tests, as shown in Table 8, suggest that the eugenol-containing polymers have a high level of antiviral activity. Both the polymers with 15 and 20 mol% eugenol reduced VSV by 100% compared to the PBS control.

Table 8. Antiviral Tests using VSV

Polymer	Eugenol Content	Titer	% Reduction
PBS	0	4.50E+04	0.00
0%-M-Eug	0	1.95E+04	56.67
15%-M-EugB	15	0	100.00
20%-M-EugB	20	0	100.00

4. Conclusions

4.1 The Ideal Synthesis Route

It was found that the best method for the preparation of a PBMS-based polymer containing eugenol was synthesis Route B. Attaching the eugenol to the mercaptosuccinic acid monomer prior to polymerization allowed for the most ideal sterics. Route A formed a main chain polymer that was too tough to allow for eugenol incorporation, while Route C formed a polymer with too much rotation around single bonds and resulted in a highly amorphous polymer.

It was also found that scandium triflate was the ideal catalyst for this polymerization because it helped to avoid unwanted crosslinking of the mercapto groups.

4.2 Overall Effects of Eugenol Content

Through this synthesis method, we were able to add a predictable eugenol concentration to the polymers. All of the obtained polymers were semi-crystalline. It was found that lower eugenol content led to polymers with better thermal properties and also to polymers that were more crystalline.

All of the target polymers reduced over 90% of bacteria compared to our PBS controls. The antibacterial studies did support our hypothesis that eugenol having pendant functional groups caused a higher antibacterial effect. The polymer that held eugenol entirely in the main chain only produced a 13.60% reduction of bacteria.

Our data did not suggest if there was a strong correlation between eugenol content and molecular weight properties. These measurements need to be confirmed further to see if eugenol content has an effect.

4.3 Effects of BHT

Adding BHT to the polymerization generally produced more crystalline, brittle polymers with higher degradation temperatures.

Adding BHT to the polymers seems to have no significant effect on antibacterial or antiviral properties.

4.4 Future Work

The molecular weight and antiviral properties of these polymers still need to be confirmed through further testing to see if any correlation exists with eugenol content.

In order to make this material even more sustainable the scandium catalyst should be recovered and reused. While these polymers have the potential to be biodegradable, the antibacterial effect of eugenol could interfere with this process. Degradation studies should be performed to confirm degradation is able to occur at a reasonable rate.

For these eugenol containing PBMS polymers to be useful for all of their potential applications, their mechanical properties such as strength and durability need to be tested and possibly improved.

The objective of this research was achieved in that we were able to synthesize semi-crystalline PBMS-based polymers containing various amounts of eugenol. These polymers are still able to have useful physical properties for many potential future uses. The ultimate goal is that industries such as food packaging or medical equipment will be able to switch to more sustainable synthetic polymers that also have more attractive functionalities than previously used materials.

5. References

[1] D. K. Schneiderman, M. A. Hillmyer, 50th Anniversary Perspective: There is a Great Future in Sustainable Polymers, *Macromolecules* 2017, **50**, 3733-3749

https://doi.org/10.1021/acs.macromol.7b00293

[2] Our Common Future, Report of the World Commission on Environment and Development, World Commission on Environment and Development, 1987. Published as Annex to General Assembly document A/42/427, Development and International Co-operation: Environment August 2, 1987

http://digitallibrary.un.org/record/139811/files/A_42_427-EN.pdf

[3] P. B. Smith, G. E. Payne, The Emergence of Renewable and Sustainable Polymers, *ACS Symposium Series* 2011, 1-10

https://doi.org/10.1021/bk-2011-1063.ch001

[4] S. Mahira, A. Jain, W. Khan, A. J. Domb, Antimicrobial Materials- An Overview, *Royal Society of Chemistry* 2019, **5**, 1-37

https://doi.org/10.1039/9781788012638-00001

[5] S. Duan, R. Wu, Y. Xiong, H. Ren, C. Lei, Y. Zhao, X. Zhang, F. Xu, Multifunctional Antimicrobial Materials: From Rational Design to Biomedical Applications, *Progress in Materials Science,* 2022, **125**, 100887

http://doi.org/10.1016/j.pmatsci.2021.100887

[6] L. Rojo, J. M. Barcenilla, B. Vazquez, R. Gonzalez, J. S. Roman, Intrinsically Antibacterial Materials Based on Polymeric Derivatives of Eugenol for Biomedical Applications, *Biomacromolecules* 2008, **9,** 2530-2535

https://doi.org/10.1021/bm800570u

[7] B. Balasubramaniam, Prateek, S. Ranjan, M. Saraf, P. Kar, S. P. Singh, V. K. Thakur, A. Singh, R. P. Gupta, Antibacterial and Antiviral Functional Materials: Chemistry and Biological Activity toward Tackling COVID-19-like Pandemics, *ACS Pharmacol. Trasl. Sci.* 2021, **4,** 8-54 https://doi.org/10.1021/acsptsci.0c00174

[8] S. Ding, J. Wang, S. Dong, A. Ashour, Y. Liu, L. Qui, B. Han, Developing Multifunctional/ Smart Civil Engineering Materials to Fight Viruses, *ACS Sustainable Chem. Eng.,* 2022, **10**, 678-690 https://doi.org/10.1021/acssuschemeng.1c07642

[9] M. Ulanowska, B. Olas, Biological Properties and Prospects for the Application of Eugenol- A Review, *Int. J. Mol. Sci.,* 2021, **22**, 3671

https://doi.org/10.3390/ijms22073671

[10] L.R. Parisi, D.M. Scheibel, S. Lin, E.M. Bennett, J.M. Lodge, M.J. Miri, Eugenol as renewable comonomer compared to 4-penten-1-ol in ethylene copolymerization using a palladium aryl sulfonate catalyst, *Polymer* 2017, **114**, 319-328 https://doi.org/10.1016/j.polymer.2017.03.009

[11] S. Gazzottia, S. A. Todiscoa, C. Picozzic, M. A. Ortenzia, H. Farinaa, G. Lesmaa, A. Silvania, Eugenol-grafted aliphatic polyesters: Towards inherently antimicrobial PLA based materials exploiting OCAs chemistry, *European Polymer Journal* 2019, **114**, 369-379 https://doi.org/10.1016/j.eurpolymj.2019.03.001

[12] Reilly, Liam T.; Miri, Massoud J., ACS National Meeting & Exposition, San Diego, CA, United States, August 25-29, 2019, POLY-0245

[13] J. Dai, Y. Jiang, X. Liu, J. Wang, J. Zhu, Synthesis of eugenol-based multifunctional monomers via a thiol–ene reaction and preparation of UV curable resins together with soybean oil derivatives, *RSC Adv.,* 2016, **6**, 17857-17866

https://doi.org/10.1039/C6RA01420H

[14] A. Corma, H. Garcia, Lewis Acids: From Conventional Homogeneous to Green Homogeneous and Heterogeneous Catalysis, *Chem. Rev.* 2003, **103**, 4307-4365

https://doi.org/10.1021/cr030680z

[15] S. Kobayashi, M. Sugiura, H. Kitagawa, W. Lam, Rare-Earth Metal Triflates in Organic Synthesis, *Chem. Rev.* 2002, **102**, 2227-2302

https://doi.org/10.1021/cr010289i

[16] A. Takasu, Y. Oishi, Y. Iio, Y. Inai, T. Hirabayashi, Room-Temperature Polycondensation of Dicarboxylic Acids and Diols Catalyzed by Water-Stable Lewis Acids, *Macromolecules* 2003, **36**, 1772

https://doi.org/10.1295/polymj.37.946

[17] K. Yamamoto, A. Takasu, Polyester Synthesis at Moderate Temperatures via the Direct Polycondensation of Dicarboxylic Acids and Diols Catalyzed by Rare-Earth Perfluoroalkanesulfonates and Bis(perfluoroalkanesulfonyl)imides, *Macromolecules* 2010, 43, 8519

https://doi.org/10.1021/ma901945u

[18] K. Fukaya, A. Takasu, Grafting of Poly(2-Oxazoline) Side Chains from Polyester Containing Oxazoline Units and Their Blends with Water Soluble Vinyl Polymers, *Macromol. Chem. Phys.* 2021, **222**, 2000344

https://doi.org/10.1002/macp.202000344

[19] Q. Lian, Y. Li, K. Li, J. Cheng, J. Zhang, Insights into the Vulcanization Mechanism through a Simple and Facile Approach to the Sulfur Cleavage Behavior, *Macromolecules* 2017, **50**, 803-810 https://doi.org/10.1021/acs.macromol.6b02335

[20] ASTM Standard E3180, 2012, Standard Test Method for Determining the Activity of Incorporated Antimicrobial Agent(s) in Polymeric or Hydrophobic Materials, ASTM International, West Conshohocken, PA, 2001 http://doi.org/10.1520/E2180-07R12

[21] D.P. Nair, M. Podgórski, S. Chatani, T. Gong, W. Xi, C. R. Fenoli, C. N. Bowman, The Thiol-Michael Addition Click Reaction: A Powerful and Widely Used Tool in Materials Chemistry, *Chem. Mater.* 2014, **26**, 724-744 https://doi.org/10.1021/cm402180t

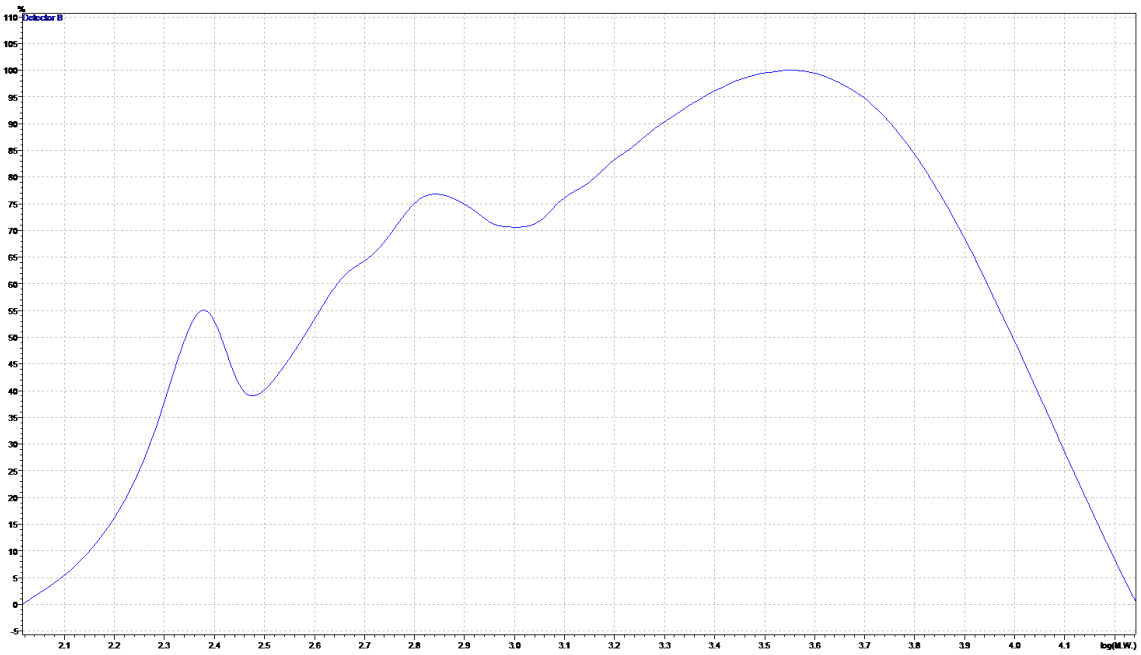
[22] M. S. Mahajan, P. P. Mahulikar, V. V. Gite, Eugenol based renewable polyols for development of 2K anticorrosive polyurethane coatings, *Progress in Organic Coatings,* 2020, **148**, 105826 https://doi.org/10.1016/j.porgcoat.2020.105826

[23] N. Wiradharma, M. Khan, L.K. Yong, C. A. E. Hauser, S. V. Seow, S. Zhang, Y. Yang, The Effect of Thiol Functional Group Incorporation into Cationic Helical Peptides on Antimicrobial Activities and Spectra, *Biomaterials,* 2011, **32**, 9100-9108 https://doi.org/10.1016/j.biomaterials.2011.08.020

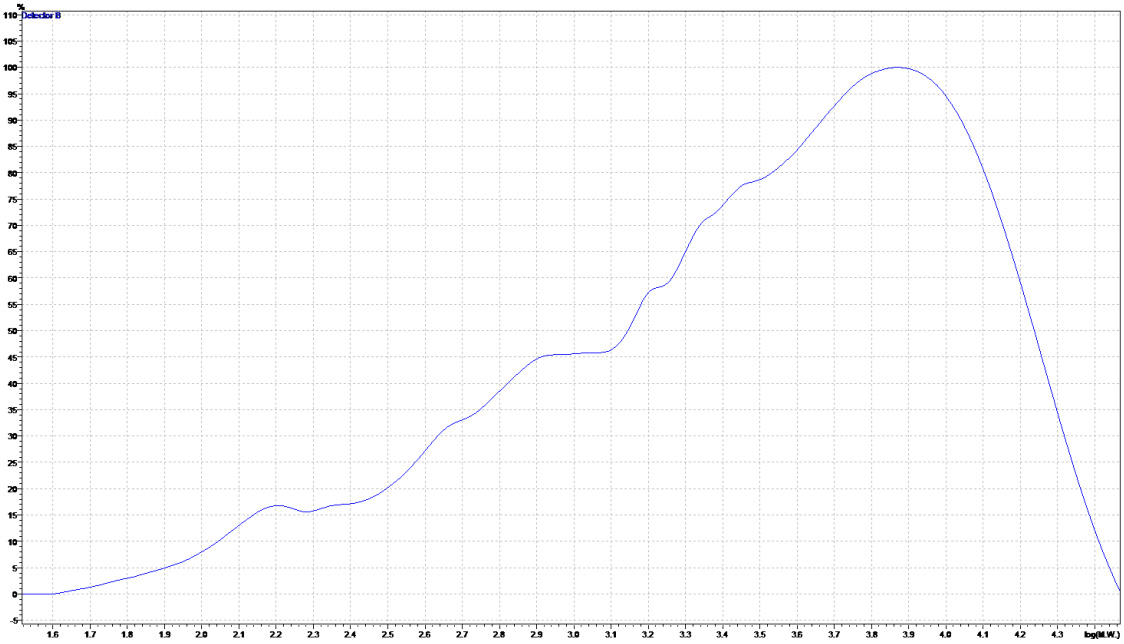
6. Appendix

6.1 GPC Curves

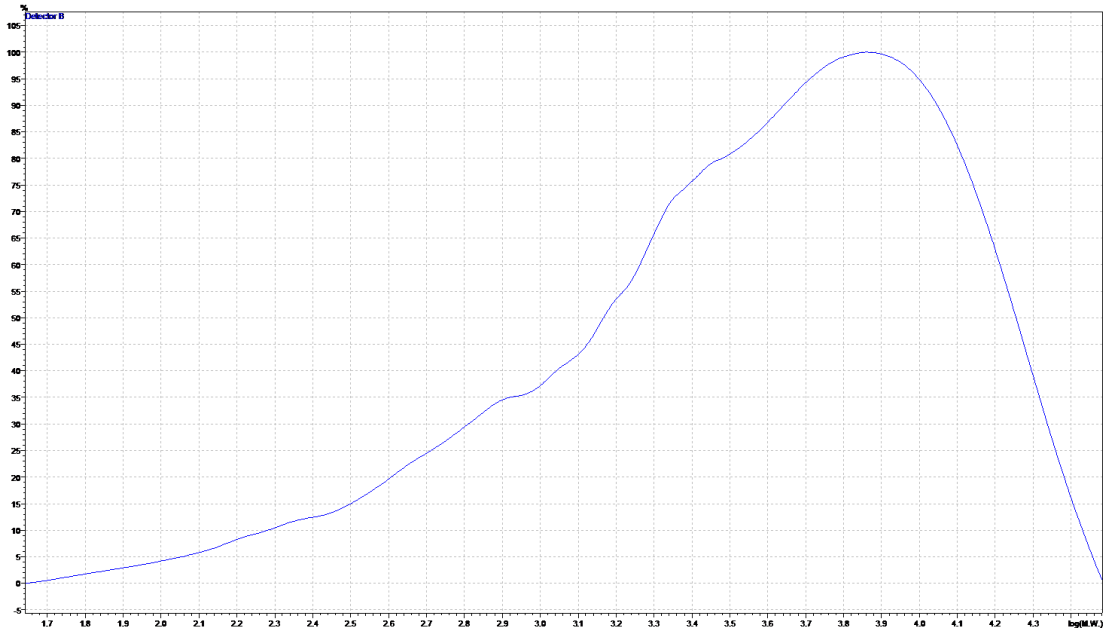
A- 1 GPC of PBS



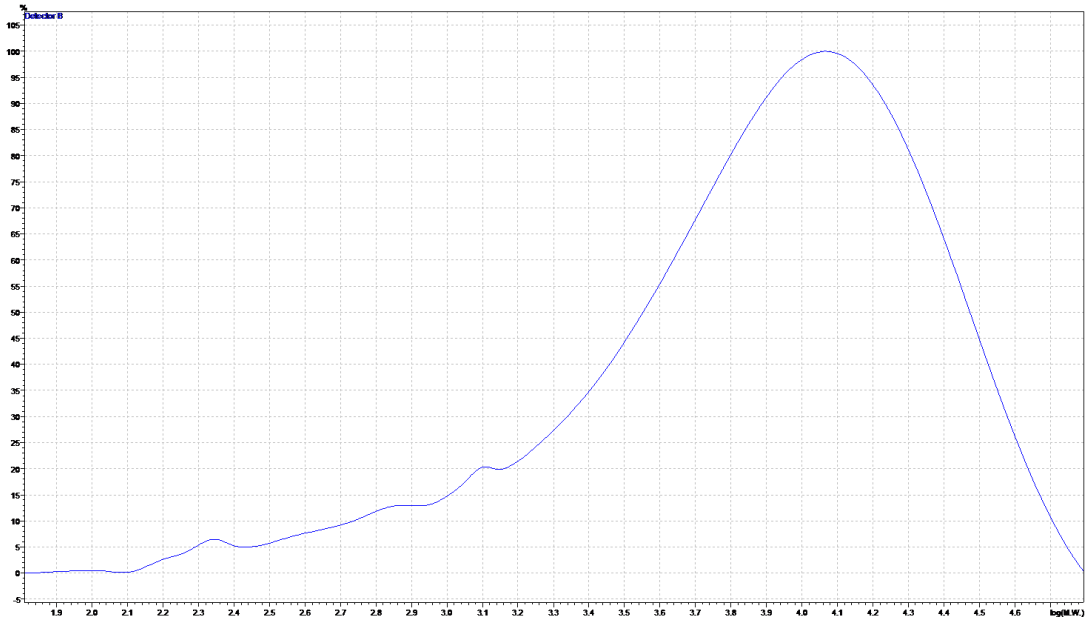
A- 2 GPC of PBMS



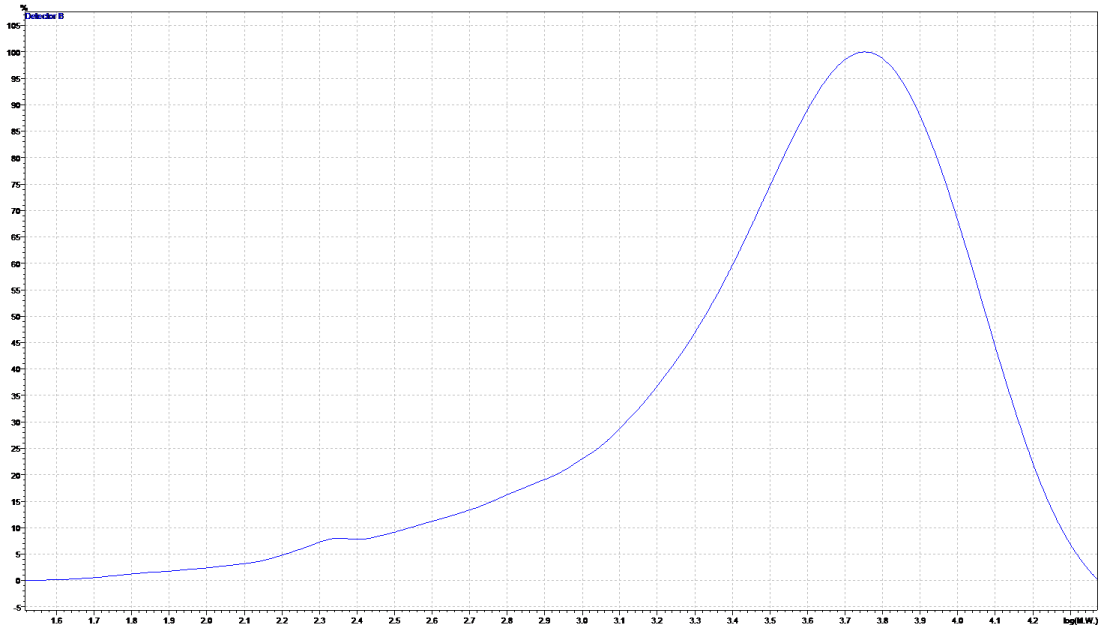
A- 3 GPC of 5%-M-Eug



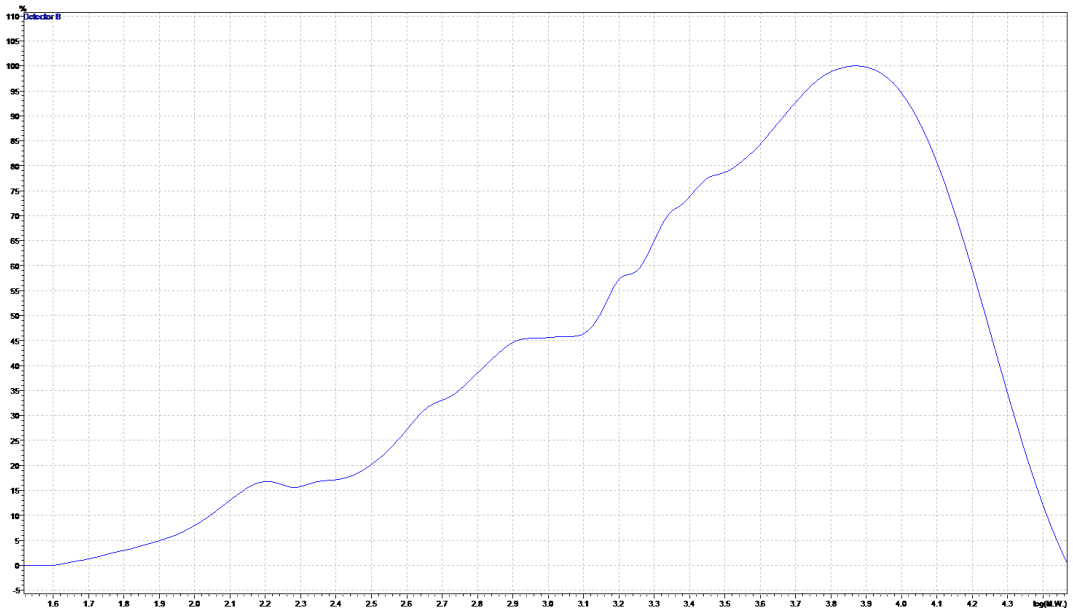
A- 4 GPC of 10%-M-Eug



A- 5 GPC of 15%-M-Eug



A- 6 GPC of 5%-M-EugB



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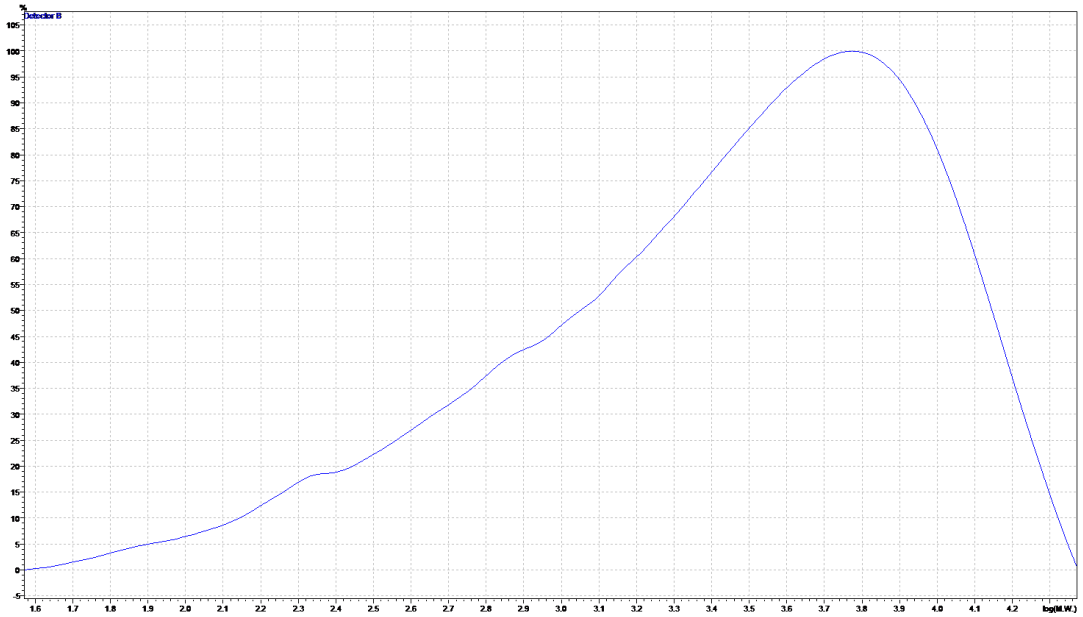
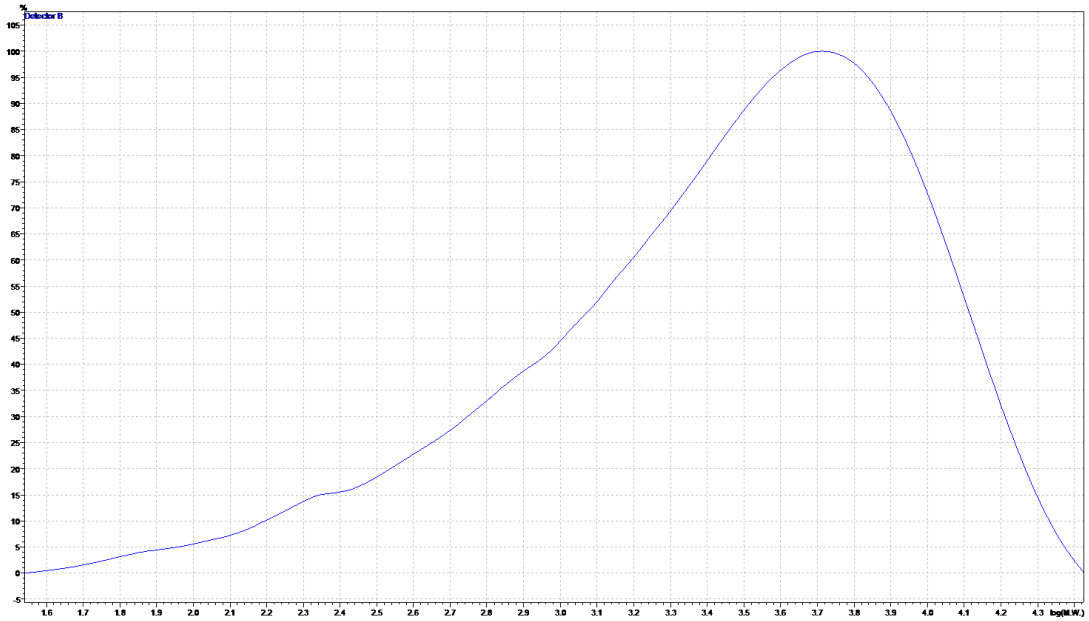
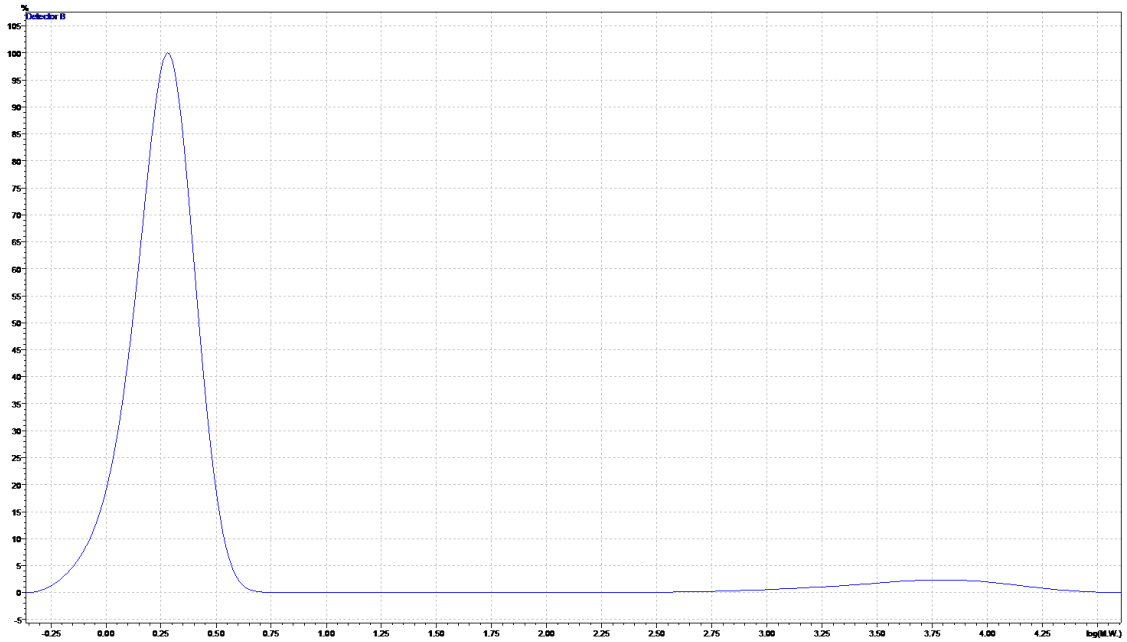


A-8 GPC of 15%-M-EugB

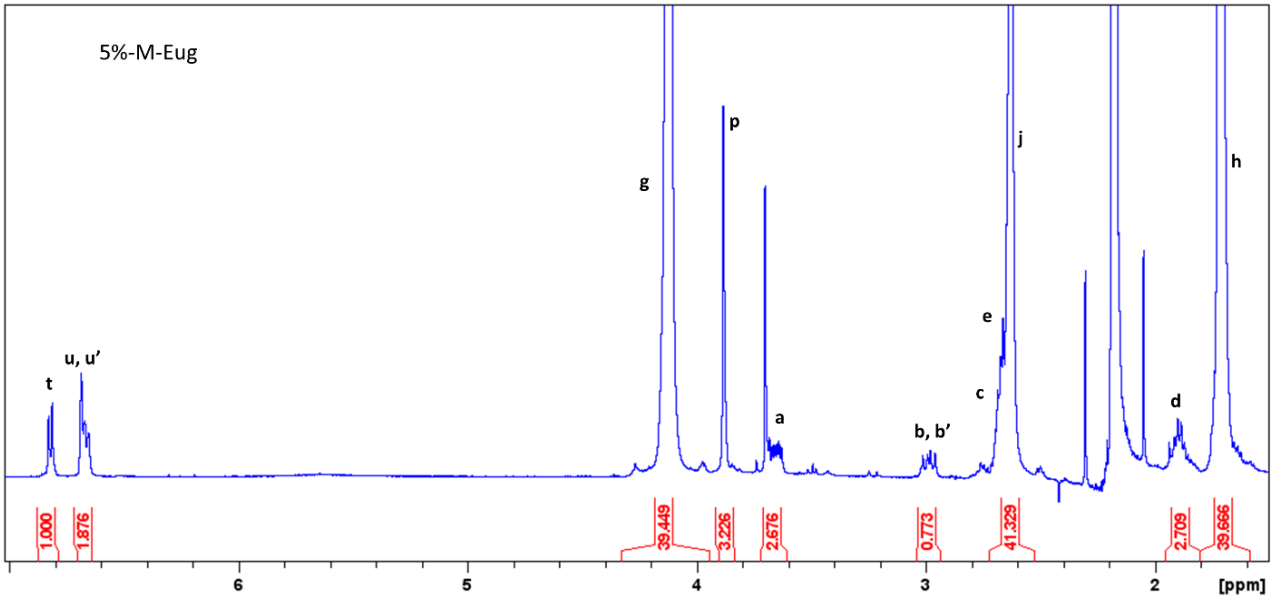


A- 9 GPC of 20%-M-EugB

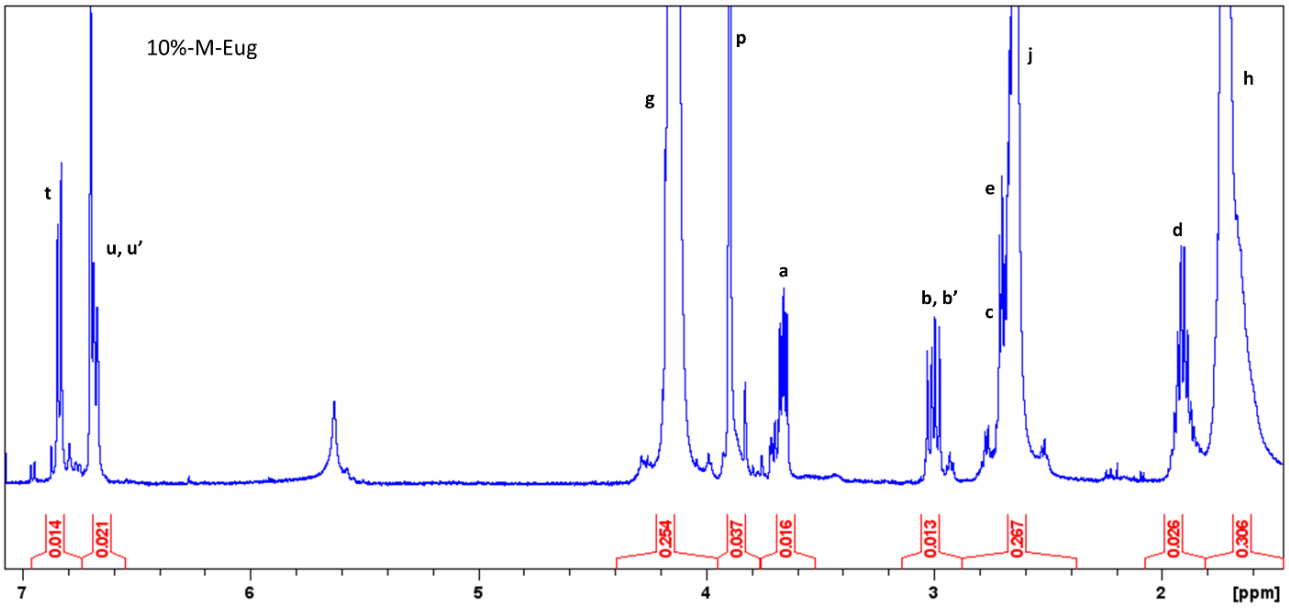


6.2 Eugenol Composition Determination

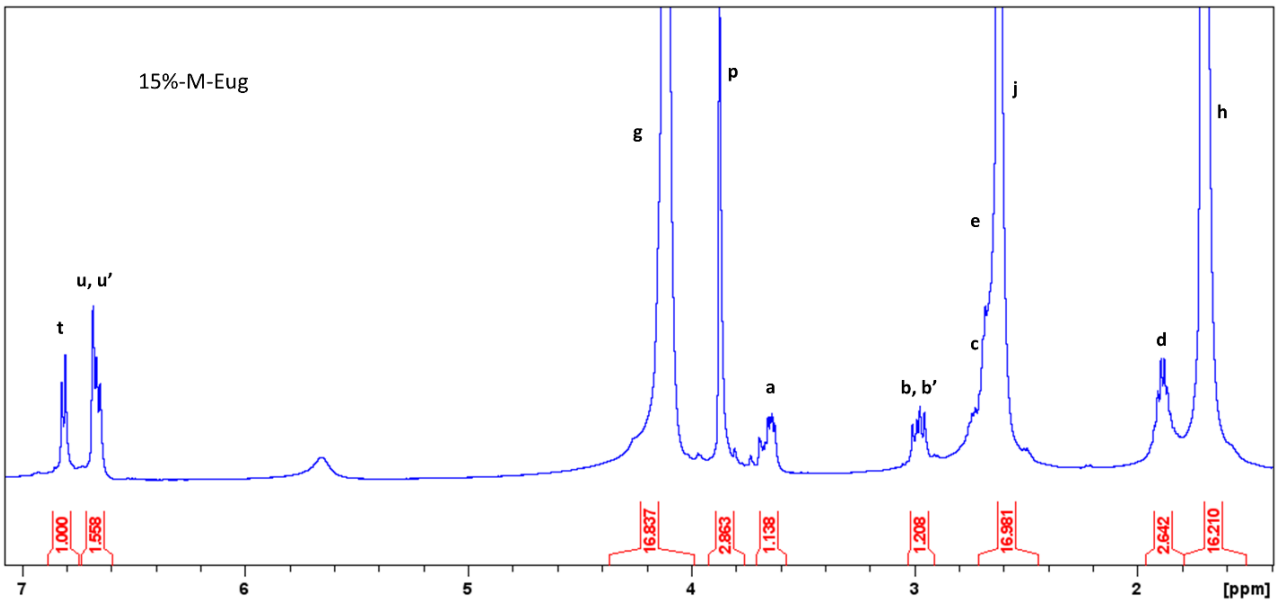
A- 10 ^{1}H NMR of 5%-M-Eug



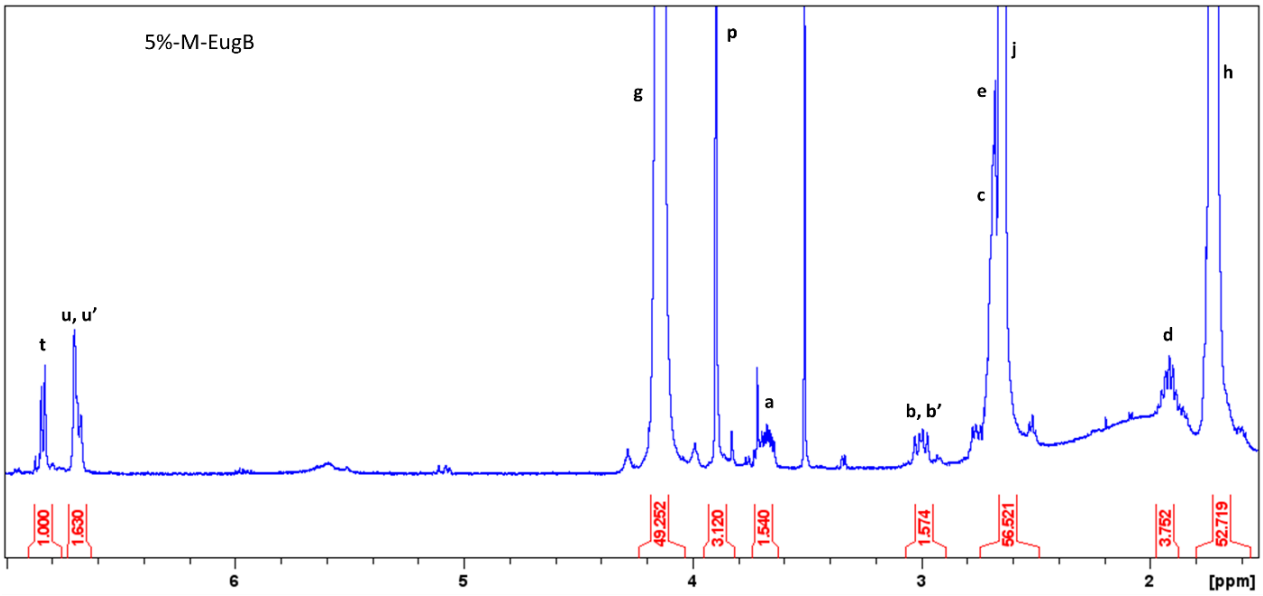
A- 11 ^{1}H NMR of 10%-M-Eug



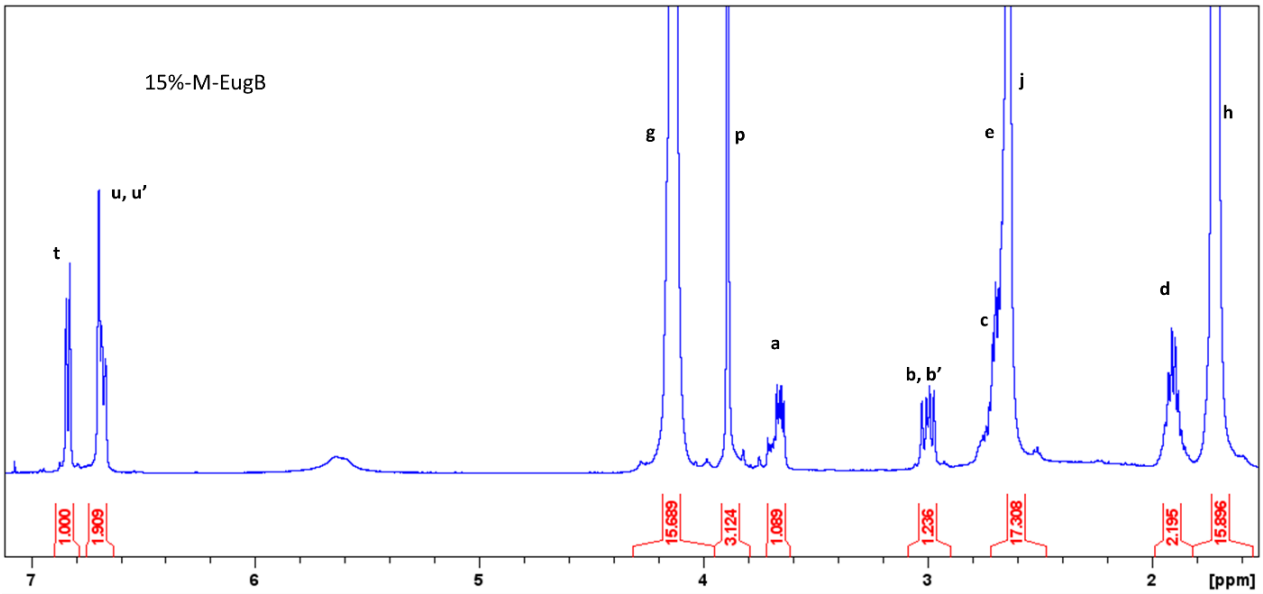
A- 12 ^{1}H NMR of 15%-M-Eug



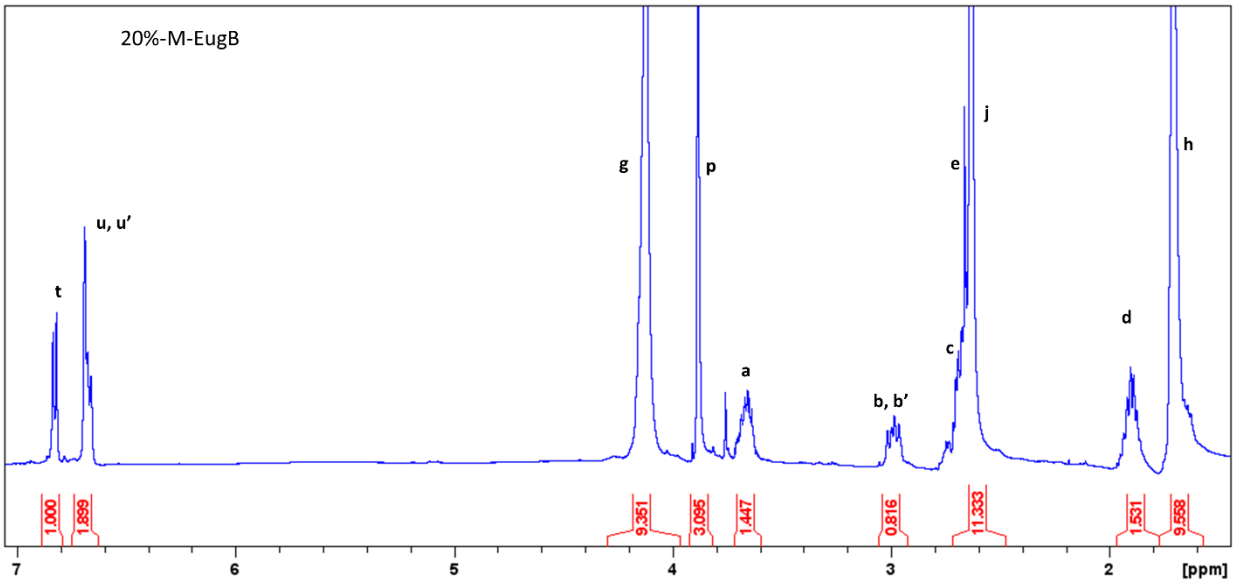
A- 13 ^{1}H NMR of 5%-M-EugB



A- 14 ^{1}H NMR of 15%-M-EugB

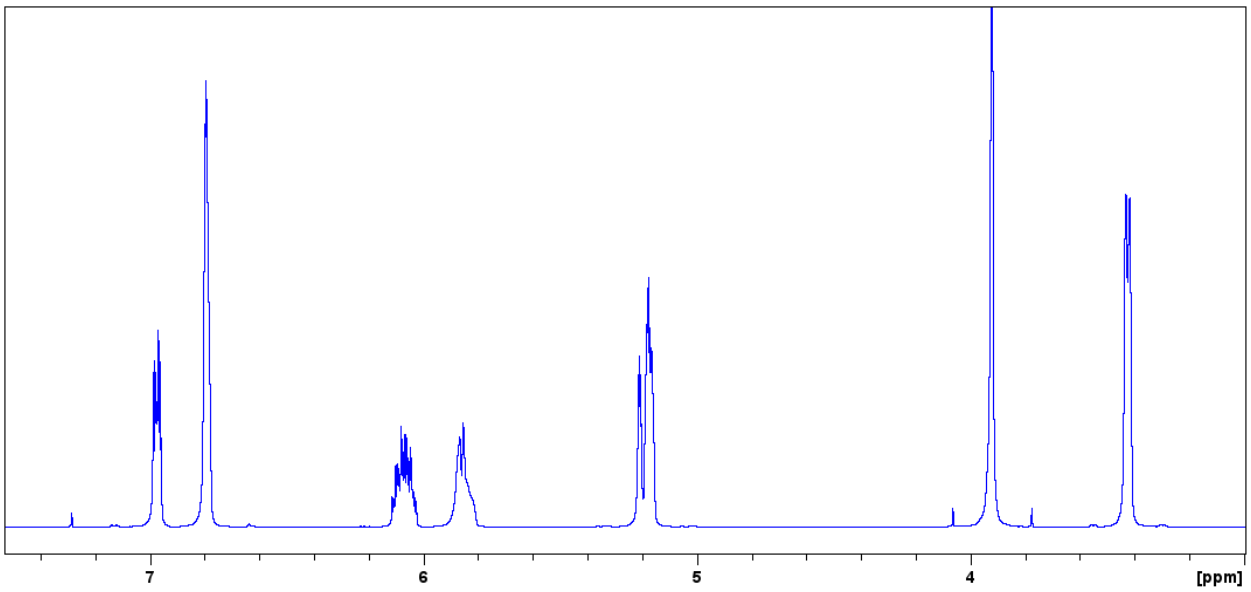


A- 15 ^{1}H NMR of 20%-M-EugB

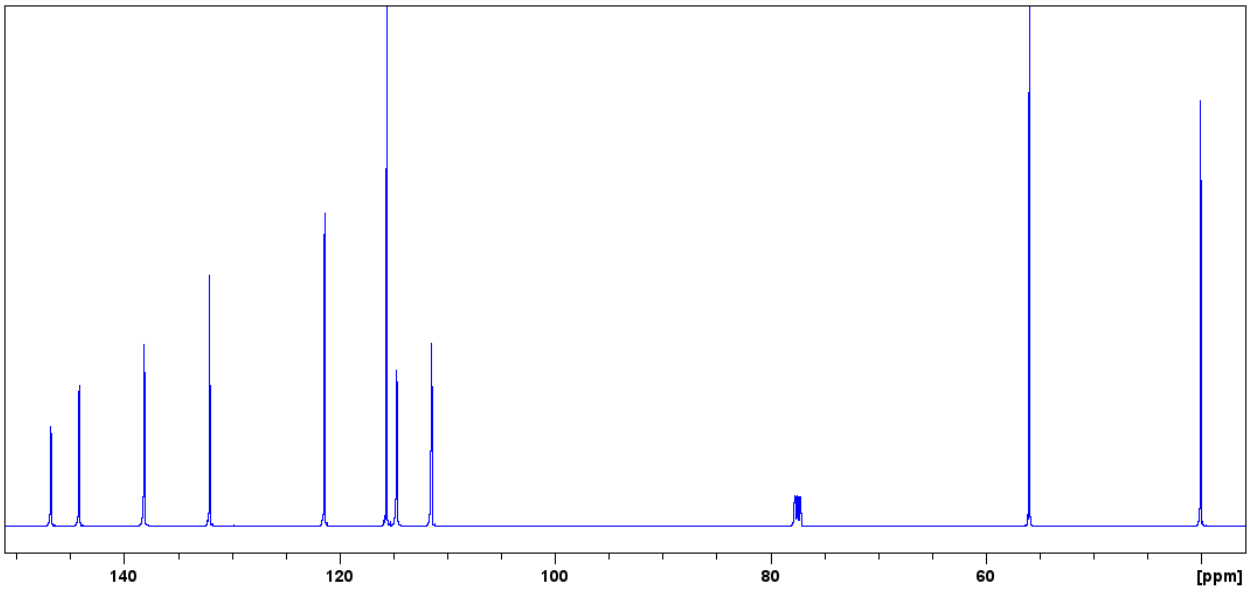


6.3 Starting Materials

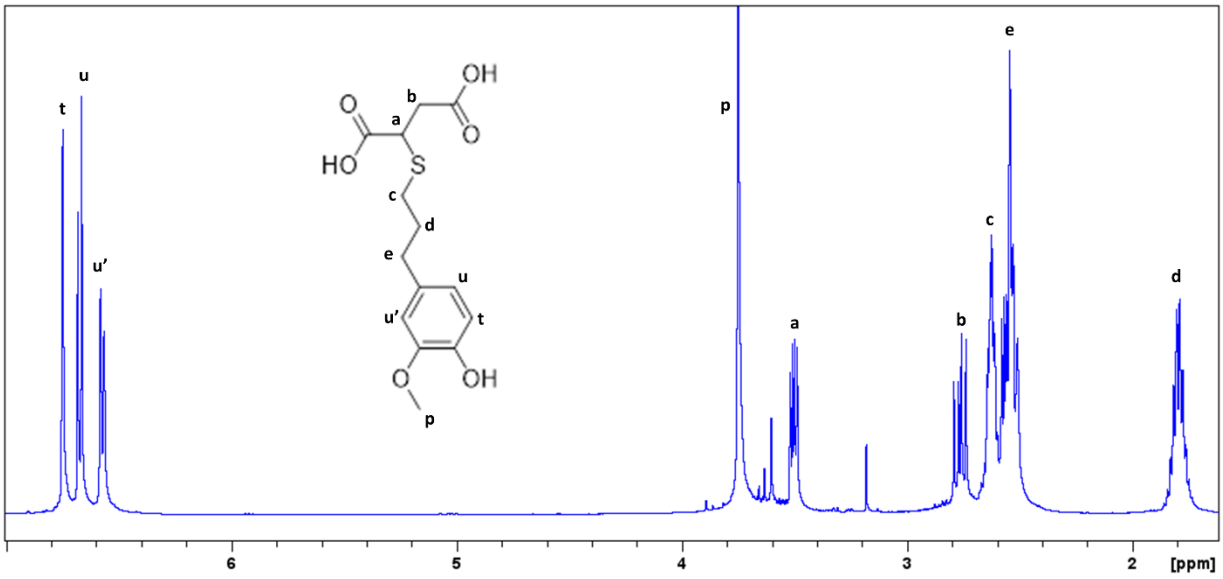
A- 16 ^{1}H NMR of Eugenol



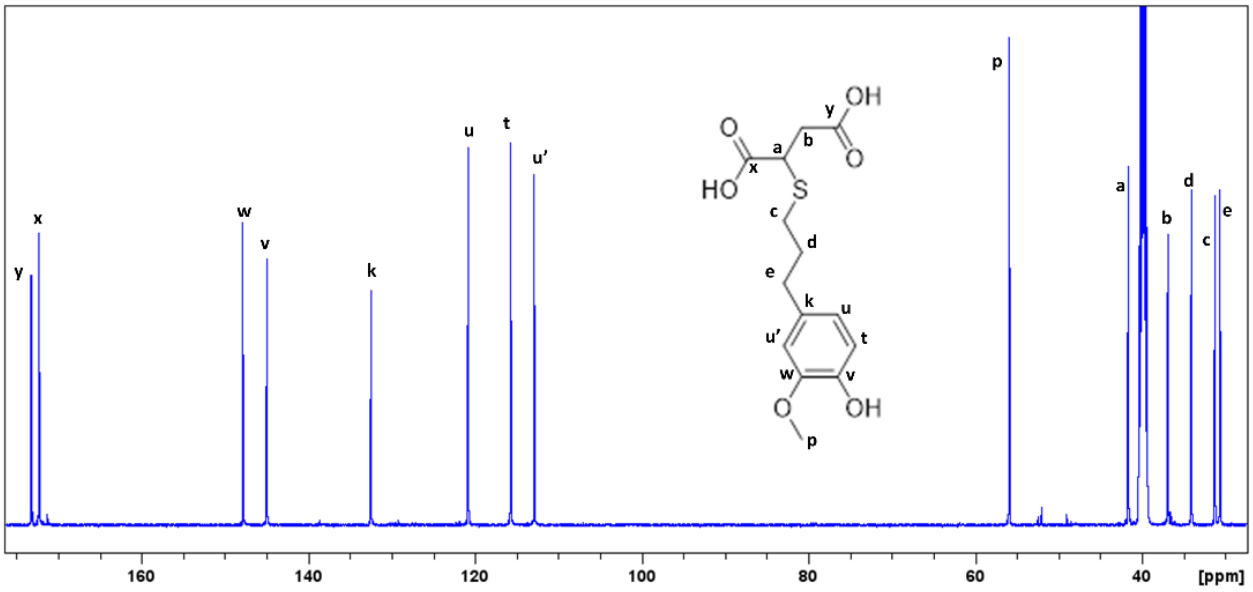
A- 17 ^{13}C NMR of Eugenol



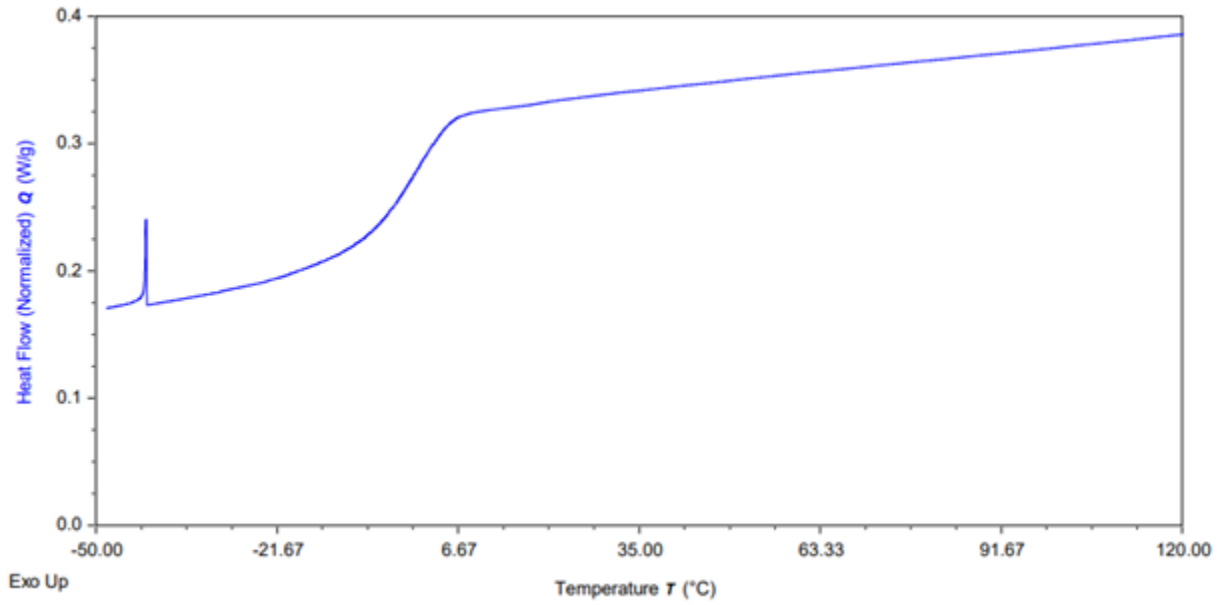
A- 18 ^{1}H NMR of Mercaptosuccinic Acid-Eugenol Monomer



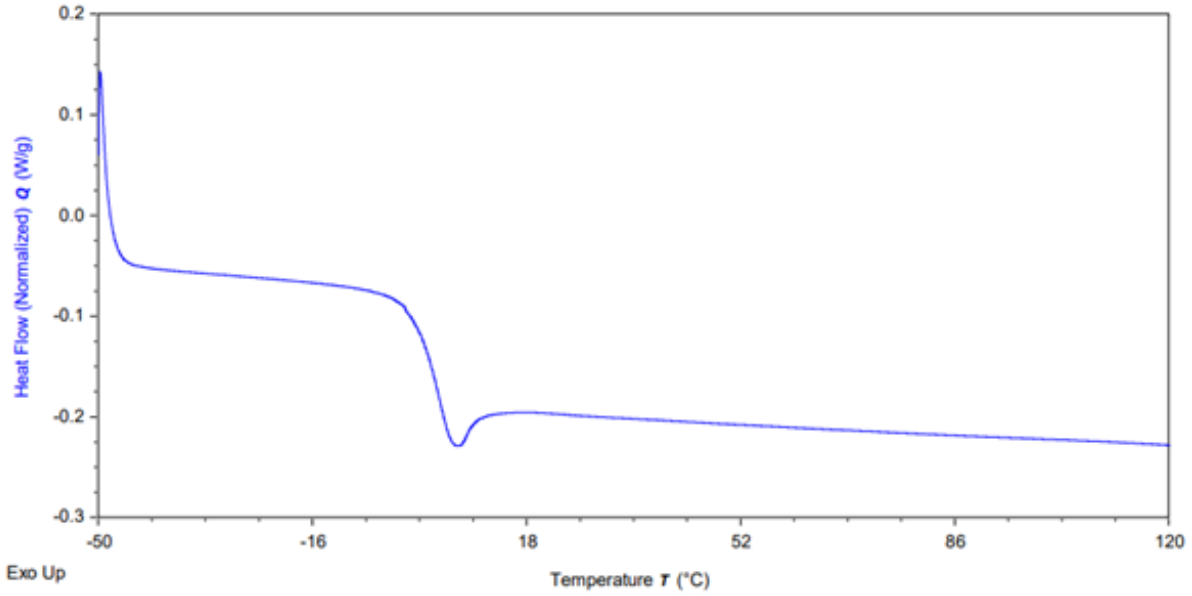
A- 19 ^{13}C NMR of Mercaptosuccinic Acid- Eugenol Monomer



A- 20 Mercaptosuccinic Acid- Eugenol Monomer Cooling Curve

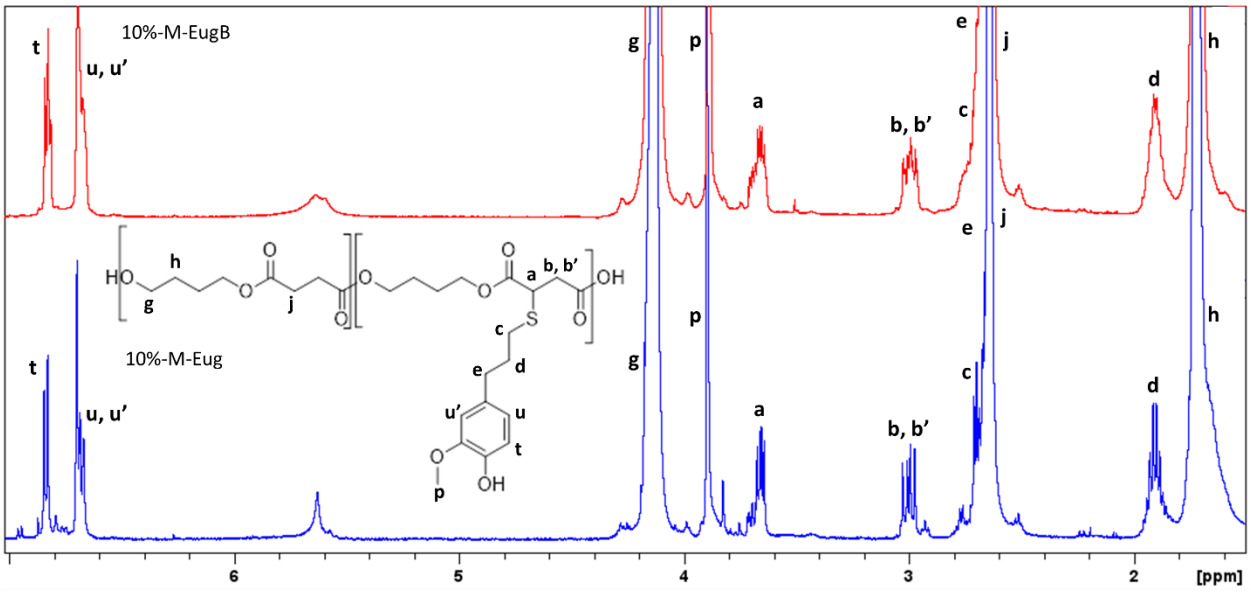


A- 21 Mercaptosuccinic Acid - Eugenol Monomer Melting Curve

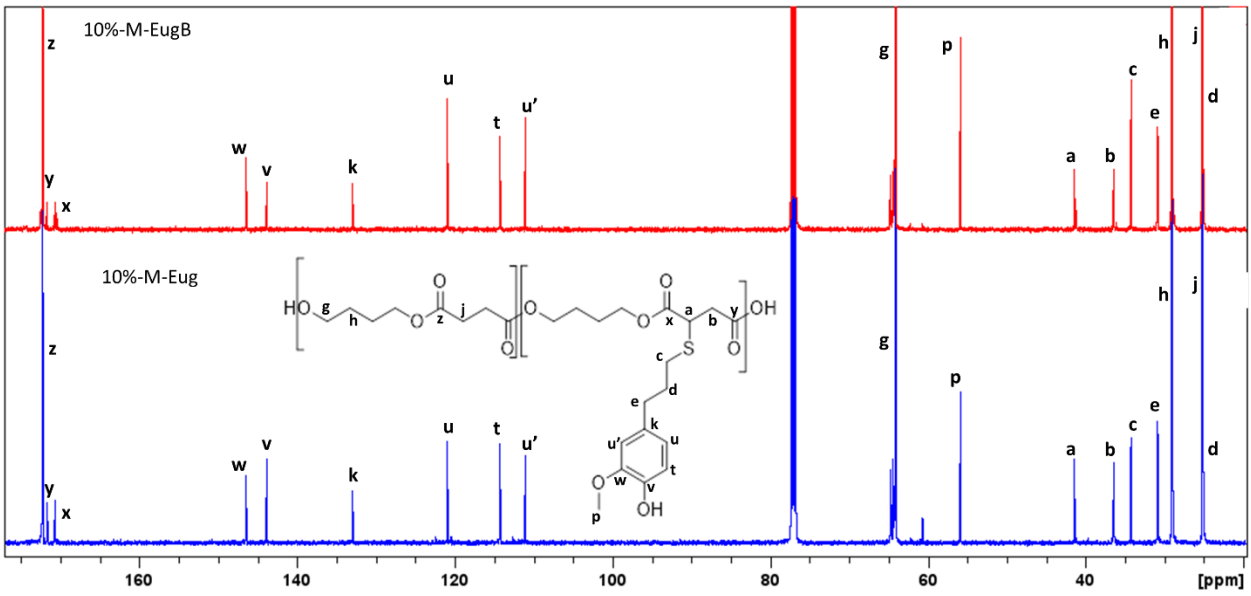


6.4 Polymers Containing BHT vs. Not Containing BHT Curves

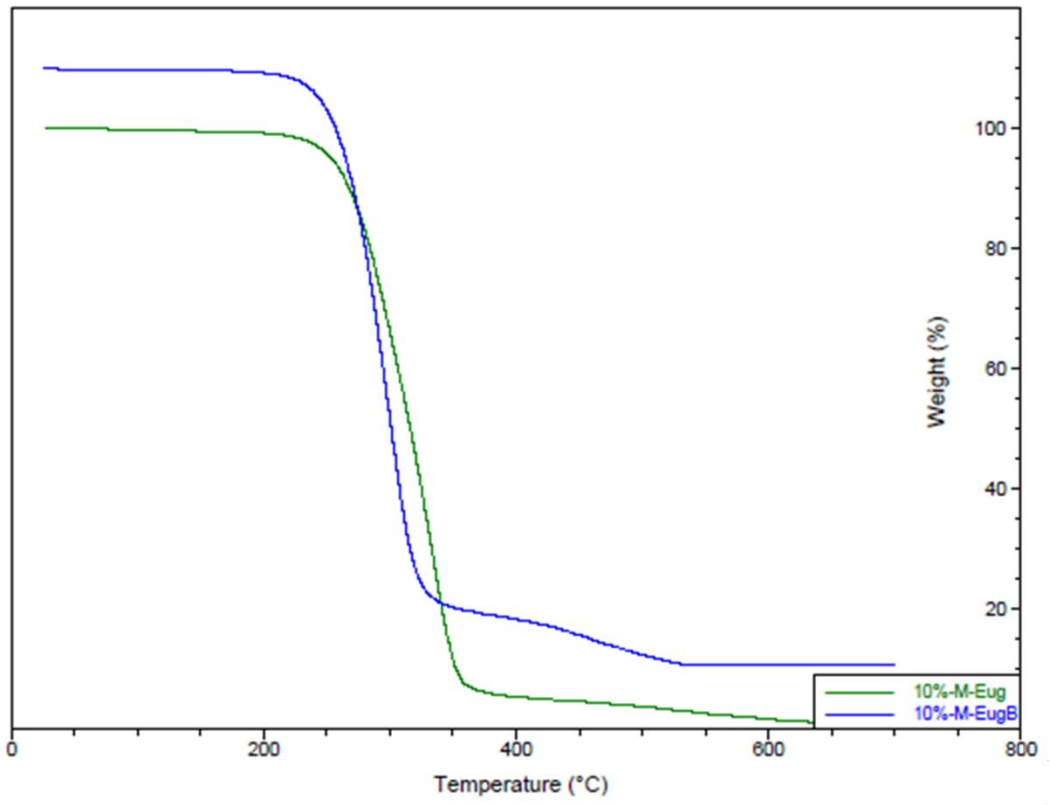
A- 22 ^{1}H NMR comparing the 10% polymers with BHT and without BHT



A- 23 ^{13}C NMR comparing the 10% polymers with BHT and without BHT



A- 24 TGA curves comparing the 10% polymers with BHT and without BHT



6.5 Antibacterial Data

1. Equation for converting CFU/mL to % Reduction

$$\%\ Reduction = \frac{((CFU/mL_{PBS}) - (CFU/mL_{Sample}))}{(CFU/mL_{PBS})} \times 100$$