

**Synthesis and Characterization Of Poly(Eugenolyl
Acrylate) and Poly (P- Styrene Eugenolyl Sulfonate)
and Study of Their Controlled Release Behavior**

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**تحضير وتشخيص بولي(يوجينوليل اكريليت)وبولي(بارا-ستايرين يوجينوليل
سلفونيت)ودراسة سلوك التحرر المسيطر عليه**

الخلاصة:

في هذا البحث تم تحضير العديد من انواع البوليمرات الدوائية. بولي(4-
يوجينوليل ستايرين سلفونيت) N2 الناتجة من تفاعل بولي(4-ستايرين سلفوناييل
كلورايد) N1 مع اليوجينول ، وبولي(يوجينول اكريليت) N5 المركب الثاني فقد
تم تحضيره من تفاعل بولي(اكريلويل كلورايد) N4 مع اليوجينول.

المركبات الكيميائية المحضرة ميزت وشخصت بأطياف الأشعة تحت الحمراء
وفوق البنفسجية. قيست الخواص الفيزيائية وتم حساب اللزوجة الجوهرية. ودرس
التحرر الدوائي باوساط PH مختلفة.

اليوجينول لديه القدرة لتخفيف ألم السن المعاب أو المريض.

ABSTRACT:

In this paper many types of drug polymers were prepared .Poly(4-eugenolyl styrene sulfonate) N₂ was prepared from reaction of poly(4-styrene sulfonyl chloride) N₁ with Eugenol and poly(Eugenolyl acrylate) N₅ was also prepared from reaction of polyacryloylchloride N₄ with Eugenol.

The prepared polymers were characterized and identified by IR,UV-spectroscopy .The physical properties and the intrinsic viscosity were measured .The drug releasing was studied with different PH media. Eugenol has the ability to relieve pain of irritated or diseased tooth .

Key words: Poly(Eugenolyl Acrylate)and Poly(p-Styrene Eugenolyl Sulfonate),Controlled

Release Behavior

1.INTRODUCTION

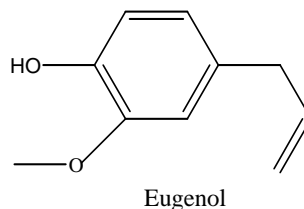
The use of functional Polymer in medicine has seen considerable growth during the past two decades(Jagur,1999). There has been a growing literature Pertaining to the use of functional polymers as delivery of agents for the therapeutic against variety of diseases states(Ottenbrite et al.,1991) .They include delivery of drugs at sustained rate , targeted delivery of drugs at specific to minimize toxicity and enhance selectivity for certain antitumor agents(Ulbrich et al.,1997) ,as well as macromolecular prodrugs with polymers acting as carrier

molecules(Duncan et al.,1984).More recently polymers have been used as non viral vectors for the delivery of genetic materials for gene therapy(Desmedt et al.,2000).

The concept of polymeric drug has been a subject of considering skepticism ,with medicinal chemists long considering synthetic polymers .Biocompatible polymeric equestrians represent an ideal class of agents for this purpose .their non absorption through the intestinal wall should offer minimal toxicity, while the incorporation of appropriate functional groups and manipulation of polymer physiochemical characteristics provides opportunities to tailor make polymers with high selectivity and capacity (Langer,1998).

Pimento leaf oil (pimento dioica (Myrtaccae)) is a native of Jamaica and Central America .Jamaica is the world leading supplier of Pimento, the spice, and Pimento leaf oil , which is used in foods and as an essential oil in the fragrance industry .

The main ingredient (95%-96%)in Pimento leaf oil , which constitutes 0.8% of the leaves , is Eugenol-1,which the main principle of a related plant, cloves (Syzygium aromaticum (Myrtaceae)(Benny et al.,2009).



A new controlled release compound was prepared by the reaction of p-styrene sulfonyl chloride and 8-hydroxy

quinoline in the presence of triethylamine as catalyst, this obtained monomer with bioactive agent moiety was polymerized with benzoyl peroxide as initiator at reflux condition under nitrogen atmosphere (Khazaei et al.,2007). Many acrylate polymers were prepared according to the modification reaction of poly acryloyl chloride or poly acrylic acid with different substituted group (Firyal,2005).

Eugenol possesses analgesic and inflammatory properties with ability to relieve pain irritated or diseased tooth pulp, thus incorporating polymers with Eugenol moieties in dental cements is attractive. An acrylic derivative of Eugenol methacrylate (EY MA) was Copolymerized with acrylic acid (AA) using radical initiator to yield a water soluble copolymer of acrylic acid and eugenol methacrylate p(AA –Co EgMA) which was then applied in the formation of glass –ionomer cements for potential application as dental cements .

2.MATERIALS AND METHODS

The following instruments were used in this work:

Melting points were determined on a Gallenkamp FB-600 melting point apparatus .

FT-IR spectra was recorded using solid KBr discs by test scan Shimadzu FTIR 800 series .

UV. spectra was recorded using Shimadzu UV-VIS recorder.

All materials were purchased from Merck and Fluka .

2.1 Materials:

All available chemical reagents were used without further purification .

2.2 Methods

2.2.1 PREPARATION OF POLY(4-STYRENE SULFONYL CHLORIDE) N₁

Chloro sulfonic acid (5 ml, 0.0497 mole) was added drop wise to a stirred mixture of Poly styrene (5.17 g, 0.0497 mole) dissolved in 20ml of chloroform and placed in a round-bottomed flask provided with condenser and separatory funnel , the suspension was cooled at 0-6 C at 1h. the white polymer was obtained , washed several times with ether, dried in a vacuum oven and characterized .The softening point was $>270\text{ }^{\circ}\text{C}$.The FT-IR spectrum gave absorption at 1170-1374 Cm^{-1} for S=O group .

2.2.2 REPARATION OF POLY(4-EUGENOLYL STYRENE SULFONATE) N₂

A mixture of Poly (4-styrene sulfonyl chloride) 5 g, 0.0246 mole and 20 ml of dioxane, and (4 ml, 0.0246 mole) of eugenol was added to reaction mixture in the presence of few drops of pyridine as a catalyst, refluxed with stirring about 1h. by using water bath .Cooled and poured into 50 ml of waters .White precipitate was isolated, dried in a vacuum oven.

The yellow –brown product of polymer N₂ was characterized by FT-IR spectra and C,H,N analysis.

2.2.3 FREE RADICAL POLYMERIZATION OF ACRYLIC ACID N₃

Five grams of the pure monomer was dissolved into 30 ml of freshly distilled dry THF in a screw-capped polymerization bottle . An amount equal to 0.02g. of azobisisobuteronitrile was added .

The bottle was flashed with argon for few minutes inside a glove bag The clear solution was maintained at 60 C⁰ in a constant temperature water bath for 1h. ,the solution was poured into about 50ml of ethanol, milky polymer was isolated and washed with ether for several times, dried in a vacuum oven over night and studied its characteristics .

The softening point of the acrylic acid was 75 C⁰ . The IR spectrum gave absorption at 3500 Cm⁻¹for -OH carboxylic acid and at 1720 C⁻¹for C=O group .

2.2.4 MODIFICATION OF POLY ACRYLIC ACID TO POLY ACRYLOYL CHLORIDE N₄

In a round –bottom flask provided with condenser and reparatory funnel containing thionylchloride (5ml,0.04 mole)was added gradually to poly acrylic acid which dissolved in 20 ml of Dioxane ,the conteints were stirred with magnatic bar at room temperature .

The excess of thionyl chloride was distilled and the poly acryloyl chloride was isolated and dried .

2.2.5 PREPARATION OF POLY (EUGENOLYL ACRYLATE) N₅

In a round bottom flask provided with condenser was placed 2g. of poly acryloyl chloride dissolved in 10 ml of dioxane , then added (2ml,0.01mole) of Eugenol oil ,the

mixture was stirred with magnetic bar, heated at 15 min., cooled and poured into 25ml of ether. Yellow-brown polymer was formed and dried in a vacuum oven before weighing. Intrinsic viscosity was calculated and equals to 0.2 dl /g.

2.2.6 ANALYSIS AND RELEASE STUDY

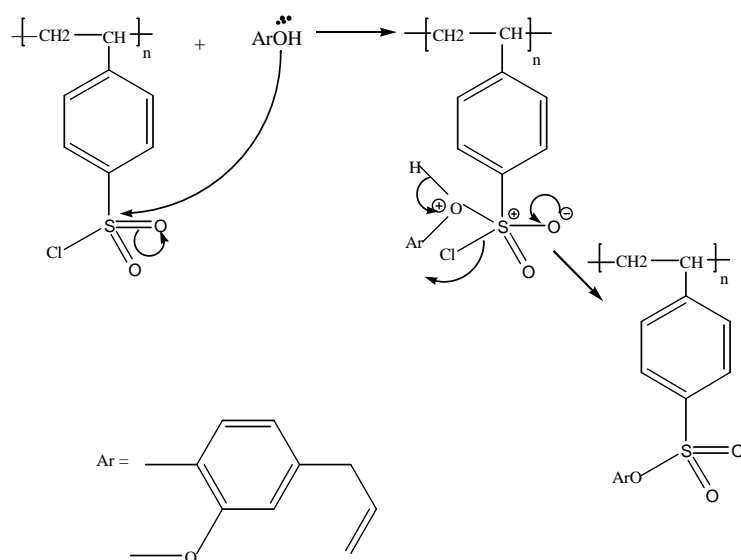
0.1g. of polymer N₂ was kept in a flask containing 50 ml buffer, at 30 °C, 50 °C, and 60 °C without stirring. A sample from the release medium was periodically withdrawn and analyzed by UV spectra at 350 nm determined the amount of the released eugenol. Every sample was replaced with new buffer for 1 day. The release study was carried out on different medium with different pH, (5, 7 and 9)⁽¹⁰⁻¹³⁾. The same controlled release study of polymer N₅ was determined in different media and different temperatures.

3. RESULT AND DISCUSSION

IR-spectra of polymer N₂, Fig.(1) shows the characteristic S=O group has resulted in strong absorption at 1374 cm⁻¹ as asymmetrical stretching absorption. The symmetrical vibration absorbs strongly near 1170 cm⁻¹. Fig (3) of IR-spectra of polymer N₅ shows the absorptions at 3060 cm⁻¹ for ν (C-H), and at 1690 cm⁻¹ indicated ν (C=O) and at 1330 cm⁻¹ due to ν (C-O), and ν (C-H) revealed absorption at 3060 cm⁻¹. Fig(4), UV spectra for polymer N₂ gave λ_{max} at 250, 360 nm due to (n- π^*) and (π - π^*) electron transition for Eugenol sulfate group substitution and Eugenol acrylate respectively.

Elemental analysis values for polymers N₂ and N₅ showed the experimental and theoretical results agreed quite well for the proposed structures .

The preparation of poly(4-Eugenolyl styrene sulfonate) N₂ was illustrated in mechanism as in scheme (1).

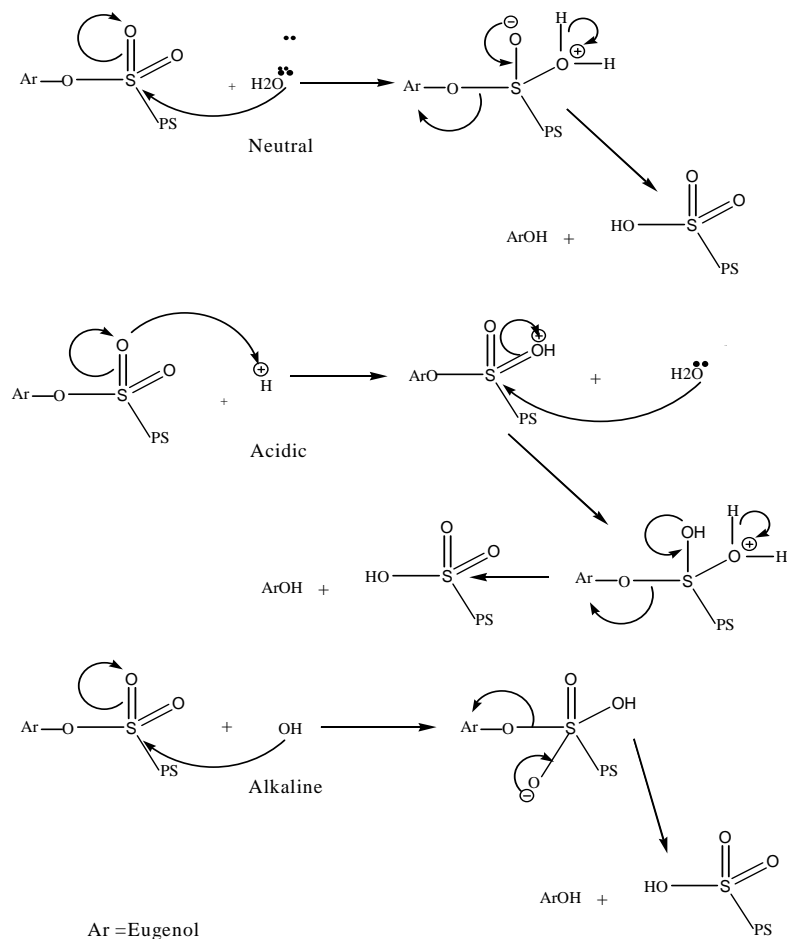


Decomposition temperature of polymer N₂ appeared at 225C⁰ ,this was because of high polarity of sulfonate group

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and aromatic groups which exist in polystyrene and in eugenol .

Scheme(2) shows the effects of temperature and PH effect on the rate of release and the ratio of the moles of eugenol at neutral , acidic and alkaline.



Scheme (2)

The mechanism of hydrolysis of sulfonation group in different media .

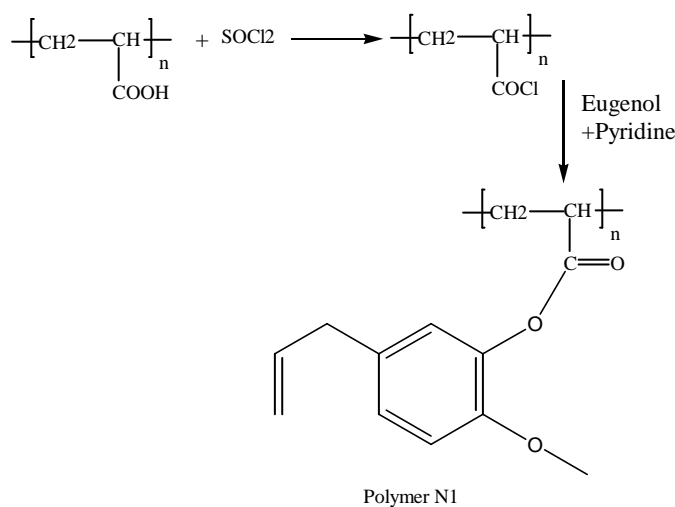
Hydrolysis of the polymer N₂ indicates the acidic media H⁺ is bonded to oxygen atom of sulfonate which increased the positive charge of the sulfur atom. It promotes the nucleophilic attack of water .

Due to the presence of OH⁻ in alkaline media which is a stronger nucleophile with respect to water ,the rate of

hydrolysis of sulfonate takes place faster than in acidic and neutral media .

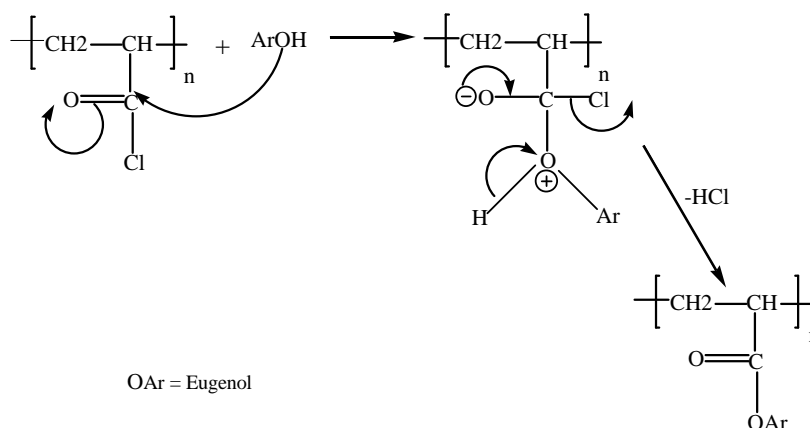
In this study, for the first time eugenol is a well known (syzygrum aromaticum (Myrtaceae) which used in dentenst applications . The Eugenolis as medical devices and dentistry uses when substituted with polymeric material to be significant advancements for delivery of therapy drug agent. These benefits may include lower toxicity ,greater specificity of action and enhanced activity due to multiple interactions and used for long considering time .

Also polymer N₅ which substituted the acrylate polymer by eugenol moiety was prepared as in scheme (3).



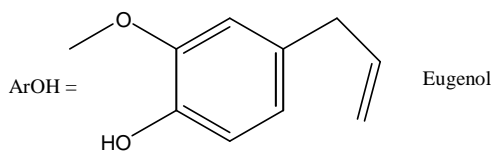
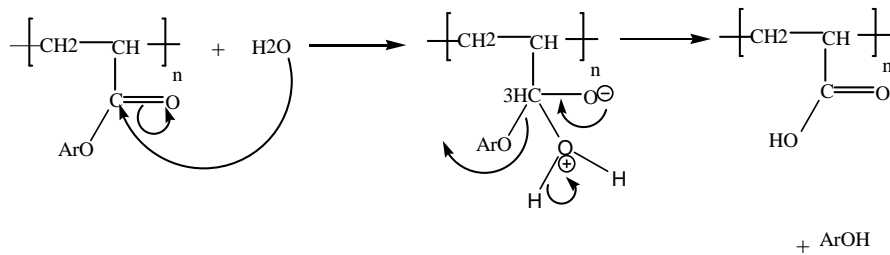
Scheme (3)

The modification of poly acryloyl chloride with eugenol is illustrated in a mechanism as in scheme (4).



Scheme (4)

Decomposition and loss of weight started above 250 C⁰, this thermal stability attributed to the presence of aromatic ring as a pendant group through the linear chains. Also the intrinsic viscosity $\delta\eta=0.75$ dl/g for polymer N₅ which enhanced the using the polymer N₅ as a dentistry drug which suitable for hydrolysis in different media such as polymer N₂, and the release Eugenol from hydrolysis of polymer N₅ was illustrated as in scheme (5).



Scheme(5)

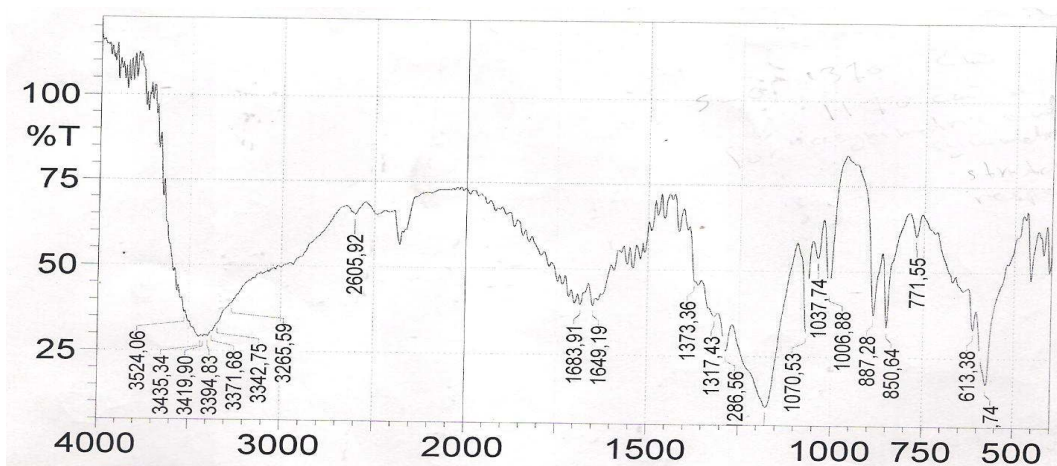


Fig.1:IR Spectrum of Poly (4- Styrene Sulfonyl Chloride)

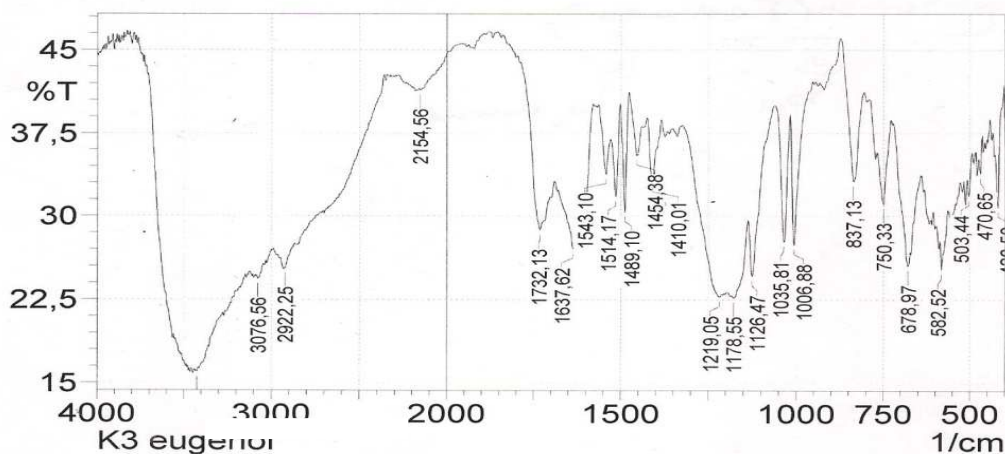
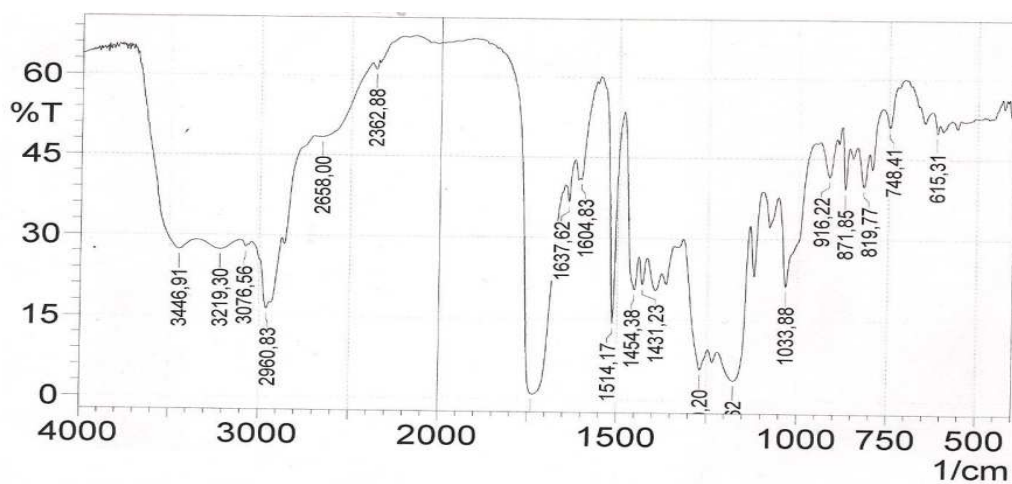
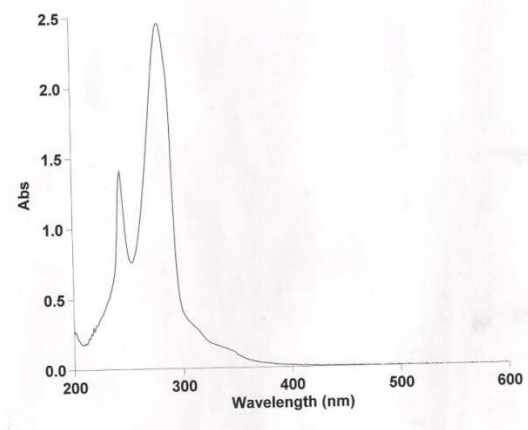


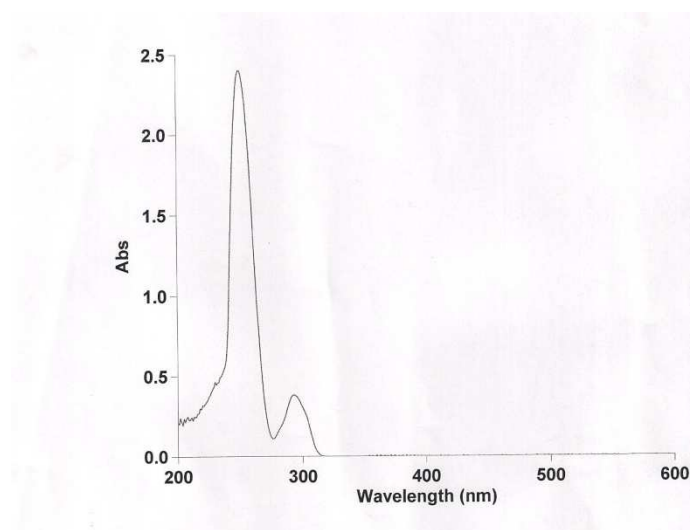
Fig (2) IR-spectrum for poly (4-Eugenolyl styrene sulfonate)



Fig(3) IR – Spectrum for poly (Eugenolyl acrylate) N5



Fig(4) UV-Spectra for polymer N1



Fig(5) UV – Spectra for polymer N5

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