Synthesis and Study Antibacterial Activity of Some New Polymers Containing Maleimide Group

Synthesis and Study Antibacterial Activity of Some New Polymers Containing Maleimide Group

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Abstract. By condensation of benzaldehyde with thiourea in absolute ethanol in the presence of glacial acetic acid as a catalyst, the Schiff base(1-benzylidenethiourea)[I] was synthesized by synthesis of 4-(3-benzylidenethioureido)-4-thioxobut-2-enoic acid compound[II] by reaction of maleic anhydride with schiff base [I] in DMF. When treating compound [II] with ammonium persulfate (NH4)2S2O8 (APS) as an ethanol initiator to obtain polymer [III], compound [III] reacted to polymer [IV] with SOCl2 in benzene. Sulfamethizole, celecoxib, salbutamol, 4-aminoantipyrine to yield polymers [V-VIII], compound [IV] reaction with different drugs. Spectral evidence established the structure of synthesized compounds: FTIR and 1HNMR, UV-Vis Spectroscopy and Elemental Analysis (C.H.N-S) . These synthesized derivatives [V-VIII] were tested for their antibacterial activity against Bacillus subtilis (G+) and Escherichia coli (G-) by agar well diffusion process, and the results showed that all polymers had a greater diameter of the growth inhibition region. This may be relative to the presence of sulfamethizole medication, maleimide group and Schiff bases, Polymer[V] demonstrated excellent inhibition against Bacillus subtilisa and E.coli.

Keyword : Schiff base , Antibacterial activity, Salbutamol , Celecoxib , Maleimide , sulfamethizole.

1. Introduction

Schiff bases are a group of compounds containing (-HC=N-) formed from condensing products of aromatic aldehydes or primary amine ketones [1]. Schiff bases are commonly used in various fields, such as medical chemistry [2], antibacterial, antiviral, pharmacological, antioxidant and cancer activities [3-5]. In addition, the Schiff base enhances the biopolymer's stability[6]. A generic formula, $H_2C_2(CO)_2NH$, has maleimide compounds. The name 'malei-mide' derives from the maleic acid and imide combination [7]. Maleimides are an essential type of heterocyclic compounds contained in natural products[8] and are used in organic and medicinal chemistry[9]. In pharmaceutical products with biological specific functions, such as antibacterial, anticancer, antitumor, tuberculostatic activity, anti-microbial, antiviral and antigenic activities, maleimides have important significance [10,11]. In order to be able to use multiple macromolecule systems, such as thermostability materials[12], self-healing systems[13], click reactions[14] and antibody-drug conjugates[15], Chemistry's

Maleimide[MI] has acquired a senior interest in both polymer and biological sciences. The structure of the alpha,β-unsaturated imide allows Maleimide to be extremely versatile. First, the two carbonyl groups have hydrogen bonding interaction power that can be used to modify the behavior of polymerization[16]. The feasibility of preparing higher and thermally stable polymers[17] is the copolymerization of maleimides with Schiff base supply. In addition to the process ability of maleimide polymer, flexible units within the polymer backbone can also be increased.

2. Experimental

Materials : *All chemicals supplied from Merck and Aldrich.*

Techniques : FTIR spectra recorded using KBr , discs on a 8400s Shimadzu spectrophotometer and FTIR spectrophotometer , Shimadzo [Ir prestige-21] . ^{1}HNMR spectra carried out by : Bruker , ultra shield 300 MHz , : Switzerland and are reported in ppm.

2.1.Synthetic Procedures:

2.1.1.Preparation of Schiff base[1-benzylidenethiourea] [I] [18]*:*

This compound was prepared from the reaction of benzeldehyde [1.06 g. , 0.01 mol] with thiourea [0.76 g. , 0.01 mol] in (30 ml.) ethanol and [3]drops of glacial acetic acid , the mixture refluxing at 70°C for 12h. . The course of the reaction was followed up using a technique TLC. When the reaction was completion , separated as yellow-colored product which was filtered , dried and recrystallized by methanol . Yield 85% ; m.p[129-131]^{0}C. Elemental Analysis , Calcd : C% = 58.53; H% = 4.87; N% = 17.07; S%= 19.51 , Found: C% = 58.67; H% = 4.98 ; N% =17.27 S% = 18.98.

2.1.2.Synthesis of 4-[3-benzylidenethioureido]-4-thioxobut-2-enoic acid[II] [19]

Mix Maleic anhydride [0.98 g. , 0.01mol] and [1.64 g. , 0.01mol] Schiff base [I] in 25ml DMF then refluxed about 4hr. , the viscous result washed with diethyl ether and then dried at room temperature. Yield 73% ; m.p[198-200]^{o}C**.** Elemental Analysis , Calcd : C% =54.96 ; H% = 3.81; N% = 10.68 ; S% = 12.21
Found: C% = 55.99 ; H% =3.90 ; N% =10.15; S% = 12.87

2.1.3.Synthesis of polymer[III] [20] *:*

[0.27g ,0.001mol] of compound [II] was mixed with (0.22gm) of ammonium per sulfate [APS] as initiator of polymerization in (15 ml.) of ethanol . The mixture stirring for 2-3 hrs at room temperature , then refluxed about 12hr. Filtered , washed with cold EtOH absolute , dried and recrystallized with ethanol to gave the required product [III].

2.1.4.Synthesis of polymer[IV] [21]

0.01 mol of compound [III] mixed with 0.01mol of thionyl chloride in 25ml. of dry benzene and reflux for (6hr) The Amount of $SOCl_2$ and benzene separated under vacuum after cooling.

2.1.5.*Synthesis of polymers [V-VIII]* [22]

A mixture [0.01mol] of compound [IV] and [0.01 mol] of drug [sulfamethizole or celecoxib or salbutamol or 4-aminoantipyrine] in 20 ml. of DMF . The mixture refluxed about 3 hr. Filtered , wash with ethanol absolute , dried and recrystallized from EtOH to gave the required product[V-VIII].

3. Result and Discussion

-1benzylidenethiourea[I] was prepared to give good yield to compound[I] by reaction of benzaldehyde with thiourea in absolute ethanol. FTIR and 1HNMR spectroscopy were used to identify this Schiff base [I]. The FTIR spectra, Fig.(1) shown at (1647)cm-1 appearance band refers to the azomethine group and two (3325,3149)cm-1 appearance bands attributable to NH2 . 1HNMR (DMSO) spectrum, Fig.(2) showed a signal at δ(2.11) ppm attributable to the NH2 group, a sharp singlet at δ(8.1) ppm for one proton attributed to CH=N and several signals for aromatic protons at δ(7.32-7.83) ppm. Compound [II] produces maleic anhydrides with Schiff base [I] in DMF from the reaction. FTIR spectroscopy detected the compound

[II]. 3400-2400 (OH), 3184 (NH) group, 3041 (C-H arom.) group, 1739 (C=O) of carboxylic acid, 1654(C=O-NH), 1641(C=N), 1591(C=C)Aromatic and 1126(C=S). FTIR absorption[a,cm-1]: Polymer [III] was synthesized with ethanol using ammonium per sulfate (APS) as the initiator via the reaction compound [II]. The stretching band referred to the O-H of the COOH moiety in the area (3406-2800)cm-1, the stretching band of the N-H group appeared at (3170) cm-1-, 3007 (C-H arom.)-, 2941,2856 (C-H aliph.) and the stretching band to (C=O) for COOH appeared at 1735cm-1.

In order to achieve transformation to a new function group, acid chloride was considered a very active intermediate, so we aimed at synthesizing compound[IV] by reaction compound[III] with thionyl chloride, the acid chloride[IV]formed as residue was used in the next reaction without further purification. Polymers [V-VIII] is synthesized with drugs (sulfamethizole or celecoxib or salbutamol or 4-aminoantipyrine) from the reacted polymer [IV] . FT-IR spectrum for compound [VII], acyl chloride absorption band disappearance and absorption band appearance at (1729) cm-1 refer to (C=O-O), N-H group stretch band appeared at (3214) cm-1 and OH, C=O-NH and C=N stretch bands appeared at(3438), (1687), (1630) cm-1 respectively. 1H NMR (δ ppm): sharp singlet signal at δ (1.17) refers to nine C(CH3)3 protons, signal at δ (2.01) due to proton NH of [NH-C(CH3)3] group, -CH=CH chemical shift disappears and shows chemical shift at δ (2.73-2.98) due to-[CH-CH]n-, doublet signal at (3.17-3.40) connected to CH2 proton and triplet signal at δ(4.47) due to CH proton signals at δ(5.65),(5.77) due to proton CH2O and (5.77) Compound FT-IR spectrum [VIII] (200, cm-1): reveals the current absorption band due to amide (C=O) in the area (1687)cm-1 and absorption band disappearance due to acyl chloride. A signal at δ (2.73) due to protons of [C[CH3]] group, -CH=CH chemical shift disappears and shows chemical shift at δ (2.98-3.23) ppm due to-(CH-CH)n-, signal at δ(3.45) refer to protons of [N(CH3)] group, signal at δ(6.02) refer to proton of (NH-C=O) group, multiple signals at δ(6.91-7.25) attributable to aromatic protons, signal at δ(7.97) attributable to CH=N, multiple signals at δ(6.91-7.25) The UV-Vis compound spectrum[VII,VIII] displays the peaks of absorption at(280-332), (290-2320) that can be attributed to(π-π*) and (n-π*).

Table1.FT-IR of polymers[V-VIII]

Comp. No.	υ (N-H)	υ (C-H) aliph.	υ (C=O) amide	υ (C=O) ester.	υ (C=N)	υ (C=S)
[V]	3351	2933-2872	1670	-	1627	1141
[VI]	3329	2924-2856	1680	-	1637	1132
[VII]	3214	2920-2850	1687	1729	1630	1157
[VIII]	3190	2964-2804	1687	-	1631	1193

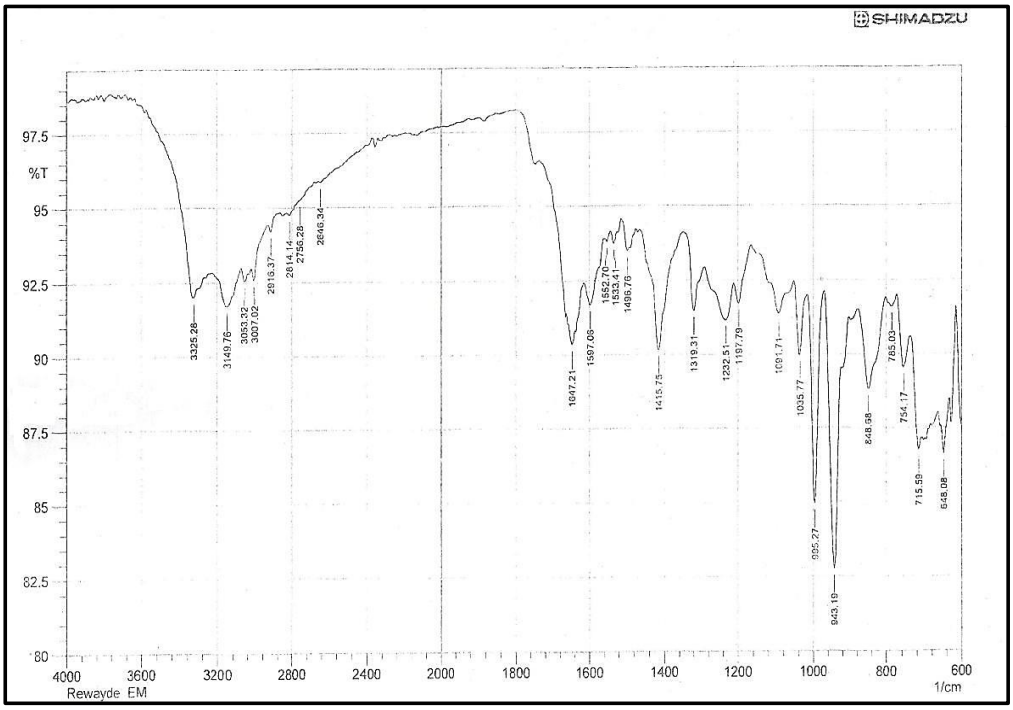


Figure1.FT-IR of compound[I]

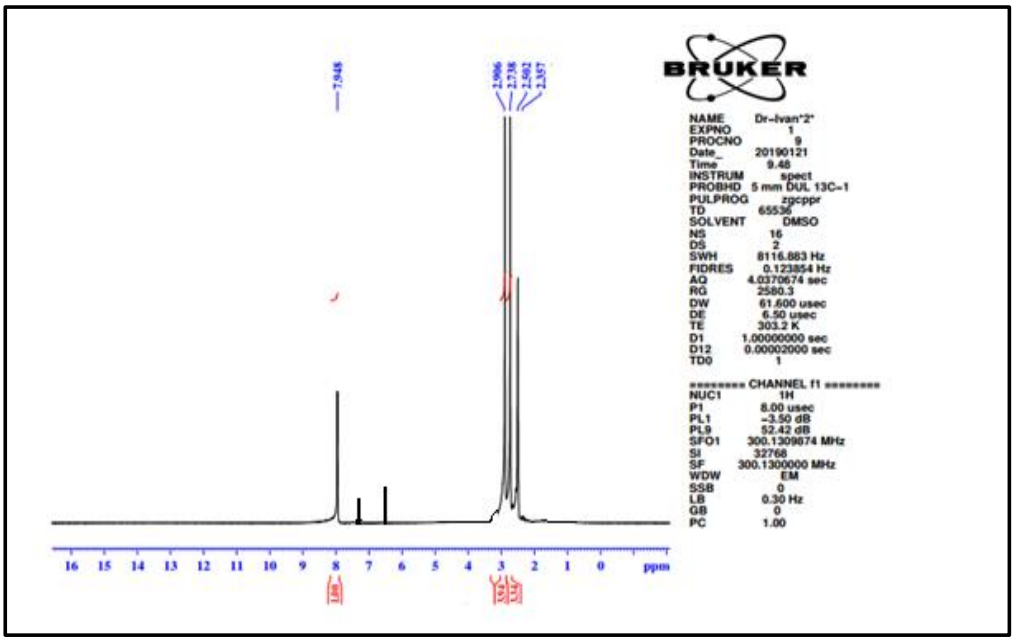


Figure 2 . [1]H-NMR of compound [I]

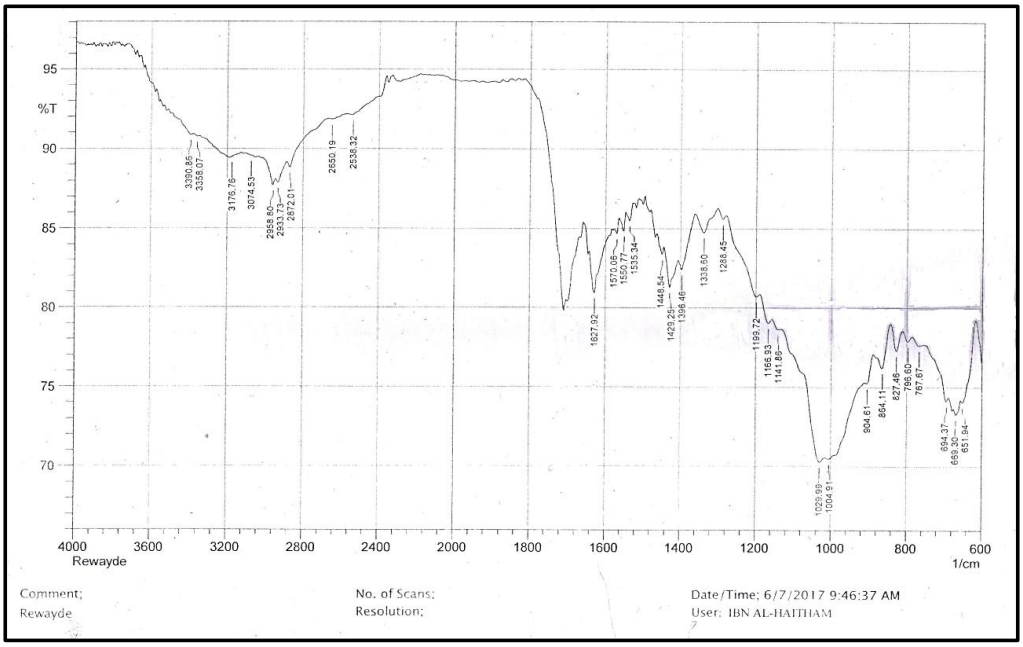


Figure 3. FT-IR of compound[V]

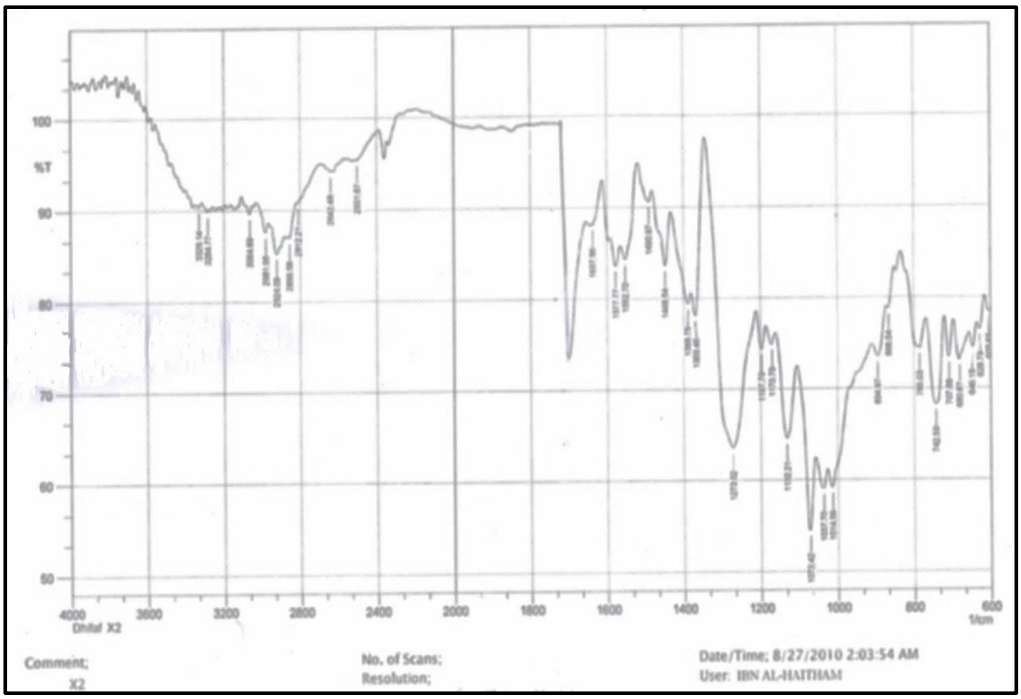


Fig.(4).FT-IR of compound[VI]

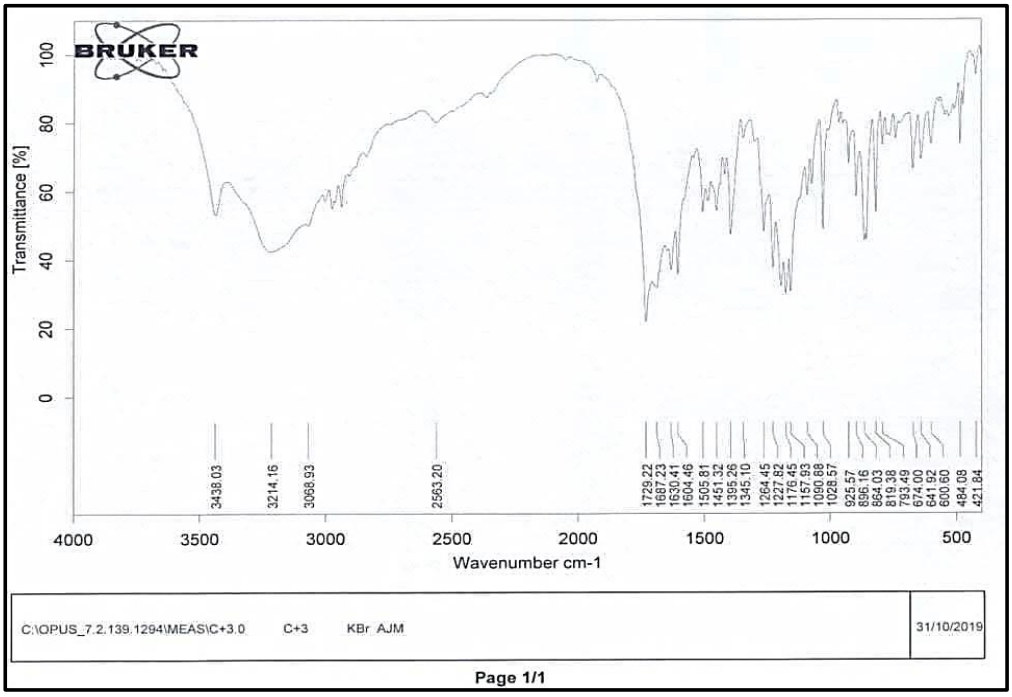


Figure 5. FT-IR of compound[VII]

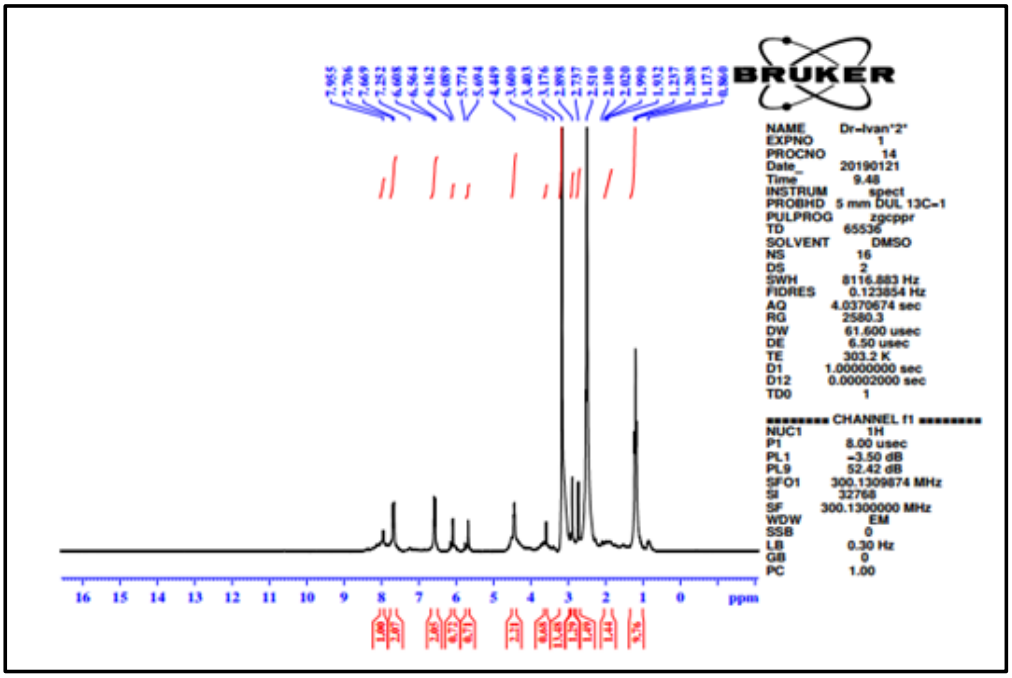


Figure 6 . ^{1}H-NMR of compound [VII]

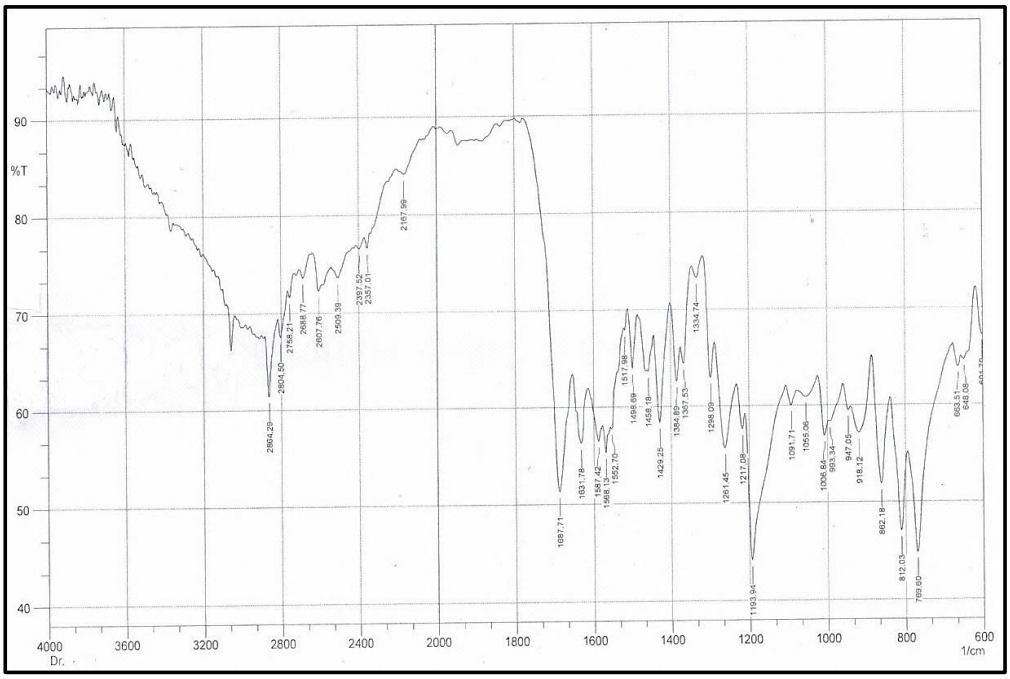


Figure 7 . FT-IR of compound[VIII]

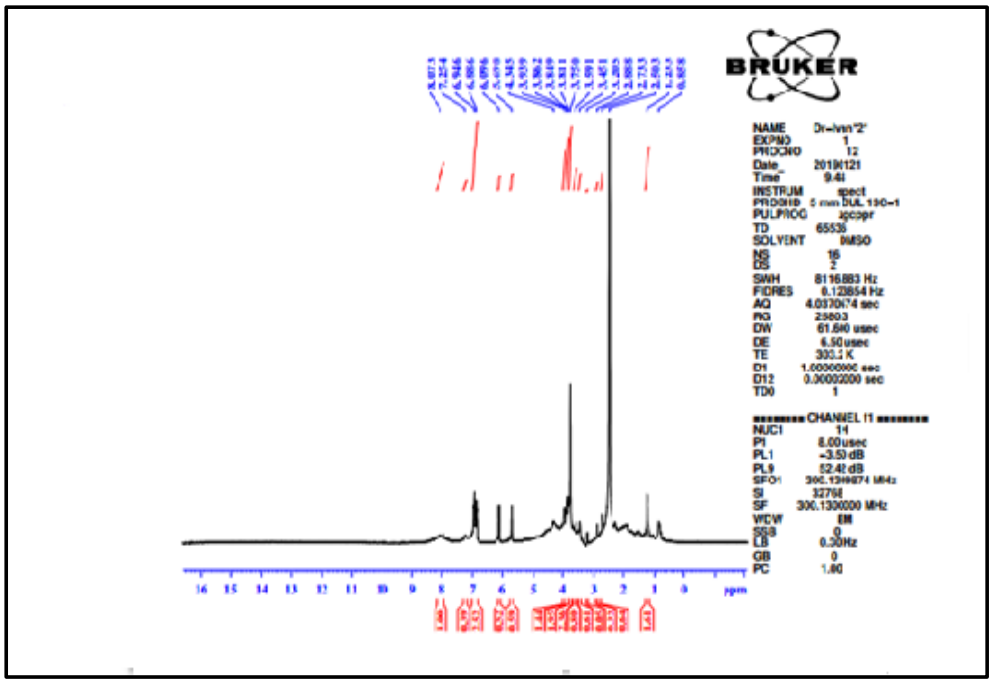


Figure 8 . ^{1}H-NMR of compound [VIII]

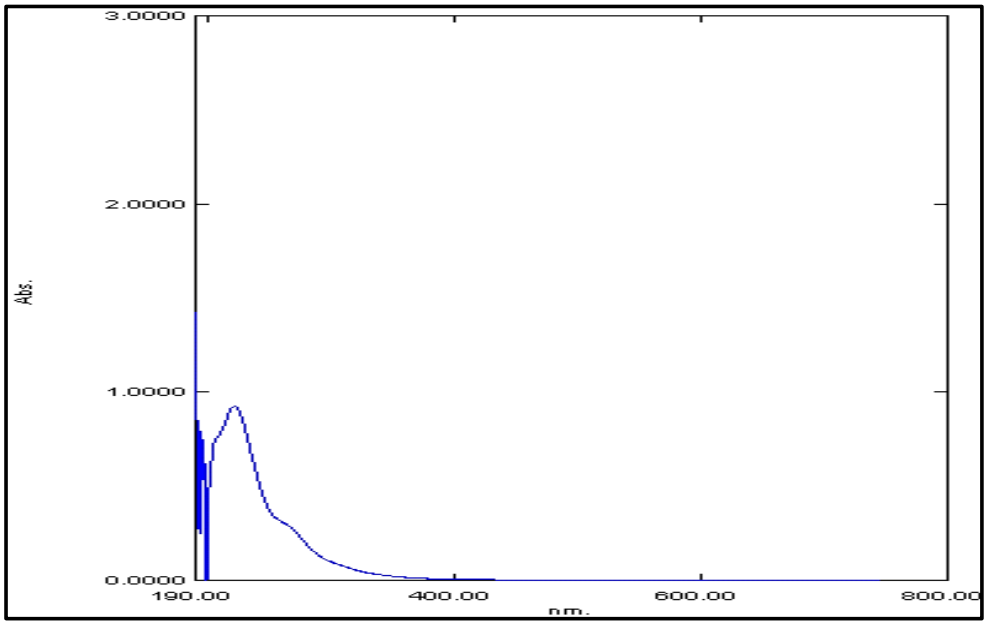


Figure 9. U.V. spectrum of compound [VII]

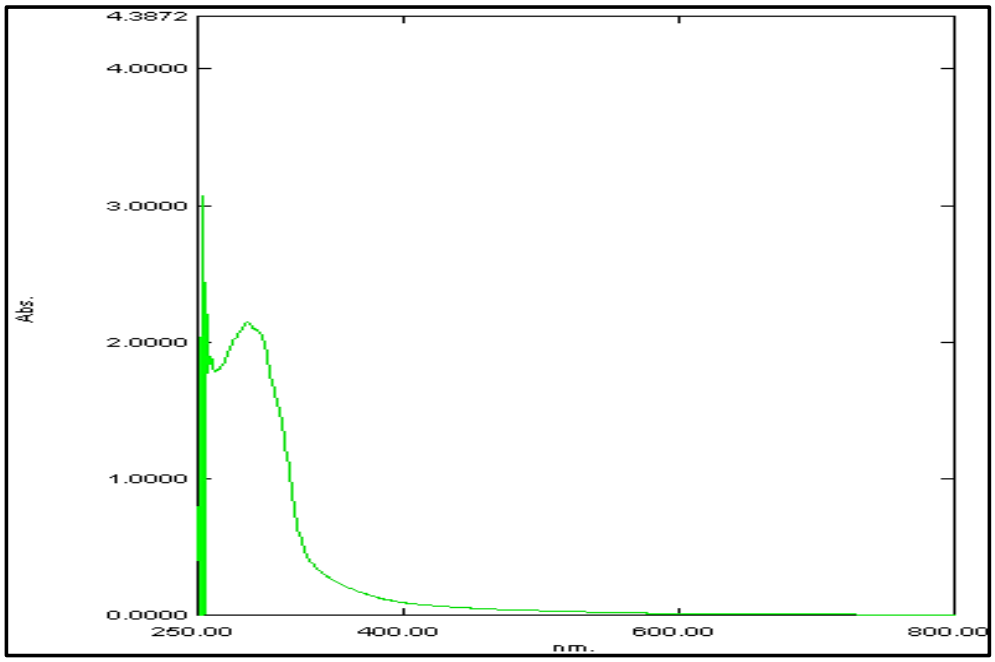


Figure 10. U.V. spectrum of compound [VIII]

4. Biological Activity:

The polymers [V-VIII] were tested by the agar well diffusion method (Barry, 1977) for their antibacterial activity against Bacillus subtilis [G+] and Escherichia coli [G-] (in vitro), the standard drug used to compare the synthesized polymers with penicillin (50µg / ml) . The results showed that the growth inhibition zone diameter of all polymers was higher. Compound[V] demonstrated strong inhibition against Bacillus subtilisa and E.coli, which may be linked to the existence of the drug sulfamethizole, since this drug is a sulfonamide-derived antibacterial. It is effective against a wide variety of gram-negative and gram-positive bacteria as an antibiotic. The polymer[V] also includes Maleimide group and Schiff bases that have strong antibacterial activity.

Table2. The inhibition zone of some synthesized compounds[V-VIII].

Comp.	E .coli	Bacillus cereus
Penicillin	17	23
[V]	28	22
[VI]	14	15
[VII]	23	20
[VIII]	16	16

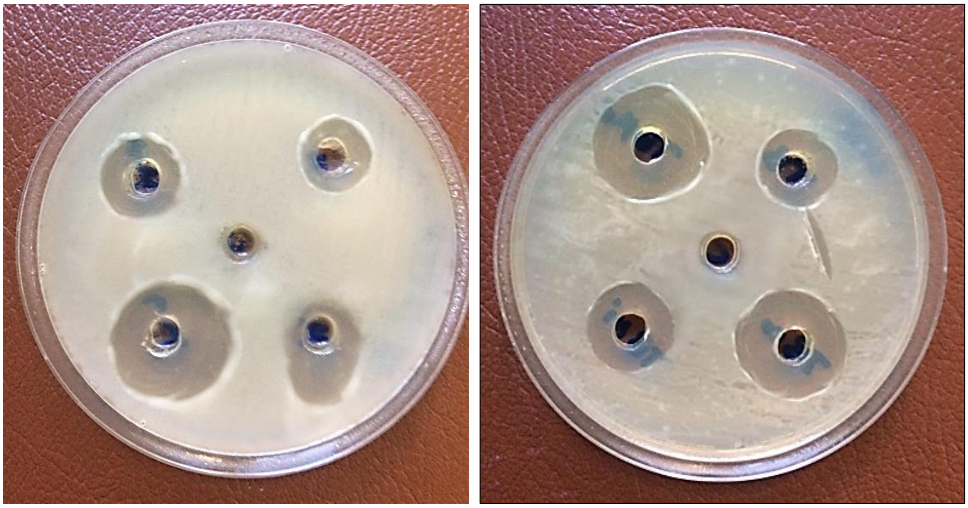
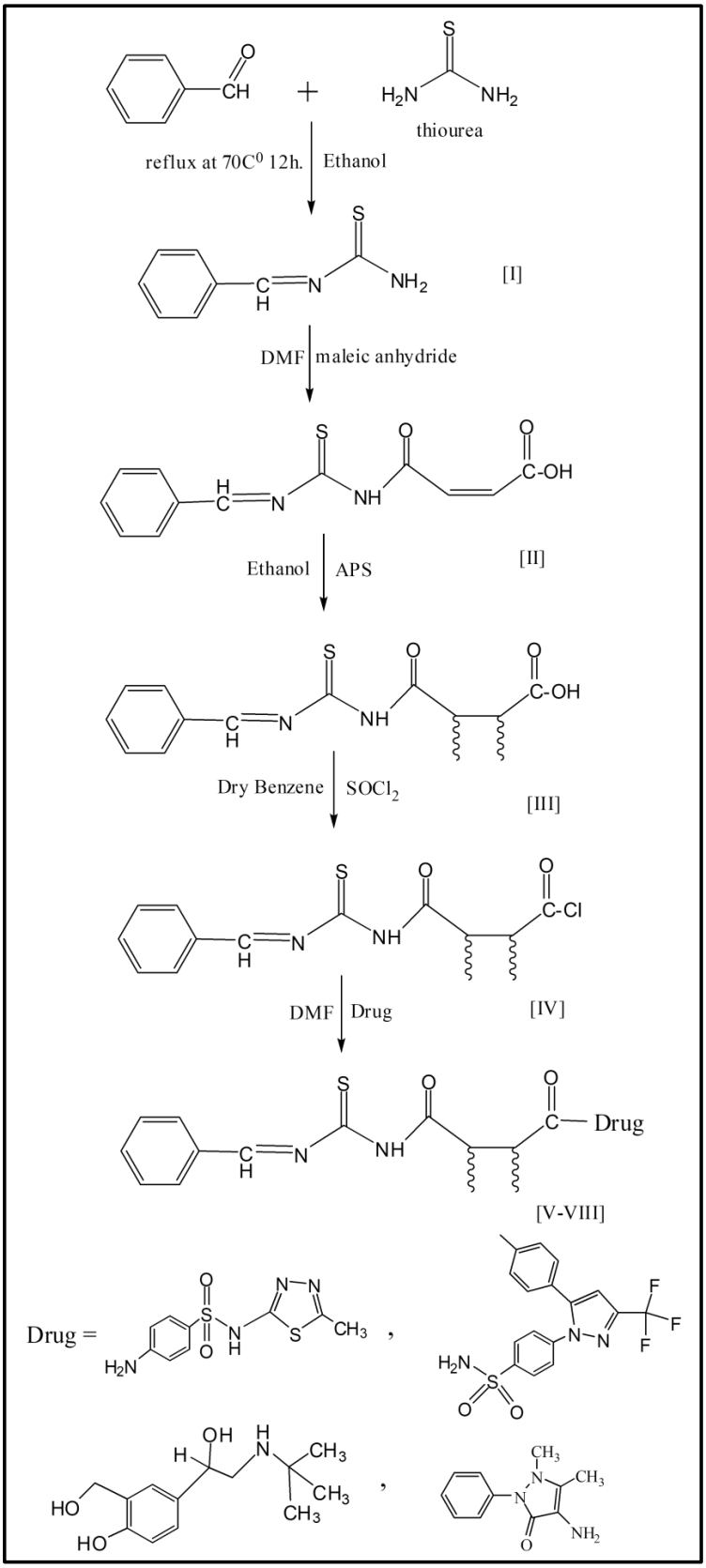


Figure 11 . Antibacterial activities of polymers



Scheme 1. The synthetic route for target derivatives[I-VIII]

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