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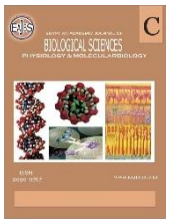

New N-Substituted Maleimide Drug Polymers: Synthesis, Drug Release and Antibacterial Activity

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ABSTRACT

In this work, new substituted drugs polymerized as new homogenous polymers with study their medicinal properties to extend the controlled drug. The first step includes the preparation of compound N-(4-hydroxyphenyl) maleimide (D_1) via a reaction of maleic anhydride with 4-aminophenol. Then compound (D_1) was converted to maleimide phenol acetic acid ether (D_2) which converted to its corresponding acyl chloride derivative which reacted with amino drugs (Ceftriaxone, Ciprofloxacin) afforded monomers (D_3 and D_4). Homogeneous polymers (D_5 and D_6) were prepared via free radical polymerization reaction of the monomers (D_3, and D_4) under nitrogen using Benzoyl peroxide (Bpo) as initiator. All these prepared monomers and polymers were characterized by FT-IR and ^{1}H-NMR, ^{13}C-NMR techniques and C.H.N.S . Study of the drug release behavior in acidic and basic media as well as the swelling ratio were achieved. The antibacterial activity and physical properties of all monomers and polymers were studied.

INTRODUCTION

Polymers are a big scientific field that has significantly improved our culture. Polymers have a range of attractive properties, including high strength or modulus-to-weight ratios (lightweight but comparatively rigid and strong), hardness, durability, corrosion resistance, and lack of conductivity (heat and electrical). Many of these properties make them ideal candidates for use in a variety of fields, including medicinal equipment, health care, food, irrigation, catalysis, electronics, environmental, green energy, and textiles (Ramazani A.*et al.*,2016).

Antimicrobial polymers are self-sterilizing and environmentally safe (Amritha CA,*et al.*,2015). They can also be quickly absorbed into fibers and extruded into fibers, and they prevent microorganisms from adhering to their surface (Witte W.1998)(Timofeeva L,*et al.*,2014) Antimicrobial polymers are formed by covalently binding biocide functional groups to the polymers (Madkour AE,*et al.*,2008)(Thamizharasi S,*et al.*,2002), giving them antimicrobial or antiseptic properties. The bulk polymer is modified, or the surface is selectively modified, using accessible reactive moieties. Antimicrobial polymeric materials can be used in the areas just described, avoiding the resistance issues that come with using antibiotics. An antimicrobial agent is a substance that prevents the development of microorganisms.

In addition, the toxicity of such antimicrobial agents is strictly proportional to their efficacy. As a result, the synthesis of effective yet non-toxic antimicrobial polymers is urgently needed (Moon W ,*et al.*,2003)(Madkour AE,*et al.*,2008)(Kao YF.2011)(Arun M. Bhagare,*et al.*,2020).

The chemical transformation of a biocide molecule into a polymerizable compound that can then be polymerized or co-polymerized with another monomer is another type of synthesis(Kareem M.M., Abaas L.A.2019) (Sabah A.A.,*et al.*,2023).Both of these types have been useful in proving the viability of non-leaching antimicrobial polymeric products. It makes sense to begin with an antibacterial agent that chemically transformed into derivatives, which polymerized, while still maintaining bioactive functional groups. An existing polymer with reactive moieties can also undergo the change. Functional moieties were chemically altered by joining a complementary reactive antimicrobial agent with hydroxyl, carboxyl, or amino groups to the polymer backbone or its pendent groups (Kareem M.M., Abaas L.A.2019).

In order to increase the drug's bioactivity through the combination of polymers, this work focused on the synthesis of N-substituted maleimide-based polymeric medicines.

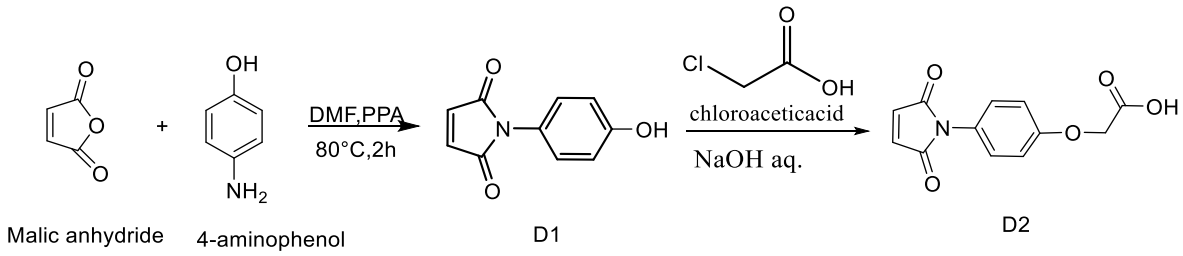
MATERIALS AND METHODS

Chemicals and reagents: Fluka, Sigma-Aldrich, CDH, and Riedel-de Haen provided all solvents and reagents, which were all analytical grade. All medicines were purchased from the SDI-Samarra Company.

Instruments: The SMP30 melting point apparatus was used to calculate melting points. PG CECIL-CE7200 double-beam spectrophotometer was used to measure UV absorption. An Ostwald viscometer was used to test the viscosity (η) of the produced polymers at 23ºC in acetone. Chemical shifts for the ^{1}HNMR spectra in dimethyl sulfoxide (DMSO-d6) were measured using a Varian INOVA 500 MHzNMR spectrometer. The Fourier Trans Infrared Spector Promoter AT-FT-IR Bruker Tensor II was used to measure the FT-IR spectra within the range (400-4000 cm^{-1}).

Synthesis of Compound [D_1]: Maleic anhydride (9.8g, 0.1mol) was dissolved in dimethylformamide, and then p-aminophenol (10.91g, 0.1mol) was slowly added into the solution. Following the addition of polyphosphoric acid (PPA), the mixture was agitated for two hours at 80°C. After cooling, the reaction mixture was added to the chilled distilled water. The orange precipitate was filtered apart and repeatedly rinsed with distilled water, recrystallized with isopropanol, filtered and vacuum-dried to afford the TLC followed the reaction process regularly (R_f = 0.45, 1 hexane: 3 ethyl acetate).(Chaudhary S, Purohit Jinger S.2017).

Synthesis of Compound [D_2]: (8.91g, 0.1mol) compound [D_1], (18.8g, 0.2mol) chloroacetic acid and 8% of NaOH solution were mixed together in 250 ml round bottom flask. The solution was refluxed for 1.5h at 100°C, and the orange clear solution was acidified with 10% HCl 7solution. The yellow precipitate was settled down and separated by gravity filtration and recrystallized with ethanol to obtain the precipitates. Table 1 lists the products' physical characteristics. TLC followed the reaction process regularly (R_f = 0.56, 1 hexane: 3 ethyl acetate). (Chaudhary S, Purohit Jinger S.2017).



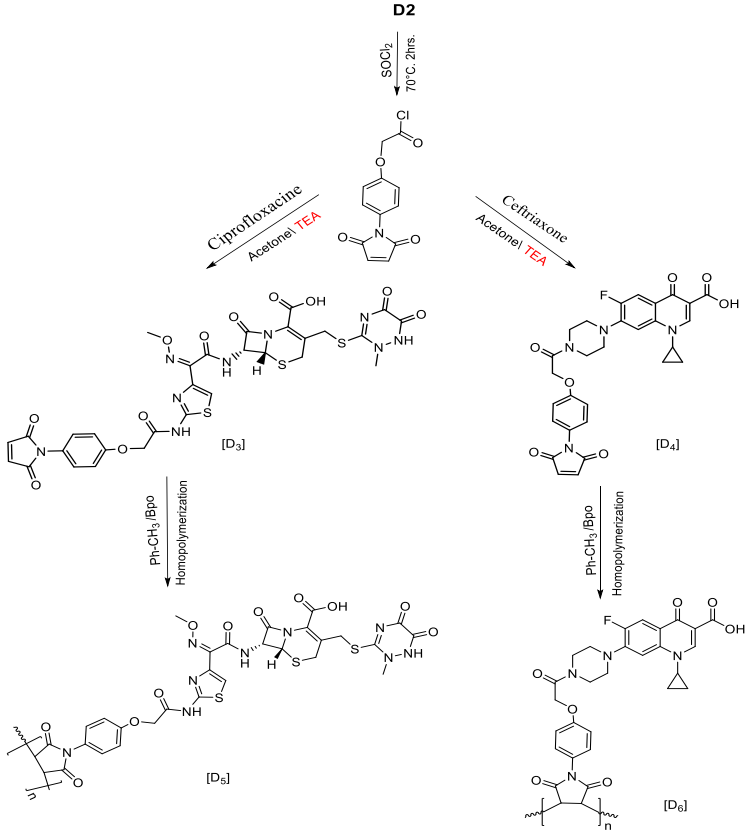
Scheme-1: Synthesis of compounds [D_1 and D_2]

Synthesis of Monomers [D_3, and D_4](One pot reaction):

In the 100 mL round bottom flask, (2.47g, 0.01 mol) of [D_2] was suspended in 8 mL of chloroform then 4 mL of ($SOCl_2$) was added. The mixture was mixed with continuous stirring for 1.5 hrs. at ambient temperature. The mixture was then at 65°C for another 2 hrs, and then the drug [Ceftriaxone (5.5g, 0.01mol.), Ciprofloxacin (3.31g, 0.01mol.)] and 1mL of triethylamine in dry acetone. The mixture was refluxed at 50°C for 2 hrs. The reaction was followed by TLC technique [7] (D_3, Rf = 0.3, 1 hexane: 3 acetone, D_4, Rf = 0.62, 1 hexane: 3 acetone).

Synthesis of Homo Polymers [D_5, and D_6]:

According to the literature (Kareem M.M.,et al.2023), the polymerization process was achieved for homogenous polymers. (0.5 g) of monomers (D_3 and D_4), 3-4 drops of dry toluene, and (0.07 g, 0.00023 mol) of the initiator Benzoyl peroxide (Bpo) were combined in a 50 mL dry two neck round bottom flask. The mixture was stirred under nitrogen gas flow for 10 minutes, and then the flask was completely sealed and heated in an oil bath for 3-4 hours at 90 °C. Following the completion of the polymerization procedure, the precipitate was filtered, washed with ether, and dried at 50°C.



Scheme-2: Synthesis route of compounds (D_3-D_6).

Swelling Ratio:

Dynamic swelling was assessed by gravimetric measures. In a beaker filled with 100 mL of water heated to 37°C, the polymeric samples were suspended. The hydrogel sample was taken out after five hours and five days, quickly wiped clear of surface water with filter paper, weighed (accuracy 0.0002), and then put back into the swelling solution. The swelling ratio was calculated using the following equation (Luten J,et al.2008)(Mohanad M.K,et al.2021).

Swelling ratio (%)= (Ws - Wd)/Wd × 100

[Wd= Weight of polymer; Ws= weight of swollen polymer]

Release of Drugs:

The drug release from the produced homo- polymers was assessed using a UV-visible spectrophotometer at a constant temperature of 37°C in different buffer solutions with pH values of (2.0, and 8.0.) 50 mL of various buffer solutions were used to submerge (0.05g) from homo-polymers for varying amounts of time at 37°C constant temperature. The hydrogel was removed from the buffer solution at the appointed time, and the amount of drug release was calculated by measuring the buffer solution's absorbance (Al Hachim Z.S,*et al.*,2022).

RESULTS AND DISCUSSION

Characterization of Compound [D_1]:

Chemical Formula: $C_{10}H_7NO_3$, Color: Orange, (90% Yield, mp 183-185°C). The N-(4-hydroxyphenyl)maleimide (HPM) infrared spectrum. As can be observed, the absorption peaks at 1697 and 1517 cm^{-1}, respectively, represent the stretching vibrations of the carbonyl groups (-C=O) of imide rings and aromatic rings. Furthermore, the asymmetric stretching vibration of the C-H bonding of olefinic groups is indicated by the absorption peak at 3111 cm^{-1}. Additionally, a peak at 3479 cm^{-1} is seen and is attributed to the O-H bond's symmetric stretching vibration. This demonstrates that HPM results from a reaction between maleic anhydride and p-aminophenol. Maleic anhydride and m-aminophenol are found to react in a polyphosphoric acid and dimethyl formamide media. At the site of the maleic anhydride's ring opening, an addition reaction. ^{1}HNMR of compound [D_1], It can be seen that the peaks are observed at the chemical shifts of 7.32 and 6,88 ppm assigned to the protons of aromatic rings. Furthermore, the peaks with the chemical shift of 6.7 and 5.1 ppm are observed, these two peaks are attributed to the protons of the imide ring and hydroxyl group. ^{13}CNMR of compound [D_1], shows different signals for different carbons as follows: The signals of aromatic carbons appeared at the range 115.70-128.23 ppm and the maleimide double bond carbons resonate at 135.16 ppm. The signal at about 161.16 ppm belongs to the maleimide carbonyl group while the signal at 156.61 ppm belongs to the carbon of C-OH groups.

Characterization of Compound [D_2]:

Chemical Formula: $C_{12}H_9NO_5$, Color: yellow, (85% Yield, mp 210-212°C). FT- IR (cm^{-1}) various absorption bands were observed at 3500-2500 (Carboxylic acid O-H), 3097 (=C-H of maleimide and aromatic), 1725 and 1701 (C=O stretch, imide ring and carboxyl groups), 1589-1490 (aromatic C=C), 1454 (-CH_2- aliphatic), 1382 (C-N), 835 (*Cis*-CH=CH bending). C=O signal backs for carboxylic acid in 1725, and 1454 (-CH_2- aliphatic) ensure the success of cyclodehydration reaction of maleamic acid. ^{1}HNMR of compound [D_2], showsa characteristic signal for methyl group (-CH_2-) at 4.49 ppm, a characteristic signal for maleimide (CH=CH) and the aromatic protons papered at the range of protons at 6.85-7.92 ppm, the broad and weak signal at 12.95ppm for carboxylic acid group.

Characterization of Compound [D_3]:

Chemical Formula: $C_{30}H_{25}N_9O_{11}S$, Color: Brownish Yellow, (80% Yield, mp 98-100 °C). FT-IR (cm^{-1}) spectrum of compound [D_3] showed strong stretching frequencies for the aromatic and maleimide (=C-H) appeared at 3086, 3034 cm^{-1}. The band at 2915 is assigned to aliphatic C-H stretching vibration of methyl groups, the amide maleimide carbonyl groups at 1710,1625 cm^{-1}, and

showing characteristic stretching bands at the range 1764cm^{-1} due to beta-lactam carbonyl and broad absorption band of carboxyl groups in drug structures around ~3500-2500 cm^{-1}. ^{1}HNMR of compound [D_3]: (500MHz, DMSO-d6, δ, ppm) shows the characteristic signal for maleimide (CH=CH) and the aromatic protons papered at the range of protons at 6.6-7.9 ppm and for beta-lactam protons at 4.1, 5.6 ppm. The signal at 9.5 ppm for amid in drug, the broad and weak signal at 12.56 ppm for carboxylic acid group of (drug) and the signal at 12.36 ppm for amid group. ^{13}CNMR of compound [D_3]: (125MHz, δ, ppm) spectrum of compound [D_3], showing the flowing signals: The alpha- carbon signal at 19.76 ppm, aromatic carbons at the range of 115.17-128.50 ppm. The maleimide double bond carbon appeared at 138.62 ppm, the carbon attached to beta-lactam appeared at 164.74 ppm, the carbonyl for amid of (drug) signal at 163.94 ppm, the signal at 161.74 ppm attributed to maleimide carbonyl and the signal at 169.795 ppm assigned to the amide carbonyl carbon.

Characterization of Compound [D_4]:

Chemical Formula: $C_{29}H_{25}FN_5O_7$, Color: Light yellow, (85% Yield, mp 250-252 °C). FT-IR (cm^{-1}) spectrum of compound [D_4] shows the broadband at 3441 cm^{-1} corresponds to the carboxylic acid of the medication Ciprofloxacin's hydroxyl group, while 3138 and 3038cm^{-1} respectively contained the (=C-H) maleimide and aromatic system. In addition, the spectrum reveals the stretching of methylene groups and aliphatic (C-H) at 2939 cm^{-1}, respectively, whereas the maleimide carbonyl, carboxylic acid carbonyl, and conjugated ketone of quinolinone emerged at 1743, 1679, and 1606 cm^{-1}, respectively(6). Other bands might be seen at 1367 cm^{-1} (C-N), 1264 cm^{-1} (C-F), and 1539-1400 cm^{-1} (C=C, aromatic).^{1}HNMR of compound [D4]: show the presence of the cyclopropyl protons' signals at 1.11 ppm (d, 4H, 2-CH2-, cyclopropyl ring), 4.84ppm for (-CH2-), 4.446 ppm (m, 1H, cyclopropyl ring), and 3.49 and 3.84 ppm (piprazine ring). The signals of maleimide (CH=CH), protons appeared at 7.052, 7.173 (s, 1H, Ar-H, quinolinone), 8.00 (s, 1H, Ar-H, quinolinone), 7.39 and 7.59 (d, 2H, benzene), 8.838 (s, 1H, vinylic proton) and broad signals at 14.24 attributed to carboxylic acid hydroxyl. ^{13}CNMR of compound [D_4]: shows different signals for different carbons as follows: the presence of the cyclopropyl carbons' at 7.7 ppm, and the signal of (-CH_2-) at 64.80 ppm. The signals of aromatic carbons appeared at the range 103.18-152.48 ppm and the maleimide double bond carbons resonated at 165.81 ppm. The signal at about 169.08 ppm belongs to the carbon amide group while the signal at 177.00 ppm belongs to the carbons of the carboxylic acid group.

Characterization of Homo-Polymer [D_5]:

Color: Light Brown, M.Wt= 13068.8. FT-IR of the Homo-polymer [D_5] show strong stretching frequencies for, the aromatic appeared at 3086 cm-1, the band at 2915, 2879 cm-1 are assigned to aliphatic C-H stretching vibration of methyl groups. The amide carbonyl groups at 1712, and 1635 cm-1, and showing characteristic stretching bands at the range of 1764cm-1 due to beta lactam carbonyl and broad absorption band of carboxyl groups in drug structures around ~3500-2500 cm-1 (190). The ^{1}H-NMR of Homo-polymer [D_5] shows the appearance of new broad bands at about (2.72) ppm belonging to the polyimide and the disappearance of the maleimide (HC=CH) protons signal (7.87 ppm). The beta-lactam proton appeared at about 4.53-5.41ppm. The amide (Ar CO-NH-) protons appeared at 9.83, and 10.689 ppm and the carboxylic proton appeared at a broad weak peak around 12.30 ppm. This indicates the success of the polymerization of this monomer besides that during the polymerization, the imide and beta-lactam ring remained intact.

Characterization of Homo-Polymer [D_6]:

Color: Red, M.Wt=8125.3. FT-IR spectrum of the [D_6] showed different bands. A band was observed at 3512 cm^{-1} due to COOH, and a band was observed at 3047 and 3037 cm^{-1} due to =C-H of aromatic rings, 2999 and 2949 cm^{-1} due to stretching vibrations of the aliphatic groups. In addition, a band was observed at 1716 cm^{-1} due to C=O

in the imide ring, and at 1647 cm^{-1} due to C=C-C=O, Quinolinone and amid carbonyl. The stretching vibration of the aromatic system was observed at 1557- 1442 cm^{-1}, the band at 1386 cm^{-1} belongs to C-N stretching, and the band at 1259 cm^{-1} due to (C-F) stretching vibration. ^{1}H-NMR of Homo-polymer [D_6]: shows different chemical shifts, a peak at 1.36 ppm belonging to the methylene protons of cyclopropyl ring. Doublet Peak for aliphatic -CH_2- the of protons at about 2.50ppm, while the single proton of this ring appeared as multiplet signal at 4.10 ppm, two peaks at 3.14 and 3.61 for polysuccinimide protons, the peaks at 3.70 for the protons of piprazine ring, and the signal at the range 4.50-4.86ppm to the -CH_2- protons. The two protons of the aromatic fused ring appeared at 7.01 and 8.01 ppm, while the aromatic protons of the meta-di-substituted benzene ring appeared at 7.43-7.92 ppm.

Table 1: Physical properties of prepared monomers [D_1, D_2, D_3, and D_4)**.**

Comp.	Colour	Yield (%)	m.p.°C	R_f
D_1	Orange	90%	183-185°C	0.45 1hexane:3ethylacetate
D_2	Yellow	85%	210-212°C	0.56 1hexane:3ethylacetate
D_3	Brownish Yellow	80%	98-100 °C	0.3 1hexane : 3acetone
D_4	Light yellow	85%	250-252°C	0.62 1hexane : 3acetone

In addition, the chemical structures of all prepared compounds were characterized by elemental analysis (CHNS) techniques and the data presented in Table 2.

Table 2: (C.H.N.S) Elementary analysis of the monomers D_3, and D_4.

Comp.	Calculated %				Found %			
	C	H	N	S	C	H	N	S
D_3	45.97	3.23	16.08	12.27	44.8	2.91	14.5	11.25
D_4	62.14	4.50	10	-	61.12	4.0	8.77	-

Solubility:

It was examined how the synthesized monomers and polymers dissolved in various solvents, including water, ethanol, $CHCl_3$, methanol, ether, toluene, DMSO, hexane, and DMF. The statistics on solubility are shown in Table 3.

Table 3: Solubility of Synthesized Monomers and Polymers D_3-D_6**.**

Comp.	H_2O	EtOH	$CHCl_3$	MeOH	Ether	Toluene	DMSO	Hexane	DMF	Acetone
D_3	Partial	+	Partial	+	-	Partial	+	-	+	+
D_4	Partial	+	Partial	+	-	Partial	+	-	+	+
D_5	Partial	Partial	Partial	+	Partial	Partial	+	-	+	Partial
D_6	Partial	Partial	Partial	+	Partial	Partial	+	-	+	Partial

Swelling Ratio:

Organic polymer gels with chemical crosslinks are known as hydrogels. When placed in good solvents, or solvents with polymer affinity, such gels enlarge but do not dissolve. The gel is known as a hydrogel when water serves as the ideal solvent. Covalent bonds, as in the majority of synthetic gels, or Van der Waal forces and hydrogen bonds can be used to cross-link hydrogel (Salewska N,Boros-majewska J, *et al.*,2012). Hydrophilic monomers can be polymerized to produce homo-polymer hydrogels, respectively **.**

Dynamic swelling was assessed by gravimetric measures. In a beaker filled with 100 mL of water heated to 37°C, the polymeric samples were suspended. The hydrogel sample was taken out after five hours and five days, quickly wiped clear of surface water with filter paper, weighed (accuracy 0.0002), and then put back into the swelling solution. The swelling ratio of homo polymers is shown in Figures 1& 2.

Release of the Drug:

By using a UV-visible spectrophotometer, drug release from the prepared polymers was determined in two different buffer solutions (pH 2.2, and 8.0) at 37°C . . Figures 3-6 demonstrate the drug release from the synthesized polymer.

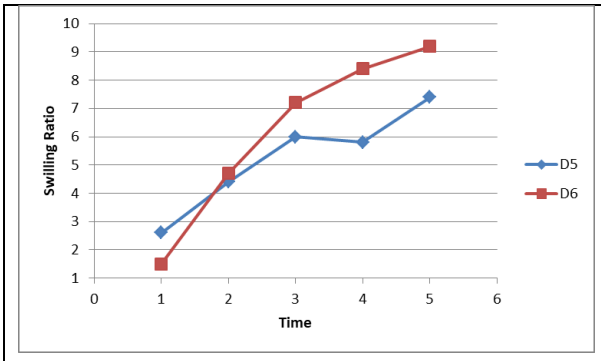


Fig. 1: The swelling ratio of homo polymer (D_5, D_6) in different hours at 37 °C

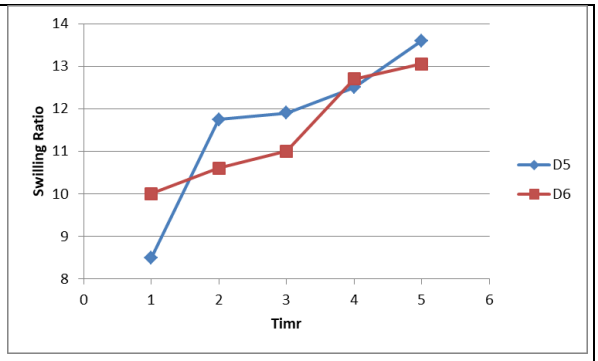


Fig. 2: The swelling ratio of homo polymer (D_5, D_6) in different days at 37 °C

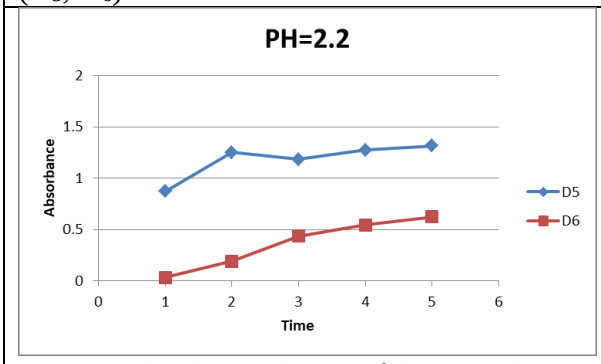


Fig. 3: The drug release of homo-polymer (D_5,D_6) in different hours in pH=2.2 at 37°C

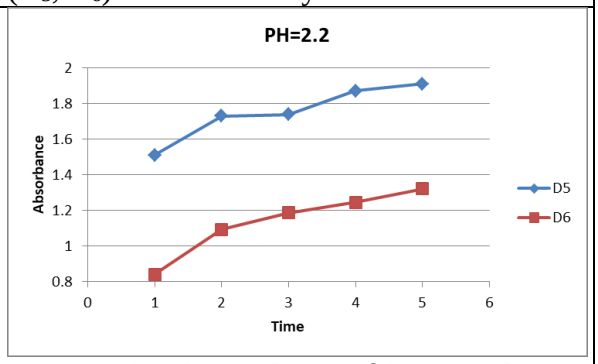


Fig. 4: The drug release of homo-polymer (D_5,D_6) in different days in pH=2.2 at 37°C

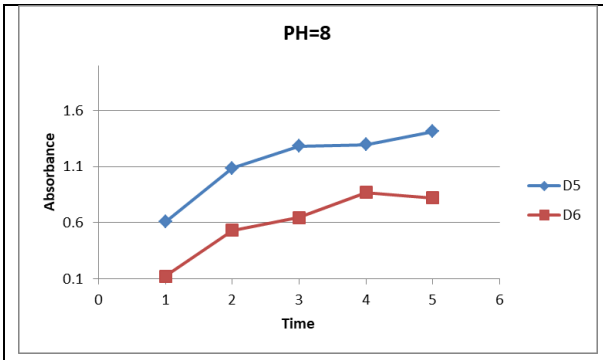


Fig. 5: The drug release of homo-polymer (D_5,D_6) in different hours in pH=8 at 37°C

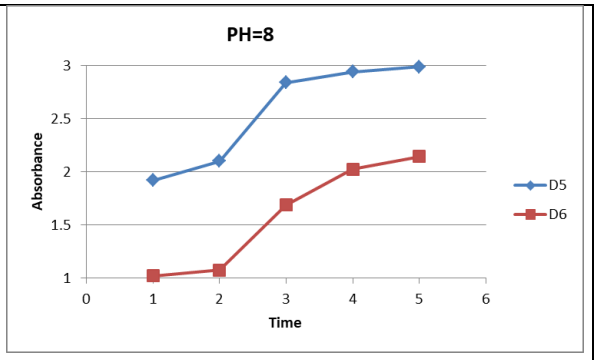


Fig. 6: The drug release of homo-polymer (D_5,D_6) in different days in pH=8 at 37°C

Maleimide-drug's Antibacterial Activity [D_3, D_4] Monomers:

Maleimides and moieties linked to them offer intriguing features, particularly when utilized as selective inhibitors of monoglyceride lipase (Dürüst Y, Karaku H , *et al.*,2012), as well as a number of other enzymes with reactive cysteinyl residues. Additionally, they were widely used for numerous biological applications such as cytotoxicity, DNA binding, and apoptosis-inducing action(Bhagare AM, Kardel A V, *et al.*,2020), antibacterial (Sabir S,*et al.*,2016), antiprotozoal (Mahle F ,*et al.*,2019), anti-inflammatory agents (Fan Yongxian ,*et al.*,2018)(Panov AA, *et al.*,2018), analgesics (Hasan.AF,*et al.*,2020)(Tabernilla A, *et al.*,2021), anti-tumor (Ahmed A, *et al.*,2022).

Additionally, due to the synergistic effect, mixing maleimide derivatives with some effective medications may change their biological properties. Table 4 lists the synthesized monomers' and their drug-loaded counterparts' antibacterial activity.

Synergistic Effects:

A situation in which the combined effects of two chemicals are greater than expected**.**

An antagonist effect:

It occurs when two or more agents work together to produce a result that is less favorable than the sum of their separate effects.

Table 4: Antibacterial activity of compounds [D_3,D4] at concentration 0.5 mg/mL

Inhibition Zone for *Staph. Coccus* of Maleimide		**Inhibition Zone for *Staph. Coccus* of Drug**		**Inhibition Zone for *E. Coli* of Maleimide**	**Inhibition Zone for *E. Coli* of Drug**
D_3	35	Ceftriaxone	30	25	20
D_4	30	Ciprofloxacin	35	30	22
DMSO	0	DMSO	0	0	0

The disk-diffusion method was used to test the antibacterial activity against pathogenic strains of Escherichia coli and Staphylococcus aureus using a solution of 0.5 mg from each chemical and each loaded medication for comparison in 1 mL of DMSO. Additionally, the DMSO activity was examined as a negative control, which demonstrates no reduction of bacterial growth.

The antibacterial activity against Gram-positive (*Staphylococcus aurous*) bacteria results in a synergistic effect for (D_3, D_4) compounds, increasing their antibacterial activity (inhibition zone) in comparison to the matching loaded medicines. However, compared to loaded medicines, maleimide derivatives exhibit greater action against Gram-negative (*E. coli*) bacteria(Khanal LN,et al.2022). This is because the maleimide

moiety is lipophilic and neutral, allowing it to easily pass through biological membranes. Gram-negative bacteria have higher antibacterial activity against *E. coli* because their cell walls are composed of one or more layers of peptidoglycan and a lipid-rich outer membrane.

Antibacterial Activity of Polymers [D_5, D_6]:

Antibacterial activity of the Homopolymers [D5, D6] against pathogenic strains of Escherichia coli and Staphylococcus aurous was performed using the disk-diffusion method employing a solution of 0.5 mg from each polymer and each loaded medication for comparison in 1 mL of DMSO. Table -5 shows the inhibition zones for [D_5, D_6] and corresponding drugs

.

Table 5: Antibacterial activity of Homopolymers [D_5, D6] at concentration 0.5 mg/mL

Inhibition Zone for *Staph. Coccus* of polymer		**Inhibition Zone for *Staph. Coccus* of Drug**		**Inhibition Zone for *E. Coli* of polymer**	**Inhibition Zone for *E. Coli* of Drug**
D_5	40	Ceftriaxone	30	30	20
D_6	20	Ciprofloxacin	35	30	22
DMSO	0	DMSO	0	0	0

The prepared homo-polymer D5 showed higher antibacterial activity toward the tested (*Staph. Coccus*) bacteria, So, if we study the biological activity after drug release on polymers at different time intervals, we may get strong evidence and may also support the idea of the safety of polymer drugs before drug release. On the other hand, when we compare the single polymer with the two bacterial strains, the results in Table 5 show that the activity of some homopolymers toward Gram-negative bacteria is higher than their counterparts. than drugs and monomers, the reason may be that the pendent drug molecules are bound in a way that prevents them from sticking to the cell wall.

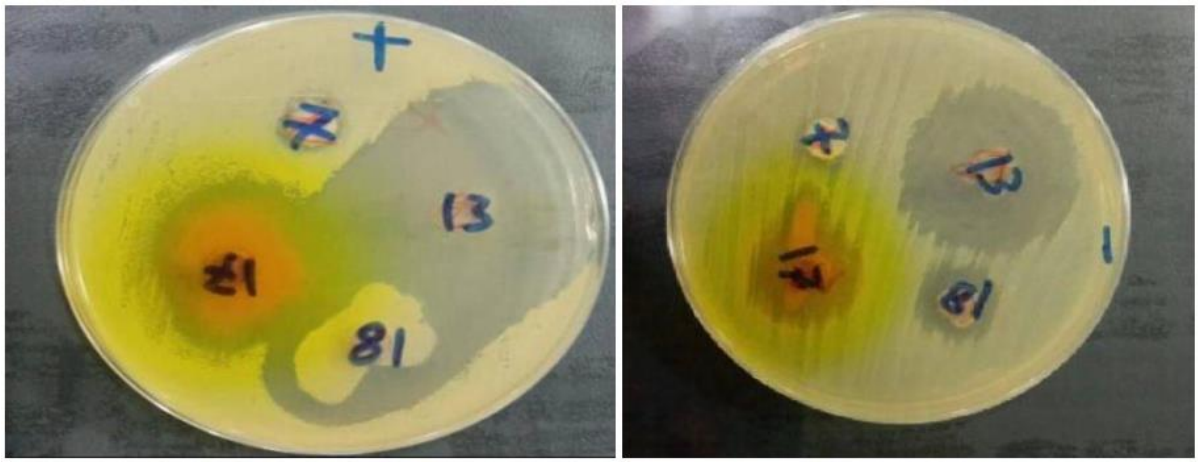


Fig. 7: Images of Petri dishes of antibacterial for synthesized monomers and polymers.

Conclusion

This study includes a reaction between maleic anhydride and 4-aminophenol to create a chemical (D_1). Then compound (D_1) was converted to maleimide phenol acetic acid ether (D_2) which was then transformed into an acyl chloride derivative. Additionally, amino Drugs (Ceftriaxone, Ciprofloxacin) are treated with acyl chloride derivative to produce (D_3,D_4) monomers (Target polymers were created by reacting a base material with Homogeneous polymers (D_5, D_6) prepared through Free radicals from the monomers (D_3,D_4) are polymerized under

nitrogen using benzoyl peroxide as an initiator. Each of the created monomers and polymers was characterized using FT-IR, ^{1}H NMR, and ^{13}C NMR spectral analysis. The controlled drug release and swelling percentage tests were carried out at a temperature of 37°C. Since different polymers have different swelling percentage values, the release of the medication may be a factor in this difference. Additionally, it was shown that the process of a medication being released in a basic medium (pH=8.0) is faster than in an acidic medium (pH=2.2).

Declarations:

Ethical Approval:Ethical Approval is not applicable.

Competing interests: The authors declare no conflict of interest.

Authors Contributions:I hereby verify that all authors mentioned on the title page have made substantial contributions to the conception and design of the study, have thoroughly reviewed the manuscript, confirm the accuracy and authenticity of the data and its interpretation, and consent to its submission.

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