Synthesis and Antimicrobial Activity of Metronidazole Containing Polymer and Copolymers

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ABSTRACT: Homopolymer and copolymers containing metronidazole (MTZ) drug were synthesized. Acryloyl chloride was reacted with MTZ (drug) to produce monomer containing MTZ, and then the monomer was copolymerized with various amounts of methyl methacrylate. The produced monomer, homopolymer, and copolymers were characterized by elemental analysis, IR, and ^{1}H-NMR. The antimicrobial activities of the synthesized polymers were tested against *Kelpsilic* as fungal organisms, and *Escherichia coli*, *Bacillus subitilus,* and *Pesudomonus areuginosa* as bacteria organisms.
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Key words: antimicrobial polymers; metronidazole; copolymers; biocide

INTRODUCTION

Recently, much attention has been paid to the problems of environmental pollution and health. Infection by pathogenic micro-organisms is of great concern in many fields, particularly in medical devices, drugs, health care products and hygienic applications, water purification systems, hospital and hospital furniture, dental surgery equipment, textiles, food packaging, and food storage, etc.[1] Pathogenic micro-organisms have caused great harm to human beings for a long time. According to the statistical result of World Health Organization in 1996, there were 52 million people died in 1995 in the world and one third of them, 17 million, were died from contagious bacteria.[2]

To get rid of these pathogenic bacteria, one has to use antimicrobial agents, also called biocides, which are materials capable of killing or inhibiting the growth of pathogenic microorganisms.[3] Low molecular weight biocides are used for sterilization of water, as antimicrobial drugs, for soil sterilization, etc. However, low molecular weight antimicrobial agents suffer from many disadvantages, such as toxicity to the environment and short-term antimicrobial ability. Also, the activity of all these compounds is temporary and thus requires repeated applications for a long time biocide effect.

To overcome problems associated with the low molecular weight antimicrobial agents, it is urgent to develop the antibacterial and antifungal agents capable of killing harmful microorganisms with a permanent or longer antimicrobial activity. The best candidates for these requirements are the antimicrobial polymers. The use of antimicrobial polymers offers promise for enhancing the efficacy of some existing antimicrobial agents and minimizing the environmental problems accompanying conventional antimicrobial agents by reducing the residual toxicity of the agents, increasing their efficiency and selectivity, and prolonging the lifetime of the antimicrobial agents.[1,4] Meanwhile, antimicrobial polymers have also attracted considerable research interests due to their nontoxicity and nonirritant properties with the improved and prolonged antimicrobial activities, compared with the ordinary low-molecular weight antibacterial agents.[5–11]

Antimicrobial materials have been developed as new ecological functional materials to meet the challenges. There have been many studies on antibacterial plastics, antibacterial fibers,[12,13] and antibacterial ceramics.[14] The continuous search for potential antimicrobial agents has lead to identification of antimicrobial biomaterials that are based on polymers or their composites.

Various types of biocidal polymers have been described previously; polymers containing quaternary nitrogen atoms,[15–18] polymers containing phosphonium salts (polymeric phosphonium materials),[19,20]

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pyridinium cations,[7] and *N*-halamine polymers.[21–25] Guanidine polymer is another series of polymer bearing guanidio groups mainly used as antimicrobial agents.[26–28]

In this work, we report the development of new polymers with antimicrobial activity. This was achieved by modification of acryloyl chloride with metronidazole drug (MTZ) to produce monomer containing MTZ drug. The monomer was copolymerized with different ratio of methyl methacrylate (MMA) to produce different ratio of copolymers with the suitable active functional group. The antimicrobial activities of the synthesized polymers were tested against *Kelpsilic* as fungal organisms, and *Escherichia coli*, *Bacillus subitilus,* and *Pesudomonus areuginosa* as bacteria organisms.

EXPERIMENTAL SECTION

Materials

MTZ was purchased from Aldrich (Milwaukee, WI) and was used as received without further purification. Acryloyl chloride was purchased from Aldrich and was used as received without further purification. Triethyl amine (TEA) was purchased from Merck-Schuchardt (Hohenbrunn, Germany) and was distilled and dried before use. Benzoyl peroxide was purchased from Aldrich and was used as received. Chloroform was purchased from Aldrich and dried from over calcium chloride and distilled before use. MMA was purchased from Aldrich and was de-inhibited before use.

Instruments

Infrared spectra were recorded from KBr pellets on a Perkin–Elmer 1430 ratio recording infrared spectrophotometer (Wellesley, MA).

Elemental analyses were recorded on Perkin-Erlmer 2400.

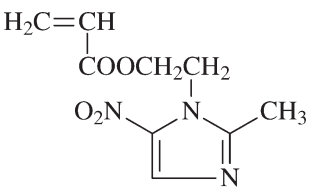
Nuclear Magnetic Resonance spectrum (^{1}H-NMR) were recorded on Varian 300 M, Mercury-oxford, and on a Jeol JNM-PM X90 SI NMR spectroscopy.

Rotary Evaporator was supplied from Buchi (Switzerland).

Monomer synthesis

Modification of acryloyl chloride with MTZ

To a solution of MTZ (5 g, 29.2 mmol) in 200 mL dry chloroform, 5 mL dry TEA was added. The mixture was cooled in an ice-salt bath and the acryloyl chloride (2.6 g, 2.3 mL, and 29.2 mmol) was added dropwise with cooling and stirring. The HCI that accumulated at the top of the reactor flask was removed via vacuum from a water aspirator. The reaction mixture was stirred overnight at room temperature for 1 day. The product was filtered off to remove the precipitated TEA hydrochloride salt. The solution was washed with 1*M* hydrochloric acid solution (2 × 200 mL), 1*M* sodium hydroxide solution (3 × 200 mL), saturated sodium chloride solution (2 × 200 mL), and washed with dry ethyl acetate and dry diethyl ether. The chloroform was evaporated on rotary evaporator and the product was filtered off and washed with dry ethyl acetate. The monomer (**I**) was yellow powder and the yield was 5 g (77%). The product (**I**) was characterized by elemental microanalysis and IR spectroscopy as shown in Tables I and II, respectively. It was also characterized by ^{1}H-NMR spectra (Fig. 1).

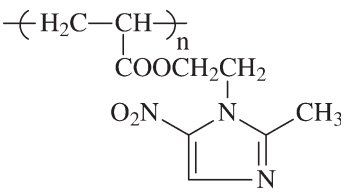


(I)

Polymer synthesis

Homopolymerization of MTZ monomer (I)

To a solution of MTZ monomer (0.6 g, 2.6 mmol) in 75 mL dry chloroform, benzoyl peroxide (0.1 g) was added. The system was stirred and refluxed in an oil bath at 90°C for 12 h. The chloroform was evaporated on rotary evaporator; the product was filtered off and washed with ethyl acetate. The polymer (**II**) yield was 0.5 g (83%), and it was characterized by elemental microanalysis and IR spectroscopy as shown in Tables I and II, respectively.



(II)

TABLE I
Elemental Analysis of Metronidazole Monomer (I) and its Copolymers

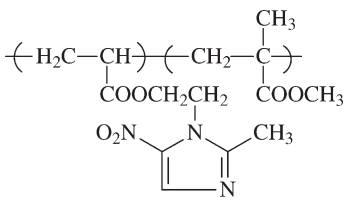
	C%		H%		N%	
Compound	Calc.	Found	Calc.	Found	Calc.	Found
I	48	44.44	4.88	3.99	18.66	18.45
II	48	46.39	4.88	5.54	18.68	17.27
III	51.69	45.56	5.84	7.84	12.92	12.38
IV	53	52.87	6.35	5.13	9.88	8.00
V	54.85	52.87	6.66	6.10	8	6.21
VI	54.68	48.23	6.88	7.99	6.72	6.75
VII	50	44.54	5.45	5.07	15.27	16.76
VIII	49.5	44.56	5.29	7.70	16.25	15.43
IX	44	40.31	4.7	4.34	15.27	14.44

TABLE II
IR. Analysis of Metronidazole Monomer (I) and its Copolymers (cm^{-1})

Compound	COOR C=O	COOR C—O	CH aliphatic	CH_3	—C=C—N	C—NO_2	—C=N—
I	1727	1261	2973	2924	1633	827, 1373, 1529	1460
II	1727	1266	2933	2741	1628	858, 1367, 1533	1474
III	1728	1266	2934	2798	1614	861, 1367, 1534	1476
IV	1727	1266	2943	2849	1614	862, 1366, 1534	1476
V	1728	1267	2930	2857	1615	861, 1368, 1533	1475
VI	1728	1266	2945	2846	1630	863, 1367, 1533	1475
VII	1728	1267	2933	2800	1630	819, 1367, 1534	1475
VIII	1728	1267	2934	2795	1629	861, 1367, 1533	1475
IX	1727	1268	2934	2934	1599	837, 1318, 1533	1459

Copolymerization of MTZ monomer (I) with MMA (1 : 1)

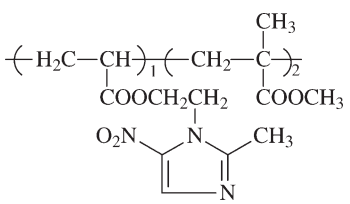
To a solution of MTZ monomer (I) (1.25 g, 5.5 mmol) in 100 mL dry chloroform, benzoyl peroxide (0.23 g) and MMA (0.55 g, 0.58 mL, 5.5 mmol) was added. The reaction mixture was stirred and refluxed in an oil bath at 90°C for 12 h; the chloroform was evaporated on rotary evaporator. The product was filtered off and washed with ethyl acetate. The polymer (**III**) yield was 1.4 g (77.7%), and it was characterized by elemental microanalysis and IR spectroscopy as shown in Tables I and II, respectively.



(III)

Copolymerization of MTZ monomer (I) with MMA (1 : 2)

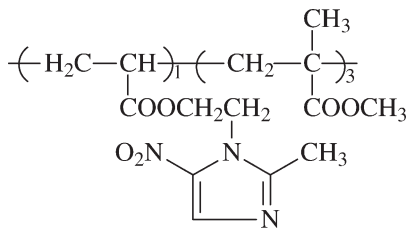
To a solution of MTZ monomer (0.6 g, 2.7 mmol) in 50 mL dry chloroform, benzoyl peroxide (0.11 g) and MMA (0.54 g, 0.57 mL, 5.4 mmol) was added. The mixture was stirred and refluxed in an oil bath at 90°C for 12 h. The chloroform was removed on rotary evaporator. The product was filtered off and washed with ethyl acetate. The polymer (**IV**) was 0.89 g (70.8%), and it was characterized by elemental microanalysis and IR spectroscopy as shown in Tables I and II, respectively.



(IV)

Copolymerization of MTZ monomer (I) with MMA (1 : 3)

To a solution of MTZ monomer (0.6 g, 2.7 mmol) in 50 mL dry chloroform, benzoyl peroxide (0.1 g) and MMA (0.8 g, 0.86 mL, 8.1 mmol) was added. The mixture was stirred and refluxed in an oil bath at 90°C for 12 h. The product was filtered off and washed with ethyl acetate and dried under vacuum at 30°C. The polymer (**V**) yield was 0.89 g (70.8%), and it was characterized by elemental microanalysis and IR spectroscopy as shown in Tables I and II, respectively.



(V)

Copolymerization of MTZ monomer (I) with MMA (1 : 4)

To a solution of MTZ monomer (1.25 g, 5.5 mmol) in 100 mL dry chloroform, benzoyl peroxide (0.23 g) and MMA (2.37 mL, 2.22 g, 22 mmol) was added. The mixture was stirred and refluxed in an oil bath at 90°C for 12 h. The product was filtered off and

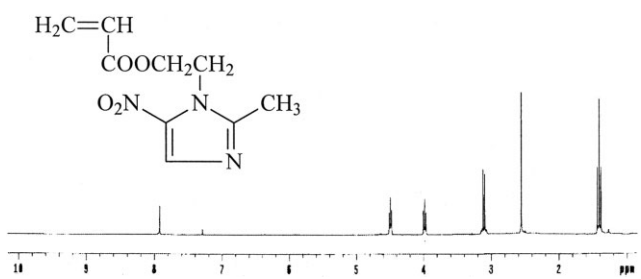
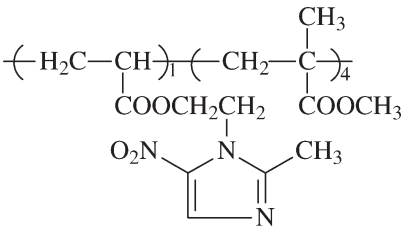


Figure 1 ^{1}H-NMR spectrum for (I).

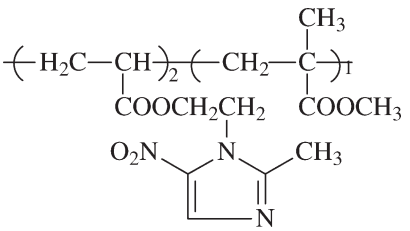
washed with ethyl acetate. The polymer (**VI**) was 1.5 g (44%), and it was characterized by elemental microanalysis and IR spectroscopy as shown in Tables I and II, respectively.



(VI)

Copolymerization of MTZ monomer (I) with MMA (2 : 1)

To a solution of MTZ monomer (0.45 g, 2 mmol) in 37 mL dry chloroform, benzoyl peroxide (0.08 g) and MMA (0.1 g, 0.1 mL, 1 mmol) was added. The mixture was stirred and refluxed in an oil bath at 90°C for 12 h. The product was filtered off and washed with ethyl acetate. The polymer (**VII**) was yellow crystals 0.49 g (40%), and it was characterized by elemental microanalysis and IR spectroscopy as shown in Tables I and II, respectively. ^{1}H-NMR spectrum as shown in Figure 2.



(VII)

Copolymerization of MTZ monomer (I) with MMA (3 : 1)

To a solution of MTZ monomer (1.35 g, 6 mmol) in 100 mL dry chloroform, benzoyl peroxide (0.26 g) and MMA (0.2 g, 0.2 mL, 2 mmol) was added. The mixture was stirred and refluxed in an oil bath at 90°C for 12 h. The product was filtered off and washed with ethyl acetate and dried under vacuum at 30°C, and it was characterized by elemental microanalysis and IR spectroscopy as shown in Tables I and II, respectively.

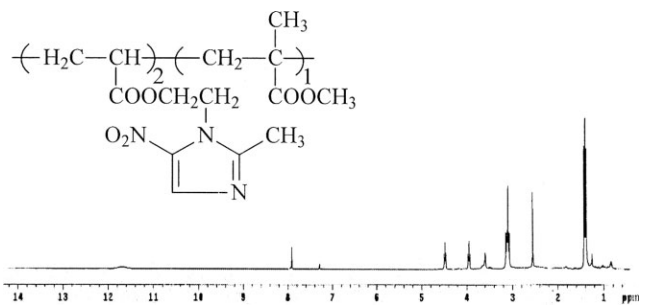
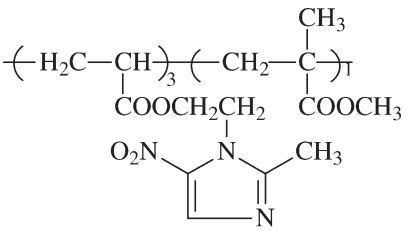


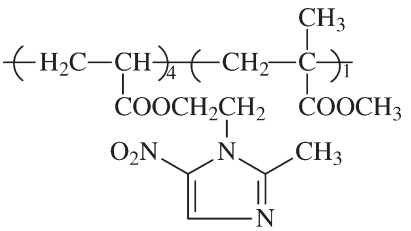
Figure 2 ^{1}H-NMR spectrum for (VII).



(VIII)

Copolymerization of MTZ monomer (I) with MMA (4 : 1)

To a solution of MTZ monomer (0.45 g, 2 mmol) in 37 mL dry chloroform, benzoyl peroxide (0.08 g) and MMA (0.05 g, 0.053 mL, 0.5 mmol) was added. The mixture was stirred and refluxed in an oil bath at 90°C for 12 h. The product was filtered off and washed with ethyl acetate. The product was collected as yellow crystals and characterized by elemental microanalysis and IR spectroscopy as shown in Tables I and II, respectively.



(IX)

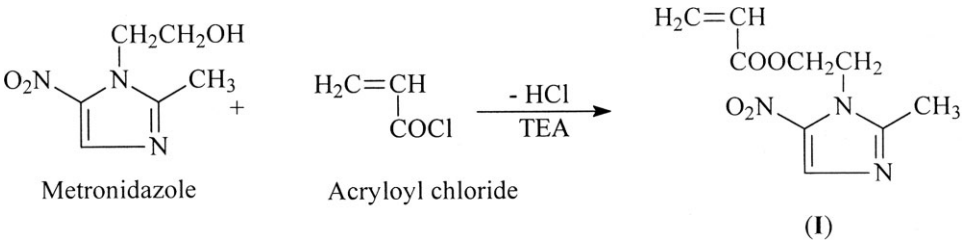
Antimicrobial assessment

Test microorganisms

These included the gram-negative bacteria, *Escherichia coli*, *Kelpsilic*, *Pesudomonus areuginosa*, and gram-positive bacteria *B. subitilus*. The bacteria strains were maintained on nutrient agar and nutrient broth.

Antimicrobial activities

The antimicrobial spectrum of the prepared polymers bearing an active functional group compounds were determined against the tested organisms on powdered samples on nutrient agar which contained per liter: 3 g peptone; 5 g NaCl; 5 g beef extract; 20



Scheme 1 Synthetic route of modified metronidazole (I).

g agar. The assay were seeded and filled with 20 mg powder synthetic polymer for the tested bacteria, after solidification, then incubated at 37°C for 24 h, after which the diameter of the inhibition zones were measured and the polymers, which produced the highest inhibition zone was further assayed at different concentration to quantify its inhibitory effect.

Minimal inhibitory concentrations

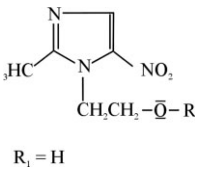
The minimal inhibitory concentrations (MICs) of the synthetic polymers against the tested microorganisms were determined by agar dilution method. The media used were nutrient broth medium for bacteria. Each culture medium was enriched with different concentrations (1.5, 3, 6, 12, 16, 20, and 24 mg/mL) of this polymers, prepared from 0.5 mL of each standard organisms suspension was mixed with 9.5 mL of diluted corresponding media in sterile test tube contained the tested polymer to give (1.5, 3, 6, 12, 16, 20, and 24 mg/mL). The results were recorded after 24 h for the tested bacteria. Number of living colonies or colony forming unit/milliliter was counted using the bioassay method. The subinhibitory concentration (sub-MICs) was used in studying the mode of action of the experimental polymer.

Toxicity test

Cell toxicity of the synthetic polymer was recorded using Brine shrimp lethality bioassay.[29] The cytotoxicity of polymer was determined by use *Artemia* for this test. Brine shrimp *Artemia* has been used for over 30 years in toxicologic studies because they provide a quick, inexpensive, and desirable alternative to testing on large animals. It is known that a positive correlation exists between *Artemia* lethality and human carcinoma cytotoxicty. In addition, Brine shrimp is used in many Prescreens for potential antitumor activity.

RESULTS AND DISCUSSION

MTZ, 2-methyl-5-nitroimidazole-1-ethanol, is a nitroimidazole derivative with activity against anaerobic protozoa, aerobic and microaerophilic bacteria. It has a heterocyclic structure consisting in imidazole-based nucleus with a nitro group in position 5.[30]

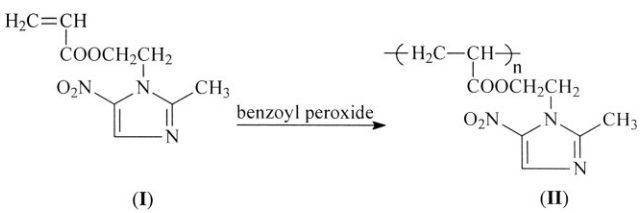


MTZ is the most used drug in the treatment of anaerobic protozoan parasitic infections caused by *E. histolytica* (amoebiasis), *T. vaginalis* (trichomoniasis), and *G. lambdia* (giardiasis), and anaerobic bacterial infections caused by *B. fragilis*, *B. melaninogenicus*, *Selenomonas*, *Clostridium*, *Peptostreptococcus*, and *Peptococcus*.[31]

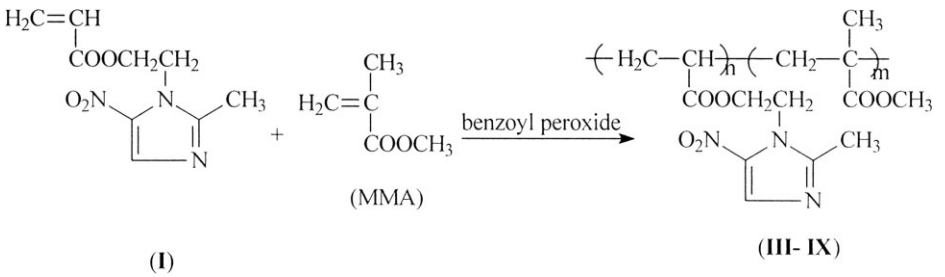
Once that MTZ enters the bacterial cell, the nitrogroup is reduced by low-redox potential electron transport proteins (such as ferrodoxin), giving a product that binds covalently to guanine and cytosine and produces single- and double-stranded DNA breaks during enzymatic degradation.[32–36]

Common adverse effects of MTZ involve the gastrointestinal tract and the neurological system with high doses. Therefore, reduction of side effects of MTZ (plasma peak levels) while prolonging its action by using controlled oral dosage forms is highly desirable.[37] This could be achieved by the attachment of the drug to a polymeric material.

Based on these general properties we prepared Polymer-MTZ conjugates using either homopolymer or copolymers with various compositions. The obtained products antimicrobial activities were investigated.



Scheme 2 Synthetic route of homopolymer from modified metronidazole (II).



Scheme 3 Synthetic route of co-polymer from modified metronidazole (I) and methyl methacrylate MMA.

Modification of acryloyl chloride with MTZ

MTZ was reacted with acryloyl chloride in the presence of dry TEA as an acid acceptor in dry chloroform under anhydrous condition. The MTZ drug of (I) is attached directly to the polymer main chain. The only precaution, here, is the control of the temperature in the first few hours as known for the reactions of the acryloyl chloride. The product washed with HCl solution then with saturated sodium chloride solution to remove TEA salt, and then was washed with dry ethylacetate and dry diethyl ether. The monomer was collected as yellow fine powder as shown in Scheme 1.

The elemental analysis of modified meternidazol (**I**) was in a good agreement with the calculated values as shown in Table I. Thus, indicated high percent of conversion to the modified drug derivatives (cf. Scheme 1). The same conclusion was confirmed from the infrared studies. The IR spectrum of the product (**I**) as in Table II showed strong band appeared at 1727 cm^{-1} region for C=O in (COOR), 1633 cm^{-1} for C=C in (C=C—N), 2924 cm^{-1} for CH_3, 2973 cm^{-1} for C—H aliphatic, the strong absorption band appearance at 1460 cm^{-1} for C=N and a peak at 1633 cm^{-1} due to C=C. The characteristic bands of the IR spectra of the monomer (**I**) are listed in Table II.

As shown in Figure 1, the ^{1}H-NMR spectrum of the product (I) showed singlet signal at $\delta = 7.9$ ppm (CH of imidazole ring), triplet signals at 3.99 ppm, 4.5 ppm (CH_2, CH_2), doublet signals at 3.1 ppm (CH_2), singlet signal at 2.55 ppm (CH_3), and triplet signal at 1.4 (CH).

Homopolymerization of MTZ monomer

The monomer (I) is easily homopolymerized by free radical techniques in dry chloroform at 90°C for 24 h utilizing benzoyl peroxide as the initiator. The initiator concentration was 0.18 mol %.

After removing the unreacted materials and the produced TEA salt, the chloroform was removed by rotary evaporator and the product washed with ethylacetate, the homopolymer was collected as yellow fine powder. The reaction is as outlined in Scheme 2.

The homopolymer (**II**) was characterized by elemental microanalysis and the data was tabulated in Table I and it was in good agreement with the calculated values, thus indicated high percent of conversion of the monomer to polymeric drug derivatives (cf. Scheme 2). The characteristic bands of the IR spectrum of the homopolymer (**II**) was as listed in Table II which showed strong band at 1727 cm^{-1} due to C=O, and strong absorption band at 1474 cm^{-1} due to C=N group, 2933 cm^{-1} due to C—H aliphatic, 2741 cm^{-1} due to CH_3 and the disappearance of CH_2=CH group at 1696 cm^{-1} which confirmed the polymerization.

Copolymerization of MTZ monomer (I) with MMA

Copolymers of MTZ monomer with MMA (Scheme 3) were prepared by free radical techniques in chloroform at 90°C utilizing benzoyl peroxide as the initiator. The initiator concentration was 0.18 mol %. Copolymers were synthesized by varying the drug monomer content ratio to vary the hydrophilic/hydrophobic nature.

TABLE III
Diameters of Inhibition Zones (mm) Produced by Monomeric and Polymeric Drug Against Various Bacteria

Test organisms/ polymer code	Inhibition zone diameter (mm)								
	I	II	III	IV	V	VI	VII	VIII	IX
E. coli	9.0	5.0	30.0	40.0	30.0	30.0	30.0	40.0	35.0
B. subitilus	23.0	10.0	0.00	10.0	0.00	25	0.00	0.00	0.00
Kelbsiella	10.0	10.0	0.00	40.0	20.0	9.00	0.00	0.00	0.00
P. aeruginosa	10.0	10.0	0.00	23.0	20.0	15.0	0.00	0.00	0.00

TABLE IV
The Ratio of Surviving Cell Numbers of Some Bacterial in the Presence of the Polymer (VI)

Test organisms	Polymer concentrations (mg/mL)							
	0	1.5	3	6	12	16	20	24
E. coli	1	0.86	0.62	0.46	0.16	0.08	0.00	0.00
B. subitilus	1	0.91	0.71	0.65	0.49	0.33	0.24	0.18
Kelbsiella sp	1	0.87	0.62	0.46	0.26	0.13	0.06	0.00

These compounds were prepared to examine the effect of different ratio of MMA and metronidazol monomer (**I**) on the antimicrobial activity, a series of polymer with different ratio of MMA and another series of polymer with different ratio of monomer (**I**).

The copolymers washed with ethylacetate and were collected as yellow fine powder as shown in Scheme 3. The resulting polymers (**III–IX**) were used in the biological evaluation experiments.

The copolymers (**III–IX**) were characterized by elemental microanalysis and the data was tabulated in Table I and its in good agreement with the calculated values, the characteristic bands of the IR spectra of the copolymers (**III–IX**) showed strong bands at 1727–1728 cm^{-1} due to C=O group, strong absorption bands at 1431–1476 cm^{-1} due to C=N and 2930–2945 cm^{-1} due to C—H aliphatic as shown in Table II.

^{1}H-NMR spectrum of polymer (**VII**) (Fig. 2) showed singlet signal at 7.9 ppm (CH of imidazole ring), triplet signals at 3.9 ppm, 4.49 ppm (CH_2, CH_2), singlet 0.9 ppm (CH_3), singlet signal 1.2 ppm (CH_3 in OCH_3-singlet), singlet 2.5ppm (CH_3), triplet 1.4 ppm (CH), multiplet 3.1 ppm (CH_2), and duplet 3.5 ppm (CH_2).

Antimicrobial activity of MTZ monomer (I) with MMA

The capability of different monomer ratio in the copolymer of the test bacteria on solid medium to inhibit the growth is as shown in Table III. It was found that the diameter of inhibition zone varied from copolymer to another according to the copolymer composition and the tested microorganism. The copolymer (**VI**) was the inhibitoriest against bacteria and therefore was selected for further investigations (diameters of inhibition zones ranged between (5 and 40 mm) after 24 h of incubation. This polymer has not showed any antifungal activity.

The results showed in generally that all copolymers were effective against *E. coli*, whereas the monomer I and homopolymer II were less effective against *E. coli*. Polymer VI was also effective against *E. coli*, *B. subitilus*, *Kelbsiella*, and *P. aeruginosa*.

Antimicrobial assessment of polymer (VI)

The antimicrobial activities of (**VI**) derivatives against *B. subitilus*, *Kelbsiella*, *P. aeruginosea*, and *E. coli* were examined as described earlier.

The growth inhibiting effect was quantitatively determined by the ratio (M/C) of the surviving cell number and the results were tabulated in Table IV and represented in Figure 3, the growth inhibitory effect of polymer (**VI**) differed on different bacteria species. The results showed that the inhibitory effect

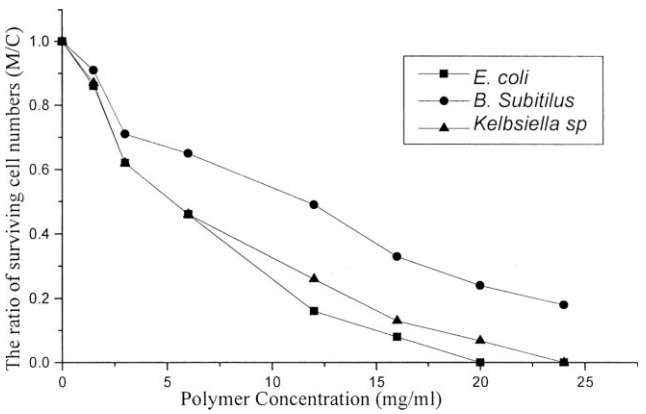


Figure 3 Growth inhibition of different concentrations of polymer (VI), the inoculation were 3×10^4 cells/ml. *E. coli*; 2×10^4 cells/ml *B. subitilus*; 2.9×10^4 cells/ml *Kelbsiella* sp.

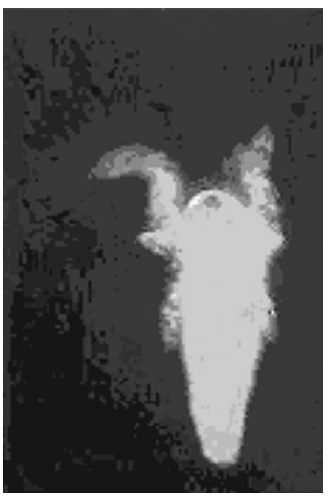


Figure 4 Artemia.

TABLE V
Lethal Dose of Polymer (VI)

Polymers	Concentration	0	10 ppm	100 ppm	1000 ppm
VI	Living *Artemia* %	100	100	100	80

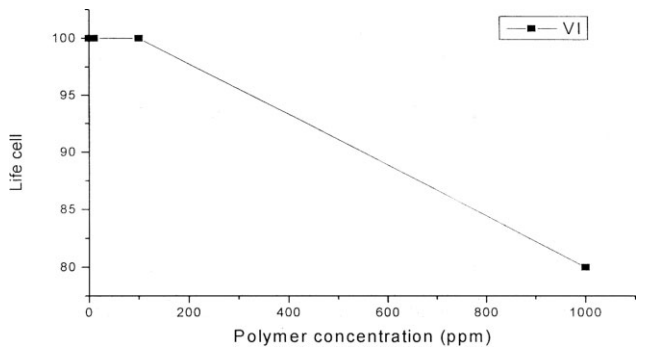


Figure 5 Lethal Dose of polymer (VI) on Artemia.

increased by increasing the concentration of the polymer.

Toxicity of polymer (VI) on *Artemia* (Fig. 4)

Brine shrimps lethality bioassay was for determination of LD_{50} of the synthetic polymer. Different concentration of 10, 100, and 1000 ppm in vials containing 5 mL of brine and 10 shrimp in each three replicates were used. Survivors were counted after 72 h. The results in Table V and Figure 5 clearly show that number of living *Artemia* was decrease by increasing the concentration of the polymer. The results show that the polymer at low concentration (10 and 100 ppm) did not affect on *Artemia*. In high concentration, the living *Artemia* is reduced to 80%. The substance not yielded the 50% dead; this means the compound under study was safe. The substance level was 1000 ppm but not exhibited the lethal dose.

CONCLUSIONS

New monomer was prepared by reaction Acryloyl chloride with MTZ. The MTZ containing monomer was copolymerized with various ratio of MMA aiming to study the effect of the copolymer microstructure on the antimicrobial properties of the copolymers. The antimicrobial activities of the synthesized polymers were tested against *Kelpsilic* as fungal organisms, and *Escherichia coli*, *Bacillus subitilus*, and *Pesudomonus areuginosa* as bacteria organisms. It was found that the antimicrobial activity is related to the polymer microstructure. In general, the polymers and copolymers showed antimicrobial activity against the tested microorganisms. However, the copolymer with 1 : 4 drug monomer : MMA ratio being the most effective on bacteria and fungi species. The cytotoxicity of copolymer VI was studied and the results showed that the copolymer was safe. The substance level was 1000 ppm but not exhibited the lethal dose.

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