Journal of Macromolecular Science, Part A
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597274

Radiation Synthesis and Characterization of Maleic Anhydride/Acrylic Acid Copolymers and Their Heterocyclic Compound Derivatives for Possible Uses as Antibacterial Agents

H. A. Abd El-Rehim[a]; T. B. Mostafa[b]; Abd El-Monem Bashindy[a]
[a] National Center for Radiation Research and Technology, Atomic Energy Authority, Nasr City, Cairo, Egypt [b] Chemistry Department Heliopolis, College For Women, Ain Shams University, Cairo, Egypt

To cite this Article El-Rehim, H. A. Abd , Mostafa, T. B. and Bashindy, Abd El-Monem(2005) 'Radiation Synthesis and Characterization of Maleic Anhydride/Acrylic Acid Copolymers and Their Heterocyclic Compound Derivatives for Possible Uses as Antibacterial Agents', Journal of Macromolecular Science, Part A, 42: 7, 853 — 867
To link to this Article: DOI: 10.1081/MA-200063124
URL: http://dx.doi.org/10.1081/MA-200063124

Journal of Macromolecular Science®, Part A: Pure and Applied Chemistry, 42:853–867, 2005

ISSN 1060-1325 print/1520-5738 online
DOI: 10.1081/MA-200063124

Radiation Synthesis and Characterization of Maleic Anhydride/Acrylic Acid Copolymers and Their Heterocyclic Compound Derivatives for Possible Uses as Antibacterial Agents

H. A. ABD EL-REHIM,[1] T. B. MOSTAFA,[2]
AND ABD EL-MONEM BASHINDY[1]

[1]National Center for Radiation Research and Technology, Atomic Energy Authority, Nasr City, Cairo, Egypt
[2]Chemistry Department Heliopolis, College For Women, Ain Shams University, Cairo, Egypt

Preparation and characterization of water-soluble maleic anhydride/acrylic acid (MAn/AAc) copolymer and its derivatives were studied for possible use as antibacterial agents. Preparation conditions that affect the copolymer yield, molecular weight and polymeric chain distribution were studied. As the irradiation dose increases, the copolymer yield, as well as molecular weight increases. The higher the MAn content in the comonomer feed solution, the lower the copolymer yield. The derivatives of MAn/AAc copolymers of different functional groups were obtained by treating MAn/AAc copolymer with various organic reagents containing reactive amino groups, such as sulpha–drug compounds and amino acid derivatives. Characterization of obtained copolymers using FTIR, ^{1}H NMR, viscometric, and elemental analysis, was carried out. The antibacterial activity of different molecular weight copolymers and their derivatives against gram negative and gram positive bacteria was investigated. The results obtained revealed that such copolymers and the water-soluble derivatives possessed a broad lethal activity against different types of bacteria and could be used as antibacterial agents.

Keywords radiation synthesis, copolymer, characterization heterocyclic compound, antibacterial agents

Introduction

Polymers have enjoyed increasing use in medical applications in recent years (1–6). Such polymers have been employed for applications as delivery of therapeutic agents, reconstruction of tissue defects, protection of damaged tissues and the like (7–10).

Polymeric disinfectants have received considerable attention in recent years with respect to important applications (11, 12). There is an unfilled need for new antimicrobial

Received October 2004; Accepted December 2004.
Address correspondence to H. A. Abd El-Rehim, National Center for Radiation Research and Technology, Atomic Energy Authority, P.O. Box 29, Nasr City, Cairo, Egypt. E-mail: ha_rehim@hotmail.com

agents suitable for use as drugs with prolonged activity and less toxicity, anti-fouling coatings, fiber finishing, water and air disinfections and preservatives, in personal care products, as well as for new biocides to which microbial strains have not yet developed resistance. Actually bactericidal and fungicidal properties are fixed to a polymer by incorporating a biocide that is slowly released in two ways: a molecular biocide is simply added to a classical binder polymer matrix, or a biocidal compound is grafted to a polymer by a bond sensitive to hydrolysis (13, 14). For these, it has been considered necessary that the antimicrobial component elute, i.e., be released, to make contact with microbes. With the release of the anitimicrobial component, however, the anti-microbial activity decreases with the elapse of time, and is lost when the component is depleted. Antimicrobial components are often hazardous to normal tissue and they, having been released, migrate also to normal tissue, whereby it is impossible to completely prevent the hazardous action. Also, the incorporation of antimicrobial agents often causes the matrix to decrease its mechanical properties. Moreover, soluble low molecular weight molecules frequently give rise to problems like toxicity and a residual agent, especially when they are applied in water treatment, foodstuffs, and packaging materials. Such problems can be solved in two ways: enfolding the bactericide or active materials compound by stable covalent bonding to polymeric carriers (15–17), or synthesis of reactive polymers possess antimicrobial activity themselves (18, 19).

In recent years, attention has been focused on the synthesis of reactive polymers having microbiological activity, which exhibits low toxicity. The materials were based on hydrophilic vinyl compounds as a potential polymer for biologically and pharmaceutical applications (20–22). In this connection, MAn and AAc were selected as comonomers for radiation synthesizing a water-soluble reactive copolymer containing anhydride and carboxylic groups suitable for further chemical treatments. The expected microbiological activity of these polymers is based on their special constitution attributing only to the final copolymer itself, not to leaching low molecular additives to the initial copolymer Therefore, some preparation conditions such as, irradiation dose and comonomer composition that affect the molecular weight and polymeric chains distribution of the prepared copolymer were studied. To enhance the microbial activity of such copolymers, treatments with different reagents such as sulfa drugs and amino acid derivatives were carried out.

Experimental

Materials and Methods

Materials. Acrylic acid and Maleic anhydride (supplied by Merck) were purified by conventional purification methods. Solvents and other chemical reagents were used as received.

Synthesis of MAn/AAc Copolymer

Copolymers were prepared by irradiation of MAn/AAc binary monomers system in acetone at different doses; 5, 10, and 20 kGy using Co-60 gamma rays as an initiator at dose rate of 7 kGy/h. After radiation polymerization completed, the copolymers were washed thoroughly with chloroform to remove residual monomers, dried in a vacuum

oven at 50°C for 24 h and then weighed. The degree of conversion was determined gravimetrically as follows:

$$\text{Degree of conversion } (\%) = \frac{\text{Wt. of total MAn/AAc copolymers}}{\text{Wt. of total MAn and AAc comonomer}} \times 100$$

FTIR spectra of homo and copolymers of AAc were recorded using FTIR Mattson 1000, Unicam, England, in the range from 400–4000 cm^{-1}

Chemical Treatment of Copolymers

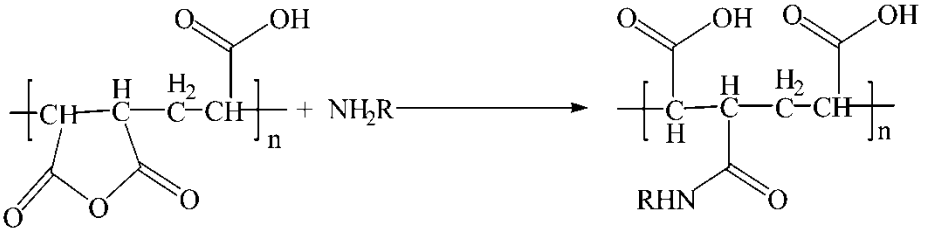
The AAc/MAn copolymers derivatives were treated with sulpha-drug, and NH_2- derivatives of pyridine or amino acids, to derivitize the copolymer anhydride rings, by heating (1 : 1) (mol/mol) of them in DMF/acetone (1 : 1 v/v) at 70°C for 12 h. The product was washed with methanol and dried at 40–50°C. The detail was described in pervious work (23). Elemental analysis, FTIR, and ^{1}H-NMR analysis were performed to estimate the conversion of anhydride groups to amide derivatives. The scheme of the reactions is shown in Scheme 1.

Viscometric Analysis

Measurements were conducted in a thermostated bath with an Ubbelohde glass capillary viscometer. The relative and intrinsic viscosity of sample solutions, with different concentrations obtained with subsequent dilutions from a 0.5 g dl^{-1} solution, were determined.

^{1}H-NMR Spectroscopy

The ^{1}H-NMR spectra of the prepared copolymers were run on a 300 MHz BRUKER NMR spectrometer.



Scheme 1. NH_2R = 1) 2-Amino pyridine, 2) 4-Amino pyridine, 3) Pyrazine Carboxamide, 4) Pyridin-4-carboxamide, 5) Amino-N-2-quinoxalinyl benzene sulphonamide, 6) 4-Amino-N-[5-methyl-3-isoxazolyl benzene sulphonamide, 7) 4-Amino-N-[4,6-dimethyl-2-pyrimidinyl benzene sulphonamide]Sodium, 8) 4-Amino-N-[4-methyl-2-pyrimidinyl benzene sulphonamide], 9) 4-Amino-N-(diamino methylene) benzene sulphonamide, 10) 4-Amino-N-(4,5dimethyl-2-oxazolyl) benzene sulphonamide, 11) 4-Amino-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one, 12) 4-Amino benzene sulphonamide, 13) N-Glycyl glycine, 14) Glycyl-L-leucine, 15) 3,5-diaminobenzoic acid, 16) O- Nitroaniline, 17) Acetyl Thiourea, 18) Anthranilic acid, 19) Urea.

Strains and Media

The synthesized AAc/MAn copolymer derivatives; sulpha-drug and NH_2- derivatives of pyridine or amino acids were tested against different species of Gram (+) and Gram (−) bacteria by examining their susceptibility to these compounds.

Bacterial species of *Bacillus pumilus*, *B.subtilis*, *B.cereas*, *Clostridum perfringens Escherichia coli*, *Pseudomonas aeruginosa Klebsella Salmonella typhimurium*, *Shegilla flexneri*, *Staphyllococcus aureus*, *S.epidermis*, *Streptococcust.fecalis, and St.pyogenes used in this study were obtained from* MERCIN and all of them are ATCC.

Tryptone glucose yeast extract medium, containing g/l tryptone 5, glucose,1 yeast extract 3, and Agar Agar, 20, was used for cultivation of Bacillus species. For growth of *Stapyhlo cocci*, Baird-Parker medium was used containing g/l tryptone, 10; lab lemeco, 5; yeast extract, 1 sodium pyruvate, 10; glycine, 12; lithium chloride,5 and Agar Agar 20. Tryptone Soya agar medium was used for growth of *Sterptococci*, containing g/l tryptone, 15; soya peptone, 5 sodium chloride, 5. and Agar Agar, 20. Brilliant green agar medium was used for cultivation of *Salmomella and shigella* containing g/l, lab lemeco, 5; peptone, 10; yeast extract, 3; disodium hydrogen phosphate, 1; sodium dihydrogen phosphate 0.6; lactose, 10; sucrose, 10; phenol red, 0.09; brilliant green, 0.0047 and Agar Agar, 20. For cultivation of *E. coli*, MacConkey Agar medium was used, containing g/l, peptone, 20; lactose, 10; bile salts, 5; sodium chloride, 5; neutral red, 0.075 and Agar Agar, 20.

The studied species were sub-cultured in TGY broth medium (in a sterile test tube, 10 ml each), incubated at the specified temperature overnight with shaking at 120 rpm. The growing subculture (1 ml) was transferred to the same medium and incubated to an optical density of 0.2 (O.D.600 = 0.2). The prepared media were left to be cooled to 55°C, to each specific medium, 1 ml of the growing culture at O.D.600 = 0.2 was added to 25 ml of the medium.

The antimicrobial activity, or the susceptibility of the studied microorganisms towards different prepared compounds was carried out as follows. The media containing microorganisms were poured into 120 mm diameter sterile Petri dishes (4 mm depth), and care was taken to pour the plates on a level so that the depth of the medium was uniform. The plates were stored at 2–8°C, after solidification of the medium, a sterile cork porer was used to make a hole for each studied compounds in the agar plates. From each compound, 100 μl was poured into the hole. Following overnight incubation, the culture was examined for no growth areas around the hole (zones of inhibition bacterial strain sensitive to the antimicrobial are inhibited at a distance from the hole whereas resistance grew, up to the edge of the disc.

Results and Discussion

Preparation of MAn/AAc Copolymer

The effect of irradiation dose and comonomer composition on the MAn/AAc copolymer yield was investigated and shown in Figures 1 and 2, respectively. It can be seen that as the irradiation dose or AAc content in the comonomer feed solution increases, the obtained copolymer yield increases. The concentration of the free radical formed during the irradiation process increased with increasing the irradiation dose. As a result, the copolymer yield increased. Meanwhile, the excess of MAn in the comonomer feed solution retarded the copolymerization process. MAn has little to no tendency for homopolymerization, consequently, causing copolymer yields from MAn-rich feed solutions to be low.

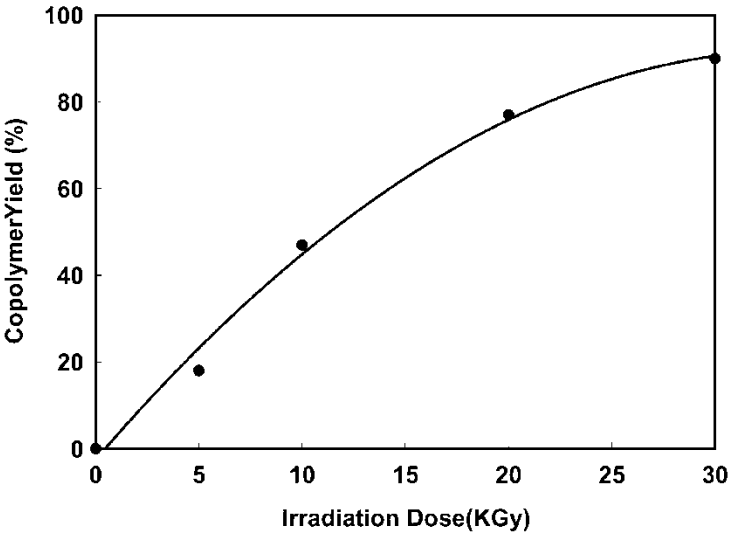


Figure 1. Effect of irradiation dose on the degree of conversion of (MAn/AAc) comonomer into copolymer; Acetone used as a duilent, comonomer composition (50/50) (mol/mol) and comonomer concentration: 70 mol%.

Copolymer Structure

For the design of synthetic polymers, such as the MAn/AAc copolymer, charge transfer complexes (CTC), as well as hydrogen bonding, has been considered to be very useful.

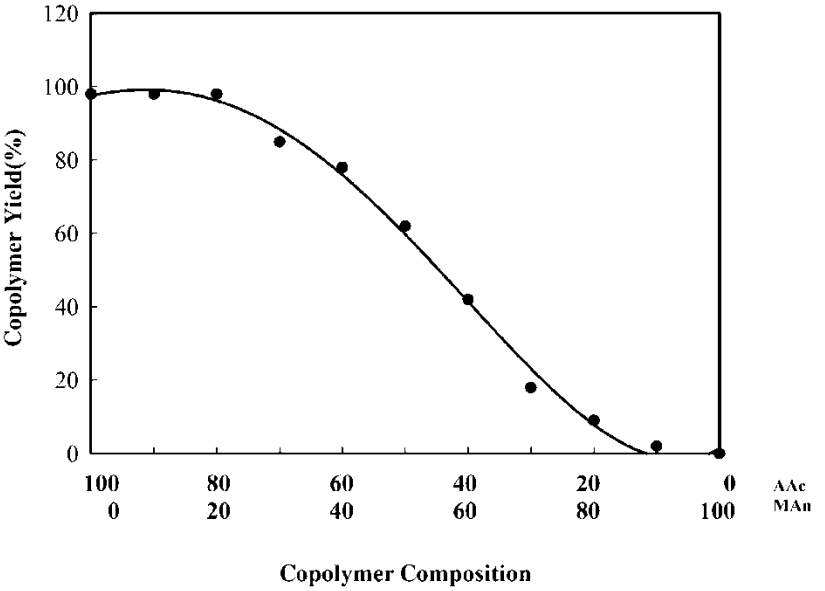


Figure 2. Effect of different (MAn/AAc) compositions (mol/mol) on the copolymer yield; Acetone used as a duilent. Irradiation dose:10 kGy, and comonomer concentration, 70 mol%.

H bonding is achieved through the complexation of two or more molecules containing proton donor and proton acceptor groups due to both electrostatic and donor-acceptor interactions in H-complexes (22, 24–26).

The effect of H-complex (–C═O. . .HO–) in radical alternating copolymerization of MAn and AAc was observed by El-Said et al. (27). They showed that copolymerization of this monomer pair proceeds through formation of a Man/AAc complex (–C═O. . .HO–), and it is possible to direct the process away from the formation of alternating copolymers to the formation of random copolymers with different composition by using naphthalene as an electron donor substance forming a donor acceptor complex with the double bond of acceptor MAn.

From the monomer structures, the formation of the intermolecular complexes, such as the H-complex between MAn (–C═O, proton acceptor) and AAc (–COOH, proton donor) is predicted and the charge transfer from AAc double bond to MAn double bond is caused by the effect of the H-complex between functional groups of comonomers. From the known values of polarity (e) for MAn as a strong acceptor monomer (e = 2.25) and AAc as a relatively weak acceptor, monomer (e = 0.77) proved that the formation of H-complex in the MAn–AAc system can be accompanied by the change of conjugation between the double bond and carbonyl group and an increase of electron density of the acrylic double bond. In this case, H-complexed AAc can be described as an electron-donor monomer. This allows easy electron transfer in the monomer mixtures from the H-complexed AAc to MAn with the formation of CTC between double bonds of the comonomers (28).

Characterization of Prepared Copolymer

The intrinsic viscosity of the copolymer obtained from different comonomer compositions was investigated using water as a diluent (Figure 3). The copolymerization of MAn with

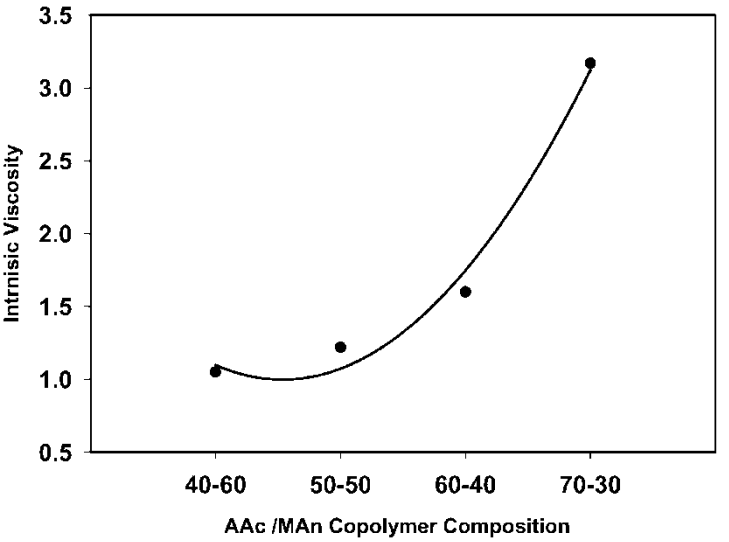


Figure 3. Relationship between intrinsic viscosity of (MAn/AAc) copolymer in water prepared from feed solutions of different comonomer compositions. Irradiation dose 20 kGy. comonomer concentration 70 mol%.

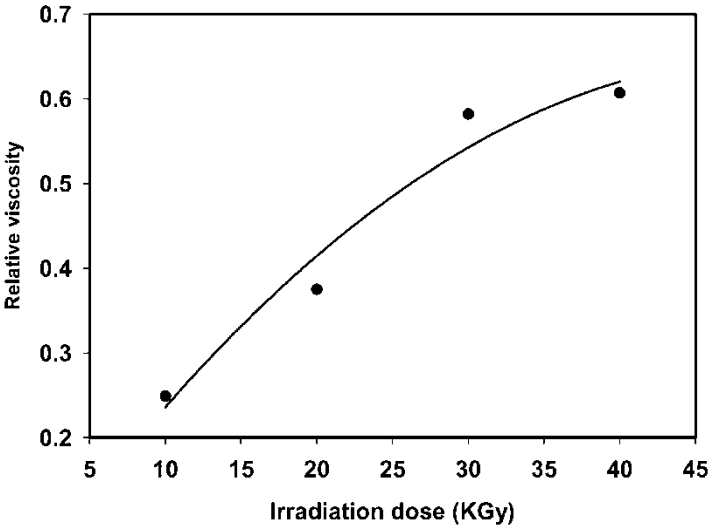


Figure 4. Relationship between relative viscosity in water of (MAn/AAc) copolymer prepared at different irradiation doses Acetone used as a duilent, comonomer composition (50/50) (mol/mol) and comonomer concentration: 70 mol%.

AAc shows a decrease in intrinsic viscosity with increasing MAn content in the comonomer feed solution. The results can be attributed to the inhibition effect of excess MAn on the copolymerization process, which retarded the rate of the propagation step. Consequently, the molecular weight, as well as the intrinsic viscosity, decreases. However, AAc has a tendency to homopolymerize and also copolymerize with MAn and an excess of AAc promotes the lengthening and molecular weight of copolymer chains. As a consequence, the copolymer intrinsic viscosity increases.

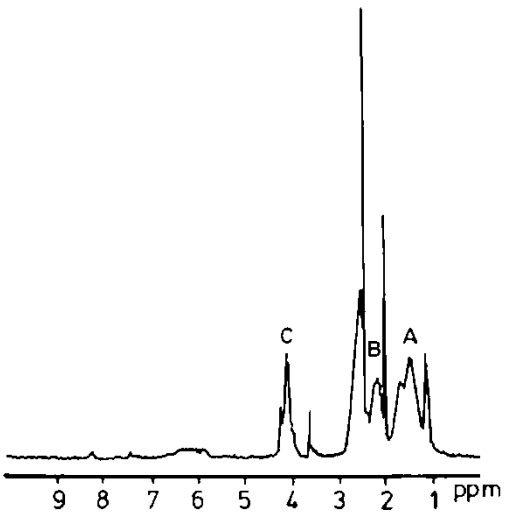


Figure 5. ^{1}HNMR-spectrum of MAn-AAc copolymer.

Table 1
Elemental and FTIR analysis of MAn/AAc copolymers reacted with different reagents

No.	Treating agents	Treated copolymer mol. formula	m.p°C	Analysis found/calculated (%)				Characterization
				C	H	N	S	
1.	2-Amino pyridine	$C_{12}H_{12}O_5N_2$ 264	115–117	54.90 54.54	4.10 4.50	10.20 10.60	—	IR: 1593 (C═N),1663 (C═O), 3280(NH)cm^{-1} ^{1}HNMR(DMSO) $\delta = 1.2–1.8$ (CH_2 of AAc) 2–2.4 (CH of AAC), 3.9–4.4(CH-CH MAn) and 6.2–8.2 (4H,Ar-H) ppm
2.	4-Amino pyridine	$C_{12}H_{12}O_5N_2$ 264	213–215	54.90 54.54	4.00 4.50	10.80 10.60	—	IR: 1593 (C═N),1663 (C═O),3280(NH)cm^{-1} ^{1}HNMR(DMSO) $\delta = 1.2–1.8$ (CH_2 of AAc) 2–2.4 (CH of AAC),3.9–4.4(CHCH MAn) and 6.2–8.2 (4H,Ar-H) ppm
3.	Pyrazine carboxamide	$C_{12}H_{11}O_6N_3$ 293	245–246	49.70 49.14	3.56 3.75	14.11 14.33	—	IR: 1593 (C═N), 1663 (C═O), 3301(NH) cm^{-1}
4.	Pyridin-4-carboxamide	$C_{13}H_{12}O_6N_2$ 292	200–202	53.70 53.34	4.13 4.10	9.20 9.59	—	IR: 1690 (C═O), 3371(NH) cm^{-1}
5.	Amino-N-2-quinoxalinyl benzene sulphonamide	$C_{21}H_{18}O_7N_4S$ 470	260–262	53.90 53.62	3.60 3.83	11.60 11.91	6.20 6.81	IR:1587(C═N),1639 (C═O),3357(NH),3436 (NH_2) cm^{-1}
6.	4-Amino-N-[5-methyl-3-isoxazolyl benzene sulphonamid	$C_{17}H_{17}O_8N_3S$ 423.3	150–153	48.00 48.19	4.20 4.02	9.75 9.92	7.10 7.56	IR: 1587(C═N),1628(C═O), 3257 (NH) 3475(NH_2), cm^{-1}

7.	4-Amino-N-[4,6-dimethyl-2-pyrimidinyl benzene sulphonamide] Sodium	$C_{19}H_{19}O_7N_4SNa$ 470.3	220–222	48.60 48.47	4.32 4.03	11.48 11.90	6.40 6.80	IR: 1590 (C═N), 1639(C═O),3439(NH_2), 2955(NH) cm^{-1}
8.	4-Amino-N-[4-methyl-2-pyrimidinyl benzene sulphonamide]	$C_{18}H_{18}O_7N_4S$ 434.3	240–242	49.90 49.73	4.30 4.14	12.70 12.89	7.60 7.37	IR: 1597(C═N), 1641 (C═O),3489(NH_2), 3225(NH) cm^{-1}
9.	4-Amino-N-(diamino methylene) benzene sulphonamide	$C_{14}H_{16}O_7N_4S$ 384.24	223–225	43.50 43.72	4.22 4.16	14.55 14.57	8.10 8.33	IR1590 (C═N), 1639(C═O),3436(NH_2), 3223(NH) cm^{-1}
10.	4-Amino-N-(4,5dimethyl-2-oxazolyl) benzene sulphonamide	$C_{14}H_{13}O_7N$ 307	225–227	54.92 54.72	4.31 4.23	4.40 4.56	— —	
11.	4-Amino-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one	$C_8H_{10}N_2O_6$ 230	185–187	41.40 41.74	4.50 4.35	12.25 12.17	—	
12.	4-Amino benzene sulphonamide	$C_{18}H_{19}O_8N_3S$ 437.3	190–192	49.60 49.39	4.31 4.34	9.70 9.60	7.12 7.32	IR: 1595 (C═N), 3370(NH) cm^{-1}
13.	N-Glycyl glycine	$C_{18}H_{19}O_6N_3$ 373	230–232	57.92 57.90	5.12 5.09	11.00 11.26	— —	IR: 1658(C═O), 3480(NH_2), cm^{-1}
14.	Glycyl-L-leucine	$C_{13}H_{14}O_7N_2$ 342.6	180–182	45.55 45.53	4.12 4.08	8.3 8.17	9.00 9.34	
15.	3,5-diaminobenzoic acid	$C_{11}H_{14}O_8N_2$ 302	280 (Dec.)	43.90 43.70	4.45 4.64	9.40 9.27	—	IR: 1659(C═O), 3225(NH), cm^{-1}
16.	–O– Nitroaniline	$C_{15}H_{22}O_8N_2$ 358	280–282	50.37 50.27	6.22 6.15	7.67 7.82	—	IR: 1665(C═O), 3235(NH), cm^{-1}

(continued)

Table 1
Continued

No.	Treating agents	Treated copolymer mol. formula	m.p°C	Analysis found/calculated (%) C	H	N	S	Characterization
17.	Acetyl thiourea	$C_{14}H_{14}O_7N_2$ 322	265–267	52.30 52.17	4.50 4.35	8.29 8.69	—	
18.	Anthranilic acid	$C_{13}H_{12}O_7N_2$ 308	123–125	50.80 50.65	3.92 3.89	8.90 9.09	—	
19.	Urea	$C_{10}H_{12}O_6N_2S$ 288	218–220	41.62 41.67	4.12 4.17	9.60 9.72	10.50 11.11	IR: 1659- (C═O), 3241 (NH) cm^{-1}

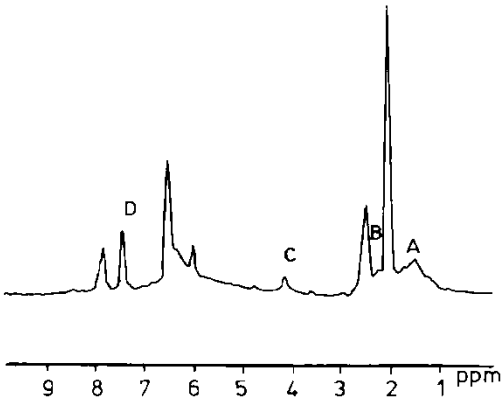


Figure 6. ^{1}H-NMR-spectrum of MAn-AAc copolymer treated with 2-amino pyridine.

By increasing the irradiation dose, required for the MAn/AAc copolymerization process, the relative viscosity of the obtained copolymer increases (Figure 4). As the irradiation dose increases, the copolymer molecular weight increases resulting in increasing in its relative viscosity.

FTIR analysis was made in order to confirm the formation of the MAn/AAc copolymer. The spectrum of AAc homopolymer showed an absorption band at 1713 cm^{-1}, due to the carbonyl groups of AAc. However, bands at 1778 and 1851 cm^{-1}, due to MAn anhydride groups, beside the band of AAc groups at 1714 cm^{-1}, clearly appeared in the FTIR spectrum of MAn/AAc copolymer.

The ^{1}H-NMR spectrum for PAAc/MAn (in DMSO) (Figure 5) shows resonance at $\delta = 1.2-1.8$ ppm (CH_2 of AAc), 2–2.4 ppm (CH of AAc) 3.9–4.4 ppm (CH-CH MAn).

Elemental and FTIR analysis were also made for MAn/AAc copolymers which reacted with different reagents, such as amino pyridine, amino acids and sulpha-drugs, to estimate the MAn conversion by such treatments (Table 1). The elemental analysis data of copolymer treated with different reagents indicated that most of the anhydride groups in the copolymer converted to amide derivatives. The FTIR spectra of MAn/AAc treated copolymers show disappearance of the MAn bands at 1778 and 1851 cm^{-1}. Meanwhile, the band around 1650 cm^{-1} which resulted from conversion of MAn groups to amide groups clearly appears (Table 1).

Table 2
Biological activity of (MAn/AAc) copolymer prepared at different irradiation doses against various types of pathogenic microorganisms

Strain copolymer prepared at	Inhibition zone (mm)			
	10 kGy	20 kGy	30 kGy	40 kGy
B. cereus	16	16	18	17
C. perfringens	18	17	19	19
E. coli	17	16	16	18

The ^{1}H-NMR spectrum for PAAc/MAn treated with 2-amino pyridine (in DMSO) (Figure 6) shows resonance at $\delta = 1.2-1.8$ ppm (CH_2 of AAc), 2–2.4 ppm (CH of AAc), 3.9–4.4 ppm (CH–CH of MAn) and 6.2–8.2 ppm (Ar H ppm).

Evaluation of MAn/AAc Copolymer and its Derivatives as Antimicrobial Agents

Contamination by microorganisms is of great concern in several areas such as medical devices, health care products, water purification systems, hospitals, food packaging, food storage, etc. Consequently, biocidal polymers have received much attention in recent years (12).

The antimicrobial activity of MAn/AAc copolymers of different molecular weight (prepared at different irradiation doses) was studied (Table 2). Insignificant changes in the activity of water-soluble copolymers prepared at different irradiation dose against the microorganism were noticed. This means that the mode of bacterial lethal action is not dependent on the copolymer chain length. The copolymer, carboxylic acid groups may be the sole factor affects the microorganism. Copolymers of 2,4-DMA could significantly inhibit the growth of microorganisms within 48 h (21).

Also, Oh and coworkers (18) synthesis copolymer and tested their bactericidal activity against *S. aureus* and *Ps. Aeruginosa.* The results showed excellent growth inhibition of these bacteria by the copolymers.

The antimicrobial activity of the treated copolymers was examined against Gram-negative and Gram-positive bacteria. Generally, all non water-soluble treated copolymers showed insignificant activity against the studied microorganisms. Meanwhile, all soluble treated copolymers proved effective against the tested microorganisms, but growth

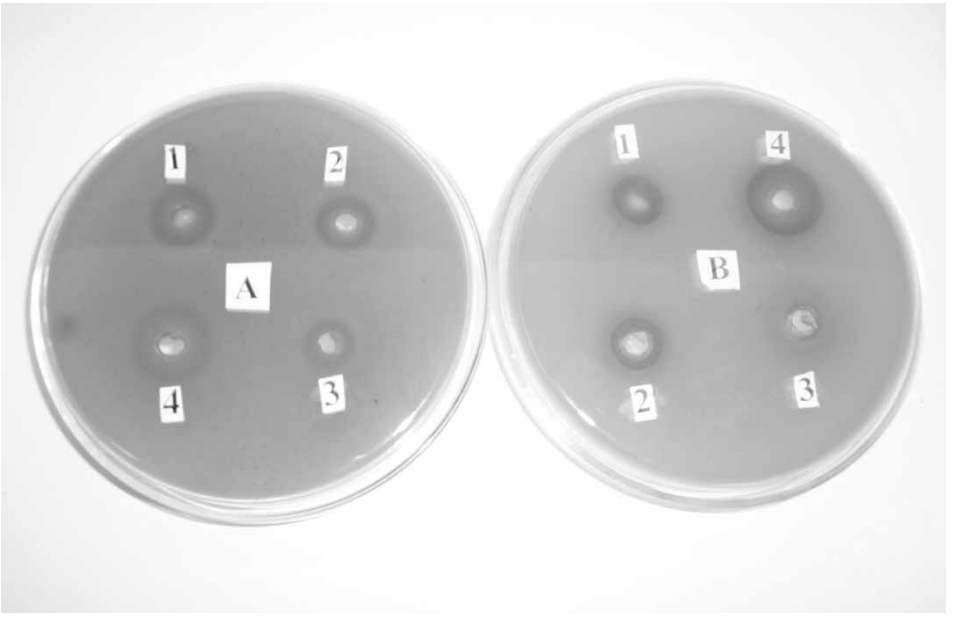


Figure 7. The activity of MAn-AAc copolymer treated with different reagents (1) 2-amino pyridine, (2)-pyridine 4-Carboxamide,(3) 4-amino-N-(diaminomethylene benzene sulphonamide) and (4)-glycyl-L-leucine against (A)-*E.Coli* and (B)-*K.aerogenes.*

Table 3
Biologial activity of (MAn/AAc) copolymer prepared at (60/40) comonomer composition, irradation dose 20 kGy treated with different reagents: (1)-4-amino pyridine (2)-pyridine 4-Carbox amide (3)-4 amino-N-(diamino methylene benzene sulphonamide) and (4)-glycyl-L-leucine against different types of microorganisms

Strain polymer type	Inhibition zone (mm)			
	1	2	3	4
B. pumilus	10	12	20	30
B. subtilis	16	14	11	18
C. perfringens	12	20	18	22
E. coli	14	13	12	18
Klebsella	14	16	16	22
Ps. aeruginosa	12	16	12	22
Salmonella typhi	15	12	14	20
Shegilla flexneri	16	18	12	22
S. aureus	15	15	16	22
S. epidermis	12	16	20	22
St. fecalis	12	20	18	22
St. pyogenes	12	16	22	30

inhibitory effects varied from one another. The soluble copolymer bearing amino acid moiety was the most effective one against both Gram-negative and Gram-positive bacteria. The diameters of its inhibition zones ranged between 18 and 30 mm after 24 h. (Figure 7 and Table 3).

Conclusion

A number of water-soluble MAn/AAc copolymers and their derivatives, which exhibited their own antimicrobial activity, were prepared by using gamma rays. The preparation conditions, such as comonomer composition and irradiation dose, have a great effect on MAn/AAc copolymer molecular weight. Characterization of the MAn/AAc copolymer was investigated. In order to enhance the antimicrobial activity of MAn/AAc copolymer, modification was carried out by treating them with different reagents such as sulfa-drugs and amino acid derivatives. The prepared copolymers and some of its soluble derivatives posses high antimicrobial activity and could be used in biomedical applications.

References

1. Ratner, D.B., Schoen, F.J., and Hoffman, A.S.J. (1997) Biomaterials Science: An Introduction to Materials in Medicine. Harcourt Brace & Company.
2. Pathak, C.P., Barman, S.P., Philbrook, C., Sawhney, A.S., Coury, A.J., Avila, L.Z., Kieras, M.T. (2003) Multiblock Biodegradable hydrogels for drug delivery and tissue treatment. USA Patents 6,639,014.

3. Lorenz, D., Hlee, C.. (2002) Gels formed by the interaction of polyvinylpyrrolidone with chitosan derivatives. USA Patents, 6,379,702.
4. Dumitriu, Severian. (2002) Polymeric Biomaterials. In , 2nd Ed; Marcel Dekker: New York.
5. Law, W.T., Kamala, N., and Busman, A.M. (2002) Biomedical Diagnostic Science and Technology. Port Science Inc: Moorestown, NJ.
6. Abd El-Rehim, H.A., Hegazy, E.A., and El-Hag, A. (1999) Use of radiation grafting polyethylene in dialysis of low molecular weight metabolites. *Polym Int.*, 48: 593–601.
7. Abd El-Rehim, H.A. and El-Arnaouty, M.B. (2004) Properties and biocompatibility of polypropylene graft copolymer films. *J. Biomed. Mater. Res., Part B: Appl. Biomat.*, 68BB: 209–215.
8. Mi, F.L., Shyup, S., Wup, Y.S., Leey, J.S., and Huangu, R. (2001) Fabrication and characterization of a sponge-like asymmetric chitosan membrane as a wound dressing. *Biomaterials*, 22: 165–173.
9. Kabanov, V.Y. (1998) Preparation of polymeric biomaterials with the aid of radiation—chemical methods. *Russ. Chem. Rev.*, 6: 77–83.
10. Garca, O., Blanco, M.D., Martn, J.A., and Teijon, J.M. (2000) 5-Fluorouracil trapping in poly(2-hydroxyethyl methacrylate-co-acrylamide) hydrogels: *In vitro* drug delivery studies. *Eur. Polym. J.*, 36: 111–122.
11. Tyagi, M. and Singh, H. (2000) Iodinated P(MMA-NVP): An efficient matrix for disinfections of water. *Appl. Polym. Sci.*, 79: 1109–1116.
12. Sun, Y. and Sun, G.J. (2001) Novel regenerable N-halamine polymeric biocides II. Grafting hydantoin-containing monomers onto cotton cellulose. *Appl. Polym. Sci.*, 81: 617–624.
13. Liu, Y., Laks, P., and Heiden, P. (2002) Controlled release of biocides in solid wood III. Preparation and characterization of surfactant-free nanoparticles. *J. Appl. Polym. Sci.*, 86: 615–621.
14. Dumitrascu, N., Borcia, G., Apetroae, N., and Popa, G. (2003) Immobilization of biological active species on PA-6 foils treated by a dielectric barrier discharge. *J. Appl. Polym, Sci.*, 90: 1985–1990.
15. Rivas, L.B.E., Pereira, D.M., Mondaca, R.J., and Saavedra, M.A. (2003) Water-soluble cationic polymers and their polymer-metal. *J. Appl. Polym. Sci.*, 87: 452–457.
16. Sun, Y., Chen, T., Worley, S.D., and Sun, G. (2001) Novel refreshable N-halamine polymeric biocides containing imidazolidin-4-one derivatives. *J. Polym. Sci. A: Polym. Chem.*, 39: 3073–3084.
17. Hartmann, M., Bauer, H., and Wermann, K. (1985) Biocide polymers14- Modification of polyvinyl alcohol with biological active N-phosphorylatd 3-amino-1,2,4-triazoles. *Angew. Makrom. Chemie*, 135: 1–9.
18. Oh, S.T., Ha, C.S., and Cho, W.J. (1994) Synthesis and biocidal activities of polymer III. Bactericical activity of homopolymer of AcDP and copolymer of AcdDP with St. *J. Appl. Polym. Sci.*, 54 (7): 859–866.
19. Song, J.W., Ghim, H.D., Choi, J.H., Ko, S.W., and Lyoo, W.S. (2001) Preparation of antimicrobial sodium alginate with chito-oligosaccharide side chains. *J. Polym. Sci A: Polym. Chem.*, 39: 1810–1816.
20. Charles, U., Pittman, J.G., and Allan, S.H. (1981) Copolymerization of pentachlorophenyl acrylate with vinyl acetate and ethyl acrylate polymer-bound fungicides. *J. Appl. Polym. Sci.*, 26: 2403–2413.
21. Mitesh, B.P., Patel, S.A., Ray, A., and Patel, R.M. (2003) Synthesis, characterization and antimicrobial activity of acrylic copolymers. *J. Appl. Polym. Sci.*, 89: 895–900.
22. Trivedi, B.C. and Culbertson, B.M. (1982) Maleic Anhydride. Plenum Press: New York.
23. Abd El-Rehim, H.A., ;, El-Hag, Ali, A., Mostafa, T.B., and Farrag, H.A. (2004) Anti-microbial activity of anhydride copolymers and their derivatives prepared by ionizing radiation. *Eur. Polym. J.*, 40: 2203–2212.
24. Kato, T., Mizoshita, N., and Kanie, K. (2001) Hydrogen-bonded liquid crystalline materials: Supramolecular polymeric assembly and the induction of dynamic function. *Macromol. Rapid Comm.*, 22: 797–814.

25. Kabanov, V.A., Zubov, V.P., and Semchikov, Y.D. (1987) Complex-Radical Polymerization Chemistry. Moscow.
26. Vinogradov, S.N. and Linnell, R.H. (1971) Hydrogen Bonding. Van Nastr and Reinhold Co., New York.
27. El'Saied, A.A., Mirlina, S.Y., and Kargin, V.A. (1969) Copolymerization of unsaturated mono- and dibasic acids The possibility of controlling copolymer composition. Polym. *Sci. USSR*, A11 (2): 314.
28. Kaplan, H., Zakir, M.O., and Guner, A. (2004) Hydrogen (H)-complex formation anhydride acrylic acid (methyl acrylate) monomer system. *J. Molecular Liquids*, 111: 77–84.