(724.6-711.4 eV), α-FeOOH (724.5-711.0 eV) and $KFeO_2$ (724.6-711.3 eV)[5] having $Fe^{3+}$ ions in the lattice. After the lithiation, Fe 2*p* core lines become sharper considerably and shift to lower B.E. region by ~1 eV (723.3-710.2 eV). The lowering of B.E. means the decreasing in valence state, from $Fe^{3+}$ to $Fe^{2+}$ in this case. The B.E.'s of Fe 2*p* electrons in $LiFeMoO_4Cl$ also coincide with other $Fe^{2+}$-containing compound such as FeO(723.8-710.3 eV)[5]. The B.E.'s of core level electrons of other elements in $FeMoO_4Cl$(*e.g.*, molybdenum, oxygen and chloriné) are not changed after lithiation. That is, intercalated lithium ions selectively reduce $Fe^{3+}$ to $Fe^{2+}$ rather than $Mo^{6+}$. Generally the XPE spectra of paramagnetic Fe 2*p* levels are highly complex and have many satellite peaks with main XPE lines (FWHM = 3.3 eV for Fe $2p_{3/2}$), which are the characteristic feature of the compounds with 3*d*-group transition metals[6]. The existence of complex satellites in the Fe 2*p* spectra confirms that $Fe^{3+}$ and $Fe^{2+}$ are in high-spin state with 5 and 4 unpaired electrons, since no shake-up satellite peaks could be expected for the diamagnetic ions like $Fe^{2+}(t_{2g}^6e_g^0)$ with low spin state.

B.E.'s of Mo $3d_{3/2}$ and $3d_{5/2}$ electrons for $FeMoO_4Cl$ and $LiFeMoO_4Cl$ are measured as (235.4 ± 0.1)eV-(232.2 ± 0.1) eV, respectively, which are almost the same as those of other $Mo^{6+}$ species such as $MoO_3$<235.6-232.5 eV>, $CoMoO_4$ <235.0-231.8 eV>, $Al_2(MoO_4)_3$<235.8-232.7 eV >and $Fe_2(MoO_4)_3$ < 235.3-232.2 eV>[7,8]. XPE lines for O 1*s*(530.3 ± 0.1 eV) and Cl 2*p*(198.2 ± 0.1 eV) in $FeMoO_4Cl$ and $LiFeMoO_4Cl$ are not changed as expected. Due to the broadening of Li 1*s* line with long tail toward high B.E. region by overlapping with other lines such as Fe 3*p* and Au 5*p*, and moreover with complicated satellites, the exact B.E. of Li 1s line could not be measured.

In summary, it has been confirmed that ferric ions in $FeMoO_4Cl$ are selectively reduced to ferrous ions upon lithium intercalation with a decrease of crystal symmetry from tetragonal to monoclinic($LiFeMoO_4Cl$). From the magnetic and XPS data along with X-ray structural analysis, it has been concluded that high spin configuration of $Fe^{2+}$ $(e_g^3b_{2g}^1a_{1g}^1b_{1g}^1)$, corresponding to $^5E_g$ ground term in $D_{4h}$ symmetry, can be stabilized by the elongation of $FeO_4ClCl'$-distorted octahedra in a weak ligand field. And both compounds show an extensive short range intralayer antiferromagnetic correlation.

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# Syntheses and Biological Activities of Copolymers Composed of Dihydropyran, Acrylic Acid and Their Derivatives

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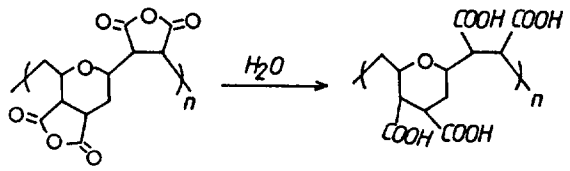
Various polyanions of both natural and synthetic origin are known to exhibit a broad spectrum of interesting biological activities.[1-5] Among those synthetic polyanions, divinyl ether-maleic anhydride (1:2) alternating copolymer (DIVEMA) has been extensively studied due to its antiviral, antitumor and interferon-inducing properties.[6-11]

The structural feature of hydrolyzed product (I), an intrinsic active form in the biological system of DIVEMA, (I) contains tetrahydropyran rings and carboxylate groups attached on the polymer backbone as functionalities.

Hypothesizing that the polymers having similar structure to that of DIVEMA would manifest relevant biological activities, we synthesized several copolymers which contained



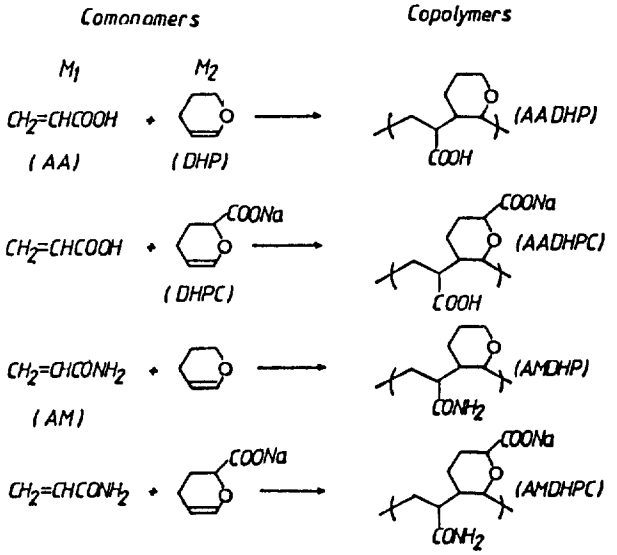

(DIVEMA) (1)

both tetrahydropyran rings and carbonyl groups. It was surprising to find that most of the polyanions synthesized and tested up to date for their biological activities were designed to contain only carboxylates as polar and/or functional groups even though sugar moieties-pyran or furan ring-may, in general, play rather important role in biological systems.

**Table 1. Copolymerization Data at 70°C**

| Copolymer | Comonomer[a] $M_1$ | $M_2$ | Initiater[b] | Polym. Solvent | Polym. time (h) | Yield (%) | Reactivity $r_1$ | Ratio $r_2$ |
|---|---|---|---|---|---|---|---|---|
| AADHP | AA | DHP | AIBN | Dioxane | 20 | 48 | 1.18 ± 0.004 | 0.00 ± 0.005 |
| AADHPC | AA | DHPC | $K_2S_2O_8$ | $H_2O$ | 2 | 41 | 2.11 ± 0.01 | 0.00 ± 0.008 |
| AMDHP | AM | DHP | AIBN | Acetone | 15 | 45 | 14.05 ± 0.01 | 0.00 ± 0.002 |
| AMDHPC | AM | DHPC | $K_2S_2O_8$ | $H_2O$ | 1 | 38 | 15.9 ± 0.1 | 0.00 ± 0.01 |

[a]Comonomer concentration: [mol/*l*]. [AA] = [DHP] = 0.725, [AA] = [DHPC] = 0.22. [AM] = [DHP] = 0.563, [AM] = [DHPC] = 0.22. [b]Initiator concentration: 1 mol% of total monomer concentration.




**Scheme 1**

In this paper we report the syntheses and biological activities of copolymers containing pyran ring and carbonyl functions. The synthetic outline of copolymers obtained by radical copolymerization are illustrated in Scheme 1.

3,4-Dihydro-2H-pyran(DHP) is known to homopolymerize[11] and copolymerize[12] with thiophenaldehyde in the presence of cationic initiators. While the radical copolymerization of DHP with maleic anhydride,[13,14] vinylidene cyanide,[15] benzaldehyde[16] and acetonitrile[17] are known, the copolymerization of DHP with acrylic acid (AA) and acrylamide (AM) are not reported. Moreover, the polymerization of sodium 3,4-dihydro-2H-pyran-2-carboxylate (DHPC) has not been attempted either by radical or by cationic initiators. The reaction conditions, initiators and reactivity ratios are summerized in Table 1.

All polymers obtained in this study are very hygroscopic and readily soluble in water. The structures were confirmed by ir, *i.e.*, characteristic peak for carboxyl groups at 1800, for carboxylate group at 1750, for amide group at 1750 and 1660, and for the ether group of pyran ring at 1200 $cm^{-1}$. The AA components incoporating poly(acrylic acid-co-3,4-dihydro-2H-pyran) (AADHP) and poly (acrylic acid-co-sodium 3,4-dihydro-2H-pyran-2-carboxylate) (AADHPC) were determined by titration of the carboxyl groups with NaOH, whereas AM Components in poly (acrylic amide-co-3,4-dihydro-2H-pyran) (AMDHP) and poly (acryl amide-co-sodium 3,4-dihydro-2H-pyran-2-carboxylate) (AMDHPC) were measured by elementary analysis of nitrogen.

**Table 2. Characterization and Biological Activities of the polymer compared with DIVEMA**

| Copolymer Composition[a] | $ID_{50}$[b] $[\eta]$[f] | ($\mu$g/ml) 3LL[c] | Bl6[d] | MEF[e] |
|---|---|---|---|---|
| $(AA)_{0.58}(DHP)_{0.42}$ | 0.05 | 1389 | 1330 | 1587 |
| $(AA)_{0.65}(DHPC)_{0.35}$ | 0.15 | 1313 | 878 | 301 |
| $(AM)_{0.75}(DHP)_{0.25}$ | 0.15 | 2061 | 1909 | 1768 |
| $(AM)_{0.85}(DHPC)_{0.15}$ | 0.07 | 2168 | 1634 | 1729 |
| $(DIVE)_{0.5}(MA)_{0.5}$ | MW = 5,500 | 2504 | 1511 | 765 |

[a]Mole fraction of monomer component in the copolymer. [b]$ID_{50}$ was defined as the concentration which reduced absorbance by 50% of control untreated wells in the MTT assay. All results represent the average of 8 wells. [c]Lewis lung carcinoma originated from C57BL/6 mouse. [d]Malignant melanoma originated from C57BL/6 mouse. [e]Secondary mouse embryofibroblast. [f]Intrinsic viscosity of the copolymer.

Determination of the reactivity ratios were performed by changing mole fractions of each of the comonomer pairs and measuring mole fraction of monomer components in the copolymer before a 10% conversion proceeds. The reactivity ratios($r_1$) for the copolymerization of AMDHP and AMDHPC were found to be one order of magnitude higher than those of AADHP and AADHPC. This result can be attributed to the fact that the rate of polymerization of AM is faster than that of AA.

Since DIVEMA is an alternating copolymer, an attempt was made in this study to synthesize copolymers having similar alternating sequences by changing the feeding mole ratios of the monomers. The DHP component incoporated in the copolymers was increased adjusting mole ratios of the DHP monomer at the onset of copolymerization. The results are summerized in Table 2. AADHP was found to be nearly an alternating copolymer while the other three copolymers contained more $\alpha$-olefins than dihydropyran components.

For the purpose of biological activity comparison, DIVEMA was made in acetone[18] and the molecular weight of the DIVEMA was regulated with tetrahydrofuran as a transfer agent.[19] Because of DIVEMA of MW range 1,000-10,000 has been shown to have high antitumor and antiviral activities while at the same time low toxicity,[1] DIVEMA having MW of 5500 with polydispersity of 1.3 was chosen for authentic sample in this study.

For biological activity measurement, MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] assay

method was applied. MTT assay is dependent on the cellular reduction of MTT by the mitochondrial dehydrogenase of viable cells to a blue formazan product which can be measured spectrophotometrically. $2 \times 10^3$ 3LL or B-16 cells, $2 \times 10^4$ MEF(mouse embryo fibroblast) cells were inoculated in each well of flatbottomed 96-well microtiter plates in 0.18 m*l* of culture medium to which 0.02 m*l* of 10× concentrated drug or medium was added. On the 4th day, the media from the plates was aspirated completely and 50 $\mu l$ of the MTT solution (1 mg/m*l*) was added to each well and incubated at 37 °C for a further 4 h. Following the incubation, to majority of the MTT solution was aspirated, in order not to disturb the formazan crystals, and 50 $\mu l$ DMSO was added to each well and plates were placed on a plate shaker for 5 min and absorbance was read at 570 nm with a enzyme-linked immunosorbent assay reader.[20]

Biological activities of polymers synthesized in this study expressed by $ID_{50}$ are summerized in Table 2. The $ID_{50}$ values of DIVEMA, AADHP and AMDHP for normal mouse embryo fibroblasts were 765, 1587, and 1768 $\mu$g/m*l* respectively. There were no striking differences between $ID_{50}$ values for normal and neoplastic cells; the $ID_{50}$ values in most cases, *in vitro* ranged from 1300 to 2500 $\mu$g/m*l*. The anticancer effects of DIVEMA *in vivo* have been speculated to be mediated via a macrophage system[21-24] which cannot be reflected by simple direct cytotoxicity *in vitro*, as shown by this experiment. Thus these results also support the findings reported by others that the cytotoxic activity of DIVEMA can not be differentiated between normal and neoplastic cells *in vitro*. Studies on the anticancer effect of DIVEMA and the copolymers synthesized in this study *in vivo* are currently in progress.

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# Catalytic Effects of Anion-Exchange Resins on the Ethylation of Ethyl 2-Ethylacetoacetate

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Synthetic polymers have been extensively employed as catalysts for organic reactions. The catalysis by the polymers may be attributed to the increased effective concentrations of reactants bound on the polymer,[1] effective pH on the polymer domain which is different from that in the bulk medium,[2] or the hydrophobicity created on the surface of the polymer.[2] In addition, ion-exchange resins catalyze some organic reactions by acting as heterogeneous sources of acids and bases.[3]