NOTES

Biomedical Polymers. III. Bacteriocidal Property of the Resins Derived from Substituted Acetophenones

INTRODUCTION

Extensive damage is inflicted by microorganism to natural polymers of fruits, vegetables, etc.[1] Such action depends on susceptibility of the polymer to penetration and degradation, which govern the application of protective treatment.

Interest in chemotherapy was initiated by the pioneering work of Dogmagk (1935), with the discovery of prontosil and the isolation of penicillin by Flory and Chain followed by the discovery of chloroamphenicol, aureomycin, streptomycin, etc. Since then, there has been rapid development in the field, with introduction of polymers which possess the extra advantage of moldability for use as general medical appliances[2] and capability to be used as a constant-release drug-delivery system.[3]

Recently, organo-Hg polyacrylates,[4] and polycarbohydrates modified through organostannate reactants have been reported[5] for use as bacteriocides. Manufacture of antibacterial plywood[6] and fibers[7,8] has also been reported.

Polymers derived from salicylic acid and its derivatives are well known for their biological activity.[9,10] Ciampa and co-workers[11-13] have extensively investigated the biological activity of a number of polymeric resins incorporating salicylic acid as one of the components. A survey of literature reveals that the antimicrobial activity of the resins prepared from substituted acetophenones has not been reported.

The work embodied in the present investigation involves preparation of resin copolymers from substituted acetophenones by reaction with various aromatic substrates such as substituted benzoic acids, phenols, and formaldehyde using acidic catalysts. The bacteriocidal properties of the resins have been evaluated.

EXPERIMENTAL

Materials

Analar grade hydroxy and amino substituted acetophenones (Sigma) were used. 4-Hydroxy phenacyl bromide was prepared by bromination of the corresponding acetophenone. Other chemicals used were of Analar grade.

For carrying out the bacteriocidal test of the polymers, various animal pathogenic organism, viz., *Staphylococcus aureus, Staphylococcus citrus, Bacillus subtillis, Klebsiela, Escherichia coli, Pseudomonus pyocyanous, Streptococcus viridius, Salmonella Typhosa para B,* and *Proteus* were employed.

Resin Synthesis

Copolymers from *o*- and *m*-hydroxy acetophenones (OHAP, MHAP) were prepared as per our earlier communication.[14] Resins from *m*-amino acetophenone (MAAP) and 4-hydroxy phenacyl bromide were prepared following procedure outlines in a previous communication.[15,16]

Antibiotic Sensitivity Test

Antibiotic sensitivity of the resins were monitored by the diffusion test, where the chemical is allowed to diffuse through a solid medium so that a gradient was established, the concentration being nearer the site of application of the drug and decreasing with distance. The test bacterium was seeded on the medium and its sensitivity to the drug was estimated from the inhibition of its growth.

The disc diffusion method uses filter paper discs, 6 mm in diameter, charged with appropriate concentration of test chemical. The discs were stored dry in cold. A suitable dilution of broth culture was flooded on the surface of a solid medium (nutrient agar). The plate was tilted to ensure uniform spreading and the excess broth was pipetted off. After drying (37°C for 30 min), antibiotic discs were supplied with sterile forceps. After overnight incubation, the degree of sensitivity was determined by measuring the zones of inhibition of growth around the discs.

Antibiotic sensitivity of the compounds were evaluated against the previously mentioned pathogens after isolation of the pathogenic bacteria from clinical specimen. Test chemicals were employed at different dilution in DMSO (5, 7, 15, 30, 40, 60% w/v).

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Table I Sensitivity Pattern in 1000 ppm (%) of Resins against Test Organisms[a]

Name of the Resin	Bacteria Strains								
	Staphylococcus		*Strepto-coccus*	*Bacillus*		*Esche-richia*	*Pseudo-monus*		*Salmonella Typhosa*
	Aureus	*Citrus*	*Viridius*	*Subtillis*	*Klebsiela*	*Coli*	*Pyocyanus*	*Proteus*	*Para* B.
1	2	3	4	5	6	7	8	9	10
OHAP-OC-F	> 30	> 30	—	> 30	> 30	> 30	> 30	> 30	—
OHAP-ASA-F	15	> 30	—	15	> 30	> 30	15	> 30	—
OHAP-SA-F	> 30	> 30	—	> 30	> 30	> 30	> 30	> 30	—
MHAP-F	> 30	> 30	—	> 30	> 30	> 30	> 30	> 30	—
MHAP-H-F	> 30	> 30	—	15	> 30	> 30	15	> 30	—
MAAP-F	> 60	> 60	—	> 60	> 60	> 60	> 60	> 60	—
MAAP-R-F	> 30	> 30	—	> 30	> 30	> 30	> 30	> 30	—
MAAP-C-F	> 30	> 30	—	> 30	> 30	> 30	> 30	> 30	—
MAAP-ASA-F	> 60	> 60	—	60	> 60	60	60	> 60	> 60
MAAP-PCBA-F	> 60	> 60	—	> 60	> 60	> 60	> 60	> 60	> 60
MAAP-MC-F	> 60	> 60	—	> 60	> 60	> 60	> 60	> 60	> 60
MAAP-H-F	7	7	—	7	7	7	7	7	7
PAAP-F	> 40	—	—	> 40	> 40	> 40	> 40	> 40	—
PAAP-PA-F	> 40	—	—	> 40	> 40	> 40	> 40	> 40	—
PAAP-MTA-F	> 40	—	—	40	> 40	> 40	> 40	> 40	—
PHPB-OTA-F	> 40	—	—	> 40	> 40	> 40	> 40	> 40	—
PHPB-MTA-F	> 40	—	> 40	> 40	> 40	> 40	> 40	> 40	—
PHPB-PCBA-F	> 40	—	40	15	40	40	40	40	—
PHPB-PNBA-F	15	—	> 40	15	15	> 40	> 40	> 40	—

[a] Key: OTA = *o*-toluic acid; MTA = *m*-toluic acid; MC = *m*-cressol; OC = *o*-cressol; PCBA = *p*-chlorobenzoic acid; PNBA = *p*-nitro benzoic acid; PA = phthalic acid; ASA = acetyl salicylic acid; SA = sulfanilic acid; C = catechol; R = resorcinol; H = hydroquinone.

The results are reported in Table I, in terms of minimum percentage (w/v), at which the sensitivity pattern is observed.

RESULTS AND DISCUSSION

Action of a polymer in a biological system takes into account the reaction and intermolecular attraction like hydrophobic effect, etc. Chemical reaction that a polymer may undergo in an organism, e.g., hydrolysis, oxidation, and conjugation to biomolecules have been extensively reviewed.[17] Polymers depending upon charge, charge density, molecular weight, hydrophobicity, conformation, and tacticity interact more or less strongly with cell membrane components like lipid protein, glycoprotein, etc.,[18,19] and displace the equilibrium of different vital processes, thereby causing death to the organism.

Examination of the results of the antibiotic activity of copolymers represented in Table I reveals that the resin copolymer prepared from *m*-amino acetophenone–hydroquinone–formaldehyde is the most active of all resin copolymers, being toxic to all the pathogenic organisms under study, marked by an obtainable sensitivity pattern at 7% concentration. One similar resin from *m*-hydroxy acetophenone, MHAP–H–F, only shows toxicity to *Bacillus subtillis* and *Pyocyanous* at 15% concentration. However, at the same concentration, *o*-hydroxy acetophenone–acetyl salicylic acid–formaldehyde resin shows higher toxicity to most of the pathogens.

Out of the copolymers prepared from *p*-hydroxy phenacyl bromide, the resins prepared with *o*- and *m*-toluic acid were least toxic even at the highest experimented dose, whereas those from *p*-chloro or *p*-nitro benzoic acid were found to have a noticeable effect at 15% concentration for some pathogens. This can be attributed to the presence of Cl or N atoms in the resin.

Biological activity of hydroquinone[20] is well established. The relatively reduced bacteriocidal sensitivity of MHAP–H–F resin may be attributed to lower composition of hydroquinone unit in the copolymer.

Antibacterial activity of the resins under study could be referred to a number of causes like injurious effect on the cell wall or cell division, effect on permeability of cell membrane and cell enzyme system, chelation, and precipitation of chemicals. Oxygen and nitrogen atoms present in the resin can act as hydrogen acceptor in the metabolic system and by doing so disturb the normal hydrogenation and dehydrogenation reactions in the cell. The reactive free radicals formed can also act as an antimetabolite.

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