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Research Article

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Biocidal efficacy of synthetic copolyesters having chalcone moiety

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ABSTRACT

Two chalcone diols (2E)-1-(4-hydroxyphenyl)-3(4-hydroxy, 3-ethoxy phenyl) prop-en-1-one and (2E)-1-(4-hydroxy-3-methoxy phenyl)-3(4-hydroxy, 3-ethoxy phenyl) prop-en-1-one were synthesized by acid catalyzed Claisen-Schmidt reaction. The synthesized chalcones were made to undergo polymerization using three aliphatic dichlorides namely glutaryl, succinyl and oxalyl chlorides. The polymers were random copolyesters and characterized by solubility and viscosity measurement. The structure of the copolyester was established by FTIR, ^{1}H-NMR and ^{13}C-NMR. The biocidal efficacy was done by Disc diffusion method and found to be nominal against the standards used. Thus these copolyesters may be considered as drug carriers.

Keywords: Chalcones, polycondensation, copolyesters, antibacterial, antifungal.

INTRODUCTION

Chalcones (α,β-Unsaturated ketones) are biogenetic precursors of flavonoids [1]. Chemically, chalcones are 1,3-diaryl-2-propen-1-ones in which two aromatic rings are joined by a three carbon bridge having a cabonyl moiety and α,β unsaturation [2]. Conventionally, chalcones are synthesized by Claisen-Schmidt condensation of arylaldehydes and acetophenones. The traditional methods for the synthesis of chalcones involves the use of strong bases such as NaOH, KOH, Ba (OH) hydrotalcites, LiHMDS, calcined NaNO3/natural phosphate. There are also some reports of acid-catalyzed aldol condensations, e.g. AlCl3, BF3, dry HCl, ZrH2/NiCl2 and RuCl3 (for cyclic and acyclic ketones).

Chalcones and its derivatives have attracted increasing attention due to numerous pharmacological applications [3]. Literature survey reveals that numerous chalcones and their derivatives exhibit a broad spectrum of pharmacological activities such as anti-amoebic[4], antibacterial, antifungal [5], anticancer [6], anticonvulsant [7], anti-inflammatory, antifungal, antibacterial [8], Antileishmanial [9], Anti-malarial [10], Anti-malarial, Anti-tubercular [11]. Senthamizh Selvi and coworkers have synthesized certain chalcone based random copolyesters and reported their biocidal behavior. [12]

Perundevi and coworkers have synthesized certain bischalcone based random copolyesters and reported their antibacterial behavior. [13]

The objective of our study is to synthesize four copolyesters by incorporating the chalcone moieties in the copolyester main chain by polycondensation process, then characterizing them analytically and to study their anti bacterial and anti fungal activity

EXPERIMENTAL SECTION

Aldrich samples of 4-hydroxy acetophenone and 3-ethoxy, 4-hydroxy benzaldehyde, 3-methoxy, 4-hydroxy acetophenone and were used as received. Ethanol (Merck) was used as non-solvent for the copolyesters and as solvent for the preparation of the two chalcone diols. Aldrich samples of succinyl chloride, oxalyl chloride, glutaryl and isopthaloyl chloride were used as such in the synthesis of the 5 copolyesters. Spectral grade DMSO-d6 was used as internal standard for recording NMR spectra.

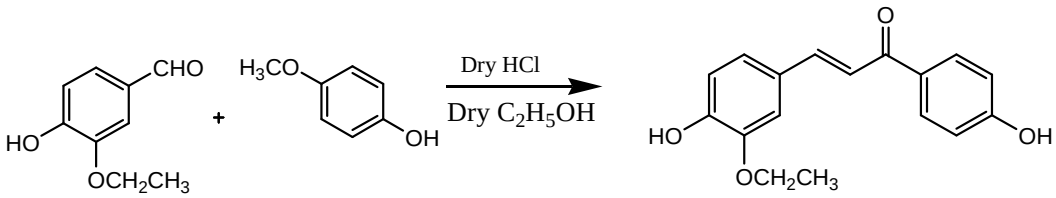
Synthesis of chalcone diols

The monomer diols namely (2E)-1-(4-hydroxyphenyl)-3(4-hydroxy, 3-ethoxy phenyl) prop-en-1-one and (2E)-1-(4-hydroxy-3-methoxy phenyl)-3(4-hydroxy, 3-ethoxy phenyl) prop-en-1-one were synthesized by the process reported by Jasmine Francis and etal. [14]

Synthesis of HHEP

Dry HCl gas was passed through a well cooled and stirred solution of 4-hydroxy acetophenone (50 mmol) and 3-ethoxy-4-hydroxy benzaldehyde (50mmol) in 100 ml of dry ethanol taken in a 250 ml round bottom flask. The yellow colored crystals of HHEP which got separated was washed with double distilled water and recrystallized from hot methanol. Yield - 90%, M.P. – 174^{o}C.

Scheme 1: Synthesis of Monomer Diol HHEP

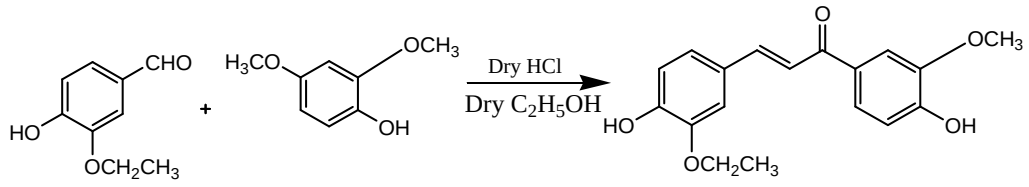


3-ethoxy-4hydroxy benzaldehyde4-hydroxyacetophenone2E)-1-(4-hydroxyphenyl)-3(4-hydroxy,3-ethoxyphenyl) prop-en-1-one

Synthesis of MHEP

Dry HCl gas was passed through a well cooled and stirred solution of 4-hydroxy-3-methoxy acetophenone (50 mmol) and 3-ethoxy-4-hydroxy benzaldehyde (50mmol) in 100 ml of dry ethanol taken in a 250 ml round bottom flask. The yellow coloured crystals of MHEP which got separated was washed with double distilled water and recrystallised from hot methanol. Yield - 74%, M.P. – 194^{o}C

Scheme 2: Synthesis of Monomer Diol MHEP



3-ethoxy-4hydroxy benzaldehyde 4-hydroxy-3-methoxy acetophenone (2E)-1-(4-hydroxy-3-methoxy phenyl)-3(4-hydroxy, 3-ethoxy phenyl) prop-en-1-one

Synthesis of Copolyesters

The procedure [13]for the synthesis of a typical aliphatic diacid chloride-based copolyester is given here. The diol HHEP (1mmol) was dissolved in 10 ml of dry DMF and taken in a 100 ml round bottomed flask. To this 0.2ml of succinyl chloride and 0.2 ml of oxalyl chloride were added with constant stirring and the temperature was maintained at 120^{o}C with continuous stirring for 3 hours. At end the reaction mixture was cooled to room temperature and poured into 100 ml of methanol when the copolyester was precipitated. It was filtered, washed with

dry methanol and dried in vaccum. The other four copolyesters were also prepared by similar method. The diols and the diacid chlorides used and the copolyester code of the four copolyesters are presented in Table 1.

Table 1:Monomers used and the copolyester code of the four copolyesters
Together with Percentage of yield and inherent viscosities (η_{inh})

Diacid chloride– I Succinyl chloride		Copolyester code	Yield (%)	η_{inh} (dL/g)
Diol	Diacid chloride II			
HHEP	Glutaryl chloride	PSGH	84.7	1.01
HHEP	Oxalyl chloride	PSOH	82.3	1.024
HHEP	Isophthaloyl chloride	PSIH	79.2	1.26
MHEP	Oxalyl chloride	PSOM	74.5	1.11
MHEP	Glutaryl chloride	PSGM	81.4	1.13

Antimicrobial Activity (Agar Disc Diffusion Method)
Antibacterial activity of sample was determined by disc diffusion method [15] on Muller Hinton agar (MHA) medium. The Muller Hinton Agar medium was weighed as 3.8gmsand dissolved in 100ml of distilled water and add 1gm of agar. Then the medium is kept for sterilization. After sterilization the media was poured in to sterile petriplates and were allowed to solidify for thirty minutes. After the medium was solidified, the inoculums were spread on the solid plates with sterile swab moistened with the bacterial suspension. Add 20 µl of sample[concentration: 1000 µg, 500 µg, 250 µg, 125 µg & 62.5 µg], negative control add 20 µl ofDMSO and positive control add 10 µl (10 µg) streptomycin on respective disc and placed on MHA plates. These plates were incubated for 24 hrs at 37ºc .Then the microbial growth was determined by measuring the diameter of zone of inhibition.

Antifungal Activity Assay
Antifungal activity of copolyester sample was determined by antifungal susceptibility test. Prepare PDA Broth and inoculate the culture. Then it is kept in shaker for a day. The potato dextrose agar was weighed as 3.9gms and dissolved in 100ml of distilled water to which 1gm of agar was added. Then the medium was kept for sterilization. After sterilization the media was poured in to sterile Petri plates and were allowed to solidify for twenty minutes. After solidification, the inoculums were spread on the solid plates with sterile swab moistened with the fungal suspension. The discs were placed in PDA plate and 20µl of sample [concentration: 500µg, 250µg, 125µg,62.5µg] were added. The plates were kept at room temperature. Then the microbial growth was determined by measuring the diameter of zone of inhibition.

RESULTS AND DISCUSSION

Solubility of all the five copolyesters synthesized were determined in various solvents qualitatively. The inherent viscosity (ηinh) of the copolyesters were determined in DMAc solution at a concentration 0.1 gdL-1 using Ubbelohde viscometer in which the pure solvent had a flow rate of 104 seconds at 30°C. FT-IR spectra of the entire random copolyesters were recorded using Shimadzu FT-IR instrument. The 1H and 13C-NMR spectra were recorded with BRUKER AV III 500 MHz NMR instrument in DMSO-d6 solvent.

Solubility
The copolyesters stated here are found to be soluble in highly polar solvents such as DMAc and dimethyl formamide, partially soluble in moderately polar solvents like tetrahydrofuran and acetone but thoroughly insoluble in least polar solvents like benzene and hexane.[16] Copolyesters with methoxy substituent in the benzene ring of the chalcone moiety had better solubility which may be attributed to their competence to disrupt the macromolecular chain. Similar explanation was offered by Perundevi and coworkers [16] in a series of copolyester.

Viscosity Measurements
The ηinh value of all the five copolyesters was determined in DMAc solution at 30°C using Ubbelohde viscometer. 25mg of each of pure dry copolyester sample was dissolved in 25ml of DMAc, kept aside for some time with occasional shaking. Then they were left undisturbed for 24 hours. The η inh was calculated from the flow time measurements.[16] The inherent viscosity values were found to be in the range of 0.73–1.10dL/g and are presented in table 1. The data shows that these copolyesters are reasonably of high molecular weight.

Spectral Studies

FT-IR spectrum of the five copolyesters were recorded using Shimadzu FT-IR instrument. The FT-IR spectrum of all the five copolyesters revealed characteristic absorption in the range of 1742–1764cm-1 due to ester C=O stretching frequency. Similar observations were made by Samuel and
Coworkers [17] in a series of copolyesters.

The NMR spectra were recorded with BRUKER AV III 500 MHz NMR instrument in DMSO-d6 solvent to categorize the repeating structural units present in the copolyester chain. The aromatic protons are observed in the range of 7.2–8.1ppm. The vinyllic protons attached to the carbonyl carbon are observed in the range of 6.7–6.9ppm. The methoxy protons in the chalcone moiety are represented in the range of 3.1–3.4ppm. The methylene protons are observed in the range of 1.3–3.3 ppm. Similar remarks were made Perundevi and coworkers [16] in a series of copolyesters derived from bischalcones.

The signals in the range of 170–205ppm and 165–175ppm in the 13C-NMR spectra of the copolyesters are due to the carbonyl carbon of theα,β-unsaturated ketone and ester groups, respectively, which indicates the formation of copolyester.

Table 2: Inhibition effects of the five copolyesters on the growth of *Staphylococcus aureus, Klebsellia pneumonia, Bacillus Subtilis, E.Coli* and *Pseudomonas aeruginosa*

Test Material	*Staphylococcus aureus*						*Klebsellia pneumoniae*					
	1000 µg	500 µg	250 µg	125 µg	62.5 µg	Streptomycin 10 µg	1000 µg	500 µg	250 µg	125 µg	62.5 µg	Streptomycin 10 µg
PGSH	6	6	-	-	-	16	7	6	-	-	-	16
POSH	9	9	9	8	8	16	13	10	12	10	10	16
POSM	5	5	5	5	5	16	6	6	6	6	6	16
PSIM	6	7	6	6	6	16	10	9	8	8	7	16
PSGM	12	9	8	8	7	16	12	11	10	10	9	16

Test Material	*Bacillus Subtilis*						*E.Coli*					
	1000 µg	500 µg	250 µg	125 µg	62.5 µg	Streptomycin 10 µg	1000 µg	500 µg	250 µg	125 µg	62.5 µg	Streptomycin 10 µg
PGSH	9	8	6	-	-	17	8	7	-	-	-	18
POSH	14	13	13	12	10	17	9	8	8	7	7	18
POSM	10	10	9	7	7	17	9	8	8	7	7	18
PSIM	10	10	9	7	7	17	9	8	8	7	7	18
PSGM	13	11	8	6	-	17	12	10	10	7	7	18

Test Material	*Pseudomonas aeruginosa*					
	1000 µg	500 µg	250 µg	125 µg	62.5 µg	Streptomycin 10 µg
PGSH	7	6	6	6	6	16
POSH	10	9	8	8	8	16
POSM	7	7	7	7	6	16
PSIM	8	8	8	8	8	16
PSGM	10	10	8	8	8	16

Bactericidal Study

The antibacterial activity [18] of the five copolyesters PSGH, PSOH, PSIH, PSOM and PSGM were assayed against (*Staphylococcus aureus, Bacillus subtillus, Klebsilla pnemoniae, Pseudomonas aeruginosa* & amp; *Escherichia coli* by disc diffusion method. [19]. Streptomycin inhibited the escalation of *Staphylococcus aureus* by 20mm, Enterrococcus faecalis

By 19mm, Bacillus cereus by 26mm, and Escherichia coli by 17mm. From table 2 it is apparent that the four copolyesters were found to be bactericidal in nature. With increase of concentration of the copolyester material it was observed that the inhibition effect increased.

Fungicidal Study

The antifungal activity [20] of the synthesized copolyesters PSGH, PSOH, PSIH, PSOM and PSGM were assayed against *A.fumigates, Aspergillus flavus, T. mentogrophyte* by disc diffusion method. Streptomycin subdued the

growth of *Candida albicans* by 14mm, *Aspergillus flavus* by 13mm, *Penicillium* by 10mm, and *T. mentogrophyte* by 10mm. From table 3 it is obvious that the five copolysters were found to be fungicidal in nature.

Table 3: Inhibition effects of the five copolyesters on the growth of *A.flavus, A. fumigates*, and *T.mentagrophyte*

Test Material	*A.flavus*					*A.fumigates*				
	1000 µg	500 µg	250 µg	125 µg	62.5 µg	1000 µg	500 µg	250 µg	125 µg	62.5 µg
PGSH	12	10	-	-	-	9	-	-	-	-
POSH	17	14	10	-	-	14	12	10	-	-
POSM	18	15	13	10	-	16	14	11	7	7
PSIM	8	-	-	-	-	18	17	13	-	-
PSGM	10	9	9	-	-	-	-	-	-	-

Test Material	T,mentagrophyte				
	1000 µg	500 µg	250 µg	125 µg	62.5 µg
PGSH	20	16	12	7	-
POSH	31	26	21	20	14
POSM	25	20	20	20	19
PSIM	22	19	19	12	10
PSGM	21	19	16	16	15

CONCLUSION

All the five copolyesters synthesized using a diacid chloride-I (Succinyl chloride), diacid chloride-II (Glutaryl chloride, oxalyl chloride and isopthaloyl chloride) and a chalcone diol. The chalcone diols are varied. The chalcone diols used are (2E)-1-(4-hydroxyphenyl)-3(4-hydroxy,3-ethoxy phenyl) prop-en-1-one (HHEP) and (2E)-1-(4-hydroxy-3-methoxy phenyl)-3(4-hydroxy,3-ethoxy phenyl) prop-en-1-one (MHEP) .The copolyesters synthesized here are highly soluble in polar organic solvents. These random copolyesters are characterized by solubility studies, viscosity measurements and spectral data. The copolyesters exhibited significant bactericidal activity against pathogenic bacteria. Some of them are also found to be fungicidal in nature.

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