Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2012, 4(1):393-397

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis, Characterisation and Antimicrobial Activity of Certain Chalcone Based Random Copolyesters

***R. Senthamizh Selvi, R. Nanthini and G. Sukanyaa**

Postgraduate and Research Department of Chemistry, Pachaiyappa's College, Chennai

---

ABSTRACT

In an effect to develop antimicrobial activity, four copolyesters were synthesised from 1, 3-bis (4-hydroxy-3-methoxyphenyl) propenone (BHMPP) and 1- (3, 5-dihydroxyphenyl)-3-(4-methoxyphenyl) propenone (DHPMPP) by Phase transfer catalysed polycondensation with adipoyl, suberoyl, azeloyl and sebacoyl chlorides. These copolyesters were characterised by solubility data and viscosity measurements. The microstructure of the repeating unit was confirmed by IR, ^{1}H and ^{13}C NMR. These copolyesters displayed potential antimicrobial activity against fungal and bacterial strains.

Keywords: Chalcones, copolyesters, polycondensation, antifungicidal and antibactericidal.

INTRODUCTION

Chalcones are 1, 3-diphenyl-2-propene-1-one, in which two aromatic rings are linked by a three carbon α, β-unsaturated carbonyl system. They possess conjugated double bonds and a completely delocalised π-electron system on both benzene rings. Molecules possessing such system have relatively low redox potentials and have a greater probability of undergoing electron transfer reactions. Chalcones represent an essential group of natural as well as synthetic products and some of them possess wide range of pharmacological activity such as antibacterial [1], antitumoural [2], anticancer [3], antitubercular, anti-inflammatory [4], antioxidant [5], antimalarial [6], antiulcerative [7] etc. The presence of reactive α, β-unsaturated keto group in chalcones is found to be responsible for their biological activity [8].

Chalcones constitute a repeated group of natural products and some of them possess a wide range of biological activities such as antimicrobial (Prasad, Y.et al.). Antimicrobial agent-bound polymers exhibit antimicrobial activities by slowly releasing active agents through hydrolysis, while some polymers are also antimicrobial by themselves.

Chalcones are natural or synthetic flavonoids displaying an impressive array of biological properties. Their antimicrobial activity and particularly the antifungal action have been largely attributed to the reactive enone moiety [9, 10]. As a Michael reaction acceptor the enone unit binds thiol groups of certain proteins. The Michael reactions of chalcones are facilitated by electron withdrawing (EW) groups at p-position in ring B.

Due to the rapid development of bacterial resistance to antibacterial agents, it is vital to discover novel scaffold for the design and synthesis of the new antibacterial agents to help in the battle against pathogenic microorganisms. It was observed that the antibacterial efficiency depends on the length of the alkyl substituents in the polymer repeat units. As the polymer became more hydrophobic (hexyl and higher alkyl chain lengths in the repeat unit) the integrity of the membrane was more efficiently disrupted [11-16]. The bactericidal effects have been related to the ability of the α,β-unsaturated ketone to undergo a conjugated addition to a nucleophilic group.

EXPERIMENTAL SECTION

Materials

Adipic acid (Ranbaxy), sebacic acid (SDS) and thionyl chloride (SDS) were purchased and used . 4-hydroxy benzaldehyde (Merck), 4-hydroxy-3-methoxy benzaldehyde (Merck) were used as received. Tetra-n-butylammonium bromide (TBABr, Fluka) was purchased and used. Spectral grade DMSO-d6 (Aldrich) containing TMS as internal standard was used as received for recording NMR spectra.

Synthesis of monomers

1, 3-bis (4-hydroxy-3-methoxyphenyl) propenone (BHMPP)

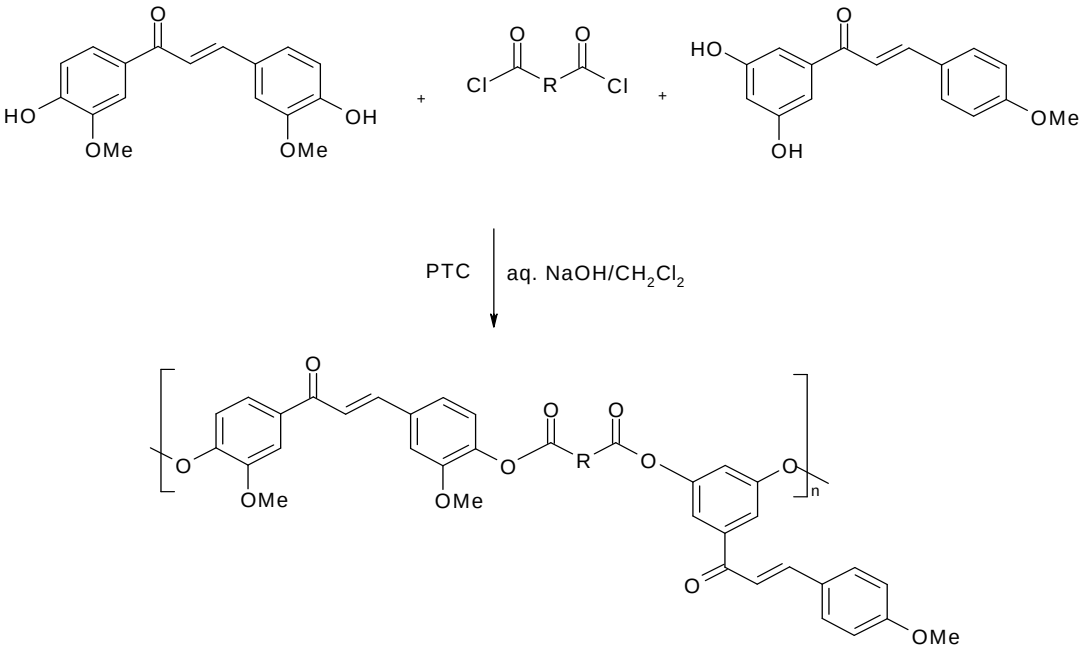
A mixture of 4-hydroxy3-methoxy benzaldehyde and 4-hydroxy-3-methoxy acetophenone kept dissolved in methanol. The reaction was allowed to proceed for an hour and then poured into ice cold water the yellow precipitate of BHMPP was filtered, dried and further recrystallised from methanol.Yield:90%, m.p:200^{o}C. FT IR (KBr): 3400 cm^{-1}(ν_{OH}); 1591 cm^{-1}($\nu_{C=C}$); 1641 cm^{-1}($\nu_{C=O}$). ^{1}H NMR (DMSO-d6):7.1-8.2δ (aromatic), 9.7 δ (S, 2H,-OH), 3.6 δ (S, 3H,-OCH_3). ^{13}C NMR (DMSO-d_6): 188.51 δ (>C=O), 158.24 δ (C-OH), 55.63 δ (-OCH_3). Molecular formula: $C_{17}H_{16}O_5$, MS (El) m/z 300[M^+].

1-(3, 5-dihydroxyphenyl)-3-(4-methoxyphenyl) propenone (DHPMPP)

1-(3, 5-dihydroxyphenyl)-3-(4-methoxyphenyl) propenone was prepared from 3,5-dihydroxy acetophenone and 4-methoxy benzaldehyde kept dissolved in methanol. The reaction was allowed to proceed for an hour and then poured into ice cold water the yellow precipitate of BHMPP was filtered, dried and further recrystallised from methanol.

Synthesis of copolyesters

Equimolar quantities of BHMPP (1 mmole) and DHPMPP (1mmole) were dissolved in 25 mL of aqueous sodium hydroxide (0.1 N) solution and taken in a round- bottomed flask (100 mL). After 15 minutes a solution of 2 mL of 2% phase-transfer catalyst was added and stirred. The mixture was stirred continuously at room temperature for 30 minutes in inert atmosphere. About 25 mL solution of adipoyl chloride (2 mmole) in dichloromethane (DCM) was added. The mixture was maintained at room temperature with continuous stirring for seven hours. The reaction mixture was poured into 100 mL of n-hexane when the solid co polyester was obtained. It was then filtered in vaccum. The crude sample was purified and used. Copolyester PBHR2, PBHR3 and PBHR4 were prepared by a similar method using suberoyl, azeloyl and sebacoyl chlorides [17]. The scheme is presented below. The aliphatic acid chlorides used in the scheme are given in Table 1.



Antimicrobial activity

The copolyesters obtained were tested against different bacterial strain (*Escherichia coli, Staphylococcus aureus, Enterococcus faecalis* and *Bacillus subtilis*) and fungal strains (*Candida albicans, Trichophyton rubrum, Aspergillus niger, Trichophyton mentagraphytes, Aspergillus flavus* and *Rhizopusoryzae*).

Table 1. Aliphatic acid chlorides used and the copolyester code of the four polyesters.

S. No.	Codes of polyesters	Acid chloride (R)
1	PBHR1	$-(CH_2)_4-$
2	PBHR2	$-(CH_2)_6-$
3	PBHR3	$-(CH_2)_7-$
4	PBHR4	$-(CH_2)_8-$

RESULTS AND DISCUSSION

The copolyesters synthesised in the present work were characterised by solubility studies, viscosity measurements and spectral data.

Solubility

All the synthesised polymers were easily soluble in aprotic polar solvents like tetrahydrofuran, dimethyl sulphoxide, dimethyl formamide, dimethylacetamide, dioxane, p-cresol and in chlorinated solvents such as methylene dichloride, chloroform and insoluble in toluene, n-hexane, benzene, xylene, diethyl ether and other hydrocarbons solvents. This may be due to the inter-molecular interactions of polar solvents with ester linkage of the polymer molecules. Some of the polymers do not dissolve in the above said solvents; which polymer does not dissolve, in which other solvent is it dissolving. This might be due to the high rigid aromatic nature of the polymers [18].

Viscosity of copolyesters

The inherent viscosity of the resulting polymers was determined in dimethyl sulphoxide solution at 30^{o}C using Ubbelohde viscometer. In each case, 25 mg of dry pure copolyester sample was dissolved in 25 ml of DMSO, kept aside for some time with occasional shaking. The η_{inh} was calculated from the flow time measurement. The inherent viscosity values of all the copolyesters are listed in Table 2. The data reveals that these polymers are of reasonably high molecular weight.

Table 2. Percentage of yield and inherent viscosities (η_{inh}) of the copolyesters

S.No	Copolyester	Yield (%)	Inherent viscosity (dL/g)
1	PBHR1	75	0.33
2	PBHR2	77	0.34
3	PBHR3	78	0.36
4	PBHR4	80	0.38

Spectral studies

IR spectra of the four copolyesters were recorded using Nicolet 510 FT-IR instrument. IR spectra of all the four copolyesters showed characteristic absorption in the range of 1742-1764 cm^{-1} due to ester C=O stretching frequency. From the spectra, it could be observed that characteristic absorption frequencies in the range 1585-1598 cm^{-1} and 976-986 cm^{-1} are characteristic of trans olefinic double bonds. The stretching vibration of methylene group show characteristic absorption band in the range 2851-2875 cm^{-1}.

The ^{1}H and ^{13}C NMR spectra were recorded with JEOL GSX-400MHz instrument in DMSO-d6 solvent to identify the structural units present in the copolyester chain. The aromatic protons are observed in the range of 7.5-8.0 ppm. The methoxy protons in the chalcone moiety are showed by a signal at 3.4 ppm. The signal in the range of 185-200 ppm and 168-172 ppm in the ^{13}C NMR spectra due to the presence of ketone carbonyl and ester carbonyl carbon (Kannappan et al.).

Antimicrobial activity of copolyesters

The antifungal activity of the synthesised copolyesters were assayed at concentrations of 15.62 µg/ml, 31.25µg/ml, 62.5µg/ml, 125µg/ml, 500µg/ml and 1000µg/ml against six plant pathogens and mould fungi. The zone of minimum inhibition against all test fungi is given in Table 3.

The presence of an enone linkage would be a structural requirement necessary but not by itself sufficient for the antifungal activity. Unexpectedly, the most active compounds PBHR1, PBHR2, PBHR3 and PBHR4 does not have electron withdrawing group in the para position of ring A [19, 20 & 21], but these compounds seem to exhibit strong antifungal activity against *Rhizopusoryzae*, *T.mentagrophytes*, *T.rubrum* and *A.niger*, which may be due to the presence of methoxy substituent (Rajan et.al.) and 4 - methoxy phenyl propanone as the pendant group present

in the para position in the main chain [22]. But the same compounds show moderate antifungal activities against *C. albicans* and *A. flavus* at high concentration in comparison with standard fungicides, fluconozole. This may be due to the presence of electron donating substituent $–OCH_3$ group in m-position in ring-B. Among these polymers, PBHR4 should possess very strong antifungal activity against all fungal strains at all concentrations which may be due to the increase in alkyl chain length (octyl and higher alkyl chain length in the repeating unit).

Table 3: Antifungal activity of copolyesters of PBHR1, PBHR2, PBHR3 and PBHR4 using broth micro dilution method MIC (µg/ml)

S.No	Tested fungi	PBHR1 (µg/ml)	PBHR2 (µg/ml)	PBHR3 (µg/ml)	PBHR4 (µg/ml)
1	*Candida albicans*	62.5	62.5	31.25	15.62
2	*Trichophyton rubrum*	31.25	31.25	31.25	15.62
3	*Aspergillus niger*	15.62	15.62	15.62	15.62
4	*Trichophyton mentagrophytes*	31.25	15.62	15.62	15.62
5	*Aspergillus flavus*	125	125	62.5	62.5
6	*Rhizopusoryzae*	15.62	15.62	15.62	15.62

The bacterial activity of the synthesised PBHR4 was probed against Gram-positive bacterias including *S. aureus, E. faecalis and B. subtilis* and Gram-negative bacteria namely *E. coli*. The experimental results indicate that, the above compound PBHR4 shows good antibacterial activity against *E. faecalis, B. subtilis* and *E. coli*, which may be due to the presence of electron releasing group such as methoxy group in both rings A and B. In addition to this, the higher bactericidal activity of the polymer may be due to the fact that polymers can more readily diffuse across the bacterial cell walls [23, 24].The results of the antimicrobial screening of the PBHR4 copolyester was given in Table 4.

Table 4: Inhibition effects of polyesters of PBHR4

Zone of inhibition (diameter in mm)					
Microorganisms	**1000µg**	**500 µg**	**250 µg**	**100 µg**	**Streptomycin 10µg**
Escherichia coli	9	8	9	8	22
Staphylococcus aureus	7	7	6	-	24
Enterococcus faecalis	9	8	9	8	26
Bacillus subtilis	9	8	8	8	17

CONCLUSION

Four copolyesters are synthesised using a diols of 1, 3 - bis-4-hydroxyl 3- methoxyphenyl) propenone (BHMPP) and 1- (3, 5-dihydroxyphenyl) - 3 - (4-methoxyphenyl) propenone (DHPMPP) coupled with aliphatic acide chlorides like adipolyl, suberaloyl, azeloyl and sebacoyl chloride. The copolyesters were characterised by viscometric and spectral studies. These copolyesters exhibited significant antimicrobial activity against fungal and bacterial starins.

REFERENCES

[1] S.S. Mokle, M.A. Sayeed, Kothawar and Chopde, *Int. J. Chem. Sci.*, **(2004)**. 2(1): 96.
[2] P.M. Siva Kumar, S.K. Geetha Babu and D. Mukesh, *Chem. Pharm. Bull,* **(2007)**. 55(1): 44.
[3] E. Francesco, G. Salvatore, M. Luigi and C. Massimo, *Phytochem,* **(2007)**. 68: 939.
[4] H.K. Hsieh, L.T. Tsao, L.T. and J.P. Wang, J. *Pharm. Pharmacol.*, **(2000)**. 52: 163.
[5] C.L. Miranda, G.L.M. Aponso, J.F. Stevens, M.L. Deinzer and D.R. Buhler, *J. Agric. Food Chem,* **(2000)**. 48: 3876.
[6] M. Liu, P. Wilairat and L.M. Go, *J. Med. Chem,* **(2001)**. 44: 4443.
[7] S. Mukarami, M. Muramatsu, H. Aihara and S. Otomo, *Biochem. Pharmacol,* **(1991)**. 42: 1447.
[8] A. Rajendra Prasad, A. Lakshmana Rao and R. Rambabu, *E. Journal of Chemistry*, **(2008)**. 5(3): 461-466.
[9] Shailendra Mandge, Hemendra P.Singh, S. Dutta Gupta and N.S. Hari Narayana Moorthy, *Trends in Appl. Sci.*, **(2007)**. 2(1): 52-56.
[10] Nowakowska. Z. Eurp. *J. Medicinal Chemistry,* **(2007)**. 42: 125-137.
[11] S. Priyarega, A. Muthusamy,K. Kaniappan and S.C. Murugavel, *Polymer*, **(2003)**. 6: 187-196.
[12] O. Nerya, R. Musa, S. Khatib, S. Tamir and J. Vaya, *Phytochemistry,* **(2004)**. 65: 1389-1395.
[13] E.B. Yang, Y.J. Guo, Y.Z. Zhang, Chen, P. Mack, *Biochim. Biophy. Acta,* **(2001)**. 1550: 144-152.
[14] A. Friis-Miranda, M. Chen, K. Fuursted, S. Christensen and B. Kharazmi, *Planta Med.*, **(2002)**. 68: 416-419.
[15] T. Fukai, A. Marumo, K. Kaitou, T. Kanda, S. Terada and T. Nomura, *Life Sci.* **(2002)**. 71:1449-1463.

[16] T. Hatano, Y. Shintani, Y. Aga, S. Shiota, T. Tsuchiya and Yoshida, *Chem. Pharm. Bull*. **(2000**). 48: 1286-1292.
[17] A. Muthusamy and S.C. Murugavel, *Polymer*, **(2006)**. 18: 227-240.
[18] K. Kaniappan and S.C. Murugavel, *J. Macro. Sci., Part-A*, **(2005)**. 42: 1589-1602.
[19] P. Ramkumar, K. Ganesan, S. Jayavelu and K. Murugasen, *Syn.Lett*. **(2006)**. 11: 1121-1124.
[20] P.M. Gurubasavaraja Swamy and Y.S. Agasimundin, *Acta. Pharm. Sci.*, **(2008)**. 50: 197-202.
[21] Y. Rajendra Prasad, P. Praveen Kumar and P. Ravi Kumar, *Eur. J. Chem*. **(2008)**. 5: 144-148.
[22] Y.C. Rajan , C.C. Kanakam, S. Periyar Selvam and K. Murugesan, *Tetrahedron Letr*. **(2007)**.48: 8562-8565.
[23] R.S. Suman, M.S. Malik,T.S. Kathpal and O.P. Malik, *Indian J. Chem*. **(1995)**. 34: 743-746.
[24]K. Jankova, J. Kops, X. Chen, W. Batsberg, *Macromol. Rapid Commun*. **(1999)**. 20: 219.