AMERICAN JOURNAL OF PHARMTECH RESEARCH

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Synthesis, Characterization and Antifungal activity of Coumarin based random copolyester

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ABSTRACT

Synthesis of coumarin based random copolyester was prepared by the reaction of biscoumarin monomer **1** and anthroquinone**3** with azeloyl chloride through interfacial polycondensation technique by using phase transfer catalyst. The chemical structure of the copolyester was investigated by Fourier-transform infrared spectroscopy (FTIR) and proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy. Disc diffusion method was employed to investigate the antifungal activity of the synthesized copolyester.

Keywords: Coumarin, Antifungal, Copolyester, Condensation.

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Received 12 May 2014, Accepted 21 May 2014

Please cite this article in press as: Swamy NK *et* Synthesis, Characterization and Antifungal activity of Coumarin based random copolyester. American Journal of PharmTech Research 2014.

INTRODUCTION

A probe through the literature indicates that there has been a rising interest in synthesizing aliphatic aromatic copolyester[1-6]. Of particular interest coumarin based random copolyester, because of its wide spectrum of pharmacological activity such as antimicrobial, antifungal, anticoagulant, anticancer, anti-inflammatory and antiviral etc. During the implantation of medical devices such as sutures, prosthesis anchor, staples and valves there is a possibility of creating a biofilm into the near vicinity of surgical implantation. The fungal within the biofilm are often resistant to antibiotics. To encounter this problem, the surgical implanted material has to be coated with polymer having antifungal activity. By considering the above facts it is necessary to develop a new class of antifungal copolyester was designed and synthesized for screening of antifungal activities against various microorganism

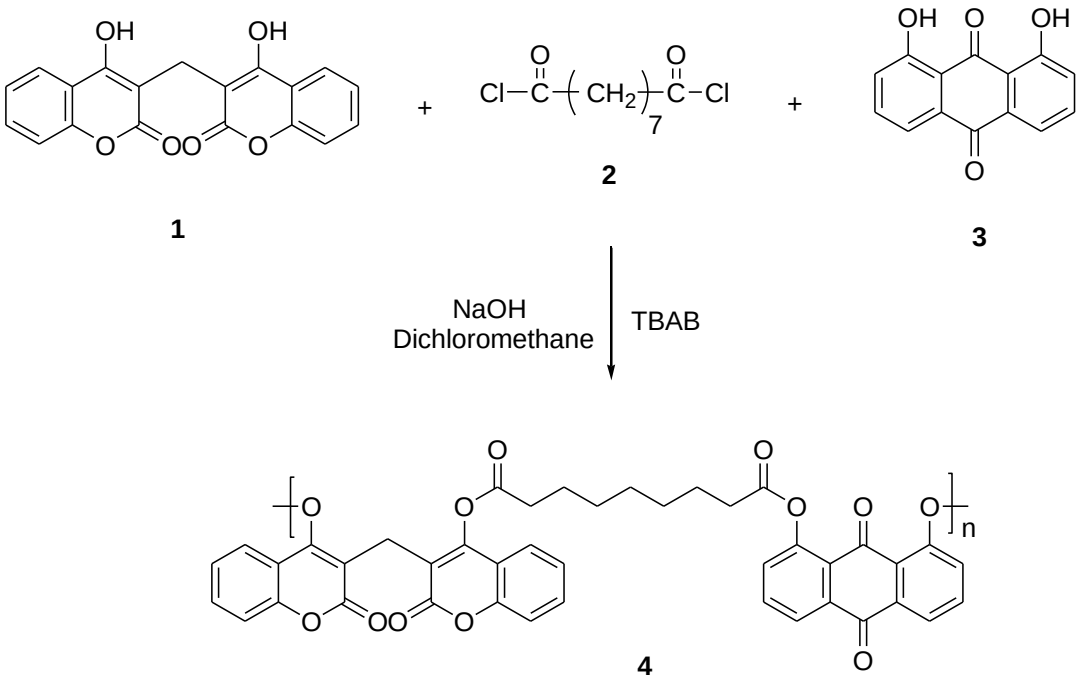
MATERIALS AND METHODS:

Dicoumarol, 1,8-dihydroxyanthraquinone and azeloyl chloride (Aldrich) were used as such. *Tetra-n-butylammonium bromide (TBAB)* and sodium hydroxide (Merck, India) were used as received. Solvents were purified according to the standard procedure in the literature[7].3% (w/v) solutions were taken as a standard for solubility of copolyester in various solvents. FT-IR spectra were recorded on Perkin Elmer 883 spectrophotometer. ^{1}H-NMR spectra for copolyester was recorded on a Bruker 400 MHz spectrometer using $CDCl_3$ as a solvent. *Aspergillus Niger, Aspergillus Flavus, Candida Albicans and Proteus Vulgaris* were the fungi which were used for the study.

Experiment:

Synthesis of copolyester (4)

In a three-neck round-bottomed flask (500 cm^3 in volume), equipped with a mechanical stirrer, dry nitrogen inlet, outlet and dropper, a mixture of 3,3′-methylene-bis(4-hydroxycoumarin)**1** and 1,8-dihydroxyanthraquinone**3** each (0.002 mmole) was taken. Sodium hydroxide (0.008 mmole) dissolved in 80 ml distilled water was added ,with continuous stirring, 2ml of 2% tetra-n-butyl ammonium bromide was added. 0.004 mmole of azeloyl dichloride, dissolved in 30ml dry methylene chloride was added and the stirring was continued for a further period of 1hr at 2000 rpm. Then reaction mixture was poured into methanol; the precipitated polymer was filtered and washed several times with water. The polymer was dissolved in chloroform and reprecipitated in methanol and dried under reduced pressure at 80^{o}C for 24h to yield 85% of pure copolyester.



Scheme 1 Synthesis of copolyester4

RESULTS AND DISCUSSION

It is noteworthy that such a synthetic methodology for rapid preparation of random copolyester affords advantages of short reaction time, high yields and simple workup. Structural assignments of the peaks coincide with the spectral data of the FT-IR analysis. The copolyester show characteristic absorption due to carbonyl stretching of the ester group at around 1725 cm^{-1}. However, it is interesting to find the peak at 1648cm^{-1} corresponding to the stretching of carbonyl group of 3,3′-methylene-bis(4-hydroxycoumarin)**1** molecule. So it can be inferred that the biscoumarin molecule is an integral part of the polymer backbone. ^{1}H NMR data are in confirmative with the structure of the molecule proposed under investigation. In the proton NMR of copolyester, bridged carbon of biscoumarin unit appeared at 3.90ppm, thus conforming the incorporation of biscoumarin monomer **1** in the polymeric chain. The characteristic peak at 1.13-2.34ppm is attributed to the aliphatic acid dichloride. The aromatic protons related to biscoumarin**1** and anthraquinone**3** in the polymer backbone appeared in the region of 8.22-7.10 ppm respectively.

***In vitro* antifungal activity:**

Synthesized copolyester was screened for antifungal activity against *Aspergillus Niger,Aspergillus Flavus, Candida Albicans and Proteus Vulgaris* were the fungi which were used for the study. Disc diffusion method on Sabouraud Dextrose agar medium has been employed to determine the Antifungal activity of extracts. A stock culture was maintained on Nutrient agar Slant at 6°C.

Active cultures for experiments were prepared by transferring a loop full of culture from the stock cultures into the test tubes containing Sabourad Dextrose broth, that were incubated at 24h at 37ºC. The activity of copolyester was given in Table 1

Antifungal activity[8,9] of copolyester was evaluated against four fungal species, viz. *Aspergillus Niger, AspergillusFlavus, Candida Albicans*and *Proteus Vulgaris*as shown in Fig 1. It was found that copolyester has good, in-vitro antifungal activity. Both monomer 1 and 3 exhibited very good activity against Candida Albicans and Proteus Vulgaris. Monomer 3 exhibited very least activity against Aspergillus Niger, AspergillusFlavus. It is inferred that the lipophilicity character of copolyester enhances the antifungal activity against microbs by penetration of cell wall and restricts further growth of organisms.

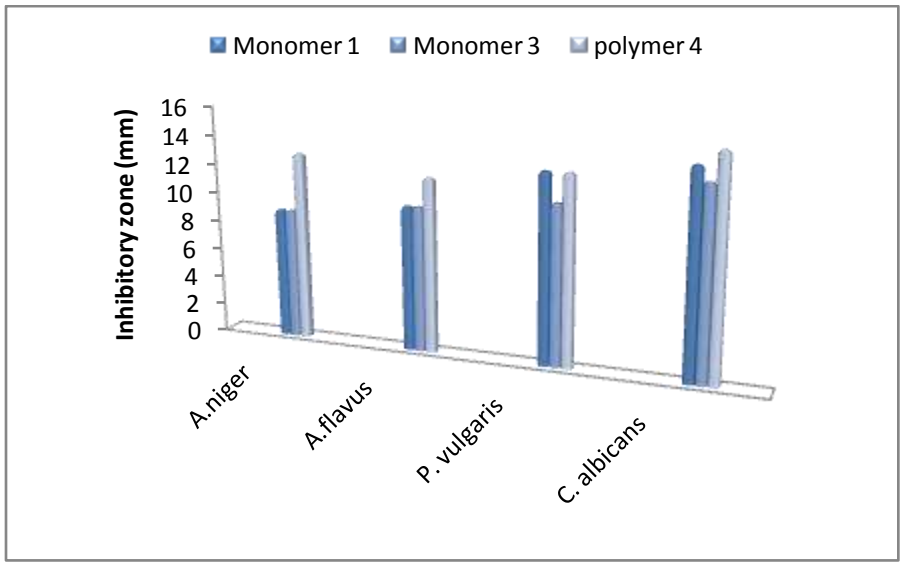


Figure 1: Comparative activities of monomers and copolyester against microbes using 60µL concentration

Table 1: Zones of inhibition (in mm) of the compounds against various microbes

	A.niger			***A.flavus***			***P. vulgaris***			***C. albicans***		
Compound	**20µL**	**40µL**	**60µL**	**20µL**	**40µL**	**60µL**	**20µL**	**40µL**	**60µL**	**20µL**	**40µL**	**60µL**
Monomer 1	-	8	9	9	10	10	-	11	13	12	12	14
Monomer 3	-	-	9	-	-	10	-	10	11	10	12	13
polymer 4	10	12	13	9	11	12	10	11	13	12	14	15

CONCLUSION:

In the present investigation, the synthesized copolyester showed promising antifungal activity against four fungal species, *Aspergillus Niger, AspergillusFlavus, Candida Albicans and Proteus Vulgaris*. It is concluded that the synthesized copolyester may be preferred as antimicrobial coating agents in various surgical implants and finds applications in variety of medical disciplines.

ACKNOWLEDGEMENT:

The authors would like to thank CLRI technical persons for their analytical support.

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