SCOPE AND OBJECTIVE OF THE PRESENT WORK

2.1 Scope and background

Development of new polymeric materials for intended specific applications have garnered interest among research scientists. Liquid crystalline polymers are a subject area of the great upsurge of interest for having potential applications in various fields, including optics, optical data storage, optoelectronic and non-linear optic devices.[1-6] Rigid polyarylates like Poly(hydroquinone terephthalate) and poly(hydroxybenzoate) exhibit high melting temperatures. The incorporation of non-coplanar 2,2'-biphenylene moiety into the polymer backcone can improve the processability by decreasing the intermolecular interactions.

Polyarylates synthesized by polycondensation of 2,2′-bibenzoyl chloride with various bisphenols had glass transition temperatures in the range of 120–250°C. Aromatic homopolyesters synthesized with 2,2'-dimethyl biphenylene units had lower phase transition temperatures and enhanced solubilities.[7] Polymers synthesized with monomer bearing a bulky side group (*tert*-butyl hydrochinone) or a crankshaft monomer (6-acetoxy-2-naphthoic acid) with the non-coplanar 2,2′-dimethyl biphenol and terephthalic acid showed nematic mesophase.[8] Thermotropic random copolyesters containing 2,2′-biphenylene rings, disclike mesogens in the polymer chain, were synthesized by Padmanaba Naidu et al.[9] Direct polycondensation of 2,2'-bibenzoic acid with various aromatic diamines improved the solubility of polymers in various organic solvents. Malcolm B. Polk et al studied the thermal properties of block and random copolyesters containing the o, o'-biphenol moiety. Replacement of 4,4'-biphenyldicarboxylate, and even terephthalate and isophthalate moieties by 2,2'-biphenyldicarboxylate moiety greatly lowers the softening point of the polymer due to the reduction in the closeness of packing of the polymer chains.

Biocompatibility and biodegradability of polyesters make it available to be used in biomedical and biomaterial fields. Diphenic acid derivatives[10] possess various pharmacological activities. [11] Owing to the wide spectrum of pharmacological applications, 2,2'-biphenyl dicarboxylic was used as a base scaffold to synthesize various copolyesters. This was suitably copolymerized using vivid aliphatic, alicyclic and aromatic monomers.

Antibiotic resistance is rising to dangerously high levels in all parts of the world. In the year 2017, the WHO has warned twelve superbugs as antibiotic resistant which includes *E. coli* and *salmonella,* which live in human and animal guts and can cause food poisoning and *Staphylococcus aureus*, which is responsible for about a third of "flesh-eating bacteria" infections in the United States. Antimicrobial polymers offer promise for enhancing the efficacy of some existing antimicrobial agents and minimizing the environmental problems accompanying the use of conventional antimicrobial agents, by reducing the residual toxicity of the agents, increasing their efficiency and selectivity and prolonging the lifetime of the antimicrobial agents. In addition, polymeric antimicrobial agents have the advantage of being nonvolatile, chemically stable and do not permeate through the skin.[12] Nurit Beyth *et al*., reported antibacterial activity of dental composites containing quaternary ammonium polyethylenimine nanoparticles against Streptococcus mutans.[13] Tom Anthierens *et al*., synthesized alkyne-containing poly (butylene adipate) functionalized with quaternary phosphonium groups as potential antimicrobial packaging material.[14] Kannapan *et al*., synthesized a series of four poly (ester-amides) by direct polycondensation of 4,4'-oxybis(benzoic acid) with arylidene diol and a diamine and studied the bactericidal efficacy.[15] Malathy *et al*., synthesized six nonlinear random copolyesters by direct polycondensation of mesogenic 4,4'-oxybis(benzoic acid) with certain aliphatic diols and arylidene diols and investigated the bactericidal activity.[16] Prompted by the biological activities of 2,2'-biphenyl dicarboxylate moiety we envisioned our approach towards the synthesis of random copolyesters

containing 2,2'-biphenyl dicarboxylic acid as a monomer with certain diols like hydroquinone, hydroquinone bis(hydroxyethyl ether), 2-hydroxyethyl-4-hydroxybenzoate, bisphenol A, 1,4-cyclohexanediol and 1,8-dihydroxyanthraquinone and specific aromatic dicarboxylic acids such as terephthalic acid, 4,4'-oxybis (benzoic acid) and 2,6-naphthalene dicarboxylicacid for antibacterial studies.

To improve the pharmacokinetic and pharmacodynamic activity of the anti-cancer drug polymers with targeted drug delivery systems are developed. Dose-limiting toxic effects, solubility and *in vivo* instability are the stumbling blocks in cancer drug development. Divema the first synthetic polymeric anticancer drug was found to be toxic because of the high molecular mass. Sun-Mi Lee *et al* synthesized anti tumor active polymers, poly(metacryloyl-2-oxy-1,2,3-propanetricarboxylic acid-co-exo-3,6-epoxy-1,2,3,6-tetrahydrophthalic acid), poly(metacryloyl-2-oxy-1,2,3-propanetricarboxylic acid-co-hydrogen ethyl-exo-3,6-epoxy-1,2,3,6-tetrahydrophthalate), poly(metacryloyl-2-oxy-1,2,3-propanetricarboxylic acid-co-hydrogen ethyl-exo-3,6-epoxy-1,2,3,6-tetrahydrophthaloyl-5-fluorouracil) of number average molecular weight ranging from 9,400 to 14,900 and the in vitro cytotoxicities of copolymers were evaluated with mouse mammary carcinoma (FM3A), mouse leukemia (P388), and human histiocytic lymphoma (U937) as cancer cell lines. The *in vivo* and *in vitro* studies show that the polymers have much improved activity than free 5-fluorouracil.[17] Woo-Moon Choi *et al* synthesized polymers containing pyrimidine derivatives and found that the cytotoxicities of the polymers on the MT-4 cell line to be much less than 3'-azido-3'-deoxythymidine (AZT). [18] The aim of this work is to synthesize anticancer active polyesters containing diphenic acid moiety. Six random copolyesters containing diphenic acid were examined against MCF-7 and A549 cell lines.

Applications of 2,2'-biphenylene moiety in various fields are given below

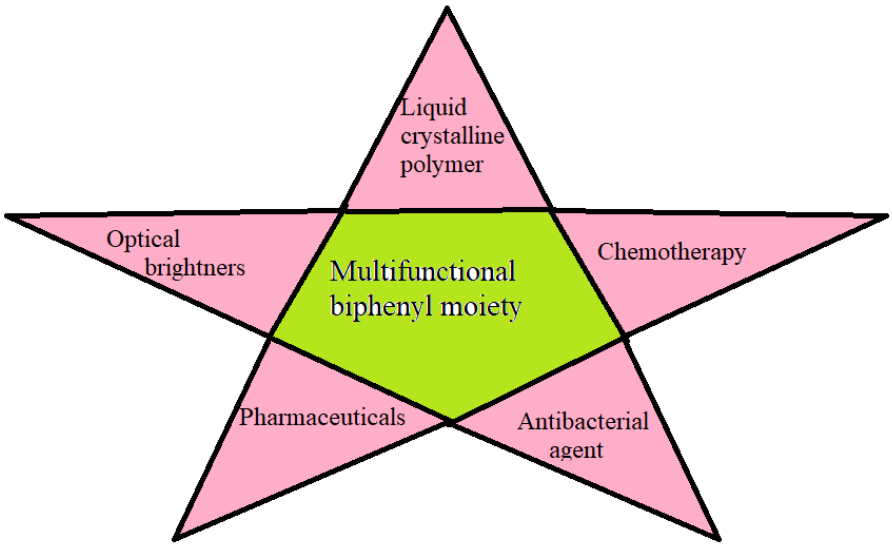
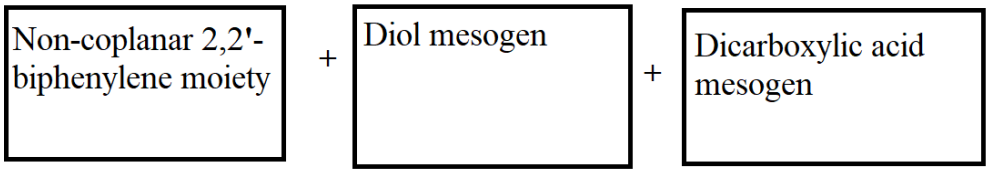


Figure 2.1 Multifunctional applications of 2,2'-biphenylene moiety

2.2 Objective

The main objective of this work is to incorporate non-coplanar 2,2'-biphenylene moiety into the polymer backbone and to study the structure-property relationship of the random copolyesters with respect to the different moieties present in the polymer backbone. The present work focuses on the synthesis, characterization and their applications of thermotropic liquid crystalline random copolyesters containing 2,2'-biphenyl dicarboxylate moiety. Due to the pharmacological applications of esters of diphenic acid, the antibacterial and anticancer activities of the random copolyesters was studied. In the present work, copolyesters were tailor made using 2,2'-biphenyl dicarboxylic acid as monomer and comonomers namely 1,4-cyclohexanediol, 2-hydroxyethyl-4-hydroxybenzoate, hydroquinone bis (hydroxyethyl ether), 1,8-dihydroxy anthraquinone, hydroquinone, Bisphenol-A with various aromatic dicarboxylic acids such as terephthalic acid, 4,4'-oxybis(benzoic acid) and 2,6-naphthalene dicarboxylic acid. Six series of novel random copolyesters containing nine fully aromatic copolyesters, five partially aromatic

copolyesters containing aliphatic moiety and three partially aromatic copolyesters containing alicyclic moiety were prepared by solution polycondensation method using diphenylchlorophosphate as a condensing agent in pyridine with LiCl. Higashi method[19] is mainly used for the polycondensation of aromatic dicarboxylic acids and aromatic diols. Synthesis of polyesters with aromatic dicarboxylic acid and alicyclic diols, aliphatic diols demonstrates the extended applicability of Higashi method. The risk of degradation of the monomers especially 1,4-cyclohexanediol is greatly reduced because of the low temperature and shorter time required for polymerization. The tedious method of preparation of acid chloride was also avoided. Esters of diphenic acid possess pharmacological activities like analgesic, antidiarrheal, antihypertensive, antispasmodic and bronchodilation, antimicrobial, wound healing, anticancer activity, antithrombic, antipyretic and antimutagenic activity. [20] Because of the wide spectrum of biological applications, 2,2'-biphenyl dicarboxylic was used as a base scaffold to synthesize various copolyesters. The skeleton of the copolyesters may be depicted as follows



The present work is on the synthesis and characterization of random copolyesters containing non-coplanar 2,2'- biphenylene moiety. It comprises of

- Preparation of monomer diol, 2-hydroxyethyl-4-hydroxybenzoate (HB).
- Characterisation of the prepared monomer diol by FT-IR, ^{1}H NMR and ^{13}C NMR spectral techniques.

- Synthesis of seventeen random copolyester by direct polycondensation with one common monomer dicarboxylic acid, six varying monomer diol and three different monomer dicarboxylic acid using diphenylchlorophosphate (DPCP) in pyridine medium.

- Determination of inherent viscosity η_{inh} of the synthesized copolyester using Ubbelohde viscometer.

- Determination of molecular weight of two typical copolyesters by Gel Permeation Chromatography (GPC).

- Characterization of all the synthesized copolyesters by FT-IR, ^{1}H NMR and ^{13}C NMR spectral techniques.

- Characterization of typical copolyesters by DEPT-135 NMR and 2D-HSQC NMR spectroscopy.

- Thermal analysis of all the synthesized copolyesters by Differential Scanning Calorimetry (DSC) to detect the glass transition temperature, melting endotherm and isotropisation temperature.

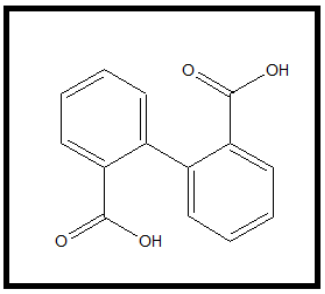
- Study of liquid crystalline textures of the synthesized copolyesters by Hot Stage Polarizing Optical Microscope (HOPM).

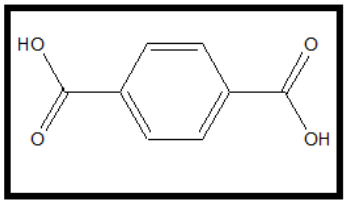
- Investigation of crystallinity of the synthesized polyesters by Wide Angle X-ray Diffraction Method (WAXD).

- Assessing the antibacterial activity of some copolyesters against human pathogenic bacteria by Disc diffusion method.

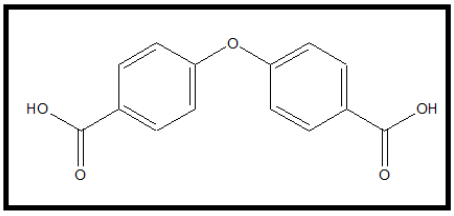
- Evaluating the *in vitro* cytotoxicity of some copolyesters.

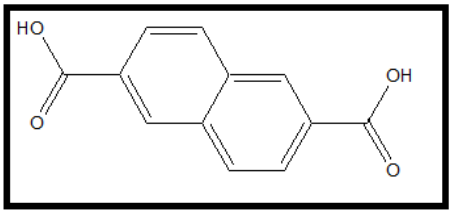
2.3 Aromatic dicarboxylic acids are used in the synthesis of copolyesters





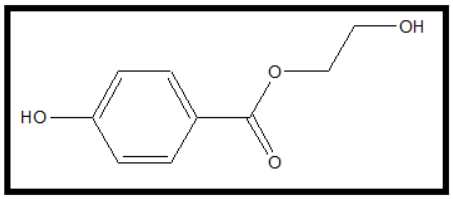
Diphenic acid (DA) Terephthalic acid (TA)

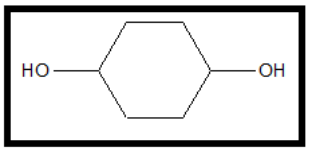




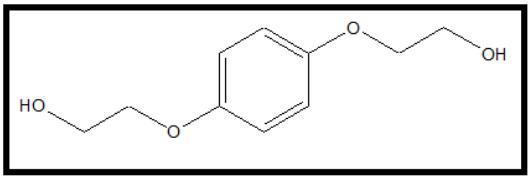
4,4'-oxybis (benzoic acid) (OBBA) 2,6-naphthalene dicarboxylicacid (NDA)

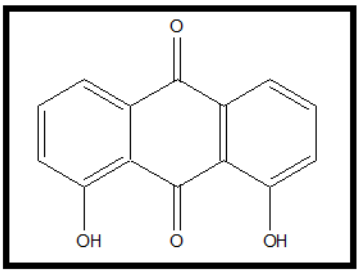
2.4 Diol comonomers used in the synthesis



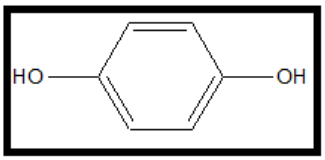


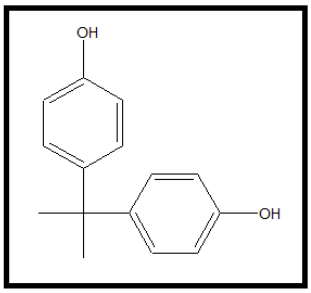
2-hydroxyethyl-4-hydroxybenzoate (HB) 1,4-cyclohexanediol (CHD)





hydroquinone bis (hydroxyethyl ether) (HE) 1,8-dihydroxy anthraquinone (AQ)





Hydroquinine (HQ) Bisphenol A (BPA)

References

1. Longcheng Gao;Zhihao Shen ;Xinghe Fan; Qifeng Zhou, *Polym. Chem.*, **2012**, 3, 1947.

2. Naoto Tamai; Hiroshi Miyasaka, *Chem. Rev.*, **2000**,100,1875-1890.

3. Henning Sirringhaus; Nir Tessler; Richard H. Friend, *Science,* **1998**, 280,1741-1744.

4. Yanlei Yu; Makoto Nakano; Tomiki Ikeda, *Nature*, **2003** , 425, 145.

5. Almeria Natansohn; Paul Rochon, *Chem. Rev.,* **2002**, 102, 4139-4175.

6. V. Percec, *Nature,* **2002**, 419,384-387.

7. Hans- Werner Schmidt, Dajian Guo, *Makromol. Chem*., 1988, 189,2029-2037.

8. Werner Grasser, Hans-Werner Schmidt, *Polymer* 2001,42,8529-8540.

9. E. Padmanaba Naidu, E. Arumugasamy, V. Kannappan, I. K. Varma & E. Ravichandran, *Molecular Crystals and Liquid Crystals Science and Technology. Section A. Molecular Crystals and Liquid Crystals*, 1996, 287: 1,1-10. M. A. Salem; M. H. Helel; Y. A. Ammar; M. S. A. El-Gaby; H. Kh. Thabet; M. A. Gouda, *Synthetic communications,* **2017**, Vol. 47, NO. 10, 935–960.

11. Anindita Deb; Sikha Barua; Dr. Biswajit Das, *Journal of Pharmacognosy and Phytochemistry*, **2016**; 5 (1): 194-197.

12. Alexandra Munoz-Bonilla; Maria L. Cerrada; Marta Fernandez-Garcia, *Polymeric materials with antimicrobial activity : from synthesis to applications*, RSC publishing, Cambridge, UK, **2013**.

13. Nurit Beytha; Ira Yudovin-Farber; Ran Bahira; Abraham J. Domb; Ervin I. Weiss, *Biomaterials*, **2006,** 27, 3995– 4002.

14. Tom Anthierens; Leen Billiet; Frank Devlieghere; Filip Du Prez, *Innovative Food Science and Emerging Technologies*, **2012**,15,81–85.

15. V. Kannapan; D. Reuben Jonathan, *Journal of Chemical and Pharmaceutical Research*, **2013**, 5, 382-386.

16. N. Malathy; D. Roop Singh**,** *Indian Journal of Science and Technology*, **2012**, 5, 2302-2306.

17. Sun-Mi Lee; Sangwook Jung; Chang-Sik Ha; Il doo Chung, *Macromolecular Research*, **2008**, 16, 510-516.

18. Won-Moon Choi; Neung-Ju Lee; Young-Woo Lee; Chang-Sik Ha; Won-Jei Cho, *Macromol.Symp.,* **1997**,118,619-624.

19. Fukuji Higashi; Atsushi Hoshio; Jun Kiyoshige, *Journal of Polymer Science: Polymer Chemistry Edition*, **1983**, 21,3241-3247.

20. Anindita Deb; Sikha Barua; Dr. Biswajit Das, *Journal of Pharmacognosy and Phytochemistry*, **2016**; 5 (1): 194-197.