ISSN:2229-6107

INTERNATIONAL JOURNAL OF PURE AND APPLIED SCIENCE & TECHNOLOGY

E-mail :
editor.ijpast@gmail.com
editor@ijpast.in

www.ijpast.in

INTERNATIONAL JOURNAL OF PURE AND APPLIED SCIENCE & TECHNOLOGY
IJPAST

ISSN 2229-6107 www.ijpast.in
Vol 13 ,Issuse 2.June 2023

SYNTHESISANDCHARACTERISATIONOFCHALCONEBASEDCOPOLYESTERSAND THEIR ANTICANCER ACTIVITY

Ms. Nayela Ghazal[1], Dr S. Satyanandam[2], Mr. Mohammed Kafeel Urrahman Khan[3]

ABSTRACT: One of the most prevalent causes of mortality among women is breast cancer.There are chemopreventive and anti-cancer properties shown by chalcone.Twocopolyesters employing different chalconediols as a monomer are part of a proactive strategy in the battle against breast cancer.PG and the solution polycondensation technique were used to synthesize aliphatic and aromatic acid chlorides. Viscosity and solubility tests defined the two copolyesters. The copolyesters' structures were determined using FT-IR, 1H NMR, 13CNMR, and MALDI.We used the MCF-7 Cell Line to study the monomer and copolyesters' anticancer activities, and the VEROCell Line using the MTT test to study their cytotoxic effects.Graph Pad Prism 7 and ED50 Plus v.1.0 were used to compute the IC50 values. Cholcone MHEP is cytotoxic, and the Selectivity index shows that chalcone HHEP and the two copolyesters are effective anticancer agents. Chemotherapy may target these copolyesters either alone or in conjunction with cancer drugs since their selectivity indices are greater than 2.

Keywords: Chalconesdiols,Copolyesters MTTassay,IC_{50},Selectivityindex

INTRODUCTION

: Cancer refers to anymalignantgrowthortumorcausedbyabnormalan d uncontrolled cell division. Breast cancer is one of the most common cancers in women. Death from cancer worldwide are projected to continue rising, with an estimated 131 millon death in 2030. Chalcones are a class of natural compounds that widely exist in a variety of plant species. They are commonly known as yellow pigments in flowers and are also widely distributed in various parts (roots, rhizomes, heartwood, leaves, flowers and seeds) [1].Chalcone derivative have shown anti-cancer, antimalarial, anti-inflammatory [2], anti-bacterial, anti-filarial, antifungal and anti-oxidant activity [3]. Concerning the chemical structural level, these compounds are open-chained molecules, in which the two aromatic rings are joined by a three-carbon α, β-unsaturated carbonyl system (1,3-diphenyl-2-prop-1-one).A large number of chemical structures have been studied, and it was reported that hydroxyl- derivatives of chalcones display marked anti- proliferative effects on cancer cells. These groups are likely necessary for the chemotherapy agents [4]. The principal aim of our work is the discovery of novel cytotoxic and anticancer agents. In the present study, we have synthesized two chalconediols by acid catalysedclaisen condensation method. Using those chalcone as monomers and varyingaciddichloridestwocopolyesterswеresynth esied to study their enhanced biological activity[5,6,7]. The newly synthesized chalconediols and polyesters are further screened for their anticancer activity.

Associate professor[1,2] Assistant professor[3]
Department of Pharmaceutical Chemistry,,
Global College of Pharmacy, Hyderabad. Chilkur (V), Moinabad (M), Telangana- 501504

INTERNATIONAL JOURNAL OF PURE AND APPLIED SCIENCE & TECHNOLOGY
IJPAST
ISSN 2229-6107 www.ijpast.in
Vol 13 ,Issuse 2.June 2023

MATERIALSANDMETHODS:

Synthesis of ChalconeDiols: The two monomer chalconediols namely(2E)-1-(4-hydroxy phenyl) 3-(4 hydroxy -3- ethoxy phenyl) prop-2- ene -1-one[HHEP] and(2E)- 1-(4 hydroxy-3- methoxy phenyl)- 3-(4 hydroxy -3- ethoxy phenyl) prop-2- ene -1 -one [MHEP]were synthesizedandreported[8].

Synthesis of HHEP: DryHCl gas (generatedasa result of reaction betweenconcentratedsulphuricacidanddrycrystals ofNaCl) was passedthroughawellcooledsolutionof3gof4-hydroxy -3-ethoxybenzaldehydeand2.7gof4-hydroxy acetophenone in 100 ml of absolute ethanol takenin a 250 ml RB flask under stirring conditions. The precipitate is poured into ice cold distilled water and allowed to settle, filtered, dried and recrytallised from methanol.Same method was adopted to synthesiseMHEPand both were reported [8].

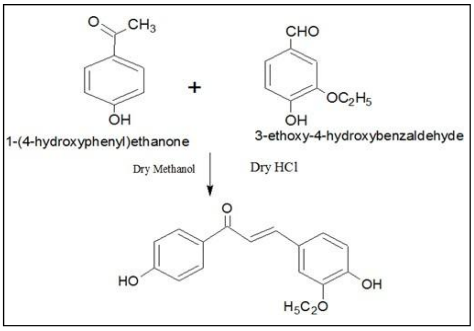


FIG.1:SYNTHESISOFHHEP

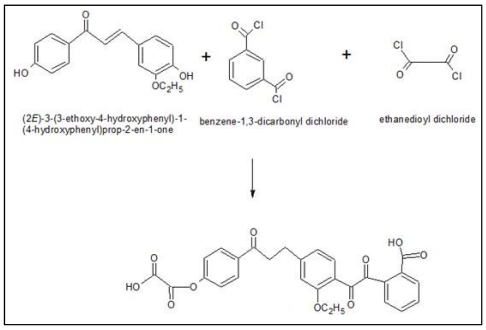


FIG.2:SYNTHESISOF PIOH

SynthesisofCopolyesters:

Synthesis of PIOH: Taken 1g of HHEP in 100 ml RB flask. Added 10 ml of dry DMF stirred till it is dissolved, then added 0.3573 g of isophthaloyl chloride and 0.1586 g of oxalyl chloride, temperature was raised to 120 °C andmaintainedat 120 °C. Left the reaction to proceed for 12 h.After the reaction time, quenched in 50 ml of *n*- hexane, filtered, dried, powered. It is then reprecipitated from methanol.

Same method was adopted to synthesise PIOM and both were reported [8]. The structure of the copoly- esters was established by FT-IR, ^{1}H NMR, ^{13}C NMRandMALDI.**Table1**givesinformationregardingthemonomersusedinthesynthesis of the two copolyesters, their respectivecopolyester code, percentage of yield and inherent viscosities.

TABLE1:MONOMERSUSED,COPOLYESTERCODE,PERCENTAGEOFYIELDANDINHERENTVISCOSITIES

Diol	Diacicdchloride-I	Diacicdchloride-II	Copolyestercode	Percentageyield	InherentViscosity(cP)
HHEP	Isophthaloylchloride	Oxalylchloride	PIOH	78	1.2890
MHEP	Isophthaloylchloride	Oxalylchloride	PIOM	85	1.0578

Cytotoxic Studies: The anticancer activity of samples on MCF-7 cells were determined by the MTT assay cells ($1x10^5$/well) were plated in 0.2 ml of medium/well in 96-well plates. Incubate at 5% CO_2 incubator for 72 h. Then, add concentrationsof the samples in 0.1% DMSO for 48 h at 5% CO_2 incubator.Afterremovalofthesamplesolutionandwashingwithphosphate-bufferedsaline(pH7.4),Viable cells were determined by the absorbance at 540nm. Measurements were performed and the concentration required for a 50% inhibition of viability (IC_{50}) was determined graphically. The effect of the samples on the proliferation of MCF-7 cells was expressed as the % cell viability, usingthe following formula:

$$\frac{\text{A540oftreated cells}}{}$$

20µl/well (5mg/ml) of 3-(4,5dimethyl-2-thiazolyl)- 2,5-diphenyl-tetrazolium bromide (MTT)

INTERNATIONAL JOURNAL OF PURE AND APPLIED SCIENCE & TECHNOLOGY
IJPAST
ISSN 2229-6107 www.ijpast.in
Vol 13 ,Issuse 2.June 2023

%cell viability=A540ofcontrolcellsx100%

phosphate-bufferedsalinesolutionwasadded. After 4 h incubation, 1 ml of DMSO was added. UsingtheGraphPadPrism,theIC_{50}valuesare calculatedandcomparedwithED_{50}plusv1.0.

FromthisSelectivityindexwasfoundusingthe following formula:IC_{50}valuesofnormalcellline

$$\text{SelectivityIndex} = \frac{50\ \text{IC}}{\text{valuesofcancercellline}}$$

Spectral Studies: FTIR spectrum of the two copolyesters namely PIOH, PIOM were recordedbymakinguseofShimadzuFT-IRinstrument.The

FT-IR spectrum of the two copolyesters displayed distinctiveabsorptionintherangeof1750-1768

RESULTSANDDISCUSSION: The twosynthesized chalocone based copolyesters were characterized by viscosity measurement, solubility studyandspectroscopicmethodsFT-IR,^{1}H and^{13}C NMRandMALDI.Cytotoxicstudywascarriedoutusing MTT assay. Solubility of the two copolyesterswas determined in various solvents and reported [8]. The outcome revealsthatthey are foundto be highly polar solvents, partially soluble in moderatelypolarsolventsbutabsolutelyinsoluble in least polar solvents. The inherent viscosity value of the twocopolyesters PIOH, PIOM was determined inDMAcsolutionat 30 °C using UbbelohdeViscometerandwerefoundto be1.0189 and 1.0632 dL/grespectively as presented in **Table 1**reveals that these copoly-estershavehighmolecularweight .cm^{-1}owingtoesterC=Ostretchingfrequency.

Nuclear Magnetic Resonance (NMR) spectroscopy is useful for characterizing the polymer samples. The ^{1}H and ^{13}C NMR spectra of the two copolyesters were recorded with BRUKER AV III 500 MHz NMR instrument in DMSO-d6 solvent and TMS as internal standard. The aromaticprotons were observed in the range 7.0 to 8.2 ppm. The vinyllic protons attached to carbonyl carbonare observed in the ranges of 6.6 to 6.9 ppm. The vinyllic protons attached to phenyl rings are observed in the ranges of 4.3 to 4.5 ppm. The methoxy protons in the chalcone moiety were observed in the range 3.1 to 3.4 ppm. The methyleneprotonsobservedintherangeof2.2to 2.9ppm and themethyl protons in 1.3 to 1.7 ppm.

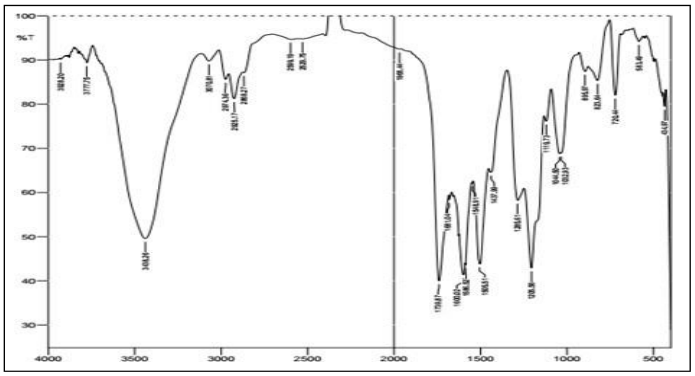


FIG.3:FT-IRSPECTRUMFOR PIOM

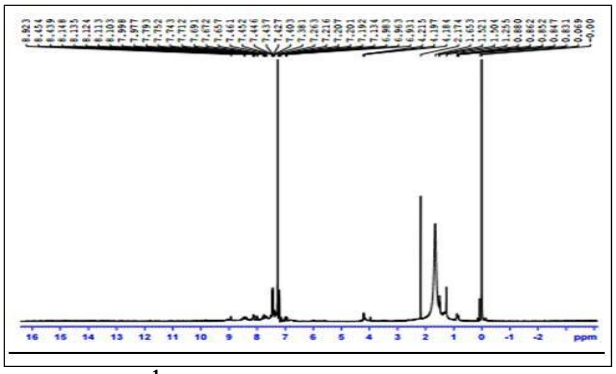


FIG.4:^{1}HNMRSPECTRUMFORPIOM

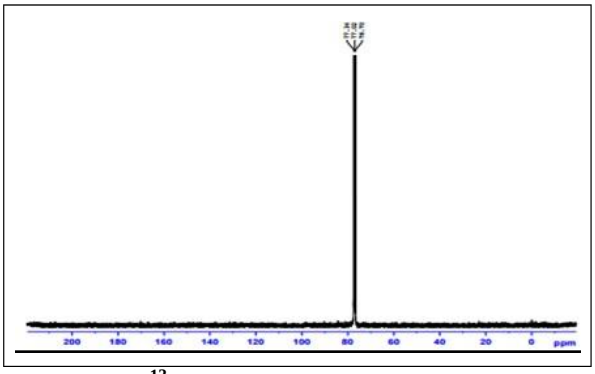


FIG.5:^{13}CNMRSPECTRUMFORPIOM

INTERNATIONAL JOURNAL OF PURE AND APPLIED SCIENCE & TECHNOLOGY
IJPAST
ISSN 2229-6107 www.ijpast.in
Vol 13 ,Issuse 2.June 2023

MALDI: MALDI-Massspectrum was useful in finding the molecular weight of the polymeric samples. MALDI -Mass spectrum of PIOM is showninthe**Fig.6**.TheMolecularweightofthe polymerwasfoundto 877.242 experimentally, which isinnearlyinagreementwiththetheoreticalmolecularweight.

***In-vitro* Cytotoxic Effect of Chalcones:** Anticancer activity of chalcone might be due to molecular alteration such as induction ofapoptosis, DNA and mitochondrial damage, inhibition of angiogenesis, tubulinn inhibition, kinases inhibition and also drug efflux protein activities [9]. Aromatic chalcones with hydroxyl group,methoxygrouponAringatposition 2 or3 are considered as lead compounds forgenerationofnewpotentialanticancer drugs [10]. Whenthetwomonomersarecomparedfor their anticancer activities, the chalconediolHHEPwasfoundtobegoodanticancera gentandMHEPascytotoxiceffect. When the two copolyestersarecompared for theiranticanceractivitiesbotharefoundtobe good anticancer agents becausethe aromatic ring has substituent alkoxygroups at the chalconebackbone.

TABLE 2:IC_{50}AND SELECTIVITY INDEX VALUES OFMONOMERSONVEROANDMCF-7CELLLINE (GraphPadPrismVersion7)

Monomer Code	GraphPadPrismVersion7		
	IC_{50}		Selectivity index
		MCF-7	
MHEP	2.499	2.349	1.0639
HHEP	12.8	2.754	4.6479

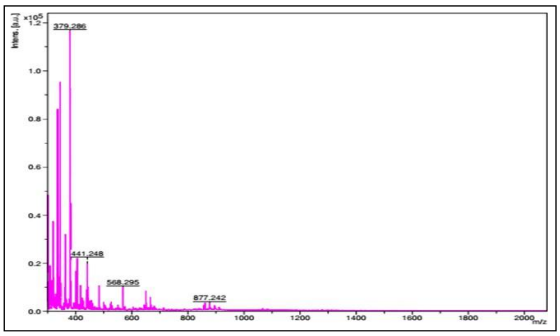


FIG.6:MALDIFOR PIOM

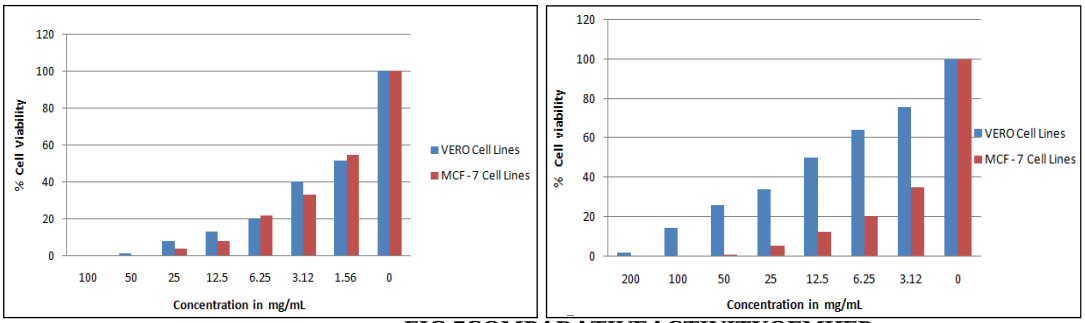
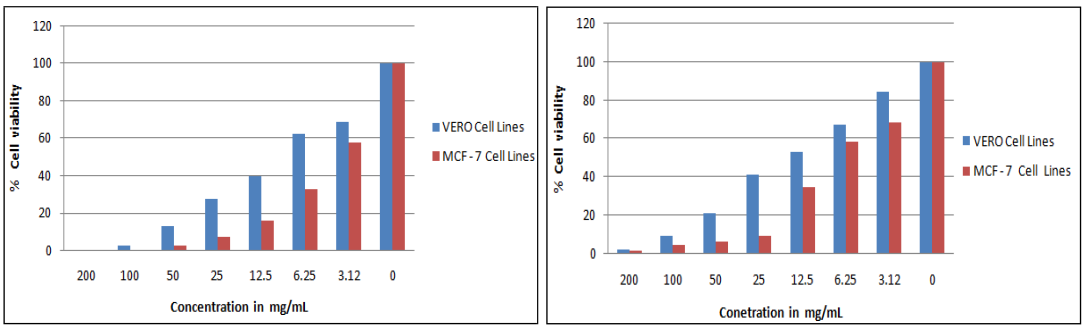


FIG.7COMPARATIVEACTIVITYOFMHEP ON VEROAND MCF-7CELLLINES



INTERNATIONAL JOURNAL OF PURE AND APPLIED SCIENCE & TECHNOLOGY
IJPAST

ISSN 2229-6107 www.ijpast.in
Vol 13 ,Issue 2.June 2023

FIG.9:COMPARATIVEACTIVITYOFPIOH ON VERO AND MCF-7 CELL LINES

TABLE3:IC_{50}ANDSELECTIVITYINDEXVALUESOFCOPOLYESTERSONVEROANDMCF-7CELLLINE(GRAPH PAD PRISM VERSION 7 AND ED_{50} PLUS V 1.0)

Copolyesters Code	GraphPadPrismVersion7			ED_{50}PlusV1.0		
	IC_{50}		Selectivityindex	IC_{50}		Selectivityindex
	Vero	MCF-7		Vero	MCF-7	
PIOH	9.351	4.387	2.1315	8.73	3.24	2.69
PIOM	14.71	7.286	2.0189	14.99	6.274	2.38

Literature surveyindicatesthatwhentheselectivity index is greater than two for a material under investigation it can be good anticancer agents[11]. The Selectivity index of the monomer HHEP and the copolyesters PIOH and PIOM are found to be more than two. Hence they can be targeted at the BreastCancerCellLinesasgoodanticanceragents.

CONCULSION: Two chalcone (HHEP and MHEP) were synthesized and characterized. These chalcone as monomers diols were used and two copolyesters were synthesized using differentdiacid chloride namely oxalyl chloride and isophthaloyl chloride by polycondensation method. These arecharacterizedand evaluated for their anticancer activity. The selectivity index reveals that one of the monomer (HHEP) and two copolyesters are potent anticancer agents. Hence they can be used as a anticancer agents. This study can be further extended on drug conjugates targeting MCF-7 Cell Line.

REFERENCES:

1. 1. An update on the anticancer activity of naturally occurring chalcones by Zhang EH, Wang RF, Guo SZ, and Liu B. Evidence-Based Complementary and Alternative Medicine, Volume 2013, Article ID 815621, published by Hindawi Publishing Corporation.
2. 2. Kataki D and Sarma JC: 1, 3-diphenylpropenones synthesized solvent-free using microwave assistance. Articles 1–7 published in the 2011 edition of the Chemistry Central Journal. "In-vitro anticancer activity of mono-substituted chalcone derivatives" (Prabhakar V, Balasubramanian R, Sathe P, Krishna CM and Juvekar A, 2003). Results from the 2014 International Journal of Tumor Therapy, Volume 3, Issue 1, Pages 1–9.
3. 4. The effect of new chalcones generated from quinoxaline on the growth of glioma cells in vitro. Authors: Bonfili, Cecarini, Amicil, and Kellar. European Journal of Medical Chemistry, 2012, 48: 255–64. ReprositorioInstitucionalPUCRS.
4. 5. A study published in Cancer-Chemotherapy in 2000 by Rosa DV, Cristiano F, Mariagrazia D, Cristiana G, Antonella R, Federica B, Franco OR, Salvatore M, and Giovanni S. was mentioned in the article.
5. The article "Anticancer Drud Des 1995; 10: 481-90" was written by De Vincenzo, Scambia, Benedettipanici, Ranelletti, Bonanno, Ercoli, Monache, Ferrari, Piantelli, and Mancuso.
6. A study published in the journal Med.Chem in 2001 by Lopez SN, Castelli MV, Zacchini SA, Dominguez JN, Lobo G, Jaime CC, Cortes JCG, Ribas JC, Devia C, Ana MR, RicardoBioorgDE:9:1999-2013.
7. 8. Biocidal effectiveness of synthetic copolyesters bearing chalcone moiety (Devi DL, Jonathan DR, and Kothai S 2007). Published in 2016 by the Journal of Chemical and Pharmaceutical Research, volume 8, issue 3, pages, 1041–
8. . Chalcone scaffold in anti-cancer arsenal: a molecular insight (Manik Das and Kunal Manna).
9. Synthesis, characterisation, and anti-cancer activity of certain pyrazoline derivatives by Devikar K, Swamy S, and Murugan V. Published in the International Journal of Pharmaceuticals and Phytopharmaceutical Research.