ISSN: 2755-0168

Journal of Biotechnology & Bioinformatics Research

SCIENTIFIC Research and Community

Research Article

Open Access

Synthesis, Characterization, In-Silico Docking Study and In-Vitro Anti-Inflammatory Activities of Novel Chalcone Derivatives

R. Bharathi[1] and N. Santhi[2]*

[1]Research and Development Centre, Bharathiar University, Coimbatore, 641046, India

[2]Department of Chemistry, Govt Arts College, C Mutlur, Chidambaram, 608102, India

ABSTRACT

A series of chalcones were synthesised by condensation of appropriate acetophenones with appropriate aromatic aldehydes, and their anti-inflammatory activities were investigated. In comparison to standard drugs, some have been found to have important activity. In silico docking, tests on chalcones were shown to be more selective to COX-2. Further anti-inflammatory results were supported by docking studies with COX-2. The results from the anti-inflammatory and docking indicate that the synthesised compounds 3b, 3g and 3h can be seen as therapeutic drugs.

***Corresponding author**

N. Santhi, Department of Chemistry, Govt Arts College, C.Mutlur, Chidambaram, 608102, India. E-mail: nsanthigac@gmail.com

Received: June 21, 2021; **Accepted:** June 25, 2021; **Published:** June 30, 2021

Keywords: Chalcone, Antiinflammatory, HRBC, Docking, COX-2

Introduction

Inflammation is a biological response of body tissues to potentially harmful stimuli such as pathogens or irritants; it is thought to be a protective response involving immune cells and blood vessels. Anti-inflammation is the ability of a substance to reduce inflammation, which directly acts on the central nervous system to stop pain signals from being sent to the brain. Chalcone is made up of an aromatic ketone and an enone, and it serves as the central core for the majority of biological compounds. Chalcones are also known as chalconoids when grouped together. Chalcones have a diverse range of biological activities, including antibacterial and even cytotoxic properties. Chalcones are typically synthesised through an aldol condensation of benzaldehyde and acetophenone in the presence of sodium hydroxide [1-6]. The biological activities of chalcones include antimalarial, antitubercular, cytotoxic, anti-HIV, antiinflammatory, antiplasmodial, immunosuppressive, antioxidant, analgesic, antiviral, and antimicrobial properties [6-16]. This broad range of activity displayed by chalcone derivatives piques the interest of many researchers who are looking for new potent molecules with antiinflammatory activity. One well-known method for studying invitro anti-inflammatory activity is HRBC membrane stabilization. NSAIDs either inhibit these lysosomal enzymes or stabilise the lysosomal membrane. As a result, the prevention of hypotonicity, which causes HRBC membrane lysis, is used to assess the anti-inflammatory activity of 1, 2-disubstituted chalcone derivatives [17-19]. Synthesised chalcone derivatives by acetanilide with formyl morphiline and tested them for anti-inflammatory activity in both in-vitro and in-silico studies, which revealed a significant activity when compared to the standard. Synthesised pyrazole-based chalcones and demonstrated that they have anti-inflammatory properties. Cyclooxygenases (COX-1 and COX-2) are important isozymes that catalyse the complex biotransformation of arachidonic acid into PGs and thromboxanes, which are ultimately responsible for a variety of physiological and pathophysiological responses. The COX-2 isozyme is primarily responsible for the production of inflammatory PGs, which cause pain, swelling, and fever. Aside from its ability to cause peripheral inflammation, COX-2 isozyme expression is increased in a variety of human cancers, including gastric, breast, lung, colon, esophageal, prostate, and hepatocellular carcinomas [20-24].

Keeping this in mind, we created some chalcone derivatives and tested them for anti-inflammatory activity in vitro. Molecular docking experiments were carried out to explain the molecular basis of the observed inhibitory activities of the investigated compounds, as reported in this paper.

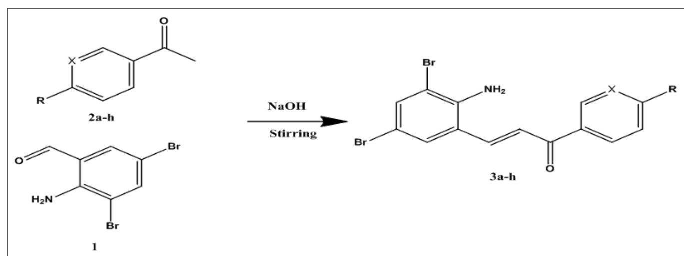
Experimental

Melting points were determined in open capillaries and are found uncorrected. IR spectra were recorded on FTIR spectrophotometer Shimadzu 8700 using KBr disc method. ^{1}H and ^{13}C NMR spectrum were recorded on BRUKER AVANCE III AMX-400 spectrometervfor the synthesized compound. The frequency of 400 MHz for the proton NMR spectrum and 100 MHz frequency for ^{13}C NMR spectrum, $CDCl_3$ used as a solvent.

Synthesis and scheme of (E)-3-(2-amino-3, 5-dibromophenyl)-1-(4-substitutedphenyl) prop-2-en-1-one (3a-h)

2-amino-3,5-dibromobenzaldehyde (1) (0.05 mol) dissolved in 30 ml of ethanol in 100 ml beaker and The substituted aryl acetophenone (2a-h) (0.05 mol) were taken and dissolved in 30 ml of ethanol in a 100 ml beaker. The above two solution were taken in a 250 ml RB flask, to this, 2 ml of 30% sodium hydroxide solution was added stirrered well until the product formed. Completion of the reaction was identified by observing on precoated TLC plates.

After completion of the reaction, the reaction mixture was poured into crushed ice, and acidified with dil HCl. The product formed were filtered, washed, dried and recrystallized using ethanol. The reaction mechanism is explained in Scheme-1. The newly prepared chalcones 3a-h are characterized by melting point, FT-IR, ^{1}H NMR, and ^{13}C NMR spectral studies.



Scheme 1

Synthesis of 4-((E)-3-(2-amino-3, 5-dibromophenyl) acryloyl) benzonitrile (3a)
Yield 78%; M.P. 156 - 157°C; M.F: $C_{16}H_{10}Br_2N_2O$; IR (KBr): 1651 (C=O), 1597 (CH=CH), 3066 (Aro C-H), 3456 (NH2), 624 (C-Br) cm^{-1} ; 1 HNMR ($CDCl_3$): δ 4.51 (s, 2H, NH_2), 7.48 (d, 1H, CH alpha), 7.64 (d, 1H, CH beta), 6.97 – 7.64 (m, 6H, ArH); ^{13} CNMR ($CDCl_3$): 189.4 (C=O), 121.4 (Cα), 142.1 ($C_β$), 108.0 – 143.3 (Aromatic carbons).

Synthesis of (E)-3-(2-amino-3, 5-dibromophenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one (3b)
Yield 65%; M.P. 167 - 169°C; M.F: $C_{15}H_{11}Br_2NO_2$; IR (KBr): 1645 (C=O), 1600 (CH=CH), 3068 (Aro C-H), 3464 (NH_2), 632 (C-Br) cm^{-1} ; ^{1}HNMR ($CDCl_3$): δ 4.86 (s, 2H, NH_2), 6.96 (d, ^{1}H, CH alpha), 7.83 (d, 1H, CH beta), 6.95 – 8.95 (m, 6H, ArH); ^{13} CNMR ($CDCl_3$): 189.4 (C=O), 121.7 (Cα), 142.1 (Cβ), 109.2 – 143.1 (Aromatic carbons).

Synthesis of (E)-3-(2-amino-3, 5-dibromophenyl)-1-(4-chlorophenyl) prop-2-en-1-one (3c)
Yield 69%; M.P. 204 - 206°C; M.F: $C_{15}H_{10}Br_2ClNO$; IR (KBr): 1631 (C=O), 1591 (CH=CH), 3061 (Aro C-H), 3479 (NH_2), 628 (C-Br) cm^{-1} ; ^{1}HNMR ($CDCl_3$): δ 4.86 (s, 2H, NH_2), 7.41 (d, 1H, CH alpha), 7.91 (d, 1H, CH beta), 7.21 – 7.93 (m, 6H, ArH); 13 CNMR ($CDCl_3$): 181.9 (C=O), 122.0 (Cα), 135.1 (Cβ), 101.9 – 136.1 (Aromatic carbons).

Synthesis of (E)-3-(2-amino-3, 5-dibromophenyl)-1-(4-methoxyphenyl) prop-2-en-1-one (3d)
Yield 80%; M.P. 148 - 150°C; M.F: C16H13Br2NO2; IR (KBr): 1674 (C=O), 1597 (CH=CH), 3047 (Aro C-H), 3475 (NH2), 628 (C-Br) cm^{-1} ; 1 HNMR ($CDCl_3$): δ 4.76 (s, 2H, NH_2), 7.23 (d, 1H, CH alpha), 7.88 (d, 1H, CH beta), 6.88 – 7.89 (m, 6H, ArH); 13 CNMR ($CDCl_3$): 187.4 (C=O), 124.6 (Cα), 140.1 (Cβ), 106.8 – 141.3 (Aromatic carbons).

Synthesis of (E)-3-(2-amino-3, 5-dibromophenyl)-1-(pyridin-3-yl) prop-2-en-1-one (3e)
Yield 77%; M.P. 83 - 85°C; M.F: $C_{14}H_{10}Br_2N_2O$; IR (KBr): 1674 (C=O), 1593 (CH=CH), 3064 (Aro C-H), 3408 (NH_2), 611 (C-Br) cm^{-1} ; ^{1}HNMR ($CDCl_3$): δ 4.89 (s, 2H, NH_2), 7.46 (d, 1H, CH alpha), 7.83 (d, 1H, CH beta), 7.46 – 9.09 (m, 6H, ArH); ^{13} CNMR ($CDCl_3$): 181.9 (C=O), 124.9 (Cα), 145.7 (Cβ), 102.3 – 146.9 (Aromatic carbons).

Synthesis of (E)-3-(2-amino-3, 5-dibromophenyl)-1-p-tolylprop-2-en-1-one (3f)
Yield 75%; M.P. 112 - 115°C; M.F: $C_{16}H_{13}Br_2NO$; IR (KBr): 1681 (C=O), 1573 (CH=CH), 3060 (Aro C-H), 3461 (NH_2), 609 (C-Br) cm^{-1} ; ^{1} HNMR (CDCl3): δ 4.76 (s, 2H, NH2), 7.21 (d, 1H, CH alpha), 7.71 (d, 1H, CH beta), 7.21–7.72 (m, 6H, ArH); ^{13} CNMR (CDCl3): 195.0 (C=O), 126.4 (Cα), 148.0 (Cβ), 113.1 – 149.0 (Aromatic carbons).

Synthesis of (E)-3-(2-amino-3, 5-dibromophenyl)-1-(4-fluorophenyl) prop-2-en-1-one (3g)
Yield 71%; M.P. 138 - 140°C; M.F: $C_{15}H_{10}Br_2FNO$; IR (KBr): 1629 (C=O), 1593 (CH=CH), 3061 (Aro C-H), 3429 (NH_2), 628 (C-Br) cm^{-1} ; ^{1} HNMR (CDCl3): δ 4.67 (s, 2H, NH2), 7.15 (d, 1H, CH alpha), 7.61 (d, 1H, CH beta), 6.68 –7.99 (m, 6H, ArH); 13 CNMR ($CDCl_3$): 188.4 (C=O), 125.9 (Cα), 142.8 (Cβ), 107.2 – 142.2 (Aromatic carbons).

2.1.8 Synthesis of (E)-3-(2-amino-3, 5-dibromophenyl)-1-(4-nitrophenyl) prop-2-en-1-one (3h)
Yield 75%; M.P. 173 - 175°C; M.F: $C_{15}H_{10}Br_2N_2O_3$; IR (KBr): 1699 (C=O), 1551 (CH=CH), 3051 (Aro C-H), 3473 (NH_2), 640 (C-Br) cm^{-1} ; ^{1} HNMR (CDCl3): δ 4.71 (s, 2H, NH_2), 7.19 (d, 1H, CH alpha), 7.65 (d, 1H, CH beta), 7.17 – 8.03 (m, 6H, ArH); 13 CNMR (CDCl3): 183.5 (C=O), 121.6 (Cα), 138.5 (Cβ), 103.2 – 145.0 (Aromatic carbons).

Anti-inflammatory activity of synthesized derivatives using HRBC assay
Fresh human blood was drawn and mixed with equal parts sterilised Alsever's solution (Dextrose 2%, Sodium citrate 0.8%, Citric acid 0.05%, Sodium chloride 0.42%, and Distilled water 100mL). This blood solution was centrifuged for 10 minutes at 3000 rpm before being washed three times with an equal volume of normal saline. The blood volume is measured and reconstituted as a 10% v/v suspension with normal saline. The reaction mixture, which included 1.0mL of test sample at various concentrations in normal saline and 0.5mL of 10% HRBC suspension, 1mL of 0.2M phosphate buffer, and 1mL hyposaline, was incubated at 37°C for 30 minutes and centrifuged at 3,000 rpm for 30 minutes. The supernatant solution's haemoglobin content was determined spectrophotometrically at 560nm. Each experiment was carried out three times. In this study, dichlorofenac sodium was used as the standard and distilled water as the control. Where the blood control represents either 100% hemolysis or 0% stability, the percentage of HRBC hemolysis calculated by formula [25].

%Hemolysis = (OpticalDensity of Test Sample / Optical Densityof Control) × 100.
The concentration of a compound, where 50% of its maximal effect is observed (IC50) using graph pad prism was measured.

Molecular docking
Chemical structures of all the synthesized compounds were drawn using Chem Draw Ultra 8.0 software. Mol2 files of all the derivatives were converted into .pdb files using Marvin Sketch. All the ligand molecules were allowed to be flexible and their torsional roots were detected and chosen. PDB files were further optimized and converted to pdbqt files for molecular docking by using AutoDock Tools 1.5.6 [26].

Results and discussion
IR spectrum of the compounds 3a-h shows that the strong absorption stretching frequency band appeared at 1629 - 1699 cm^{-1} is due to C=O of chalcone moiety and a stretching frequency

band strongly appeared at 1551 - 1600 cm-1is due to CH=CH of the chalcone. The stretching frequency band present in the region of 3408 - 3479 cm^{-1} is due to N-H bond. Stretching frequency range at 3051 - 3068 cm^{-1} is reveals that the presence of aromatic C-H group. In ^1H NMR spectra, the strong singlet appeared at 4.51 – 4.89 ppm is due to ring NH_2 proton. The H-α and H-β protons of chalcones occur as two doublets in the ranges 6.96 – 7.48 ppm (H- α) and 7.61 – 7.91 ppm (H- β) in the ^1H NMR spectra. The other aromatic protons usually appear in between δ 6.68 – 9.09, depending on the type of aromatic/ heteroaromatic ring and also based on the electronic effects of the substituents present on these rings. ^{13}C NMR spectrum of compound shows that the carbonyl carbon of the chalcones usually appears δ 181.9 – 195.0 in its ^{13}C NMR spectrum. The α- and β- carbon atoms with respect to the carbonyl group give rise to characteristic signals in between δ 121.4 – 126.4 and δ 135.1 – 148.0 respectively. Phenyl ring aromatic carbon signals are appeared from 101.9 to 149.0 ppm.

The in-vitro anti-inflammatory activity revealed that the chalcone derivatives exhibited significant activity when compared to the standard, diclofenac sodium. Table 1 shows the percentage of anti-inflammatory activity of chalcone derivatives 3a-h. All inhibitors offered adequate protection in a dose-dependent manner. Due to the resemblance of RBC membrane with the lysosomal membrane, it may possibly inhibit the release of the lysosomal contents of neutrophils at the site of inflammatory reactions. Such neutrophil lysosomal constituents include bactericidal enzymes and proteases, which upon extracellular release cause further inflammation and tissue damage. At 500µg/ml, the highest effect of stabilization was presented by compound 3a with 82.29% protection. It was followed by compound 3d (81.02%), compound 3e (80.43 %) and compound 3b (79.94 %). At the lowest concentration (100µg/mL.), same pattern was observed. These results may be due to prevention of chemical mediator-release or stabilization of the human RBC membrane properties which could be attributed to the inhibition of hypotonicity-induced lysis of membrane [27]. Additionally, it may be assumed that anti-oxidant and radical scavenging activities of the chalcone play a key role in preventing human RBC membrane lysis [28]. However, the anti-inflammatory activity was found to be lower than that of diclofenac sodium (86.61%) in the case of all chalcone derivatives. Although the precise mechanism of membrane protection action is not deciphered by this study, it may be assumed that the inhibitory compound might mediate membrane protection action by changing its surface area/volume ratio of the cells leading to an increase in the membrane dimensions or shrinking of the cells or by interactions with the membrane proteins [29].

Table 1: IC50 Values of Compounds 3a-h Calculated Based on HRBC Membrane Stabilization Assay

Compound	Concentration (µg/ml)	% Inhibition	ic50
3a	100	33.47	172.86
	250	61.61	
	500	82.29	
3b	100	37.88	147.83
	250	65.24	
	500	79.94	
3c	100	25.33	213.37
	250	56.22	
	500	68.67	
3d	100	36.80	155.87
	250	62.98	
	500	81.02	
3e	100	25.04	238.81
	250	51.61	
	500	80.43	
3f	100	37.59	157.31
	250	59.65	
	500	72.39	
3g	100	32.20	174.27
	250	62.88	
	500	79.45	
3h	100	33.86	180.85
	250	57.88	
	500	74.55	
DFS	100	41.90	127.25
	250	67.49	
	500	86.61	

In-vitro anti-inflammatory activity of eight chalcone derivatives by HRBC method showed IC50 value greater than 100µg/ml. whereas the IC50 value of compound 3b was calculate to be 147.83 µg/ml. Out of the eight compounds studied, the compound 3b showed the minimum IC50 value 147.83µg/ml. The observed IC50 value showed that compound 3b exhibited highest anti-inflammatory activity. Among the eight compounds, the compound 3a showed maximum percentage inhibition of 82.29% at the concentration of 500µg/ml which is comparable with that of standard drug diclofenac sodium which showed the percentage inhibition of 86.61% at the concentration of 500µg/ml.

Molecular Docking Studies of Chalcone Derivatives with PDB: 3LN1

The docking study was performed using the Autodock 4.2. All the eight chalcone derivatives (3a-h) were docked into the active site of the enzymes COX-2 (PDB ID: 3LN1) which showed better docking scores than the reference compounds diclofenac sodium. The synthesized compounds/ligands inhibition activity was assessed using the Autodock vena and interaction displayed using Discovery Studio Ver 2017. The docking studies were carried out by targeting the active sites of the protein with the synthesized compounds.

Table 2: Amino Acid Residue Interaction for Compounds 3a-h with 3LN1

S.No	Compounds	Binding score (kcal/mole	Hydrogen bond Interactions	No of Hydrogen bond Interactions
1	3a	7.1	PHE 504, MET 508	2
2	3b	-6.5	PHE 504, MET 508	2
3	3c	-6.9	MET 508	1
4	3d	-7.7	MET 508, MET 509	2
5	3e	-6.6	MET 508, ARG 499	2
6	3f	-7.4	MET 508	1
7	3g	-7.6	MET 508	1
8	3h	-7.9	MET 508, VAL 509, PHE 504, ILE 503	4
9	DFS	-7.5	GLN 178, PHE 504	2

Figure 1: Three & Two Dimensional Image for Compounds 3a-3c Docking with 3*LN1* protein

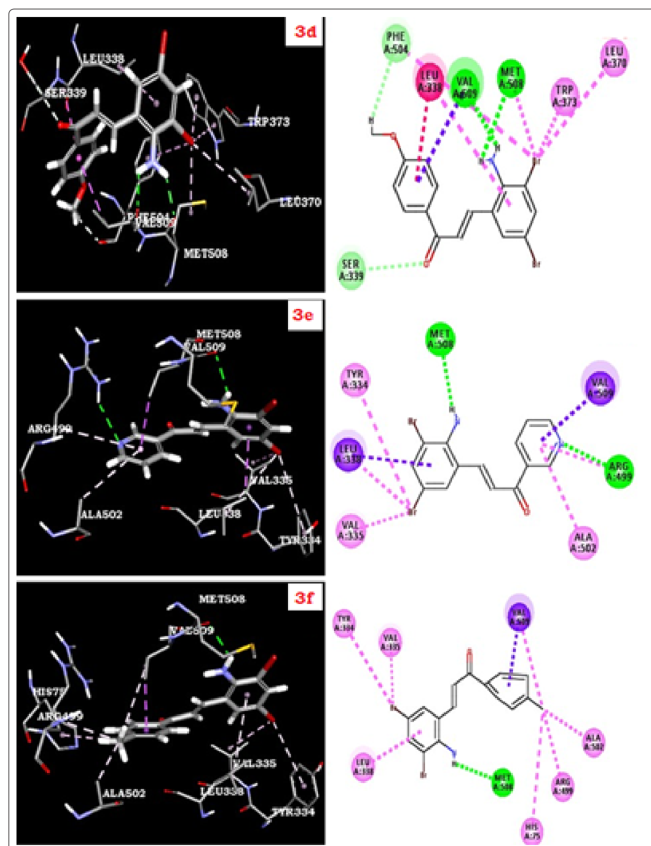


Figure 2: Three & Two Dimensional Image for Compounds 3d-3f & DFS Docking with *3LN1* protein

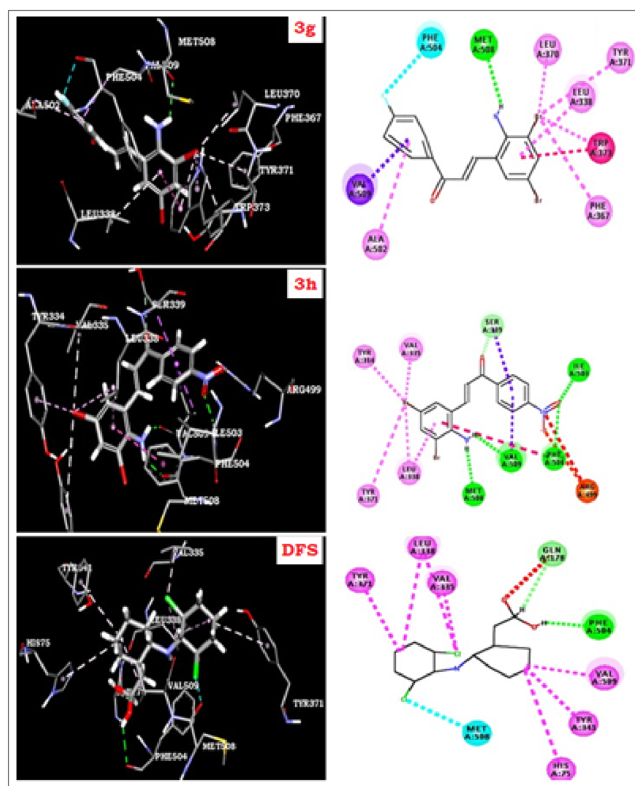


Figure 3: Three& Two Dimensional Image for Compounds 3g, 3h & DFS Docking with *3LN1* protein

The docking study was conducted for the eight compounds/ligands and their numbers are 3a–3h. The results of the molecular docking as the binding score were shown in Table 2. Among the eight ligands under study, the compounds 3h and 3d were shown good binding score with the target protein (3*ln1*). The 2D and 3D ligand interaction of the compound 3a–3h are given in Figure 1 to 3. The binding orientation of the synthesized compound 3d and 3h were shown an interaction by hydrogen bond with amino acid residue such as

VAL 508, VAL 509 for compound 3d and MET 508, VAL 509, PHE 504, ILE 503 for compound 3h as well as Pi - Pi - T Shaped interaction of compound 3h with TYR 334, VAL 335, TYR 371, LEU 338, SER 339, ARG 499. These interactions were clearly demonstrated in the 2D images of docking studies.

Conclusion

(E)–3-(2-amino-3, 5-dibromo phenyl)-1-(4-substituted phenyl) prop-2-en-1-one and their derivatives (3a-h) have been synthesized by treating 2-amino-3, 5-dibromobenzaldehyde (1) stirred with substituted aryl acetophenones (2a-h) in ethanol solvent. The structure of synthesized compounds 3a-h were confirmed by their melting point, FT-IR, 1H NMR and ^{13}C NMR spectral studies. Biological activities of the synthesized compounds were evaluated by anti-inflammatory. The hydroxy substituted compounds 3b show better activity in anti-inflammatory activity. On the basis of molecular docking studies compounds 3g (fluoro) and 3h (nitro) have maximum binding score in the case of 3LN1 receptor.

References

1. Jin K, Luo Z, Zhang B, Pang Z (2018) Biomimetic nanoparticles for inflammation targeting. Acta Pharmaceutica Sinica B, 8: 23-33.
2. Ji RR, Xu ZZ, Strichartz G, Serhan CN (2011) Emerging roles of resolvins in the resolution of inflammation and pain. Trends in neurosciences, 34: 599-609.
3. Rammohan A, Reddy JS, Sravya G, Rao CN, Zyryanov GV (2020) Chalcone synthesis, properties and medicinal applications: a review. Environmental Chemistry Letters, 18: 433-458.
4. Kedar MS, Shirbhate MP, Chauhan R, Sharma S, Verma A (2020) Design Synthesis and Evaluation of Anticancer Pyrazole Derivatives of Chalcone Scaffold. Research Journal of Pharmacy and Technology, 13: 342-346.
5. Romanelli G, Pasquale G, Sathicq Á, Thomas H, Autino J, et al. (2011) Synthesis of chalcones catalyzed by aminopropylated silica sol–gel under solvent-free conditions. Journal of Molecular Catalysis A: Chemical, 340: 24-32.
6. Li R, Kenyon GL, Cohen FE, Chen X, Gong B, et al. (1995) In vitro antimalarial activity of chalcones and their derivatives. Journal of medicinal chemistry, 38: 5031-5037.
7. Hans RH, Guantai EM, Lategan C, Smith PJ, Wan B, et al. (2010) Synthesis, antimalarial and antitubercular activity of acetylenic chalcones. Bioorganic & medicinal chemistry letters, 20: 942-944.
8. Go ML, Wu X, Liu XL (2005) Chalcones: an update on cytotoxic and chemoprotective properties. Current medicinal chemistry, 12: 483-499.
9. Cole AL, Hossain S, Cole AM, Phanstiel IV O (2016) Synthesis and bioevaluation of substituted chalcones, coumaranones and other flavonoids as anti-HIV agents. Bioorganic & medicinal chemistry, 24: 2768-2776.
10. Viana GSB, Bandeira MAM, Matos FJA (2003) Analgesic and antiinflammatory effects of chalcones isolated from Myracrodruon urundeuva Allemão. Phytomedicine, 10:189-195.
11. Wu X, Tiekink ER, Kostetski I, Kocherginsky N, Tan AL, et al. (2006) Antiplasmodial activity of ferrocenyl chalcones: investigations into the role of ferrocene. European journal of pharmaceutical sciences, 27: 175-187.
12. Luo Y, Song R, Li Y, Zhang S, Liu ZJ, et al. (2012) Design, synthesis, and biological evaluation of chalcone oxime derivatives as potential immunosuppressive agents. Bioorganic & medicinal chemistry letters, 22: 3039-3043.
13. Anto RJ, Sukumaran, K., Kuttan, G., Rao, M. N. A., Subbaraju, V., & Kuttan, R. (1995). Anticancer and antioxidant activity of synthetic chalcones and related compounds. Cancer letters, 97(1), 33-37.
14. Viana GSB, Bandeira MAM, Matos FJA (2003) Analgesic and antiinflammatory effects of chalcones isolated from Myracrodruon urundeuva Allemão. Phytomedicine, 10: 189-195.
15. Mateeva N, Eyunni SV, Redda KK, Ononuju U, Hansberry TD, et al. (2017) Functional evaluation of synthetic flavonoids and chalcones for potential antiviral and anticancer properties. Bioorganic & medicinal chemistry letters, 27: 2350-2356.
16. Nowakowska Z, Kędzia B, Schroeder G (2008) Synthesis, physicochemical properties and antimicrobial evaluation of new (E)-chalcones. European journal of medicinal chemistry, 43: 707-713.
17. Gomes MN, Muratov EN, Pereira M, Peixoto JC, Rosseto LP, et al. (2017) Chalcone derivatives: promising starting points for drug design. Molecules, 22: 1210.
18. Nagaharika Y, Rasheed S (2013) Anti-inflammatory activity of leaves of Jatropha gossypifolia L. by HRBC membrane stabilization method. Journal of Acute Disease, 2: 156-158.
19. Nielsen VG, Webster RO (1987) Inhibition of human polymorphonuclear leukocyte functions by ibuprofen. Immunopharmacology, 13: 61-71.
20. Ahamed AA, Sihabudeen MM (2017) Synthesis and biological evaluation of some novel heterocyclic Chalcone derivatives. Asian Journal of Pharmacy and Pharmacology, 3: 247-250.
21. Chavan HV, Bandgar BP, Adsul LK, Dhakane VD, Bhale PS, et al. (2013) Design, synthesis, characterization and anti-inflammatory evaluation of novel pyrazole amalgamated flavones. Bioorganic & medicinal chemistry letters, 23: 1315-1321.
22. Rouzer CA, Marnett LJ (2009) Cyclooxygenases: structural and functional insights. Journal of lipid research, 50: S29-S34.
23. Vane JR, Botting RM (1998) Anti-inflammatory drugs and their mechanism of action. Inflammation Research, 47: 78-87.
24. Agarwal S, Reddy GV, Reddanna P (2009) Eicosanoids in inflammation and cancer: the role of COX-2. Expert review of clinical immunology, 5: 145-165.
25. Nagaharika Y, Rasheed S (2013) Anti-inflammatory activity of leaves of Jatropha gossypifolia L. by HRBC membrane stabilization method. Journal of Acute Disease, 2: 156-158.
26. Kumar A, Kumar S, Jain S, Kumar P, Goyal R (2013) Study of binding of pyridoacridine alkaloids on topoisomerase II using in silico tools. Medicinal Chemistry Research, 22: 5431-5441.
27. Padmanabhan P, Jangle SN (2012) Evaluation of in-vitro anti-inflammatory activity of herbal preparation, a combination of four medicinal plants. International journal of basic and applied medical sciences, 2: 109-116.
28. Kamble MA, Mahapatra DK, Dhabarde DM, Ingole AR (2017) Pharmacognostic and pharmacological studies of Bombax ceiba thorn extract. Journal of Pharmacy & Pharmacognosy Research, 5: 40-54.
29. Khadka NK (2019) Modulations of Lipid Membranes Caused by Antimicrobial Agents and Helix 0 of Endophilin.

Copyright: ©2021 N. Santhi. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.