WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 15, 862-867. Research Article ISSN 2277– 7105

SYNTHESIS, CHARACTERIZATION AND *IN-VITRO* ANTI-INFLAMMATORY AND ANTI OXIDANT ACTIVITY OF SOME NOVEL CHALCONE BASED ACETAMINOPHEN DERIVATIVES

***[1]M. Loganathan, [2]K. S. Dinesh, [3]V. Prabhakar and [4]Dr. A. Chithra and [5]M. Muthuraj**

[1,5]Assistant Professor, Department of Pharmaceutical Chemistry, Vellalar College of Pharmacy, Tamil Nadu.

[2]Assistant Professor, Department of Pharmaceutical Analysis, The Erode College of Pharmacy, Tamil Nadu.

[3]Assistant Professor, Department of Pharmacology, Vellalar College of Pharmacy, Tamil Nadu.

[4]Associate Professor, Department of Pharmaceutical Chemistry, JKKMMRF College of Pharmacy, Tamil Nadu.

Article Received on
08 September 2022,
Revised on 29 Sept. 2022,
Accepted on 19 Oct. 2022
DOI: 10.20959/wjpr202215-25996

***Corresponding Author**
M. Loganathan
Assistant Professor,
Department of
Pharmaceutical Chemistry,
Vellalar College of
Pharmacy, Tamil Nadu.

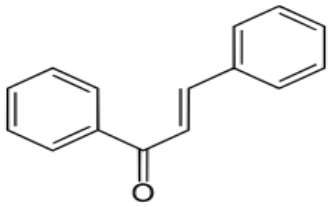
ABSTRACT

Chalcones are the naturally occuring flavanoid compounds which are now becoming trend in synthetic research because of its wider pharmaceutical application. Chalcones and their derived products are known to possess variety of biological activities such as antimicrobial, anticancer, antitubercular, antioxidant, anti-inflammatory, antileishmanial, enzyme inhibitory acquiring an unique place in medicinal chemistry. In the present study, chalcones based compounds are synthesized by claisen schmidt reaction using acetaminophen and various aldehydes to get the title compound. Four different compounds are formed using different aldehydes like chromene 3 carbaldehyde, para Anisaldehyde, furfuraldehyde, formaldehyde. The compounds formed are characterized by IR spectroscopy and NMR spectroscopy and evaluated for *in-vitro* anti oxidant activity using DPPH radical scavenging assay and anti inflammatory activity by Inhibition of albumin denaturation. From the studies it was concluded that the compound formed from chromene 3 carbaldehyde shows maximum inhibition of albumin denaturation and anti oxidant activity.

KEYWORDS: chalcones, aldehydes, acetaminophen, anti inflammatory, anti oxidant.

INTRODUCTION

Chalcones are organic flavanoid compounds, found naturally in plants. Naturally they occur mainly in petal pigments, also found in the heartwood, bark, leaf, fruit and root. Chemically it belongs to the class α,β-unsaturated ketone. Chalcone skeleton contains two aromatic rings linked by an aliphatic three-carbon chain. The two rings of chalcone are interconnected by a highly electrophilic three-carbon α,β-unsaturated carbonyl system that assumes linear or nearly planar structure. They possess conjugated double bonds and a completely delocalized π-electron system on both the aromatic rings.[1] The structural modifications of the chalcone rings have led to a high degree of diversity that has proven useful for the development of new medicinal agents, and thus chalcones have become an object of interest. The chalcones are well documented for a broad spectrum of biological activities including antimicrobial, anticancer, cytotoxic, antioxidative, anti-inflammatory, antiviral, and others. Currently, chalcone derivatives have been widely used for the treatment of viral disorders, cardiovascular diseases, stomach cancer, antimicrobial, anticancer, antitubercular, antioxidant, anti-inflammatory, and miscellaneous applications in biological and medicinal fields.[2]



General Structure of chalcone

Practically chalcones are prepared by using claisen schmidt reaction which involves reaction between an aldehyde or ketone having an α-hydrogen with an aromatic carbonyl compound lacking an α-hydrogen. The Paracetamol (N-(4-hydroxyphenyl)acetamide) is made to react with different aldehydes as like the same procedure of claisen schmidt reaction and evaluated for anti inflammatory and anti oxidant activity.[2]

MATERIALS AND METHODS

The chemicals used for the synthesis of title compounds were obtained from Nice chemicals and are laboratory grade. Analytical TLC was performed on Precoated sheets of silica gel G/UV-254 of 0.2mm thickness (Macherey-Nagel, Germany) using analytical grade solvent and visualized with iodine spray (10% w/w I2 in silica gel) or UV light. IR spectra were taken as KBr pellets for solids on Perkin Elmer. Spectrum FT-IR. 1H NMR (400MHz) and

13C NMR (100 MHz) spectra wererecorded in DMSO-d6 solution with TMS as an internal standard on Bruker instrument.

A.Procedure for Synthesis of title compounds

Equal moles of paracetamol and various aldehyde were taken in clean conical flask and dissolved in 10mL of ethanol. Then 10mL of 40% NaOH solution was added to above reaction mixture drop by drop with continuous stirring. The time taken for addition of NaOH solution should be above 30 minutes and the stirring process was contiunued for 5 – 6 hours using stirrer.After that dilute HCl was added in the sides of the flask slowlyThe product [substituted chalcones] obtained was filtered, washed with ethanol.The Scheme of the reaction was given below.

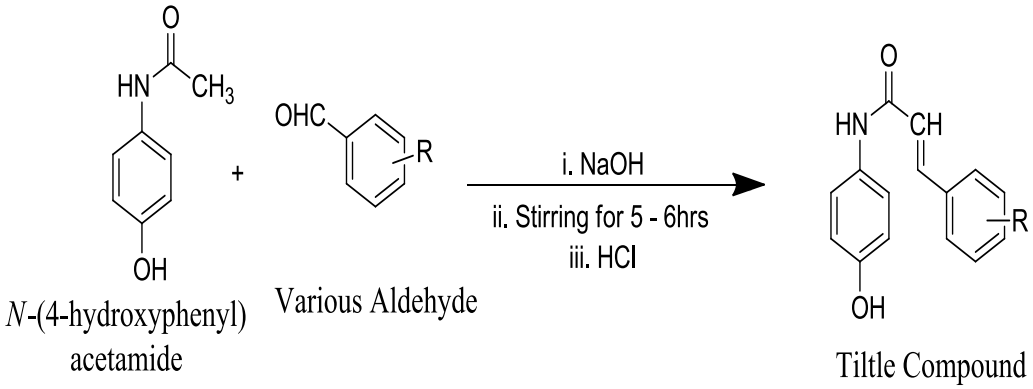


Table 1: Title compounds.

Compound IUPAC Name	Aldehyde used	Compound Code
(E)-N-(4-hydroxyphenyl)-3-(4-methoxyphenyl)acetamide	P-Anisaldehyde	PAA
(E)-N-(4-hydroxyphenyl)-3-(4-oxo-4H-chromen-3-yl)acetamide	Chromene 3 – carbaldehyde	PCA
(E)-3-(furan-2-yl)-N-(4-hydroxyphenyl)acetamide	Furfuraldehyde	PFA
N-(4-hydroxyphenyl)acetamide	Formaldehyde	PFF

Table 2: Characterization of the title compounds.

Compound	Molecular formula	Colour	Molecular weight	Melting point	Percentage yield
PFA	$C_{13}H_{11}NO_3$	Yellowish solid	229 gm	249 – 253	69 %
PCA	$C_{18}H_{13}NO_4$	Dark brown	269 gm	201 – 204	67%
PAA	$C_{16}H_{15}NO_3$	Blackish brown solid	269 gm	331 – 333	85%
PFF	$C_9H_9NO_2$	Chocolate brown solid	329 gm	282 – 283	86 %

Spectral data for synthesized compounds

PFA - IR (KBr in cm-1)3475.78 (NH str), 3423.41 (OH str), 3120.61 (CH str alkene), 1681.81 (CH str aromatic), 1608.58 (C-O str), 1544.88 (C=O str amide), 1473.51 (NH vibration), 810.05 (CH bending Aromatic:;), **1^H NMR (DMSO, δ ppm):** 9.41 (1H, OH proton), 9.17 (1H, NH proton), 8.57, 8.02, 7.69, 7.49, 7.33, 7.21, 6.98, 6.94 (aromatic proton).

PCA - 3322 (NH str), 2921 (CH str alkene), 1661 (CH str aromatic), 1551 (C-O str), 813(CH bending Aromatic; **1^H NMR (DMSO, δ ppm):** 5.35 (OH proton, 1H), 7.45&7.41 (ethylene proton, 2H), 10.12 (NH proton, 1H), 7.45 (benzene proton, 2H), 6.93 (benzene proton, 2H), 7.47, 7.55, 7.56 & 8.08 (benzene proton, 4H), 5.29 (pyran ring proton, 1H).

PAA - 3318 (NH str), 2214 (CH str alkane), 16811 (CH str aromatic), 1565 (C-O str), 1510 (C=O str amide), 1459 (NH vibration), 782 (CH bending Aromatic); **1^H NMR (DMSO, δ ppm):** 9.43 (1H, hydroxy proton), 9.27 (1H, NH proton), 7.73, 7.71, 7.36, 7.21, 6.98 (aromatic proton), 7.13 (1H, alkene proton), 7.48 (1H, alkene proton), 3.36 (3H, methoxy proton**).**

PFF - : 3303 (NH str), 2194 (CH str alkene), 1552 (C-O str), 1403 (C=O str amide), 772 (CH bending Aromatic). **1^H NMR (DMSO, δ ppm):** 9.41 (1H, OH proton), 9.17 (1H, NH proton), 8.57, 8.02, 7.69, 7.49, 7.33, 7.21, 6.98, 6.94 (aromatic proton).

B. Anti – Inflammatory activity[3]

Inhibition of albumin denaturation was done to assess Anti inflammatory activity.The reaction mixture consists of an equal volume of title compounds of different concentrations (100–500 µg/ml) prepared using ethanol and 1% aqueous solution of bovine albumin (Fraction V). The pH of the reaction mixture was adjusted using a small amount of 1N HCl. The sample extracts were incubated at 37°C for 20 min and then heated to 51°C for 20 min. The absorbance was measured after cooling the samples at room temperature. The turbidity formed was measured at 660 nm using ultraviolet (UV)-visible spectrophotometer (Model: Shimadzu UV-1800). The percentage inhibition of protein denaturation was calculated as follows.

$$\%\,\text{inhibition} = \frac{\text{Abs control} - \text{Abs sample}}{\text{Abs control}} \times 100$$

The anti-inflammatory study was compared with a standard drug diclofenac. Results of in-vitro anti-inflammatory activity of the compounds were expressed as percentage values. The results obtained are tabulated in table 3.

C.Anti-Oxidant activity[4]

DPPH radical assay

Antioxidant capacity assay was carried out using DPPH as radical. Briefly, 2,2-diphenyl-1picrylhydrazyl (DPPH) radical in ethanol (250mM, 2 mL) was added to 2 mL of an ethanolic solution of the test compounds. Final concentration of the test compounds in the reaction mixtures was 50 mM. Each mixture was then shaken vigorously and held for 30 min at room temperature in the dark. The decrease in absorbance of DPPH at 517 nm was then measured. Ethanol was used as a blank and a DPPH solution (2 mL) in ethanol (2 mL) as the control solution. All tests were performed in triplicate. The results were compared with the standard Ascorbic acid. The results obtained are tabulated in the table 4.

Table 3: % Albumin denaturation.

Concentration (µg/mL)	PFA	PCA	PAA	PFF	Standard Diclofenac
100	15.25±2.0	35.56±1.3	31.05±1.8	15.25±2.0	51.84±1.5
200	22.89±2.1	41.05±1.4	39.04±1.9	22.89±2.1	63.33±1.6
300	28.28±1.4	68.42±1.5	65.56±0.4	28.28±1.4	76.76±1.4
400	33.25±1.6	77.68±1.4	72.36±1.7	33.25±1.6	85.89±1.1
500	47.80±1.75	97.55±1.45	79.02±1.0	47.80±1.7	99.37±1.3

Table 4: Anti – oxidant activity.

Concentration (µg/ml	PFA	PCA	PAA	PFF	Standard Ascorbic acid
12.5	87.05	95.01	92.99	81.71	75.17
25	85.27	91.91	91.92	79.57	71.63
50	78.38	74.34	85.86	77.43	68.08
100	74.58	56.53	83.61	76.12	64.53
200	69.35	42.75	81.94	74.1	57.44
IC50value	**>200**	**156.13**	**>200**	**>200**	**<12.5**

RESULTS AND DISCUSSION

All the synthesized title compounds were purified by successive recrystallization using ethanol. The purity of the synthesized compounds was checked by performing TLC. The structures of the synthesized compounds were determined on the basis of their FTIR and 1HNMR spectral data. Primarily the inhibition of protein (albumin) denaturation was found to be maximum in ethanolic solution of Compound coded PCA(Chromene 3 aldehyde) with

97.55±1.45% at concentration of 500 µg/mL. Similarly them compound PCA exhibited good anti-oxidant activity compared to the standard due to the presence of hydroxy group in its structure.

CONCLUSION

The chemistry of chalcones remains a fascination among researchers in the 21st century due to the large number of replaceable hydrogens that allows a large number of derivatives and a variety of promising biological activities Anti inflammatory and anti oxidant activity of the synthesized derivatives was done in comparison with the standards to reveal the potency of synthesized derivatives. Furthermore research in the compound showing better activity (PCA) makes to the development of chalcone derivatives with therapeutic values.

REFERENCES

1. Joffina higgs, Chalcone derivatives: synthesis, *in vitro* and *in vivo* evaluation of their anti-anxiety, anti-depression and analgesic effects, national library of science, 2019 Mar; 19(5).
2. Nadia A. A. Elkanzi Synthesis of Chalcones Derivatives and Their Biological Activities: A Review, *ACS Omega*, 2022; 7(32): 27769–27786.
3. Vrinda RS, Michael CA, Rajeev G, Anju H, Ronald MD. Ester and Amide Prodrugs of Ibuprofen and Naproxen: Synthesis,Anti-inflammatory Activity, and Gastrointestinal Toxicity. J. Pharm Sci, 1992; 149(98).
4. Siham Abdelrahmane Lahsasni Synthesis, characterization and evaluation of antioxidant activities of some novel chalcones analogues, Chem Cent J., 2014; 8: 32.