Pharmacophore 2013, Vol. 4 (2), 59-69 ISSN 2229 – 5402 USA CODEN: PHARM7

Pharmacophore

(An International Research Journal)

Available online at http://www.pharmacophorejournal.com/

Original Research Paper

MICROWAVE ASSISTED SYNTHESIS AND BIOLOGICAL ACTIVITY OF CERTAIN 4-HYDROXY CHALCONES

R. Revathi[1], C. Ratna Sree[1], R.Jayakumar[3], **D.Visagaperumal[1, 2]***, N.Anbalagan[4]

[1]Department of Pharmaceutical Chemistry, Bapatla College of Pharmacy, Bapatla, Andhrapradesh, India
[2]Department of Pharmacy, Acharya Nagarjuna University, Guntur, Andhrapradesh, India
[3]Astra Zeneca India Pharma limited, Bellary road, Yalahanka, Bangalore, Karnataka, India
[4]Department of Pharmaceutical Chemistry, Pydah College of Pharmacy, Kakinada, Andhrapradesh, India

ABSTRACT

A facile synthesis of some 4-hydroxychalcones (3a-3j) by the condensation of various substituted benzaldehydes and 4-hydroxyacetophenone has been described. It is prepared by Claisen-Schmidt condensation. This is a comparative study of synthesizing compounds by conventional as well as non-conventional microwave irradiation in a commercially modified microwave oven and thus confirms the possible intervention of specific (non-thermal) microwave effect. The research is focused on the remarkable reaction rate enhancement by the use of various non-conventional microwave irradiations which minimizes the time and solvents in reactions. The microwave method offers several advantages like simple procedure, fast reaction rate, mild reaction condition and improved yields as compared to conventional methods. Variety of functional groups such as nitro, chloro, dimethylamino, methoxy, methyl and hydroxy survived under the reaction conditions. The structures of newly synthesized compounds have been established on the basis of IR and ^{1}H NMR spectral data.

Keywords: 4-Hydroxychalcones, Analgesic, Anti-inflammatory.

INTRODUCTION

Inflammation is produced due to the liberation of endogenous mediators like histamine, serotonin, bradykinin, prostaglandin, etc., in the body. Prostaglandins are ubiquitous substances that indicate and modulate cell and tissue responses involved in inflammation and even in small quantities they can elicit pain response. Pain is produced during dropped muscular activities. In order to comprehend the inflammatory process, an antagonist for these mediators is generally required. The existence of two cyclooxygenase COX-1 and COX-2[1], that are regulated and expressed differently, which are responsible for production of prostaglandins were detected independently during early 1990s. It was found that COX-1 provided cytoprotection in the gastrointestinal tract (GIT), whereas inducible COX-2 selectively mediates inflammatory signals. NSAID's are widely used for treating pain and inflammation by blocking the metabolism of arachidonic acid through the enzyme cyclooxygenase (COX). Most of the currently available NSAIDs in the market show greater selectivity for COX-1 than COX-2, chronic use of NSAIDs, may elicit appreciable GI irritation, bleeding and ulceration and this incidences are very high (30%) and may cause some patients to abandon NSAID therapy. This is generally attributed to two factors-Local irritation by the direct contact of carboxylic acid

moiety of NSAID with GI mucosal cells (Ulcerogenic effect) and decreased tissue prostaglandin production in tissues which undermines the physiological role of cytoprotective prostaglandins in maintaining GI health and homeostasis. The discovery of COX-2, expressed in response to inflammatory stimuli, present in the CNS, not in the gastric mucosa has provided a unique opportunity to develop NSAIDs that lack the ulcerogenic effect.[2] Thus, it has led to the hypothesis that selective inhibitor of COX-2 over COX-1 may be better anti-inflammatory agent with less adverse effects than the classical NSAIDs. Selective COX-2 inhibitors having better safety profile are now marketed as new generation NSAIDs.[2,3] But these selective COX-2 inhibitors (coxibs) are found to have some unexpected cardiovascular adverse effects[4], increased systemic blood pressure and hypersensitivity[5] and some of them are already withdrawn from market.[6] So, design and development of NSAIDs with enhanced safety profile is still a necessity and challenge for the pharmaceutical industry. Chalcones are the aromatic ketones belonging to 1,3-diaryl-2-propen-1-ones. Chalcones are considered as the precursors of flavonoids and isoflavonoids and are widely present in edible plants. The chemistry of chalcones generated intensive scientific studies throughout the world, specially interesting for their biological applications. Chalcones are coloured compounds because of the presence of the chromophore and auxochromes. The compounds with backbone of chalcones have been reported to possess various biological activities such as antimicrobial[7], anti-inflammatory[8], analgesic[9], antiplatelet[10], antiulcerative[11], antimalarial[12], anticancer[13], antiviral[14], antileishmanial[15], antioxidant[16], antitubercular[17], antihyperglycemic[18], anti-HIV[19], carboxygenase inhibitor[20], insecticidal[21,22], bactericidal[23,24], fungicidal[25] activities. Chalcones are very common in natural products chemistry and some of the derivatives are used as sweeteners, drugs, and sunscreen agents.[26] Chalcones synthesized can be used as intermediates for synthesizing various heterocyclic compounds.

Several strategies for the synthesis of the system based on the formation of carbon-carbon bond have been reported. Among them the direct aldol condensation and Claisen Schmidt condensation still occurs prominent position. The main method for the synthesis of chalcones is the classical Claisen-Schmidt condensation in the presence of aqueous alkali[27,28], $Ba(OH)_2$, ultrasound irradiation.[29] However many of this methods suffered from harsh reaction conditions, toxic reagents, strong acidic/basic conditions, prolonged reaction time, poor yield and low selectivity. Although, several modification have been made to counter these problems. There is still a need for the development of selective and better strategies for the synthesis of α, β-unsaturated carbonyl compounds. Recently, microwave radiation has gained the attention of chemists due to its unique advantages, such as shorter reaction times, cleaner reaction products, higher yields and better selectivities, being a valuable alternative to accomplish more efficient syntheses of a variety of organic compounds with a considerable simplicity of operation and milder reaction conditions, when combined with the solvent-free approach, as it provides an opportunity to work with open vessels.[30,31] Keeping in view of these findings, herein we had described the synthesis of chalcones under microwave irradiation and compared with conventional method and also evaluated for analgesic and anti-inflammatory activity.

MATERIAL AND METHODS

All solvents used were of laboratory grade and were obtained from SD fine chemicals (Mumbai, India), Merck (Mumbai, India) and Loba Chemie. Melting points were determined in open glass capillary tubes and were uncorrected. Compounds were routinely checked for their purity on Silica gel G (Merck) thin layer chromatography (TLC) plates. Iodine chamber were used for visualization of TLC spots. The IR spectra were recorded in KBr pellets on FT-IR spectrophotometer. ^1H NMR spectra were

recorded on Bruker DPX-300 NMR spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard. The chemical shifts were reported in ppm scale. All reactions were carried out in a commercially available LG microwave oven (MB-3947C) having a maximum power output of 800 W operating at 2450 MHz.

Synthesis of Chalcones

Conventional method

Equimolar quantities of substituted benzaldehydes (0.01 mol) and 4-hydroxyacetophenone (0.01 mol) were dissolved in minimum quantity of alcohol with 3-4 drops of concentrated sodium hydroxide. The solution was stirred with magnetic stirrer for 2-3 h and was placed overnight in a refrigerator. The mixture was then filtered, washed, dried in air and recrystallized from ethanol.

Microwave method

An equimolar mixture of 4-hydroxyacetophenone and substituted benzaldehydes was dissolved in minimum amount of ethanol in a conical flask and NaOH was added to it. The conical flask was covered with a funnel and then the flask was placed in a domestic microwave oven. The reaction mixture was irradiated under 160-320 watt for 60-120 sec. The progress of the reaction was monitored by TLC for every 30 sec. Then the reaction mixture was cooled and the obtained solid was recrystallized from ethanol.

Animals

Adult albino mice of both sexes weighing 20-25 g were fasted for 12-24 h and used for the assessment of the analgesic activity. Adult male albino rats weighing 150–180 g were fasted for 12 h and used for the evaluation of the anti-inflammatory activity. All animals were obtained from the animal house of Bapatla College of Pharmacy, Bapatla. Animals were allowed free access to water and fed with standard diet. The research was conducted in accordance with the ethical rules on animal experimentation, approved by the Ethics Committee of Bapatla College of Pharmacy, Bapatla.

Analgesic Activity

The synthesized compounds were used for evaluating their analgesic activity in acetic acid induced writhing response in albino mice following the method of Turner[32] and Collier[33] *et al.* Seventy two mice were selected and divided into 12 groups (six in each group), starved for 16 h and pretreated as follows: the first group which served as a positive control was orally received 1% CMC in appropriate volumes. The second to eleventh groups were receiving the aqueous suspension of synthesized compounds while the last group received diclofenac sodium. The test compounds were administered orally at the dose level of 20 mg/kg and Diclofenac sodium at the dose of 10 mg/kg (p.o.) was administered as standard drug for comparison. After 30 min, each mouse was administered 1% of an aqueous solution of acetic acid (10 mL/kg) and the mice were then placed in transparent boxes for observation. The number of writhes was counted for 15 min after acetic acid injection at 0.5, 1, 1.5 and 2 h. The number of writhes in each treated group was compared to that of a control group. The number of writhing was recorded and the percentage protection was calculated using the following ratio and the results are presented in table-3:

$$\% \text{ Protection} = [(\text{Control mean} - \text{Treated mean}) / \text{Control mean}] \times 100\%$$

Anti-inflammatory Activity

The anti-inflammatory activity was evaluated by using carrageenan-induced rat paw oedema model.[34] In this the animals were divided into groups (control, reference and test groups) each of 6 animals. Acute inflammation was produced by subplantar injection of 0.05 mL of 1 % suspension of carrageenan in saline into the plantar tissue of one (right) hind paw of the rat, one hour after oral administration of the test compound at dose levels of 20 mg kg^{-1}. The control group received equal volume of saline into the other (left) hind paw. The reference group was orally administered with indomethacin (5mg kg^{-1}) suspended in saline as reference drugs. The average mass of oedema

was calculated for control, reference and the test groups after drug administration. The percentage of inhibition of oedema was evaluated as per Winter *et al.*[35] The results were analyzed for statistical significance (expressed as mean ±SEM) between the zero hour administrations with other durations for the treated groups using one-way ANOVA followed by multiple comparisons by Dunnett's tests.

Acute Toxicity

Acute toxicity tests were performed according to the organization of economic co-operation and development (OECD) guideline for testing of chemicals. Acute toxicity of chalcone derivatives was determined in Wister albino mice. Each group of 3 animals was fasted for 24 hours prior to the administration of the test compounds. The test compounds are administered orally in doses up to 500 mg/kg by suspending in 1% C.M.C solution and were kept under observation for period of 24 hours.

Statistical Analysis

The data was expressed as Mean ± SEM (standard error of mean). Analysis of variance (ANOVA) followed by Dunnett test was used to statistically analyze data. P values less than 0.001 ($P<0.001$), 0.01 ($P<0.01$), 0.05 ($P<0.05$) were considered as significant.

RESULTS AND DISCUSSION

The synthesis of the chalcones was accomplished according to the Claisen-Schmidt condensation of 4-hydroxyacetophenone with appropriate substituted aromatic aldehyde under microwave irradiation and conventional method, as indicated in Scheme1 and Table1. The corresponding reactions proceeded smoothly and gave good to excellent yields (26-84 %) in microwave method when compared conventional method which had the yield of 9-75%. An important feature of this procedure is the survival of variety of functional groups such as nitro, chloro, dimethylamino, methoxy and methyl under the reaction conditions. The structures of the products were deduced from their IR and ^{1}H NMR spectral as indicated in table2. For example the IR spectrum of compound 3a-j exhibited characteristic band absorption for conjugated C=O group in the region of 1610-1700 cm^{-1}. The absorptions bands at around 1570-1620 cm^{-1} were assigned to the existing of C=C. Similarly, the peaks in ^{1}H NMR spectra of the synthesized compounds were in accordance with assigned structures. The analgesic activity was evaluated by acetic acid induced writhing response method. The percent protection in mice brought about by administration of the drugs is shown in Table3. The compounds tested showed analgesic activity in the range of 19.05 to 35.85% with this method as compared to 58.54% protection with diclofenac sodium. Compounds (3a-3j) were further tested for analgesic activity at the same dose as used for anti-inflammatory activity. The anti-inflammatory activity of compounds was carried out at an oral dose relative to 5 mg/kg of indomethacin. The percent edema inhibition relative to control was measured after 1 h, 2 h and 3 h of the treatment. The inhibition of swelling in carrageenan induced edema in rat paw brought about by oral administration of the drug is shown in Table4. All the synthesized compounds tested for anti-inflammatory activity had shown the inhibition of edema ranging from 4.6 to 8.05%. The statistical significance testing using one way analysis of variance (ANOVA) followed by Dunnett's test showed that the anti-inflammatory activity of all the newly synthesized compounds were ineffective in comparison with the standard. The anti-inflammatory effect was observed in the compounds in the similar way to analgesic effects.

CONCLUSIONS

In this work, we have demonstrated the synthesis of chalcones using microwave irradiation and compared with conventional method. The use of microwave has shown the advantages like high yields, relatively short reaction times, low cost, simple experimental and as isolation procedures, and finally, it is in agreement with the green chemistry protocols. The activity data obtained

during the study will be certainly useful to go for further research for drug designing and synthesizing new chalcone derivatives and also for heterocyclic moieties.

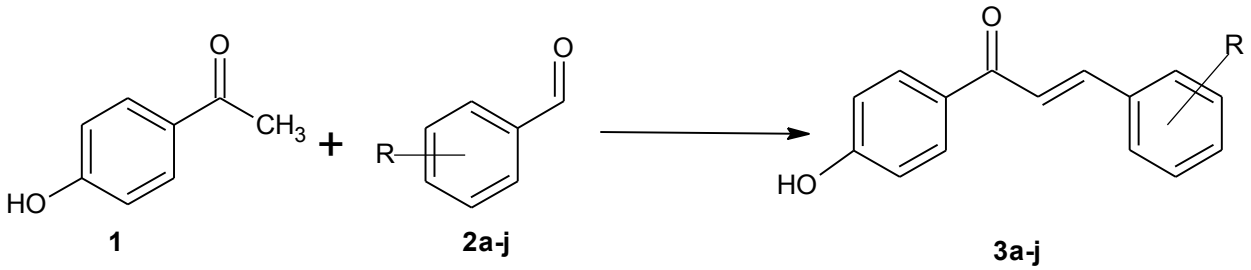
Table 1: Chemical data for the chalcones (3a-j)

Comp.	Reactants	Chalcones	Molecular formula	Molecular weight
3a	4-hydroxyacetophenone+ benzaldehyde	1-(4-hydroxyphenyl)-3-phenylprop-2-en-1-one	$C_{15}H_{12}O_2$	224
3b	4-hydroxyacetophenone+3-nitrobenzaldehyde	1-(4-hydroxyphenyl)-3-(3-nitrophenyl)prop-2-en-1-one	$C_{15}H_{11}NO_4$	269
3c	4-hydroxyacetophenone+4-nitrobenzaldehyde	1-(4-hydroxyphenyl)-3-(4-nitrophenyl)prop-2-en-1-one	$C_{15}H_{11}NO_4$	269
3d	4-hydroxyacetophenone+4-dimethylaminobenzaldehyde	3-[4-(dimethylamino) phenyl]-1-(4-hydroxy phenyl)prop-2-en-1-one	$C_{17}H_{17}NO_2$	267
3e	4-hydroxyacetophenone+4-methoxybenzaldehyde	1-(4-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one	$C_{16}H_{14}O_3$	254
3f	4-hydroxyacetophenone+4-methylbenzaldehyde	1-(4-hydroxyphenyl)-3-(4-methylphenyl)prop-2-en-1-one	$C_{16}H_{14}O_2$	238
3g	4-hydroxyacetophenone+2-chlorobenzaldehyde	3-(2-chlorophenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one	$C_{15}H_{11}ClO_2$	259
3h	4-hydroxyacetophenone+4-chlorobenzaldehyde	3-(4-chlorophenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one	$C_{15}H_{11}ClO_2$	259
3i	4-hydroxyacetophenone+4-hydroxybenzaldehyde	1,3-bis(4-hydroxy phenyl)prop-2-en-1-one	$C_{15}H_{12}O_3$	240
3j	4-hydroxyacetophenone+3-hydroxy-4-methoxybenzaldehyde	3-(3-hydroxy-4-methoxy phenyl)-1-(4-hydroxy phenyl)prop-2-en-1-one	$C_{16}H_{14}O_4$	270

Table 2: Spectral data, yield and melting point of compounds

Compounds	IR-Spectrum (KBr), cm^{-1}	^{1}H-NMR spectrum (δ, ppm)	Yield (%)		m.p. (°C)
			Conven	MV	
3a	3384 (OH), 3082 (C-H aromatic), 1683 (C=O), 1576 (C=C)	7.56 (d, 1Hα), 7.99 (d, 1Hβ), 7.01–7.5(m, 9H, Ar-H), 12.9 (s, 1H, OH)	39	45	120-121
3b	3372 (OH), 3062 (C-H aromatic), 1689 (C=O), 1582 (C=C)	7.51 (d, 1Hα), 7.91 (d, 1Hβ), 7.05–8 (m, 8H, Ar-H), 12.3 (s, 1H, OH)	75	84	182-184
3c	3379 (-OH), 3079 (C-H aromatic), 1692 (C=O), 1585 (C=C)	7.54 (d, 1Hα), 7.94 (d, 1Hβ), 7.02–7.07 (m, 8H, Ar-H), 12.5 (s, 1H, OH)	26	49	58

3d	3381 (OH), 3014 (C-H aromatic), 1669 (C=O), 1595 (C=C), 1370 (C-N)	2.94 (s, 6H, N-$(CH_3)_2$), 6.5 (d, 1Hα), 8.72 (d, 1Hβ), 6.81–8.76 (m, 8H, Ar-H), 9.68 (s, 1H, OH)	47	65	112-113
3e	3385 (OH), 3029 (C-H aromatic), 1659 (C=O), 1582 (C=C), 1171 (OCH_3)	3.72 (s, 3H, OCH_3), 6.81 (d, 1Hα), 7.92 (d, 1Hβ), 6.72–8.13 (m, 8H, Ar-H), 12.76 (s, 1H, OH)	35	51	179–181
3f	3449 (OH), 3018 (C-H aromatic),1679 (C=O), 1594 (C=C)	2.31 (s, 3H, CH_3), 7.26 (d, 1Hα), 7.73 (d, 1Hβ), 7.01–8.2 (m, 8H, Ar-H), 12.72 (s, 1H, OH)	30	49	114–116
3g	3455 (OH), 1692 (C=O), 1618 (C=C), 835 (Ar-Cl)	7.48 (d, 1Hα), 8.14 (d, 1Hβ), 6.35–8.2 (m, 8H, Ar-H), 12.76 (s, 1H, OH)	41	46	180
3h	3451 (OH), 1696 (C=O), 1615 (C=C), 830 (Ar-Cl)	7.41 (d, 1Hα), 8.16 (d, 1Hβ), 6.42–8 (m, 8H, Ar-H), 12.74 (s, 1H, OH)	16	55	190
3i	3462 (OH), 3010 (C-H aromatic), 1661 (C=O), 1581 (C=C)	7.82 (d, 1Hα), 7.53 (d, 1Hβ), 6.29–8.21 (m, 8H, Ar-H), 10.18 (s, 1H, OH)	9	25	287–289
3j	3412 (OH), 3012 (C-H aromatic), 1618 (C=O), 1591 (C=C), 1162 (OCH_3)	3.79 (s, 3H, OCH_3), 7.67 (d, 1Hα), 7.42 (d, 1Hβ), 6.32–8.33 (m, 8H, Ar-H), 10.23 (s, 1H, OH)	14	26	260



R=H,3-NO_2,4-NO_2,4-$N(CH_3)_2$,4-OCH_3,4-CH_3,2-Cl,4-Cl,4-OH,3-OH-4-OCH_3

Scheme 1: Synthesis of chalcone derivatives

Table 3: Analgesic effect of selected investigated compounds

S. No.	R	Dose (mg/kg)	Mean value ± S.E. at different time interval (in seconds)				% Protection	
			30 min	60 min	90 min	120 min	90 min	120 min
3a	H	20	4.833±0.6009	5.167±0.4014	5.333±0.4216	5.167±0.4773	35.85	34.6
3b	3-NO_2	20	4±0.5744	4.333±0.7149	4.667±0.6667	4.333±0.4216	27.66	20.93
3c	4-NO_2	20	4.167±0.6009	4.333±0.7601	4.667±0.6667	4.167±0.4773	27.66	19.05
3d	4-$N(CH_3)_2$	20	5.167±0.4773	5.333±0.6146	5.5±0.5627	5.333±0.4216	38.18	35.85
3e	4-OCH_3	20	4.5±0.7638	5.333±0.8819	5.5±0.7188	5.333±0.4944	38.18	35.85
3f	4-CH_3	20	4.5±0.4282	4.667±0.8028	5.167±0.7032	4.667±0.7149	33.33	27.66
3g	2-Cl	20	4.333±0.6667	4.5±0.5627	4.667±0.7149	4.333±0.4216	27.66	20.93
3h	4-Cl	20	4.667±0.5578	5±0.7303	5.167±0.7032	4.883±0.6009	33.33	29.17
3i	4-OH	20	4.833±0.6009	5.167±0.8724	5.333±0.8028	5±0.8165	35.85	32
3j	3-OH,4-OCH_3	20	4.667±0.8819	5.333±0.5578	5.5±0.6191	5.167±0.4773	38.18	34.6
STD	Diclofenac Sodium	20	6.333±0.6667	7.167±0.9458	9.167±0.8333	8.167±0.9068	60.47	58.54

Significance levels compared with 30 min administration (ANOVA followed by Dunnett's test). Each value represents ± SE (n = 6).

Table 4: Anti-inflammatory effects of selected investigated compounds

S.No.	R	Drug Conc.	Paw volume measured after				% inhibition at	
			30 min	1 h	2 h	3 h	2 hr	3 hr
3a	H	20	0.4333±0.08819	0.7167±0.2072	1.383±0.1302**	1.45±0.1478***	4.6	2.24
3b	3-NO_2	20	0.4333±0.1054	0.75±0.1688	1.383±0.1815***	1.45±0.1057***	4.6	2.44
3c	4-NO_2	20	0.4333±0.1145	0.7333±0.1909	0.383±0.1740***	1.467±0.1406***	4.6	1.12
3d	4-$N(CH_3)_2$	20	0.4333±0.1085	0.7333±0.1838	1.333±0.1944**	1.417±0.1302***	8.05	4.49
3e	4-OCH_3	20	0.4333±0.1202	0.7333±0.2155	1.367±0.1382**	1.467±0.1282***	5.74	1.12
3f	4-CH_3	20	0.4333±0.1022	0.75±0.1455	1.367±0.2362**	1.467±0.1085***	5.74	1.12
3g	2-Cl	20	0.4333±0.1145	0.7333±0.08819	1.383±0.1662***	1.433±0.1116***	4.6	3.37
3h	4-Cl	20	0.4333±0.1453	0.7167±0.1014	1.383±0.14***	1.467±0.1406***	4.6	1.12
3i	4-OH	20	0.4333±0.06667	0.7333±0.1358	1.367±0.08819***	1.45±0.07638***	5.74	2.24
3j	3-OH, 4-OCH_3	20	0.4333±0.09189	1.35±0.1522***	1.433±0.1647***	0.7167±0.1352	6.9	3.37
STD	Indomethacin	5	0.2167±0.4014	0.2833±0.06009	0.3667±0.05578	0.4167±0.6009	74.71	71.91

Significance levels *P< 0.05, **P< 0.01, ***P<0.001 compared with respective zero hour administration (ANOVA followed by Dunnett's test). Each value represents ± SEM (n = 6)

REFERENCES

1. Silverstein, FE; Faish, G; Goldstein, JL; Simon, LS; Pinus, T; Whelton, R., Makuch, R; Eisen, G; Agrawal, NM; Stenson, WF; Burr, AM; Zhao, WW; Kent, JD; Lefkowith, JB; Verburg, KM; Geis, GS (2000), "Gastrointestinal toxicity with celecoxib vs non-steroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis", ***J Am Med Assoc***, Vol. 284 (10), 1247-1255.
2. Kalgutkar, AS (1999), "Selective cyclooxygenase-2 inhibitors as non-ulcerogenic anti-inflammatory agents", ***Expert Opin. Therap Patents***, Vol.9 (7), 831-849.
3. Tally, JJ; Bertenshaw, RS; Brown, DL; Carter, JS; Graneto, MJ; Kellogg, MS; Kobolt, CM; Yuan, J; Zhang, YY and Seibert, K (2000), "N-[[(5-Methyl-3-phenylisoxazol-4-yl)- phenyl] sulfonyl] propanamide, Sodium Salt, Parecoxib Sodium: A Potent and Selective Inhibitor of COX-2 for Parenteral Administration", ***J. Med. Chem***, Vol.43, 1661-1663.
4. Dogne, JM; Supuran, CT and Pratico, D (2005), "Adverse Cardiovascular Effects of the Coxibs", ***J Med Chem***, Vol.48 (7), 2251-2257.
5. De Gaetano, G; Donati, MB and Cerletti, C (2003), "Prevention of thrombosis and vascular inflammation: benefits and limitations of selective or combined COX-1, COX-2 and 5-LOX inhibitors",***Trends Pharmacol Sci***, Vol.24 (5), 245-252.
6. Rathish, IG; Javed, K; Ahmad, S; Bano, S; Alam, MS; Pillai, KK; Singh, S and Bagchi, V (2009), "Synthesis and anti-inflammatory activity of some new 1,3,5-trisubstituted pyrazolines bearing benzene sulfonamide", ***Bioorg Med Chem Lett***, Vol.19 (1), 255-258.
7. Shah, M; Patel, P; Korgaokar, S and Parekh, H (1996), "Synthesis of pyrazolines, isoxazoles and cynopyridines as potential antimicrobial agents", ***Indian J Chem***, Vol.35 (12), 1282-1284.
8. Rangari, V; Gupta, VN and Atal, CK (1990), "Synthesis, anti-inflammatory and anti-arthritic activity of newer beta-boswellic acid derivatives", ***Indian J Pharm Sci***, Vol.52 (3), 158-60.
9. Viana, GSB; Bandeira, MAM and Matos, FJA. (2003), "Analgesic and anti-inflammatory effects of chalcones isolated from *Myracrodruon urundeuva* Allemão", ***Phytomedicine***, Vol.10 (2-3), 189-195.
10. Zhao, LM; Jin, HS; Sun, LP; Piao, HR and Quan, ZS (2005), "Synthesis and evaluation of antiplatelet activity of trihydroxychalcone derivatives", ***Biorg. Med. Chem. Lett***, Vol.15 (22), 5027-5029.
11. Murakami, S; Muramatsu, M; Aihara, H and Otomo, S (1991), "Inhibition of gastric H^+, K^+-ATPase by the anti-ulcer agent, sofalcone", ***Biochem, Pharmacol***, Vol.42 (7), 1447-1451.
12. Liu, M; Wilairat, P and Go, LM (2001), "Antimalarial Alkoxylated and Hydroxylated Chalones: Structure Activity Relationship Analysis", ***J Med Chem***, Vol.44 (25), 4443-4452.
13. Francesco, E; Salvatore, G; Luigi, M and Massimo, C (2007), "Chemistry and pharmacology of oxyprenylated secondary plant metabolites", ***Phytochem***, Vol.68 (7), 939-953.
14. Binder, D; Noe, CR; Holzer, W and Rosenwirth, B (1985), "Thiophene as a Structural Element of Physiologically Active Compounds, XII: Thiophene Analogues of Antiviral Chalcones", ***Archiv Der Pharmazie***, Vol.318 (1), 48-59; (1985*)*, ***Chem. Abstr,*** Vol.102, 149025u.
15. Nielsen, SF; Chen, M; Theander, TG; Kharazmi, A and Christensen, SB (1995), "Synthesis of antiparasitic licorice chalcones", ***Bioorg Med Chem Lett***, Vol.5 (5), 449-452.
16. Miranda, CL; Ivanov, V; Stevens, JF; McCall, M; Frei, B; Deinzer, ML and Buhler DR (2000), "Antioxidant and Prooxidant Actions of Prenylated and Nonprenylated

Chalcones and Flavanones in Vitro", ***J Agric Food Chem***, Vol.48 (9), 3876-3884.

17. Siva Kumar, PM; Geetha Babu, SK and Mukesh, D (2007), "QSAR Studies on Chalcones and Flavonoids as Anti-tuberculosis Agents Using Genetic Function Approximation (GFA) Method", ***Chem Pharm Bull***, Vol.55 (1), 44-49.
18. Satyanarayana, M; Tiwari, P; Tripathi, BK; Srivastava, AK and Pratap, R (2004), "Synthesis and antihyperglycemic activity of chalcone based aryloxypropanolamines", ***Bioorg Med Chem***, Vol.12 (5), 883-889.
19. Cheenpracha, S; Karalai, C; Ponglimanont, C; Subhadhirasakul, S and Tewtrakul, S (2006), "Anti-HIV-1 protease activity of compounds from *Boesenbergia pandurata*", ***Bioorg Med Chem***, Vol.14 (6), 1710-1714.
20. Satoshi, S; Yasunori, N; Hiroki, U; Akihiro, I; Tokutaro, M; Hitoshi, M and Toshio, S (1993), "3,4-Dihydroxychalcones as potent 5-lipoxygenase and cyclooxygenase inhibitors", ***J Med Chem*****,** Vol.36 (24), 3904-3909; (1994), ***Chem Abstr***, Vol.120: 133956j.
21. Nissan Chemical Industries Ltd. (1983), ***Japan Kokai Tokkyo Koho Japan***, Vol 58, 08, 035; (1983), ***Chem Abstr***, 98, 178947a.
22. Seele, R *et al.* (1989), "***Eur Pat Appl Ep*****"**, Vol.337, 198 (Cl C07D, 249/08); (1990), ***Chem Abstr***, Vol.113, 178990s.
23. Bowden, K; Dal, PA. and Shah, CK (1990), "Structure-activity relations. Part 5. Antibacterial activity of a series of substituted (E)-3-(4-phenylbenzoyl)acrylic acids, -chalcones, -2-hydroxychalcones and -alpha-bromochalcones; addition of cysteine to substituted 3-benzoylacrylic acids and related compounds", ***J Chem Res Synop***, Vol.12, 2801-2830; (1991), ***Chem Abstr*****,** Vol.114, 160570m.
24. Inamori, Y; Baba, K; Tsujibo, H; Taniguchi, M; Nakata, K and Kozawa, M. (1991), "Antibacterial Activity of Two Chalcones, Xanthoangelol and 4-Hydroxyderricin, Isolated from the Root of *Angelica keiskei* KOIDZUMI", ***Chem Pharm Bull***, Vol.39 (6), 1604-1605; (1991), ***Chem Abstr*****,** Vol.115, 105547c.
25. Pedersen, AK and Fitzgerald, GA (1985), "Preparation and analysis of deuterium-labeled aspirin: Application to pharmacokinetic studies", J ***Pharm Sci***. Vol.74 (2), 188-192; (1985), ***Chem Abstr***, Vol.103, 87592m.
26. Li, J-T, Yang, W-Z; Wang, S-X; Li, S-H and Li, T-S (2002), "Improved synthesis of chalcones under ultrasound irradiation", ***Ultrasonics Sonochemistry***, Vol.9 (5), 237-239.
27. Prasad, YR; Rao, AL; Rambabu, R and Kumar, PR (2007), "Synthesis and biological evaluation of some novel chalcone derivatives", ***Oriental J. Chem***, Vol.23 (3), 927-937.
28. Rao, SM; Kotesh, J; Marukulla, R and Duddeck, H (2004), "Synthesis and spectroscopic characterization of some chromanochalcones and their dihydro derivatives", ***Arkivoc***, Vol.2004 (xiv), 96-102.
29. Calvino, V; Picallo, M; Lopez-Peinado, AJ; Martin-Aranda, RM and Duran-Valle, CJ (2006), "Ultrasound accelerated Claisen–Schmidt condensation: A green route to chalcones", ***Appl Surf Sci***, Vol.252 (17), 6071-6074.
30. Varma, RS (1999), "Solvent-free organic syntheses using supported reagents and microwave irradiation", ***Green Chem*****,** Vol.1 (1), 43-55.
31. Hayes, BL (2002), "***Microwave Synthesis: Chemistry at the Speed of Light***", Matthews, NC, CEM Publishing.
32. Turner, RA (1965), "***In Analgesics: Screening Methods in Pharmacology***". Turner, R.A., Ed. Academic Press, London, 100.
33. Collier, HDJ; Dinnin, LC; Johnson, CA and Schneider, C (1968), "The abdominal response and its suppression by analgestic drugs in the mouse", ***Br. J. Pharmacol and Chemother***, Vol.32 (2), 295-310.

34. Obukowicz, MG; Welsch, DJ; Salsgiver, WJ; Berger, M; Chinn, KS and Duffin, KL (1998), "Novel, selective delta6 or delta5 fatty acid desaturase inhibitors as anti-inflammatory agents in mice", ***J Pharmacol Exp Ther***, Vol.287 (1): 157-162.

35. Winter, CA; Risely, EA and Nuss, GW (1963), "Anti-inflammatory and antipyretic activities of indomethacin, 1-(p-chlorobenzyl)-5-methoxy-2-methyl-indole-3-acetic acid", ***J Pharmacol Exp Ther***, Vol.141 (1), 369-376.

Correspondence Author:
D.Visagaperumal
Associate Professor
Department of Pharmaceutical Chemistry
Bapatla College of Pharmacy
Bapatla, Guntur Dt
Andhra Pradesh, India-522101
Email: vishak_dr@yahoo.co.in

Cite This Article: R, Revathi; C Ratna, Sree; R, Jayakumar; D,Visagaperumal and N, Anbalagan (2013), "Microwave Assisted Synthesis And Biological Activity Of Certain 4-Hydroxy Chalcones", ***Pharmacophore***, Vol. 4 (2), 59-69.

Pharmacophore
(An International Research Journal)