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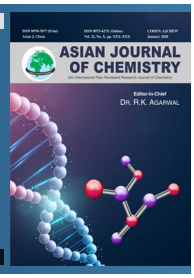

Synthesis, Characterization and Anti-inflammatory Activity of (2*E*)-3-(2-Bromo-6-hydroxy-4-methoxyphenyl)-1-(naphthalene-2-yl)prop-2-en-1-one

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(2*E*)-3-(2-Bromo-6-hydroxy-4-methoxyphenyl)-1-(naphthalene-2-yl)prop-2-en-1-one (**d1**) was synthesized by the Claisen-Schmidt condensation method and characterized by ^{1}H NMR, ^{13}C NMR spectral studies. The anti-inflammatory activity was conducted in Swiss albino rats for paw edema model. Edema was actuated with 1 % carrageenan to every one of the animals following 1 h of the oral medicines. Paw thickness was checked at t = 1, 2, 3, 4, 5 and 24 h. Stair climbing score and motility score were surveyed at t = 24 h. Compound **d1** signicant decline in paw thickness at $p < 0.001$ diminished by 32 % in paw thickness. The compound **d1** signicantly expanded the stair climbing and motility score. This study suggested that the compound **d1** exhibits remarkable anti-inflammatory activity when compared with that of the standard drug.

Keywords: Naphthalene chalcones, Anti-inflammatory activity, Paw edema.

INTRODUCTION

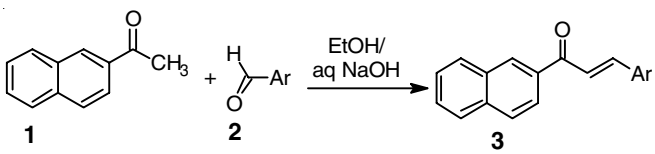
Malignant development is one in all the most medicinal issues inside the human populace and one of the various purposes behind death. A tad bit of the normally happening mixes is dynamically enthused about threatening tumor meds in various human dangerous developments [1-5]. Chalcones are available flavonoid exacerbates that go about as chemotherapeutic operators owing to their natural movement. Consequently, we look to incorporate new atoms from the plant beginning [6]. Fundamentally, chalcones incorporate an aliphatic three-carbon chain joins that links 2 aromatic rings. Chalcones or 1,3-disubstituted-prop-2-en-1-ones (R1COCH=CHR2), are α,β-unsaturated ketones comprising of 2 aromatics having an assorted cluster of substituents and that they grouped commonly of the indispensable subgroups of flavonoids and its frameworks showing medicative and natural properties. Chalcones are benzyl bunch acetophenone or benzylideneacetophenone and their rings are interconnected by incredibly characteristic activity 3 carbon α,β-unsaturated carbonyl framework that expects straight or almost planar structure [7-9]. Mixes of this classification demonstrate an enormous assortment of the organic movement, together with antibacterial [10], dangerous tumor [11-13] antifungal, fourteen enemies of inflammatory [14-16], antiprotozoal tranquilize [17] and antitubercular exercises [18]. The perception expresses that once electron-rich naphthyl rings are a blessing in chalcones, they will partake in π-π communication, picture stacking collaborations and this could assume a critical job in dimensioning inhibitors among the dynamic locales of chemicals [19]. There are various components to a fiery response that will add to the related side effects and tissue damage. Edema, leukocytes penetration and tumor arrangement speak to such parts of inflammation. The reason that chalcone hydrocarbon ring might be utilized as a profitable moiety inside the meaning of the most recent threatening tumor experts in various human malignant growths. Different naphthalene subordinates have been accounted to indicate anticancer activity by subduing tubulin polymerization [20,21]. For the amalgamation of mixes **d1** the Claisen-Schmidt condensation reactions between equimolar amounts of 2-acetylnaphthalene and the suitable aldehyde within the sight of watery sodium hydroxide arrangement, was utilized to incorporate novel naphthalene containing chalcone as shown in **Scheme-I**. Prompted by these considerations, we have incorporated and portrayal of chalcone containing 2-naphthyl substituents.

EXPERIMENTAL

All the compounds are available commercially and used as received. Reactions were monitored by TLC, performed on silica gel glass plates containing and visualization on TLC was achieved by UV light or iodine indicator. ^{1}H and ^{13}C NMR spectra were recorded on V NMRS-400 Agilent NMR instrument. Chemical shifts (δ) are reported in ppm downfield from internal TMS standard, with tetramethylsilane (TMS) as the inside standard in DMSO. Carrageenan was acquired from Hi-Media, India. Standard anti-inflammatory drug indomethacin was acquired from Recon, Bangalore, India.

Animals: Swiss albino, BALB/c female rats, matured 150-160 g were housed under standard research centre conditions and encouraged an eating routine of animal food and water not obligatory all through the analysis. The rats were kept up at room temperature (22 ± 2 °C) with ventilation for a 12 h day/night cycle. Swiss albino rats (120 g each) were utilized for the present examination. They were encouraged with standard pellet diet and water not obligatory. All the animals were acclimatized for something like a multi-week before the trial session. All animal's experimentations were endorsed by the Institutional Animal Ethics Committee (IAEC), (Approval No: BCP/IAEC/EXTP/05/2018) Bharathi College of Pharmacy, Bharathi Nagara, Mandya District, India. As per the Committee for control and supervision of experiments on animals (CPCSEA) rules for the animals' research facility.

Synthesis of (2*E*)-3-(2-Bromo-6-hydroxy-4-methoxyphenyl)-1-(naphthalene-2-yl)prop-2-en-1-one (d1): An aqueous solution of NaOH (50 % w/v, 5 mL) was added to equimolar mixtures (0.58 mmol of each component) of 2-acetylnaphthalene and appropriate aldehydes The mixtures were then stirred at ambient temperature for 4 h, an excess of ice-cold water was added and the resulting solid products were collected by filtration and dried in air, obtained desire products (**Scheme-I**). Yield 81.92 %, Yellow powder, m.p.: 162-164 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.58 (s, 1H), 8.17-7.89 (m, 6H), 7.60-7.57 (m, 2H), 6.99-6.97 (d, J = 7.6, 1H), 6.47-6.45 (d, J = 6.8 1H), 5.96-5.92 (t, J = 7.6, J_2 = 7.1 1H), 3.61 (s, 3H); ^{13}C NMR: 153.441, 146.708, 137.913, 134.741, 132.853, 129.632, 129.643, 126.563, 128.281, 127.999, 126.967, 125.002, 123.455, 121.402, 112.306, 111.595, 107.198.



Scheme-I: Synthesis of compound **d1**, an aqueous sodium hydroxide solution (50 % w/v, 5 mL) was added to equimolar mixtures (0.58 mmol of each component) of 2-acetylnaphthalene and the appropriate aldehyde

Carrageenan-induced acute inflammatory model: For the anti-inflammatory evaluation of acute inflammation, animals were separated into four groups. Group A (normal) did not get any oral treatment; Group B (control), Group C (positive control) animals were managed with indomethacin and Group D (**d1** Treated) (150 mg/Kg body weight). Anti-inflammatory action was estimated utilizing carrageenan-induced rat paw edema measure [22,23]. Edema was prompted by subplantar infusion of 100 µL of 1 % of carrageenan in refined water into the left hind paws of each rat of the considerable number of groups aside from the group A, B, C, D. Paw thickness were estimated just prior to the carrageenan infusion, *i.e.*, at 0 h, and at that point at 1, 2, 3, 4 and 24th h after carrageenan infusion. Increment in paw thickness was estimated as the distinction in paw thickness at "0 h" and paw thickness at separate hours.

Stair climbing activity test: Medium-term fasting creatures were prepared for the multi-week to climb a staircase with ventures at 5, 10 and 15 cm having water at the second and nourishment at the third step. The climbing capacity of the rat in the above groups was scored 0 if the rat did not climb; 1, if the rat climbed onto stage 1; 2, if the rat climbed onto stage 2; 3, if the rat could climb all the three stages [23].

Motility test: The motility example of the rats was observed for a time of 5 min and scored 0, if the rats strolled with trouble and abstained from contacting the toes of the kindled paw to the floor; 1, if the rat strolled with nearly nothing trouble, yet with toe contacting the floor; 2, if the rat strolled effectively [25].

RESULTS AND DISCUSSION

Carrageenan-induced inflammation: Infusion of carrageenan into the rear paw incited dynamic edema achieving its highest at 4 h. If there should arise an occurrence of Group A animals paw thickness found at t =0 was 0.48 ± 0.0408 and this remaining parts consistent toward the finish of 24 h. The group B creatures had demonstrated an expansion in paw thickness at every hour, which was signicant at $P < 0.001$. At 0 h the thickness was 0.48 ± 0.040 cm, which expanded to 1.18 ± 0.049 at t = 4 h. At 24 h, the thickness was observed to be 1.5 ± 0.025. The paw thickness of Group C creatures was 0.45 ± 0.028 cm, which demonstrated a gentle increment toward the finish of the 2nd h, that is, 0.70 ± 0.0102 cm. After the 2nd h it decreased to 0.65 ± 0.077, 0.60 ± 0.0489, 0.56 ± 0.0053 and 0.52 ± 0.024 toward the finish of 3, 4 and 24 h, separately. Gathering C animals demonstrated an expansion up to the 2nd h. 0.78 ± 0.065 thickness was found toward the finish of the 3rd h, which diminished to 0.55 ± 0.0024 cm at t = 24 h. Groups C showed a measurably signicant decline in paw thickness ($P < 0.0001$). These qualities were observed to be factually signicant at $P < 0.0001$ (Fig. 1).

Stair climbing activity: Hyperalgesia was instigated *via* carrageenan in Group A rats. Their stair climbing action was 0.28 ± 0.244, while the most astonishing score was seen in Group A animals at 3 ± 0.00 (measurably signicant; $P < 0.0001$). Lactobacillus treatment signicantly expanded the stair climbing score of 2.57 ± 0.489 and 2.71 ± 0.408 for Group C and Group D, respectively (signicant at $P < 0.0001$). Group B creature score was most minimal in contrast with Groups A, C and D animals (Fig. 2).

Motility: Walking ability of the rats to climb the staircase at the season of peak inflammation was checked by motility score. Group C and Group D animals were demonstrating the highest score of 2.42 ± 0.489 and 2.5 ± 0.32 (signicant at $P < 0.001$). The score for Group A creatures was 3 ± 0.00 through 0.14 ± 0.244 was found in the event of gathering B creatures.

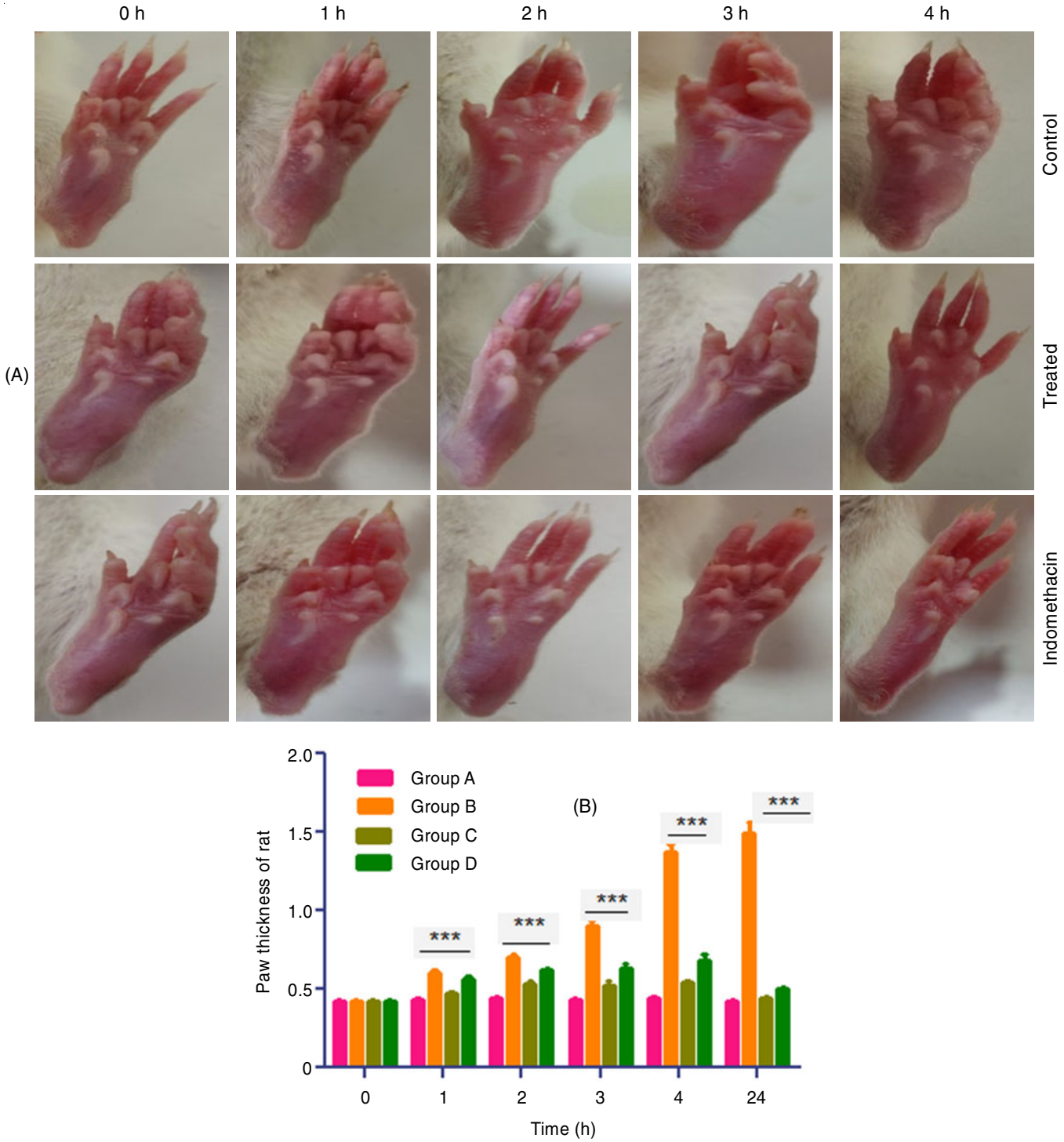


Fig. 1. (A) Change in paw thickness at t = 0, 1, 2, 3, 4 and 24 h. n = 5 (signicant at P < 0.0001). Edema was induced by injecting 0.1mL of 1 % solution of carrageenan into the subplantar surface of the left hind paw. (B) Group A: normal; Group B: carrageenan control; Group C: indomethacin; Group D: treated

This was observed to be the most minimal when looking at Group B animals (Fig. 2).

Carrageenan-induced rat paw edema model is an appropriate test for assessing hostile to inflammatory drugs, which has habitually been utilized to survey the antiedematous effect of the medication. In this model of inflammation, **d1** had an extremely reliable enemy of inflammatory action and in this manner indicated a significant decline in the paw thickness of rat (Group C and D). The present outcomes recommend that **d1** the first period of carrageenan-actuated paw edema, confirming an NSAID-like property. The current examination demonstrated that **d1** has both pains relieving and against inflammatory properties.

Statistical analysis: The paw edema volume is expressed as the mean ± SEM of five perceptions. The stair climbing capacity test and motility are communicated as middle scores and the Kruskal-Wallis test was used to think about the animals. Data were analyzed using Graph Pad Prism 5.0 software.

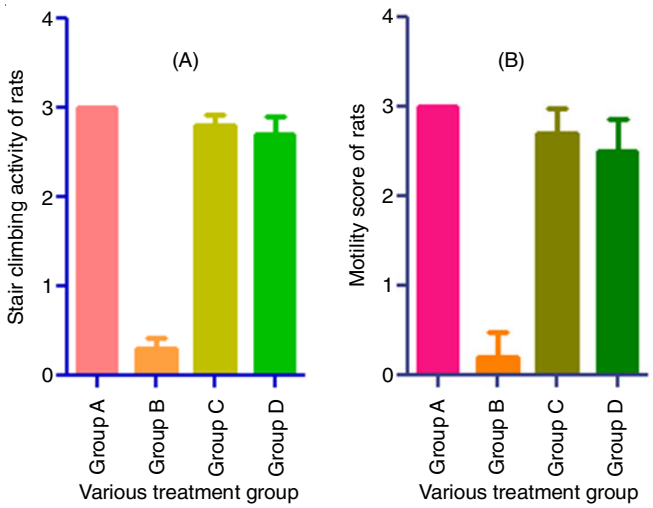


Fig. 2. (A) the drugs were administered half-hour orally before injecting inflammation. Stair climbing activity was discovered at the time of peak inflammation (4 h for carrageenan). Group A: normal; Group B: carrageenan control; Group C: indomethacin; Group D: treated; (B) The motility score was discovered at the time of peak inflammation (4 h for carrageenan).Group A: normal; Group B: carrageenan control; Group C: indomethacin; Group D: treated

Conclusion

In the present study, naphthalene chalcone **d1** were synthesized by the Claisen condensation and carried out the anti-inflammatory activity results show that compound with electron donating group exhibits the superior activity.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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