WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 10, 1294-1308. Research Article ISSN 2277– 7105

DESIGN, SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF *β, β* -DIPHENYL PROPIONIC ACID DERIVATIVES ON ALBINO WISTAR RATS FOR PHARMACEUTICAL INTERESTS

Punet Kumar[1]*, Sangam[2] and Vidhan Chand Bala[3]

[1]Drug Design Laboratory, Shri Gopichand College of Pharmacy, Bagpat, 250609, (U. P.) India.

[2]Department of Pharmaceutical Chemistry, Faculty of Oxford College of Pharmacy, Hapur, 201001, (U.P.) India.

[3]Department of Pharmacology, Faculty of Oxford College of Pharmacy, Hapur, 201001, (U.P.) India.

Article Received on
04 July 2019,

Revised on 24 July 2019,
Accepted on 14 August 2019,

DOI: 10.20959/wjpr201910-15699

***Corresponding Author**
Prof. Punet Kumar
Drug Design Laboratory,
Shri Gopichand College of Pharmacy, Bagpat, 250609,
(U. P.) India.

ABSTRACT

Phenyl propionic acid is as safer and more potent analgesic and inflammatory compound. The present scenario studies the synthesis of β, β--diphenyl propionic acid derivatives. *β, β* -diphenyl propionyl chloride (Intermediate compound) was prepared by the reaction of β,β-diphenyl propionic acid, and thionyl chloride. β, β-diphenylpropanoyl chloride was reacting to a number of aromatic amines in the presence of potassium carbonate in acetone. The synthesized compound is characterized by physical properties, IR, 1HNMR, Mass spectral data. Synthesis derivatives are examined to find out an analgesic activity (the method of working hot plates and tails Flik method) and anti -inflammatory activity (a method induced by Carrageenan induced edema) with Diclofenac and Indomethacin as standard drug. AK-3 (Morpholine derivative) and AK-5(diphenylamine derivative) are potent analgesics and anti-inflammatory compounds. The derivatives of Arylpropionic acid have pain relief and a great space for further development as a similar and anti-inflammatory agent.

KEYWORDS: Aryl propionic acid derivatives, *β, β*-diphenyl propionyl chloride, inflammation, Albino rats, Diclofenac sodium, Analgesia, Eddy's Hot Plate Method.

INTRODUCTION

Aryl propionic acid derivatives are an important and valuable family of NSAIDs. They are often applied to treat several of skeletal diseases and skeletal muscle diseases. One of the derivatives of propionic acid, such as ibuprofen, 2-(4-isobutyl phenyl) propionic acid, is a well-known pain reliever that has strong pain relief, especially in arthritis, antipyretic and anti-inflammatory properties. Long-term use of agents results in gastrointestinal ulceration, bleeding, and neptrotoxicity. Inflammation is an immune response to damage or infection that causes disease, redness, heart, and inflammation in the affected area. It involves a number of events that can be obtained through various events (for example, the agent of ischemia infections and other physical damage). The inflammatory response is characterized by the following symptoms: Redness of the localized area.

The inflammation is two types:-

Acute inflammation

With a short process, for example (days to a few weeks) increase the migration of blood flow from leukocytes, increasing the temperature of the nucleus.

Chronic inflammation

With a longer duration of action, it is likely to destroy much more tissue.

The cause of inflammation can be classified as follows:-

- **Microbes, e.g**. bacteria, viruses, protozoa, fungi.
- **Physical agent,** such as head, cold, mechanical damage, ultraviolet and ionizing radiation.
- **Chemical agents**

Organic for example:- Toxic microbial, organic poison.

Inorganic, for example:- Acids, alkalis**.**

Analgesia (illness) is an unspecified and unpleasant sensation usually raised by external or internal stimulus stimuli. The medicine, which changes the sensitivity of the pain, eliminates pain, is called painkillers or analgesics. The emergence of better $NSAID_S$ continues with the possible details of the perfect anti-inflammatory agents, coxibs, in continuous treatment. The synthetic procedures mainly based upon structure modification to found a molecule, which has improved safety profile. Among the derivatives of aryl propionic acid, there is a huge quantity of compounds, which display anti-inflammatory activity. Aryl propionic acid

derivatives are under the category of synthetic compounds with a wide variety of pharmacological activities in the accumulation with anti-inflammatory activity such as antimicrobial, analgesic, hypoglycaemic, anticancer, anticonvulsant, etc. In our attempt to find out more effective and safer agents for the dealing of inflammatory conditions, we report the synthesis, spectral characterization (IR, 1 HNMR, and Mass spectra) and pharmacological evaluation of a series of β, β -diphenyl propionic acid derivatives. The reaction scheme is presented in Fig. 1-2.

MATERIALS AND METHOD

All chemicals are purchased at CDH (Central Drug House Pvt. Ltd, New Delhi, India) and used for the reaction. Solvents are dry and cleaned by standard methods. All solvents and anhydrous solution are sprayed for at least 12 hours, which are dried in the oven. And put in dehydrating notes with KOH. The melting points of the prepared compounds, as well as the intermediate ones, are determined and corrected by the by open capillary methods. The reactions are controlled by thin layer chromatography (TLC) with coated silica gel plates. Iodine vapor for spot detection. The IR spectrum of designing compounds has been captured on the bromide discs of the spectrum in the FT-IR spectrophotometer (MODEL 8300, SHIMADZU Co). The 1HNMR spectra were recorded in the $CDCl_3$ solvent on an NMR spectrophotometer (Broker Joel, 300MHz) and TMS was used as an internal standard. The precise molecular mass of synthesized compounds was recorded in a mass spectrophotometer (MODEL WATERS, Q-TOF MICROMASS). The elementary analysis is executed on the element analyzer (Carlo Erba-1108) and the values are lies in appropriate limit of the calculated values. The spectroscopic characterization was done at Punjab University, Chandigarh, India.

Synthesis procedure of β, β -diphenyl propionyl chloride

A mixture of *β,β*-diphenyl propionic acid (0.01 mole) and thionyl chloride (0.05 mole) was heated in a water bath in reflux for 8 hours and excess thionyl chloride is removed under reduced pressure to reduce *β, β*-diphenylpropanoyl chloride. The product is recrystallized from ethanol. Reaction Scheme of Synthesis of *β,β* -diphenyl propionyl chloride are presented in figure 1.

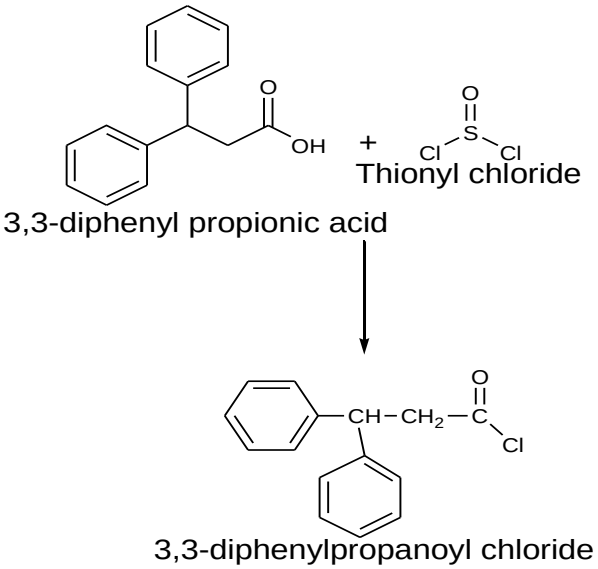


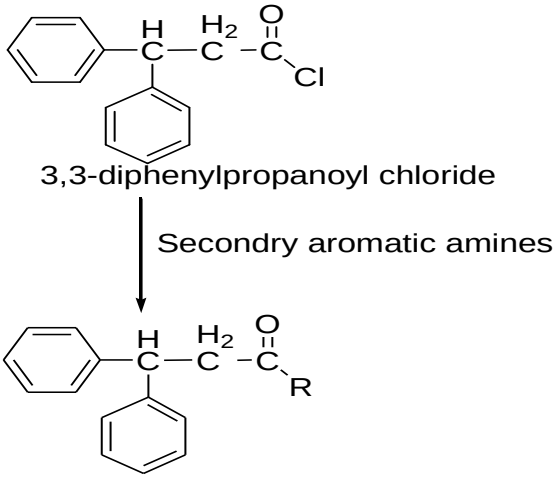
Fig. 1: Reaction Scheme of Synthesis of *β,β* -diphenyl propionyl chloride.

β, β -diphenylpropanoyl chloride interpretation

1H-NMR (400 MHz, CDCl3) δ (ppm): 7.15-7.32 (10 H, Aro.); 4.42-4.46 (1H, CH); 3.48-3.38 (2H, CH2) **IR (KBr) cm-1:** 1590.9 (C-C Str. Aro.); 1453 (C=C Str. Aro.); 3028.3 (C-H Str. Aro.); 706.2 (C-H ben. Aro.); 925.6 (C-C Str. Alk.); 491.12 (C-C ben. Alk.); 1451.5 (C-H ben. Alk.); 1270.9 (C-H ben. methylene); 1622 (C=O str.); 694.2 (C-Cl Str.) **MS:** m/z 246.21 (M+).

General method to the Synthesis of different derivatives (AK-1 to AK-5)

0.02 moles of β, β -diphenyl propionyl chloride was fused in 150 ml of acetone to 250 ml of RBF, and 0.04 ml K_2CO_3 anhydrous were added and kept at reflux for 1 hour. After the addition of 0.02 Mol of secondary aromatic amines [diphenylamine (PK1), Ethylpiprazine (PK2), morphine (PK3), Piprazine (PK4), Pyrrolidine (PK5)]. The reaction mixture was reflux for 8 hours with a magnetic stirrer there is a mobilization Continuous. Excess solvent is removed and the final residue is washed with water and dried. Ethanol is used for crystallization. The results of physical, analytical data and elementary analysis of the synthetic product are shown in table 4. Reaction scheme to Synthesize of different derivatives (PK-1 to PK-5) are presented on figure 2.



General structure of final compounds

Where,

R= Diphenylamine (PK1), Ethyl Piprazine (PK2), Morpholine (PK3), Piprazine (PK4), Pyrrolidine (PK5)

Fig. 2: Reaction scheme to Synthesize of different derivatives (PK-1 to PK-5).

Interpretation of different Derivatives (PK-1 to PK-5)

β,β -diphenyl-1-(piprazin-1-yl)propan-1-one (PK-1)

1H-NMR (400 MHz, CDCl3) δ (ppm): 7.14-7.37 (10H, Aro.); 4.41-4.45 (1H, CH); 2.82-3.00 (2H, CH2); 1.91-3.46 (9H, Piprazine) **IR (KBr) cm-1:** 1574.31 (C-C Str. Aro.); 1410.39 (C=C str. Aro.); 3026.57 (C-H Str. Aro.); 702.68 (C-H ben. Aro.); 891.58 (C-C Str. Alk.); 476.78 (C-C ben. Alk.); 1409.7 (C-H ben. Alk.); 1280.50 (C-H ben. methylene); 1662.82 (C=O str.); 760.63 (C-N Str.) **MS:** m/z 295.01 (M+).

1-(4-ethylpiprazin-1-yl)- β, β -diphenylpropan-1-one (PK-2)

1H-NMR (400 MHz, CDCl3) δ (ppm): 6.9-7.19 (10H, Aro.); 4.41-4.48 (1H, CH); 2.81 (2H, CH2); 2.50-3.29 (8H, Piprazine); 0.8-1.39 (5H, C2H5) **IR (KBr) cm-1:** 1574.90 (C-C str. Aro.); 1433.91 (C=C str. Aro.); 3035.67 (C-H str. Aro.); 701.95 (C-H ben. Aro.); 892.68 (C-C str. Alk.); 476.69 (C-C ben. Alk.); 14031.3 (CH ben. Alk.); 1162.83 (C-H ben. methylene); 1667.70 (C=O str.); 751.96 (C-N Str.) **MS:** m/z 323.28 (M+).

1-morpholino- β, β -diphenylpropan-1-one (PK-3)

1H-NMR (400 MHz, CDCl3) δ (ppm): 6.90-7.31 (10H, Aro.); 4.40 (1H, CH); 3.09 (2H, CH2); 2.7-3.0 (8H, Morpholine) **IR (KBr) cm-1:** 1556.15 (C-C str. Aro.); 1494.14 (C=C str. Aro.); 3026.96 (C-H str. Aro.); 701.38(C-H ben. Aro.); 854.56(C-C str. Alk.); 475.53(C-C

ben. Alk.); 1432.20 (C-H ben. Alk.); 1277.92(C-H ben. methylene); 1661.38(C=O str.); 752.96(C-N str.) **MS:** m/z 298 (M+).

β, β -diphenyl-1-(pyrrolidin-1-yl)propan-1-one (PK-4)

1H-NMR (400 MHz, CDCl3) δ (ppm): 6.81-7.33 (10H, Aro.); 4.39-4.45 (1H, CH); 3.01-3.13 (2H, CH2); 1.81-2.00 (8H, pyrolidine) **IR (KBr) cm-1:** 1584.90 (C-C str. Aro.); 1435.91 (C=C str. Aro.); 3038.50 (C-H str. Aro.); 707.84 (C-H ben. Aro.); 893.68 (C-C str. Alk.); 478.79 (C-C ben. Alk.); 14035.70 (C-H ben. Alk.); 1164.90 (C-H ben. methylene); 1669.92 (C=O str.); 751.87 (C-N Str.) **MS:** m/z 282.29 (M+).

N, N, β, β -tetraphenylpropanamide (PK-5)

1H-NMR (400 MHz, CDCl3) δ (ppm): 6.92-7.30 (19H, Aro.); 4.21-4.43 (1H, CH); 2.86-3.11 (2H, CH2) **IR (KBr) cm-1:** 1593.34 (C-C str. Aro.); 1451.24 (C=C str. Aro.); 3028.38 (C-H str. Aro.); 702.38 (C-H ben. Aro.); 882.39 (C-C str. Alk.); 475.69 (C-C ben. Alk.); 1451.18 (C-H ben. Alk.); 1244.49 (C-H ben. methylene); 1664.39 (C=O str.); 747.44 (C-N Str.) **MS:** m/z 379.09 (M+).

Pharmacological Evaluation

Investigational Animals

Pharmacological activity was evaluated using Albino rats (male/female) in a range of 150 to 250g. Albino Wistar Rats was found at the Institutional Animal home on IFTM University Moradabad, India. These animals have been preserved in acrylic road cages and are generally in laboratory conditions (temp. 25 + 2)°C, relative humidity of 50 to 5%, maintenance of dark and light cycles (12/12 hours). Animals are patting for freshwater particles and a normal diet libitum. All animals adapt to laboratory conditions within a week before the experiment begins. All experimental methods and protocols described in this study must be considered and approved by CPCSEA (The Committee for the Purpose of Control and Supervision of Experiments on Animals).

Preparation of Test Compounds

Examination samples and references are set up as a suspension to 1% of Tween 80. A group (control) has taken with 0.1 ml of tween 80 suspensions for oral administration. The second (standard) group is treated with Diclofenac sodium suspension at a dose of 50 mg/kg. The test group was given a dose of 150 mg / kg of synthesize compound.

Examination of acute toxicity study

The Examination acute toxicity study was conducted in accordance with OECD guidelines for the selection of test compounds for approval by the Ethics Commission.[17] The animals are divided into seven groups of 6 animals per group (n=6). On the day of biological evaluation, the test compounds were administered to animals (Oral) at different doses of 10, 20, 100, 200 and 1000 mg/kg body weight (b.w). The animals were monitored for 3 hours to confirm any regular animal reaction, neurological and autonomic behavior. The test lasts 24 hours in an interval of 30 minutes or until death. Findings from the toxicity study showed that animals were safely found at the highest dose of 1000 mg/kg body weight. In general, there are a small number of changes that have arisen in response to behaviors such as sensitivity, alertness and discomfort. Therefore, 1/10 the highest tolerated dose, i.e. 100 mg/k b.w. was selected for the study.

Evaluation of the analgesic activity

Evaluation of analgesic activity with Eddy's Hot Plate method

All synthesized compounds (PK-1 to PK-5) were analyzed to determine analgesic activity using Eddy's hot plate method. The animals are divided into seven groups with 6 animals per group for each dose (n=6). In this process hot plate method is used and is composed of an electrically heated surface, used in the current study. In this method temperature 55-56°C was maintained. Experimental animals are placed on a hot plate and time until their jump, are recorded by stopwatch. Observation is made before and after 0, 30, 60 and 90 minutes after a standard oral or subcutaneous examination (sc) or test samples.[18,19]

There are seven groups which consist of six animals in each group are as follow:

Served as control considered in group-1

Diclofenac sodium 50 mg/kg is used as standard in group-2

(PK-1) 100mg/kg is used as suspension of test compound in group-3

(PK-2) 100mg/kg is used as suspension of test compound in group-4

(PK-3) 100mg/kg is used as suspension of test compound in group-5

(PK-4) 100mg/kg is used as suspension of test compound in group-6

(PK-5) 100mg/kg is used as suspension of test compound in group-7

Table 1 and figure 3 shows analgesic response by using the Hot Plate method.

Table 1: Hot Plate method is used for Analgesic response.

Treatment Group	Animal dose/body weight (mg/kg	Analgesic percentage response by hot plate method Mean time in min. SEM			
		30 min.	60 min.	90 min.	180 min.
Control	5 mg/kg	3.20±0.11	3.54±0.10	3.10±0.11	3.13±0.14
Diclofenac	50 mg/kg	43.61±2.42**	67.32±4.96**	83.70±5.00**	33.32±7.57**
AK-1	100 mg/kg	5.4±1.71	4.72±0.12	17.30±2.10	16.01±6.21
AK-2	100 mg/kg	22.72±0.20*	30.02±1.11*	27.44±10.10*	24.97±6.72*
AK-3	100 mg/kg	32.92±10.3*	61.74±12.10*	75.51±10.00*	50.70±10.76*
AK-4	100 mg/kg	14.72±7.41*	37.30±6.90ns	33.40±6.69**	20.37±8.44ns
AK-5	100 mg/kg	38.43±5.46***	65.98±4.99***	76.40±7.86***	39.83±8.76**

Expressed values are as mean ± SEM. n=6;*P< 0.05, **P<0.01 and ***P<0.001 measured as significant. Bonferroni Post Test is used in Two-way ANOVA.

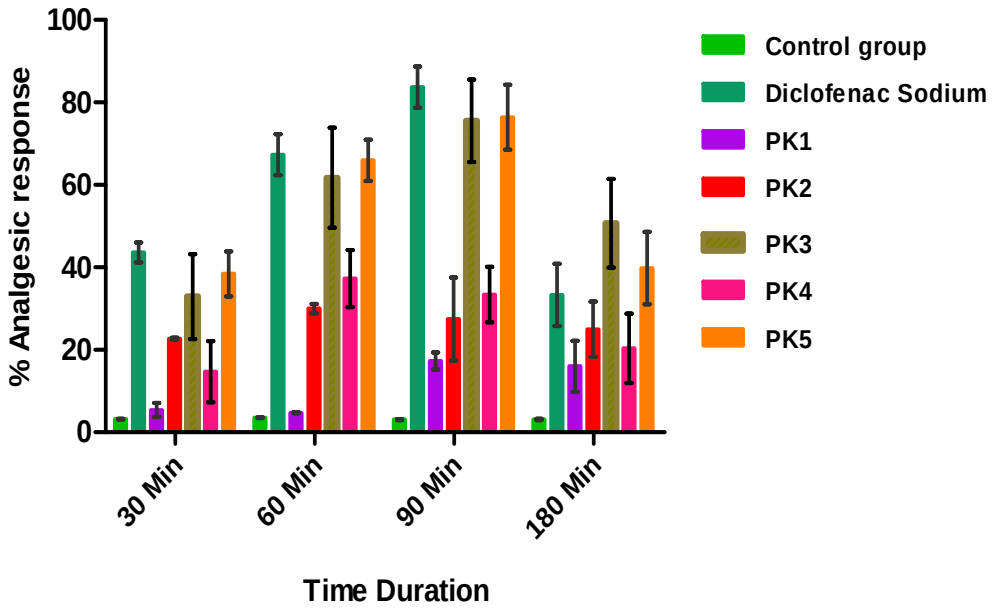


Fig. 3: Analgesic percentage response by Hot Plate Method.

Tail Flick Test Method

All compounds are also evaluated using a tail flick method for analgesic activity. Animals of either sex, with a weighting of between 150-200 gm were selected for study. The animals were divided into seven groups with 6 animals per group for each dose (n=6). The hot water was used in the tail flick method. The water was kept at a temperature of 55-56°C and the tail of the mouse up to two cm was submerged in hot water. The procedure was used to note the response time, which is known at the time it takes for the laboratory animal to deflect its tails in unfavorable situations. Discarded reading was first. Reaction time was recorded as the average of three consecutive values. The latent period of the rapid tail response was recorded

and considered an analgesia index and reached before and 30, 60 and 90 minutes after administration of the medicinal product. The maximum possible analgesia (MPA) was calculated.[20,21] The animals were divided into seven groups with 6 animals per group for each dose (n=6) are as follows.

Served as control considered in group-1

Diclofenac sodium 50 mg/kg is used as standard in group-2

(PK-1) 100mg/kg is used as suspension of test compound in group-3

(PK-2) 100mg/kg is used as suspension of test compound in group-4

(PK-3) 100mg/kg is used as suspension of test compound in group-5

(PK-4) 100mg/kg is used as suspension of test compound in group-6

(PK-5) 100mg/kg is used as suspension of test compound in group-7

Table 2 and figure 4 shows analgesic response by using the tail flick method.

Table 2: Analgesic percentage response by tail flick method.

Treatment groups	Dose /body weight(mg/kg)	Analgesic percentage response by tail flick methods Reaction time in sec. SEM			
		0 min	15min	30 min	45 min
Control	5 ml/kg	3.17±0.74	3.82±0.32	4.69±0.39	4.49±0.09
Diclofenac	25 mg/kg	6.99±3.38***	10.40±0.92***	11.07±2.09***	12.38±1.12***
AK-1	100 mg/kg	3.02±1.20ns	3.31±1.69 ns	5.40±1.39 ns	4.40±1.95 ns
AK-2	100 mg/kg	3.68±4.69 ns	4.00±3.10 ns	4.95±1.32 ns	4.89±1.93 ns
AK-3	100 mg/kg	4.98±2.29*	8.81±.139**	9.30±2.11**	10.11±1.42**
AK-4	100 mg/kg	3.00±0.16 ns	3.89±1.40 ns	4.81±0.81 ns	5.16±1.70 ns
AK-5	100 mg/kg	5.92±1.40**	8.79±0.99**	9.53±1.00**	10.42±0.95**

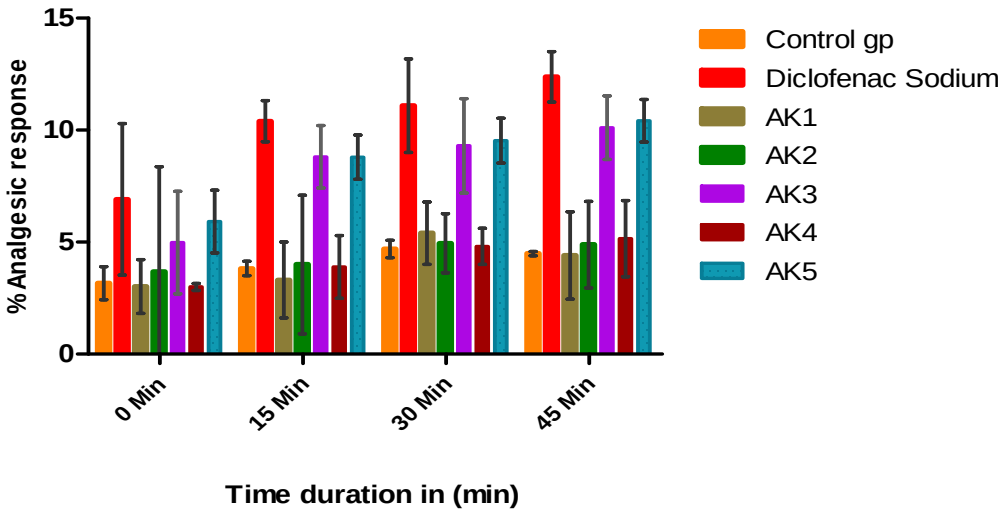


Fig. 4: Analgesic response by tail flick method.

Evaluation of Anti-inflammatory Activity

Carrageenan Induced Rat Paw Edema Method

The use of Carrageenan-induced rat leg edema method to check the anti-inflammatory effects of new synthesized compounds (AK-1 to AK-5). The animals were divided into seven groups with 6 animals per group for each dose (n=6) are as follows:

Served as control considered in group-1

Indomethacin 25 mg/kg is used as standard in group-2

(PK-1) 100mg/kg is used as suspension of test compound in group-3

(PK-2) 100mg/kg is used as suspension of test compound in group-4

(PK-3) 100mg/kg is used as suspension of test compound in group-5

(PK-4) 100mg/kg is used as suspension of test compound in group-6

(PK-5) 100mg/kg is used as suspension of test compound in group-7

Indomethacin (25 mg/kg body weight) is used as a standard drug. After 1 hour of oral administration of test compounds in a group of 3 to 7 animals and Indomethacin in groups of 2 animals was found to be acute inflammation. After 1 hour of oral management of the drug, inflammation was caused by the preparation of the Carrageenan water suspension (1% w/v, 0.1 ml), which is injected into the right hind legs in the sub planter of each rat area. Using the marker, the sign of identity was made with the right foot in malleolus to make undemanding testimonies. The strength of the paw of rats is calculated in plethysmometrically after 30, 60, 90 and 120 minutes after Carrageenan injection. The % inhibition is calculated for given formula:

$$\% \text{ Inhibition} = 1 - \frac{Vt}{Vc} \times 100$$

Where, Vt and Vc indicate the average change in the volume of feet of rats (treatment and control) respectively. The findings of the rat paw edema method caused by Carrageenan are presented in table 3 and figure 5.[22]

Table 3: Anti-inflammatory effect of synthesized compounds using Carrageenan induced paw edema method.

Treatment	Initial Paw volume	Paw volume after induction						% inhibition
		1 hr	2 hr	3 hr	4 hr	5 hr	6 hr	
Control	1.20±0.14	1.20±0.13	1.20±0.13	1.20±0.13	1.20±0.13	1.20±0.13	1.20±0.13	--
Indomethacin (25mg/kg)	1.07±0.07	2.10±0.22**	1.55±0.14**	1.45±0.21**	1.31±0.17*	1.20±0.11**	1.10±0.15*	55.18
AK-1 (100mg/kg)	1.17±0.14	1.39±0.1 7ns	1.90±0.11 ns	1.87±0.17 ns	1.84±0.21 ns	1.77±0.18 ns	2.12±0.42 ns	69.9
AK-2 (100mg/kg)	1.14±0.08	1.35±0.21 ns	1.40±0.13 ns	1.38±0.07*	1.38±0.11 ns	1.38±0.05 ns	1.63±0.11 ns	94.6
AK-3 (100mg/kg)	1.23±0.11	1.38±0.17 ns	1.87±0.22 ns	1.89±0.41 ns	1.91±0.31 ns	2.11±0.03 ns	1.24±0.05*	46.26
AK-4 (100mg/kg)	1.01±0.04	1.41±0.11 ns	1.71±0.20 ns	1.51±0.22 ns	1.39±0.17 ns	1.31±0.13*	2.14±0.14 ns	94.5
AK-5 (100mg/kg)	1.21±0.13 ns	2.10±0.22 ns	1.55±0.14 ns	1.45±0.21*	1.31±0.17**	1.20±0.11**	1.28±0.17 ns	97.19

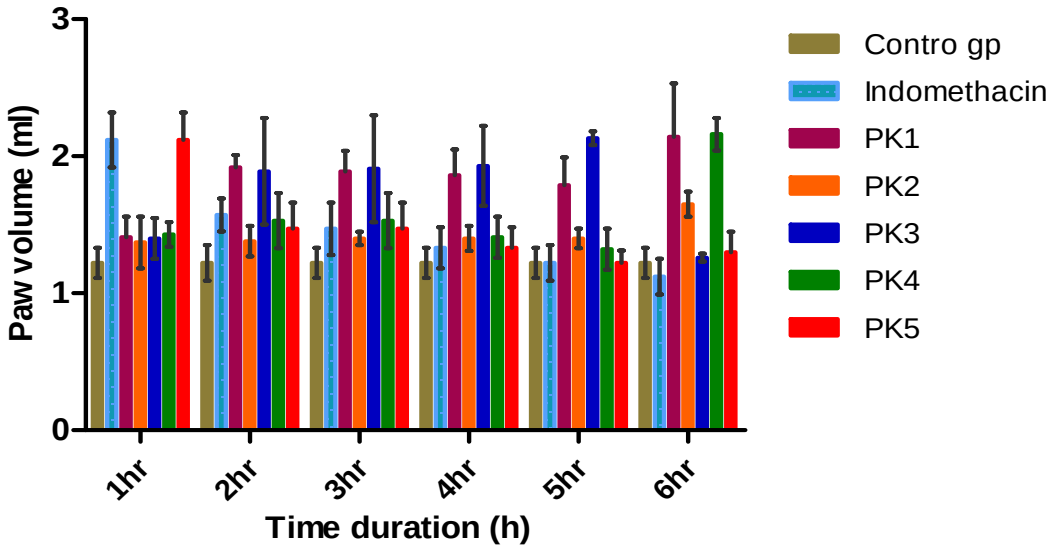


Fig. 5: Anti-inflammatory effects of synthesized compounds by using Carrageenan induced paw edema method.

RESULT AND DISCUSSION

The results of physical, analytical data and elementary analysis of the synthetic product are shown in table 4. A number of titles derived from diphenyl propionic acid (PK-1 to PK-5) were synthesized according to the fig. 1. The structure of newly synthesized compounds was confirmed by spectral data (IR, 1H NMR, mass spectroscopy and elemental analysis). All PK-1 to PK-5 synthesized compounds are subject to a toxicity study initially in accordance with OECD guidelines. After a toxicity test, the animals were found safe with a higher dose of 1000 mg/kg body weight. Unauthorized changes are found in behavioral responses, such as pressure, alertness, and insecurity. For this reason, 1/10 is the maximum allowable dose (100 mg/kg), which is considered a therapeutic dose.[23] The analgesic activity is carried out

by the technique of the hot plate and tail flick method. Use Diclofenac sodium as a standard of reference. The analgesic activity of the synthesized compounds PK-3 and PK-5 showed significant responses (Tables 2 and 3). Many researchers have worked on determining anti-inflammatory activity using the Carrageenan-induced edema method in the Wistar albino rat using the random sampling method and using Indomethacin (20 mg/kg) as a general standard drug.[24,26] Anti-inflammatory activity is estimated by the Carrageenan induced rat paw edema method. Indomethacin is used as standard drug. AK-5 shows the most sensitive and most potent anti-inflammatory response in all assay analyzes (Table 4). A study on alpha-(pthenoylphenyl)-propionic acid, it has been shown that the compound has anti-inflammatory, analgesic and antipyretic activities.[27]

The largest groups of non-narcotic analgesics. Are the arylalkanoic acid derivatives, comprising derivatives of aryl acetic acid, heteraryl acetic acid, indole acetic acid and especially propionic acid. Common attribute among all of these compounds is that they causes inhibition of prostaglandin biosynthesis, which contributes to their analgesic and other pharmacological properties as well as to their principal side effect, gastrointestinal irritation.[28] Apart from analgesics and anti-inflammatory effects, propionic acid derivatives are being studied for double-blind comparison ibuprofen and a fenamate (Mefenamic acid) in the treatment of dysmenorrheal also and the findings suggested no clinical difference between a propionic acid derivative such as ibuprofen and a fenamate such as Mefenamic acid in the treatment of dysmenorrheal.[29] As the synthesized compounds exhibited analgesic and anti-inflammatory activity, prostaglandin inhibition may be the chief reason behind its potent action.

CONCLUSION

The readings discovered the information that prepared compounds PK-3 (Morpholine derivative) and PK5 (diphenylamine derivative) are potent analgesic and anti-inflammatory compounds. The results indicate that arylpropionic acid products have excellent potential for further development as beneficial analgesics and anti-inflammatory agents. Further experiments were required to explain their mechanism of action.

ACKNOWLEDGEMENTS

Authors are thankful to Dr. Arun Kumar Mishra, IFTM University, Moradabad and Dr. Pradeep Kumar, Shri Gopichand College of Pharmacy, Bagpat (U.P.) for motivation and facilities provided to conduct this work.

CONFLICT OF INTEREST

The authors declare no conflict of interest or otherwise.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Institutional Animal Ethics Committee approved the protocols before start of the experiment.

HUMAN AND ANIMAL RIGHTS

All the laboratory animals based experimental procedures and protocols described in this study were reviewed and approved by the Institutional Animal Ethics Committee (Reg. No. 837/PO/Re/S/04/CPCSEA).

REFERENCES

1. Sosa S, Balicet MJ, Arvigo R, Esposito RG, Pizza C, Altinier GA. Screening of the topical anti-inflammatory activity of Some Central American plants. J. Ethanopharmacol, 2002; 8: 211-215.
2. Hossain MS, Alam MB, Chowdhury NS, Asadujjaman M, Zahan R, Islam MM, Mazumder MEH, Haque ME, Islam A. Antioxidant, analgesic and anti-inflammatory activities of the herb Eclipta prostrata. J. Pharmacol. Toxicol, 2011; 6(5): 468-480.
3. Mishra D, Ghosh G, Kumar PS, Panda, P.K. An experimental study of analgesic activity of selective cox-2 inhibitor with conventional nsaids. Asian J. Pharm. Clin. Res., 2011; 4(1): 78-81.
4. Pilotto A, Franceschi M, Leandro G, Paris F, Niro V, Longo MG, Dambrosio LP, Andriulli A, Mario FD. The risk of upper gastrointestinal bleeding in elderly users of aspirin and other non-steroidal anti-inflammatory drugs: the role of gastroprotective drugs. Aging Clin. Exp. Res., 2003; 15(6): 494-499.
5. Conforti F, Sosa S, Marrelli M, Menichini F, Statti GA, Uzunov D, Tubaro A, Menichini F. The protective ability of Mediterranean dietary plants against the oxidative damage: The role of radical oxygen species in inflammation and the polyphenol, flavonoid and sterol contents. Food Chem., 2009; 112(3): 587-594.
6. Robert A. Antisecretory, antiulcer, cytoprotective and diarrheogenic properties of prostaglandins. Adv. Prostaglan. Thromboxane Res., 1976, 2: 507-520.
7. Verrico MM, Weber RJ, Mc Kaveney TP, Ansani NT, Towers AL. Adverse drug events involving COX-2 inhibitors. Ann. Pharmacother, 2003; 37(9): 1203-1213.

8. Semwal A. A novel, -diphenyl propionic acid amide derivatives showing anti-inflammatory and anticonvulsant activity. Int. J. Med. Sci. Clin. Invent, 2014; 1: 15-24.
9. Rayam P, Anireddy JS, Polkam N, Allaka TR, Chepuri K, Nadendla M. Synthesis and biological activity of novel acyl hydrazone derivatives of 3-(4,5-diphenyl- 1,3-oxazol-2-yl) propanoic acid as anticancer, analgesic and anti-inflammatory agents. J. Pharm. Res., 2015; 9(2): 157-164.
10. Dilber SP, Dobric SL, Juranic ZD, Markovic BD, Vladimirov SM, Juranic IO. Docking studies and anti-inflammatory activity of -hydroxy--arylpropanoic acids. Molecules, 2008; 13: 603-615.
11. Vasincu I, Apotrosoae, M, cu D, Profire L. New derivatives of arylpropionic acid. Synthesis and biological evaluation. Rev. Med. Chir. Soc. Med. Nat. Iasi., 2013; 117(2): 532-537.
12. Husain A, Ajmal M. Synthesis of novel 1, 3, 4-oxadiazole derivatives and their biological properties. Acta Pharm, 2009; 59: 223-233.
13. Husain A, Ahuja P, Sarafroz. Synthesis and biological evaluation of aroylpropionic acid based 1,3,4-oxadiazoles. Ind. J. Pharm. Sci., 2009; 71(1): 62-66.
14. Wolff HP, Kühnle HF. Synthesis and hypoglycemic activity of N-alkylated hydrazonopropionic acids. J. Med. Chem., 1985; 28(10): 1436-1440.
15. Sharma SV. Synthesis and anticancer activity of some L-cystine derivatives. Ind. J. Phar. Sci., 2002; 64(3): 200-204.
16. Asif M, Singh A, Bilkanti L. In-vivo anticonvulsant and in-vitro antitubercular activity of methyl indole derivative of some 6-aryl-4, 5-Dihydropyridazin-3(2H)-ones and their expected anticonvulsant mechanisms. Iran. J. Pharm. Sci., 2013; 9(1): 67-80.
17. OCED/OCDC. OECD guidelines for testing of chemicals. Revised draft guidelines 423, acute oral toxicity class method, October 2000.
18. Ghule BV, Ghante M. Analgesic, anti-inflammatory activity of Lagenaria siceraria Stand. Pharmacogn. Mag., 2006; 2(8): 232-236.
19. Yutaka K, Motoharu K, Yasunori, Akira, David BB, KenIchiro I, Masataka K, Ryoji Y, Timothy H, Hajime S. 15deoxy-D12,14-PGJ2 induces synoviocyte apoptosisand suppresses adjuvant-induced arthritis in rats. J. Clin. Inv., 2000; 106: 189-197.
20. Vaghasiya RG, Banerjee A, Shrivastava N. Analgesic activity of hydro-alcoholic extract of Morus alba Linn. Ind. Drugs, 2007; 44(5): 364-368.
21. Jaiswal SR, Sontakke SD. Experimental evaluation of analgesic and anti-inflammatory activity of simvastatin and atorvastatin. Indian J. Pharmacol, 2012; 44(4): 475-479.

22. Alam MM, Shaharyar M, Hamid H, Nazreen S, Haider S, Alam MS. Synthesis of novel 8-hydroxy quinolin based 1,3,4oxadiazoles and S-substituted 1,2,4-triazole derivatives and evaluation of their anti-inflammatory, analgesic, ulcerogenic and antimicrobial activities. Med. Chem., 2016; 7: 663-673.
23. OCED/OCDC and OECD, Guidelines for testing of chemicals. Revised draft guidelines 423, acute oral toxicity class method, revised document, 2000.
24. Charles Dorni AI, Vidyalaxmi KS, Hannah RV, Dubey GP. Anti-inflammatory activity of Plumbago capensis. Pharmacogn. Mag., 2006; 2(8): 239-242.
25. Adeyemi OO, Okpo SO, Ogunti OO. Analgesic and anti-inflammatory effects of the aqueous extract of leaves of Persea americana Mill (Lauraceae). Fitoterapia, 2002; 73(5): 375-380.
26. Winter CA, Risley EA, Nuss GW. Carrageenan induced edema in hind paw of rat as assay for anti-inflammatory drugs. Proc. Soc. Exp. Biol. Med., 1962; 111: 544-547.
27. Fujimura H, Tsurumi K, Hasegawa J, Yanagihara M, Hiramatsu Y, Maekawa K. Anti-inflammatory, analgesic and antipyretic activities of alpha-(p-thenoylphenyl)-propionic acid (TN762). Nihon Yakurigaku Zasshi, 1982; 79(3): 123-136.
28. Brogden RN. Non-steroidal anti-inflammatory analgesics other than Salycilates. Drugs, 1986; 32(4): 27-45.
29. Roy S. A double-blind comparison of a propionic acid derivative (ibuprofen) and a fenamate (mefenamic acid) in the treatment of dysmenorrhea. Obstet. Gynecol, 1983; 61(5): 628-632.