ISSN 1996-5052

Current Research in Chemistry

Knowledgia SCIENTIFIC
A Place to Publish Outstanding Research

http://knowledgiascientific.com

Current Research in Chemistry 4 (4): 99-109, 2012
ISSN 1996-5052 / DOI: 10.3923/crc.2012.99.109

Synthesis of 2,4,5-Triphenylimidazoles Novel Mannich Bases as Potential Antiinflammatory and Analgesic Agents

[1]Rashmi Arora, [1]N.S. Gill, [1]Ramit Kapoor, [1]Amit Aggarwal and [2]A.C. Rana
[1]Department of Pharmaceutical Chemistry, [2]Department of Pharmacology, Rayat Institute of Pharmacy, Railmajra-144533, Punjab, India

Corresponding Author: Rashmi Arora, Department of Pharmaceutical Chemistry, Rayat Institute of Pharmacy, Railmajra-144533, Punjab, India

ABSTRACT

The 2,4,5-triphenylimidazole was synthesized by refluxing benzoin, benzaldehyde and ammonium acetate in equimolar quantities. The Mannich bases were synthesized by using abstractable hydrogen present in 2,4,5-triphenylimidazole because various drugs obtained from Mannich reaction have proved more effective and less toxic than their parent drugs. Various Mannich Bases of 2,4,5-triphenylimidazole i.e., 5(a); 5-((2,4,5-triphenyl-1H-imidazol-1-yl)methyl)-1H-benzo[d]imidazole,5(b);5-((2,4,5-triphenyl-1H-imidazol-1-yl)methyl)-1H-benzo[d][1,2,3]triazole, 5(c); 3-(2,4,5-triphenyl-1H-imidazol-1-yl) methyl)morpholine, 5(d); N,N-dimethy l(2,4,5-triphenyl-1H-imidazol-1-yl)methanamine, 5(e); N-ethyl-N-((2,4,5-triphenyl-1H-imidazol-1-yl)methyl) ethanamine, were synthesized with yield of 61.4, 66.7, 78, 75.2, 73%, respectively. Synthesized compounds were evaluated for analgesic and antiinflammatory activities. Compound 5(a), 5(c) and 5(d) showed maximum percentage inhibition of paw edema i.e., 51.19, 52.8 and 50%, respectively, as compare to standard drug diclofenac sodium, at dose of 200 mg kg^{-1}. Compound 5(c) and 5(d) showed maximum analgesic activity with lapse time of 6.94±0.15 and 6.99±0.22°C, respectively. All the synthesized compounds were characterized on the basis of their elemental analysis, IR and ^{1}HNMR spectroscopic data. All the tested compounds have shown moderate to good antiinflammatory activity by carrageenan-induced rat paw edema method as well as analgesic activity on Eddy's hot plate.

Key words: Triphenylimidazole, mannich reaction, benzotriazoles, antiinflammatory, analgesic

INTRODUCTION

Medicinal chemistry is concerned about the influence of various chemical structures on the activity leading to the formation of diverse heterocyclic compounds having wide range of biological activities (Shalini *et al*., 2010; Sandhar *et al*., 2012). Imidazole basically is a five member structure with nonadjacent two nitrogen elements, which determines its basicity and acidity (Fig. 1). It is amphoteric in nature (Yasodha *et al*., 2009; Kumar *et al*., 2011). Its molecular formula is $C_3H_4N_2$ (Bhatnagar *et al*., 2011). The simplest member is imidazole itself. Among the imidazole derivatives trisubstituted imidazoles basically 2,4,5-triphenylimidazole have found to possess maximum antiinflammatory activity (Amir *et al*., 2011) (Fig. 1).

The Mannich reaction usually occurs with secondary amines, a carbonyl compound accomplied with formaldehyde resulting in loss of water molecule to form a compound mainly known as

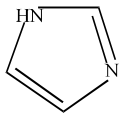

Fig. 1: Basic structure of imidazole

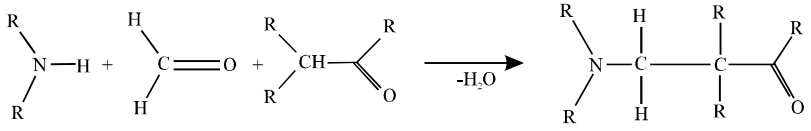

Fig. 2: Synthesis of mannich base

a mannich base (Manikpuri *et al.*, 2010; Sahoo *et al.*, 2006). Mannich Bases of various diverse compounds have shown to possess many pharmacological activities and also found themselves in various industrial uses like in polymers, lubricating oil and medicinal chemistry (Fig. 2).

Imidazoles are probably the most well known heterocycle which is common and important feature of a variety of natural products and medicinal agents. Derivatives of imidazole were reported for antiinflammatory (Fatimi *et al.*, 1994; Suzuki *et al.*, 1992), analgesic, anticonvulsant (Abiqnente *et al.*, 1981), tuberculostatic, antimicrobial and anticancer activities. Prompted by the broad spectrum activities of 2,4,5-triphenylimidazole derivatives, it was intended to synthesize various derivatives of 2,4,5-triphenyl-1-substituted imidazoles and to evaluate them for their antiinflammatory and analgesic activities.

MATERIALS AND METHODS

Chemicals: Carrageenan was obtained from HiMedia Labs, Mumbai. All other chemical reagents were used of analytical grade, which were procured from different companies (Loba Chem, Merck Limited and S D Fine). The progress of the reaction was monitored on readymade silica gel plates (Merck) using chloroform-methanol (1:1) as a solvent system. Iodine was used as a developing agent. Melting points were determined with a Buchi 530 melting point apparatus in open capillaries. IR spectra were recorded on KBr discs, using a Perkin-Elmer Model 1600 FT-IR spectrometer. The proton magnetic resonance spectra (^{1}H-NMR) were recorded on Perkin Elmer Spectrophotometer-300 MHz in DMSO-*d6* using TMS as an internal standard. Elemental analysis was performed by CHNS (O) analyzer.

Animals: The Wistar albino rats (150-200 g) of either sex were obtained from Zoin Co. Biologicals, near science market, Ambala. They were kept at standard laboratory diet, environmental temperature and humidity. A 12 h light and dark cycle was maintained throughout the experimental protocol.

Synthesis

Synthesis of 2,4,5-triphenylimidazole (4): Benzoin (1) (5 g, 0.023 M) was reacted with benzaldehyde (5 mL, 0.05 mol) (2) in presence of ammonia (3) and refluxed for 4 h and the resulting mixture was cooled, filtered to get 2,4,5-triphenylimidazole (4). The precipitate was filtered, dried and recrystallized from ethanol (Lunt *et al.*, 1987; Hoffman, 1953; Bredereck *et al.*, 1959).

General synthesis of mannich bases of 2,4,5-triphenylimidazoles (5a-5e): 2,4,5-triphenylimidazole (1) (2.5 g, 0.006 mol) was added in dimethyl formamide (2) (10 mL, 0.131 mol). Formaldehyde (2) (10 mL, 0.131 mol) was added drop wise. The mixture was subjected to stirring for 30 min to yield a methyl derivative. To the another beaker various secondary amines (5a-5e) (3) (2.5 g, 021 mol) was added in dimethyl formamide (2) (10 mL, 0.131 mol). The methyl derivative was transferred to secondary amines and was stirred for few minutes. The contents of the beaker were refluxed for 4 h, the reaction procedure was monitored over TLC. The precipitate was filtered, dried and recrystallized using (methanol:chloroform) (Table 1, Fig. 3).

Antiinflammatory activity

Carrageenan-induced rat paw edema: The carrageenan-induced rat paw edema assay was carried out according to Winter *et al.* (1962). Wistar rats were divided into 7 groups each consisting of 6 animals (Gill *et al.*, 2010):

- **Group I: Disease control:** Carrageenan (1%) was administered in the plantar surface of rat (p.o.)
- **Group II: Standard:** Suspension of Diclofenac sodium (10 mg kg^{-1}) in 1% Gum acacia (p.o.)+Carrageenan
- **Group III-VII: test:** Suspension of test compounds 5a to 5e respectively (200 mg kg^{-1}) in 1% Gum acacia (p.o.)+Carrageenan

Edema was induced on the left hind paw of the rats by subplantar injection of 0.1 mL of a solution of 1% (w/v) carrageenin in a 0.9% NaCl (w/v). The paw volume was measured at intervals of 60, 120, 180 min by the mercury displacement method using a plethysmograph after administration of the suspension of test compounds in 1% Gum acacia orally. The average paw edema volume of all the groups were calculated and compared with that of control. The percentage inhibition of paw edema in drug treated group was compared with the carrageenan control group and calculated according to the following equation:

$$\text{Inhibition of drug (\%)} = \frac{Vc - Vt}{Vc} \times 100$$

where, Vc is the inflammatory increase in paw volume of control group of animals and Vt is the inflammatory increase in paw volume of drug-treated animals.

Analgesic activity: Swiss albino mice of either sex were divided into 7 groups each consisting of 6 animals:

Table 1: Physicochemical parameters of some novel 2,4,5-triphenylimidazoles mannich bases (5a-5e)

Compound	X	Molecular formula	M.Wt. (g M^{-1})	Yield (%)	M.pt (°C)	Rf
5a	Benzimidazole	$C_{29}H_{22}N_4$	427.18	61.4	257-262	0.55
5b	Benzotriazole	$C_{28}H_{21}N_5$	427.18	66.7	273-275	0.57
5c	Morpholine	$C_{26}H_{25}N_5O$	395.5	78	247-250	0.60
5d	Dimethyl amine	$C_{24}H_{23}N_3$	353.5	75.2	251-255	0.61
5e	Diethyl amine	$C_{26}H_{27}N_3$	381.22	73.0	262-268	0.54

*M.Wt.: Molecular weight, M.pt: Melting point, Rf: Retention factor

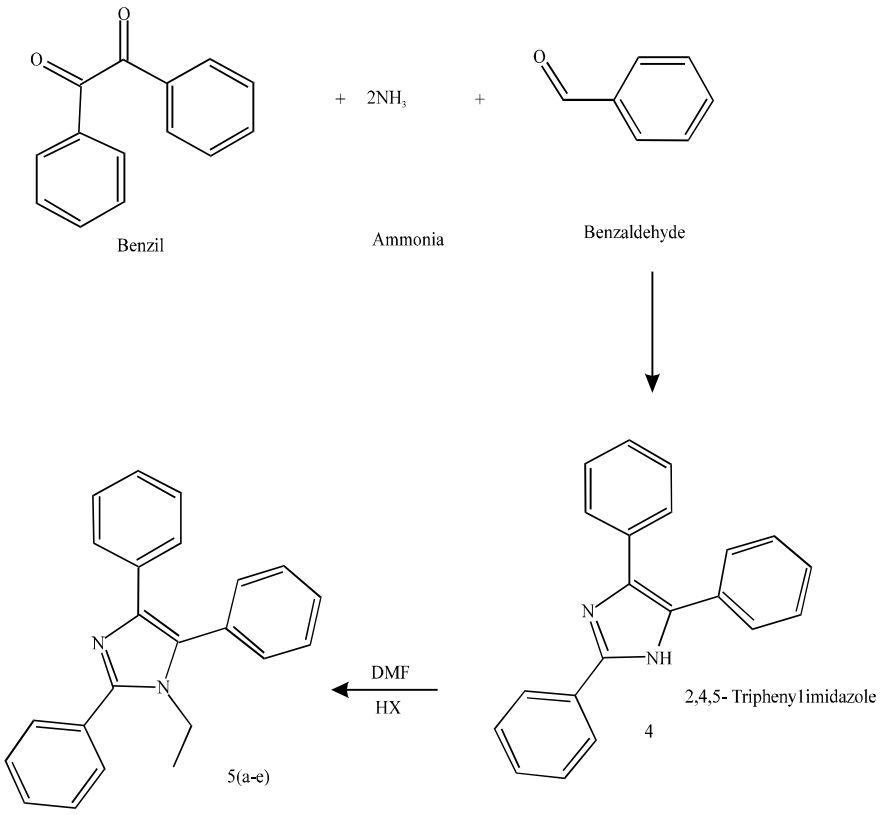

Fig. 3: Synthesis of some novel 2,4,5-triphenylimidazoles mannich bases (5a-5e)

- **Group I: Control:** 1% Gum acacia (p.o.)
- **Group II: Standard:** Suspension of Diclofenac sodium (10 mg kg^{-1}) in 1% Gum acacia (p.o.)
- **Group III-VII: Test:** Suspension of test compounds 5a to 5e respectively (200 mg kg^{-1}) in 1% Gum acacia (p.o.)

Eddy's hot plate method: The analgesic activity of the test compounds (5a-5e) were measured by hot-plate method. The rats were placed on a hot plate maintained at 55±0.5°C. The reaction time was taken as the interval from the instant animal reached the hot plate until the moment animal licked its feet or jumped out (Zakaria *et al.*, 2006; Franzotti *et al.*, 2001; Sahu *et al.*, 2012). The reaction time was recorded before and after 0, 30, 60 and 90 min following oral administration of tests compounds (5a-5e) and standard drug in the form 1% Gum acacia suspension. Following groups were made and latency period in which rat responded to hot plate was calculated.

Statistical analysis: All the results were expressed as Standard Error of Means (SEM). The data was statistically analyzed by one way Analysis of Variance (ANOVA) followed by Tukey using GraphPad Prism 5 Software. The p-value<0.05 was considered to be statistically significant.

RESULTS

The synthesis of various derivatives of 2,4,5-triphenylimidazole (5a ,b, c, d, 5e) were carried out. Characterization data of the synthesized compounds is given below and physical

Table 2: Antiinflammatory effect of some novel 2,4,5-triphenylimidazoles mannich bases on carrageenan induced paw edema (5a-5e)

		Mean paw volume (mL)			
Treatment groups	Dose (mg kg^{-1}) orally	60 min	120 min	180 min	Inhibition (%)
Control	-	0.73±0.009	0.78±0.007	0.84±0.006	-
Standard	10	0.54±0.01[a]	0.44±0.018[a]	0.34±0.009[a]	59.51
5a	200	0.61±0.009[a]	0.49±0.046[a]	0.41±0.008[a]	51.19
5b	200	0.60±0.005[a]	0.50±0.003[a]	0.48±0.006[a]	42.85
5c	200	0.58±0.048[a]	0.48±0.057[a]	0.40±0.023[a]	52.38
5d	200	0.59±0.035[c]	0.51±0.006[a]	0.42±0.005[a]	50.00
5e	200	0.62±0.015[b]	0.52±0.007[a]	0.45±0.006[a]	46.45

Values are Mean±SEM (n = 6), Each group was compared with control at [a]p<0.001, [b]p<0.01 and [c]p<0.05

Table 3: Analgesic activity of some novel 2,4,5-triphenylimidazoles mannich bases (5a-5e) on Eddy's hot plate

		Lapse time (sec)			
Groups	Dose (mg kg^{-1}) orally	0 min	30 min	60 min	90 min
Control	-	3.30±0.083	3.32±0.19	3.40±0.062	3.35±0.053
Standard	10	3.33±0.15	5.77±0.06[a]	7.45±0.12[a]	9.45±0.28[b]
5a	200	3.04±0.095	3.45±0.15	4.12±0.05[c]	6.03±0.18[b]
5b	200	3.10±0.069	3.51±0.21	4.18±0.09[c]	6.08±0.13[b]
5c	200	3.16±0.030	3.54±0.11	4.36±0.26[b]	6.94±0.15[c]
5d	200	3.27±0.083	3.55±0.11	4.41±0.19[b]	6.99±0.22[c]
5e	200	3.17±0.049	3.52±0.10	4.24±0.04[b]	6.08±0.09[b]

Values are Means±SEM (n = 6), Each group was compared with control at [a]p<0.001, [b]p<0.001 and [c]p<0.05

properties of compounds were given in Table 1. Biological activities like analgesics as well as antiinflammatory activity were performed on the newly synthesized compounds and their result (analgesic) were given in Table 3 and antiinflammatory was given in Table 2.

All the newly synthesized compounds 5-((2,4,5-triphenyl-1H-imidazol-1-yl)-1H imidazole derivatives was confirmed on the basis of spectroscopic data given below.

2,4,5-triphenylimidazole: The derivative was synthesized by reaction between ammonia, benzaldehyde and benzoin. The contents of the beaker were refluxed for 4 h, the reaction procedure was monitored over TLC. The precipitate was filtered, dried and recrystallized using (methanol: chloroform). The %age yield was found out to be 77%, m.p. 251-253°C and Rf 0.63. Further the compound was characterized by IR and ^{1}HNMR:

- **FTIR (cam^{-1}) :**1636 cm^{-1} (C = C), 1600 cm^{-1} (C = N), 1636 (N-H)
- **^{1}HNMR (DMSO-d6):**7.2-7.4(15H, m, Ar-H), 13.2 (1H, s, N-H)

5-((2,4,5-triphenyl-1H-imidazol-1-yl)methyl)-1H-benzo[d]imidazole (5a): The compound 5-((2,4,5-triphenyl-1H-imidazol-1-yl) methyl)-1H-benzo[d]imidazole (5a) was synthesized by adding 2,4,5-triphenylimidazole in Dimethyl formamide Formaldehyde was added drop wise. The mixture was subjected to stirring for 30 min to yield a methyl derivative. To the beaker Benzimidazole was added in Dimethyl formamide. The methyl derivative was transferred to secondary amines and was stirred for few minutes. The contents of the beaker were refluxed for

h, the reaction procedure was monitored over TLC. The precipitate was filtered, dried and recrystallized using (methanol: chloroform). The percentage yield was found out to be 61.4%, m.p. 257-262°C and Rf 0.55. Further the compound was characterized by IR and ^{1}HNMR:

- **FTIR (cam^{-1}):** 3432 (N-H), 1659 (C = C), 1600 (C = N), 1357 (C-N)
- **^{1}HNMR (DMSO-d6, δ ppm):** 5.3 (1H, s, N-H), 8.0901 (1H, s, C-H), 7.0-7.9 (15H, m, Ar-H), 5.11(2H, t, -CH = N-)
- **Elemental analysis:** $C_{30}H_{23}N_3$: C, 84.64%; H, 5.45%; N, 9.87%. Found: C, 84.65%; H, 5.7%; N, 9.7%

The compound was evaluated for analgesic as well as antiinflammatory activities. The compound was evaluated for antiinflammatory activity in albino rats by carrageenan induced rat paw edema method. The compound (5a) showed slightly less moderate activity in the range of 51.19% at a dose of 200 mg kg^{-1} at time interval of 3 h of carrageenan challenge when compared with standard Diclofenac sodium at the same time period exhibited 59.51% of activity respectively at a dose of 10 mg kg^{-1} (Table 2).

The analgesic activity of the synthesized compounds was evaluated in albino rats by Eddy's hot plate method. The compound (5a) showed maximum activity at a dose of 200 mg kg^{-1} in the range of 6.03±0.18b at 90 min when compared with standard drug Diclofenac sodium at a dose of 5 mg kg^{-1} in the range of 9.45±0.28 at 90 min (Table 3).

5-((2,4,5-triphenyl-1H-imidazol-1-yl)methyl)-1H-benzo[d][1,2,3]triazole (5b): The compound 5-((2,4,5-triphenyl-1H-imidazol-1-yl)methyl)-1H-benzo[d]imidazole (5b) was synthesized by adding 2,4,5-triphenylimidazole in Dimethyl formamide. Formaldehyde was added drop wise. The mixture was subjected to stirring for 30 min to yield a methyl derivative. To the other beaker Benzotriazole was added in dimethyl formamide. The methyl derivative was transferred to secondary amines and was stirred for few minutes. The contents of the beaker were refluxed for 4 h, the reaction procedure was monitored over TLC. The precipitate was filtered, dried and recrystallized using (methanol: chloroform). The% age yield was found out to be 66.7, m.p. 273-275°C and Rf: 0.57. Further the compound was characterized by IR and ^{1}HNMR:

- **FTIR (cam^{-1}):** 3368 (N-H), 3181 (=C-H), 1652 (C = N), 1492 (C = C), 1388(C-N)
- **^{1}HNMR (DMSO-d6, δ ppm):** 7.0-7.6 (15H, m, Ar-H), 4.9 (1H, s, N-H), 7.8 (1H, s, fused Ar-H)
- **Elemental analysis: for $C_{28}H_{21}N_5$:** C, 78.67%; H, 4.95%; N, 16.38%; Found: C, 79.13%; H, 2.15%; N, 16.39%

The compound was evaluated for analgesic as well as antiinflammatory activities. The compound was evaluated for antiinflammatory activity in albino rats by carrageenan induced rat paw edema method. The compound (5b) showed slightly less moderate activity in the range of 42.85% at a dose of 200 mg kg^{-1} at time interval of 3 h of carrageenan challenge when compared with standard Diclofenac sodium at the same time period exhibited 59.51% of activity at a dose of 10 mg kg^{-1} (Table 2).

The analgesic activity of the synthesized compounds was evaluated in albino rats by Eddy's hot plate method. The compound (5b) showed maximum activity at a dose of 200 mg kg^{-1} in the range of 6.08±0.13 at 90 min when compared with standard drug diclofenac sodium at a dose of 5 mg kg^{-1} in the range of 9.45±0.28 at 90 min (Table 3).

3-((2,4,5-triphenyl-1H-imidazol-1-yl)methyl)morpholine (5c): The compound 5((2,4,5-triphenyl-1H-imidazol-1-yl)methyl)-1H-benzo[d]imidazole (5c) was synthesized by adding 2,4,5-triphenylimidazole was added in Dimethyl formamide. Formaldehyde was added drop wise. The mixture was subjected to stirring for 30 minutes to yield a methyl derivative. To the other beaker Morpholine was added in dimethyl formamide. The methyl derivative was transferred to secondary amines and was stirred for few minutes. The contents of the beaker were refluxed for 4 h the reaction procedure was monitored over TLC. The precipitate was filtered, dried and recrystallized using (methanol: chloroform). The %age yield was found out to be 78%, m.p. 257-262°C and Rf 0.60. Further the compound was characterized by IR and ^{1}HNMR:

- **FTIR (cam^{-1}):** 3432 (N-H), 1650 (C = N), 1456 (C = C), 1397(C-N), 1065(C = O)
- **^{1}HNMR (DMSO-d6, δ ppm):** 7.0-7.5 (15H, m, Ar-H), 3.8 (2H, d, C-H), 2.8 (1H, p, C-H), 2.9 (1H, m, fused Ar-H)
- **Elemental analysis for $C_{26}H_{25}N_3O$:** C, 78.96%; H, 6.37%; N, 10.62%; O, 4.05%; Found: C, 78.59%; H, 6.50%; N, 10.50%; O, 4.41%

The compound was evaluated for antiinflammatory activity in albino rats by carrageenan induced rat paw edema method. The compound (5c) showed maximum activity in the range of 52.38% at a dose of 200 mg kg^{-1} at time interval of 3 h of carrageenan challenge when compared with standard Diclofenac sodium at the same time period exhibited 59.51% of activity at a dose of 10 mg kg^{-1} (Table 2).

The analgesic activity of the synthesized compounds was evaluated in albino rats by Eddy's hot plate method. The compound (5c) showed moderate activity at a dose of 200 mg kg^{-1} in the range of 6.94±0.15 at 90 min when compared with standard drug diclofenac sodium at a dose of 5 mg kg^{-1} in the range of 9.45±0.28 at 90 min (Table 3).

N, N-dimethyl(2,4,5-triphenyl-1H-imidazol-1-yl)methanamine (5d): N, N-dimethyl (2,4,5-triphenyl-1H-imidazol-1-yl)methanamine (5d) was synthesized by adding 2,4,5-triphenylimidazole in dimethyl formamide. Formaldehyde was added drop wise. The mixture was subjected to stirring for 30 min to yield a methyl derivative. To the another beaker dimethyl amine was added in dimethyl formamide. The methyl derivative was transferred to secondary amines and was stirred for few minutes. The contents of the beaker were refluxed for 4 hour, the reaction procedure was monitored over TLC. The precipitate was filtered, dried and recrystallized using (methanol: chloroform). The% age yield was found out to be 75.2%, m.p. 247-250°C and Rf 0.61. Further the compound was characterized by IR and ^{1}HNMR:

- **FTIR (cam^{-1}):** 3455 (N-H), 1662 (C = N), 1488 (C = C), 1393(C-N)
- **^{1}HNMR (DMSO-d6, δ ppm):** 7.2-7.5 (15H, m, Ar-H), 2.7 (1H, s, fused C-H)
- **Elemental analysis for $C_{24}H_{23}N_3$:** C, 81.55%; H, 6.56%; N, 11.89%; Found: C, 81.59%; H, 6.52%; N, 11.88%

The compound was evaluated for antiinflammatory activity in albino rats by carrageenan induced rat paw edema method. The compound (5d) showed slightly less moderate activity in the range of 50.00% at a dose of 200 mg kg^{-1} at time interval of 3 h of carrageenan challenge when compared with standard Diclofenac sodium at the same time period exhibited 59.51% of activity at a dose of 10 mg kg^{-1} (Table 2).

The analgesic activity of the synthesized compounds was evaluated in albino rats by Eddy's hot plate method. The compound (5d) showed maximum activity at a dose of 200 mg kg^{-1} in the range of 6.99±0.22 at 90 min when compared with standard drug Diclofenac sodium at a dose of 5 mg kg^{-1} in the range of 9.45±0.28 at 90 min (Table 3).

N-ethyl-N-((2,4,5-triphenyl-1H-imidazol-1-yl)methyl) ethanamine (5e): N,N-dimethyl (2,4,5-triphenyl-1H-imidazol-1-yl)methanamine (5e) was synthesized by adding 2,4,5-triphenylimidazole in Dimethyl formamide. Formaldehyde was added drop wise. The mixture was subjected to stirring for 30 min to yield a methyl derivative. To the another beaker. Diethyl amine was added in Dimethyl formamide. The methyl derivative was transferred to secondary amines and was stirred for few minutes. The contents of the beaker were refluxed for 4 h the reaction procedure was monitored over TLC. The precipitate was filtered, dried and recrystallized using (methanol: chloroform). The %age yield was found out to be 73.0 %, m.p. 262-268°C and Rf 0.54. Further the compound was characterized by IR and ^{1}HNMR:

- **FTIR (cam^{-1}):** 3355 (N-H), 3085 (=C-H-), 1667 (C = N), 1495 (C = C), 1391(C-N-)
- **^{1}HNMR (DMSO-d6, δ ppm):** 7.0-7 (15H, m, Ar-H), 4.8 (2H, d, C-H), 3.43 (2H, m, fused C-H), 2.2(3H, t, fused C-H)
- **Elemental analysis for $C_{26}H_{27}N_3$:** C, 81.85%; H, 7.13%; N, 11.01%; Found: C, 82.01%; H, 7.15%; N, 10.83%

The compound was evaluated for antiinflammatory activity in albino rats by carrageenan induced rat paw edema method. The compound (5e) showed slightly less moderate activity in the range of 46.45% at a dose of 200 mg kg^{-1} at time interval of 3 h of carrageenan challenge when compared with standard Diclofenac sodium at the same time period exhibited 59.51% of activity at a dose of 10 mg kg^{-1} (Table 2).

The analgesic activity of the synthesized compounds was evaluated in albino rats by Eddy's hot plate method. The compound (5e) showed mild activity at a dose of 200 mg kg^{-1} in the range of 6.08±0.09 at 90 min when compared with standard drug Diclofenac sodium at a dose of 5 mg kg^{-1} in the range of 9.45±0.28 at 90 min (Table 3).

Antiinflammatory activity: The development of edema in the paw of the rat after injection of carrageenan is a biphasic event. The edema occurs due to inflammatory mediators like serotonin, histamine, kinin and prostaglandin (Emma *et al.*, 2010). Inhibition of edema observed in carrageenan models may be due to the ability of the different compounds to inhibit these chemical mediators of inflammation, or a stabilizing effect on lysosomal membranes. Imidazole derivatives showed good antiinflammatory activity with morpholine derivative showing maximum activity. Benzotriazoles derivatives were seemed to be less potent as compared with others which are showing significant activity.

The positive control, diclofenac and test compounds (5a-5e) significantly inhibited the paw edema response in comparison to control group. Diclofenac showed an inhibition of 59.51% after 3 h. Compound 5c showed maximum activity with an inhibition of 52.38% and compound 5b showed minimum activity with an inhibition of 42.85% after 3 h (Table 2).

Analgesic activity: The mechanism of pain transmission is very complex and many different neuromodulators and receptors could be involved. The central analgesic activity of the synthetic

compounds was studied using Eddy's Hot plate method and significantly increased reaction time was observed. Again morpholine derivative showed maximum central analgesic activity.

Diclofenac showed marked analgesic response. All the test compounds (5a-5e) also showed good analgesic activity with compound 5c having maximum activity and compound 5a with minimum analgesic activity (Table 3).

From the literature it may be concluded that Mannich bases of 2,4,5-triphenylimidazole showed their antiinflammatory and analgesic activity by inhibiting the microsomal prostaglandin E2-synthase 1 (mPGES-1) like other imidazole derivatives.

DISCUSSION

The Mannich Bases of Novel 2,4,5-triphenylimidazole were synthesized. All the newly synthesized Mannich bases of 2,4,5-triphenylimidazoles were evaluated for their analgesic and antiinflammatory activities (Shalini *et al.*, 2011; Puig Parellada, 1985). Previous studies showed that the chloro group in place of abstractable hydrogen in 2,4,5-triphenylimidazole showed potent antiinflammatory activity (Yasodha *et al.*, 2009). The substitution at C-2 benzene nucleus with benzyl, benzoyl, para amino benzoyl showed antifungal activity (Yadav *et al.*, 2011). The 2,4,5-triphenyl nucleus had been synthesized by microwave technique as well (Pandit *et al.*, 2011). The trimethoxy benzene nucleus at the 2 position of imidazole ring results in antiinflammatory and antifungal activities (Umarani *et al.*, 2011). Addition of thiol group in 2,4,5-triphenylimidazole resulted in increased activity (El Ashry *et al.*, 2007). Azole ring in place of abstractable hydrogen in 2,4,5-triphenylimidazole ring showed potent antibacterial and antiinflammatory activity (Amir *et al.*, 2011). Conversion into benzimidazole and 1, 2, 3, 4-tetrahydroquinoline ring resulted in compounds possessing better activity (Verma *et al.*, 1982, 1984; Bhatnagar *et al.*, 2011). Inclusion of thiazolidine-2, 4-diones in imidazole moiety was explored as new potential human CB1 cannabinoid receptor ligands (Muccioli *et al.*, 2006). Thus in accordance with the above findings, all the newly synthesized compounds 5-((2,4,5-triphenyl-1H-imidazol-1-yl)-1H imidazole derivatives were tested *in vivo* in order to evaluate them for their antiinflammatory and analgesic activities (Achar *et al.*, 2010).

CONCLUSION

The various Mannich bases of 2,4,5-triphenylimidazole have been synthesized and evaluated for their antiinflammatory and analgesic activity. The mannich bases showed good responses when compared to the standard drug. It is concluded that the mannich bases of 2,4,5-triphenylimidazoles are potent antiinflammatory and analgesic agents.

ACKNOWLEDGMENTS

Thanks to Professor A.C. Rana and all faculty members of Rayat Institute of Pharmacy for their encouragement and support.

REFERENCES

Abiqnente, E., F. Arena, P. De Caprariis, R. Nuzzetti and E. Marmo *et al.*, 1981. Research on heterocyclic compounds. X.-Imidazo[1,2-a]pyrazine derivatives: Synthesis and antiinflammatory activity. Farmaco Sci., 36: 61-80.

Achar, K.C.S., K.M. Hosamani and H.R. Seetharamareddy, 2010. *In vivo* analgesic and antiinflammatory activities of newly synthesized benzimidazole derivatives. Eur. J. Med. Chem., 45: 2048-2054.

Amir, M., I. Hasan, W. Akhter, S.A. Khan and I. Ali, 2011. Design and synthesis of some azole derivatives containing 2,4,5 triphenyl Imidazole moiety as anti-inflammatory and antimicrobial agents. Ind. J. Chem., 50: 207-213.

Bhatnagar, A., P.K. Sharma and N. Kumar, 2011. A review on Imidazoles: Their chemistry and pharmacological potentials. Int. J. PharmTech Res., 3: 268-282.

Bredereck, H., R. Gompper and D. Hayer, 1959. Formamid-reaktionen, XIII. Imidazole aus α-diketonen. Chemische Berichte, 92: 338-343.

El Ashry, E.S.H., N. Rashed, L.F. Awad, E. Ramadan, S.M. Abdel-Maggeed and N. Rezki, 2007. MAOS versus conventional synthesis of 4,5-di- and 3,4,5-triphenylimidazole-2-thione and their derivatives. ARKIVOC, 7: 30-40.

Emma, T., J.M Ziebell, A.V Leonard and R. Vink, 2010. Kinin receptor antagonists as potential neuroprotective agents in central nervous system injury. Molecules, 15: 6598-6618.

Fatimi, J., J.F. Lagorce, J.L. Duroux, M.L. Chabernaud, J. Buxeraud and C. Raby, 1994. 1,4,5-trialkyl imidazole system anti-inflammatory properties of new substituted derivatives. Chem. Pharm. Bull., 42: 698-701.

Franzotti, E.M., C.V.F. Santos, H.M.S.L. Rodrigues, R.H.V. Mourao, M.R. Andrade and A.R. Antoniolli, 2001. Anti-inflammatory, analgesic activity and acute toxicity of *Sida cordifolia* L. (Malva-branca). J. Ethnopharmacol., 72: 273-277.

Gill, N.S., K. Dhiman, J. Bajwa, P. Sharma and S. Sood, 2010. Evaluation of free radical scavenging, anti-inflammatory and analgesic potential of *Benincasa hispida* seed extract. Int. J. Pharmacol., 6: 652-657.

Hoffman, K., 1953. Imidazole and its Derivatives. Interscience Publisher, New York, USA., pp: 143-145.

Kumar, N., P.K. Sharma, V.K. Garg and P. Singh, 2011. Synthesis and anticonvulsant activity of novel substituted phenyl indoloimidazole derivatives. Curr. Res. Chem., 3: 114-120.

Lunt, E., C.G. Newton, C. Smith, G.P. Stevens and M.F. Steven *et al.*, 1987. Antitumor imidazotetrazines. 14. Synthesis and antitumor activity of 6- and 8-substituted imidazo[5,1-d]-1,2,3,5-tetrazinones and 8-substituted pyrazolo[5,1-d]-1,2,3,5-tetrazinones. J. Med. Chem., 30: 357-366.

Manikpuri, A.D., S. Joshi and P.V. Khadikar, 2010. Synthesis and antimicrobial study of the mannich bases of 4-{(dipropylamino)[bis (methylene)] sulfanyl}benzamide. J. Eng. Sci. Manage. Educ., 2: 29-33.

Muccioli, G.G., J. Wouters, C. Charlier, G.K. Scriba and T. Pizza *et al.*, 2006. Synthesis and activity of 1,3,5-triphenylimidazolidine-2,4-diones and 1,3,5-triphenyl-2-thioxoimidazolidin-4-ones: Characterization of new CB1 cannabinoid receptor inverse agonists/antagonists. J. Med. Chem., 49: 872-882.

Pandit, S.S., S.K. Bhalera, U.S. Aher, G.L. Adhav and V.U. Pandit, 2011. Amberlyst A-15: Reusable catalyst for the synthesis of 2, 4, 5-trisubstituted and 1,2,4,5-tetrasubstituted-1H-imidazoles under MW irradiation. J. Chem. Sci., 123: 421-426.

Puig Parellada, P., 1985. Analgesic, anti-inflammatory and oxy-radical scavenger activity of imidazole and imidazole derivatives. Int. J. Tissue React., 7: 509-512.

Sahoo, S., T. Joseph and S.B. Halligudi, 2006. Mannich reaction in Bronsted acidic ionic liquid: A facile synthesis of β-amino carbonyl compounds. J. Mol. Catal., 244: 179-182.

Sahu, R.K., A. Singh, R. Gupta, A. Roy and J. Dwivedi, 2012. Development and evaluation of antipyretic and antinociceptive activity of polyherbal formulation containing some indigenous medicinal plants. Int. J. Pharm., 8: 271-276.

Sandhar, A., D.N. Prasad, A. Kapoor and R.K. Singh, 2012. Efficient p-amino benzoic acid catalyzed eco-friendly synthesis of 1,5-benzodiazepines among various amino acids under solvent free conditions. Curr. Res. Chem., 4: 68-75.

Shalini, K., N. Kumar and P.K. Sharma, 2011. Synthesis of N-((2-Substituted Phenyl)-4, 5-Diphenyl-1H-Imidazol-1yl) (Phenyl) Methyl) substituted amine derivatives, spectral characterization and their pharmacological evaluation. Biointerface Res., 1: 184-190.

Shalini, K., P.K. Sharma and N. Kumar, 2010. Imidazole and its biological activities: A review. Chem. Sin., 1: 36-47.

Suzuki, F., T. Kuroda, T. Tamura, S. Sato, K. Ohmori and S. Ichikawa, 1992. New antiinflammatory agents. 2. 5-Phenyl-3H-imidazo[4,5-c][1,8]naphthyridin-4(5H)-ones: A new class of nonsteroidal antiinflammatory agents with potent activity like glucocorticoids. J. Med. Chem., 35: 2863-2870.

Umarani, N., K. Ilango, G. Garg, B.K. Srinivas and V. Hemalatha, 2011. Exploring the effects of newer three component Aminobenzylated reactions of triphenyl imidazole motif as potent Antimicrobial and Antiinflammatory agents. Int. J. Pharm. Pharm. Sci., 3: 62-65.

Verma, M., V.R. Gujrati, M. Sharma, A.K. Saxena and T.N. Bhalla *et al.*, 1982. Indolyl compounds as antiinflammatory agents. Arch. Pharmazie, 315: 358-363.

Verma, M., V.R. Gujrati, M. Sharma, A.K. Saxena and T.N. Bhalla *et al.*, 1984. Anti-inflammatory activity of amino acyl benzoate. Pharmacol. Res. Commun., 16: 9-20.

Winter, C.A., E.A. Risley and G.W. Nuss, 1962. Carrageenan induced edema in hind paw of the rat as an assay for anti-inflammatory drug. Proc. Soc. Exp. Biol. Med., 111: 544-547.

Yadav, S.K., S.M. Mali Patil and B.K. Mishra, 2011. Synthesis, spectral characterization & biological screening of some novel synthesized imidazoles. Int. J. Drug Dis. Herbal Res., 1: 27-31.

Yasodha, A., A. Sivakumar, G. Arunachalam and A. Puratchikody, 2009. Synthesis and Biological evaluation of some 2, 4, 5 Triphenyl Imidazole derivatives. J. Pharm. Sci. Res., 1: 127-130.

Zakaria, Z.A., R.N.S.R.M. Nor, M.R. Sulaiman, Z.D.F.A. Ghani, G.H. Kumar and C.A. Fatimah, 2006. Antinociceptive and anti-inflammatory properties of *Melastoma malabathricum* leaves chloroform extract in experimental animals. J. Pharmacol. Toxicol., 1: 337-345.