

## Synthesis and Pharmacological Evaluation of Some Potent 2-(4-Substitutedphenyl)-4,5-Diphenyl-1*H*-Imidazoles.

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**The reaction between benzil and ammonium acetate with appropriate aldehyde(s) in glacial acetic acid readily gives 2-(4-substitutedphenyl)-4,5-diphenyl-1*H*-imidazole (1-10). The spectra (IR, <sup>1</sup>H and <sup>13</sup>C NMR and MS) and analytical data have supported their structures. Toxicity of 1-10 has been determined. Analgesic, antiinflammatory, antiepileptic and locomotor activities of the compounds 1-10 have been evaluated by standard methods.**

Compounds containing imidazole nucleus have been of great interest to synthetic and medicinal chemists for a long time due to their unique chemical and biological properties mainly related to analgesics<sup>1</sup>, antiinflammatory<sup>2</sup>, antiparasitic<sup>3</sup>, platelet aggregation inhibitors<sup>4</sup>, and antiepileptic agents<sup>5</sup>. Further, imidazole and its derivatives comprise the ring system in a number of naturally occurring compounds such as histamine, histidine, pilocarpine and allantoin, which have a wide range of biological activities. Several derivatives of imidazoles have been marketed as biologically active products such as clonidine, tolazoline, fenmetazole, phenytoin, trifluoromethoxy, for hypertension, angina, depression, epilepsy and thrombosis, respectively. It is also found that the imidazoles are associated with many other pharmacological activities. Hence, synthesis of new imidazoles is being continuously reported. Aliphatic carboxylic esters of 2-(4-hydroxyphenyl)-4,5-diphenylimidazoles<sup>6</sup>, alkylthioimidazoles<sup>7</sup>, 4-( $\omega$ -phenylalkyl)imidazoles<sup>8</sup>, cis-1-(2-phenyl-4-(phenoxy or phenylthio)methyl-1,3-dioxolan-2-yl)-1*H*-imidazole<sup>9</sup>, 1,2-substituted-4,5-bis(hydroxymethyl)imidazoles<sup>10</sup>, 1-ethyl-2-furyl-4,5-diphenylimidazoles<sup>11</sup>, 2-aryl-4-(3-thienyl)imidazole<sup>12</sup> were reported and screened for various pharmacological activities such as lipase activity, ACAT inhibiting activity,  $\beta$ -glucosidase inhibiting activity,

antimicrobial, antineoplastic, analgesic and antiinflammatory to mention some. The literature survey on imidazole reveals that so far no works are reported on 2-(4-substitutedphenyl)-4,5-diphenyl-1*H*-imidazoles. Following this, and in continuation of our research on imidazoles<sup>5</sup>, we attempted to synthesize certain new imidazoles of this kind with a view to screening the biological activities in relation to chemical modifications.

### MATERIALS AND METHODS

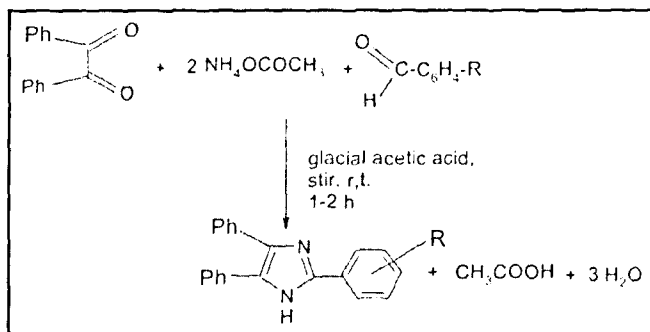
Melting points determined were uncorrected. IR (KBr) of the compounds 1-10 were recorded in Perkin Elmer 1600 FT spectrophotometer, <sup>1</sup>H and <sup>13</sup>C NMR spectra in DMSO-*d*<sub>6</sub> or CDCl<sub>3</sub> Brucker, 300 MHz spectrometer using TMS as internal standard and mass spectra on a Shimadzu QP-5000 mass spectrometer.

### General procedure for the preparation of compounds 1-10<sup>13</sup>:

A mixture of benzil (5.25 g, 0.025 mol), ammonium acetate (10g, 0.129mol) and required 4-substitutedbenzaldehyde(s) (0.018 mol) in glacial acetic acid (50 ml) was heated under reflux for 1-2 h. The progress of the reaction was monitored by TLC (silica gel E Merck plates) test using ethyl acetate as eluent. The reaction mixture was allowed to stand to attain room temperature. The solid that appeared after the addition of water (150 ml) was filtered. The filtrate was neutralized with ammonium hydroxide to give solid

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Scheme 1: Synthetic route

R groups used were 1. 4-F, 2. 4-Cl, 3. 4-Br, 4. 4-I, 5. 4-NO<sub>2</sub>, 6. 4-NH<sub>2</sub>, 7. 4-NMe<sub>2</sub>, 8. 4-OH, 9. 4-CH<sub>3</sub> and 10. 4-OCH<sub>3</sub>

and was filtered. The solid mass obtained from first and second crop was washed well with toluene, dried in vacuum and recrystallised from aqueous ethanol. Yield and melting point of the product(s) were determined.

### 2-(4-Fluorophenyl)-4,5-diphenyl-1H-imidazole 1:

IR: 3420, 3029, 1658, 1608, 1493, 1451, 1158 and 737 cm<sup>-1</sup>; <sup>1</sup>H NMR: δ 12.82 (s, 1H (NH)), 8.14 (d, 2H, (C<sub>3</sub> and C<sub>5</sub> H of 2-phenyl)), 7.95 (d, 2H, (C<sub>2</sub> and C<sub>6</sub> H of 2-phenyl)) and 7.83-7.20 (m, 10H, (4 and 5-diphenyl)), ppm; <sup>13</sup>C NMR: δ 158.04, 148.07, 145.10, 142.02, 141.25, 133.64, 132.04, 131.06, 129.84, 129.34, 128.84, 127.45, 120.62, 112.16 and 104.20 ppm; MS (FAB): m/z 314 (M<sup>+</sup>, 100%), 193, 178, 165 and 103 for C<sub>21</sub>H<sub>15</sub>N<sub>2</sub>F.

### 2-(4-Chlorophenyl)-4,5-diphenyl-1H-imidazole 2:

IR: 3418, 3062, 1660, 1597, 1485, 1449 and 731 cm<sup>-1</sup>; <sup>1</sup>H NMR: δ 12.80 (s, 1H, (NH)), 8.12 (d, 2H, (C<sub>3</sub> and C<sub>5</sub> H of 2-phenyl)), 8.04 (d, 2H, (C<sub>2</sub> and C<sub>6</sub> H of 2-phenyl)) and 7.84-7.20 (m, 10H, (4 and 5-diphenyl)), ppm; <sup>13</sup>C NMR: δ 143.24, 142.49, 141.12, 139.37, 138.58, 136.29, 134.65, 131.65, 130.51, 129.68, 128.07, 128.72, 127.54, 118.14 and 112.04 ppm; MS (FAB): m/z 330 (M<sup>+</sup>, 100%), 297, 194, 178, 165, 115 and 105 for C<sub>21</sub>H<sub>15</sub>N<sub>2</sub>Cl.

TABLE 1: PHYSICAL DATA OF COMPOUNDS 1-10

Compd No	mp (°)	Yield (%)	Nature	Mol. Formula	CHN analysis: found (calcd.) (%)		
					C	H	N
1	239-41	79	Colorless crystalline solid	C <sub>21</sub> H <sub>15</sub> N <sub>2</sub> F	80.16 (80.25)	4.81 (4.78)	8.59 (8.92)
2	246-48	80	Colorless solid	C <sub>21</sub> H <sub>15</sub> N <sub>2</sub> Cl	77.26 (76.36)	4.65 (4.54)	8.52 (8.48)
3	221-23	68	Pale brown solid	C <sub>21</sub> H <sub>15</sub> N <sub>2</sub> Br	67.36 (67.37)	4.05 (4.01)	7.49 (7.48)
4	197-99	65	Brown solid	C <sub>21</sub> H <sub>15</sub> N <sub>2</sub> Br	59.26 (59.71)	4.88 (4.55)	6.23 (6.63)
5	250-51	79	Dark yellow solid	C <sub>21</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub>	73.72 (73.90)	4.19 (4.39)	12.18 (12.32)
6	211-12	73	Colorless crystalline solid	C <sub>21</sub> H <sub>17</sub> N <sub>3</sub>	80.98 (81.02)	5.28 (5.47)	13.45 (13.50)
7	225-27	70	Pale brown solid	C <sub>23</sub> H <sub>19</sub> N <sub>3</sub>	81.78 (81.89)	5.60 (5.63)	12.39 (12.46)
8	237-39	78	Colorless crystalline solid	C <sub>21</sub> H <sub>16</sub> N <sub>2</sub> O	85.18 (85.16)	5.38 (5.81)	9.09 (9.03)
9	221-23	76	Colorless solid	C <sub>22</sub> H <sub>18</sub> N <sub>2</sub>	80.72 (80.76)	5.08 (5.13)	8.87 (8.97)
10	210-12	82	Colorless crystalline solid	C <sub>22</sub> H <sub>18</sub> N <sub>2</sub> O	80.96 (80.98)	5.28 (5.52)	8.48 (8.58)

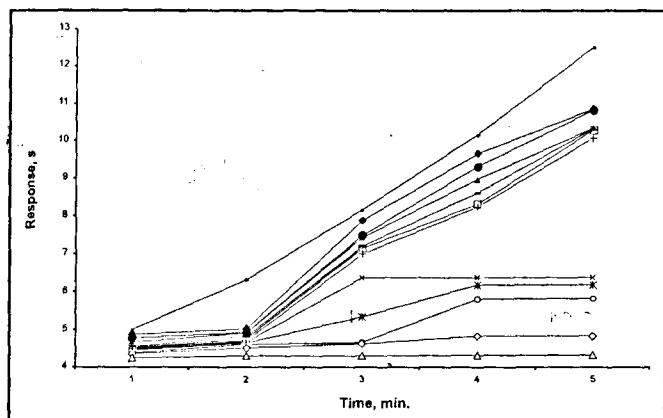


Fig. 1: Analgesic activity of compounds 1-10 by hot plate method

Effect of test compounds on hot plate induced analgesia in mice. Compound 1 is represented by (●—), 2 by (▲—), 3 by (x—), 4 by (✕—), 5 by (○—), 6 by (■—), 7 by (□—), 8 by (—), 9 by (◇—), 10 by (◆—), control (△—), standard pentazocine (▣—)

#### 2-(4-Bromophenyl)-4,5-diphenyl-1H-imidazole 3:

IR: 3415, 3028, 1638, 1618, 1483, 1432 and 715  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$ :  $\delta$  12.80 (s, 1H, (NH)), 8.11 (d, 2H, ( $\text{C}_3$  and  $\text{C}_5$  H of 2-phenyl)), 7.83 (d, 2H, ( $\text{C}_2$  and  $\text{C}_6$  H of 2-phenyl)) and 7.81-7.20 (m, 10H, (4 and 5-diphenyl)), ppm;  $^{13}\text{C NMR}$ :  $\delta$  142.58, 141.68, 140.73, 139.50, 137.78, 136.02, 132.34, 131.37, 130.12, 129.68, 128.88, 128.66, 127.82, 126.06 and 119.22 ppm; MS (FAB): m/z 374 ( $\text{M}^+$ , 100%), 297, 175, 165, 115 and 105 for  $\text{C}_{21}\text{H}_{15}\text{N}_2\text{Br}$ .

#### 2-(4-Iodophenyl)-4,5-diphenyl-1H-imidazole 4:

IR: 3416, 3026, 1659, 1618, 1481, 1430 and 500  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$ :  $\delta$  12.76 (s, 1H, (NH)), 8.12 (d, 2H, ( $\text{C}_3$  and  $\text{C}_5$  H of 2-phenyl)), 7.95 (d, 2H, ( $\text{C}_2$  and  $\text{C}_6$  H of 2-phenyl)) and 7.64-7.21 (m, 10H, (4 and 5-diphenyl)), ppm;  $^{13}\text{C NMR}$ :  $\delta$  144.59, 142.69, 141.49, 139.36, 133.87, 133.14, 132.60, 131.50, 130.12, 129.05, 128.07, 128.73, 128.73, 128.58, 127.92, 127.49 and 126.74 ppm; MS (FAB): m/z 422 ( $\text{M}^+$ , 100%), 296, 194, 178, 165, 115 and 105 for  $\text{C}_{21}\text{H}_{15}\text{N}_2\text{I}$ .

#### 2-(4-Nitrophenyl)-4,5-diphenyl-1H-imidazole 5:

IR: 3434, 3039, 1693, 1658, 1493, 1521, 1407, 1350 and 835  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$ :  $\delta$  12.68 (broad hump, 1H, (NH)), 8.11 (d, 2H, ( $\text{C}_3$  and  $\text{C}_5$  H of 2-phenyl)), 8.09 (d, 2H, ( $\text{C}_2$  and  $\text{C}_6$  H of 2-phenyl)) and 8.00-7.11 (m, 10H, (4 and 5-diphenyl)), ppm;  $^{13}\text{C NMR}$ :  $\delta$  146.49, 135.36, 133.14, 132.92, 132.70, 130.12, 129.05, 128.73, 128.58, 128.24, 127.92, 127.49, 126.74 and 116.21 and 126.74 ppm; MS (FAB): m/z 341

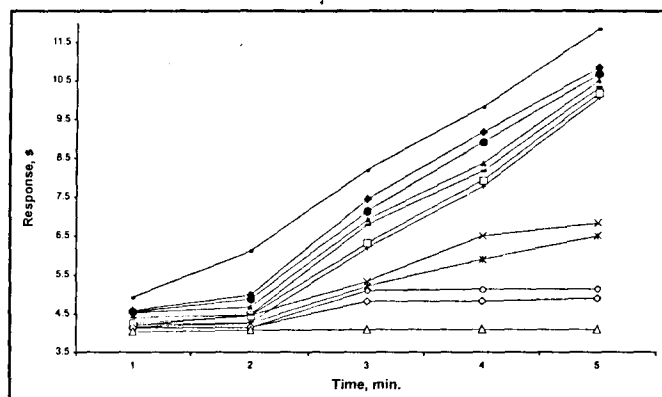


Fig. 2: Analgesic activity of compounds 1-10 by tail flick method

Effect of test compounds by tail flick induced analgesia in mice. Compound 1 is represented by (●—), 2 by (▲—), 3 by (x—), 4 by (✕—), 5 by (○—), 6 by (■—), 7 by (□—), 8 by (—), 9 by (◇—), 10 by (◆—), control (△—), standard pentazocine (▣—)

( $\text{M}^+$ , 100%), 296, 194, 178, 165, 115 and 105 for  $\text{C}_{21}\text{H}_{15}\text{N}_3\text{O}_2$ .

#### 2-(4-Aminophenyl)-4,5-diphenyl-1H-imidazole 6:

IR: 3426, 3438, 1660, 1600, 1479 and 1449  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$ :  $\delta$  12.63 (broad hump, 1H, (NH)), 8.15 (d, 2H, ( $\text{C}_2$  and  $\text{C}_6$  H of 2-phenyl)), 7.92 (d, 2H, ( $\text{C}_3$  and  $\text{C}_5$  H of 2-phenyl)) and 7.90-6.91 (m, 10H, (4 and 5-diphenyl)), ppm;  $^{13}\text{C NMR}$ :  $\delta$  156.26, 154.78, 153.27, 151.26, 149.28, 148.52, 132.38, 131.55, 130.73, 129.64, 128.58, 128.19, 127.64, 126.33 and 118.80 ppm; MS (FAB): m/z 311 ( $\text{M}^+$ , 100%), 295, 194, 178, 165 and 106 for  $\text{C}_{21}\text{H}_{17}\text{N}_3$ .

#### 2-(4-Dimethylaminophenyl)-4,5-diphenyl-1H-imidazole 7:

IR: 3428, 3038, 2888, 1642, 1612, 1444 and 1407  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$ :  $\delta$  12.46 (broad hump, 1H, (NH)), 8.17 (d, 2H, ( $\text{C}_2$  and  $\text{C}_6$  H of 2-phenyl)), 8.05 (d, 2H, ( $\text{C}_3$  and  $\text{C}_5$  H of 2-phenyl)), 7.90-6.42 (m, 10H, (4 and 5-diphenyl)) and 2.74 (s, 6H, ( $\text{N}(\text{CH}_3)_2$ )) ppm;  $^{13}\text{C NMR}$ :  $\delta$  154.38, 152.67, 149.78, 145.68, 149.28, 137.50, 136.02, 135.46, 131.37, 130.12, 128.88, 128.53, 127.82, 127.81, 126.06 and 22.13 ppm; MS (FAB): m/z 339 ( $\text{M}^+$ , 100%), 324, 297, 194, 178, 165, 115 and 105 for  $\text{C}_{23}\text{H}_{19}\text{N}_3$ .

#### 2-(4-Hydroxyphenyl)-4,5-diphenyl-1H-imidazole 8:

IR: 3426, 3031, 1638, 1610, 1492, 1458, 1240 and 1067  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$ :  $\delta$  12.27 (broad hump, 1H, (NH)), 10.70 (s, 1H, (OH)), 8.20 (d, 2H, ( $\text{C}_2$  and  $\text{C}_6$  H of 2-phenyl)), 7.58 (d, 2H, ( $\text{C}_3$  and  $\text{C}_5$  H of 2-phenyl)) and 7.56-7.03 (m, 10H, (4

TABLE 2: ANTIINFLAMMATORY ACTIVITY OF COMPOUNDS 1-10

Compd. No	Dose (mg/kg)	Increase in paw volume after 3 h (mean±SEM)	Decrease in paw volume (%) (mean±SEM)
1	106.45	0.01 ± 0.00 **	44.13 ± 0.12
2	121.81	0.01 ± 0.00 **	48.28 ± 0.18
3	107.96	0.17 ± 0.01**	22.99 ± 0.21
4	109.17	0.31 ± 0.02	10.54 ± 0.11
5	120.63	0.42 ± 0.02	4.60 ± 0.24
6	106.29	0.09 ± 0.01**	33.33 ± 0.31
7	109.17	0.02 ± 0.00 **	45.98 ± 0.21
8	106.29	0.01 ± 0.00 **	52.87 ± 0.21
9	102.67	0.38 ± 0.02	8.05 ± 0.12
10	105.18	0.04 ± 0.00 **	40.23 ± 0.12
Control	5 ml/kg	---	---
Standard	10 mg/kg	0.02 ± 0.00	48.28 ± 0.34

\*\*P < 0.01, Vs Standard

and 5-diphenyl)), ppm; <sup>13</sup>C NMR: δ 161.30, 158.02, 152.78, 147.52, 145.25, 144.48, 134.22, 129.79, 129.50, 128.68, 128.38, 127.09, 124.24, 115.99 and 113.29 ppm; MS (FAB): m/z 312 (M<sup>+</sup>, 100%), 297, 194, 165, 115 and 105 for C<sub>21</sub>H<sub>16</sub>N<sub>2</sub>O.

**2-(4-Methylphenyl)-4,5-diphenyl-1H-imidazole 9:**

IR: 3420, 3030, 2868, 1669, 1600, 1493 and 1449 cm<sup>-1</sup>; <sup>1</sup>H NMR: δ 12.16 (broad hump, 1H, (NH)), 7.92 (d, 2H, (C<sub>2</sub> and C<sub>6</sub> H of 2-phenyl)), 7.82 (d, 2H, (C<sub>3</sub> and C<sub>5</sub> H of 2-phenyl)), 7.60-7.50 (m, 10H, (4 and 5-diphenyl)) and 1.57 (s, 3H, (CH<sub>3</sub>)), ppm; <sup>13</sup>C NMR: δ 142.86, 141.23, 140.62, 139.82, 137.80, 133.38, 132.41, 130.12, 129.02, 128.88, 128.66, 127.53, 127.03, 126.06, and 21.13 ppm; MS (FAB): m/z 310 (M<sup>+</sup>, 100 %), 296, 178, 165, 115 and 103 for C<sub>22</sub>H<sub>18</sub>N<sub>2</sub>.

**2-(4-Methoxyphenyl)-4,5-diphenyl-1H-imidazole 10:**

IR: 3422, 3028, 2871, 1662, 1604, 1450, 1402, 1211 and 1067 cm<sup>-1</sup>; <sup>1</sup>H NMR: δ 12.12 (broad hump, 1H, (NH)). This signal is disappeared by deuterium exchange. 8.14 (d, 2H, (C<sub>2</sub> and C<sub>6</sub> H of 2-phenyl)), 7.94 (d, 2H, (C<sub>3</sub> and C<sub>5</sub> H of 2-phenyl)), 7.84-6.84 (m, 10H, (4 and 5-diphenyl)) and 3.34 (s, 3H, (OCH<sub>3</sub>)), ppm; <sup>13</sup>C NMR: δ 159.45, 155.78, 149.37, 146.52, 145.63, 135.51, 131.32, 129.55, 128.37, 127.32,

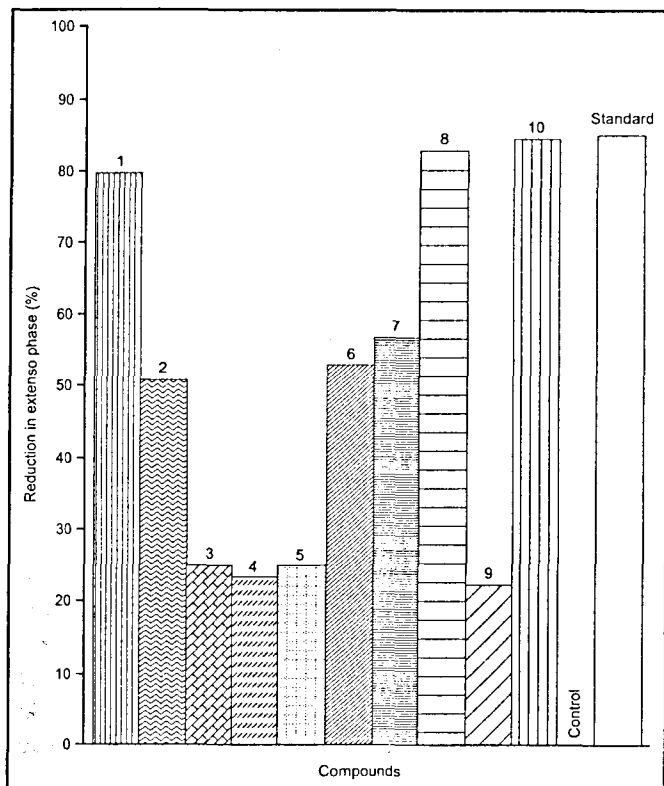
126.73, 125.21, 123.17, 114.10 and 55.21 ppm; MS (FAB): m/z 326 (M<sup>+</sup>, 100%), 312, 297, 194, 178, 165, 115 and 107 for C<sub>22</sub>H<sub>18</sub>N<sub>2</sub>O.

**Acute toxicity studies :**

Swiss mice of either sex were divided into fifty groups containing ten animals of each and treated i.p. with the dose range from 40 to 220 mg/kg test drugs. The animals were observed for mortality till 72 h and the LD<sub>50</sub> was calculated using graphical method<sup>14</sup>.

**Animal experimentation :**

Biological evaluation of synthesized compounds 1-10 was carried out in the Department of Animal Biotechnology, Bharathidasan University, Tiruchirappalli, Tamilnadu. Animal facility of this institute is approved by CPCSEA (Reg.No.418). The animals were maintained at a well ventilated, temperature controlled (30±1°) animal room for 7 days prior to the experimental period. The animals were provided with food and water *ad libitum*. Animals were acclimatized to laboratory conditions before the test. Each animal was used only once. The experimental protocols for the analgesic, antiinflammatory, antiepileptic and locomotor activities have been approved by the Institutional Animal Ethics Committee and conducted according to the Indian



**Fig.3: Antiepileptic activity of compounds 1-10**

Figure shows action test compounds on maximal electro shock induced seizures in rats. Compound 1 is represented by (▣), 2 by (▤), 3 by (▥), 4 by (▦), 5 by (▧), 6 by (▨), 7 by (▩), 8 by (▪), 9 by (▫), 10 by (▬), control (□), standard phenytoin (▣)

National Science Academy guidelines for the use and care of experimental animals.

#### Analgesic activity:

The analgesic activity was screened by hot plate<sup>15</sup> and tail flick methods<sup>16</sup>. Swiss mice (20-25 g) were divided into twelve groups each consisting of six. One group served as negative control (received 0.2% Tween suspension 5 ml/kg, i.p), the second group served as positive control (received pentazocine 10 mg/kg i.p). The other groups received between 10.26 and 12.18 mg/kg of compounds 1-10 i.p. The basal reaction time of animal was noted by placing the animals in the hot plate at  $55 \pm 0.5^\circ$  before and 15, 30, 60 and 120 min after the administration of test drugs. Cut-off time was kept at 15 s in order to avoid injury to the tail. Tail flick response was evoked by placing rat tail over a wire heated electrically. The intensity of heat was adjusted (current 3.0 A) so that baseline tail flick latency averaged 3 to 4 s in all the animals. Cut-off time was kept at 12 s in

order to avoid injury to the tail. The increase in reaction time against control group was calculated. The results are expressed as mean  $\pm$  standard error. The test of significance was analyzed by students 't' test<sup>17</sup>.

#### Antiinflammatory activity:

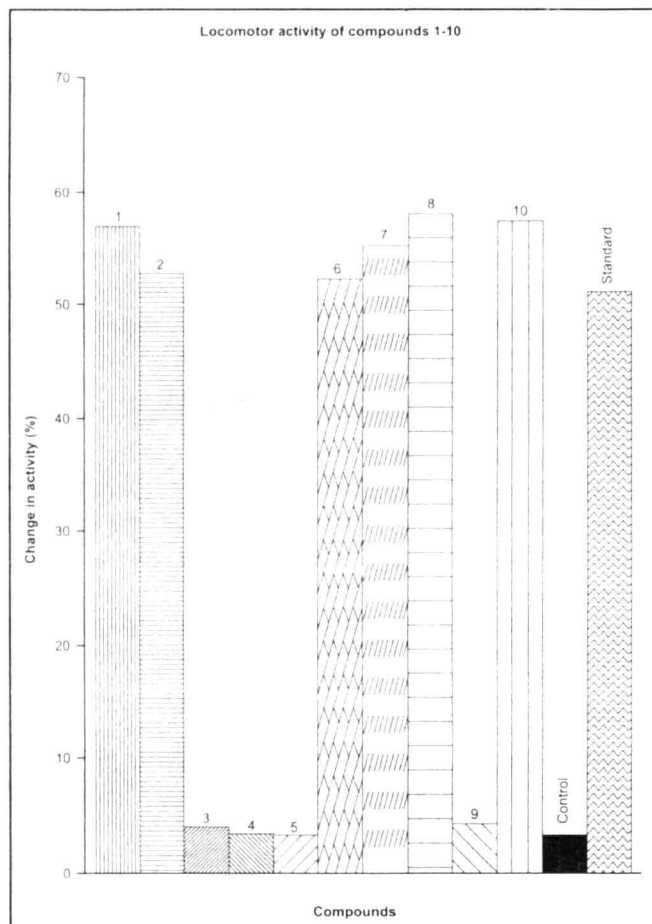
Antiinflammatory activity was determined by carrageenan-induced rat paw edema method<sup>18</sup>. Wistar rats (120-150 g) of either sex were used in this study and worked-up as above method. The positive control used here was indomethacine (10 mg / kg, ip). The control group received 0.2% Tween suspension (5 ml/kg ip). The test groups received between 10.26 and 12.18 mg/kg of compounds 1-10 ip. After the carrageenan injection the paw volume was measured immediately and at 1, 2, and 3 h by plethysmometer (UGO-Basile, Italy). The difference between the left and right paw was taken as a measure of edema. Any significant reduction in the volume of the paw compared to the control group was considered as antiinflammatory response.

#### Antiepileptic activity:

Electro shock method<sup>19,20</sup> was followed to study the antiepileptic activity. Wistar rats (120-150 g) of either sex were used in this study and worked-up as above method. The positive control used here was phenytoin (25 mg/kg ip). The control group received 0.2% Tween suspension (5 ml/kg ip). The test groups received between 10.26 and 12.18 mg/kg of compounds 1-10 i.p. Supramaximal electroshock of 150 mA for 0.2 s by a techno convulsimeter was given to the rats. Animals which showed positive hind limb tonic extensor response during pre- screening were selected and the test drugs were injected i.p. half an hour before the supramaximal shock. The protective index was defined as the abolition or reduction of the hind limb tonic extension component of the seizure.

#### Locomotor activity:

Actophotometer<sup>21</sup> was used to evaluate the locomotor activity. The Swiss mice (20-25 g) were divided into twelve groups each consisting of six. The test compounds were injected i.p. to the 10 groups of six mice each. One group received standard chlorpromazine (3 mg/kg) and one group received 0.2% tween suspension (5 ml/kg, i.p). The test groups received between 10.26 and 12.18 mg/kg of compounds 1-10 i.p. The locomotor activity score of all the animals was noted by placing the animals in the square area of the instrument for 10 min. The test compounds 1-10 were administered i.p., Each mouse was retested for activity



**Fig. 4: Locomotor activity of compounds 1-10**

Figure shows locomotor activity of test compounds 1-10. Compound 1 is represented by (▣), 2 by (▤), 3 by (▥), 4 by (▦), 5 by (▧), 6 by (▨), 7 by (▩), 8 by (▪), 9 by (▫), 10 by (▬), control (■), standard chlorpromazine (▭)

score after 30 min. The difference in the activity before and after the administration of test compounds was noted. The per cent decrease in motor activity (%) was calculated.

## RESULTS AND DISCUSSION

2-(4-Substitutedphenyl)-4,5-diphenyl-1*H*-imidazole (1-10) was synthesized by condensation reaction involving three reagents such as benzil, appropriate benzaldehyde(s) and ammonium acetate in glacial acetic acid (Scheme 1).

The physical data of the compounds 1-10 were collected and are presented in Table 1. The yields of 1-10 fall in the range of 65-82%. Most of them are colorless crystalline solids. The spectral (IR, <sup>1</sup>H, <sup>13</sup>C NMR and MS) and analytical data are in good agreement with their

structures.

The infrared spectra of 1-10 showed the characteristic absorption bands. The NMR spectral data of the compounds correspond to their structures. The <sup>13</sup>C spectra of 1-10 agree with the assigned structures. The mass spectra of these compounds show the molecular ion peak as base peak (100%) with expected mass.

The toxicity study of compounds 1-10 indicate the LD<sub>50</sub> values lie in between 10.26 and 12.18 mg/kg, body weight. The therapeutic dose of the drug is considered as 1/10 of LD<sub>50</sub> value. Hence, the LD<sub>50</sub> values used for recording various biological response is in between 10.26 and 12.18 mg/kg, body weight.

The results in fig. 1 and 2 show the analgesic activity of compounds by hot plate and tail flick methods respectively. These are useful only for detecting narcotic analgesics<sup>23</sup>. The compounds 1, 2, 6, 7, 8, and 10 showed their potency as analgesic agents by their greater increase in reaction time. The group such as -F, -Cl, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub>, -OH and -OCH<sub>3</sub> at *p*-position of 2-phenyl-4,5-diphenylimidazole produces significant activity (P < 0.01)

The results in Table 2 indicate that the compounds 1, 2, 6, 7, 8 and 10 are show significant antiinflammatory activity (P < 0.01). The compounds 1, 2, 6 and 8 are equipotent active with the standard. Moreover, compounds 6 and 10 exhibit antiinflammatory activity. Carrageenan-induced paw oedema was taken as a prototype of exudative phase of inflammation. The development of oedema has been described as biphasic<sup>24</sup>. The initial phase is due to the release of histamine, serotonin and kinins in the first hour. after injection of carrageenan. More pronounced second phase is related to the release of prostaglandin like substances in 2-3 h. Hence, the significant antiinflammatory effect may be due to an inhibitory effect exerted predominantly on the mediators of inflammation induced by phlogogenic stimuli.

The compounds 1, 2, 6, 7, 8 and 10 exhibit significant antiepileptic activity (P < 0.01). The compounds 1, 8 and 10 show equipotent activity with standard and the compounds 2, 6 and 7 show antiepileptic activity (fig. 3). Drugs like phenytoin, methytoin, and ethytoin have nucleus of reduced form of imidazole. Hence the antiepileptic activity of the compounds may be attributed to the fact that these drugs may either block the initiation of electrical impulses from the focal area or spread of abnormal electrical discharge to adjacent brain tissues. This may cause for the decrease in

post tetanic potentiation which may be responsible for the spread of seizure activity<sup>25</sup>. Screening results of locomotor activity reveal (fig. 4) that the compounds 1, 2, 6, 7, 8 and 10 show significant activity ( $P < 0.01$ ). whereas, these compounds are showing higher activity when compared with the standard. The presence of group such as -F (1), -Cl (2), -NH<sub>2</sub> (6), -N(CH<sub>3</sub>)<sub>2</sub> (7), -OH (8) and -OCH<sub>3</sub> (10) in the 2-(4-substitutedphenyl)-4,5-diphenylimidazole reduces the aggressiveness. This may be due to modification of mesolimbic system or some other mechanism<sup>26</sup>.

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