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STRUCTURE AND SYNTHESIS OF SOME IMIDAZOLE DERIVATIVES CONTAINING 2-(4-CHLOROPHENYL)-4, 5-DIPHENYL IMIDAZOLE MOIETY AS ANTI-INFLAMMATORY AND ANTIMICROBIAL AGENTS

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Abstract
A series of imidazole derivatives (4**a-e**)have been synthesized from2-(4-chlorophenyl)-4, 5-diphenyl-1*H*-imidazole-1-yl)-acetic acid hydrazide under various reaction conditions. Elemental analysis, IR, ^{1}HNMR and mass spectral data confirmed the structure of the newly synthesized compounds. All the synthesized imidazole derivatives have been investigated for their anti-inflammatory, anti-bacterial and antifungal effect and showed moderate to good activity.

Keywords:2-(4-chlorophenyl)-4, 5-diphenyl-1*H*-imidazole, anti-inflammatory, antimicrobial, antifungal

Introduction
The nonsteroidal anti-inflammatory drugs ($NSAID_S$) are commonly used in the treatment of rheumatoid arthritis, and other inflammatory diseases. Even with the advent of COX-2 inhibitors, their long term use has been associated with gastrointestinal ulceration, bleeding and nephrotoxicity[1].The tendency of many acidic drugs to accumulate in the stomach walls soon after oral absorption, as evidenced by radio autography, has been considered as a contributory factor for GI irritation[2]. The adverse effect of NSAID's are mediated via inhibition of prostaglandin synthesis from arachidonic acid by non-specific blocking of the enzyme cycloxygenase leading to vasoconstriction and reversible mild renal impairment[3]. It has been reported in the literature that certain five membered heterocyclic compounds possess interesting anti-inflammatory activity with lesser GIside effect[3,4]. Among heterocyclic compounds, imidazole ring bearing compounds are reported to have significant anti-inflammatory activity[5, 6]. Multi drug treatment of inflammatory conditions associated with microbial infections poses a unique problem especially for patients with impaired liver or kidney functions. Hence, mono therapy with a drug having both anti-inflammatory and antimicrobial activities is highly desirable, both from the pharmaco-economic as well as

patient compliance points of view[7-15]. Encouraged by these observations and in continuation of the research programme on the synthesis of five membered heterocyclic compounds, herein is reported the synthesis of various derivatives of 2-(4-chlorophenyl)-4, 5-diphenyl-1*H*-imidazole.

The reaction sequence leading to the formation of the desired heterocyclic compounds are outlined in **Scheme I**. 2-(4-chlorophenyl)-4, 5-diphenyl-1*H*-imidazole-1-yl)-acetic acid hydrazide**3** was prepared by treating 2-(4-chlorophenyl)-4, 5-diphenyl-1*H*-imidazole with ethyl chloroacetate in the presence of anhydrous acetone and potassium carbonate followed by reaction with hydrazine hydrate in absolute ethanol. Hydrazide**3** is treated with phenylisothiocynates derivatives. Hydrazide**3** on treatment with various substituted phenylisothiocynates gaveN^1-(2-(4-chlorophenyl)-4,5-diphenyl-imidazol-1-yl-ethanoyl)-N^4-substitutedphenyl thiosemicarbazide.

The ^{1}H NMR spectra of compound **4a** showed a multiplet δ7.2-7.5 for 19 aromatic protons of phenyl ring of imidazole derivatives. A peak was also obtained at δ 8.12 showing the presence of 1H of NH. A singlet was obtained at another δ 4.52-4.55 for NCH_2 protons. Furthermore, two singlets were also obtained at δ 12.70 and δ 10.88 of CONH and CSNH-group respectively.

The ^{1}H NMR spectra of compound **4b** showed a multiplet δ6.91showing the presence of 16 aromatic protons of phenyl ring attached to imidazole derivatives. A doublet was also observed at δ 8.08-8.11 showing the presence of remaining two protons of phenyl ring attached to imidazole. Singlets were obtained at δ3.73, δ4.45 and δ12.75 for methoxy, N-CH_2 protons and –CONH- group respectively and a singlet was also obtained at 12.41 for one proton of CSNH group. The IR spectrum of compound showed absorption peaks at 1502 cm^{-1}, C=C stretching;1606 cm^{-1}, C=N; 1456cm^{-1}, C-N stretching; 3032cm^{-1}, ArC-H stretching,1751cm^{-1}, -CONH- stretching, 1208 cm^{-1}, C=S stretching, and 1166cm^{-1} methoxy stretching.

The ^{1}H NMR spectra of **4c** compound showed a multiplet at δ 7.21-7.53 for 16 aromatic protons of phenyl rings attached to imidazole. A doublet was also observed at δ 8.07-8.09 showing the presence of remaining two protons of phenyl ring attached to imidazole. Two singlets were also obtained at δ 2.28 and δ 4.53 for CH_3 and N-CH_2 protons respectively. Furthermore, another singlet was also obtained at δ 12.59 of –CONH- proton, 12.41 for one proton of CSNH group and one peak at 8.08 for one proton of –NH- group. The IR spectrum of compound showed absorption peaks atδ 1539 (C=C), (aromatic C-H), 3196 (NH), δ 1892 (CONH), 1668 (C=O), 1596 (C=N), 1207 cm^{-1} (C=S) stretching.

The ^{1}H NMR spectra of **4d** compound showed a multiplet at δ7.21-8.02 for 18 aromatic protons of phenyl rings attached to imidazole. A singlet was obtained at δ 4.52 for N-CH_2 protons. Three singlets were also obtained at δ12.80, δ8.14 and δ11.08 of –CONH-, -NH- and -CSNH- group respectively. The IR spectrum of compound showed absorption peaks at δ 4.99 (C-Cl), δ3032 (aromatic C-H), δ 3196 (NH), δ 1751 (CONH), 1651 (C=O), 1606 (C=N), 1208 cm^{-1} (C=S) stretching.

The ^{1}H NMR spectra of **4e** compound showed a multiplet at δ 7.22-7.67 for 18 aromatic protons of phenyl rings attached to imidazole. A singlet was obtained at δ 4.49 for N-CH_2 protons. Three singlet were also obtained at δ 12.83, δ11.16 and δ 12.69 of –CONH-, -NH-

and -CSNH- group respectively. The IR spectrum of compound **4e** showed absorption peaks at 499 cm^{-1} (C-Cl), 3032 cm^{-1} (aromatic C-H), 3196 cm^{-1} (NH), 1751 cm^{-1} (CONH), 1651 cm^{-1} (C=O), 1591 cm^{-1} (C=N), 1101 cm^{-1} (C=S), 1547 cm^{-1} (C=C) stretching. The structure of **4e** compound was further characterized by mass spectra: molecular ions peaks at m/z M^+ 500.2. Further peaks at m/z = 383, 319 and 297.

Biological Studies

Adult male Wister strain rats of either sex, weighing 180-200 g were used. The animals were allowed food and water *adlibitum*. They were housed at room at 25 ± 2^oC, and 50 ± 5% of relative humidity with 12 hr light/dark cycle. The animals were randomly allocated into groups at the beginning of all the experiment. All the test compounds and reference drug were administered orally, suspended in 0.5% carboxymethylcellulose (CMC) solution.

Anti-inflammatory activity

The test was performed by the method of Winter*etal*.[16] on the group of six animals in each. Carrageenan solution (0.1% in sterile 0.9% NaCl solution) in a volume of 0.1 ml was injected subcutaneously into the subplantar region of the right hind paw of each rat, 1 hr after the administration of test compounds and standard drug indomethacin(10mg/kg, p.o). One group was kept as control, receiving only 0.5% carboxymethylcellulose solution. The right hind paw volume was measured before and after 4hr of carrageenan treatment by means of a plethysmometer. The percentage anti-inflammatory activity was calculated according to the following formula.

Percentage anti-inflammatory activity = (1-Vt/Vc)× 100, where Vt represents the mean in paw volume in rats tested with test compounds and Vc represents the mean increase in paw volume in control group of rats.

Data are expressed as mean ± SEM.The student *t*-test was applied to determine the significance of the difference between the control group and rats treated with the test compounds. The anti-inflammatory activity of the newly synthesized compounds 4a, 4b, 4c, 4d and 4e were compared with the standard drug indomethacin. At the same oral dose, indomethacin showed 71.56% inhibition of rat paw edema whereas the tested compounds (4a-e) showed inhibition ranging from 41.90 to 83.40% after 4 hr (**Table I**). The compounds 4c and 4d having methyl, 4-Fluoro groups showed moderate activity(53.90and 54.01%) in comparison to standard drug indomethacin (71.56%). The compounds 4e having 4-chloro group showed better activity (83%) in comparison to standard drug indomethacin (71.56%). It was noted that when the phenyl ring of thiosemicarbazide of triphenylimidazole moiety was substituted by methylphenylgroup(4c) and fluorophenyl groups (4d), there was marked increase in the anti-inflammatory activity (from 40.81% to 54%) respectively. The compounds 4e having 4-chlorophenylgroup showed enhanced activity (83.40 %) greater than the standard drug indomethacin (71.56%).

The other two imidazole derivatives 4a and 4b having phenyl and 4-methoxy phenyl group respectively showed poor anti-inflammatory activity (40.81 and 41.90 %). It was observed that chlorogroup substitution resulted in the significant increase of anti-inflammatory activity (83.40 %). The results of anti-inflammatory activity clearly indicated that among all fourimidazole derivatives, the chlorophenyl substituted imidazolederivative were the most active compounds of the series.

Antibacterial and antifungal activities

All the compounds have been screened for both antibacterial and antifungal activities using cup plate agar diffusion method[17] by measuring the inhibition zone in mm. Ofloxacin (100µg/mL) was used as standard drug for antibacterial activity, and Voriconazole

(100μg/mL) as a standard drug for antifungal activity.The compounds were screened for antibacterial activity against *E. coli*, *B.subtalis* and *S.aureus* in nutrient agar medium, and for antifungal activity against*Candida albicans* in Sabouraud's dextrose agar medium. These sterilized agar media were poured into Petri-dishes and allowed to solidify. On the surface of the media microbial suspensions were spread with the help of sterilized triangular loop. A stainless steel cylinder of 8 mm diameter (pre-sterilized) was used to bore cavities. All the synthesized compounds (100μg/ml) were placed serially in the cavities with the help of micropipette and allowed to diffuse for 1 hr. DMF was used as solvent for all compounds and as control. These plates were incubated at 37^{o}C for 34hr and 28^{o}C for 48hr, for antibacterial and antifungal activity respectively. The zone of inhibition observed around cup after respective incubation was assured and percent inhibition of the compounds was calculated. Results were presented in Table II.

The 2-(4-chlorophenyl)-4, 5-diphenyl-1*H*-imidazole derivative 4e, 4b and 4chaving 4-chlorophenyl group, 4-methoxyphenyl group and 4-methylphenyl group showed highest activity(75%, 72% and 69% respectively) against *S.aureous.* The compound 4c and 4d having 4-methylphenyl group and 4-fluorophenyl group showed highest activity (67% and 62.5% respectively) against *E.coli* when compared with standard drug Ofloxacin. Rest of the compound showed moderate to good activity against *E.coli, B.subtalis* and *S.aureus*. The derivative 4e having chloro phenyl group showed highest activity against (75%).
All the derivatives (4a-e) showed good antifungal activity (68 to 75%) against *Candida Albicans*. The derivative 4a and 4b having phenyl and 4-methoxy phenyl ring showed highest antifungal activity (75%) against *C.albicans*. The compound 4d also showed good activity. When 4-methoxy phenyl group replaced by 4-methylphenyl in compound 4c and 4-chlorophenyl incompound 4erespectively, there was slight decrease of antifungal activity (58.6% and 68.5 %). The imidazole derivative having 4-methylphenyl group showed minimum activity. Thus, it is concluded from the screening results that imidazole derivative 4a and4b were most effective against at a concentration of 100μg/ml. Overall screening result show variable trend of effect of imidazole derivative (4a-e)) against all the micro-organism.

Experimental Section

Materials and Measurements

All the chemicals used in the synthesis were supplied by E.Merck and S.D. Fine Chemicals. Melting point was determined by open capillary tube method and is uncorrected. Homogeneity of the compounds were checked on thin layer chromatography using iodine vapors as visualizing agent. IR spectra were obtained on a Perkin-Elmer 1720 FT-IR spectrometer (KBr pellets). ^{1}H NMR spectra were obtained on a Bruker DRX-300 (300MHz FT NMR) spectrometer in $CDCl_3$ using tetramethysilane (TMS) as the internal reference (chemical shifts in δ, ppm). Mass spectra were recorded on aJeol SX-102 spectrometer. Synthesis of 2-(4-chlorophenyl)-4, 5-diphenyl-1*H*-imidazole **1** was carried out by using chlorobenzaldehdye by the methods reported in literature[18].

Synthesis of 2-(4-chlorophenyl)-4, 5-diphenyl-1*H*-imidazole (1): Eqimolar quantity of benzyl (0.01 mol), ammonium acetate (0.01 mol) and chlorobenzaldehdye (0.01 mol) were dissolved in 50 mL glacial acetic acid in a 100 mL round bottom flask, and this reaction solution was stirrered on a magnetic stirrer. The reaction mixture was refluxed for 5 hrs on an oil bath. 300 mL cooled water was added to reaction mixture and product was precipitated out. The product immediately filtered off and neutralized with 5% ammonium solution. The compound was recrystallized from absolute ethanol to yield colourless crystalline compound

2. Yield 65%; m.p. 260°C;^{1}H-NMR ($CDCl_3$) of compound shows a double doublet at δ7.92-7.94 ;δ 8.21-8.50 and δ 8.50-8.53 respectively showing presence of 4H-protons of 2-phenyl ring attached to imidazole. A multiplet was obtained at δ7.32-7.78 showing the presence of remaining 10H protons of 4, 5-diphenyl rings. A singlet was also obtained at 13.09 showing the presence of NH protons.

Synthesis of 2-(4-chlorophenyl)-4, 5-diphenyl-imidazole-1-yl)-acetic acid ethyl ester 2: A mixture of 2-(4-chlorophenyl)-4, 5-diphenyl-1*H*-imidazole (0.03 mol) and ethyl chloroacetate (0.01 mol) in dry acetone (40 mL) was refluxed on a heating mantle for 30 hrs. The reaction mixture was cooled to RT. The crystals thus obtained was filtered, washed with water, dried and purified by recrystallization from ethanol to yield colourless crystalline compound **2**.Yield 66%;m.p. 260°C; IR (KBr, cm^{-1}): 550-490 cm^{-1} (C-Cl); 3026.85 cm^{-1} (aromatic C-H); 1668 (C=O), 1595 cm^{-1} (C=N); ^{1}H-NMR ($CDCl_3$): δ1.31-1.37 (t, 3H, CH_3), δ 4.08-4.16 (q, 2H, CH_2), δ 4.48 (s, 2H, NCH_2), δ 7.20-7.45 (m, 10H, ArH), δ 8.04-δ8.10 (4H, 3d, ArH); MS: *m/z*382 (M^+).Anal. Calcd for $C_{25}H_{21}N_2O_2Cl$.

Synthesis of 2-(4-chlorophenyl)-4,5-diphenyl-imidazole-1-yl)-acetic acid hydrazide 3: A mixture of2-(4-chlorophenyl)-4, 5-diphenyl-imidazole-1-yl)-acetic acid ethyl ester (0.01 mol) and hydrazine hydrate (0.05 mol) in ethanol (50 mL) was refluxed on water bath for 12 hrs. The reaction mixture was cooled to RT. The crystals thus obtained were filtered, washed with water, dried and purified by recrystallization from ethanol to yield colourless crystalline compound **3**.Yield 68%; m.p. 240°C; IR (KBr): 550-490 cm^{-1} (C-Cl); 3026.85 cm^{-1} (aromatic C-H); 1595 cm^{-1} (C=N); 3038 cm^{-1} (NH), 1694 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ5.35 (s, 2H, NCH_2), δ 5.1(d, 2H, NH_2), δ 7.20-7.5 (m, 10H, ArH), δ 8.04-8.10 (4H, 2d, ArH); δ 9.8 (bs, 1H, s, CONH); MS: *m/z*368 (M^+).Anal. Calcd for $C_{23}H_{19}N_4OCl$.

General method of synthesis of N^1-(2-(4-chlorophenyl)-4,5-diphenyl-imidazol-1-yl-ethanoyl)-N^4-substitutedphenylthiosemicarbazide: A mixture of acidhydrazide (0.01 mol) and substituted phenylisothiocynate (0.01 mol) in absolute ethanol (50 mL) was refluxed on a water bath for 6 hrs. The reaction-mixture was concentrated and allowed to stand at RT overnight. The needle shaped crystals of thiosemicarbazide thus obtained were filtered, washed with petroleum ether and purified by re-crystallization from ethanol.

N^1-(2-(4-chlorophenyl)-4,5-diphenyl-imidazol-1-yl-ethanoyl)-N^4-phenylthiosemicarbazide, 4a:Yield 52%; m.p. 228°C; IR (KBr): 1502 cm^{-1} (C=C), 3032 cm^{-1} (aromatic C-H), 3196 cm^{-1} (NH), 1751 cm^{-1} (CONH), 1683 cm^{-1} (C=O), 1597 cm^{-1} (C=N), 1099 cm^{-1} (C=S). **^{1}H-NMR ($CDCl_3$):** δ 4.53 (s, 2H, NCH_2), δ 7.2-7.5 (m, 19H, ArH), δ 8.12 (bs, 1H, NH) δ 10.88 (bs, 1H, CSNH), δ 12.70 (bs, 1H, CONH); MS: *m/z* 533 (M^+). Anal. Calcd for $C_{30}H_{24}N_5O_2SCl$.

thiosemicarbazide, 4b:Yield 49.3%; m.p. 230°C; IR (KBr): 1502 cm^{-1} (C=C), 3032 cm^{-1} (aromatic C-H), 3196 cm^{-1} (NH), 1751 cm^{-1} (CONH), 1668 cm^{-1} (C=O), 1606 cm^{-1} (C=N), 1208 cm^{-1} (C=S) and 2988 cm^{-1} alkyl –CH- stretching; **^{1}H-NMR ($CDCl_3$):** δ 3.73 (s, 3H, OCH_3), δ 4.45 (s, 2H, NCH_2), δ 6.91 (m, 16H, ArH), δ 8.08-8.11(d, 2H, ArH),

N^1-(2-(4-chlorophenyl)-4,5-diphenyl-imidazol-1-yl-ethanoyl)-N^4-4-methoxyphenyl δ **1**0.91 (bs, 1H, NH), δ 12.41 (bs, 1H, CSNH), δ 12.75 (bs, 1H, CONH); (M^+).*m/z* 530 (M^+). Anal. Calcd for $C_{31}H_{26}N_5O_2SCl$.

N^1-(2-(4-chlorophenyl)-4,5-diphenyl-imidazol-1-yl-ethanoyl)-N^4-4-methylyphenyl thiosemicarbazide, 4c:Yield 52%; m.p. 238^{o}C; IR (KBr): 1539 cm^{-1} (C=C), 1044 cm^{-1} (C-F), 3037 cm^{-1} (aromatic C-H), 3196 cm^{-1} (NH), 1892 cm^{-1} (CONH), 1668 cm^{-1} (C=O), 1596 cm^{-1} (C=N), 1207 cm^{-1}(C=S) and 2988 cm^{-1} alkyl –CH- stretching; **^{1}H-NMR ($CDCl_3$):** δ 2.28 (s, 3H, CH_3), δ 4.53 (s, 2H, NCH_2), δ 7.21-7.53 (m, 16H, ArH), δ 8.07-8.09 (d, 2H, ArH), δ 8.08 (bs, 1H, NH), δ 12.41 (bs, 1H, CSNH), δ 12.59 (bs, 1H, CONH); MS: *m/z* 517 (M^+).Anal. Calcd for $C_{31}H_{26}N_5O2SCl$.

N^1-(2-(4-chlorophenyl)-4,5-diphenyl-imidazol-1-yl-ethanoyl)-N^4-4-flourophenyl thiosemicarbazide,4d:Yield 48.8%; m.p. 251^{o}C; IR (KBr): 499 cm^{-1} (C-Cl), 1044 cm^{-1} (C-F), 3032 cm^{-1} (aromatic C-H), 3196 cm^{-1} (NH), 1751 cm^{-1} (CONH), 1651 cm^{-1} (C=O), 1606 cm^{-1} (C=N), 1208 cm^{-1} (C=S); **^{1}H-NMR ($CDCl_3$):** δ 4.52 (s, 2H, NCH_2), δ 7.21-8.02 (m, 18H, ArH), δ 8.14 (bs, 1H, NH), δ 11.08 (bs, 1H, CSNH), δ 12.80 (s, 1H, CONH); MS: *m/z*521(M^+); Anal. Calcd for $C_{30}H_{23}FN_5OSCl$.

N^1-(2-(4-chlorophenyl)-4,5-diphenyl-imidazol-1-yl-ethanoyl)-N^4-4-chlorophenyl thiosemicarbazide, 4e:Yield 48%; m.p. 223^{0}C; IR (KBr): 499 cm^{-1} (C-Cl), 3032 cm^{-1} (aromatic C-H), 3196 cm^{-1} (NH), 1751 cm^{-1} (CONH), 1651 cm^{-1} (C=O), 1591 cm^{-1} (C=N), 1101cm^{-1} (C=S); **^{1}H NMR ($CDCl_3$):** δ 4.49 (s, 2H, NCH_2), δ 7.22-7.67 (m, 18H, ArH), δ 11.16 (bs, 1H, NH), δ 12.69 (bs,1H, CSNH), δ 12.83 (bs, 1H, CONH); MS: *m/z*538(M^+), 540 (M^++2). Anal. Calcd for $C_{30}H_{23}Cl_2N_5OS$.

Conclusions:

This paper reports, design and synthesis of some imidazole derivatives containing 2-(4-chlorophenyl)-4, 5-diphenyl imidazole moiety as anti-inflammatory and antimicrobial agents. The Synthesis of 2-(4-chlorophenyl)-4, 5-diphenyl-1*H*-imidazole-1 was carried out by using chlorobenzaldehdye by the methods. The compounds were screened for antibacterial activity against *E. coli*, *B. subtalis* and *S. aureus* in nutrient agar medium, and for antifungal activity against *Candida albicans* in Sabouraud's dextrose agar medium. All the derivatives (4a-e) showed good antifungal activity. The derivative 4a and 4b having phenyl and 4-methoxy phenyl ring showed highest antifungal activity.

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References

1 Kimmey M B, NSAID, ulcers and prostaglandins, *J Rheumatol*, 19, **1992**, 68-73.
2 Shen T Y, Toward more selective antiarthritic therapy, *J Med Chem*, 24, **1981**, (1), 1-5.
3 Ejaz P, Bhojani K, Joshi V R, NSAIDs and kidney, J Assoc Physicians India, Vol. 51, Aug. 2004, PP- 632-640.
4 Boschelli D H, Conner D T, Bornemeir D A, Dyer R D, Kennedy J A, Kuipers P J, Okonkwo G C, Schreir D J & Wright C D,1,3,4-Oxadiazole, 1,3,4-thiadiazole, and 1,2,4-triazole analogs of the fenamates: in vitro inhibition of cyclooxygenase and 5-lipoxygenase activities, *J Med Chem*, 36, **1993**, 1802-10.
5 Tozkoparan B, Gokhan N, Aktay G, Yesilada E &Eartan M,6-Benzylidenethiazolo[3,2-b]-1,2,4-triazole-5(6H)-ones substituted withibuprofen: synthesis, characterization and evaluation of anti-inflammatory activity**,** *Eur J Med Chem*, 35, **2000**, 743.

6 Suzuki F, Kuroda T &Tamura T, *J Med Chem*, 35, **1992**, 2863.
7 El-Feky S A&Abd el-Samii Z K, *Pharmazie*, 50, **1995**, 341.
8 Amir M, Khan M S Y&Zaman M S, *Indian J Chem*, 43B, **2004**, 2189.
9 Plaska E,Shahin G, Kelicen P, Duslu T N & Altinok G, *Il Farmaco*, 57, **2002**, 101.
10 Murthy S N &Srinivasa V*, Indian J Pharmacol*, 35, **2003**, 61.
11 Parekh H, Khunt R&Ladoon K, *Orient J Chem*, 18, **2002**, 135.
12 Patil L R, MandhareR P N, Bondge S P, Munde S B &Mane R A*, Indian JHeterocyclChem*, 12, **2003**, 245.
13 Dundar O B, Ozgen O, Menteşe A, Altanlar N, Atlı O, Kendi E&Ertan R, *Bioorg MedChem*, 15, **2007**, 6012.
14 Farghaly A M, Bekhit A A&Park J Y, *Arch Pharm Med Chem*, 333, **2003**, 53.
15 Bekhit A A&Azeim T A, *Bioorg MedChem*, 12, **2004**, 1935.
16 Bekhit A A, Ashour H M A &Guemei A, *Arch PharmChem Life Sci*, 338, **2005**, 167.
17 Barry A L, *The Antimicrobial Susceptibility test: Principle and Practice*(Lea &Febiger Philadelphia),**1976**, 180.
18 Winter CA, Risley E A &Nuss GW, *ProcSocExpBiol Med,*111, **1962**, 544.
19 Harwood L M, Moody C j & Percy J M, *Experimental Organic Chemistry*, 2nd Edn, (Blackwell Scientific Publications, London), **1994**, 644.

Table I-Anti-inflammatory activity of compounds **4a, 4b, 4c, 4d and 4e**

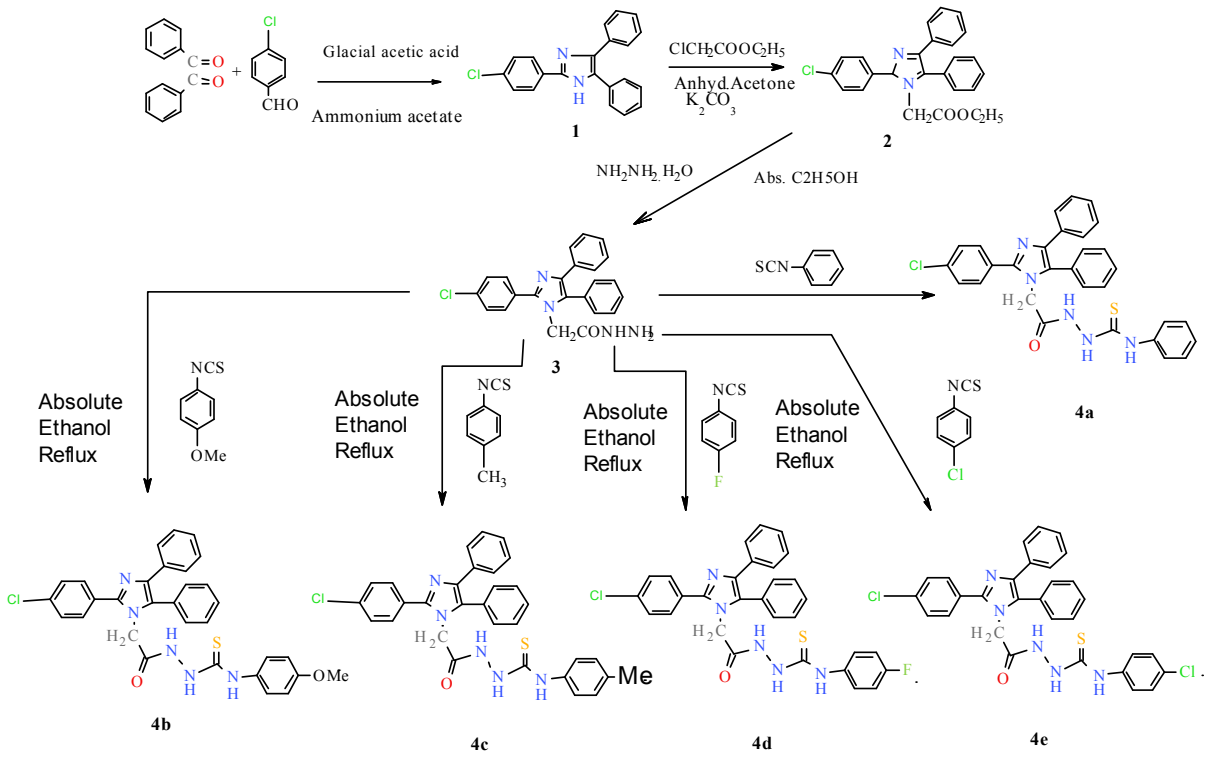
Compd.	Mean values (±SEM) of oedema Volume		Anti-inflammatory activity (% inhibition±SEM)	
	3hr	4hr	3hr	4hr
Control	1.74±0.076	1.62±0.082	----	---
Indomethacin	0.50±0.026	0.46±0.029	71.10±1.42	71.56±1.42
4a	1.06±0.048	0.97±0.047	39.32±1.37*	40.81±1.40*
4b	1.05±0.042	0.94±0.043	40.73±1.87*	41.90±1.21*
4c	0.82±0.031	0.74±0.035	53.00±1.67*	53.90±1.39*
Xd	0.83±0.028	0.75±0.028	52.44±1.28*	54.01±1.24*
Xe	0.32±0.031	0.25±0.018	81.98±1.77**	83.40±1.06*

Anti-inflammatory activity of the test compounds were compared w.r.t. standard drug. Data were analyzed by student's *t* test for n=6; *p<0.0001, **p<0.01, ***p<0.5

TableII- Antibacterial and antifungal activityof compounds **4a, 4b, 4c, 4d and 4e**

Compd.	Antibacterial activity						Antifungal activity	
	E.coli		*B.subtalis*		*S.aureus*		*C.albicans*	
	Zone of inhibition (mm)	% inhibition	Zone of inhibition (mm)	% inhibition	Zone of inhibition (mm)	% inhibition	Zone of inhibition (mm)	% inhibition
4a	22	61.11	14	43	14	48	20	75
4b	22	61.11	15	47	21	72	20	69

4c	23	67	15	47	20	69	17	58.6
Xd	22.5	62.5	20	62	19	65.5	20	69
Xe	19	52	12	50	22	75	20	685
Ofloxacin	36	100	32	100	29	100	---	---
Voriconazole	---	---	---	---	---	---	29	100



Scheme I

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