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N-Substituted-3-chloro-2-azetidinones: Synthesis and characterization of new novel anti-inflammatory agents

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ABSTRACT

Various substituted 4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-substituted (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloro azetidin–2–one containing different functional groups have been synthesized by treating fluorochloroaniline with KSCN in presence of bromine in glacial acetic acid and ammonia to get 2-amino-6-fluoro-7-chloro-(1,3)-benzothiazole, which was treated with anthranillic acid in presence of dry pyridine to get 2-amino-*N*-(6-fluoro-7-chloro-(1,3)-benzothiazol-2-yl) benzamide. To the above, refluxed with vanillin and alcohol in presence of Conc.HCl to get 2-(3-hydroxy-4-methoxy benzylidene amino phenyl amido)-6-fluoro-7-chloro-(1, 3)-benzothiazole or Schiff's base. A Solution of Schiff's base in 1,4-dioxane was added to well-stirred mixture of chloroacetyl chloride and triethylamine to get Azetidinone. To the above product different primary and secondary aromatic amines in presence of DMF were treated to get newly targeted compound through replacing at 7th position chlorine.

The lead compounds were characterized by melting point, TLC, calculated elemental analysis, UV, IR and ^{1}H NMR spectral studies. The compounds were tested for anti-inflammatory activity (*in-vitro*) by protein denaturation method and showed significant activity at low and high concentration compared to standard; still further studies are requested.

KEYWORDS: Fluorine, Benzothiazole, Azetidinone, Anti-inflammatory activity.

Introduction

2-Azetidinones, commonly known as β-lactams, are well-known heterocyclic compounds among the organic and medicinal chemists. The activity of the famous antibiotics such as penicillins, cephalosporins and carbapenams are attributed to the presence of 2-azetidinone ring in them. Recently, some other types of biological activity besides the antibacterial activity have been reported in compounds containing 2-azetidinone ring [1]. Such biological activities include antimicrobial[2], anti-tuburcular[3], carbonic anhydrase inhibitors[4], local anaesthatics[5], anti-inflammatory[6], anthelmintic[7], anticonvulsant[8], hypoglycemic activity [9].

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The β-lactams also serve as synthons for many biologically important classes of organic compounds.[10] Due to this, the investigation of chemistry and biology of these compounds continue to appeal the synthetic and medicinal organic chemists.

It is well known that the introduction of fluorine atom into an organic molecule causes dramatic changes in its biological profile, mainly due to high electro negativity of fluorine, the strong carbon-fluorine bond and increased solubility in lipids.[11] In search for new biodynamic potent molecule, it was thought worthwhile to incorporate some additional heterocyclic moieties in the β-lactam nucleus and study their biological and pharmacological activity.[12] The review of literature reveal prompted us to synthesize substituted fluorobenzothiazole, azetidinone targeted compounds and those

will be screened for anti-inflammatory activity.

Materials and Methods
Experimental Section

Step I: 4-fluoro-3-chloro aniline 1.45g (0.01 mol) was treated with potassium thiocyanate (KSCN) 8gm (0.08mol) in presence of glacial acetic acid (20ml) and bromine to get 2-amino-6-fluoro-7-chloro-benzothiazole.

Step II: 2-amino-6-fluoro-7-chloro-benzothiazole (5.22 g, 0.026 mol), treated with Anthranillic acid (4.0 g, 0.029 mol) in presence of Pyridine (20 ml, 0.25 mol) to get 2-(o-amino phenyl amido)-6–fluoro -7-chloro (1,3) benzothiazole.

Step III: 2-(o-amino phenyl amido)-6–fluoro -7-chloro (1, 3) benzothiazole (0.01 mol) refluxed with vanillin (0.015 mol) and ethanol (20ml) in presence of Conc.HCl (3-4 drops) to get 2-(3-hydroxy-4-methoxy benzylidene amino phenyl amido)-6-fluoro-7-chloro-(1,3) benzothiazole or Schiff's base.

Step IV: A Solution of Schiff's base (0.01 mol) in 1, 4-dioxane (50ml) was added to well-stirred mixture of chloroacetyl chloride (0.95 ml, 0.012 mol) and triethylamine (1.08 ml, 0.02 mol) at 0^{o} C. The reaction mixture was then stirred for 18 - 20 hrs and kept aside for 3 days at room temperature. The product was recrystallised from N,N' Dimethyl formamide (DMF).

Step V: Azetidine were treated with double the quantities of various substituted aniline, anisidine, PABA and piperazine, refluxed for 2 hours in presence of N,N-dimethyl formamide (DMF). The mixture was cooled and poured into crushed ice. The solid separated was filtered off, dried and crystallized from alcohol and benzene **(Table No. 1)**.

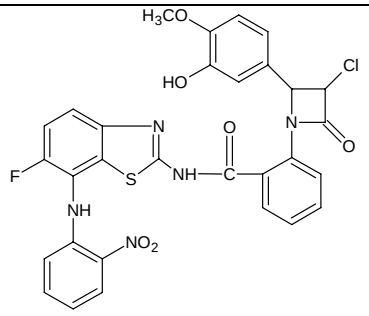
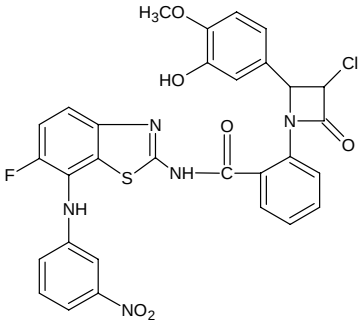
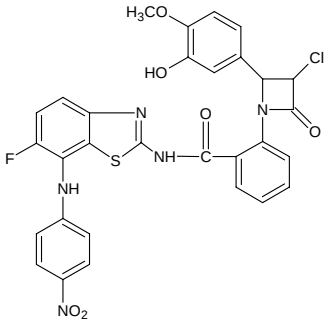
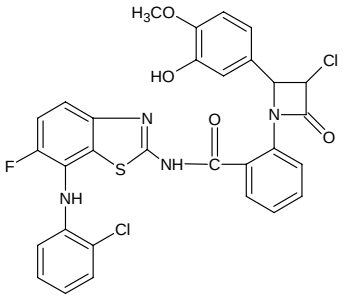
Identification and Characterization:

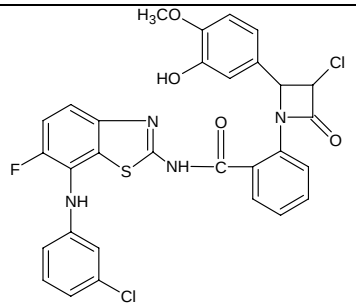
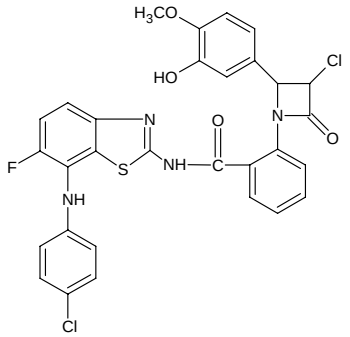
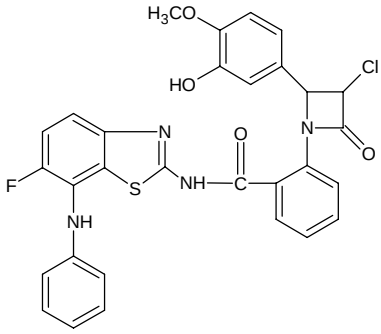
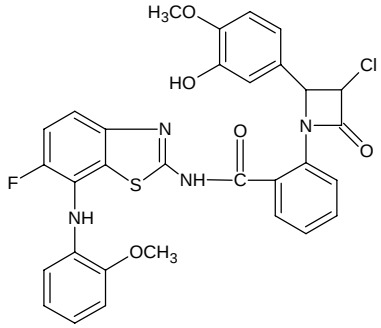
Melting points were determined in open capillaries and are uncorrected. IR spectra (KBr pellet technique) were recorded using a Perkin-Elmer 237 spectrophotometer. ^{1}H NMR spectra were recorded on Bruker AM 400 instrument (at 400 MHz) using tetramethylsilane (TMS) as an internal standard and DMSO-*d6* as a solvent. Chemical shifts are given in parts per million (ppm). Splitting patterns are designated as follows: s- singlet, d- doublet, t- triplet, q- quartet and m-multiplet. Mass spectra (MS) were recorded on Shimadzu GC-MS operating at 70eV. All the synthesized compounds were purified by recrystallization. The reactions were followed up and the purity of compounds was monitored on pre-coated TLC plates and visualizing the spots in ultraviolet light.

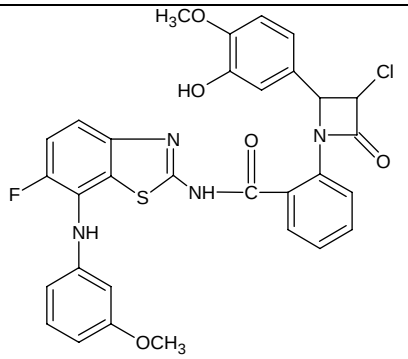
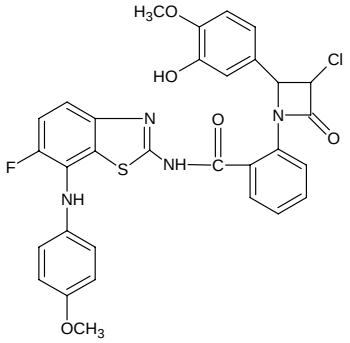
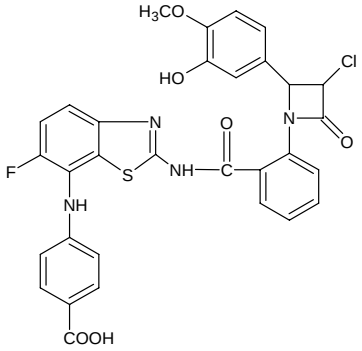
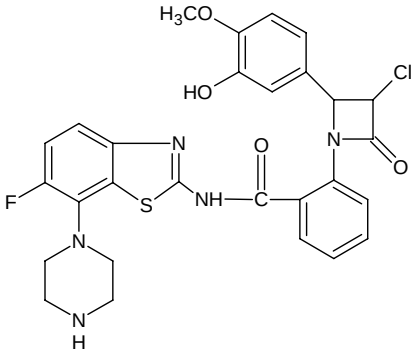
4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-o-nitroanilino (1, 3)-benzothiazol-2'-yl) amido-2-ph enyl]-3-chloro azetidin–2–one (A_1). Yield 78%; mp 190^{o}C; IR (KBr) ν (cm^{-1}); 3350 (Ar-NH); 1750 (C=0); 1550 (C=N); 1710 (C=C); 1450 (NO_2); 1130 (C-F); 720 (C–S); 1300 (Sec.Ar.Amine); 840 (C–Cl); 1250 (C-O-C); 1390 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.5 (s, 1H, -NH-); 9.2 (s, 1H, -NH-); 8.4 (s, 1H, -OH); 7.0 to 8.0 (m, 13H, Ar-H); 6.8 (d, β lactum 2H – Proton); 3.7 (s, 3H, $-OCH_3$); Analysis Calcd. for $C_{30}H_{21}O_6SN_5FCl$; C, 56.83%; H, 3.34%; N, 11.05%; Found; C, 56.81%; H, 3.33%; N, 11.01%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-m-nitroanilino (1, 3)-benzothiazol-2'-yl) amido-2-ph enyl]-3-chloro azetidin–2–one (A_2). Yield 82%; mp 178^{o}C; IR (KBr) ν (cm^{-1}); 3370 (Ar-NH); 1710 (C=0); 1525 (C=N); 1680 (C=C); 1450

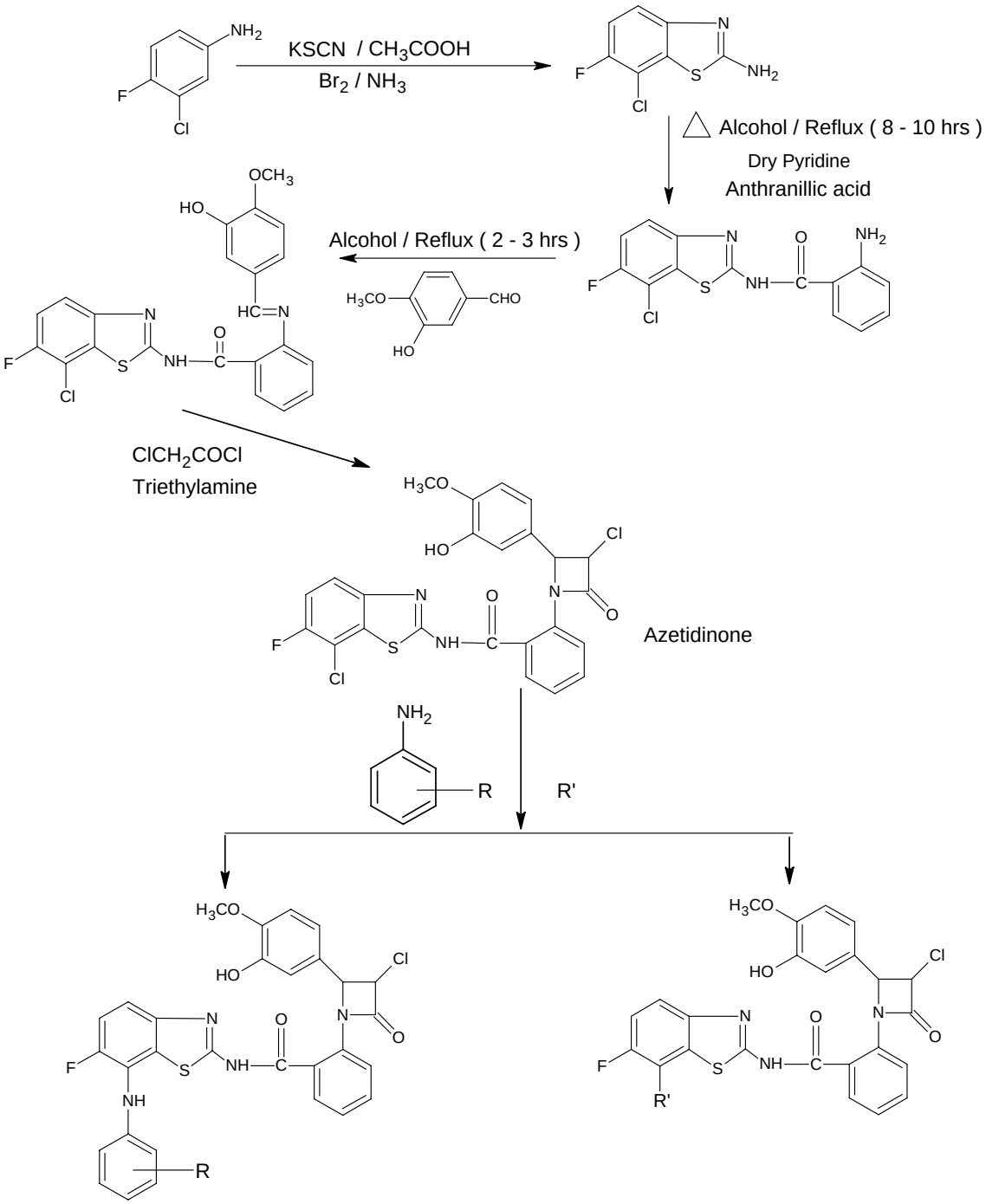
Table No. 1 List of compounds synthesized

Sl. No.	Compound Code	Structure Chemical	Name
1	A_1		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-o-nitroanilino(1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloro azetidin–2–one
2	A_2		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-m-nitroanilino(1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloro azetidin–2–one
3	A_3		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-p-nitroanilino (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloro azetidin–2–one
4	A_4		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-o-chloroanilino (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloro azetidin–2–one

Sl. No.	Compound Code	Structure Chemical	Name
5	A_5		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-m-chloroanilino (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloro azetidin–2–one
6	A_6		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-p-chloroanilino (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloro azetidin–2–one
7	A_7		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- anilino (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloro azetidin–2–one
8	A_8		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- o-methoxyanilino (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloroazetidin–2–one

Sl. No.	Compound Code	Structure Chemical	Name
---	---		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- m - methoxyanilino (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloroazetidin–2–one
9	A_9	
10	A_{10}		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- p - methoxyanilino (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloroazetidin–2–one
11	A_{11}		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- p – carboxyanilino (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloroazetidin–2–one
12	A_{12}		4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- piperzino (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloroazetidin–2–one

Scheme


KSCN / CH3COOH
Br2 / NH3
Alcohol / Reflux (8 - 10 hrs)
Dry Pyridine
Anthranillic acid
Alcohol / Reflux (2 - 3 hrs)
ClCH2COCl
Triethylamine
Azetidinone
R
R'
R = o-NO2, m-NO2, p-NO2 aniline
o-Cl, m-Cl, p-Cl aniline
aniline
o,m,p, anisidine
PABA
R' = piperazine

(NO_2); 1160 (C-F); 720 (C–S); 1340 (Sec.Ar.Amine); 840 (C–Cl); 1250 (C-O-C); 1390 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.6 (s, 1H, -NH-); 9.4 (s, 1H, -NH-); 8.2 (s, 1H, -OH); 7.0 to 8.0 (m, 13H, Ar-H); 6.8 (d, β lactum 2H – Proton); 3.6 (s, 3H, -OCH_3); Analysis Calcd. for $C_{30}H_{21}O_6SN_5FCl$; C, 56.83%; H, 3.34%; N, 11.05%; Found; C, 56.82%; H, 3.32%; N, 11.04%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-p-nitroanilino (1,3)-benzothiazol-2'-yl) amido-2-ph enyl]-3-chloro azetidin–2–one (A_3). Yield 75%; mp 183^{o}C; IR (KBr) ν (cm^{-1}); 3370 (Ar-NH); 1700 (C=0); 1540 (C=N); 1660 (C=C); 1420 (NO_2); 1160 (C-F); 725 (C–S); 1310 (Sec.Ar.Amine); 850 (C–Cl); 1255 (C-O-C); 1380 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.6 (s, 1H, -NH-); 9.3 (s, 1H, -NH-); 8.6 (s, 1H, -OH); 7.2 to 8.0 (m, 13H, Ar-H); 7.0 (d, β lactum 2H – Proton); 3.6 (s, 3H, -OCH_3); MS (m/z) 634 (M^+) 517.5, 379.4, 201.3, Analysis Calcd. for $C_{30}H_{21}O_6SN_5FCl$; C, 56.83%; H, 3.34%; N, 11.05%; Found; C, 56.81%; H, 3.32%; N, 11.01%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-o-chloroanilino (1,3)-benzothiazol-2'-yl) amido-2-ph enyl]-3-chloro azetidin–2–one (A_4). Yield 72%; mp 164^{o}C; IR (KBr) ν (cm^{-1}); 3380 (Ar-NH); 1730 (C=0); 1540 (C=N); 1680 (C=C); 1155 (C-F); 720 (C–S); 1300 (Sec.Ar.Amine); 850 (C–Cl); 1250 (C-O-C); 1380 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.6 (s, 1H, -NH-); 9.4 (s, 1H, -NH-); 8.6 (s, 1H, -OH); 7.0 to 7.8 (m, 13H, Ar-H); 6.9 (d, β lactum 2H – Proton); 3.8 (s, 3H, -OCH_3); Analysis Calcd. for $C_{30}H_{22}O_4S_2N_4FCl$; C, 57.79%; H, 3.39%; N, 8.99%; Found; C, 57.73%; H, 3.35%; N, 8.92%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-m-chloroanilino (1,3)-benzothiazol-2'-yl) amido-2-ph enyl]-3-chloro azetidin–2–one (A_5). Yield 74%; mp 132^{o}C; IR (KBr) ν (cm^{-1}); 3400 (Ar-NH); 1765 (C=0); 1540 (C=N); 1690 (C=C); 1170 (C-F); 725 (C–S); 1310 (Sec.Ar.Amine); 820 (C–Cl); 1250 (C-O-C); 1380 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.3 (s, 1H, -NH-); 9.0 (s, 1H, -NH-); 8.6 (s, 1H, -OH); 7.2 to 8.0 (m, 13H, Ar-H); 6.8 (d, β lactum 2H – Proton); 3.8 (s, 3H, -OCH_3); Analysis Calcd. for $C_{30}H_{22}O_4S_2N_4FCl$; C, 57.79%; H, 3.39%; N, 8.99%; Found; C, 57.72%; H, 3.33%; N, 8.96%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-p-chloroanilino (1,3)-benzothiazol-2'-yl) amido-2-ph enyl]-3-chloro azetidin–2–one (A_6). Yield 73%; mp 126^{o}C; IR (KBr) ν (cm^{-1}); 3290 (Ar-NH); 1720 (C=0); 1530 (C=N); 1680 (C=C); 1160 (C-F); 725 (C–S); 1300 (Sec.Ar.Amine); 840 (C–Cl); 1250 (C-O-C); 1380 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.5 (s, 1H, -NH-); 9.2 (s, 1H, -NH-); 8.4 (s, 1H, -OH); 7.0 to 8.0 (m, 13H, Ar-H); 6.8 (d, β lactum 2H – Proton); 3.7 (s, 3H, -OCH_3); MS (m/z) 634 (M^+) 613.9, 454.7, 369.8, 203.8; Analysis Calcd. for $C_{30}H_{22}O_4S_2N_4FCl$; C, 57.79%; H, 3.39%; N, 8.99%; Found; C, 57.74%; H, 3.36%; N, 8.94%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- a nilino (1,3)-benz othiazol-2'-yl) amido-2-phenyl]-3-chloro az etidin–2–one (A_7). Yield 76%; mp 112^{o}C; IR (KBr) ν (cm^{-1}); 3390 (Ar-NH); 1755 (C=0); 1510 (C=N); 1690 (C=C); 1150 (C-F); 720 (C–S); 1255 (Sec.Ar.Amine); 840 (C–Cl); 1220 (C-O-C); 1380 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.6 (s, 1H, -NH-); 9.2 (s, 1H, -NH-); 8.2 (s, 1H, -OH); 7.4 to 8.2 (m, 14H, Ar-H); 6.8 (d, β lactum 2H – Proton); 3.6 (s, 3H, -OCH_3); Analysis Calcd. for $C_{30}H_{22}O_4S_2N_4FCl$; C, 61.17%; H, 3.76%; N, 9.51%; Found; C, 61.14%; H, 3.72%; N, 9.46%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- o-methoxyanilino (1,3)-benzothiazol-2'-yl) amido-2-ph enyl]-3-chloroazetidin–2–one (A_8). Yield 65%; mp 124°C; IR (KBr) ν (cm^{-1}); 3350 (Ar-NH); 1720 (C=0); 1540 (C=N); 1685 (C=C); 1165 (C-F); 725 (C–S); 1310 (Sec.Ar.Amine); 830 (C–Cl); 1250 (C-O-C); 1390 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.5 (s, 1H, -NH-); 9.2 (s, 1H, -NH-); 8.4 (s, 1H, -OH); 7.0 to 8.0 (m, 13H, Ar-H); 6.8 (d, β lactum 2H – Proton); 3.8 (s, 3H, $-OCH_3$); 3.6 (s, 3H, $-OCH_3$); Analysis Calcd. for $C_{31}H_{24}O_5SN_4FCl$; C, 60.14%; H, 3.91%; N, 9.05%; Found; C, 60.13%; H, 3.87%; N, 9.01%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- m - methoxyanilino (1,3)-benzothiazol-2'-yl) amido-2-ph enyl]-3-chloroazetidin–2–one (A_9). Yield 69%; mp 118°C; IR (KBr) ν (cm^{-1}); 3310 (Ar-NH); 1730 (C=0); 1550 (C=N); 1650 (C=C); 1130 (C-F); 725 (C–S); 1310 (Sec.Ar.Amine); 840 (C–Cl); 1245 (C-O-C); 1380 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.5 (s, 1H, -NH-); 9.2 (s, 1H, -NH-); 8.4 (s, 1H, -OH); 7.0 to 8.0 (m, 13H, Ar-H); 6.8 (d, β lactum 2H – Proton); 3.8 (s, 3H, $-OCH_3$); 3.6 (s, 3H, $-OCH_3$); 6.4 (d, β lactum 2H – Proton); Analysis Calcd. for $C_{31}H_{24}O_5SN_4FCl$; C, 60.14%; H, 3.91%; N, 9.05%; Found; C, 60.12%; H, 3.88%; N, 9.02%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- p - methoxyanilino (1,3)-benzothiazol-2'-yl) amido-2-ph enyl]-3-chloroazetidin–2–one (A_{10}). Yield 83%; mp 158°C; IR (KBr) ν (cm^{-1}); 3400 (Ar-NH); 1750 (C=0); 1560 (C=N); 1660 (C=C); 1170 (C-F); 730 (C–S); 1300 (Sec.Ar.Amine); 850 (C–Cl); 1230 (C-O-C); 1385 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.5 (s, 1H, -NH-); 9.2 (s, 1H, -NH-); 8.4 (s, 1H, -OH); 7.0 to 8.0 (m, 13H, Ar-H); 6.8 (d, β lactum 2H – Proton); 3.8 (s, 3H, $-OCH_3$); 3.6 (s, 3H, $-OCH_3$); Analysis Calcd. for $C_{31}H_{22}O_6SN_4FCl$; C, 60.14%; H, 3.91%; N, 9.05%; Found; C, 60.11%; H, 3.89%; N, 9.01%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'- p – carboxyanilino (1,3)-benzothiazol-2'-yl) amido-2-ph enyl]-3-chloroazetidin–2–one (A_{11}). Yield 77%; mp 260°C; IR (KBr) ν (cm^{-1}); 3320 (Ar-NH); 1700 (C=0); 1530 (C=N); 1640 (C=C); 1165 (C-F); 730 (C–S); 1310 (Sec.Ar.Amine); 840 (C–Cl); 1270 (C-O-C); 1380 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 10.2 (s, 1H, -COOH); 9.5 (s, 1H, -NH-); 9.2 (s, 1H, -NH-); 8.4 (s, 1H, -OH); 7.0 to 8.0 (m, 13H, Ar-H); 6.8 (d, β lactum 2H – Proton); 3.8 (s, 3H, $-OCH_3$); 3.6 (s, 3H, $-OCH_3$); Analysis Calcd. for $C_{31}H_{22}O_6SN_4FCl$; C, 58.82%; H, 3.50%; N, 8.85%; Found; C, 58.77%; H, 3.47%; N, 8.82%.

4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-piperzino (1,3)-benz othiazol-2'-yl) amido-2-phenyl]-3-chloroaz etidin–2–one (A_{12}). Yield 85%; mp 308°C; IR (KBr) ν (cm^{-1}); 3300 (Ar-NH); 1650 (C=0); 1550 (C=N); 1650 (C=C); 1190 (C-F); 740 (C–S); 1290 (Sec.Ar.Amine); 850 (C–Cl); 1290 (C-O-C); 1380 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ 9.5 (s, 1H, -NH-); 8.4 (s, 1H, -OH); 7.0 to 8.0 (m, 9H, Ar-H); 6.8 (d, β lactum 2H – Proton); 3.8 (s, 3H, $-OCH_3$); 2.6 (t, 4H, $(CH_2)_2$); 2.4 (t, 4H, $(CH_2)_2$); Analysis Calcd. for $C_{30}H_{22}O_4S_2N_4FCl$; C, 57.78%; H, 4.33%; N, 12.03%; Found; C, 57.74%; H, 4.30%; N, 12.81%.

In vitro anti-inflammatory study

The synthesized compounds are screened for anti-inflammatory activity by using inhibition of albumin denaturation technique.

The Ibuprofen was used as standard drug. Both standard and test drugs were dissolved in minimum amount of dimethyl formamide

(DMF) and diluted with phosphate buffer (0.2 M, pH 7.4). Final concentration of DMF in all solutions was less than 2.5%. Test solution (1 ml) containing different concentrations of drug was mixed with 1 ml of albumin solution in phosphate buffer and incubated at 27˚ ± 1˚ C in BOD incubator for 15 min. Denaturation was induced by keeping the reaction mixture at 60˚ ± 10˚ C in water bath for 10 min. After cooling the denaturation (concentration of albumin) was measured at 660 nm (UV-Visible spectrophotometer SL-159, Elico India Ltd.). Percentage inhibition of denaturation was calculated from control where no drug was added. Each experiment was done in triplicate and average was taken **(Table No. 2)**.[13]

$$\% \text{ of inhibition} = 100 \times \left(\frac{Vt}{Vc} - 1 \right)$$

Table No. 2 Anti-inflammatory activity of synthesized compounds (*In-vitro* models)

Sl No	Name of the compounds	Absorbance value (Mean ± SE)	Inhibition of denaturation in (%)
01	Control	0.098 ± 0.009	--
02	Ibuprofen	0.190 ± 0.002	93.87
03	A_1	0.138 ± 0.004	62.92
04	A_2	0.136 ± 0.004	20.40
05	A_3	0.137 ± 0.003	50.00
06	A_4	0.139 ± 0.002	40.80
07	A_5	0.129 ± 0.002	73.80
08	A_6	0.130 ± 0.002	68.02
09	A_7	0.131 ± 0.001	23.46
10	A_8	0.132 ± 0.004	79.93
11	A_9	0.112 ± 0.003	73.80
12	A_{10}	0.118 ± 0.002	53.74
13	A_{11}	0.119 ± 0.001	40.81
14	A_{12}	0.120 ± 0.003	76.53

Results and Discussion

Synthesized compounds of 4-(m-hydroxy-p-methoxy phenyl)-1-[(6'-fluoro-7'-substituted (1,3)-benzothiazol-2'-yl) amido-2-phenyl]-3-chloro azetidin–2–one were tested for anti-inflammatory activity by *in-vitro* method and compared with standard Ibuprofen; showed significant anti-inflammatory activity.

Among compounds tested A_5, A_8, A_9 and A_{12} showed significant anti-inflammatory activity when compared to standard drug Ibuprofen.

Conclusion

Result of present study demonstrate that, a new class of different aromatic primary and secondary amines encompassing azetidinone to get targeted molecules were synthesized and evaluated for anti-inflammatory activity (*in-vitro*) by protein denaturation method. The tested compounds are showing appreciable inhibition of protein denaturation compared to standard. Among the tested A_5, A_8, A_9 and A_{12} showed better anti-inflammatory activity. It can be concluded that this class of compounds certainly holds great promise towards good active leads in medicinal chemistry. A further study to acquire more information concerning pharmacological activity is in progress.

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References

1. Girija, S. Singh., Elbert Mbukwa., Tshepo Pheko., *ARKIVOC*, 2007 (ix), 80-90.
2. Sutoris, V., Halgas, J., *Chem. Abstr.,* 1984, 100, 103234 s.

3. Ares Jaffrey., *Chem. Abstr.,* 1991, 114, 71453 d.

4. Wollesdrof, O.W. Jr., Schwam, H., *Chem. Abstr.,* 1989, 111, 194656 x.

5. Costakes, E., Tsatsas. G., *Chem. Abstr.,* 1979, 90, 203935 q.

6. Srinivasa, G.M., Jayachandran, E., Shivakumar, B., Sreenivasa Rao, D., *Oriental Journal of Chemistry*, 2004, 20(1), 103-110.

7. Sreenivasa, G.M., Shivkumar, B., Jayachandran. E., *Indian Drugs*, 2006, 43 (4).

8. Turner, R.A., XV edn., (Ed. Turner RA), Academic Press, New York, 1965, 165-172.

9. Chernykh, V.P., Sidorenko, O.F., *Chem. Abstr.*, 1983, 98, 89233 x.

10. Conte, L., et al., *J. Fluorine Chem*, 1995, 70, 175-179.

11. Desbois Michel., Eur Pat., APP.l EP. 248746 (IPC Co7Co85/00), *Chem. Abstr*., 1987, 108, 159896 a.

12. Biological assays, *Indian Pharmacopoeia Published by Govt. of India*, 1996, 2, 88.

13. Sreenivasa Rao, D., Jayachandran, E., Sreenivasa, G.M., Shivakumar, B., *Oriental J. of Chemistry*, 2005, 21(1), 113-116.