Synthesis and Anti-inflammatory Activity of Some Novel 3-(6-Substituted-1, 3-benzothiazole-2-yl)- 2-[(4-substituted phenyl) amino] methyl] quinazolines-4 (3*H*)-ones

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Abstract: A series of novel 3-(6-substituted-1, 3-benzothiazole-2-yl)-2-[(4-substituted phenyl) amino] methyl] quinazolines-4(3*H*)-ones were synthesized by treating 2-(chloromethyl)-3-(6-substituted-1, 3-benzothiazole-2-yl) quinazoline-4-(3*H*)-one (**II_{a-d}**) with various substituted amine. The compounds (**II_{a-d}**) prepared by treating 2-[(chloroacetyl) amino] benzoic acid with different 2-amino-6-substituted benzothiazole. Elemental analysis, IR, ¹HNMR and mass spectral data confirmed the structure of the newly synthesized compounds. Synthesized quinazolines-4-one derivative were investigated for their anti-inflammatory and antibacterial activity.

Keywords: Quinazoline, Benzothiazole, Anti-inflammatory activity.

Introduction

Quinazoline 4-one ring system have been consistently rewarded as a promising molecule because of its broad spectrum pharmaceutical activity like antihistaminic activity¹, anti-inflammatory², antibacterial³, antidiabetic⁴, anticancer⁵, antifungal⁶, anthelmintics⁷ and antitubercular activities⁸.

Benzothiazole is one of the oldest and potent heterocyclic compounds having anti-inflammatory activities⁹⁻¹⁰, anthelmintic activity¹¹. Structure activity relationship studies of quinazoline ring system revealed in various literature¹⁻⁸.

As these two heterocycles are potent as biologically active compound, in the present study we are planned to prepared compounds containing both quinazoline fused with benzothiazole. In view of these observations, we report herein the reaction of substituted benzothiazole with 2-[(chloroacetyl) amino] benzoic acid to get 2-(chloromethyl)-3-(6-substituted-1, 3-benzothiazole-2-yl) quinazoline-4(3*H*)-one (**II_{a-d}**).

Final derivatives were prepared by treating **II_{a-d}** with different substituted amines to get (**III_{a1,a4} – III_{d1-d4}**) and performed their anti-inflammatory and antibacterial activity.

o-Amino benzoic acid is reacted with chloroacetyl chloride in the presence of benzene to form 2-[(chloroacetyl) amino] benzoic acid (**I**) which on reaction with different substituted benzothiazole in the presence of toluene and PCl_5 gives 2-(chloromethyl) 3[6(substituted) 1,3-benzothiazole-2-yl] quinazoline-4(3*H*)-ones (**II_{a-d}**) which were later treated with different substituted amine to yield 2-(amilomethyl)-3-(6-substituted-1, 3-benzothiazole-2-yl) quinazolin-4 (3*H*)-ones (Scheme 1).

Scheme 1.

The IR spectra of 2-[(chloroacetyl) amino] benzoic acid showed characteristic absorption band at $3200\text{--}3300\text{ cm}^{-1}$ was attributed to NH, which were disappeared by the formation of 2-(chloromethyl) 3[6(substituted) 1,3-benzothiazole-2-yl] quinazoline-4(3*H*)-ones. The ^1H NMR, LCMS, IR and elemental analysis supported the structure of title compounds. Physical and analytical data of title compound and its other substituted derivatives are given in Table 1.

Experimental

All the chemicals were purchased from Merck and used without purification. Analytical TLC was performed on silica Gel F₂₅₄ plates (Merck) with visualization by UV light. Melting points were determined in open capillaries on a ThermoNik melting point apparatus, Mumbai, India and are uncorrected. The IR spectra (KBr, γ max, cm^{-1}) were run on Shimadzu-8400 FTIR spectrophotometer. ^1H NMR (δ ppm, $\text{CDCl}_3/\text{DMSO-d}_6$) spectra were recorded using Bruker WM-400 spectrometer with TMS as internal standard. Mass spectra were recorded on Micromass Q-TOF and Shimadzu LCMS 2010A Mass spectrometer. Elemental analysis was performed on Thermo Finnigan FLASH EA 1122 CHNS analyzer and was within 0.4% theoretical values.

Synthesis of 2-[(chloroacetyl) amino] benzoic acid (I)

Anthranilic acid (0.1 mol) is taken in round bottom flask to this 100 mL of benzene is added and made homogenous by stirring on a magnetic stirrer for 30 min. The chloro acetyl chloride (0.1 mol) is added and stirred for 2 h. After the completion of reaction the solution is poured on crushed ice and obtained solid was filtered and dried. The product is recrystallized from chloroform: alcohol (9:1). Yield: 95%; M.P: $188\text{--}189^\circ\text{C}$.

Table 1. Physical and analytical data of title compound and its other substituted derivatives.

Compound	R	Mol. formula	FW	Yield, %	Melting point, °C
III a₁	H	C ₂₃ H ₁₈ N ₄ OS	398	38	165-167
III a₂	CH ₃	C ₂₄ H ₂₀ N ₄ OS	412	53	150-152
III a₃	OCH ₃	C ₂₄ H ₂₀ N ₄ O ₂ S	428	45	Above 300
III a₄	Cl	C ₂₃ H ₁₇ N ₄ OSCl	432	47	128-130
III b₁	H	C ₂₃ H ₁₈ N ₄ O ₂ S	414	41	Above 300
III b₂	CH ₃	C ₂₄ H ₂₀ N ₄ O ₃ S	444	45	Above 300
III b₃	OCH ₃	C ₂₄ H ₂₀ N ₄ O ₂ S	428	48	Above 300
III b₄	Cl	C ₂₃ H ₁₇ N ₄ O ₂ SCl	448	41	88-90
III c₁	H	C ₂₂ H ₁₅ N ₄ OSCl	418	51	98-100
III c₂	CH ₃	C ₂₃ H ₁₈ N ₄ OSCl	433	45	138-140
III c₃	OCH ₃	C ₂₃ H ₁₈ N ₄ O ₂ SCl	449	43	158-160
III c₄	Cl	C ₂₂ H ₁₅ N ₄ OSCl ₂	453	49	163-165
III d₁	H	C ₂₂ H ₁₅ N ₄ OSF	402	52	Above 300
III d₂	CH ₃	C ₂₃ H ₁₈ N ₄ OSF	417	46	Above 300
III d₃	OCH ₃	C ₂₃ H ₁₈ N ₄ OSF	433	42	255-257
III d₄	Cl	C ₂₂ H ₁₅ N ₄ OSFCl	437	49	Above 300

2-[(Chloroacetyl) amino] benzoic acid (I)

IR (KBr, cm⁻¹): 2923 (Aromatic CH stretching), 1650 (C=O Stretching), 1478 (C=N), 815 (1,4- disubstituted benzene), 671 (C-S). ¹H NMR (DMSO-d₆) δ: 13.6-13.9 (s, 1H of COOH), 11.6 (s, 1H of NH), 7.2-8.6 (m, 4H of Aro-H), 4.4 (s, 2H of CH₂Cl). mass spectra (*m/z*): M⁺ = 214. Elemental data: cal, C, 55.26; H, 3.09; N, 7.16; Found: C, 55.06; H, 3.10; N, 7.11.

Synthesis of 2-(chloromethyl)-3-(6-substituted-1,3-benzothiazol-2-yl) quinazolin-4(3H)-one (II a-d)

A solution of compound (2-[(chloroacetyl) amino] benzoic acid) (**I**) (0.1 mol) and 2-amino-6-substituted benzothiazole (0.1 mol) in dry toluene (40 mL) was taken in a dropper and was added drop wise with constant stirring to a mixture of PCl₃ (6 g) in dry toluene (20 mL) placed in a round bottomed flask. The reaction mixture was stirred at reflux temperature for 3 h. After the completion of the reaction the solvent was removed in vacuum under pressure and the residue obtained was treated with a 5% solution of Na₂CO₃ (100 mL), the obtained solid was filtered, washed with water, dried and recrystallized with suitable solvent.

2-(Chloromethyl)-3-(6-methyl-1, 3-benzothiazol-2-yl) quinazolin-4(3H)-one (IIa)

IR (KBr, cm⁻¹): 2923, 2865(Aromatic CH stretching), 1648 (C=O Stretching), 1523,1478 (C=N). 815,760 (1,4- disubstituted benzene), 678(C-S). ¹HNMR (DMSO-d₆) δ: 6.9-8.2 (m, 7H, Ar-H), 4.2 (s, 2H, CH₂Cl), 1.2 (s, 3H, CH₃).mass spectra (*m/z*): M⁺ = 347. Elemental data: cal, C, 59.73; H, 3.54; N, 12.29; Found: C, 59.26; H, 3.36; N, 12.13. Yield: 65%. MP: 97- 98 °C.

2-(Chloromethyl)-3-(6-methoxy-1, 3-benzothiazol-2-yl) quinazolin-4(3H)-one (IIb)

IR(KBr,cm⁻¹): 2923, (Aromatic CH stretching), 1650 (C=O Stretching), 1478 (C=N). 815 (1,4- disubstituted benzene), 671 (C-S). ¹HNMR (DMSO-d₆) δ: 6.7-8.1 (m, 7H, Ar-H), 4.3 (s, 2H, CH₂Cl), 1.4 (s, 3H, CH₃). mass spectra (*m/z*): M⁺ = 358. Elemental data: cal, C, 57.06; H, 5.38; N, 11.47; Found: C, 56.98; H, 5.32; N, 11.57. Yield: 67%. MP: 152- 153 °C.

3-(6-Chloro-1,3-benzothiazol-2-yl)-2-(chloromethyl)quinazolin-4(3H)-one (IIc)

IR(KBr,cm⁻¹): 2919,2860 (Aromatic CH stretching), 1658 (C=O Stretching), 1520,1472 (C=N). 813,758 (1,4- disubstituted benzene), 668(C-S). ¹HNMR (DMSO-d₆) δ: 7.1-8.2 (m, 7H, Ar-H), 4.3 (s, 2H, CH₂Cl). Mass Spectra (*m/z*): M⁺= 362. Elemental data: cal, C, 53.05; H, 2.50; N, 11.60; Found: C, 53.01; H, 2.41; N, 11.49. Yield: 73%. MP: 177- 178 °C.

2-(Chloromethyl)-3-(6-fluoro-1,3-benzothiazol-2-yl)quinazolin-4(3H)-one (IIId)

IR(KBr,cm⁻¹): 2923, (Aromatic CH stretching), 1650 (C=O Stretching), 1478 (C=N). 815 (1,4- disubstituted benzene), 671 (C-S). ¹HNMR (DMSO-d₆) δ: 6.8-8.1 (m, 7H, Ar-H), 4.4 (s, 2H, CH₂Cl). Mass Spectra (*m/z*): M⁺= 346. Elemental data: cal, C, 55.58; H, 2.62; N, 12.15; Found: C, 55.41; H, 2.46; N, 11.98. Yield: 67%. MP: 98- 90 °C.

Synthesis of 3-(6-substituted-1, 3-benzothiazole-2-yl)-2-[(4-substituted or unsubstituted phenyl) amino] methyl] quinazolines-4(3H)-ones (IIIa₁-a₄), (IIIb₁-b₄), (IIIc₁-c₄), (IIId₁-d₄).

A mixture of compound **IIa-d** (0.01 mol.), substituted amine (0.01 mol) & 25 mL of pyridine is taken in a round-bottomed flask and refluxed for 4 to 6 hours. After the completion of the reaction the contents of the flask is poured on crushed ice, the solid separated was filtered and dried. The product was recrystallized with suitable solvents.

2-(Anilinomethyl)-3-(6-methyl-1, 3-benzothiazol-2-yl) quinazolin-4(3H)-one (IIIa₁)

IR (KBr,cm⁻¹): 2930, (Aromatic CH stretching), 1645 (C=O Stretching), 1465 (C=N). 835 (1,4- disubstituted benzene), 675 (C-S). ¹HNMR (DMSO-d₆) δ: 6.9-8.2 (m, 12H, Ar-H), 4.2 (s, 2H, CH₂Cl), 1.3 (s, 3H, CH₃). Mass Spectra (*m/z*): M⁺= 399. Elemental data: cal, C, 69.32; H, 4.55; N, 14.06; Found: C, 68.89; H, 4.48; N, 13.98. Yield: 64%. MP: 165- 167 °C.

3-(6-Methyl-1,3-benzothiazol-2-yl)-2-[(4-methylphenyl) amino] methyl] quinazolin-4(3H)-one (a₂)

IR(KBr,cm⁻¹): 2930, (Aromatic CH stretching), 1645 (C=O Stretching), 1465 (C=N). 835 (1,4-disubstituted Benzene), 675 (C-S). ¹HNMR (DMSO-d₆) δ: 6.9-8.1 (m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 1.2-1.4 (m, 6H, CH₃), 6.6 (s, 1H, NH). Mass Spectra (*m/z*): M⁺= 413. Elemental data: cal, C, 69.88; H, 4.89; N, 13.58; Found: C, 69.58; H, 4.79; N, 13.48. Yield: 76%. MP: 150- 152 °C.

2-[(4-Methoxyphenyl) amino] methyl]-3-(6-methyl-1,3-benzothiazol-2-yl) quinazolin-4(3H)-one (IIIa₃)

IR(KBr, cm⁻¹): 2945, (Aromatic CH stretching), 1655 (C=O Stretching), 1435 (C=N). 845 (1,4-disubstituted benzene), 667 (C-S). ¹HNMR (DMSO-d₆) δ: 6.9-8.2 (m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 1.2-1.4 (m, 6H, CH₃ and OCH₃), 6.5 (s, 1H, NH). Mass Spectra (*m/z*): M⁺= 429. Elemental data: cal, C, 67.27; H, 4.70; N, 13.07; Found: C, 67.19; H, 4.68; N, 12.98. Yield: 74%. MP: 150- 152 °C.

2-[(4-Chlorophenyl)amino]methyl]-3-(6-methyl-1,3-benzothiazol-2-yl) quinazolin -4(3H)-one (IIIa₄)

IR(KBr,cm⁻¹): 2943, (Aromatic CH stretching), 1648 (C=O Stretching), 1441 (C=N). 843 (1,4-disubstituted benzene), 669 (C-S). ¹HNMR (DMSO-d₆) δ: 7.2-8.9 (m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 1.3 (s, 3H, CH₃), 6.8 (s, 1H, NH). Mass Spectra (*m/z*): M⁺= 434. Elemental data: cal, C, 63.51; H, 3.96; N, 12.94; Found: C, 63.50; H, 3.89; N, 12.87. Yield: 78%. MP: above 300 °C.

2-(Anilinomethyl)-3-(6-methoxy-1, 3-benzothiazol-2-yl) quinazolin-4 (3H)-one (IIIb₁)

IR(KBr,cm⁻¹): 2955, (Aromatic CH stretching), 1645 (C=O Stretching), 1456 (C=N). 864 (1,4-disubstituted benzene), 686 (C-S). ¹HNMR (DMSO-d₆) δ: 7.0-8.2 (m, 12H, Ar-H), 4.2 (s, 2H,

CH₂), 1.4 (s, 3H, OCH₃), 6.8 (s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 445. Elemental data: cal, C, 66.64; H, 4.38; N, 13.52; Found: C, 66.57; H, 4.37; N, 13.60. Yield: 68%. MP: above 300 °C.

2-(-(4-Methyl)anilinomethyl)-3-(6-methoxy-1,3-benzothiazol-2-yl)quinazolin-4 (3H)-one (IIIb₂)

IR(KBr,cm⁻¹): 2942, (Aromatic CH stretching), 1625 (C=O Stretching), 1434 (C=N). 878 (1,4-disubstituted benzene), 664(C-S). ¹HNMR (DMSO-d₆) δ: 6.8-8.2 (m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 1.3-1.5 (m, 6H, CH₃ and OCH₃), 7.3 (s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 429. Elemental data: cal, C, 67.27; H, 4.70; N, 13.07; Found: C, 67.24; H, 4.68; N, 13.02. Yield: 71%. MP: above 300 °C.

2-(-(4-Methoxy) anilinomethyl)-3-(6-methoxy-1, 3-benzothiazol-2-yl) quinazolin-4 (3H)-one (IIIb₃)

IR(KBr,cm⁻¹): 2952, (Aromatic CH stretching), 1636 (C=O Stretching), 1447 (C=N). 865 (1,4-disubstituted benzene), 657(C-S). ¹HNMR (DMSO-d₆) δ: 6.8-8.2 (m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 1.2-1.4 (m, 6H, OCH₃), 6.5(s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 445. Elemental data: cal, C, 64.85; H, 4.54; N, 12.60; Found: C, 64.79; H, 4.49; N, 12.57. Yield: 77%. MP: above 300 °C.

2-[(4-Chlorophenyl) amino] methyl}-3-(6-methoxy-1, 3-benzothiazol-2-yl) quinazolin-4(3H)-one (IIIb₄)

IR(KBr,cm⁻¹): 2948, (Aromatic CH stretching), 1634 (C=O Stretching), 1456 (C=N). 878 (1,4-disubstituted benzene), 687(C-S). ¹HNMR (DMSO-d₆) δ: 7.2-8.9 (m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 1.5 (s, 3H, OCH₃), 6.7 (s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 449. Elemental data: cal, C, 61.53; H, 3.82; N, 12.48; Found: C, 61.48; H, 3.79; N, 12.46. Yield: 71%. MP: 88-90 °C.

2-(Anilinomethyl)-3-(6-chloro-1,3-benzothiazol-2-yl)quinazolin-4(3H)-one (IIIc₁)

IR(KBr,cm⁻¹): 2954 (Aromatic CH stretching), 1636 (C=O Stretching), 1446 (C=N). 868 (1,4- disubstituted benzene), 685 (C-S). ¹HNMR (DMSO-d₆) δ: 7.2-8.9 (m, 12H, Ar-H), 4.3 (s, 2H, CH₂), 6.8 (s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 419. Elemental data: cal, C, 63.88; H, 3.61; N, 13.37; Found: C, 63.87; H, 3.57; N, 13.27. Yield: 76%. MP: 98-100 °C.

3-(6-Chloro-1, 3-benzothiazol-2-yl)-2-[(4-methylphenyl) amino] methyl} quinazolin-4(3H)-one (IIIc₂)

IR(KBr,cm⁻¹): 2956 (Aromatic CH stretching), 1632 (C=O Stretching), 1448 (C=N). 862 (1,4-disubstituted benzene), 678 (C-S). ¹HNMR (DMSO-d₆) δ: 6.9-8.1(m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 1.4 (s, 3H, CH₃), 6.7(s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 434. Elemental data: cal, C, 63.81; H, 3.96; N, 12.94; Found: C, 63.78; H, 3.94; N, 12.89. Yield: 68%. MP: 138-140 °C.

3-(6-Chloro-1, 3-benzothiazol-2-yl)-2-[(4-methoxyphenyl) amino] methyl} quinazolin-4(3H)-one (IIIc₃)

IR(KBr,cm⁻¹): 2942 (Aromatic CH stretching), 1637 (C=O Stretching), 1442 (C=N). 866 (1,4-disubstituted benzene), 674 (C-S). ¹HNMR (DMSO-d₆) δ: 7.1-8.1 (m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 1.4 (s, 3H, OCH₃), 6.5(s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 450. Elemental data: cal, C, 61.53; H, 3.82; N, 12.48; Found: C, 61.49; H, 3.79; N, 12.43. Yield: 77%. MP: 158-160 °C.

3-(6-Chloro-1, 3-benzothiazol-2-yl)-2-[(4-chlorophenyl) amino] methyl} quinazolin-4(3H)-one (IIIc₄)

IR(KBr,cm⁻¹): 2945 (Aromatic CH stretching), 1642 (C=O Stretching), 1433 (C=N). 876 (1,4- disubstituted benzene), 668 (C-S). ¹HNMR (DMSO-d₆) δ: 6.9-8.1 (m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 6.7(s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 454. Elemental data: cal, C, 58.29; H, 3.11; N, 12.36; Found: C, 58.26; H, 3.09; N, 12.39. Yield: 69%. MP: 163-165 °C.

2-(Anilinomethyl)-3-(6-fluoro-1,3-benzothiazol-2-yl) quinazolin-4(3H)-one (III**_d₁)**

IR(KBr,cm⁻¹): 2943 (Aromatic CH stretching), 1638 (C=O Stretching), 1438 (C=N). 873 (1,4- disubstituted benzene), 664 (C-S). ¹HNMR (DMSO-d₆) δ: 7.2-8.7 (m, 12H, Ar-H), 4.4 (s, 2H, CH₂), 6.8 (s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 403. Elemental data: cal, C, 65.66 ; H, 3.76; N, 13.92; Found: C, 65.67; H, 3.75; N, 13.90; Yield: 78%. MP: above 300 °C.

3-(6-Fluoro-1, 3-benzothiazol-2-yl)-2-[(4-methylphenyl) amino] methyl} quinazolin-4(3H)-one (III**_d₂)**

IR(KBr,cm⁻¹): 2942 (Aromatic CH stretching), 1632 (C=O Stretching), 1432 (C=N). 867 (1,4- disubstituted benzene), 666 (C-S). ¹HNMR (DMSO-d₆) δ: 7.1-8.2(m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 1.3 (s, 3H, CH₃), 6.8 (s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 418. Elemental data: cal, C, 66.33; H, 4.11; N, 13.45; Found: C, 66.32; H, 4.09; N, 13.43. Yield: 82%. MP: above 300 °C.

3-(6-Fluoro-1, 3-benzothiazol-2-yl)-2-[(4-methoxyphenyl) amino] methyl} quinazolin-4(3H)-one (III**_d₃)**

IR(KBr,cm⁻¹): 2947 (Aromatic CH stretching), 1645 (C=O Stretching), 1436 (C=N). 864 (1,4-disubstituted benzene), 655 (C-S). ¹HNMR (DMSO-d₆) δ: 7.1-8.2 (m, 11H, Ar-H), 4.4 (s, 2H, CH₂), 1.4 (s, 3H, OCH₃), 6.5 (s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 434. Elemental data: cal, C, 63.88; H, 3.96; N, 12.96; Found: C, 63.81; H, 3.93; N, 12.92. Yield: 78%. MP: 255-258 °C.

2-[(4-Chlorophenyl) amino] methyl}-3-(6-fluoro-1, 3-benzothiazol-2-yl) quinazolin-4(3H)-one (III**_d₄)**

IR(KBr,cm⁻¹): 2947 (Aromatic CH stretching), 1645 (C=O Stretching), 1436 (C=N). 864 (1,4- disubstituted Benzene), 655 (C-S). ¹HNMR (DMSO-d₆) δ: 7.1-8.1 (m, 11H, Ar-H), 4.3 (s, 2H, CH₂), 6.7 (s, 1H, NH). Mass Spectra (*m/z*): M⁺ = 438. Elemental data: cal, C, 60.48; H, 3.23; N, 12.82; Found: C, 60.40; H, 3.30; N, 12.86. Yield: 73%. MP: above 300 °C.

Anti-inflammatory activity

Data in Table 2 & 3 and Figure 1 showing anti-inflammatory activity of quinazoline derivatives in Carrageenan induced acute rat paw oedema model.

Results and Discussion**Anti-inflammatory activity**

The synthesized derivatives were tested for anti-inflammatory activity at the dose of 200 mg/ kg in acute-inflammatory models in Rats. The compounds under study-exhibited moderate to significant Anti-inflammatory activity and the results are tabulated in the table. Compound **III**_a₄, **III**_b₄, **III**_c₃, **III**_c₄, **III**_d₃ and **III**_d₄ shown reduction in Oedema volume of 68.96%, 65.51%, 68.96%, 51.27%, 70.68% and 67.27% respectively and compound **III**_a₃, **III**_b₃, **III**_b₂, **III**_b₃, **III**_c₁, **III**_c₂, **III**_d₁ and **III**_d₂ exhibited a moderate Inhibition of 31.03%, 41.37%, 37.92%, 48.27%, 37.27%, 31.03%, 38.27% and 34.48% respectively. Where the rest of the compounds tested, exhibited a minimum inhibition compared to the standard diclofenac sodium, which shown a reduction in Oedema volume by 83.78% in carrageenan induced Rat hind paw Oedema model.

Structure activity relationship studies for anti-inflammatory activity reveals that compound like **III**_a₄, **III**_b₄, **III**_c₃, **III**_c₄, **III**_d₃ and **III**_d₄ showed significant activity may be due to the presence of electron withdrawing group *i.e.* Cl, F as substituents on benzothiazole ring, which is attached to third position of Quinazoline nucleus, which may be responsible for marked anti-inflammatory activity.

Table 2. Anti-inflammatory activity of compounds **IIIa₁-a₄**, **IIIb₁-b₄**, **IIIc₁-c₄** & **IIId₁-d₄**.

Group	Treatment	Dose mg/kg	<i>Paw oedema volume</i>							
			After 1 st h		After 2 nd h		After 3 rd h		After 4 th h	
			Mean	% ROV	Mean	% ROV	Mean	% ROV	Mean	% ROV
1	Control	0.5 mL	0.16	-	0.21	-	0.26	-	0.29	-
2	Standard	20	0.15	6.96	0.12	41.20	0.88	66.30	0.01	83.78
3	IIIa₁	200	0.13	15.62	0.17	19.04	0.23	11.53	0.26	10.34
4	IIIa₂	200	0.15	6.25	0.19	9.52	0.19	26.92	0.20	31.03
5	IIIa₃	200	0.14	12.50	0.18	14.28	0.17	34.61	0.17	41.37
6	IIIa₄	200	0.12	25.00	0.14	33.33	0.13	50.00	0.09	68.96
7	IIIb₁	200	0.15	6.25	0.19	9.52	0.20	23.07	0.22	24.13
8	IIIb₂	200	0.13	18.75	0.15	28.57	0.18	30.76	0.18	37.93
9	IIIb₃	200	0.14	12.50	0.17	19.04	0.16	38.46	0.15	48.27
10	IIIb₄	200	0.13	18.75	0.16	23.80	0.15	42.30	0.10	65.51
11	IIIc₁	200	0.13	15.62	0.15	26.19	0.18	28.07	0.18	37.24
12	IIIc₂	200	0.14	11.25	0.17	19.04	0.19	24.23	0.20	31.03
13	IIIc₃	200	0.06	59.37	0.10	52.23	0.16	38.46	0.09	68.96
14	IIIc₄	200	0.15	6.25	0.16	23.80	0.17	34.61	0.14	51.72
15	IIId₁	200	0.13	18.75	0.16	23.80	0.18	28.07	0.17	38.27
16	IIId₂	200	0.12	25.00	0.14	30.95	0.18	30.76	0.19	34.48
17	IIId₃	200	0.14	09.37	0.18	14.28	0.14	46.15	0.08	70.68
18	IIId₄	200	0.10	37.50	0.12	42.85	0.12	53.38	0.09	67.27

ROV- Reduction in paw Oedema volume.

Figure 1. Anti-inflammatory activity of quinazoline derivatives*Antibacterial activity*

The results of the newly synthesized compounds are reported as MIC against *staphylococcus aureus* (*S. aureus*), *bacillus subtilis* (*B. subtilis*), (gram-positive bacteria), *pseudomonas aeruginosa* (*P. aeruginosa*), *bacilis pumillus* (*b. pumillus*). Structure activity relationship studies for antibacterial activity, it was found that the entire compound showed poor activity as compared to standard (Ampicillin 50 and 100 / mL). The poor activity may be due to the presence of bulkiness of substituents on quinazolines nucleus.

Table 3. Anti-inflammatory activity of Compound **IIIa₁-a₄**, **IIIb₁-b₄**, **IIIc₁-c₄**, **IIId₁-d₄**.

	1 h	2 h	3 h	4 h
Std	6.96	41.2	66.3	83.78
IIIa₁	15.62	19.04	11.53	10.34
IIIa₂	6.25	9.52	26.92	31.03
IIIa₃	12.5	14.28	34.61	41.37
IIIa₄	25.00	33.33	50.00	68.96
IIIb₁	6.25	9.52	23.07	24.13
IIIb₂	18.75	28.57	30.76	37.93
IIIb₃	12.5	19.04	38.46	48.27
IIIb₄	18.75	23.8	42.3	65.51
IIIc₁	15.62	26.19	28.07	37.24
IIIc₂	11.3	19.0	24.2	31.0
IIIc₃	59.37	52.23	38.46	68.86
IIIc₄	6.25	23.8	34.61	51.72
IIId₁	18.75	23.8	28.07	38.27
IIId₂	25	30.95	30.76	34.48
IIId₃	9.37	14.28	46.16	70.68
IIId₄	37.5	42.85	53.38	67.27

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