Structure–Activity Relationship and Docking Analysis of Benzothiazoles as Emerging Anti-Inflammatory Agents: An Overview

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Abstract

The heterocyclic class of bicyclic chemicals includes benzothiazole. Benzothiazole derivatives have a wide range of biological actions, including those against diabetes, convulsants, analgesics, leishmaniasis, malaria, histamine, and fungus. They also have effects against cancer, inflammation, tumours, viruses, bacteria, and proliferative cells. Inhibiting cycloxygenase-2 is one of benzothiazole derivatives' most important uses (COX-2). In this work, the anti-inflammatory and analgesic properties of benzothiazole derivatives are highlighted using a thorough literature review. Different substituted benzothiazoles combined with azetidinones, indoles, oxazoles, oxadiazoles, sulphonamides, triazoles, pyrimidines, and pyrazolines exhibit notable anti-inflammatory and analgesic activity. The current study thus focuses on the and anti-inflammatory properties of variously modified benzothiazole derivatives.

Keywords – *Benzothiazole, Anti-inflammatory, COX, LOX*

1. Introduction –

Inflammation and discomfort are frequently results of bacterial infections. Typically, analgesic and anti-inflammatory medications are provided at the same time. **[19]** Inflammation is a complex process, it shows the bodies response to diverse stimuli and is caused due to several problems such as arthritis, asthma, and psoriasis, which require prolonged or repetitive therapy. Analgesic and anti-inflammatory medications specifically target Cyclooxygenase-2, which is produced by inflammatory stimulation like bacterial endotoxin and cytokines **[6]**. COX-1 and COX-2 are two kinds of COX proteins that are produced by our bodies, While COX-1 is present in the majority of human tissues, COX-II is present at very undetectable levels in some tissue **[21].** Cyclooxygenase-2 is a crucial enzyme for prostaglandin synthesis in inflammatory cells, which implies that it is the main mediator of inflammation and is competitively suppressed by NSAIDs. NSAIDs are an excellent option for treatment of various inflammation related disease, including rheumatoid arthritis and gout.

Heterocyles are significant pharmcophores that plays a key role in generation of special chemical compounds with pharmacological properties. Five membered heterocyclic which incorporate oxygen, nitrogen and sulphur are found in broad spectrum therapeutic agents which plays a significant role in drug discovery and drug development **[2]**. Benzothiazole is a flexible heterocyclic moiety which consist of 5-membered thiazole ring fused to benzene ring that serves as a key structural component of many artificial and naturally occurring marine creatures, together with plant-based compounds **[1,20]**. Benzothiazole is a weakly basic heterocyclic organo-sulfur compound. They are frequently utilized in product development bioorganic and medicinal chemistry **[4]**. Reported data showed that benzothiazole showed different types of pharmacological activity viz. anticancer, antimicrobial, anti-inflammatory, analgesic, antioxidant, antiviral antimalarial, antidiabetic etc **[1,6,9,20,21]**. Moreover, the benzothiazoles are known to present in a variety of therapeutically effective medicines, pramipexole ethoxzolamide, zopolrestat and riluzole are a few examples **[19]**.

Figure 1. 2D and 3D structure of Benzothiazole (C_7H_3NS)

The extensive study on the anti-inflammatory potential of Benzothiazole derivatives that is discussed in the current review will be useful in the future discovery of new drugs and the development of medications as anti-inflammatory and analgesics.

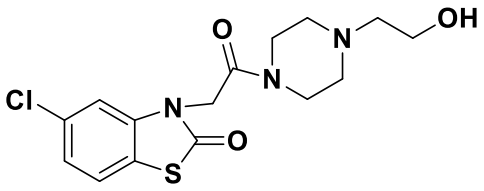


Figure 2. Benzothiazole ring containing anti-inflammatory drug.

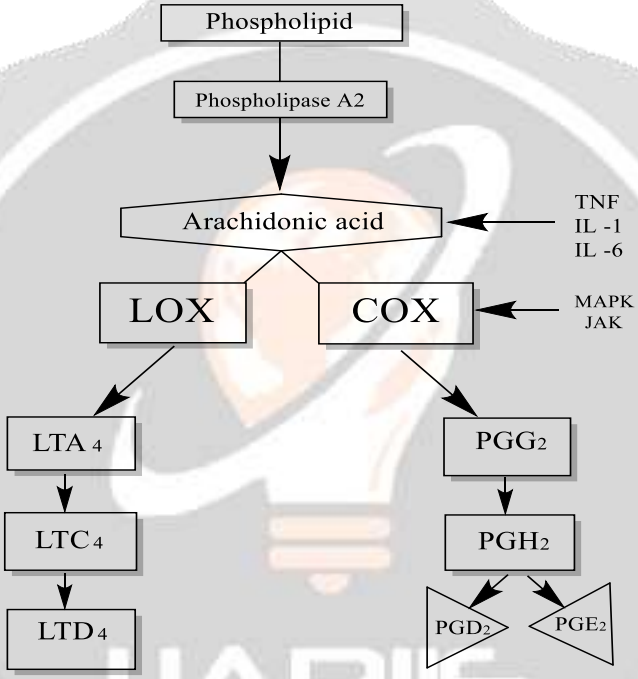


Figure 3. Process of inflammation

COX - cyclooxygenase; **LOX** - lipoxygenase, **IL** - leukotriene, **TNF** - tumour necrosis factor, **MAPK**—mitogen activated protein kinase

Benzothiazoles perform their anti-inflammatory activity mainly by interacting with receptors cyclooxygenase (COX-1 and COX-2), Cannabinoid receptor, 5-lipoxygenase, MAP kinase and TNF – alpha **[44]** (Figure 4).

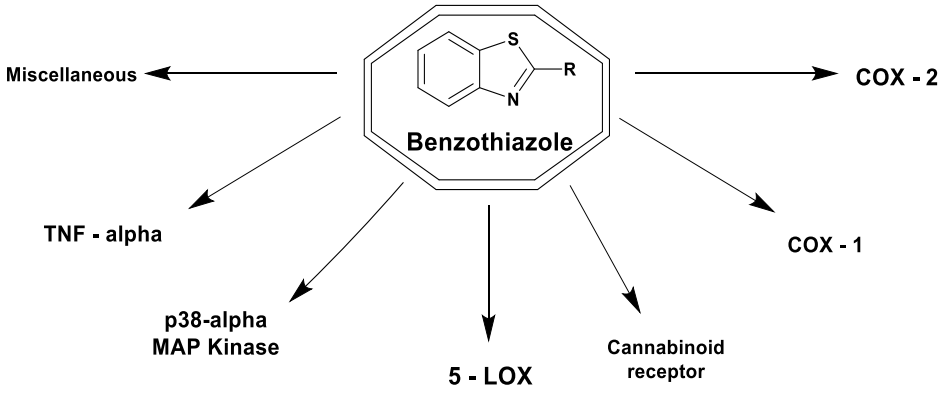


Figure 4. Benzothiazole interactions with clinically approved targets.

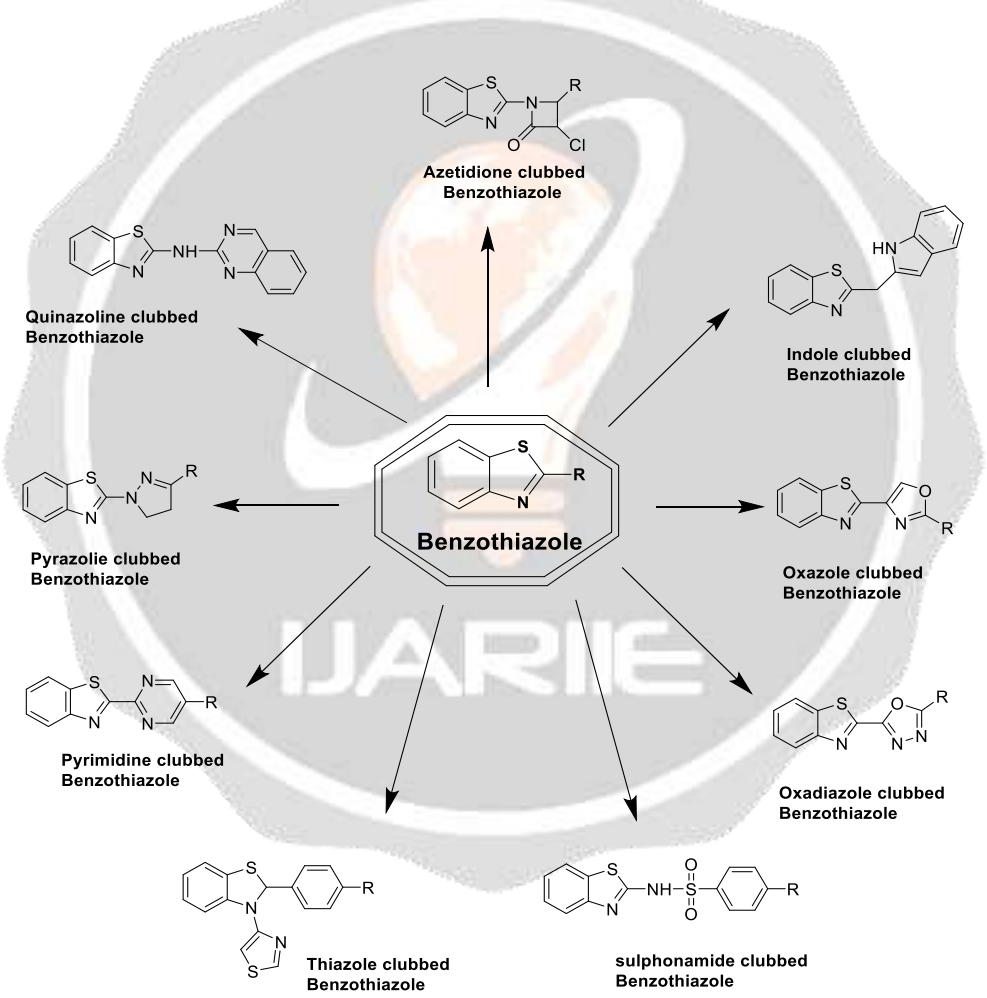


Figure 5. Different derivatives of Benzothiazoles

2. Benzothiazole Derivatives as Anti-Inflammatory agents–

2.1 COX - 2 Inhibition

Deb et al. (2014) Synthesised N-(benzothiazol-2-yl)-2-(substituted) acetamide scaffolds and investigated them for anti-inflammatory activity using carrageenan rat paw edema assay. Among the studied compounds, compound **1** depict maximum anti-inflammatory activity (% inhibition = 74.44), and activity was found to be significant of standard drug Indomethacin (% inhibition = 78.89). SAR studies revealed that the substitution of 4-fluoroaniline with amide group increased the anti-inflammatory activity. Molecular docking analysis demonstrated that compound **1** depicted maximum interaction among the synthesised compounds with human **COX-2**[5].

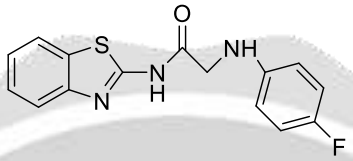


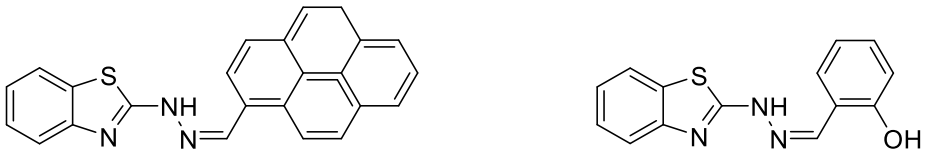
Figure 6. Substituted Acetamide clubbed Benzothiazole derivatives (1)

Raghavendra et al. (2012) Synthesized acetamide based benzothiazoles derivatives and evaluate them for anti-inflammatory activity by using carrageenan induced paw oedema method. Among all the studied compounds, compound **2a** (% inhibition = 41.30%) and **2b** (% inhibition = 34.78%) was found to showed most significant activity as compared to the standard drugs Naproxen (% inhibition = 71.70%) and rofecoxib (% inhibition = 81.01%). SAR studies suggested that the presence of unsubstituted piperazine ring and piperazine ring containing phenyl ring at N_4 enhanced the anti-inflammatory activity. Molecular docking study of these compounds suggested that compound **2a (**docking score = -6.48 kcal/mol) and **2b** (docking score = -6.23 kcal/mol) interacts with **COX-2** enzyme more efficiently than rofecoxib (docking score = -6.13 kcal/mol)[31].

(2a) **(2b)**

Figure 7. Substituted Acetamide clubbed Benzothiazole derivatives (2a and 2b)

Govindaiah et al. (2021) – reported benzothiazoles-hydrazone analogues and evaluate the anti-inflammatory activity by using Bovine serum albumin method and Egg serum albumin methods. Among all the studied compounds, Compound **3a** (IC50 = 26.99 µg/mL) and **3b** (IC50 = 26.69 % µg/mL) showed most potent anti-inflammatory activity as compared to the standard drug diclofenac sodium (IC50 = 22.57 µg/mL). Docking studies revealed that compound **3a** (docking score = -9.2 kcal/mol) and **3b** (docking score = -9.6 kcal/mol) showed significant docking score with **COX-2** enzyme when compared to standard drug Diclofenac Sodium[13].



(3a) **(3b)**

Figure 8. Hydrazone based benzothiazoles derivative (3a and 3b)

Wang et al. (2017) Synthesised benzothiazole based hydrazone analogues and investigated them for their in vitro anti-inflammatory activity using Human erythrocyte method and Hypotonic solution-induced method. Among the studied compound **4** ((IC50 = 90.74 μg/mL) depicted maximum anti-inflammatory activity, significant of standard drug Indomethacin ((IC50 = 40.04 μg/mL). Molecular docking analysis demonstrated that compound **4** (docking score =-8.90) depicted maximum interaction among the studied compounds when docked with human **COX-2**. SAR analysis indicated that substitution of aliphatic side chain with hydrazide moiety enhanced the anti-inflammatory activity [45].

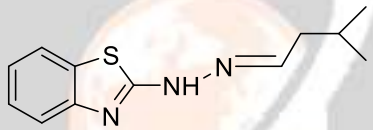


Figure 9. Hydrazone based benzothiazoles derivative (4)

Yatam et al. (2018) reported the synthesis of Mercapto-benzothiazole clubbed 1,2,4-oxadiazole derivatives and evaluated as anti-inflammatory agent using **COX-2**. Among the studied compounds **5a** (IC50 = 6.8 μg/mL) and **5b** (IC50 = 5.0 μg/mL) showed maximum inhibition against selective **COX-2** inhibitors with higher anti-inflammatory action than standard Ibuprofen[49].

(5a) **(5b)**

Figure 10. Substituted Oxadiazole clubbed Benzothiazole derivatives (5a-5b)

Zheng et al. (2020) Synthesised benzothiazole derivatives clubbed 1,3,4 - oxadiazole and screened them for In-Vivo Anti-inflammatory activity with the help of para-xylene-induced mice ear swelling model. The most potent anti-inflammatory activity is showed by compound **6** (% inhibition = 57.35%) significant of standard drug (% inhibition = 43.62%). The docking study also showed that compound **6** indicated highest binding affinity with **COX-2** enzyme among the studied compounds[50].

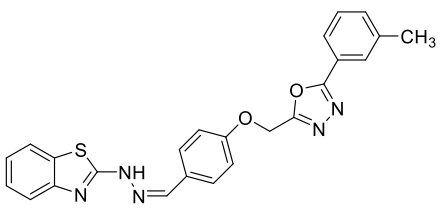


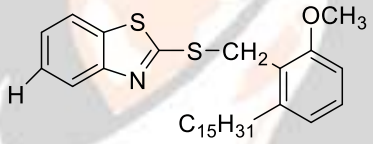
Figure 11. Substituted 1,3,4 - Oxadiazole clubbed Benzothiazole derivative (6)

Shafi et al. (2012) Synthesised 1,2,3-triazoles containing 2-mercapto benzothiazole scaffold, and tested for anti-inflammatory activity by using biochemical cyclooxygenase (COX) assays and carrageenan-induced hind paw edema method. Amongst the studied Compounds, compound **7a** (% inhibition = 78.11%) and **7b** ((% inhibition = 81.13%), depicted excellent anti-inflammatory activity as compared to standard drug Ibuprofen ((% inhibition = 71.69%). Molecular docking analysis demonstrated that compound **7a** (docking score = -12.54 kcal/mol) and **7b** (docking score = -12.38 kcal/mol) depicted maximum interaction when docked with human **COX-2**. The SAR studies reveal that substitution of para fluoro aniline greatly enhances the anti-inflammatory activity[37].

(7a) **(7b)**

Figure 12. Substituted Triazole clubbed Benzothiazole derivatives (7a and 7b)

Paramashivappa et al. (2013) prepared 2-[[2-alkoxy-6-pentadecylphenyl)methyl]thio]-1H-benzothiazoles, derivates and examined as anti-inflammatory agents. Compounds **8** exhibited maximum COX-2 inhibitory action (IC50 = 1.06 µg/mL) and activity was found to be significant as standard drug rofecoxib (IC50 = 10.057 µg/mL). SAR studies revealed that the presence of methoxy substitution at 2nd position of phenyl ring enhance the anti-inflammatory activity[29].

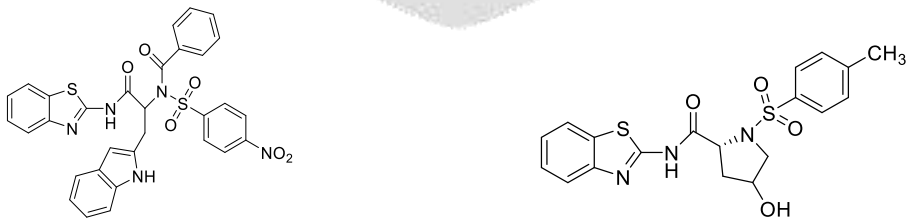


(19)

Figure 14. Benzothiazole derivatives (8)

2.2 COX - 1 inhibition

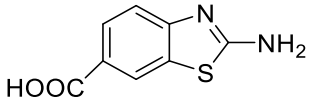
Ugwu et al., (2018) reported sulphonamide derivatives of benzothiazole, and tested for anti-inflammatory activity. Results indicated that compound **9a** (% inhibition = 89.20) and **9b** (% inhibition = 78.50) demonstrated excellent anti-inflammatory activity as compared to standard drug celecoxib (% inhibition = 61.10). The SAR study indicated that substitution of indole ring at acetamide moiety improve the anti-inflammatory activity. Molecular docking analysis demonstrated that compound **8a** depicted maximum interaction (docking score = -12.50 kcal/mol) among the studied compounds when docked with **COX-1**[41].



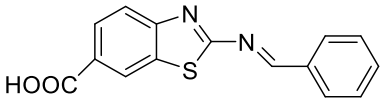
(8a) **(8b)**

Figure 13. Substituted sulfonamide clubbed Benzothiazole derivatives (8a and 8b)

Hashmi et al. (2022) Synthesised disubstituted-benzothiazole and evaluate them for anti-inflammatory activity using carrageenan-induced paw edema model in rats. Among the studied compound **10a** (% inhibition = 59.6) and compound **10b** (% inhibition = 54.7) depicted maximum anti-inflammatory activity. However, activity was found to be significant as standard drug nimesulide (% inhibition = 63.7). The SAR studies demonstrated that carboxyl group at 4th position improved the activity[15].



(10a)



(10b)

Figure 15. Miscellaneous benzothiazoles derivatives (10a and 10b)

2.3 Cannabinoid (CB2) inhibitor

Ghonim et al. (2019) Synthesised a series of benzothiazoles derivatives and evaluated all for anti-inflammatory activity, using CB1 EC50 assay and CB2 EC50 assay. Compound **11a** was found to be the most potent anti-inflammatory agent and showed significant inhibition as compared to standard drug Indomethacin (% inhibition = 75.40). The SAR studies showed that substitution of trifluoro methyl group at 3rd position of phenyl ring enhanced the anti-inflammatory activity. The molecular docking studies of the studied compound shows that compound **11a** showed maximum binding energy when docked with **CB2 receptor**[12].

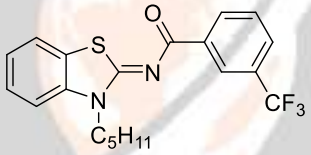
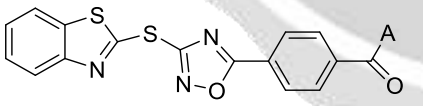


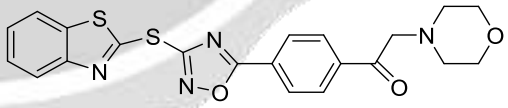
Figure 16. Benzothiazole derivative (11a)

2.4 5-LOX inhibition

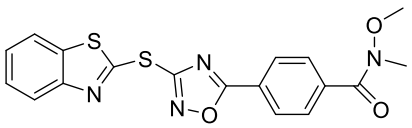
Yatam et al. (2018) reported the synthesis of mercapto-benzothiazole integrating 1,2,4-oxadiazole derivatives and biologically evaluated them using COX-2 and 5-LOX assays. The In-vivo studies indicated that Compounds **12a** (IC50 = 6.8 μg/mL) and **12b** (IC50 = 5.0 M μg/mL) were discovered to be strong, selective COX-2 inhibitors with higher anti-inflammatory action than standard Ibuprofen. Compounds **12c** and **12d** were showed to be strong inhibitors of **5-LOX** (IC50 = 5.1 M and IC50 = 5.5 M, respectively)[49].



(12a)



(12b)



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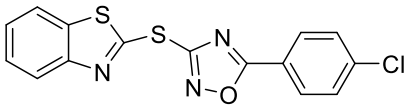


(12d)

Figure 17. Substituted Oxadiazole clubbed Benzothiazole derivatives (12a-12d)

Haroun et al. (2022) synthesised benzothiazole-based thiazolidinones derivatives investigated for their anti-inflammatory activity by using carrageenan-paw oedema method and LOX assay. Amongst the studied Compounds, **13a** (Inhibitory % = 69.57) depicted excellent anti-inflammatory activity as compared to standard drug indomethacin (Inhibitory % = 91.0) and compound **13a** (Inhibitory % = 91.00) also exhibited maximum activity in **5-LOX**. The SAR studies reveal that substitution of methoxy groups at para position of benzyl group greatly enhances the anti-inflammatory activity. Molecular docking analysis demonstrated that compound **13a** (docking score = −8.52 kcal/mol), depicted maximum interaction with human **5-LOX**[14].

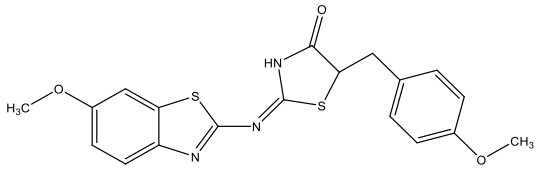
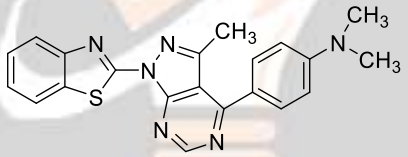


Figure 18. Substituted Oxadiazole clubbed Benzothiazole derivatives (13a)

2.5 p38α MAP kinase inhibition –

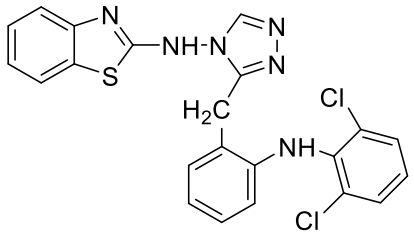
Azam et al. (2013) reported the synthesis of Pyrazolopyrimidines based benzothiazole derivatives, investigated anti-inflammatory activity using carrageenan induced method in Wistar albino rats. SAR studies revealed that the presence of OH group and $N(CH_3)_2$-C_6H_4 group at the para position of the pyrazolopyrimidine ring enhanced the activity. Compound **14a** showed maximum activity (% inhibition = 59.6) as compared to the reference drug diclofenac sodium (% inhibition = 62.6). Molecular docking analysis demonstrated that compound **14a** depicted maximum interaction when docked with **p38α MAP kinase enzyme**[3].



(14a)

Figure 19. Substituted pyrazolopyrimidines based benzothiazoles derivatives (14a)

Tariq et al. (2017) prepared bis-heterocycles containing 1,2,4-triazole-based benzothiazole-2-amines scaffold, and are tested for anti-inflammatory activity by using BSA denaturation inhibition assay and p38α MAP kinase inhibitory activity. Amongst the studied Compounds, compound **15a** (Inhibitory % = 68.05) depicted better anti-inflammatory activity as compared to standard drug diclofenac Sodium (Inhibitory % = 65.64). SAR studies revealed that substitution of 2-[(2,6-dichlorophenyl) amino] benzyl group at 3rd position of the triazole moiety increases the anti-inflammatory activity. Molecular docking analysis demonstrated that compound **15a** (docking score =-8.993 kcal/mol), **15b** (docking score = -88.14 kcal/mol), and **15c** (docking score =-8.673 kcal/mol) depicted maximum interaction when docked with **p38α MAP kinase**[38].



(14a)

Figure 20. Triazole based benzothiazoles derivatives (15a)

Tariq et al. (2018) reported the 1,2,4-Triazole containing benzothiazoles derivatives, all of the synthesised compounds were initially tested for anti-inflammatory activity. The in-vitro studies showed that Compound **16a** exhibited the maximum anti-inflammatory activity (% inhibition = 85.36) which is greater than standard drug Diclofenac (% inhibition = 82.54). In-vivo studies also indicated that compound **16a** shows best anti-inflammatory activity (% inhibition = 84.43) as compared to the standard drug diclofenac (% inhibition = 82.48). SAR studies indicated that the presence of p-fluoro aniline with triazole moiety enhanced the anti-inflammatory activity. Molecular docking analysis demonstrated that compound **16a** depicted maximum interaction (docking score = -7.353 kcal/mol) with **p38α MAP Kinase enzyme**[39].

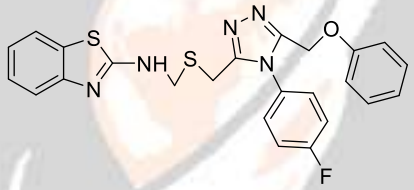
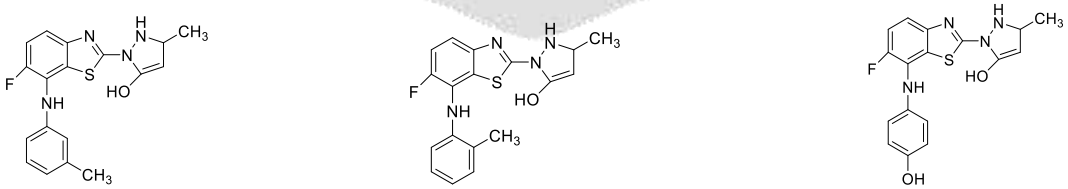


Figure 21. Substituted Triazole clubbed Benzothiazole derivative (16a)

2.6 TNF – alpha inhibition

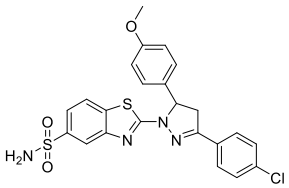
Ravi et al. (2013) **–** Synthesised fluorinated benzothiazoles derivatives and screened them for In-vivo anti-inflammatory activity using Carrageenan induced rat hind paw model using reference drug Diclofenac at different time intervals 0,1,2,3 and 4 hours. The most potent anti-inflammatory activity was showed by compound **17a** (% inhibition = 43.42%), **17b** (% inhibition = 42.29%), **17c** (% inhibition = 42.28%), and activity was found to be significant as compared to standard drug diclofenac (% inhibition = 38.59%). Docking studies revealed that among the studied compounds, Compound **17b** shows highest binding energy when docked with **TNF – alpha**. The SAR studies illustrated that the presence of o-methyl group and p-hydroxy group at the aniline moiety enhances the activity [32].



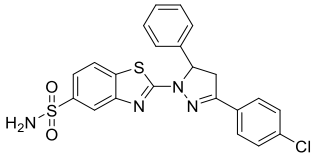
(17a) **(17b)** **(17c)**

Figure 22. Substituted fluorinated derivatives of benzothiazoles (17a-17c)

Kharbanda et al. (2014) obtained hybrid of pyrazolines clubbed benzothiazoles moiety using a carrageenan-induced paw edoema model, the anti-inflammatory efficacy of synthetic compounds was evaluated. Among all the studied compounds **19a** (% inhibition = 47.8%)**, 19b** (% inhibition = 49.1%), **19c** (% inhibition = 45.9%) and **19d** (% inhibition = 44.7%) shows significant activity a standard drug celecoxib (% inhibition = 73.1%). The SAR studies indicated that substitution of phenyl and p-methyl phenyl moiety at the 2nd position of pyrazole enhanced the anti-inflammatory activity. Molecular docking analysis demonstrated that compound **19a** and **19b** depicted maximum interactions as compared to standard drug celecoxib with **TNF-alpha**[18].



(19a)



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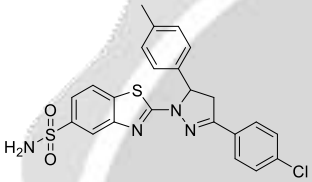

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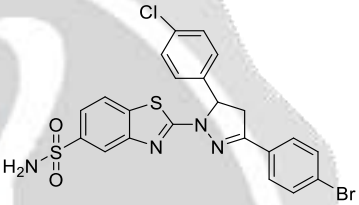
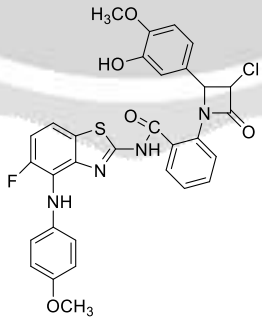


(19d)

Figure 24. Substituted Pyrazoline clubbed benzothiazole derivatives (19a-19c)

2.7 Miscellaneous

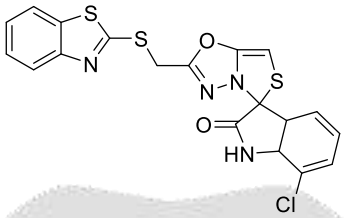
Kumar et al. (2012) Synthesised N-substituted-3-chloro-2-azetidinones clubbed benzothiazole derivatives, and evaluate anti-inflammatory activity. Among the studied compound **19a** depicted maximum anti-inflammatory activity (% inhibition = 79.93). However, activity was found to be significant as compared to standard drug ibuprofen (% inhibition = 93.87). SAR studies showed that the presence of methoxy group at the para position of aniline moiety increased the anti-inflammatory activity [23].



(20a)

Figure 25. Substituted Azetidinone clubbed Benzothiazole derivatives (20a)

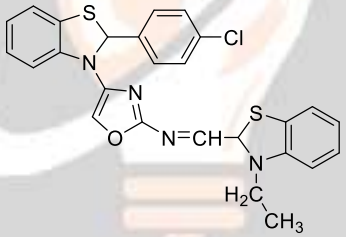
Kaur et al. (2012) reported the synthesis of indole-based benzothiazole derivatives, and investigated their anti-inflammatory potential using the carrageenan induced test (in-vivo). Among these Compound **20a** showed the strongest anti-inflammatory action (% inhibition = 69.2) even greater than reference drug (% inhibition = 63.4%) SAR analysis deduced that substitution of chloro group at the 3rd position of indolyl moiety improved the anti-inflammatory activity[17].



(21a)

Figure 26. Substituted Indole based benzothiazole derivatives (21a)

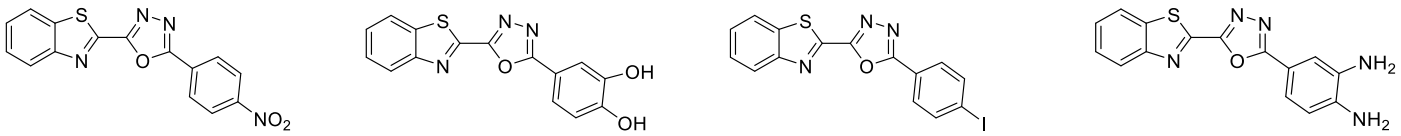
Kumar et al. (2021) obtained the oxazole based benzothiazoles derivatives and these compounds was tested for anti-inflammatory activity in albino rats. The compound **21c** showed highest anti-inflammatory activity (% inhibition = 33.8%), the activity was found to be significant as compared to the standard drug phenyl-butazone (% inhibition = 66.5). SAR studies deduced that the substitution of ethyl group at third position of benzothiazole moiety improved the anti-inflammatory activity[22].



(22a)

Figure 27. Substituted oxazole based benzothiazole derivatives (22a-22c)

Kumar et al. (2015) synthesised 3-benzothiazole-2-carbohydrazide derivatives as anti-inflammatory agent and activity was tested in Wistar rats using the carrageenan-induced rat paw edoema method. The Compounds **22a** (% inhibition = 81.91%), **22b** (% inhibition = 80.23%), **22c** (% inhibition = 80.23%), and **22d** (% inhibition = 81.54%) have showed equipotent anti-inflammatory action to standard drug diclofenac (% inhibition = 82.14%) [24] The SAR studies demonstrated that substitution of 4-nitro, 3,4-dihydro, 4-iodo and 3,4-diamino groups on the phenyl moiety increased the anti-inflammatory activity.

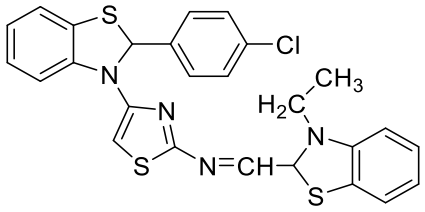


(23a) **(23b)** **(23c)**

(23d)

Figure 28. Substituted Oxadiazoles clubbed Benzothiazole derivatives(23a-23d)

Kumar et al., (2021) obtained the oxazole based benzothiazoles derivatives and tested for anti-inflammatory activity in albino rats. Among the all studied compounds **10a** showed significant anti-inflammatory activity (% inhibition = 34.7%) in comparison with standard drug phenyl-butazone (% inhibition = 66.5). The SAR studies revealed that the compound with ethyl substitution at third position of benzothiazole moiety improved the anti-inflammatory activity [22].



(24a)

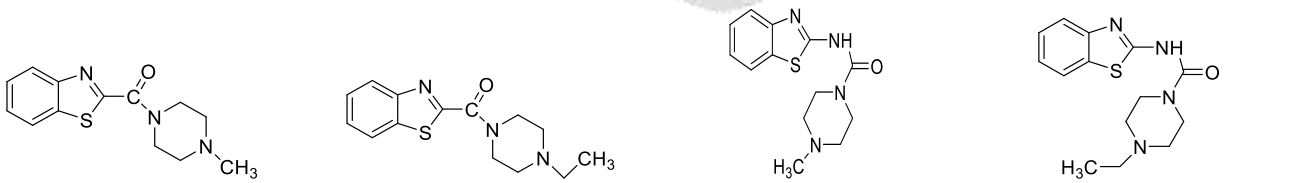
Figure 29. Substituted Thiazole clubbed benzothiazole derivative (24a and 24b)

Deodhar et al., (2012) - Synthesised thiazolidine clubbed benzothiazoles derivatives and evaluated their anti-inflammatory activity using Carrageenin induced hind-paw edema method. The compound **25a** (% inhibition = 65.5%) and compound **25b** was found to be the most potent anti-inflammatory agents (% inhibition = 62.29%) which was found significant to be significant as compared to standard drug Indomethacin (% inhibition = 75.40). The SAR studies showed that the presence of ethyl and methyl groups at the 5th position of benzothiazole moiety enhanced the anti-inflammatory [28].

(25a) **(25b)**

Figure 30. Substituted thiazolidine clubbed benzothiazole derivatives (25a-25b)

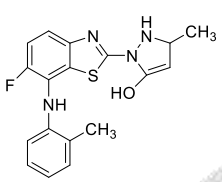
Vamsi et al., (2013) reported the synthesis of benzothiazole containing piperidines derivatives and evaluated for their anti-inflammatory activity. Compounds **26a** and **26b** showed moderate anti-inflammatory activity. The SAR of the studied compounds reveals that ethyl piperazine and methyl piperazine enhances the activity and presence of NH group between benzothiazole and carbonyl group didn't alter the activity **(26c and 26d)**[43].



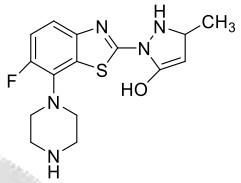
(26a) **(26b)** **(26c)** **(26d)**

Figure 31. Substituted piperidine clubbed benzothiazole derivatives (26a-26d)

Ravi et al., (2013) Synthesised pyrazolebased derivatives of benzothiazoles and screened them for In-vivo anti-inflammatory activity with the help of carrageenan induced rat hind paw model. The most potent anti-inflammatory activity is showed by **27b** (% inhibition = 45.52) and **27c** (% inhibition = 47.80) which is significant as compared to the standard drug (% inhibition = 49.80%). The SAR studies demonstrated that the substitution of toluidine and piperazine moiety at the 4th position of benzothiazoles improved the anti-inflammatory activity[32].



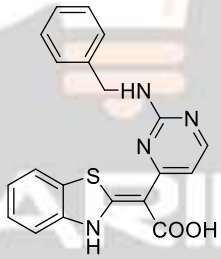
(27b)



(27c)

Figure 32. Substituted Pyrazole clubbed benzothiazole derivatives (27a-27b)

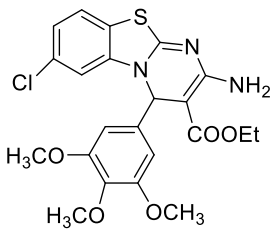
Doma et al., (2014) synthesised pyrimidine clubbed benzothiazole derivatives and evaluated for anti-inflammatory activity in a carrageenan-induced rat paw edoema model. Among the studied compounds **27b** (% inhibition = 63.1%) showed similar anti-inflammatory activity as compared to standard drug diclofenac (% inhibition = 64.4), SAR revealed substitution of COOH at benzothiazole moiety increases the anti-inflammatory activity.



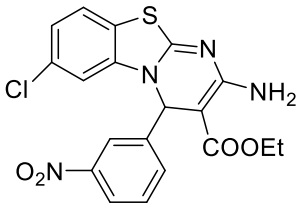
(28b)

Figure 33. Substituted Pyrimidine based benzothiazoles derivatives (28a-28e)

Nalawade et al., (2013) synthesised substituted pyrimido-benzothiazole-3- carboxylate derivatives and tested them for anti-inflammatory activity using the inhibition of albumin denaturation technique. Compound **29a** (% inhibition = 89.47%) compounds **29b** (% inhibition = 84.21%) demonstrated very good activity which was found to be significant to the standard drug diclofenac sodium (% inhibition = 94.73%). SAR illustrated that presence of 3-nitro and 3,4,5-trimethoxy groups on the phenyl ring attached with pyrimidine ring enhanced the anti-inflammatory activity [27.]



(29a)



(29b)

Figure 34. Substituted Pyrimido-benzothiazole derivatives (29a-29d)

Conclusions -

Benzothiazole is a common pharmacophore in medicinal chemistry. According to this research, there is an increasing interest in the development of lead or hybrid compounds containing the BTA moiety as an anti-inflammatory and analgesic drug. The current study investigates the efficacy of Benzothiazole in the treatment of inflammation and pain when combined with azetidinones, indoles, oxazoles, oxadiazoles, sulphonamides, triazoles, pyrimidines, and pyrazolines. SAR investigations revealed that the anti-inflammatory and analgesic effect of Benzothiazole scaffolds is complex and difficult to explain. The abundance of research on the anti-inflammatory character of BTA derivatives discussed in this study, as well as their rationalisation based on these compounds pharmacological targets, where possible, may be valuable for the creation of novel such drugs.

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