Benzothiazoles: A New Profile of Biological Activities

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The small and simple benzothiazole nucleus is present in compounds involved in research aimed at evaluating new products that possess interesting biological activities, such as antitumor, antimicrobial, anthelmintic, antileishmanial, anticonvulsant and antiinflammatory. The present review focuses on the benzothiazoles with potential activities that are now in development.

Benzothiazoles are bicyclic ring system with multiple applications. In the 1950s, a number of 2-aminobenzothiazoles were intensively studied as central muscle relaxants. Since then medicinal chemists have not taken active interest in this chemical family. Biologist's attention was drawn to this series when the pharmacological profile of Riluzole[1] was discovered. Riluzole (6-trifluoromethoxy-2-benzothiazolamine, PK-26124, RP-25279, Rilutek) was found to interfere with glutamate neurotransmission in biochemical, electrophysiological and behavioral experiments. After that benzothiazole derivatives have been studied extensively and found to have diverse chemical reactivity and broad spectrum of biological activity.

Although they have been known from long ago to be biologically active[2-4], their varied biological features are still of great scientific interest. Benzothiazoles show antitumor activity, especially the phenyl-substituted benzothiazoles[5-7], while condensed pyrimido benzothiazoles and benzothiazolo quinazolines exert antiviral activity[8]. Recently, Racane *et al.*[9] have described the synthesis of bis-substituted amidino benzothiazoles as potential anti HIV agents. Substituted 6-nitro-and 6-aminobenzothiazoles[10] show antimicrobial activity. Given below is a brief account of various alterations conducted on benzothiazole ring and their associated biological activities.

Antitumor activity:

A series of potent and selective antitumor agents mostly from substituted 2-(4-aminophenyl) benzothiazoles were developed and examined, *in vitro*, their antitumor activity in ovarian, breast, lung, renal and colon carnicoma human cell lines[11-21]. Pyrimido benzothiazole and benzothiazolo quinoline derivatives[22], imidazo benzothiazoles[23,24] as well as, polymerized benzothiazoles[25] showed antitumor activity.

2-(4-Aminophenyl) benzothiazoles[26,27] (1) comprise a novel mechanistic class of antitumor agents. Their unusual activity was first recognized from the distinctive biphasic-dose response relationship shown in *in vitro* assays against sensitive breast tumor cell lines, e.g., MCF-7 and MDA-468. Potency against these breast lines and others was independent of the estrogen or growth factor receptor status of the cells. Introduction of methyl or halogen substituent into the 3'-position of the 2-phenyl group enhances potency and extends the spectrum of action to certain colon, lung, melanoma, renal and ovarian cell lines.

6-Amidino-substituted-2-aminobenzothiazoles (2), *N*-methyl-2-(4-cyanostyryl) benzothiazolium, cyano-substituted-2-styryl benzothiazoles (3) and amidino and bis-amidino-substituted 2-styryl benzothiazoles (4) were prepared by Caleta *et al*[28]. All new compounds were tested on cytostatic activities against malignant cell lines. The compounds exerted a different inhibitory effect, depended on concentration and type of the cells. The best inhibitory effect was achieved with compounds (3) and (4) with slight differences among them. All of them inhibited the growth of examined tumor cell lines and also normal fibroblasts. Other examined compounds exhibited a moderate inhibitory effect, depending on type of the cells.

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Fluorinated analogues of 2-(4-aminophenyl) benzothiazoles have been synthesized which successfully block C-oxidation by Hutchinson *et al*[17]. 2-(4-Amino-3-methylphenyl)-5-fluorobenzothiazoles (5) is the favored analogue for clinical consideration possessing enhanced efficacy *in vitro* and superior potencies against human breast and ovarian tumor xenografts implanted in nude mice.

Quinol esters and ethers[29] (6) derived from the oxidation of 2-(4-hydroxyphenyl) benzothiazoles and quinine monoketals (7) from the oxidation of 2-(3-hydroxyphenyl benzothiazoles, respectively, have significantly improved and extended antitumor potency *in vitro* against pairs of breast and colon human tumor cell lines.

The oxidation reactions of 2-(4-hydroxy-3-methoxyphenyl) benzothiazole (8) were studied by Wells *et al*[30]. In *in vitro* growth inhibition tests against the human breast cancer cell lines MCF-7 and MDA-468 (over 7 and 10 d, respectively) determined by MTT assay, the phenolic benzothiazole gave IC_{50} values (dose to inhibit cell growth by 50%) of 0.62 and 0.06 μM, respectively. Beneteau *et al.*[31] have described the synthesis of 2-cyano-4,7-dimethoxybenzothoiazoles (9). The 2-cyano derivatives exhibit interesting *in vitro* antitumor activity. As for the 4,7-dimethoxybenzothiazoles, removal of the cyano substituent present in the 2-position of the dioxino-benzothiazole ring involved the lost of activity (IC_{50} >100 μM).

Antimicrobial activity:

Benzothiazoles show a wide spectrum of chemotherapeutic activity and a considerable amount of work has been done on the synthesis of new potent antibacterial and antifungal benzothiazoles. Bhusari *et a1*[32], prepared some new 2-(substituted phenylsulfonamido)-6-substituted benzothiazoles (10) and screened them for their antibacterial activity against *Bacillus subtilis*, *Salmonella typhi* and *S. dysentery*. Compounds with R=Br and R'=CH_3, NH_2 and I were found more active and others were less or moderately active.

Various benzothiazolo triazole derivatives (11) were prepared by Sreenivasa *et al*[33] and found to possess good activity against *S. aureus, E. coli* and *C. ablicans.* Some 6-fluoro-7-(substituted)-(2-*N*-p-anilinosulfonamido) benzothiazoles (12) (R =o-nitroanilino, m-nitroanilino, p-nitroanilino, o-chloroanilino, m-chloroanilino, p-chloroanilino, anilino, morpholino, piperazino, dimethylamino) were synthesized and studied for their antibacterial and antifungal activities. All compounds showed moderate activity against *S. aureus, S. albus* and *C.ablicans*[34].

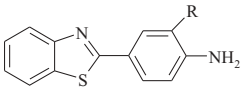
Ojha *et al.*[35], reported various benzothiazolyl carboxamido pyrazoline derivatives (13) and studied their antimicrobial activity. They found that when R=CH_3 and R_1=o-OCH_3 C_6H_4, compound showed no activity and when R = Cl and R_1 = p-OCH_3 C_6H_4, the compound was active against *S. aureus*. The rest of the compounds showed activity against, *S. aureus, E. coli, Pseudomonas aeruginosa, Klebsiella pneumoniae* and *Proteus mirabilis.*

Some 8-[(6'-substituted-1',3'-benzothiazol-2'-yl)aminomethyl] substituted hydroxy coumarins (14) were screened for antibacterial activity against *S. aureus* and *E. coli* and also antifungal activity against *Alternaria brassicicola* and *Fusarium udam.* All these compounds showed moderate activity[36].

Barede *et al.*[37] worked on a few 5,6-disubstituted-2-(substituted phenyl carboxamido) benzothiazoles (15) and found them active against *M. tuberculosis, S. typhi, S. aureus, C. ablicans, Trichophyton rubrum* and *Trychophyton mentagrophyles*. The compounds were also active against some helmenths like *Hymenolepis nana.* A few 2-[(4-amino/2, 4-diaminophenyl) sulfonyl derivatives of benzothiazoles (16) have been found to possess good activity against *E. coli*[38].

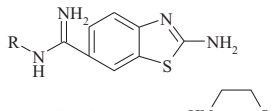
Yilidiz-Oren *et al*.[39] has synthesized a series of multisubstituted benzoxazoles, benzimidazoles and benzothiazoles (17) as non-nucleoside fused isosteric heterocyclic compounds and tested for their antibacterial activities against *Staphylococcus aureus*, *Streptococcus faecalis*, *Bacillus subtilis* as gram positive and *E. coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* as gram negative bacteria and yeast *Candida albicans* using twofold serial dilution technique. The synthesized compounds possessed a broad spectrum of activity against the tested microorganisms at MIC values between 100 and 3.12 μg/ml. Benzothiazole ring system enhanced the antimicrobial activity against *Staphylococcus aureus.*

Latrofa *et al.*[40] prepared a series of *N*-cycloalkylidene-2,3-dihydro-1,3-benzothiazoles (18), *N*-cycloalkyl-2-acylalkylidene-2,3-dihyro-1,3-benzothiazoles (19), and *N*-alkyl-2-acylalkylidene-2,3-dihydro-1,3-benzothiazoles (20) and tested for *in vitro* antibacterial and antifungal activities against four gram positive and five gram negative bacteria. The findings obtained showed that some of the tested compounds were effective against bacterial strains,



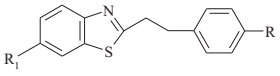
R = H, CH3, Cl, I, Br

(1)



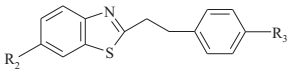
R = $CH(CH_3)_2$, CH_2CH_2 HN O

(2)



R = R_1 = H, CN

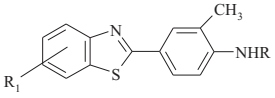
(3)



R_2 = R_3 = H, C(=NH)NHCH$(CH_3)_2$

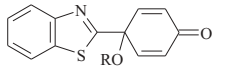
C(=NH)$NHCH_2CH_2$ HN O

(4)



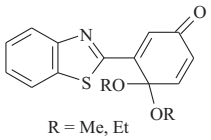
R = H; R_1 = 5-F

(5)



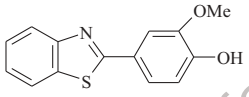
R = AO, Me, Et, Pr, $CH_2C{\equiv}CH$

(6)

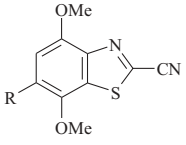


R = Me, Et

(7)

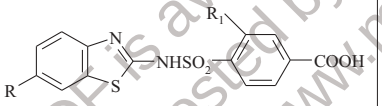


(8)



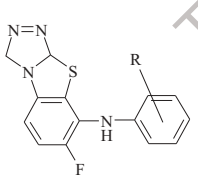
R = H, NHAc

(9)



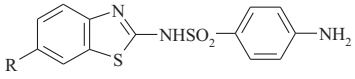
R = Cl, Br, CH_3, OCH_3; R_1 = I, CH_3, NH_2

(10)



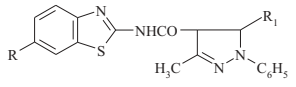
R = *o*-NO_2, *p*-NO_2, *m*-NO_2, H, *o*-Cl, *m*-Cl

(11)



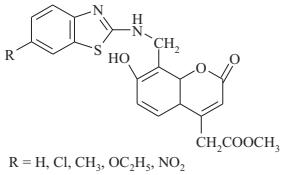
R = o-nitroanilino, m-nitroanilino, p-nitroanilino, o-chloroanilino, m-chloroanilino, p-chloroanilino, morpholino, piprazino, dimethylamine

(12)



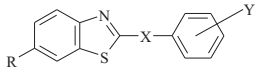
R = Cl, CH_3; R_1 = C_6H_5, *o*-$CH_3C_6H_4$, *p*-$OCH_3C_6H_4$

(13)



R = H, Cl, CH_3, OC_2H_5, NO_2

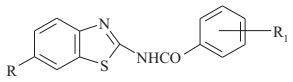
(14)



X = S, SO_2

Y = 4-NH_2, 2,4-diNH_2, 2,4-diNHAc

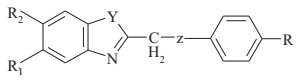
(15)



R = 5-Cl, 6-F, 5,6-diCl

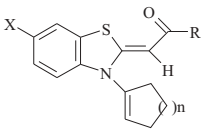
R_1 = H, 2-F, 3-F, 4-F, 2-CF_3, 3-CF_3, 2,6-diF

(16)



Y = O; Z = S; R = H; R_1 = H, Cl, NO_2; R_2 = H, NO_2

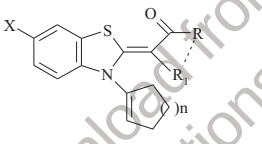
(17)



X = H, F, CH_3, OCH_3; n = 8,3

R = CH_3, C_2H_5, C_3H_7, C_4H_9, C_6H_{13}

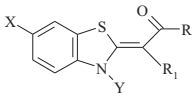
(18)



X = H; n = 8,3

R = CH_3, C_2H_5, C_6H_5, $(CH_2)_3$; R_1 = H, $(CH_2)_3$

(19)

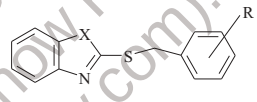


X =H; Y = C_4H_9

R = C_6H_5, -CH_2-N($CH_2C_6H_5$)-$(CH_2)_2$

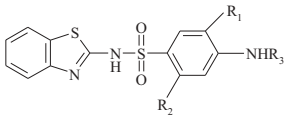
R_1 = H, CH_2-N($CH_2C_6H_5$)-$(CH_2)_2$

(20)



X = O, S; R = H, 2-NO_2, 3-NO_2, 4-NO_2, 3,5-NO_2, 2,4-NO_2, 3-CN, 4-CN

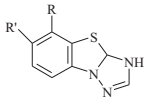
(21)



R_1 = H, CH_3, COOH; R_2 = H, Cl, Br, NO_2

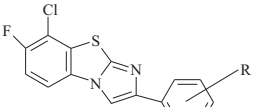
R_3 = H, $COCH_3$

(22)



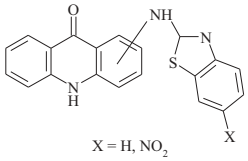
R= anilino, o-nitroanilino,m-nitroanilino, p-nitroanilino, o-chloroanilino,o-methylanilino guanidino, hydrazino, p-methylanilino, diphenylamino, 2-carboxyanilino, 4-carboxyanilino, morpholino, piprazino; R^1 = F, Br

(23)



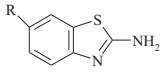
R = H, 4-F, 5-F, 3-CF_3, 4-OCH_3, 2-OH, 3-NO_2, 4-NO_2, 2,4-diCl,3,4-diCl, 5-chlorothienyl

(24)



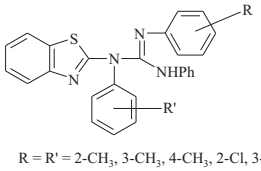
X = H, NO_2

(25)



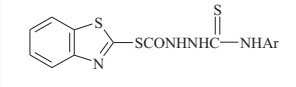
R = CH_3, C_2H_5, *n*-prop, *i*-prop, *n*-but, *n*-pent, t-pent, $OCHF_2$, OCH_3, CF_3, C_2H_5, OC_2H_5, CF_3, 4-OCF_3, 5-OCF_3, 7-OCF_3

(26)



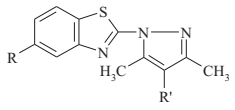
R = R' = 2-CH_3, 3-CH_3, 4-CH_3, 2-Cl, 3-Cl, 4-Cl, 2-OCH_3, 4-OCH_3, 4-Br

(27)



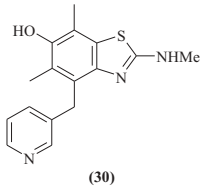
Ar = C_6H_5, o-$CH_3C_6H_4$, m-$CH_3C_6H_4$, p-$CH_3C_6H_4$
o-$OCH_3C_6H_4$, p-$OCH_3C_6H_4$, p-ClC_6H_4, p-BrC_6H_4

(28)



R = H, CH_3, Cl, F, OCH_3, NO_2
R' = H, CH_3, C_2H_5, i-C_3H_7, Br, CH_2COOH

(29)



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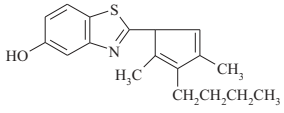
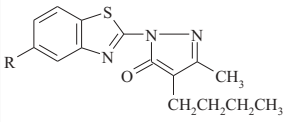


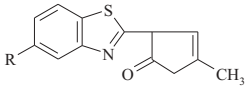
R = H, Cl, F, CH_3, OCH_3

(31)



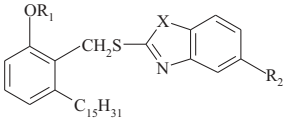
R = H, CH_3, OCH_3, Cl, F

(32)



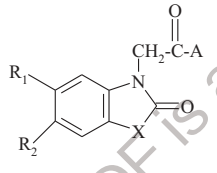
R = H, CH_3, C_6H_5, p-Cl-C_6H_4

(33)



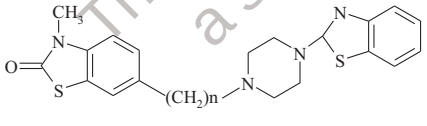
	R	R_2	X
a	H	OCH_3	NH
b	CH_3	H	S

(34a-b)



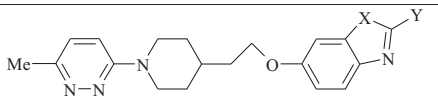
X = O, S ; R_1 = H, Cl ; R_2 = H, CH_3, C_6H_5-CO, (o) Cl-C_6H_4-CO
A = 1-morpholinyl, 1-pyrrolidinyl diethylamino, OCH_3, OC_2H_5, OH

(35)



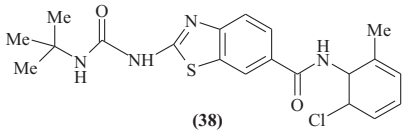
n = 2,3 or 4

(36)

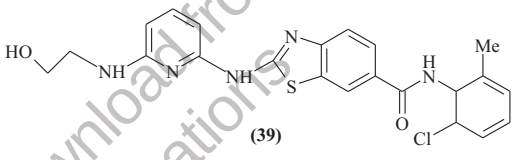


X = O, S, NMe
Y = CH_3, CH_2CH_3, SCH_3, OCH_2CH_3, SCH_2CH_3, OCH_3, $OCH_2CH_2CH_3$
$CH_2CH_2CH_3$, $(CH_2)_3CH_3$, OCH_2CH_3, SCH_2CH_3

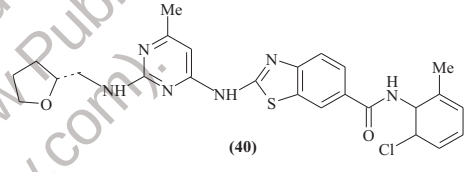
(37)



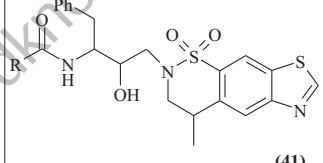
(38)



(39)



(40)



R = 2(R)-methyl-3-methylsulfonylethyl,
3-pyridylmethoxy, 5-thiazolylmethloxy

(41)

whereas, only few compounds exhibited a moderate antifungal activity against the yeast strains evaluated.

The series of 2-benzylsulfanyl derivatives of benzoxazole and benzothiazoles (21) were synthesized by Koci *et al*,[41] and evaluated for their *in vitro* antimycobaterial activity against *Mycobaterium tuberculosis* and non tuberculous mycobateria, and the activity was expressed as the minimum inhibitory concentration (MIC) in µMl/l. The substances bearing two nitro groups or a thioamide group exhibited appreciable activity particularly against non-tuberculous strains.

Various substituted 2-(4-acetamidophenylsulfonamido) benzothiazoles and 2-(4-amino phenyl sulfonamido) benzothiazoles (22) containing different functional groups have been synthesized and all the compounds have been screened for their antitubercular activity *in vitro* and compared with standards (Streptomycin and isoniazid). Among the compounds tested, compounds with R_1 =CH_3 and R_2 = Br, were found to be most potent. Overall the compounds having electron-with drawing substituents (NO_2, COOH and halogens) showed better activity than unsubstituted one[42].

Anthelmintic activity:

Recent reports of resistance to benzimidazoles have now forced the researchers to urgently develop new drugs with anthelmintic activity, to fight helminthiasis, which is

causing untold misery to the infected individuals. This prompted synthesis of benzothiazole derivatives, which is sulfur isostere of benzimidazole, in the hope of achieving better anthelmintic activity.

In the search of new anthelmintic agents of benzothiazole series, Nargund,[43] synthesized few novel 8-fluoro-9-substituted(l,3)benzothiazolo (5, 1-b)-1,3,4-triazoles (23). All these compounds were studied for their anthelmintic activity against earthworm, *Perituma posthuma*. The compound with R= *o*-nitroanilino substituent was found to possess markedly higher anthelmintic activity, than other compounds compared with standard. But all the other compounds are found to possess interestingly low level of activity, whereas 8-bromo-9-substituted (1, 3) benzothiazolo [5, 1-b]-1, 3, 4-triazoles (23) have been synthesized and screened for their anthelmintic activity against earthworm, *Perituma posthuma*. Among the compounds tested, compounds with substituent R=4-carboxyanilino and morpholino were found to be the most potent in the series[44]. Some substituted imidazobenzothiazoles (24) were tested for *in vivo* anthelmintic activity against *H. nana* infection and were found to show good to moderate activity[45].

Antileishmanial activity:

Delmas *et al.*[46] synthesized (1,3-benzothiazol-2-yl) amino-9- (10*H*)-acridinone derivatives (25) and were assessed for their *in vitro* antileishmanial and anti HIV activities 1-(6-amino-benzothiazol-2-ylamino)-10*H*-acridin-9-one, revealed a selective antileishmanial activity, mainly due to amastigote-specific toxicity. Results suggested that the addition of a benzothiazoles group on a parent amino-9-(10*H*)-acridinone ring could enhance antileshmanial abilities, the presence of a 6-amino-benzothiazole group on position 2 amino chain or a 6-nitro-benzothiazole group. On position 4 amino chain was essential for specific antiamastigote properties.

Florence Delmas *et al*,[47] has synthesized position 2 substitution-bearing 6-nitro and 6-amino benzothiazoles and their corresponding anthranilic acids and assessed the *in vitro* antiparastic activity of each derivative against the parasites of the genus *Leishmania infantum* and *Trichomonas vaginalis* compared to their toxicity towards human monocytes. The antiprotozal properties depended greatly on the chemical structure of the position 2 substitution-bearing group.

2-[(2-Chloro-benzothiazol-6-yl) amino] benzoic acid, demonstrated an interesting antiproliferative activity towards parasites of the species *Trichomonas vaginalis*, while compound.

2-({2-[(2-Hydroxyethyl) amino]-benzothiazol-6-yl} amino) benzoic acid exhibited a promising activity against parasites of the species *Leishmania infantum* in their intracellular amastigote form.

Anticonvulsant activity:

A large number of benzothiazole derivatives were evaluated for anticonvulsant activity and found to possess significant activity against various types of seizures. In the search of new anticonvulsant agents having benzothiazole nucleus, Jimonet *et al.*[48] have synthesized a lot of substituted-2-benzothiazolamines (26). All these compounds were found to possess significant activity.

A series of benzothiazolyl guanidines (27) were synthesized by Siddiqui *et al.*[49] The compounds with R=4-CH_3 and 4-Cl were found to be equipotent (100%) in activity to phenobarbitone in maximal electroshock seizure test and blocked subcutaneous pentylenetetrazole and strychnine induced seizures to some extent. All other compounds also had significant anticonvulsant activity.

Singh *et al*,[50] synthesized some 2-(4-arylthiosemicarbazidocarbonylthio) benzothiazoles (28). The compounds were screened for their anticonvulsant activity against pentylenetetrazole induced convulsions in mice and found that all the compounds possess measurable anticonvulsant activity. A large number of 2-(3*H*)-benzothiazolone derivatives (29) have been synthesized and evaluated for their anticonvulsant activity in mice and were found to be significantly active[51].

Antiinflammatory activity:

Pyrazolones and pyrazolinones rank among the more venerable non-steroidal antiinflammatory agents. Phenylbutazone and its congeners incorporating a pyrazoline-3,5-dione structure are more potent antiinflammatory agents. In the recent years a number of Benzothiazole derivatives have been synthesized and found to display antiinflammatory activity.

In vitro pharmacological profiles of E3040 (30), 6-hydroxy-5,7-dimethyl-2-(methylamino)-4-(3-pyridylmethyl) benzothiazoles were investigated by Oketani *et al.*[52] against the 5-lipooxygenase activity of rat basophilic leukaemia cells, E 3040 and Zileuton (a-5-lipooxygenase inhibitor) had an IC_{50} of 0.23 and 0.93 µM, respectively. This result indicates that E 3040 potently inhibited 5-

lipooxygegnase and thromboxane A_2 synthetase and blocked leukotriene B_4 and thromboxane B_2 production in rat peritoneal and human blood cells. Sawhney *et al.*[53] have prepared some novel 2-(2-benzothiazolyl)-6-aryl-4,5-dihydro-3(2*H*)-pyridazinone (31) and found that they possessed low to moderate antiinflammatory activity.

Singh *et al*.[54] prepared some new 2-(4'-butyl-3',5'-dimethylpyrazol-1'-yl)-6-substituted benzothiazoles (32) and 4-butyl-1-(6'-susbtituted-2'-benzothiazolyl)-3-methylpyrazol-5-ones (33) and were found to display significant antiinflammatory activity. Paramshivappa *et al.*[55] prepared a series of 2-[(2-alkoxy-6-pentadecylphenyl) methyl] thio]-1*H*-benimidazoles/ benzothiazoles and benzoxazoles from an anacardic acid and investigated their ability to inhibit human cycloxygenase-2-enzyme (COX-2). The active compounds were screened for cyclooxygenase-1 (COX-1) inhibition. Compound (34a) is 384 fold and (34b) is more than 470 fold selective towards COX-2 compared to COX-1. Dogruer *et al*.[56] synthesized sixteen (2-benzothiazolone-3-yl and 2-benzoxazolone-3yl) acetic acid derivatives (35) and tested them for antinociceptive and antiinflammatory activity. 4-[2-(6-Benzoyl-2-benzoxazolone-3-yl) acetyl] morpholino, 4-{2-[6-(2-chloro-benzoyl)-2-benzoxazolone-3-yl] acetyl} morpholino, 4-{2-[6-(2-chloro-benzoyl)-2-benzoxazolone-3yl] acetyl} morpholine, 1-[2-(5-chloro-2-benzoxazolone-3-yl) acetyl] pyrrolidine, methyl ((6-methyl-2-benzoxazolone-3-yl) acetate and *N, N*-diethyl-2- (2-benzothiazolone-3-yl) acetamide have shown more potent antinonciceptive activity than others.

Miscellaneous:

Diouf *et al*.[57] synthesized original derivatives of 2-piperazinyl benzothiazoles (36) and studied as mixed ligands for serotoninergic 5-HT_{1A} and 5-HT_3 receptors. The studied compounds exhibited significant affinities for these two serotoninergic receptor subtypes. The pharmacological profile of these ligands was agonist for 5-HT_{1A} receptors and antagonist for 5-HT_3 receptor sub sites. Compounds with such a pharmacological profile are of clinical relevance in the treatment of psychotropic diseases. e.g., anxiety, depression and schizophrenia.

Brown *et al*,[58] reported a series of pyridazinylpiperidinyl capsid-binding compounds with novel bicyclic substituents and screened against human rhinovirus (HRV). HRV cause approximately one-half of all cases of respiratory tract infection (colds). Several 2-alkoxy and 2-akylthio-benzoxazole and benzothiazoles derivatives (37) showed excellent anti HRV activity. When tested against a panel of 16 representatives HRV types, the 2-ethxoy-benzooxazole derivatives, 13 was found to have superior HRV activity (median EC_{50} 3.88 ng/mL) to known capsid-binders pleconaril and pirodavir.

Das *et al*,[59] prepared a series of structurally novel benzothiazoles based small molecule inhibitors of $p56^{lck}$ was prepared to elucidate their structure-activity relationships (SAR), respectively and cell activity in the T-cell proliferation assay. $p56^{lck}$ (Lck), a member of the Src family of non-receptor protein tyrosine kinase is expressed primarily in T-lymphocytes and natural killer cells.

Selective inhibitors of Lck may have potential therapeutic utility in the treatment of T-cell mediated disorders such as autoimmune and inflammatory diseases and in the prevention of solid organ transplant rejection[60]. BMS-243117[61] (38) is identified as a potent and selective Lck inhibitor with good cellular activity (IC_{50}=1.1 µM), whereas BMS-350751 (39) and BMS-358233 (40) are identified as potent Lck inhibitors with excellent cellular activities against T-cell proliferation.

Srinivasan *et al.*[62] have shown that the replacement of the urea moiety by benzothiazolesulfonamide provided inhibitors of HIV-1 protease with improved potency and antiviral activities. Certain members of the class showed good oral bioavailability in rats; most notably compounds are shown in (41).

CONCLUSIONS

The reviewed new class of 2-substituted aminobenzothiazoles has shown a wide spectrum of biological activities. The substituted benzothiazolylimino dithiazolidines and the 2-(2'-aryl-1,3,4-oxadiazol-5-yl)mercaptomethyl benzothiazoles are having significant antibacterial activity. Significant antiinflammatory activity is displayed by some new 2-(4'-butyl-3'-5'-dimethylpyrazol-1-yl)-6-substituted benzothiazoles and 4-butyl-1-(6'-substituted -2'-benzothiazolyl)-3-methylpyrazol-5-ones.

In search of new anticonvulsants, riluzole and benzothiazolylguanidines are found to have potent activity. Potent antitumor activity was demonstrated by a number of 2-(4-aminophenyl) benzothiazoles. The 2-(4-acetamido-2-bromo-5-methylphenyl sulfonamide) benzothiazole is found to be effective as antituberculor agents, whereas ethoxazolamide and o-acyl derivatives of 6-hydroxybenzothiazole-2-

sulfonamides are found to show the carbonic anhydrase inhibitory action. The biological profiles of these new generation of benzothiazoles represents much progress with regard to the older compounds.

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