Journal of Skin Health and Cosmetics

Research Article Open Access

Antifungal Efficacy of Novel C-6 Methyl-Substituted Benzothiazole Derivatives Against Candida albicans

Akhilesh Gupta*

Kunwar Haribansh Singh College of Pharmacy, Jaipur (UP), India

***Corresponding Author:** Akhilesh Gupta, Kunwar Haribansh Singh College of Pharmacy, Jaipur (UP), India, Tel: +917440963440; E-mail: 81.akgupta@gmail.com

Received: Feb 16 2024, **Accepted:** Mar 19 2024; **Published:** Mar 22, 2024, DOI: 10.59462/jishc.1.1.102

Citation: Akhilesh Gupta (2024) Antifungal Efficacy of Novel C-6 Methyl-Substituted Benzothiazole Derivatives Against Candida albicans. Journal of Skin Health and cosmetics,1(1):102.

Abstract

Background: Candida species, especially *C. albicans* has commonly colonized the human skin surface and cause infection. However, skin barrier level defence mechanisms are very efficient. Therefore, the skin is an effective barrier against fungal infection.

Methods: C-6 methyl substituted benzothiazole derivatives were synthesized by reaction of methyl-chloro substituted aniline with potassium thiocyanate under temperature control and presence of bromine in glacial acetic acid and ammonia. Substituted nitrobenzamides then synthesized by condensation of C-6 methyl, 7-chloro and 2-amino substituted benzothiazole with 2 (3 or 4)-nitrobenzoylchloride acid in presence of dry pyridine and acetone.

Finally, newly synthesized derivatives (D-01 to D-09) were synthesized through replacing at 7^{th} position chlorine by reaction with 2-nitroaniline, 3-nitroaniline, and 4-nitroaniline in presence of DMF. Antifungal activity was performed against *C. albicans* by cup plate method (diffusion technique) using Griseoflavin as standard.

Results: Compound D-02 and D-08 showed potent antifungal activity against *C. albicans* while compound D-01 and D-04 showed moderate inhibitory activity at both concentrations 50 µg/mL and 100 µg/mL as compared to standard.

Conclusion: Present work was based on the synthesis of substituted benzothiazole derivatives in order to find out the antifungal activity against *C. albicans*, since *Candida albicans* is mainly responsible for skin infection, especially in the epithelial cells of the vagina. The present work focused on the synthesis of newer derivatives having methyl substitution at a C-6 position of benzothiazole while 2-(3 or 4)-aryl-NO2 considered as rotating substitution at C-2 and C-7 position of benzothiazole nucleus.

Keywords: *Candida albicans*; Skin infection; Vaginal infection; Benzothiazole; Antifungal activity; 2-substituted benzothiazole; 7-substituted benzothiazole; Nitro-benzothiazole; Cyclization of benzothiazole nucleus; Cup plate method (diffusion technique)

Introduction

In the current scenario, different fungi especially *C. albicans* has been identified as human skin commensals that colonized on human skin [1,2]. Around 20%-25% of the world population is affected by symptomatic fungal skin infections caused by *C. albicans* [3]. Ue common symptoms of symptomatic fungal skin infections caused by *C. albicans* are thickening of the skin, hyperkeratosis, and erythema. Ue skin and mucosal surface infection caused by *C. albicans* is referred to as chronic mucocutaneous candidiasis, which occurs mainly in individuals with primary or acquired immunodeficiencies [4,5]. In the commensal, non-invasive state, *C. albicans* exists in the yeast form on the tissue surface. Yeast cells can be detected through the dectin-1 receptor (Dec1) that is expressed by Langerhans cells in the epidermis [6-11]. Interleukin-6 (IL-6)-dependent U17 response was achieved by activation of Langerhans cells (LCs) and antimicrobial peptide production by keratinocytes and superficial antifungal defence. Commensal skin bacteria are also involved in preventing invasion of *C. albicans* into the skin by direct and indirect mechanisms [12-18]. *C. albicans* invading the epidermis can moreover be detected by sensory neurons that promote IL-23 secretion by dermal dendritic cells and subsequent proliferation and IL-17 secretion of skin resident γδ T cells. Upon breaching of the epidermis, *C. albicans* is detected in the dermis by dermal dendritic cells which induce an IL-12- dependent U1 response required for systemic immunity against the fungus. Antimicrobial defence supported by dermal fibroblasts directly in the dermis upon activation through TLR2 by *C. albicans* and IL-1β secretion and autoactivation. Secretion of IL-1β by dermal fibroblasts requires an additional yet unidentified signal from $CD4^+$ T cells [19-24].

Benzothiazole is a therapeutically important privileged bicyclic ring system contains sulphur and nitrogen as a heteroatom. Synthesis and screening of benzothiazole derivatives have great importance in heterocyclic chemistry because of its potent and significant biological activities [25-29]. Substitution at C-2, C-6 and C-7 at benzothiazole nucleus has emerged in its usage as a core structure in the diversified therapeutically applications [30-36]. As per reported biological activities of benzothiazole derivatives it was found that change of the structure of substituent group at C-2 and C-7 position commonly results in the change of its bioactivities. Commonly change of substitution at C-2 and C-7 at benzothiazole nucleus especially with methyl at C-6 has already been proven its therapeutic importance. Till

date various biological activities for benzothiazole derivatives have been reported as antitumor, antitubercular, antimalarial, anticonvulsant, anthelmintic, analgesic, anti-inflammatory, antibacterial and antifungal, a topical carbonic anhydrase inhibitor and an antihypoxic [37-39]. 2-substituted benzothiazole derivatives were first discovered in 1887 by A. W. Hofmann as simple cyclization mechanism and number of the synthetic scheme has been reported. Ue most common and classical method was reported as direct method that involved condensation of an ortho-amino thiophenol with a substituted aromatic aldehyde, carboxylic acid, acyl chloride or nitrile to synthesize C-2 substituted benzothiazoles, but it was found that this method is not appropriate for majority of substituted C-2 aryl benzothiazoles because main difficulty encountered in synthesis of the readily oxidisable 2-amino thiophenols bearing substituent groups. For above said reason some other methods were reported and extensively used in the laboratories that based on the use of the potassium ferricyanide radical cyclization of thiobenzanilides. Uis method was named as Jacobsen cyclization and popularized because it produced only one product. As per reported method, it involved cyclization onto either carbon atom ortho to the anilido nitrogen.

Because of selective product synthesis, the Jacobsen cyclization was considered as a highly effective strategy for benzothiazole synthesis e.g. for the synthesis of C-6 substituted benzothiazoles, radical cyclization of the 3-fluoro-or 3,4-difluoro-substituted thiobenzanilides. Ue literature review also reveals that change of substituents at C-2, C-6 and C-7 interestingly changed bioactivity and considered to established structure-activity relationship [40-42].

Materials and Methods

Synthesis of substituted benzothiazole (compound code 1-SB)

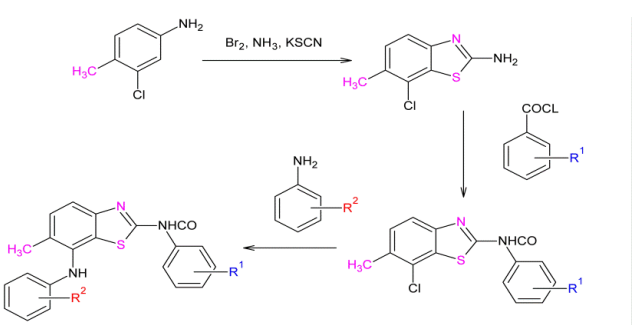
Synthesis of substituted benzothiazole nucleus was achieved by adding 8 gm (0.08 mol) of potassium thiocyanate and 1.45 g (0.01 mol) of substituted aniline into 20 mL cooled glacial acetic acid in such a way that the temperature not exceeded above room temperature. Freezing mixture of ice and salt was used to control the temperature of reaction with continuous mechanical stirring. Again temperature control was maintained during the addition of a solution of 1.6 mL of bromine in 6 mL of glacial acetic acid using dropping funnel. Ue time of addition of bromine also considered to take around 105 mins to control temperature. During the addition of bromine, temperature was controlled to never rise beyond the room. As the addition of bromine was completed the solution stirred for 2 h but below room temperature. Aler that solution was again stirred at room temperature for 10 h and allowed to stand overnight to get precipitate followed by heating at 850°C on a steam bath aler addition of 6 mL water and filtered hot (Filtrate-01). In the resulting precipitate 10 mL of glacial acetic acid was added and heated with at 850°C and filtered hot (Filtrate-02). Finally, both filtrate combined and cooled at room temperature followed by neutralization with concentrated ammonia solution to pH-6 to get precipitate. Ue resulting product treated with animal charcoal and recrystallized from benzene, ethanol of (1:1) to get substituted benzothiazole (1-SB, 66% yield).

Synthesis of nitrobenzamide (compound code 2-SB, 3-SB, and 4-SB)

5.36 g (0.026 mol) of 2-(3 or 4)-nitrobenzoylchloride was dissolved in dry acetone. Product 1-SB separately dissolved in dry pyridine and added drop wise into the solution of 2-(3 or 4)-nitro-benzoylchloride with continuous stirring at room temperature. Aler complete addition stirring was continued for another 30 mins then transferred into 200 mL ice cold water. Finally recrystallized with ethanol to get intermediate nitrobenzamide compound 2-SB, 3-SB and 4-SB

Synthesis of compound D-01 to D-09

0.008 mol of 2 (3 or 4) nitro-substituted aniline was refluxed with 2.7 g (0.0075 mol) of compound 2-SB, 3-SB and 4-SB separately for 2 h in the presence of DMF (Dimethylformamide). Aler 2 h reflux, mixture cooled at room temperature and poured into crushed ice. Ue solid was separated, dried and recrystallized with super dry alcohol to get novel benzothiazole derivatives D-01 to D-09 (Figure 1).



Comp. Code	R^1	R^2	Comp. Code	R^1	R^2	Comp. Code	R^1	R^2
D-01	2-NO_2	2-NO_2	D-04	3-NO_2	2-NO_2	D-07	4-NO_2	2-NO_2
D-02	2-NO_2	3-NO_2	D-05	3-NO_2	3-NO_2	D-08	4-NO_2	3-NO_2
D-03	2-NO_2	4-NO_2	D-06	3-NO_2	4-NO_2	D-09	4-NO_2	4-NO_2

Figure 1: Synthetic scheme

Analytical characterization

Uin layer chromatography (TLC) was used to monitor reaction progress, completion and identification of newly synthesized compounds from starting material using solvent system butanol: ethyl acetate: benzene (1:2:1) and detection performed by exposing them to iodine vapors. Ue melting point of compounds was determined using open capillaries method. Structure elucidation of compounds was done by IR and 1HNMR spectral study.

SHIMADZU (8400S) used for IR spectral study (KBr pellet technique). For the structure elucidation using IR, frequency range for Ar-C=C, C=O, C-S, C-NO_2 were considered. Bruker AM 400 1H NMR instrument (at 400 MHz) was used using $CDCL_3$ as a solvent and tetramethylsilane (TMS) as an internal standard. For structure elucidation by 1HNMR, NH proton that characterized benzothiazole was considered.

Antifungal activity against *C. albicans*

Ue synthesized compounds are screened against selected fungal strains *C. albicans* by using diffusion method and griseofulvin as a standard drug. Under the aseptic condition, 48 h old fungal culture

was inoculated into the nutrient broth and incubated for 48 h at 37°C ± 20°C in an incubator. Potato-dextrose agar media (20%) mixed with inoculated culture and poured into petri plates. Five bores are made at an equal distance by using sterile steel cork borer (8 mm in diameter) aler solidification. Different concentrations (50 µg/mL and 100 µg/mL) of standard drug and synthesized compounds along with control (Dimethyl formamide) introduced in this plates and placed in a refrigerator at 8°C-100°C as cold incubation for two hours that allowed proper diffusion of the drug and synthesized compounds. Ue petri plates were transferred to the incubator and maintained at 37°C ± 20°C for 24-36 h aler cold incubation. Zone of inhibition was observed by using vernier scale. Ue mean value of the zone of inhibition was measured in millimeter of two preparation of synthesized compounds (D-01 to D-09) and standard drug.

Result and Discussion

Ue skin is similar to mucosal surfaces such as the oral and vaginal mucosa, as they are all stratified squamous epithelia. Yet there are also substantial differences, like different degrees of cornification in these tissues, and importantly, their local environment. Ue mechanisms underlying skin colonization and invasion by *Candida species* as well as host defense mechanisms are consequently overlapping with those found for mucosal surfaces. Uese findings have revealed both mechanisms of fungal recognition as well as immunological networks required to control these infections. Simple, oIen unicellular *in vitro* models furthermore have revealed initial mechanisms of pathogenesis in Candida infections. Recently, complex 3D tissue models of human origin containing defined elements of the immune system have been shown to be particularly amenable for identifying and Modelling aspects of the antifungal defence of the human skin. Uese recent advances in setting up complex 3D-tissue models have shown great promise already and therefore will most likely offer additional approaches to dissect and study Candida-skin interactions in great detail in the near future. Benzothiazole contains sulphur and nitrogen as hetero atom but imparts biological activity while substitution at C-2, C-6 and C-7 position. In the present work, methyl substitution was at the C-6 position while 2-(3 or 4)-aryl-nitro considered as rotating substitution at C-2 and C-7 position of benzothiazole nucleus. Ue novel derivatives (D-01 to D-09) evaluated for antifungal activity against *C. albicans*. In the present work nitro group consider as rotating basis on ortho, meta and para position. Ue reason behind considering nitro group as substituent is the fungi rarely acquire resistance. TLC, melting point, IR and 1HNMR were used for analytical characterization. In the TLC, the distance traveled by compound D-01 to D-09 was found to be different from that of the starting compound that proved synthesized compounds were different from parent one, even during TLC performance every time single spot was obtained, hence it also reveals that synthesized compounds were free from impurity as well as reaction was completed. Structure elucidation by IR spectroscopy frequency range for Ar C=C, C=O, C-S, C-NO_2 was considered. In case of structure elucidation of by 1HNMR sharp characteristic signal at 7.14-7.60 ppm is observed and consider as NH proton (benzothiazole) in all the synthesized compounds (Table 1).

Compound Code	**%Yield**	**Melting point (°C)**	**TLC (RF-value)**	**IR**	**^{1}HNMR (400 Hz, DMSO-d6)**
D-01	74	265	0.48	1469 cm^{-1}Ar C=C, 1648 cm^{-1}C=O, 1255 cm^{-1}C-S, 1540 cm^{-1}C-NO_2.	δ 7.61, 7.64(s, 2H, NH), δ 3.37(s, 3H, CH_3), δ 7.19-7.76 (m, 10H, Ar-H)
D-02	71	259	0.52	1424 cm^{-1}Ar C=C, 1634 cm^{-1}C=O, 1265 cm^{-1}C-S, 1547 cm^{-1}C-NO_2.	δ 7.58, 7.62(s, 2H, NH), δ 3.35(s, 3H, CH_3), δ 7.15-7.70 (m, 10H, Ar-H)
D-03	65	268	0.51	1423cm^{-1}Ar C=C, 1622cm^{-1}C=O, 1215cm^{-1}C-S, 1534cm^{-1}C-NO_2.	δ 7.63, 7.75(s, 2H, NH), δ 3.33(s, 3H, CH_3), δ 7.17-7.72 (m, 10H, Ar-H)
D-04	68	270	0.55	1421cm^{-1}Ar C=C, 1665cm^{-1}C=O, 1243cm^{-1}C-S, 1537cm^{-1}C-NO_2.	δ 7.65, 7.79(s, 2H, NH), δ 3.39(s, 3H, CH_3), δ 7.13-7.65 (m, 10H, Ar-H)
D-05	66	256	0.59	1440 cm^{-1}Ar C=C, 1629 cm^{-1}C=O, 1217cm^{-1}C-S, 1532cm^{-1}C-NO_2.	δ 7.59, 7.55(s, 2H, NH), δ 3.31(s, 3H, CH_3), δ 7.23-7.71 (m, 10H, Ar-H)
D-06	70	269	0.48	1421cm^{-1}Ar C=C,	δ 7.65, 7.81(s, 2H, NH),

				1615cm^{-1}C=O, 1212cm^{-1}C-S, 1554cm^{-1}C-NO_2	δ 3.34(s, 3H, CH_3), δ 7.22-7.77 (m, 10H, Ar-H)
D-07	55	264	0.65	1443cm^{-1}Ar C=C, 1626cm^{-1}C=O, 1222cm^{-1}C-S, 1543cm^{-1}C-NO_2	δ 7.62, 7.66(s, 2H, NH), δ 3.37(s, 3H, CH_3), δ 7.17-7.70 (m, 10H, Ar-H)
D-08	65	255	0.62	1421cm^{-1}Ar C=C, 1621cm^{-1}C=O, 1258cm^{-1}C-S, 1523cm^{-1}C-NO_2	δ 7.62, 7.81(s, 2H, NH), δ 3.41(s, 3H, CH_3), δ 7.21-7.70 (m, 10H, Ar-H)
D-09	58	267	0.54	1467cm^{-1}Ar C=C, 1660cm^{-1}C=O, 1244cm^{-1}C-S, 1521cm^{-1}C-NO_2	δ 7.61, 7.74(s, 2H, NH), δ 3.32(s, 3H, CH_3), δ 7.13-7.79 (m, 10H, Ar-H)

Table 1: Analytical characterization of newly synthesized compounds

Antifungal activity performed at two concentration 50 and 100 µg/mL using griseofulvin as a standard drug against *C. albicans*. Compound D-02 and D-08 showed potent antifungal activity against *C. albicans* while compound D-01 and D-04 showed moderate inhibitory activity at both concentrations 50 µg/mL and 100 µg/mL as compared to standard (Table 2).

Compound code	***C. albicans***	
	50 µg/mL	**100 µg/mL**
Griseoflavin	18	28
D-1	07	12
D-2	17	26
D-3	09	16
D-4	10	18
D-5	11	21
D-6	10	18
D-7	11	19
D-8	17	25
D-9	13	22

Table 2: Result of antifungal activity

Conclusion

In the present work C-6, methyl substituted novel benzothiazole derivatives were synthesized and screened for antifungal activity against *C. albicans.* Ue paucity of data showed that compound D-02 and D-08 showed potent activity and could be considered for further clinical trials as antifungal agents.

References

1. Findley K, Yang J, Conlan S, Deming C, Meyer JA, et al. (2013) Topographic diversity of fungal and bacterial communities in human skin. Nature 498: 367-370.
2. Oh J, Freeman AF, NISC Comparative Sequencing Program, Park M, Sokolic, R Candotti F, et al. (2013) the altered landscape of the human skin microbiome in patients with primary immunodeficiencies. Genome Res 23: 2103-2114.
3. Havlickova B, Czaika VA, Friedrich M (2008) Epidemiological trends in skin mycoses worldwide. Mycoses 4: 2-15.
4. Mohandas V, Ballal M (2011) Distribution of Candida species in different clinical samples and their virulence: Biofilm formation, proteinase and phospholipase production: A study on hospitalized patients in southern India. J Glob Infect Dis 3: 4-8.
5. Kashem SW, Kaplan DH (2016) Skin immunity to Candida albicans. Trends Immunol 37: 440-450.
6. Wachtler B, Citiulo F, Jablonowski N, Forster S, Dalle F, et al. (2012) Candida albicans-epithelial interactions: Dissecting the roles of active penetration, induced endocytosis and host factors on the infection process. PLoS One 7: e36952.
7. Dalle F, Wachtler B, L'Ollivier C, Holland G, Bannert N, et al. (2010) Cellular interactions of Candida albicans with human oral epithelial cells and enterocytes. Cell Microbiol 12: 248-271.
8. Sohn K, Senyurek I, Fertey J, Konigsdorfer A, Joffroy C, et al. (2006) An in vitro assay to study the transcriptional response during adherence of Candida albicans to different human epithelia. FEMS Yeast Res 6: 1085-1093.
9. Dieterich C, Schandar M, Noll M, Johannes FJ, Brunner H, et al. (2002) In vitro reconstructed human epithelia reveal contributions of Candida albicans EFG1 and CPH1 to adhesion and invasion. Microbiology 148: 497-506.
10. Schaller M, Korting HC, Schafer W, Bastert J, Chen W, et al. (1999) Secreted aspartic proteinase (Sap) activity contributes to tissue damage in a model of human oral candidosis. Mol Microbiol 34: 169-180.
11. Schaller M, Bein M, Korting HC, Baur S, Hamm G, et al. (2003) Ue secreted aspartyl proteinases Sap1 and Sap2 cause tissue damage in an in vitro model of vaginal candidiasis based on reconstituted human vaginal epithelium. Infect Immun 71: 3227-3234.

12. Schaller M, Schackert C, Korting HC, Januschke E, Hube B (2000) Invasion of Candida albicans correlates with expression of secreted aspartic proteinases during experimental infection of human epidermis. J Investig Dermatol 114: 712-717.
13. Lermann U, Morschhauser J (2008) Secreted aspartic proteases are not required for invasion of reconstituted human epithelia by Candida albicans. Microbiology 154: 3281-3295.
14. Correia A, Lermann U, Teixeira L, Cerca F, Botelho S, et al. (2010) Limited role of secreted aspartyl proteinases sap1 to sap6 in Candida albicans virulence and host immune response in murine hematogenously disseminated candidiasis. Infect Immun 78: 4839-4849.
15. Mayer FL, Wilson D, Hube B (2013) Candida albicans pathogenicity mechanisms. Virulence 4: 119-128.
16. Moyes DL, Wilson D, Richardson JP, Mogavero S, Tang SX, et al. (2016) Candidalysin is a fungal peptide toxin critical for mucosal infection. Nature 532: 64-68.
17. Netea MG, Brown GD, Kullberg BJ, Gow NA (2008) An integrated model of the recognition of Candida albicans by the innate immune system. Nat Rev Microbiol 6: 67-78.
18. Willment JA, Marshall AS, Reid DM, Williams DL, Wong SY, et al. (2005) Ue human beta-glucan receptor is widely expressed and functionally equivalent to murine dectin-1 on primary cells. Eur J Immunol 35: 1539-1547.
19. LeibundGut-Landmann S, Gross O, Robinson MJ, Osorio F, Slack EC, et al. (2007) Syk- and card9-dependent coupling of innate immunity to the induction of t helper cells that produce interleukin 17. Nat Immunol. 8: 630-638.
20. Gantner BN, Simmons RM, Underhill DM (2005) Dectin-1 mediates macrophage recognition of Candida albicans yeast but not filaments. EMBO J 24: 1277-1286.
21. Nieto-Patlan A, Campillo-Navarro M, Rodriguez-Cortes O, Munoz-Cruz S, Wong-Baeza I, et al. (2015) Recognition of Candida albicans by dectin-1 induces mast cell activation. Immunobiology 220: 1093-1100.
22. De Jong MA, Vriend LE, Ueelen B, Taylor ME, Fluitsma D, et al. (2010) C-type lectin langerin is a beta-glucan receptor on human langerhans cells that recognizes opportunistic and pathogenic fungi. Mol Immunol. 47: 1216-1225.
23. Joly S, Ma N, Sadler JJ, Soll DR, Cassel SL, et al. (2009) Cutting edge: Candida albicans hyphae formation triggers activation of the nlrp3 inflammasome. J Immunol. 183: 3578-3581.
24. Jaeger M, Van Der Lee R, Cheng SC, Johnson MD, Kumar V, et al. (2015) Ue RIG-I-like helicase receptor mda5 (IFIH1) is involved in the host defense against candida infections. Eur J Clin Microbiol Infect Dis. 34: 963-974.
25. Bradshaw TD, Wrigley S, Shi DF, Schultz RJ, Paull KD, et al. (1998) 2-(4-aminophenyl)benzothiazoles: novel agents with selective profiles of in vitro antitumor activity. Br J Cancer 77: 745-752.
26. Alang G, Kaur R, Singh A, Budhlakoti P, Singh A, et al. (2010) Synthesis, Characterization and antifungal activity of certain (E)-1-(1-(substitutedphenyl) ethylidene)-2-(6-methylbenzo[d]thiazol-2-yl) hydrazine analogues. IJPBA 1: 56-61.
27. Suresh CH, Rao JV, Jayaveera KN (2010) Synthesis of 4-(2'-substituted benzothiaozles)-5-mercapto-3-(substituted)-1,2,4-triazole derivatives for possible antimicrobiological activities. RJPBCS 1: 635-640.
28. Basavaraja KM, Somashekhar B, Shivakumar B (2010) Synthesis of 2-[(1-phenyl) (aryl) azo] methyleneimino-6-chloro/ fluoro benzothiazoles and their antibacterial activity. Int J PharmTech Res 2: 1139-1143.
29. Vedavathi M, Somashekar B, Sreenivasa GM, Jayachandran E (2010) Synthesis, characterization and anti-microbial activity of fluoro benzothiaozle incorporated with 1,3,4-thiadiazole. J Pharm Sci & Res 2: 53-63.
30. Pandurangan A, Sharma A, Sharma N, Sharma P.K., Visht S (2010) Synthesis and structural studies of novel benzothiazole derivative and evaluation of their antimicrobial activity. Der Pharma Chemica 2: 316-324.
31. Rajeeva B, Srinivasulu N, Shantakumar SM (2009) Synthesis and antimicrobial activity of some new 2-substituted benzothiazole derivatives. E-Journal of Chemistry 6: 775-779.
32. Malik JK, Manvi FV, Nanjwade BK, Singh S (2009) Synthesis and screening of some new 2-amino substituted benzothiazole derivatives for antifungal activity. Drug Invention Today 1: 32-34.
33. Patel NB, Shaikh FM (2010) Synthesis of new pyridine based 4-thiazolidinones incorporated benzothiazoles and evaluation of their antimicrobial activity. JSciences 21: 121-129.
34. Barot HK, Mallika G, Sutariya BB, Shukla J, Nargund LVG (2010) Synthesis of nitrogen mustards of flouro-benzothiazoles of pharmacological interest. Research J PBCS 1: 124-129.
35. Dua R, Sonwane SK, Srivastava SK, Srivastava SD (2010) Greener and expeditious synthesis of 2- azetidinone derivative from 2-mercaptobenzothiazole and their pharmacological screening of the compounds using microwave irradiation. World J Chem 5: 52-56.
36. Bhusari KP, Amnerkar ND, Khedekar PB, Kale MK, Bhole RP (2008) Synthesis and in vitro antimicrobial activity of some new 4-amino-N-(1,3-Benzothiazol-2-yl) benzenesulphonamide derivatives. Asian J Research Chem 1: 53-58.
37. Sathe BS, Jayachandran E, Jagtap VA, Sreenivasa GM (2011) Anthelmintic activity of newly synthesized moieties of fluoro benzothiazole Schiff's bases. RJPBCS 2: 510-515.
38. Sreenivasa GM, Jyachandran E, Shivakumar B, Jayaraj KK, Kumar V (2009) Synthesis of bioactive molecule fluoro benzothiazole comprising potent heterocyclic moieties for anthelmintic activity. Arch Pharm Sci & Res 1: 150-157.
39. Venkatesh P, Pandeya SN (2009) Synthesis, characterization and anti-inflammatory activity of some 2-amino benzothiazole derivatives. Int J ChemTech Res 1: 1354-1358.
40. Shashank D, Vishawanth T, Prasha A, Balasubramaniam V, Nagendra A, et al. (2009) Synthesis of some substituted benzothiazole derivatives and its biological activities. Int J ChemTech Res 1: 1224-1231.
41. Kaur H, Kumar S, Singh I, Saxena KK, Kumar A (2010) Synthesis, characterization and biological activity of various substituted benzothiazole derivatives. DJNB 5: 67-76.
42. Muttu CT, Bhanushali MD, Hipparagi SM, Tikare VP, Karigar A (2010) Microwave assisted synthesis and evaluation of some fluoro, chloro 2-N(substituted schiff's bases) aminobenzothiazoles derivatives for their anti-inflammatory activity. IJRAP 1: 522-528.