A Review: Medicinally Important Nitrogen Sulphur Containing Heterocycles

Praveen K. Sharma1*, Andleeb Amin1 and M. Kumar2

1Department of Chemistry, School of Chemical Engineering and Physical Sciences, Lovely Professional University, Phagwara, Punjab, India
2Department of Chemistry, University of Rajasthan, Jaipur, India

Abstract:
Nitrogen sulphur containing heterocycles have specific properties due to which they can be used as a potential material in a different type of industries such as medicinal/pharmaceutical, paint, packing and textile, required for various chemical, physical operations and their use as products. Especially dyes, paint, agrochemicals, medicine, etc. make them more significant. In present days, Nitrogen-Sulfur heterocycles are repeatedly attracting the interest of chemists due to their exceptional bioactive behavior. The present study is a review of the work carried out by a chemist in the discovery of new, effective, medicinally important heterocyclic compounds. The present review basically focused on nitrogen-sulfur heterocycles of potential therapeutic interest, especially with thiazole, thiazine, pyrimidine, morpholine and piperazine heterosystems, benzothiazines, pyrazole-benzothiazines, morpholine-benzothiazines, piperazine-benzothiazines and pyrimidine-benzothiazoles, mainly due to their unique structural features, which enable them to exhibit a number of biological and pharmacological activities. Due to a novel mode of action, a broad spectrum of activity, lesser toxicity towards mammalian cells, and suitable profiles towards humans have triggered the use of Nitrogen Sulphur containing heterocycles in designing and synthesizing their derivatives with better properties. The overall objective of the review is to discuss the importance of novel biodynamic structurally diverse heterocycles of potential therapeutic interest: pyrimidine, morpholine, piperazine, pyrazole, benzothiazoles, pyrimidobenzothiazoles, 4H-1,4-benzothiazines, pyrazolyl-benzothiazines, morpholinyl-benzothiazines and piperazinyl-benzothiazines in order to have access to important commercial molecules for the search of better future.

Keywords: Pyrimidobenzothiazoles, Morpholinylbenzothiazines pharmacophores, Antimicrobial, Antiviral, Benzothiazoles, Benzothiazines, Pyrazolylbenzothiazines, Piperazinylbenzothiazines.

1. INTRODUCTION

Heterocycles are considered as the largest section of chemistry, especially organic chemistry. A greater part of the natural compounds produced by biotic component has heterocyclic rings as a constitutional part of their molecules. Different types of commercially important compounds alkaloids like vinblastine, reserpine, morphine, ellipticine, antibiotics like cephalosporin, penicillin etc., cardiac glycosides and different type of pesticides are heterocycles of meaning for animal and human health. The majority of the important advances have been developed by synthesizing new heterocycles which imitate natural products with similar biological activities. For that reason, scientists/researchers/chemist communities are on a nonstop search to develop better pesticides, pharmaceuticals, fungicides, compost material, weed killers, insecticides, etc. Heterocycles' role in biological system is very important. Biochemical processes of components of living organisms like RNA, DNA etc. are based on heterocycles. Except for this present life pattern and civilization, there are additional significant applications of heterocycles in the fields of cosmetics, additives, antioxidants, vulcanization accelerators dyestuffs, photographic material, reprography, data storage, solvents, and plastics. Eventually, heterocyclic chemistry is an infinite supply of exceptional compounds. A large number of models of carbon, heteroatoms and hydrogen, can be produced, which have various biological, physical and chemical properties [1 - 7]. The expansion of newly discovered processes and the planned use of recognized procedures for the development of heterocycles continue to strengthen the vast domain of organic chemistry.

A specific class of heterocycles having sulfur-nitrogen heteroatoms includes very important aromatic compounds that show physicochemical properties with significance in the development of futuristic materials such as magnets and molecular conductors. At present, interest has been promptly growing in accepting modifications and the characteristics of sulphur-nitrogen based heterocycles. Aromatic heterocycles containing Nitrogen (N) and sulfur(S) are resulting from aromatic carbocycles with the replacement of one or more
carbon by a heteroatom in the ring. Whereas, the occurrence of sulfur and nitrogen atoms in the cyclic ring is usually related to the complexity and instability in the synthesis, however, the established nitrogen and sulfur containing heterocycles with significant properties have repeatedly been synthesized. On account of the availability of electrons (unshared pairs) and the distinction in electronegativity between carbon and heteroatoms, heterocycles are very significant in the cyclic molecular structures. Therefore, the nitrogen-sulphur heterocycles exhibit physicochemical properties and reactivity fairly diverse from the precursor carbocyclic compounds [8 - 12]. The sulphur-nitrogen heterocycles form a fascinating class of heterocycles and inviting the attention of the researchers due to their structural heterogeneity and biomedical properties. In view of the structural modifications with the presence of heteroatoms and the relationship of structures with the pharmacological and biological activities. In this review article, we focused on nitrogen-sulfur heterocycles of biological and pharmacological significance inculcating multi-dimensional structural features due to distinctiveness in substituents, heterocyclic systems and adjoined pharmacologically active functional groups for making them accessible for biological evaluation and SAR (structural activity relationship) studies. In this review, we have focused on nitrogen-sulfur heterocycles of potential therapeutic interest especially with thiazole, thiazine, pyrimidine, morpholine and piperazine heterosystems, benzothiazines, pyrazolylbenzothiazines, morpholinybenzothiazines, piperazinylbenzothiazines and pyrimidobenzothiazoles, mainly due to their unique structural features, which enable them to exhibit a number of biological and pharmacological activities. The pharmacological/biological activities of heterocyclic compounds mainly depend on the structural specificity and the strength of interaction between a drug and receptors present in the biological system.

2. REVIEW OF LITERATURE

2.1. Medicinally Important Pyrimidine, Benzothiazole Fused Heterosystem: Pyrimidobenzothiazole

Pyrimidine and Thiazole nuclei are treated preferred structures as both these heterocyclic systems constitute the pharmacophore of diverse biological active molecules [13 - 19] Fig. (1). In medicinal chemistry, the therapeutic applications of pyrimidine derivatives are well known. RNA and DNA activities are based on nucleic acids Uracil, Thymine and cytosine, which have pyrimidine unit. Pyrimidine nucleus compounds acquire a wide variety of biological activities, like stavudine and zidovudine as antiHIV, sulphamethazine trimethoprim, and sulphadiazine as antibacterial, idoxuridine and trifluridine as antiviral, barbiturates e.g. phenobarbitone as sedative, 5-fluorouracil as anticancerprazosin and minoxidil as antihypertensive, hypnotics and anticonvulsant, thionyzalmine as H₂-antithiamine, and fervenuline and toxoflavin as antibiotics, propylthiouracil as antithyroid, sulphadoxin as antimalarial and antibacterial, etc [20]. Pyrimidine and their derivatives are very well known anti-inflammatory, analgesic and antipyreptic agents [21 - 33].

In the same way, substituted benzothiazoles show interesting biological activities, like antiviral, anti-inflammatory, anticonvulsant, antitumor, antimicrobial and antagonists, etc [34 - 45]. The adjoining of one biodynamic heterocyclic system with another biodynamic heterosystem results in a molecule with structural variability and improved pharmacological activity. The fusion of heterosystems has been proven to be useful and attractive for the design of new molecular framework of therapeutically interesting drugs. With the object of discovery of exploring new heterocyclic therapeutics, we focused on pyrimidobenzothiazoles, a new class of heterocycles, incorporating two pharmacologically important heterocyclic systems, benzothiazole and pyrimidine [46 - 56].

Pyrimidobenzothiazoles reportedly exhibited an extensive choice of pharmacological and biological activities such as anticonvulsant [57], anti-inflammatory [58], antitumor [59], etc. Pyrimidobenzothiazoles can also act as GABA receptor binding agents [60 - 62].

2.2. Biodynamic Heterosystem: Benzothiazine and their Derivatives

Benzothiazines are structural analogues of phenothiazines [63 - 69] and exhibit similar structural flexibility along with structural specificity, fold along nitrogen and sulfur axis, as in phenothiazines. The direction of folding and the magnitude of folding angle depend to a larger extent on the position as well as the type of the other substituents on the ring system, which consequently affect the therapeutic activities considerably. The structural specificity along nitrogen-sulfur axis in phenothiazines and 4H-1,4-benzothiazines has been considered as a significant factor to be responsible for their activities and made both the series important from not only structural point of view but also from pharmacological as well as industrial view point [70 - 72]. The structural presentation of phenothiazine and 4H-1,4-benzothiazine ring systems according to Gordon’s model is presented to show the structural similarity of both the heterosystems Fig. (2).

Benzothiazines have also been established for their pharmacological/biological behavior such as antihypertensive [73], antiinflammatory [74], antianginal [75], antihistaminic [76], antipsychotic [77], antiemetic [78], neuroleptic [79], antibacterial [80], antioxidant properties [81], etc. 4H-1,4-Benzothiazines have also been used as colour photographic developers and dye stuffs in the industry [82 - 84]. Some 4H-1,4-benzothiazines along with their biopharmaceutical activities are presented in Table I.
Fig (1). Pyrimidobenzothiazole.

![Pyrimidobenzothiazole](image)

Fig (2). Gordon’s model.

![Gordon’s model](image)

Table 1. Pharmacological activities of Nitrogen-Sulphur containing heterocycles.

| Nitrogen-Sulphur Containing Heterocycles | Activity                        | Reference |
|----------------------------------------|---------------------------------|-----------|
| ![10H- Phenothiazine](image)            | Vasorelaxant/ KATP-Channel Openers | [85]      |
| ![4H-1,4-Benzothiazine](image)         |                                 |           |

\[ R = H, CF_3, Br, NO_2, CF_3, CN \]
\[ R1 = H, CH_2=CH_2, COCH_2Cl, CSNHCH_2Ph \]
\[ X = CO, CH_2 \]
| Nitrogen-Sulphur Containing Heterocycles | Activity | Reference |
|-----------------------------------------|----------|-----------|
| \[
\begin{align*}
\text{H}_2\text{N} & - & \text{N} & - & \text{H} & - & \left(\text{NH}_\text{n}\right)\text{COOH} \\
\text{A}_{\text{=S}} & , & n & = & 1, 2 & (\text{MX}-68) \\
\text{MTX Derivatives}
\end{align*}
\] | Anti-rheumatic Anti-proliferate | [86] |
| \[
\begin{align*}
\text{F}_3\text{C} & - & \text{H} & - & \text{O} & - & \text{Br} \\
\text{OH} & - & \text{OMe}
\end{align*}
\] | Vasorelaxant | [87] |
| \[
\begin{align*}
\text{F} & - & \text{F} & - & \text{F} \\
\text{N} & - & \text{H} & - & \text{N} \\
\text{S} & - & \text{O} & - & \text{S} \\
\text{O} & - & \text{COOH}
\end{align*}
\] | Antidiabetic | [88] |
| \[
\begin{align*}
\text{N} & - & \text{O} \\
\text{N} & - & \text{O}
\end{align*}
\] | KATP Channel Openers Vasorelaxant | [89] |
| \[
\begin{align*}
\text{O} & - & \text{N} & - & \text{O}
\end{align*}
\] | Apoptosis | [90] |
| Nitrogen-Sulphur Containing Heterocycles | Activity | Reference |
|----------------------------------------|----------|-----------|
| ![Chemical Structure](image1) | Intercellular adhesion molecule-I (Icam-I) | [91] |
| ![Chemical Structure](image2) | Intercellular adhesion molecule-I (Icam-I) | [92] |
| ![Chemical Structure](image3) | Anti-inflammatory | [93] |
| ![Chemical Structure](image4) | Antimalarial (Against a rodent malaria parasite *Plasmodium berghei*) | [94] |

*NR_{1}R_{2} = \[
\begin{array}{c}
N \\
N \\
N \end{array}
\]

X=NHCOMe, NHSO_{2}Me, CH_{2}NHSO_{2}Me, CH_{2}CH_{2}NHSO_{2}Me, NHSO_{2}Ph, NHSO_{2}NMMe_{2}, NHSO_{2}NH_{2}, HN SO_{2}N, HN SO_{2}NO

R_{1}= 6-Cl, 7-Cl, R_{2}= 3-Cl, 3,4-dichloro, 2-Me
| Nitrogen-Sulphur Containing Heterocycles | Activity | Reference |
|----------------------------------------|----------|-----------|
| ![Chemical Structure 1] | Lipoygenase inhibitor | [95] |
| ![Chemical Structure 2]  
R₁ = CF₃, R₂ = F, CF₃, R₃ = CH₃, C₆H₅, R₄ = 3-ClC₆H₄, 3-BrC₆H₄ | Antimicrobial (Antibacterial activity against *Bacillus subtilis*, *Bacillus mega*, *Escherichia coli*, *Aspergillus arogen* and antifungal activity against *Aspergillus awamori*) | [96] |
| ![Chemical Structure 3] | Anti-Candida | [97] |
| ![Chemical Structure 4] | Antifungal against *Candida albicans* | [98] |
| ![Chemical Structure 5]  
R = -Et, -Bn | Antagonistic | [99] |
## Nitrogen-SulphurContainingHeterocycles

| Nitrogen-Sulphur Containing Heterocycles | Activity | Reference |
|-----------------------------------------|----------|-----------|
| ![Chemical Structure 1](image1.png)    | Antibacterial against *Staphylococcus aureus* | [100] |
| ![Chemical Structure 2](image2.png)    | Antibacterial against *Neisseria gonorrhoea* | [101] |
| ![Chemical Structure 3](image3.png)    | Antimicrobial against *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Enterococcus faecalis* and *Enterococcus faecium* | [102] |
| ![Chemical Structure 4](image4.png)    | Antimicrobial against *Staphylococcus aureus*, *Streptococcus pneumoniae* | [103] |
| ![Chemical Structure 5](image5.png)    | Anti-autoimmune | [104] |

*(Table 1) contd.....*
| Nitrogen-Sulphur Containing Heterocycles | Activity                     | Reference |
|----------------------------------------|------------------------------|-----------|
| ![Chemical Structure](image1)           | Antitumor, anti HIV          | [105]     |
| ![Chemical Structure](image2)           | Natural pigments             | [106]     |
| ![Chemical Structure](image3)           | Antimicrobial against S. aureus | [107]     |
| ![Chemical Structure](image4)           | Renin Inhibitor              | [108]     |
| ![Chemical Structure](image5)           | Antiviral against zika virus | [109]     |
| ![Chemical Structure](image6)           | Anti-inflammatory            | [110]     |

(Table 1) contd....
2.3. Pharmaceutically Important Pyrazole Derivatives: Pyrazolylbenzothiazine

Pyrazole derivatives, a set of heterocycles, occupy a significant place in pesticide and medicinal chemistry by means of a large collection of bioactivities. Pyrazole derivatives are well known and reported to show antibacterial, fungicidal, herbicidal, antimicrobial, antiinflammatory, and anticancer activities [117 - 127]. Pyrazophos, the fungicide was marketed by Hoechst AG in 1974, which have the ability to control powdery mildew in vegetables. The significance like a novel mode of action, broad spectrum of activity, lesser toxicity towards mammalian cells, and suitable profiles towards humans have triggered the use of pyrazole in designing and synthesizing its derivatives with better...
properties. Recently, pyrazole compounds, like pyraclostrobin (BASF, 2001) and pentaipyrid (Mitsui Toatsu Chemicals, 1995), are found to be latent antifungal agents for the control of various plant diseases. In recent years, researchers have given considerable attention to the synthesis of pyrazole and their derivatives due to their wide ranging bioactivities obtained through modification of structural profile by a change of the substituents in pyrazole ring [128].

In view of the structural relationship with bioactivities, the synthesis of substituted 1,4-benzothiazines Fig. (3), incorporating both benzothiazine and pyrazole heterosystems with this assumption that the synthesized heterocycles will exhibit better features caused by co-existence of two types of pharmacophoric interactions with different action of mechanism have also been reported.

2.4. Medicinally Important Morpholine/Piperazine and their Derivatives: Morpholinyl/Piperazinylbenzothiazines

The systems containing morpholine fragments have attracted interest as potential biologically active compounds [129 - 135]. Morpholines show a wide spectrum of properties varying from medicinal field applications to agricultural use [136]. Reboxetine acts as an antidepressant drug and is applied to treat panic disorder, clinical depression, hyperactivity disorder [137]. Fenpropimorph is a broadly used leaf fungicide and is predominantly used to limit fungal diseases in cereals [138]. Trioxazine, ofloxacin, ethmosine, dextromoramide, etc. containing morpholine nucleus have also found their applications in medicine. Morpholine derivatives have been the area of interest for the pharmaceutical industry as these act as bioactive compounds and effective substrates for further elaboration. In this regard, a number of patents elucidating the biological significance of such compounds have been published [139 - 143]. The literature survey reveals that the compounds with morpholine Fig. (4) show enormous therapeutic uses that include antimalarial [144], antibacterial [145], antimicrobial [146], anticonvulsant agents, antidepressant [147], leukemia [148], tranquilizers [149] and antituberculous agents [150].

Similarly, the piperazine ring is a preferrable heterosystem in medicinal-pharmaceutical chemistry and is frequently found in the structure of various enzyme inhibitors as well as clinical therapeutics [151]. Piperazine and its derivatives act as useful synthetic building blocks and have been regularly used in the preparation of important biologically active compounds. Piperazine and its derivatives have also been shown to exhibit a wide spectrum of pharmacological and biological activities such as, antibacterial [152, 153], antineoplastic [154], antinociceptive [155], antimalarial [156], antiproliferative activity [157], Na channel blocker [158], antitumor [159], antagonistic [160], antimicrobial [161], etc. Taking into account the significance of piperazine scaffold in a wide range of applications [162 - 174], we apprehended that it might be worthwhile to incorporate the piperazine heterosystem alongwith 1,4-benzothiazine Fig. (5), to synthesize therapeutically interesting heterocycles with structural diversity [175 - 179].

Fig (3). Pyrazolylbenzothiazine.

Fig (4). Morpholinylcarbonyl-4H-1,4-benzothiazines.
Fig (5). Piperazinylcarbonyl-4H-1,4-benzothiazines.

CONCLUSION

Literature reveals that nitrogen and sulphur containing heterosystems are truly important for the development of human and associated society. These heterosystems play an important and key role in curing process against life threatening diseases, which directly influence the growth of humans and animals. The overall objective of the review is to discuss the importance of novel biodynamic structurally diverse heterocycles of potential therapeutic interest, pyrimidine, morpholine, piperazine, pyrazole, benothiazoles, pyrimidobenzothiazoles, 4H-1,4-benzothiazines, pyrazolylbenzothiazines, morpholinyl-benzothiazines and piperazinylbenzothiazines in order to have access to important commercial molecules for the search of better future.

CONSENT FOR PUBLICATION

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Katritzky, A.R.; Rees, C.W. Comprehensive Heterocyclic Chemistry, 1st ed; Pergamon Press: New York, 1984.
[2] Katritzky, A.R.; Rees, C.W.; Scriven, E.F.V. Comprehensive Heterocyclic Chemistry, 2nd ed; Pergamon Press: New York, 1996.
[3] Balaban, A.T.; Onciu, D.C.; Katritzky, A.R. Aromaticity as a cornerstone of heterocyclic chemistry. Chem. Rev., 2004, 104(5), 2777-2812.
[4] Martins, M.A.P.; Cunico, W.; Pereira, C.M.P.; Flores, A.F.C.; Bonacorso, H.G.; Zanatta, N. 4-Alkoxycarbonyl-1H-1,2-dithiole-3-thione: Preparation and applications in heterocyclic synthesis. Curr. Org. Synth., 2004, 1, 391-403.
[5] Druzhinin, S.V.; Balenkova, E.S.; Nenajdenko, V.G. Recent advances in the chemistry of α,β-unsaturated trifluoromethylketones. Tetrahedron, 2007, 63, 7753-7808.
[6] Ghose, A.K.; Viswanadhan, V.N.; Wendoloski, J.J. A knowledge-based approach in designing combinatorial or medicinal chemistry libraries for drug discovery. 1. A qualitative and quantitative characterization of known drug databases. J. Comb. Chem., 1999, 1(1), 55-68.
[7] Xu, J.; Stevenson, J. Drug-like index: A new approach to measure drug-like compounds and their diversity. J. Chem. Inf. Comput. Sci., 2000, 40(5), 1177-1187.
[8] Marcos, C.F.; Polo, C.; Rakitin, O.A.; Rees, C.W.; Torroba, T. From Hunig’s Base to Bis[1,2]dithiole-3-thiones in One Pot: The Fast Route to Highly Sulfurated Heterocycles. Angew. Chem., 1997, 26, 281-283.
[9] [http://dx.doi.org/10.1002/anie.199702811]
[10] Marcos, C.F.; Polo, C.; Rakitin, O.A.; Rees, C.W.; Torroba, T.; White, A.J.P.; Williams, D.J. Tertiary amine-S,S chemistry: interception of reaction intermediates. Chem. Commun. (Camb.), 1998, 4, 453-454.
[11] [http://dx.doi.org/10.1039/a708396c]
[12] Marcos, C.F.; Rakitin, O.A.; Rees, C.W.; Torroba, T.; White, A.J.P.; Williams, D.J. Bis[1,2]dithiole[3,4-b][4,3-e][1,4]thiazine-3,5-dione, a planar 1,4-thiazine. Chem. Commun. (Camb.), 1999, 1, 29-30.
[13] Garcia-Valverde, M.; Pascual, R.; Torroba, T. Synthesis, chemistry, and dynamic NMR study of new atropisomeric 4-dialkylamino-5-chloro-1,2-dithiole-3-thiones. Org. Lett., 2003, 5(6), 929-932.
[14] [http://dx.doi.org/10.1021/ol034145x]
[15] Kappe, C.O. 100 years of the biginelli dihydropyrimidine synthesis. Tetrahedron, 1993, 49, 597-606.
[16] [http://dx.doi.org/10.1021/jm000040a010]
[17] Dandia, A.; Khatura, S.; Sarawgi, P.; Jain, A. One-Pot Three-Component Condensation Reaction in Water: An Efficient and Improved Procedure for the Synthesis of Pyrimido[2,1-b]benzothiazoles. Phosphorus Sulphur, 2007, 182, 2529-2539.
[18] Varma, R.S. Solvent-free organic syntheses using supported reagents and microwave irradiation. Green Chem., 1999, 1, 43-45.
[19] [http://dx.doi.org/10.1039/a00223e]
[20] Atwal, K.S.; Swanson, B.N.; Unger, S.E.; Floyd, D.M.; Moreland, S.; Hedberg, A.; O’Reilly, B.C. Dihydropyrimidine calcium channel blockers. 3. 3-Carbamoyl-4-carboxylic acid esters as orally effective antihypertensive agents. J. Med. Chem., 1991, 34(2), 806-811.
[21] [http://dx.doi.org/10.1021/jm00106a048]
[22] Rovnyak, G.C.; Atwal, K.S.; Hedberg, A.; Kimball, S.D.; Moreland, S.; Gougoutas, J.Z.; O’Reilly, B.C.; Schwartz, J.; Malley, M.F. Dihydropyrimidine calcium channel blockers. 4. Basic 3-substituted-4-aryl-1,4-dihydropyrimidine-5-carboxylic acid esters. Potent antihypertensive agents. J. Med. Chem., 1992, 35(17), 3254-3263.
[23] [http://dx.doi.org/10.1021/jm00095a023]
[24] Khania, F.L.; Sillinietse, G.O.; Ozel, G. Dabur.; Ozel, Ya. Ya.; Yakimenis, A. A. Khim.Pharm. Zh, 1998, 78, 1321.
[25] Cho, H.; Uen, M.; Shima, K.; Mizuno, A.; Hayashimatsu, M.; Ohnaka, Y.; Takeuchi, Y.; Hamaguchi, M.; Aisaka, K.; Hidaka, T. Dihydropyrimidines: novel calcium antagonists with potent and long-lasting vasodilative and antihypertensive activity. J. Med. Chem., 1989, 32(10), 2399-2406.
[http://dx.doi.org/10.1021/jp100109a] [PMID: 2553119]

[20] Belcema, M.; Baneker, A.; Nguyen, V.; Benillou, F.; Ouettel, C.; Marinier, A.; Roy, S.; Yung, X.; Zhang, Y.; Zuei, C. PCT Int. Appl. WO 2003084, Through. Chem. Abstr., 2003, 13937987X

[21] Pirsigroh, R.; Bianchini, F.; Banchelli, G.; Iiglesi, G.; Raimondi, L.; Cecotti, V.; Fattorini, L. Pharmacological activity of FFP028 (2-phénylpyrazol-4-ethyl-4,7-dihydro-[1,5]pyrimidine-7-one) as a new non-steroidal anti-inflammatory agent. Pharmaco Lett. Res. Comm., 1986, 1(3), 241-256.

[22] Modica, M.; Samantagi, M.; Santagati, A.; Gunilli, V.; Mangano, N.; Caruso, A. Synthesis of new [1,3,4]thiadiazol(2,3- d)pyrimidine derivatives with anti-inflammatory activity. Farmazie, 2000, 55(7), 500-502.

[23] Cenicola, M.L.; Donnoli, D.; Stella, L.; De Paola, C.; Costantino, M.; Abignente, E.; Arena, F.; Rurouschi, E.; Saturnino, C. Research on heterocyclic compounds. Antiinflammatory activity of some imidazol[1,2-d]pyrimidines. Pharmaz. Res., 1990, 2(Suppl. 3), 80-81.

[24] Nargund, L.V.G.; Badiger, V.V.; Yarral, S.M. Synthesis and antimicrobial and anti-inflammatory activities of substituted 2-mercaptop-[3,4-(4-substituted-phenyl)-1,6-cycloamino-5H-[1]benzopyrano[4,3-d]pyrimidines endowed with in vivo antiplatelet activity. J. Med. Chem., 2001, 44(15), 2828-2843.

[25] Nargund, L.V.G.; Badiger, V.V.; Yarral, S.M. Synthesis and antimicrobial and anti-inflammatory activities of substituted 2-mercaptop-[3,4-(4-substituted-phenyl)-1,6-cycloamino-5H-[1]benzopyrano[4,3-d]pyrimidines endowed with in vivo antiplatelet activity. J. Med. Chem., 2001, 44(15), 2828-2843.

[26] Lee, C.H.; Jung, M.; Cowart, G.; Gfess, G.; Perner, R.; Kim, K.H.; Gu, Y.G.; Williams, M.; Jarvis, M.F.; Kowalk, E.A.; Stewart, A.O.; Bhagwat, S.S. Discovery of 4-amino-5-(3-bromophenyl)-7-(6′-substituted-1′, 3′-biphenyl)-2-pyrazolines. J. Med. Chem., 2001, 44(13), 2133-2138.

[27] Boyle, D.L.; Kowalk, E.A.; Jarvis, M.F.; Lee, C.H.; Bhagwat, S.S.; Williams, M.; Firestone, G.S. Anti-inflammatory effects of AIB-702, a novel non-nucleoside adenine kinase inhibitor, in rat adjuvant arthritis. J. Pharmacol. Exptl. Ther., 2001, 296(2), 495-500. [PMID: 1160636]

[28] Molina, P.; Aller, E.; Lorenzo, A.; Lopez-Cremades, P.; Rioja, I.; Ubeda, A.; Terencio, M.C.; Alcaraz, M.J. Solid-phase synthesis and inhibitory effects of some pyrido[2,3-d]pyrimidines derivatives on leukocyte formations and experimental inflammation. J. Med. Chem., 2001, 44(6), 1011-1014. [PMID: 11300882]

[29] Vidal, A.; Ferrandi, M.L.; Ubeda, A.; Acero-Alarcon, A. Sepulveda-Arques, J.; Alcaraz, M.J. Effect of some hexahydridiazol[1,2-c]pyrimidines in inflammatory responses involving leukocytes and macrophages. J. Pharmacol. Pharm., 2001, 53(10), 1379-1385.

[30] Bruno, O.; Bruolo, C.; Ranise, A.; Schenone, S.; Bondavalli, F.; Barocelli, E.; Ballabeni, V.; Chiavarini, M.; Tognolini, M.; Impicciatore, M. Synthesis and pharmacological evaluation of 2,5-cycloamo-5H-[1]benzopyran(3,4-d)pyrimidines endowed with in vivo antinociceptive activity. Bioorg. Med. Chem. Lett., 2001, 11(11), 1397-1400. [http://dx.doi.org/10.1016/S0960-894X(01)00221-9] [PMID: 1137363]

[31] Bahad, S.S.; Shinde, D.B. Synthesis and anti-inflammatory activity of some [2-amino-6-(4-disubstituted aryl)-4-(4-disubstituted phenyl)-1,6 dihydropyrimidine-5(4H)-yl] acetic acid derivatives. Acta Pharm., 2003, 53(3), 223-229. [PMID: 14769245]

[32] Sawhney, S.N.; Bhutani, S. Dharmanir. Synthesis of some 2-(2-benzothiazolyl)-9′-2-(benzimidazole)-6′-aryl-4,5-dihydro-3 (211)-pyrazidinones as potential anti-inflammatory agents. Indian J. Chem., 1987, 26B, 348-350.

[33] Singh, S.P.; Vaid, R.K. Synthesis and anti-inflammatory activity of some 2-[4′-aryl-3′-[2-(diethylamino)-4-pheny]-5′-disubstituted benzothiazole and 4-butyl-1′-6′-substituted-2-benzothiazolyl]-3-methyl pyrazole-5-ones. Indian J. Chem., 1986, 25B, 288-291.

[34] Dugr, D.S.; Ulu, S.; Sahin, M.F.; Yelisada, E. Synthesis of 2-((benzothiazole-3-yl) and 2-benzothiazole-3-yl) acetic acid derivatives and Evaluation of their Antinociceptive and Anti-inflammatory Activity. Farmacie, 1998, 53, 80. [http://dx.doi.org/10.1016/S0960-894X(97)00017-7] [PMID: 943729]

[35] Dion, O.; Deperreux, P.; Lesieur, D.; Poupaert, J.H.; Caigot, D.H. Synthesis and evaluation of new 2-piperazinebenzothiazoles with high 5-HT1A and 5-HT3 affinities. Eur. J. Med. Chem., 1995, 30, 715-719.

[36] Sikorski, J.A.; Walsh, J.; Roy, S.; Yung, X.; Zhang, Y.; Zucchi, C. PCT Int. Appl. WO 2003084, Through.

[37] Vidal, A.; Ferrandi, M.L.; Ubeda, A.; Acero-Alarcon, A. Sepulveda-Arques, J.; Alcaraz, M.J. Effect of some hexahydridiazol[1,2-c]pyrimidines in inflammatory responses involving leukocytes and macrophages. J. Pharmacol. Pharm., 2001, 53(10), 1379-1385.

[38] Bruno, O.; Bruolo, C.; Ranise, A.; Schenone, S.; Bondavalli, F.; Barocelli, E.; Ballabeni, V.; Chiavarini, M.; Tognolini, M.; Impicciatore, M. Synthesis and pharmacological evaluation of 2,5-cycloamo-5H-[1]benzopyran(3,4-d)pyrimidines endowed with in vivo antinociceptive activity. Bioorg. Med. Chem. Lett., 2001, 11(11), 1397-1400. [http://dx.doi.org/10.1016/S0960-894X(01)00221-9] [PMID: 1137363]

[39] Bahad, S.S.; Shinde, D.B. Synthesis and anti-inflammatory activity of some [2-amino-6-(4-disubstituted aryl)-4-(4-disubstituted phenyl)-1,6 dihydropyrimidine-5(4H)-yl] acetic acid derivatives. Acta Pharm., 2003, 53(3), 223-229. [PMID: 14769245]
biological properties of fluorinated 2-(4-aminophenyl)benzothiazole. *Mol. Pharmacol.*, 2003, 63(3), 766-772.

Bradshaw, T.D.; Trapani, V.; Vasselin, D.A.; Westwell, A.D. The ary1 hydrocarbon receptor in anticancer drug discovery: friend or foe? *Curr. Pharm. Des.*, 2002, 8(27), 2475-2490.

Bradshaw, T.D.; Biggio, G.; Liso, M.; Zimmermann, J.; Bauer, H.H.; Hohorst, H.J.; Voelcker, G. Synthesis of new thienopyrimidobenzothiazoles and pyrimido[2,1-b]benzothiazoles as Novel antitumor 2-(4-amino-3-methylphenyl)-5-fluorobenzothiazole. *Mol. Immunol.*, 2001, 38(4), 239-246.

Shi, D.F.; Bradshaw, T.D.; Chua, M.S.; Westwell, A.D.; Stevens, M.F. Antitumor benzothiazoles. 14. aminophenyl)benzothiazoles to reactive intermediates by cytochrome *Mol. Immunol.*, 2001, 38(4), 239-246.

Cecchetti, V.; Schiaffella, F.; Tabarrini, O.; Fravolini, A. (1,4-dicarbethoxy-5-methylcyclohexanones and their testing for antiallergic drugs on histamine release from rat peritoneal mast cells. *Br. J. Pharmacol.*, 1999, 127(2), 283-288.

Lang, C.; Deniaud, I.; Devlin, M.; Reliquet, A.; Meslin, J.C. Efficient regioselective synthesis of trihydroxycoumarins: imidazol[1,2,4]-2H-pyrazino[3,4-f]imidazopyridin]-2(1H)-benzothiazoles as Novel Anticonvulsant Agents. *Sci. Pharm.*, 2001, 69(1), 53-61.

Futaki, T.; Ishida, Y.; Nakamichi, T.; Noda, S.; Yamaoka, S.; Harada, T.; Ishihara, H.; Sato, Y.; Inoue, K. Synthesis and spectroscopic studies of new fluorinated benzothiazoles. *J. Health. Sci.,* 1994, 40, 569-578.

Zimmermann, J.; Baur, H.H.; Hofsrät, H.J.; Voolcker, G. Synthesis of 1-aldolesfamoside-phenythiodiazines. *Arzneimittelforschung, 2000, 50(9), 843-847.* (PMID: 11050703)

Landreau, C.; Deniaud, I.; Devlin, M.; Reliquet, A.; Meslin, J.C. Efficient regioselective synthesis of trihydroxycoumarins: imidazol[1,2,4]-2H-pyrazino[3,4-f]imidazopyridin]-2(1H)-benzothiazoles and pyrimido[2,1-b]benzothiazoles. *J. Chem. Soc., Perkin Trans. 2, 2002, 1, 741-745.* (PMID: 103991116369)

Inoue, K.; Futaki, T.; Ishida, Y.; Nakamichi, T.; Noda, S.; Yamaoka, S.; Harada, T.; Ishihara, H.; Sato, Y.; Inoue, K. Synthesis and spectroscopic studies of new fluorinated benzothiazoles. *J. Health. Sci.,* 1994, 40, 569-578.

Kanda, A.; Hashimoto, H. Effects of semotiadil fumarate, a novel calcium antagonist, on blood pressure and heart rate in conscious spontaneously hypertensive rats. *Jpn. J. Pharmacol.*, 1993, 63(1), 121-124.

Sugimoto, Y.; Tanji, T.; Zhao, Q.E.; Fujii, Y.; Kamei, C. Effects of prochlorperazine buccal controlled analgesia with morphine following abdominal surgery. *Methods Find. Exp. Clin. Pharmacol.*, 1998, 20(6), 457-462.

Williams, P.I.; Smith, M. An assessment of prochlorperazine buccal controlled analgesia with morphine following abdominal surgery. *Methods Find. Exp. Clin. Pharmacol.*, 1998, 20(6), 457-462.

Teague, S.J.; Davis, A.M.; Oprea, T. The design of leadlike combinatorial libraries. *Angew. Chem. Int. Ed. Engl.*, 1999, 38(24), 3743-3748.

Armstrong, R.W.; Combs, A.P.; Tempes, P.A.; Brown, S.D.; Keating, T.A. Multiple-component condensation strategies for combinatorial library synthesis. *Acc. Chem. Res.*, 1999, 32(3), 313-320.

Kubayashi, T.; Strobek, M.; Schwartz, A.; Mori, Y. Inhibitory effects of a new neuropeptide diltiazem analogue, T-477, on cloned brain Ca2+ channels expressed in Xenopus oocytes. *Eur. J. Pharmacol.*, 1997, 332(3), 313-320.

http://dx.doi.org/10.1016/S0022-1139(00)80093-7

Gupta, R.R.; Kumar, M.; Gupta, V. Heterocyclic Chemistry. 2nd ed. *Springer-Verlag: Germany*, 1999.

http://dx.doi.org/10.1007/978-3-642-72276-9

Gupta, R.R.; Kumar, M.; Gupta, V. Heterocyclic Chemistry. 1st ed. *Springer-Verlag: Germany*, 1998.

http://dx.doi.org/10.1007/978-3-642-60775-3

Varga, J.M.; Kalchschmid, G.; Klein, G.F.; Frische, P. Mechanism of allergic cross-reactions-I. Multispecific binding of ligands to a mouse monoclonal anti-DNP IgE antibody. *Mol. Immunol.*, 1991, 28(6), 641-654.

http://dx.doi.org/10.1016/0161-5890(91)90133-5

Mettewally, M.A.; El-Hossini, M.S.; El-Alblak F.Z.; Khalil, A.M. Pharmacize, Synthesis of condensed heterocyclics from 3-aryl-2,4-dicarboxy-5-methylcyclohexanones and their testing for antimicrobial activity. *J. Pharm. Sci.,* 1992, 71(5), 336-339.

Li, H.; Dryhurst, G. Irreversible inhibition of mitochondrial complex I by 7-(2-aminoethyl)-3,4-dihydro-5-hydroxy-7H-1,4-benzothiazine-3-carboxylic acid (DHBT-I): A putative nigral endotxin of relevance to Parkinson’s disease. *J. Neurochem.*, 1997, 69(4), 1530-1541.

http://dx.doi.org/10.1046/j.1471-4159.1997.6904153.x

Gupta, R.R. It does not appear in the database of scientometric database. *Mol. Immunol.*, 2000, 36(4), 367-368.
62 The Open Medicinal Chemistry Journal, 2020, Volume 14

Sharma et al.

[108] Sabatini, S.; Kato, G.W.; Rossolini, G.M.; Brandini, D.; Fravolini, A.
From phenothiazine to 3-phenyl-1,4-benzothiazine derivatives as inhibitors of the Staphylococcus aureus NorA multidrug efflux pump. J. Med. Chem. 2008, 51(4), 4321-4330.

[109] Miller, W.H.; Rouse, M.B.; Seeffel, M.A. Antibacterial agents. WO2006014580 A1, 2006.

[110] Miller, W.H.; Pedrak, I.; Seeffel, M.A. Antibacterial agents. WO 2006020474 A1, 2006.

[111] Hubscherweser, C.; Survet, J.P.; Acklin, C.Z. Beta-aminocarboxyl antibiotics. WO2006098484 A1, 2006.

[112] Singh, R.; Argade, A.; Payan, D.G.; Clough, J.; Keim, H.; Sylvain, C.; Li, H.; Brahmi, S. Methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compounds. WO2006021574 A2, 2006.

[113] Ebara, T.; Hidomi, Y.; Kinoshi, K.; Masuya, K. Substituted piperidines as renin inhibitors. WO200615261 A1, 2006.

[114] Badsha, S.L.; Ahmad, N.; Ur Rehman, A.; Khan, K.; Ullah, A.; Alsayari, A.; Muhisbin, A.B.; N Mahboub, Y. Molecular docking and simulation of Zika virus NS3 helicase. BMC Chem. 2019, 13(1), 67-74.

[115] Kaul, B.L.; Piaux, B.; Wolf, V. Pigments, the process of their manufacture and their use. EP 10667882 A2, 2006.

[116] Bar, D.; Hubscherweser, C.; Survet, J.P.; Zumbrunn Acklin, C. New antibiotic derivatives. WO 2006021574 A2, 2006.

[117] Pierau, S.; Dale, G. Novel compounds having an anti-bacterial activity. WO 2006021484 A1, 2006.

[118] Strobel, H.; Nemeczek, C.; Louise, D.; Ruf, S.; Guenstern, St.; Lebrun, A.; Ritter, K.; Mallorren, J.L. Heterocycle -substituted cyclic urea derivatives. Preparation of pharmaceutical and pharmaceutical use thereof as kinase inhibitors. EP 1625391 A1, 2006.

[119] Yuji, O.; Fujimaki, A.; Akihiko, M.; Satoru, I. Process for the preparation of (+)-1,4-benzothiazine-2-acetic acid derivatives. WO2006070595 A1, 2006.

[120] Cali, P.; Hjelmencrantz, A.; Naern, L. Peptide deformylase inhibitors. WO2005092872 A1 20051006, 10.

[121] Molteni, V.; He, X.; He, Y.; Kreusch, A.; Nabakka, J.; Yang, K. Bicyclic compounds and compositions as pdf inhibitors. WO 200501161 A2 20050210, 2005.

[122] Bhushan, L.B.; Bhushan, L.V.; Channaveerappa, B.A.; Shivaramayya, K.; Rajagopalan, R.; Ranjan, C. Bicyclic compounds, process for their preparation and pharmaceutical compositions containing them. WO 2006070595 A1, 2006.

[123] Liu, X.H.; Cui, P.; Song, B.A.; Ibdoury, P.S.; Zhu, H.L.; Wang, S.F. Synthesis, structure and antibacterial activity of novel 1-(4S)-substituted-3-substituted-4,5-dihydro-2-ylfpeptide oxime ether derivatives. Bioorg. Med. Chem. 2008, 16(7), 4047-4052.

[124] Taniate, A.; Oyamada, Y.; Ofuji, K.; Kyoya, Y.; Suzuki, I.; Ito, H.; Kawaski, M.; Nagai, K.; Wachi, M.; Yamagishi, J. Design, synthesis and structure-activity relationship studies of novel indazole analogues as DNA gyrase inhibitors with Gram-negative antibacterial activity. Bioorg. Med. Chem. Lett., 2004, 14(11), 2857-2862.

[125] Velaparthy, S.; Brunsteiner, M.; Udinn, R.; Wan, B.; Franzblau, S.G.;
Petukhov, P.A. 5-tert-butyl-N-pyrrozol-4-yl-4,5,6,7-tetrahydrobenzo[4,5]isoxazole-3-carboxylic derivatives as novel potent inhibitors of Mycobacterium tuberculosis panthothenate synthetase: initiating a quest for new antibacterial drugs. J. Med. Chem. 2008, 51(7), 1999-2002. [http://dx.doi.org/10.1021/jm071372u] [PMID: 18335947]

[120] Magedov, I.V.; Manpadi, M.; Slambrouck, S.V.; Steelean, W.F.; Rozhkova, E.; Przheval'ski, N.M.; Rogelj, S.; Kornienko, A. Discovery and investigation of antiprofibrillar and apoptosis-inducing properties of new heterocyclic podophyllotoxin analogues accessible by a one-step multicomponent synthesis. J. Med. Chem. 2007, 50(21), 5183-5192. [http://dx.doi.org/10.1021/jm0705288] [PMID: 17894440]

[121] Rovnyak, G.C.; Millenig, R.C.; Schwartz, J.; Shu, V. Synthesis and antifungal activity of hydroxyhydropyrazines, oxazepanes and related analogues. J. Med. Chem. 1982, 25(12), 1482-1488. [http://dx.doi.org/10.1021/jm00340a018] [PMID: 6218302]

[122] Wächter, G.A.; Hartmann, R.W.; Sergeyev, T.; Grün, G.L.; Ledergerber, D. Tetrahydropyranophthalenes: influence of heterocyclic substituents on inhibition of steroid enzymes P450 arom and P450 17. J. Med. Chem. 1996, 39(4), 834-841. [http://dx.doi.org/10.1021/jm950377t] [PMID: 8632407]

[123] Armenise, D.; Trapani, G.; Arrivo, V.; Morlacchi, F. Preparation of potent bioactive ara and thiazolylicyclic compounds containing a bridgehead nitrogen atom. Synthesis of pyrrole[1,2-d:4,1]benzothiazine derivatives. J. Heterocycl. Chem. 1990, 27, 1521-1525. [http://dx.doi.org/10.1002/jhet.5570270601]

[124] Vicentini, C.B.; Mares, D.; Tartari, A.; Manfrini, M.; Forlani, G. Synthesis of pyrazole derivatives and their evaluation as photosynthetic electron transport inhibitors. J. Agric. Food Chem. 2004, 52(7), 1898-1906. [http://dx.doi.org/10.1021/jf035115b] [PMID: 15053526]

[125] Waldrep, T.W.; Beck, J.R.; Lynch, M.P.; Wright, F.L. Synthesis and herbicidal activity of 1-arylsulfonyl-5-halo and 1-aryl-(sulfonyl)hydropyrazole-4-carboxamides. J. Agric. Food Chem. 1990, 38, 541-544. [http://dx.doi.org/10.1021/jf00024a045]

[126] Minakata, S.; Hamada, T.; Komatsu, M.; Tsuboi, H.; Kikuta, H.; Obiryo, Y. Synthesis and Biological Activity of 1H-Pyrrole[2,3-d]pyridine Derivatives: Correlation between Inhibitory Activity against the Fungus Causing Rice Blast and Ionization Potential. J. Agric. Food Chem. 1997, 45, 2345-2348. [http://dx.doi.org/10.1021/jf960773o]

[127] Vicentini, C.B.; Romagnoli, C.; Andreotti, E.; Mares, D. Synthesis of pyrazole derivatives as growth inhibitors of some phytopathogenic fungi. J. Agric. Food Chem. 2007, 55(25), 10331-10338. [http://dx.doi.org/10.1021/jf070277d] [PMID: 18001038]

[128] Li, Y.; Zhang, H.Q.; Liu, J.; Yang, X.P.; Liu, Z.J. Stereoselective synthesis and antifungal activities of (E)-alpha-(methoxyimino)benzoxacetate derivatives containing 1,3,5-substituted pyrazole ring. J. Agric. Food Chem. 2006, 54(10), 3636-3640. [http://dx.doi.org/10.1021/jf060074q] [PMID: 17213777]

[129] Mashkovskii, M.D. Lekarstvennye sredstva (Drugs); Moscow: Novaya Volna, 2002, pp. 1, 253-263.

[130] a)Wijmants, R.; Vink, M.K.S.; Schoemaker, H.E.; van Delph, F.L.; Blaauw, R.H.; Fijten, P.J.T.; Biological Relevance and Synthesis of C-Substituted Morpholine Derivatives. Synthesis., 2004, 641-662. and references therein. Wilkinson, M. C. Asymmetric synthesis of an aminoalcohol morpholine via double allylic substitution. Tetrahedron Lett., 2005, 46, 4773. b)Lamann, B.A.; Myers, A.G. Efficient, C-Substituted Morpholine Derivatives: Correlation between Inhibitory Activity against the Fungus Causing Rice Blast and Ionization Potential. J. Agric. Food Chem. 1997, 45, 2345-2348. [http://dx.doi.org/10.1021/jf960773o]

[131] Abravamova, T.V.; Bakharev, P.A.; Vasilevva, S.V.; Silnikov, V.N. Synthesis of morpholine nucleoside triphosphates. Tetrahedron Lett., 2004, 45, 4361-4364. [http://dx.doi.org/10.1016/j.tetlet.2004.03.193]

[132] Ito, K.; Imahayashi, Y.; Kuroda, T.; Eno, S.; Saito, B.; Katsumi, T. Palladium-catalyzed asymmetric tandem allylic substitution using chiral 2-(phosphino)phenyl)pyridine ligand. Tetrahedron Lett., 2004, 45, 7277-7281. [http://dx.doi.org/10.1016/j.tetlet.2004.08.014]

[133] Clark, S.M.; Oshorn, H.M. Synthetic entry to functionalised morpholines and [1,4]-oxazepanes via reductiveamination reactions of carbohydrate derived dialdehydes. Tetrahedron Asymmetry, 2004, 15, 3643-3652. [http://dx.doi.org/10.1016/j.tetasy.2004.10.002]

[134] Bremner, E.; Baldwin, R.M.; Tamagnan, G. Asymmetric synthesis of (+)-5,3,5-S,4-reboxetine via a stereoselective oxindole synthesis. J. Chem. Soc., Perkin Trans. 1, 2000, 1999-2001. [http://dx.doi.org/10.1039/a908319f] [PMID: 10287013]

[135]版本: 0.1.0

Sharma, P.K. Synthesis and Antimicrobial Activity of Morpholinylpiperezin-1,4-benzothiazinones. Med. Chem. Res., 2012, 20(8), 2072-2078.

Sharma, P.K. Synthesis and Antimicrobial activity of Structurally flexible Heterocycles with the 1,4-Thiazine Heterosystem. Res. Chem. Intermed., 2011, 37, 178, 1103-1111.

Sharma, P.K. Synthesis and Antimicrobial Activity. Chin. Chem. Lett., 2015, 26, 3443-3451.

Sharma, P.K. Antibacterial, Antifungal and Antioxidant activities of substituted pyrazolylbenzothiazines. Der Pharmacia Lettre, 2016, 8(11), 79-82.

Sharma, P.K. Antibacterial, Antifungal and Antioxidant activities of substituted 4H-1,4-benzothiazines. Pharma Chem., 2016, 8(11), 156-159.

Sharma, P.K. Antibacterial and Antifungal activity of Piperazinylbenzothiazine. Pharma Chem., 2016, 8(5), 191-193.

Sharma, P.K. Morpholino[1,4]benzothiazine consider as bioactive compound. Der Pharmacia Lettre, 2016, 8(4), 86-90.

Sharma, P.K. Synthesis of Bioactive substituted pyrazolylbenzothiazinones. Res. Chem. Intermed., 2015, 41(9), 6141-6148.

Sharma, P.K. Synthesis and Antimicrobial Activity of Morpholinyl[1,4]benzothiazinones. Med. Chem. Res., 2012, 20(8), 2072-2078.

http://dx.doi.org/10.1039/e010600007a004 [PMID: 8393489]

Sharma, P.K. Synthesis and Antimicrobial activity of Structurally flexible Heterocycles with the 1,4-Thiazine Heterosystem. Res. Chem. Intermed., 2011, 37, 178, 1103-1111.

Sharma, P.K. Synthesis and Antimicrobial Activity. Chin. Chem. Lett., 2015, 26, 3443-3451.

Sharma, P.K. Antibacterial, Antifungal and Antioxidant activities of substituted pyrazolylbenzothiazines. Der Pharmacia Lettre, 2016, 8(11), 79-82.

Sharma, P.K. Antibacterial, Antifungal and Antioxidant activities of substituted 4H-1,4-benzothiazines. Pharma Chem., 2016, 8(11), 156-159.

Sharma, P.K. Antibacterial and Antifungal activity of Piperazinylbenzothiazine. Pharma Chem., 2016, 8(5), 191-193.

Sharma, P.K. Morpholino[1,4]benzothiazine consider as bioactive compound. Der Pharmacia Lettre, 2016, 8(4), 86-90.

Sharma, P.K. Synthesis of Bioactive substituted pyrazolylbenzothiazinones. Res. Chem. Intermed., 2015, 41(9), 6141-6148.

http://dx.doi.org/10.1039/e010600007a004 [PMID: 8393489]

Sharma, P.K. Synthesis and Antimicrobial Activity of Morpholinyl[1,4]benzothiazinones. Med. Chem. Res., 2012, 20(8), 2072-2078.

http://dx.doi.org/10.1039/e010600007a004 [PMID: 8393489]