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BIOLOGICAL ACTIVITIES OF SOME BENZOFURAN DERIVATIVES CONTAINING 4-THIAZOLIDINONE, THIAZOLE AND PYRIDINE HETEROCYCLIC MOIETIES

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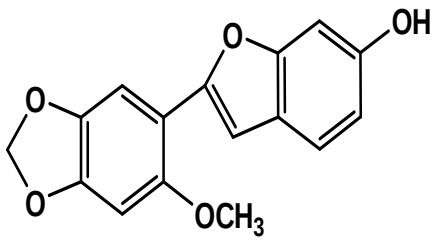
ABSTRACT

Benzofurans are exceptionally fascinating heterocycles, which are accessible in nature and demonstrate an extensive variety of pharmacological activities like anti-inflammatory, analgesic anti-microbial and so forth. Consequently, unique benzofurans containing 4-thiazolidinones, thiazole and pyridine moieties were synthesized with the end goal of various pharmacological activities.

KEYWORDS: Benzofurans, Thiazolidinones, Pyridine, Pharmacological Activities.

INTRODUCTION

Natural products play vital roles in both drug discovery and chemical biology. Different therapeutics and medication hopefuls are gotten from regular sources [1,2]. Benzofurans are regularly present in normally happening and manufactured mixes are appealing to physicists for their organic exercises and parts in plant barrier frameworks. The hydroxylated benzofurancicerfuran (1) was first accomplished from the underlying foundations of a wild types of chickpea, Cicerbijugum, and assume a noteworthy part in the resistance framework against Fusarium shrink. These benzofurans are one the most concentrated auxiliary units in both engineered and restorative science. They are generally established in different organically fascinating normal mixes and engineered subordinates [3]. Some benzofuran mixes are referred to go about as pain relieving mixes (BRL 37959, 2) with low gastric irritancy and some others as potential against disease specialists (3 and 4) [4]. Benzofuran rings are the regular themes in normal items, agrochemicals and pharmaceuticals [5].



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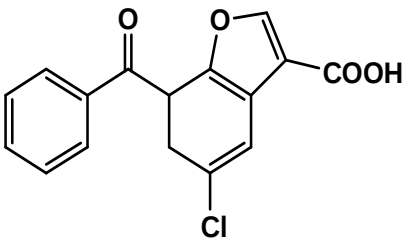

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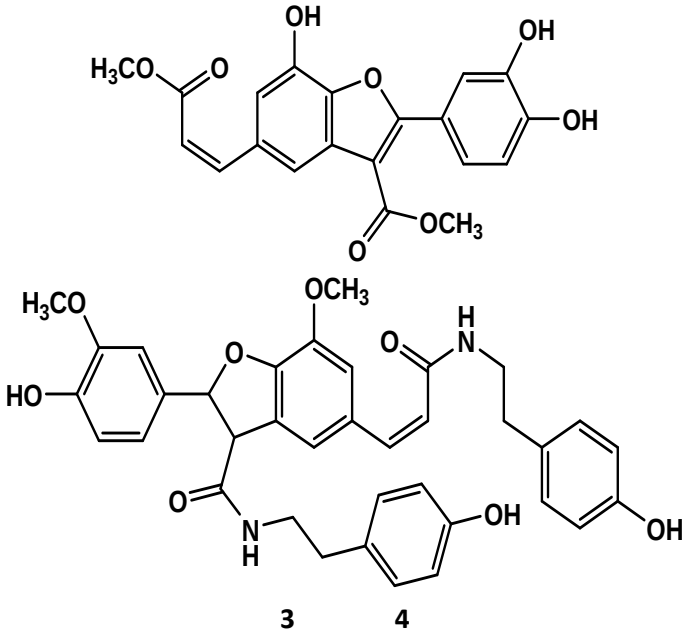

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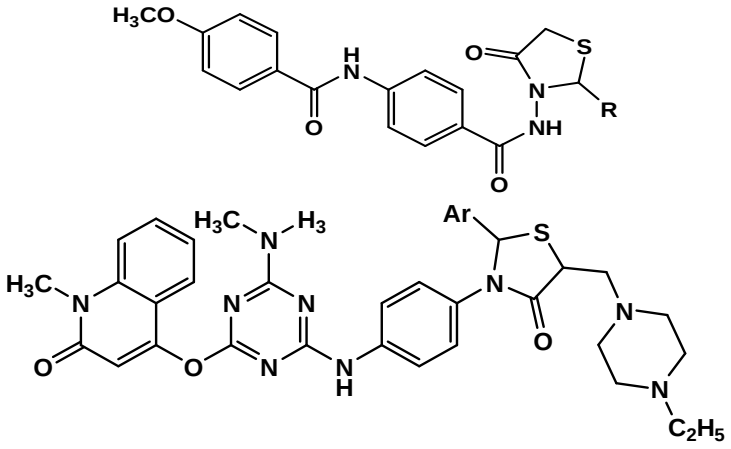
Benzofurans with thiazolidinones at 3rd position of benzofuran ring has not been explored much. Substituted benzofurans find applications as anti-oxidants, brightening agents and in different fields of chemistry and agriculture [6].

Some of the benzofurans are also used in the treatment of asthama, rheumatism and ulcers [7].

THIAZOLIDINONES

Thiazolidinonesare the derivatives of thiazolidine which belong to anvital class of heterocyclic compounds containing sulfur and nitrogen in a five membered ring with a carbonyl group. Thiazolidinonesnucleus is known to be important since it gives derivatives of different biological activities [8]. The structures of 4-thiazolidinones are studied for their biological activities [9,10]. These derivatives are well-known for their anti-TB (**5**) [11,12] and anti-fungal (**6**) [13,14] activities.



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Some other 4-thiazolidinone derivatives are useful for their anti-TB (5,7) [11,15], anti-inflammatory (8,9) [16, 17] and anti-HIV (10, 11, 12) activities [18,19].

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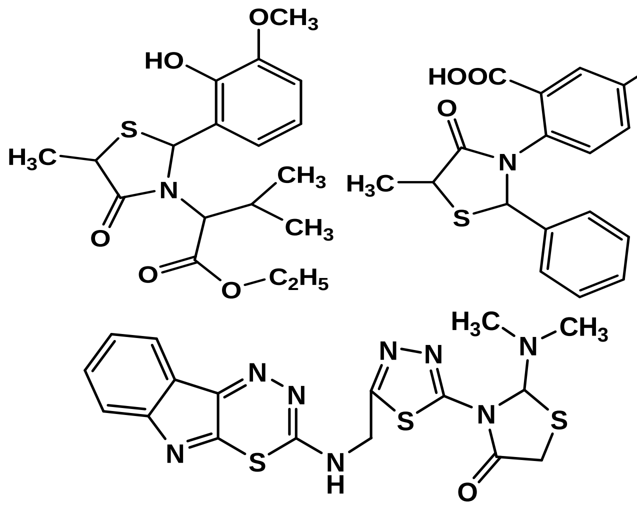

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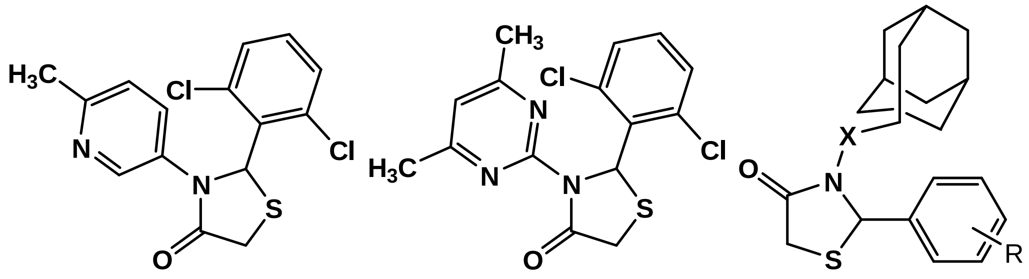

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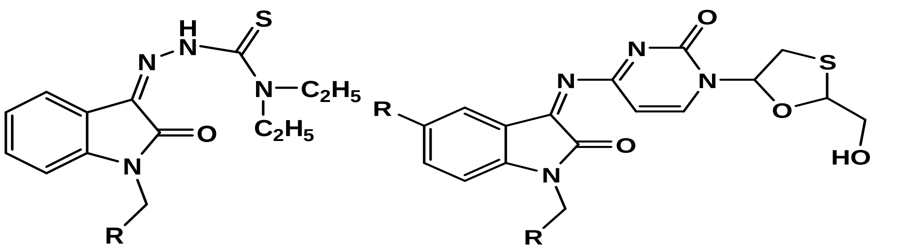
The imino group (C=N), containing compounds typically known as schiff bases, form a significant class of compounds in medicinal chemistry with different biological activities [20]. Schiff bases also play a major role in bioinorganic chemistry as they exhibit significant biological activities. These are useful due to their biological activities. Many of their ramifications have been used as antifebrile, pain and anti-rheumatism agents [21]. Schiff bases show good anti-microbial and other biological activities [22]. Schiff bases are reported to exhibit broad-spectrum of chemotherapeutic activities like anti-viral (13) [23,24], anti-TB (14) [25,26], antifungal (15) [27] and antibacterial activities (16) [28, 29].



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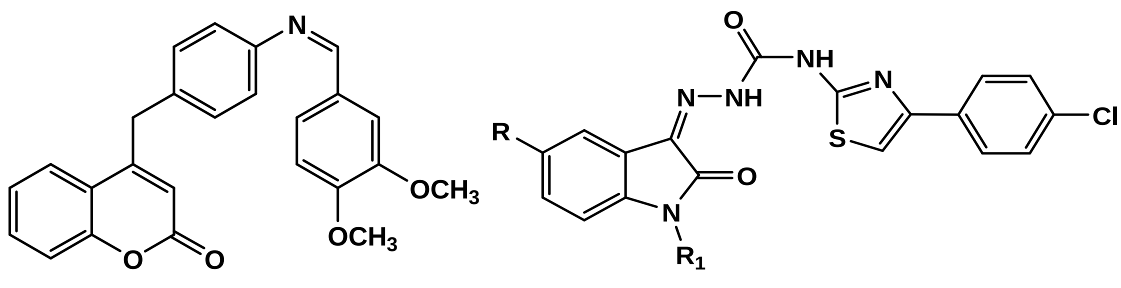

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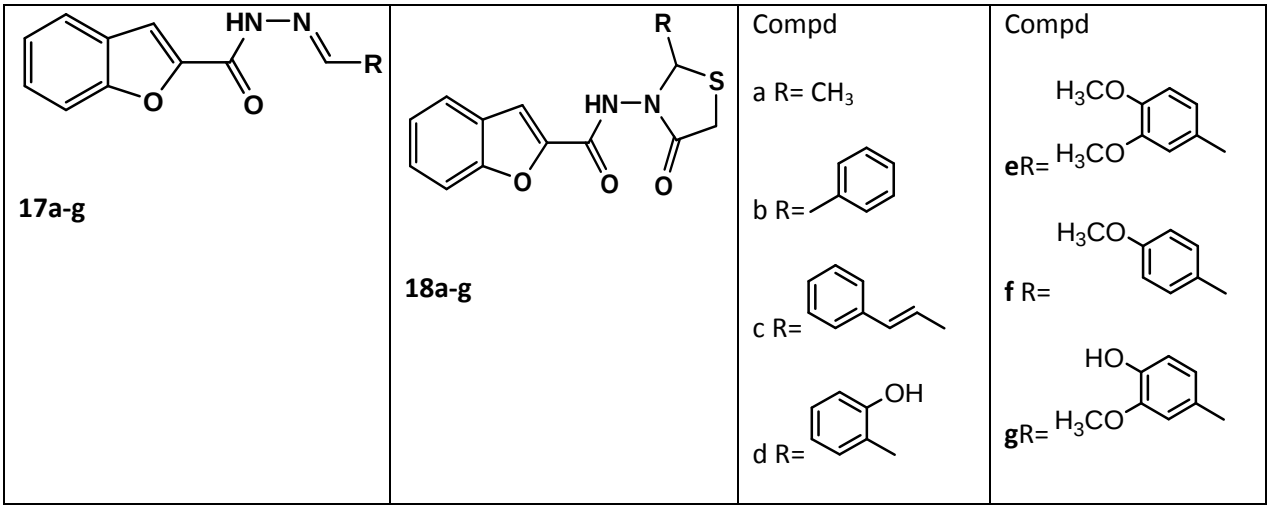
Some schiff bases of benzofuran derivatives containing thiazolidinone moietywere tested for their pharmacological activities like anti-inflammatory and analgesic,antibacterial, and anti-fungal. The compound **5a** has shown good anti-inflammatory activity [30].



ANTI-INFLAMMATORY AND ANALGESIC ACTIVITY

The compounds (17a-g and 18a-g) were tested for their anti-inflammatory activity.All the compounds were exhibited marked anti-inflammatory activity, compound 17a, which is a schiff base showed promising activity while the remaining compounds were showed moderate to low anti-inflammatory activity compared with the standard drug, indomethacin. The compounds (17a-g and 18a-g) were tested for their analgesic activity and cmpare with standard drug, tramadol hydrochloride. The analgesic activity showed that all the compounds exhibited moderate to good analgesic activity compared to that of the reference drug. The compound17c was exhibited the most significant analgesic activity; the compounds, 17a, 17d and 18c were showed the significant activity; the compound17e showed moderately significant activity while the rest exhibited low activity.

ANTI-MICROBIAL ACTIVITY

The compounds (17a-g and 18a-g) were tested for their anti-microbial activities like anti-bacterial and anti-fungal. Both anti-bacterial and anti-fungal activities were examined against bacteria; *Escherichia coli* (*E. coli*), *Staphylococcus aureus*(*S. aureus*), *Bacillus subtilis*(*B. subtilis*), *Salmonella typhi*(*S. typhi*), and fungus; *Aspergillusniger*(*A. niger*), *Candida albicans*(*C. albicans*), *Aspergillusflavus*(*A. flavus*), *Neurosporacrassa*(*N. crassa*) were used for their respective anti-microbial activities.The anti-bacterial studies showed that all the compounds were exhibited moderate to good anti-bacterial activity against all the tested bacterial strains compared with gentamycin.

The compound 18c exhibited very good activity against the bacteria *B. subtilis*at a MIC of 25 µg and has shown good activity against the other three microorganisms (*E. coli, S. aureus*and *S. typhi*) at a MIC of 100 µg, whereas the moderate activity was observed for the compounds 17e and 17g against *E. coli;* 17e, 18b and 18d against *B. subtilis*, and 17e and 18f against *S. typhi*with MIC of 400 µg. The compounds, 17c and 18f against *E. coli*, the compounds 17a, 17c, 17e, 18a, 18e and 18f against *S. aureus*, the compounds 17a-d, 17f, 6a and 6e against *B. subtilis*and the compounds 17b, 17c and 18d against *S. typhi*have shown low activity at a MIC of 800 µg. Rest of the

compounds showed no activity against all the four organisms.

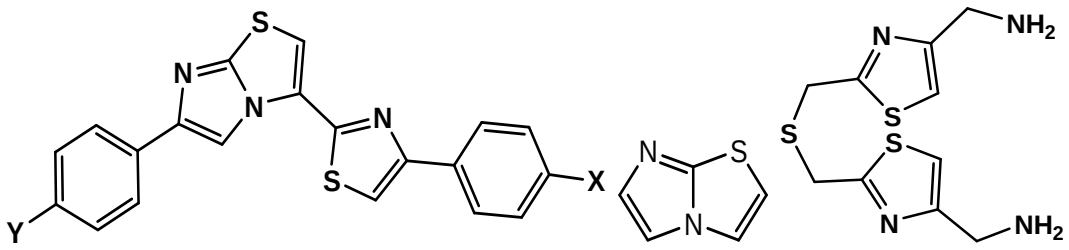
ANTI-FUNGAL STUDIES

The compounds 17e and 6b have shown moderate activity at a MIC of 400 µg and the compounds 17b, 17d, 6b, 6d, 6e and 6g have shown least activity at a MIC of 800 µg, whereas the remaining compounds did not show the activity (> 800 µg) against the fungi *C. albicans*.

The compounds 6c, 6d and 6f have shown moderate activity at a MIC of 400 µg and the compounds 17e, 17f, 6a, 6b and 6e have exhibited least activity at a MIC of 800 µg, whereas the remaining compounds have not shown the activity (> 800 µg) against the fungi *A. niger*. The compound 18c has shown very good activity (MIC 400 µg, standard also) and the compounds 17e, 18b, 18e and 18f exhibited moderate activity at a MIC of 800 µg, while the remaining compounds showed low activity (> 800 µg) against *A. flavus*. Compound 18c was showed very good activity (MIC 400 µg, standard also) and the compounds 18b, 18d and 18f were shown moderate activity at a MIC of 800 µg, while that of the remaining compounds have shown lesser activity (> 800 µg) against the fungi *N. cressa*.

THIAZOLES

Small and simple heteroaromatics have complex biological properties and belong to one of the most important classes of compounds in medicinal chemistry [31,32]. For instance, amines containing five membered heteroaryl groups such as furans, thiophenes, thiazoles, pyrazolesetc are usually found in natural products and drugs [33-35]. Among these,thiazolesconstitute an important class of S, N containing heterocycles [36]. Thiazole is an important heterocyclic ring and present in several pharmacologically active compounds [37-39]. Thiazole derivatives find applications as bacteriostatics and antibiotics (19) [40-42]. Imidazo[2,1-b]thiazoles are possess fungicidal and anti-histaminic activities (20) [43]. Thiazolesand their derivatives is attributed to their biological significance as constituents of biomolecules including antibiotics (21) [44]. The thiazolyl group is also of great importance in treating biological systems. Compounds of this functional group showed anti-microbial [15,16], analgesic [45,46], anti-tumour [47,48], anti-inflammatory [49] and anti-pyretic [46,50] activitiess. Some thiazoles exhibited a wide range of biological activities such as anti-tumor, anti-filarial (22), anti-bacterial, anthelmintic, anti-fungal and anti-inflammatory (23) [51].



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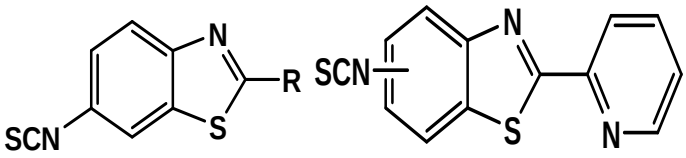

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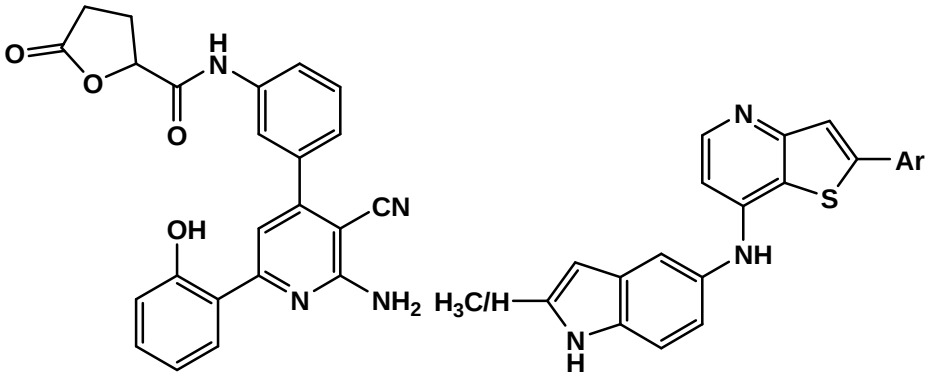
PYRIDINES

Poly-substituted pyridines are the vital class of compounds owing to their abundance in biologically important natural compounds and their usefulness as synthetic intermediates in organic synthesis [52]. Many naturally occurring and synthetic compounds containing the pyridine scaffold possesses interesting pharmacological properties [53]. Among these compounds, 2-amino-3-cyanopyridines have been identified as IKK-β-inhibitors (24) [54]. They are useful intermediates in preparing variety of heterocyclic compounds [55,56]. Several thieno[3,2-*b*]pyridines were showed important biological activities like antitumor and antiangiogenesis or dual activity, essentially by acting as inhibitors of tyrosine kinase receptors 25[57], 26[58] and 27[59] or non receptor28[60] which have been implicated in the growth and progression of various human cancers, and, therefore, have been crucial in the development of anticancer drugs.



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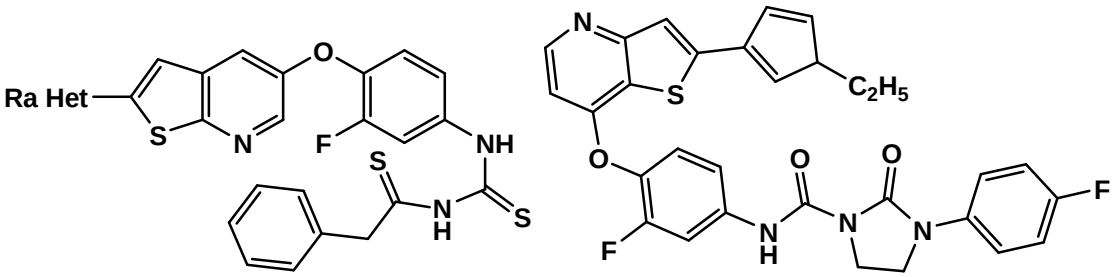

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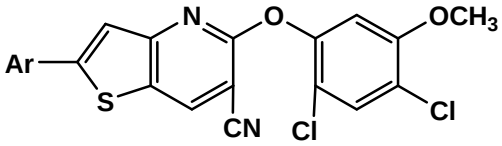

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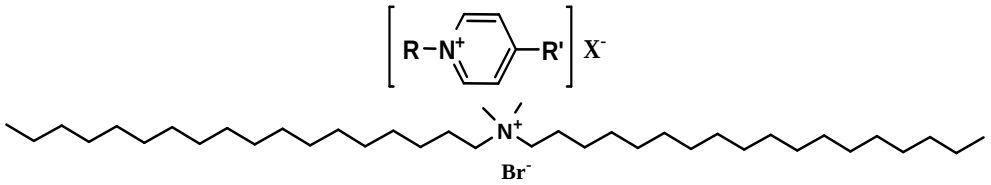
Benzyl-alkyl-ammonium salts and pyridinium salts are the cationic surfactants, which are most famously utilized as disinfectants (29, 30) [61,62]. The pyridinium salts are powerful against different microorganisms. These are utilized to wound recuperating and in the treatment of urological diseases (31) [61]. Cetylpyridinium chloride controls supragingival plaque and gingivitis (31) [61,63]. It has coordinate calming action and hinders activity on a few framework metalloproteinase proteins which cause aggravation. The pyridine subsidiaries are likewise utilized as disinfectants for eating and drinking utensils and nourishment preparing supplies. Their against microbial action has been utilized as a part of dairy industry for cleansing of drain jars and drain machines [64,65]. The 2-substituted-

imidazo[4,5-b]pyridines have distinctive synthetic and pharmacological highlights (32) [66,67], which grant them differing natural properties like hostile to malignancy (33, 34, 35) [68,69], against viral (36, 37) [70,71], against mitotic (38) [72], calming (39) [73] and tuberculostatic [74] action.



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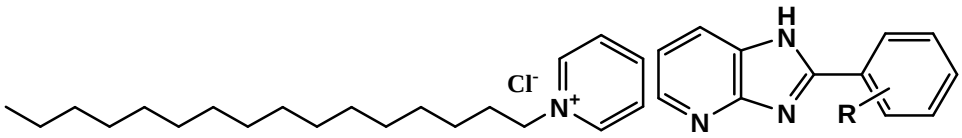

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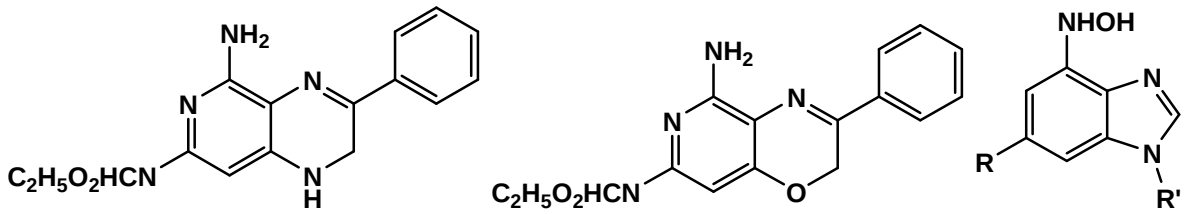

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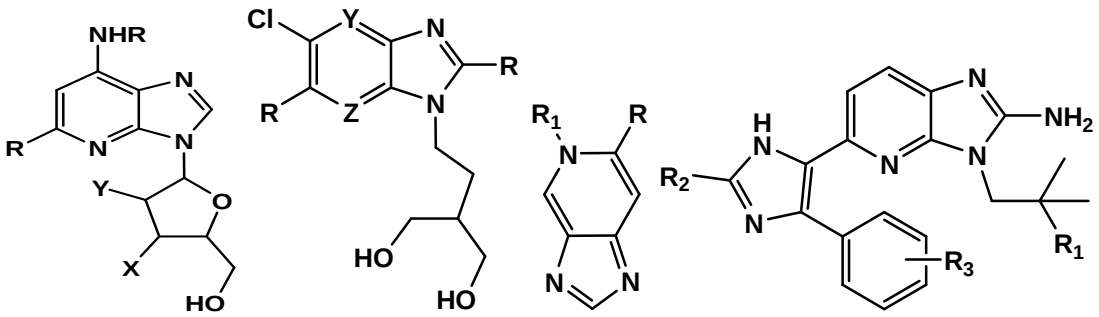

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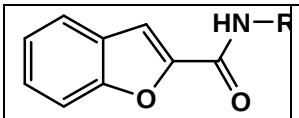
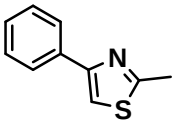
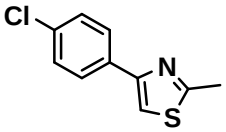
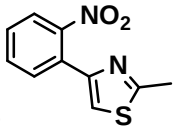
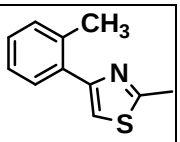
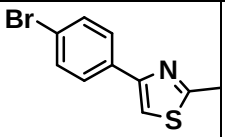
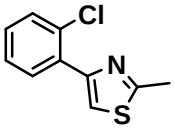
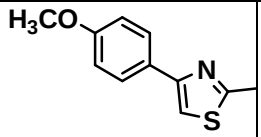
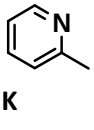
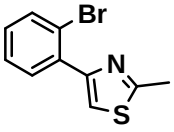
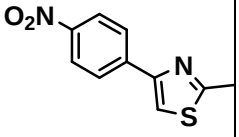
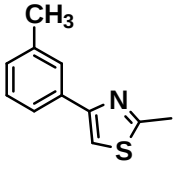
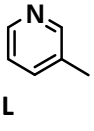
 **Compound 40a-l**	 a	 d	 g	 j
	 b	 E	 h	 K
	 c	 f	 I	 L

Some benzofuran subordinates containing thiazole and pyridine moieties were tried for mitigating, pain relieving, hostile to bacterial and against contagious exercises.

ANTI-INFLAMMATORY ACTIVITY

Anti-inflammatory activity of the compounds (40a-l) weretested, the compound 40c was exhibited promising anti-inflammatory activity compared to the standard drug, indomethacin. The compounds 40a, 40d, 40e and 40g have showed moderate activity while the remaining compounds exhibited low anti-inflammatory activity compared to the standard drug. The compounds, 40a, 40c, 40d, 40e and 40g have exhibited higher activity.

ANALGESIC ACTIVITY

All the compounds exhibited comparable analgesic activity compared to the control group the compound, 40b has shown the most significant analgesic activity. The compounds, 40a, 40d, 40e and 40j have exhibited the significant analgesic activity compared to the standard drug, tramadol hydrochloride.

ANTI-BACTERIAL ACTIVITY

The results indicated that all the compounds showed higher activity. Among all the compounds, the compound 40j (against the bacteria *E. coli*), the compounds 40a, 40e, 40g, 40j and 40k (against *S. aureus*), the compounds 40e, 40i and 40j (against *B. subtilis*) and 40g (against *S. typhi*) exhibited moderate anti-bacterial activity compared to the standard drug, gentamycin with MIC values of 400 µg. However, rest of the compounds showed low activity.

ANTI-FUNGAL ACTIVITY

The anti-fungal activity of newly synthesized compounds. It was noticed from the compound, 40j exhibited better anti-fungal activity against the fungi *N. cressa*whereas the compounds 40g (against *A. albicans*)40a, 40c, 40e and 40k (against *A. niger*) and the compound 40f (against *A. flavus*) exhibited moderate anti-fungal activity. The rest of the compounds showed low activity against all the four fungal strains. These results were compared with the standard anti-fungal drug, amphotericin.

CONCLUSIONS

Some benzofuran derivatives consisting of thiazolidinone moieties have been synthesized. The compounds were subjected to biological activities like anti-inflammatory, analgesic and anti-microbial. Among all the compounds, 17a has shown good anti-inflammatory activity while the compounds 17c and 17e have exhibited good analgesic activity.The compound 40c has shown promising anti-inflammatory activity and the compounds 40b and 40e have shown good analgesic activity.

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