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Review Article

Furan: A Promising Scaffold for Biological Activity

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Abstract

It was shown that several bioactive aromatic compounds with biological applications have the furan nucleus watch numerous significant synthetic compounds include furan scaffold, which offers a helpful therapeutic idea and is found with strong affinity for a range of receptors, assisting in the synthesis of novel, advantageous derivatives The antibacterial, antifungal, antiviral, anti-inflammatory, analgesic, antidepressant, antianxiolytic, anti-Parkinson, anti-glaucoma, muscle-relaxant, antihypertensive, diuretics, anti-ulcer, anti-aging, and anti-cancer effects of furan derivatives make them frequently utilized. Diverse furan derivatives have piqued the interest of researchers. Furan is a colourless liquid that boils almost at ambient temperature and is highly volatile and combustible.

Keywords: Furan, Heterocyclic Compound, Biological activity.

Introduction

The five-membered aromatic ring of the furan organic compounds has one oxygen atom and four carbon atoms [1-7]. 1,4-epoxybuta-1,3-diene is the IUPAC name for the furan systematic 2-(4-hydroxyaryl)–*N'*-[{5'-(substitutedaryl)-furan-2'-yl}-methylidene]- [8]. Oxacyclopenta-2,4-diene. Other names for the furan are oxale, oxa (5) annulene, epoxy 1,4-butadiene, 1,3-five-oxa, cyclopenta-1,3-diene, five-oxacyclo-1,3-diene, furfural, and divinylene oxide. Furan is a colorless liquid that boils almost at ambient temperature and is highly volatile and combustible [9]. It is soluble in a variety of typical organic solvents, such as acetone, ether, alcohol, and bran, which is used to make furfural. 2-furoic acid was the first furan derivative that Carl Wilhelm Scheel described in 1780 [10]. Furfural compounds that are soluble in water are another significant derivative [11]. It is order being strong chloroform like. The Latin furfur is the source of the furan names, which Johann Wolf-gang Dobereiner first recorded in 1831 [12] and described by John Stenhouse nine years later [4]. The corresponding derivatives of dihydro naphthalene are produced via the Diels-Alder reaction of furan with aryne and are a useful intermediary in the synthesis of various polycyclic aromatic compounds. Compounds with five members that are heteroaromatic rings have been thoroughly investigated with regards to their relative reactivity and particular physicochemical characteristics [13]. Generally speaking, the degree of

aromaticity is thought to be in the following order:

thiophene > pyrrole > furan [14]

Properties of Furan

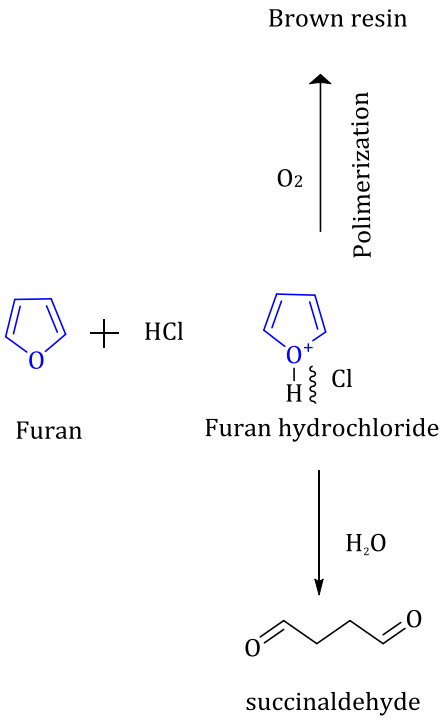
Physical characteristics: furan is a liquid with no colour. Boiling point 32 °C smells like chloroform. It dissolves in most organic solvents but is relatively weakly soluble in water.

Chemical Properties

Some of the important chemical reactions of furan are:

Basic Character

Similar to pyrrole, furan is a weak base. On unstable salts containing mineral acids, it forms (Scheme 1).



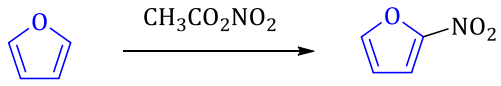
Scheme 1: Reaction of furan

Electrophilic Substitution

Similar to pyrrole, furans also experience electrophilic substitution reactions, primarily at position c-2. Substitution at position c-3 only happens when both 2-positions are already blocked. Strong acids prevent furan from undergoing its electrophilic substitution Methods: reaction because they cause polymerization to occur.

Nitration

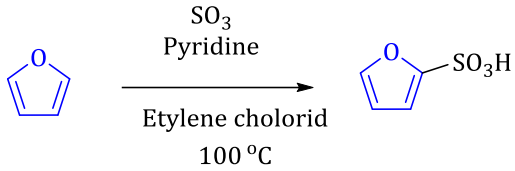
2-nitrofuran can be created by nitrating furan with a cold solution of nitric acid in acetic anhydride (Scheme 2).



Scheme 2: Nitration of furan

Sulfonation

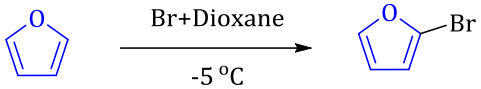
Furan 2-sulfonic acid can be produced by sulfonating furan with sulphur trioxide in pyridine at 100 °C (Scheme 3).



Scheme 3: Sulfonation of furan

Halogenation

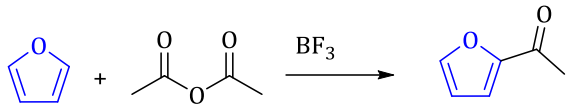
Furan does not react at all with iodine, but it reacts violently with bromine at room temperature to produce polyhalogenated product. Monobromide derivatives must be obtained under conditions that are much milder (Scheme 4).



Scheme 4: Halogenation of furan

Friedel-crafts Acylation

2-Acetyl furan can be produced by acetylating furan with acetic anhydride at 0 °C while BF3 (or Sncl4) is present (Scheme 5).



Scheme 5: Friedel-crafts Acylation of furan

Pharmacological actions and structure

Furans are well-known heterocyclic compounds that are widely present in a variety of therapeutic agents and play important roles in them. With five members, the planar ring furan dissolves in a wide range of organic solvents [4]. It is the most reactive of all the five-membered heterocyclic compounds. It's a nonpolar substance [14]. Furan's electrophilic substitution reactions ideally occur in two positions. Compared to other compounds, its high reactivity requires the use of very mild reagents. In general, compounds with the furan ring make good solvents [7]. Certain substances can mix well with hexane and water. The ether oxygen contributes polarity and hydrogen bonding potential. Numerous pharmaceutical products contain compounds with the furan or tetra hydro furan ring because they are biologically active. An intermediary of the diuretic furosemide is furfuryl amine. Tetra hydro furfuryl amine might find use in medicine as well.5. An intermediary used to prepare the ulcer-treating drug ranitidine is (dimethyl amine methyl) furfuryl alcohol.

The synthesis of cefuroxime, a penicillin derivative, requires the intermediate acetyl furan, which is made from acetic anhydride and furan [16]. Furfural is oxidized to produce furoic acid. Fury chloride and furoic acid are both employed as pharmacological intermediates. Applications are also found for tetrahydro furoic acid [17]

Based on a variety of literature reviews, furan derivatives exhibit a range of pharmacological properties

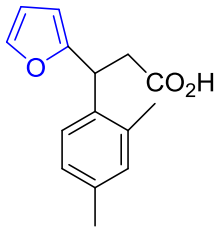
- Antidepressant activity
- Antibacterial agent
- Anti-anxiolytic properties
- Both anti-inflammatory and analgesic properties [6]
- Drugs that relax muscles
- Antihypertensive medications
- Antiarrhythmic medications
- The two types of activity are antimicrobial and steroidal
- Anti-ulcer properties
- An antidiuretic agent
- Prevents the production of sickle cells [18]
- Anti-parkinsonian
- Antihistaminic and anticholinergic properties
- Antineoplastic properties
- Insecticide usage

Many derivatives of substituted furans that combine a mono and fused furan with other heterocyclic compounds have been approved. You can find a list of medications along with their noteworthy pharmacological activities.

Biological Significance of Furan

Furan as an Anti-Bacterial Agent

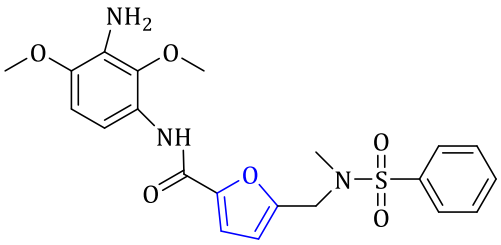
The effectiveness of derivatives of 3-aryl-3(furan-2-yl) propanoic acid as an antibacterial agent was studied. Compound **1** exhibited the most favourable outcomes, inhibiting *Escherichia coli* growth at a MIC of 64 ug/mL (Scheme 6) [19,20].



1

Scheme 6: 3-(2,4-dimethylphenyl)-3-(furan-2-yl)propanoic acid

Derivatives of furan 2,4-disubstituted **2** demonstrated superior antibacterial activity, particularly against *Escherichia coli and Proteus vulgaris* (Scheme 7) [21].



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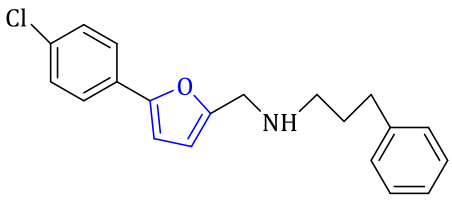
Scheme 7: *N*-(3-amino-2,4-dimethoxy phenyl)-5-((*N*-methyl phenyl sulfonamido)methyl) furan-2-carboxamide

It was discovered that a novel ARY furan derivative **3** exhibited significant action against *Escherichia coli* and *Staphylococcus aureus*, two gram-positive and gram-negative bacteria suggesting a range of actions for this novel compound (Scheme 8) [22].



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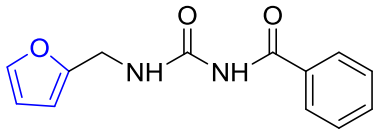
Scheme 8: *N*-((5-(4-chlorophenyl)furan-2-yl)methyl)-3-phenylpropan-1-amine

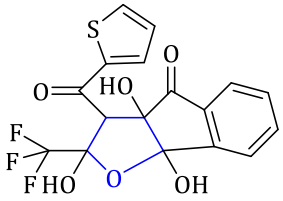
1- Benzoyl-3- furan-2- ylmethyl-thiourea **4** demonstrated antibacterial activity against *Listeria monocytogenes, Staphylococcus aureus, and Bacillus cereus* (Scheme 9) [23].



4

Scheme 9: *N*-((furan-2-ylmethyl)carbamoyl)benzamide

The antibacterial activity of compound **5** was evaluated after it was successfully synthesized. This substance was discovered to exhibit broad antibacterial activity against thirteen different bacterial strains, outperforming both streptomycin and tetracycline in terms of activity against *Pseudomonas fluorescence* (Scheme 10) [24].



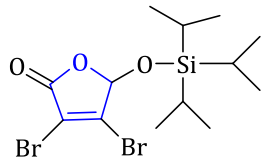
5

Scheme 10: 2,3a,8b-trihydroxy-3-(thiophene-2-carbonyl)-2-(trifluoromethyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[1,2-b]furan-4-one

Biological Significance of Furan as an Anti-Cancer Agent

Mucobromic acid (MBA) sialylation of the 5-hydroxyl group with a furan-2(SH)-one core leads to the creation of a novel class of medications with increased cytotoxicity against cancer cells [25]

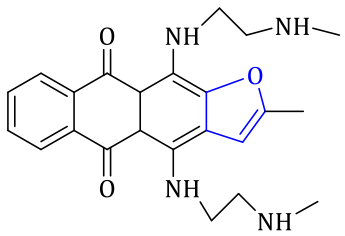
Remarkably, compound **6** was shown to be the most successful in suppressing colorectal cancer cell lines (Scheme 11).



6

Scheme 11: 3,4-dibromo-5-((triisopropylsilyl)oxy)furan-2(5*H*)-one

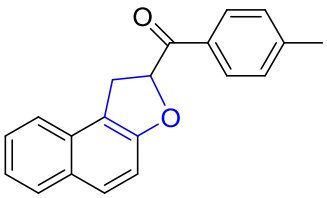
Shchekotikhin *et al*. successfully synthesized a number of anthrafuran Dione analogues of the anticancer drug ametantrone. Research assessing Compound **7** anti-proliferative effectiveness on a subset of mammalian tumour cell lines revealed that it outperformed other medications in terms of effectiveness against drug-resistant cell lines that had p53 gene deletion or P-glycoprotein overexpression. Moreover, this derivative inhibited topoisomerase I-mediated DNA uncoiling in *vitro* at low micromolar concentrations (Scheme 12) [26].



7

Scheme 12: 2-methyl-4,11-bis((2-(methylamino)ethyl)amino)-4a,10a-dihydroanthra[2,3-b]furan-5,10-dione

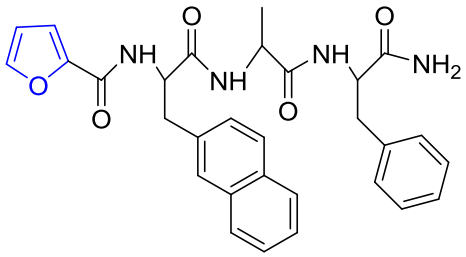
The ability of several 1,2-dihydronaphthols to inhibit cell proliferation A comparison between human triple negative Breast cancer cells MDA-MB468 and MCF-7 lines and 2,1-bifuran derivatives was made of twenty-one compounds that were synthesized. Based on the findings of multiple biochemical and microscopic investigations, Compound **8** was determined to have the best anti-proliferative activities (Scheme 13) [27].



8

Scheme 13: (1,2-dihydronaphtho[2,1-b]furan-2-yl)(p-tolyl)methanone

Several furans conjugated tripeptides were developed and evaluated against human cervical cancer cells using HeLa cells as a model. Even so, some conjugates showed interesting inhibitory activity against HeLa cells. The most effective conjugation was found to be 9, with an ICso of 0.15 ± 0.05 µg/MI. Conjugate 10's proposed mode of action against cervical cancer cells is based on mitochondrial modification and the membranolytic effect (Scheme 14) [28].

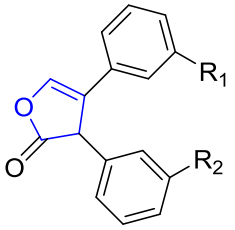


9

Scheme 14: *N*-(1-((1-((1-amino-1-oxo-3-phenylpropan-2-yl)amino)-1-oxopropan-2-yl)amino)-3-(naphthalen-2-yl)-1-oxopropan-2-yl)furan-2-carboxamide

Biological Significance of Furan as Anti-Inflammatory an Analgesic Agent

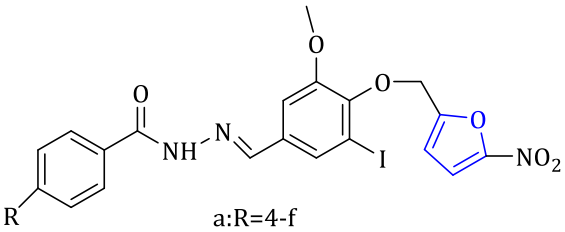
As selective COX-2 inhibitors, a number of series of diary furanone derivatives **10** have been thoroughly developed and studied; the majority of these compounds demonstrated COX-2 inhibitory potency that was on par with or even higher than that of rofecoxib (Scheme 15) [29].



10

Scheme 15: furanone derivatives

Using an inflammatory rat model induced by carrageenan, a series of hydrazide-hydrazone derivatives linking furan moiety were synthesized and evaluated for their anti-inflammatory properties. Compound **11** demonstrated noteworthy anti-inflammatory properties (Scheme 16) [30].

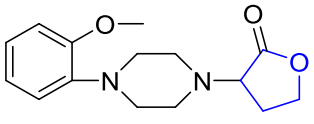


a:R=4-f
b:R=4-OH
c;R=4-SO2CH3
d;R=2,4-difluoro
e;R=3,4,5-trimethoxy

11

Scheme 16: anti-inflammatory furan

Using the hot plate and writhing test, a number of 3-substituted derivatives of dihydrofuran-2(3*H*)-one were synthesized, and their analgesic efficacy was assessed. Strong analgesic activity was demonstrated by derivative **12** [31], surpassing that of the reference compounds (morphine and acetylsalicylic acid) (Scheme 17).

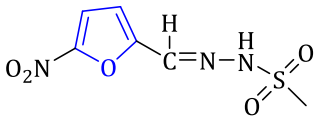


12

Scheme 17: 3-(4-(2-methoxyphenyl) piperazin-1-yl)dihydrofuran-2(3*H*)-one

Biological Significance of Furan as an Anti-Glaucoma Agent

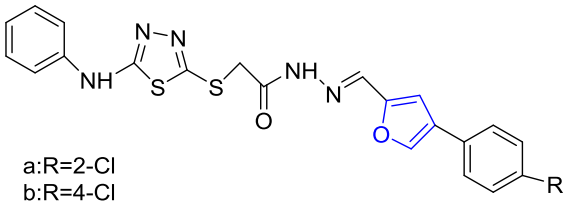
The inhibitory potential of carbonic anhydrase was evaluated for three furan sulfonyl hydrazone derivatives. Compound **13** with a withdrawing group (NO_2) was the most effective at inhibiting the hCA 1 isozyme among them (Scheme 18) [25, 32].



13

Scheme 18: *N*′-((5-nitrofuran-2-yl) methylene)methanesulfonohydrazide

Second, *N*-(2-hydroxyfuran-5-yl) It was created and assessed whether methylene-2-[(5-(phenylamino)-1,3,4-thiadiazol-2-yl) thioacetohydrazide derivatives could inhibit the human carbonic anhydrase isozymes (hCA I and hCA II). In particular. Compound 14 was found to be a potential hCA I inhibitor with an ICso value of 0.14 nm when compared to acetazolamide (IC50 = 5.8 nm), and compound 15 was found to be a potential CA II inhibitor with a ICs value of 0.15 nm when compared to AAZ (IC5=6.7mM) (Scheme 19) [31].



a:R=2-Cl
b:R=4-Cl

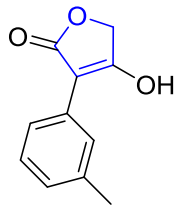
14

Scheme 19: methylene-2-[(5-(phenylamino) -1,3,4-thiadiazol-2-yl) thioacetohydrazide derivatives

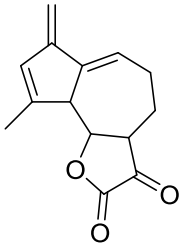
Biological Significance of Furan as an Anti-ulcer Agent

Dehydroleucodine **15a**, xanthatin **15b**, and 3-Benzyloxymethyl-5*H*-furan-2-one

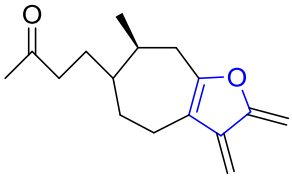
15c, which have recently demonstrated significant gastrointestinal cytoprotective activity, have been found to be effective in an animal model of stomach ulcers induced by mast cell stimulation. These findings imply that lactones may be useful in the treatment of peptic ulcer disease in humans and could also be important resources for the design and development of novel therapeutic agents for digestive disorders linked to inappropriate mast cell activation (Scheme 20) [33].



15a



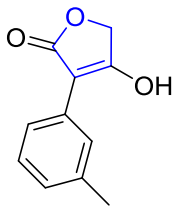
15b



15c

Scheme 20: Dehydroleucodine **15a**, xanthatin **15b**, and 3-Benzyloxymethyl-5H-furan-2-one **15c**

Twenty 3-arylfuran-2(5*H*)-ones were tested for their capacity to eliminate Helicobacter pylori and inhibit urease. In comparison to acetohydroxamic acid, 3-(3-methylphenyl) furan-2(5*H*)-one **16** exhibited the highest anti-H. pylori activity [34] (2.6 g/mL) when it came to urease inhibitory activity (Scheme 21) [35].

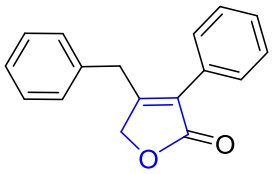


16

Scheme 21: 4-hydroxy-3-(m-tolyl)furan-2-(5*H*)-one

Biological Significance of Furan as an Anti- Hypertensive Agent

4-Benzyl-3-phenyl-SH-furan-2-one **17** was discovered after screening Malbranchea filamentous for bioactive compounds that inhibit Ca-induced vasoconstriction in rat aortic rings pretreated with high K or norepinephrine (Scheme 22) [36].



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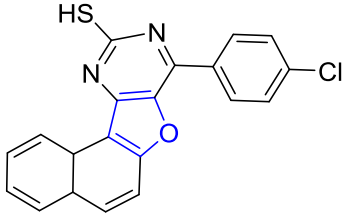
Scheme 22: 4-Benzyl-3-phenyl-SH-furan-2-one

A variety of 2-Macropto-4-substituted naphthol[2,1-b] furo[3,2-d] pyrimidines have been studied for their diuretic potential. Compared to furosemide, compound **18** showed a notable diuretic effect (Scheme 23) [31].

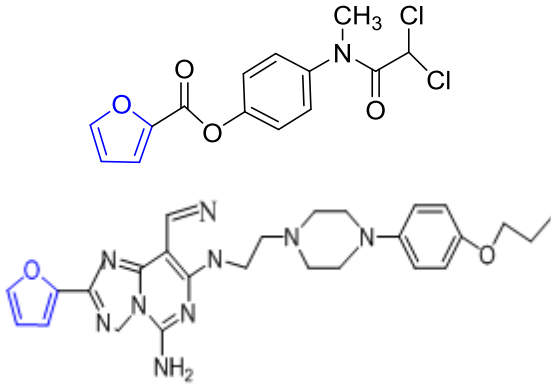


18

Scheme 23: 8-(4-chlorophenyl)-4a,11c-dihydronaphtho[1',2':4,5]furo[3,2-d]pyrimidine-10-thiol

Biological Significance of Furan as an Anti-Protozoal Agent

Diloxanide furoate is a carboxylic ester that is produced by the formal condensation of the carboxy group of furan-2-carboxylic acid with the hydroxy group of 2,2-dichloro-*N*-(4-hydroxyphenyl)-*N*-methyl acetamide. This medication is used to treat asymptomatic amebiasis (Scheme 24).



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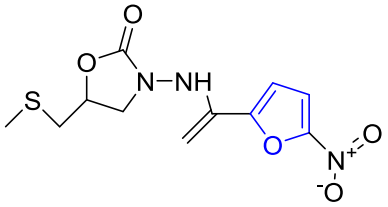
Scheme 24: Diloxanide furoates

An innovative furan derivative's effectiveness in treating UTIs was evaluated. Nifuratel (Magmilor)*N*-(5-nitro-2-furfurylidene)-3-amino-5-methylmercaptomethyl-2- oxazolidinone is its chemical name (Scheme 25).



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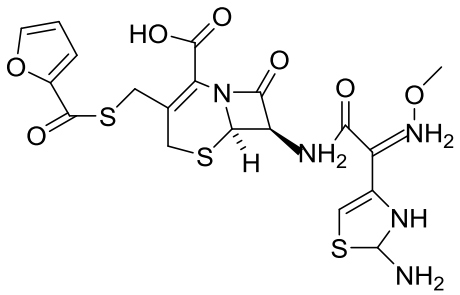
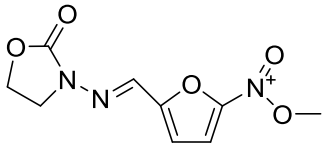
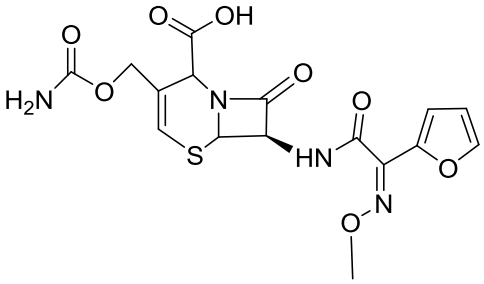
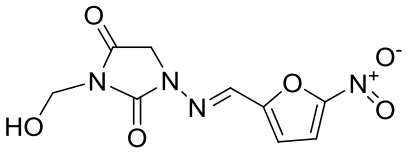
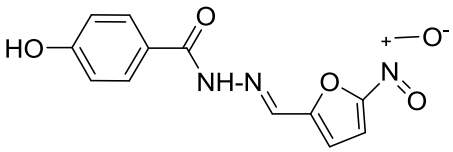
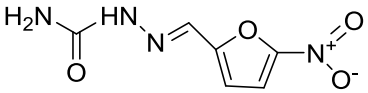
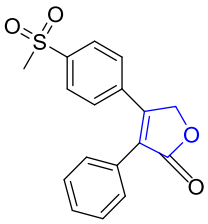
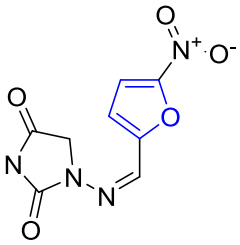
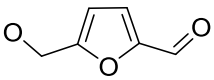
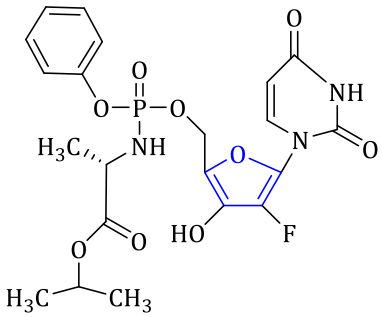
Scheme 25: 5-((methylthio)methyl)-3-((1-(5-nitrofuran-2-yl)vinyl)amino)oxazolidin-2-one

One of Schering-Plough's products was a strong and selective adenosine A2A receptor antagonist. It was being investigated as a possible treatment for Parkinson's disease. The source 2. (furanyl–2) [7–[2-[4–[4–(2-methoxyethoxy) phenyl] ethyl] Piperazinyl (IUPAC name1)7-*H* pyrazole[4,3-e] 2, 4, 1 1,5-c 5-amine thiopyrimidine zolo [31].

Furan ring containing drug listed in Table 1-3.

Table 1. List of furan ring containing drug currently available in market

Sr. no	Name of the drug	Structure	Approved activity
1	Ceftiofur		Antibacterial activity.
2	Furazolidone		Antibacterial Activity

Sr. no	Name of the drug	Structure	Approved activity
3	Cefuroxime		Antibacterial activity
4	Nifurtoinol		Antibacterial Activity
5	Nifuroxazide		Antibacterial Activity
6	Nitrofurazone		Antibacterial Activity
7	Rofecoxib		Analgesic and anti-inflammatory activity
8	Nitrofural		Antibacterial activity
9	Nitrofurantoin		Antibacterial activity
10	5-hydroxymethylfurfural		Antioxidant activity
11	Sofosbuvir		Cure hepatitis C

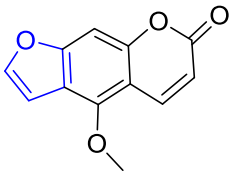
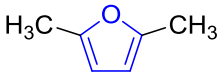
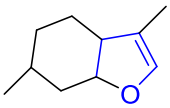
12	5-Methoxy-psoralen		Skin photochemotherapy activity
13	2,5-dimethylfuran		Antifungal activity
14	Methofuran		Antioxidant activity
15	Nitrofural		Antibacterial activity

Table 2. List of furan ring containing drug Withdrawal from market

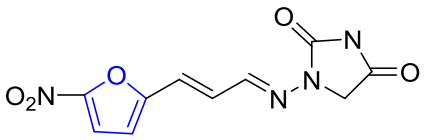
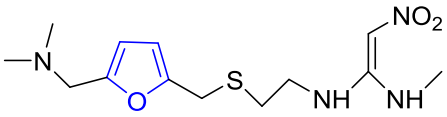
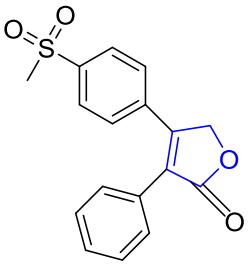
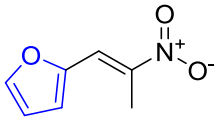
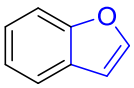
Sr. No.	Name	Structure
1	Faradizing [37]	
2	Ranitidine	
3	Rofecoxib	

Table 3. List of furan ring containing Novel drug market

Sr. No.	Name	Structure
1	2-(2-methyl-2-nitrovinyl)-furan [38]	
2	Furan-2-yl [39]	
3	Novel benzo furan	

Hypothesis

Functional Group Diversity: These changes could enhance selectivity for particular targets or impart particular biological activity.

Bioisosterism

Compounds containing furan have the ability to act as bioisosteres for other aromatic moieties, which opens up new avenues for sensible medication design. Changing our current pharmacophores.

Objective

The following are some broad goals to be considered while studying furan scaffolds for biological activity:

The process of identifying bioactive chemicals involves investigating the possibility that molecules containing furans may have bioactive properties, such as antibacterial, anti-inflammatory, anticancer, or other pharmacological actions. This entails making a wide variety of furan derivatives and testing them for particular biological activity.

Study the potential of furan-containing compounds to modify particular biological targets, such as signaling pathways, enzymes, or receptors. Creating furan derivatives with structural characteristics that selectively interact with the intended target may be one way to do this.

Research on the Structure-Activity Relationship (SAR)

Recognize the connection between the biological actions of compounds containing furans and their structural makeup. Modify furan derivatives' chemical structures systematically to see how these modifications affect their potency and efficacy. Furan scaffolds can be used as a basis for the design and development of novel drug candidates. To improve the efficacy, selectivity, and safety of furan-containing compounds as possible therapeutic agents, their pharmacokinetic and pharmacodynamic properties must be optimized.

Investigation of Natural Goods

Examine and assess the biological activity of natural goods that include furan moieties. Draw ideas for the creation of synthetic analogs with enhanced pharmacological characteristics from these natural sources.

Investigate furan rings as bioisosteres for other aromatic moieties in currently available medicinal compounds. Examine the effects of adding furan rings to specific functional groups to see how the compounds overall pharmacological profile changes.

Future Prospect of Furan Scaffold

Furfural and 5-hydroxymethyl furfural (HMF) are platform molecules derived from biomass that are the precursors of various interesting compounds such as solvents, biofuels and monomers used in polymer synthesis. All of these compounds are industrially produced *via* chemical synthesis. 5-hydroxymethyl-2-furancarboxylic acid (HMFCA) is a furan compound used for the production of interleukin inhibitors, fibres, plastics and pharmaceutical products. This furan compound is an intermediate of interest for the synthesis of surfactants, biofuels and resins [40]. It is used in the production of resins and lacquers, agrochemicals, and pharmaceuticals.

Conclusions

The reviewed furan moiety's biological and therapeutic value has been established by scientists and researchers.

This heterocyclic moiety is present in a number of medications that are available for purchase. Several substituted furan derivatives have antimicrobial (antibacterial, antifungal, and antiviral) and central nervous system (antidepressant, anxiolytic, anticonvulsant, and antiparkinsonian) properties in addition to their impact on Alzheimer's disease. In addition, they contain analgesic, antioxidant, anti-inflammatory, anti-glaucoma, anti-cardiovascular, and anti-ulcer qualities. These various endeavours serve as evidence of the furan moiety's special significance in medicinal chemistry.

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