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RECENT ADVANCES IN THE PHARMACOLOGICAL DIVERSIFICATION OF FURAN DERIVATIVES

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Abstract:

Furan is a heterocyclic organic compound consisting of a five-membered aromatic ring with four carbon atoms and one oxygen atom. The class of compounds containing such rings is also referred to as furans. Furan is a colorless, flammable, highly volatile liquid with a boiling point 31.3°C close to room temperature. Furan derivative is an imperative class of heterocycliccompound that has important biological properties. Furan is rapidly and extensively absorbed from the intestine and the lung. It can pass through biological membranes, and enter various organs. Compounds comprising the furan or tetrahydrofuran ring are biologically active and are existent in a number of pharmaceutical products. comprehensive review on Furan and it's biological activity has unveiled the versatile nature of furan compounds, these molecules exhibit a wide range of biological activities, including anti-malarial, anti-bacterial, anti- cancer, anti-convulsant, anti-oxidant activities. The importance of furan derivatives plays a major role in drug devolpment and therapeutic interventions and it holds premises for the development of novel treatments and medicines, benefitting both scientific advancements and human health.

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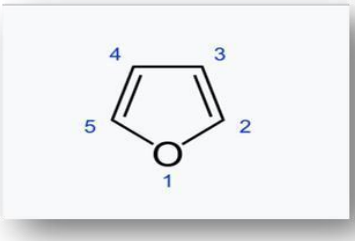
INTRODUCTION:

Furan is a heterocyclic organic compound consisting of a five-membered aromatic ring with four carbon atoms and one oxygen atom. The class of compounds containing such rings is also referred to as furans. Furan is a colorless, flammable, highly volatile liquid with a boilingpoint 31.3°C close to room temperature. Furan derivative is an imperative class of heterocyclic compound that has important biological properties. Furan is rapidly and extensively absorbed from the intestine and the lung. It can pass through biological membranes, and enter various organs. Compounds comprising the furan or tetrahydrofuran ring are biologically active and are existent in a number of pharmaceutical products. Furfuryl amine is intermediate in the diuretic, furosemide.5-(Di methyl amine methyl) furfuryl alcoholis an intermediate in the synthesis of cefuroxime, a penicillin derivative.2-Furoic acid is prepared by the oxidation of furfural, Both furoic acid and furoyl chloride are used as pharmaceutical intermediates. The compounds and its



derivatives are naturally occurring in many foods.

FIG:1 Structure of furan

PHYSICAL PROPERTIES

- It is colourless liquid
- Boiling point at 32^0c.
- Smell is like chloroform
- Slightly soluble in water
- Dissolves in most organic solvents
- It is flammable

EASIEST METHOD OF CHEMICAL SYNTHESIS OF FURANDERIVATIVES

Paal-Knorr synthesis: A smooth Paal-Knorr transformation of triketones of the type 5 to the corresponding furans was achieved by employing titanium tetrachloride as the dehydrating agent in toluene at 80°C. Several symmetric tetracarbonyl compounds were also converted to the respective furans using this method.(1)

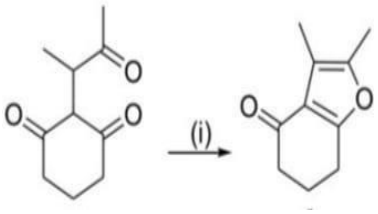


FIG:2 Paal-Knorr synthesis

Recent Literature:

Titanium enolates, in situ-generated from readily available ketones and titanium tetraisopropoxide, undergo domino cross-coupling/cyclodehydration or domino Aldol-addition/cyclocondensation with a-chloroketones to provide synthetically valuable furan derivatives.(3)

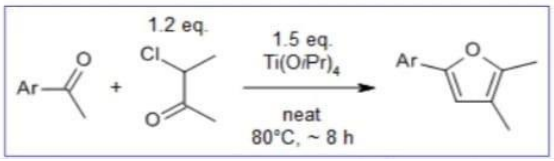


FIG:3

5- hydroxymethyl furfural is a biomass-derived commodity chemical that is ideal to prepare next-generation value- added products. Decarboxylative cross-couplings enable an efficient access to 2,5-diaryl furans. A key finding was that the presence of the hydroxymethyl handle enhances the yields ofthe first palladium-catalyzed decarboxylative cross-coupling reaction.(2)

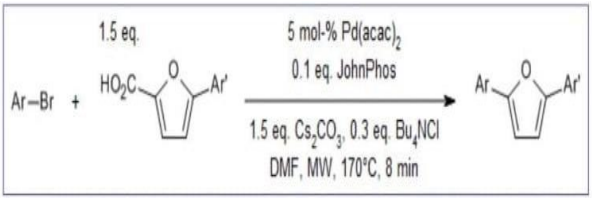


FIG:4

Synthesis of Furans via catalysis by Rhodium and Palladium salts:

Zhao and Zhang synthesized fused furans and carbocyclic furans by the Rh(I) catalyzed cycloisomerization reaction of alkynyl alkenones. The presence of external nucleophiles gave fused furans whereas their absence led to fused carbocyclic furans by the insertion of CO. Wide substrate scope with very few exceptions and the tolerance of nucleophiles including water are some of the highlights of this method.(4,5)

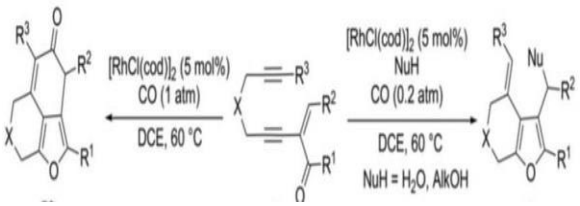


FIG:5 Synthesis of rhodium and palladium of furan via catalysisCopper catalyzed Furan synthesis:

Wang reported a Cu(I)-catalyzed synthesis of 2,3,5-trisubstituted furans by a cascade coupling of terminal alkynes with z-alkyl substituted diazoesters . The copper carbenoid species generated during the reaction may insert into the triple bond to form the corresponding cyclopropenyl ester which then undergoes a ring-opening cycloisomerization to yield chemoselectively (>99:1) the 2,3,5-trisubstituted furans over the competing alkynoate .[6]

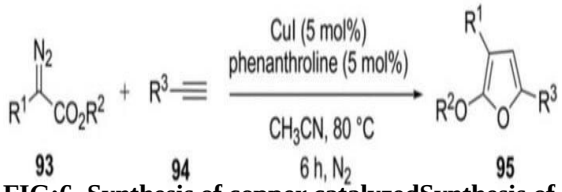


FIG:6 Synthesis of copper catalyzedSynthesis of Bioactive Benzo furan derivatives:

Benzo[b]furan derivatives have demonstrated a fascinating array of biological and pharmaceutical activities, including antitumor properties. For instance, Flynn et al. described the discovery of 7-hydroxy- methoxy-2-methyl-3-(3,4,5-trimethoxybenzoyl) benzo[b]furan) a potent and selective antiproliferative agent. They achieved the synthesis of various derivatives, many of which were obtained through a modified Larock-type coupling between o-iodophenol 1a,b and 3- silyl-1-arylpropinone 2, yielding 2- silylbenzo[b]furans 3a,b in 59% and 69% yields, respectively.[7]

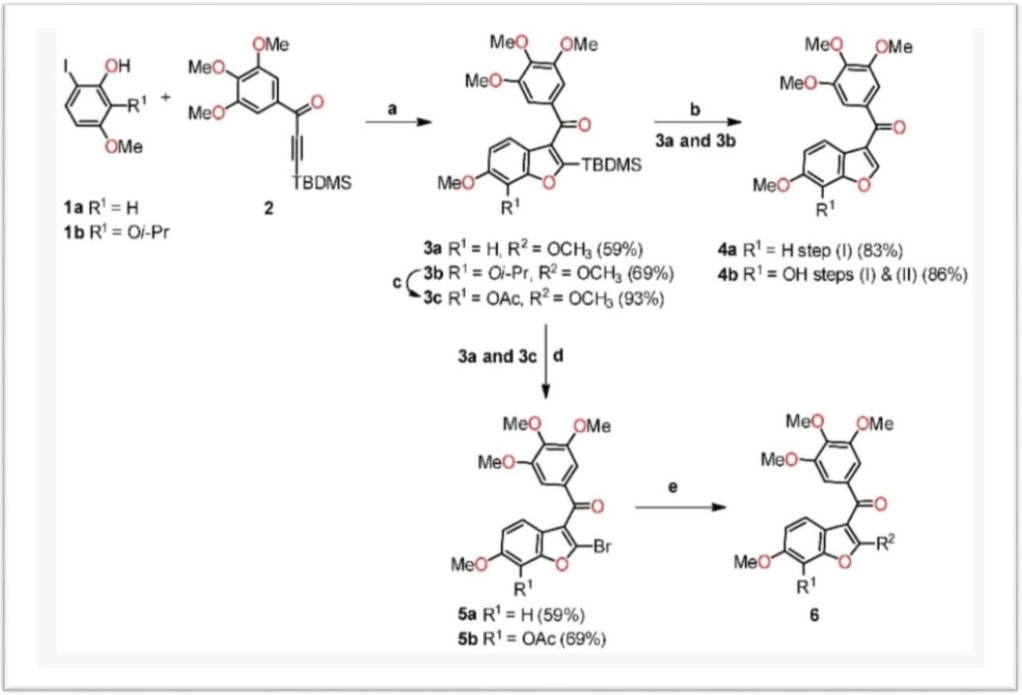


FIG:7 Synthesis of Bioactive benzo furan derivative

PHARMACOLOGICAL ACTIVITIES OF FURAN:

Furan pharmaceuticals provide a wider range of potential treatments for differentclinical conditions. Furan has a number of therapeutic benefits, including being antimicrobial like antibacterial or antifungal or antiviral, anti-inflammatory, analgesic, antidepressant, anti- anxiolytic, anti-parkinsonian, anti-glaucoma, muscle relaxant, antihypertensive, diuretic, anti-ulcer, anti-ageing, anti-viral and anticancer.[8]

Biological activity of furan as anti-microbial agents:

3-aryl-3-(furan-2-yl) propanoic acid derivatives were created and their antibacterial effectiveness was assessed. The best result demonstrated by compound, which suppressed the growth of Escherichia coli at a concentration of MIC 64 µg/ml.[9]

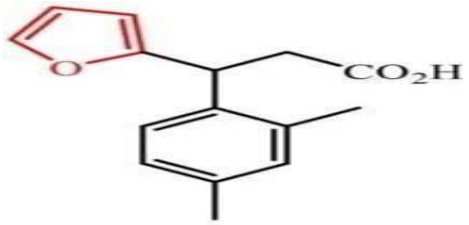


FIG:8 Anti- microbial activity of furan derivative

Biological activity of furan as central nervous system agents:

A series of 3-(furan-2-yl)-5-(substituted phenyl)-4,5-dihydro-1,2-oxazole derivatives were synthesized as antidepressant and antianxiety agents. Out of these 4-13-(furan-2-yl)-4,5- dihydro-1,2-oxazol-5-yl]phenol emerged as the most potent antidepressant agent acting through MAO inhibition without any significant neurotoxicity. The observed MAO inhibitory action could also be responsible for its promising antianxiety effects.[10]

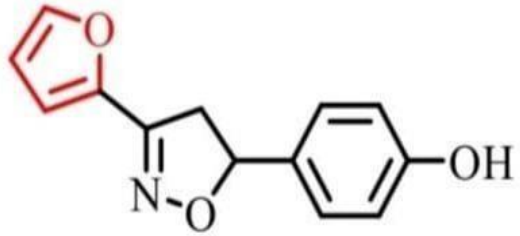


FIG:9 Central nervous system activity of furan derivative

Antibacterial activity:

Hatem A. Abdel-Aziz et al synthesized compound that showed a variable potencies against tested bacteria. The tested compound exhibited weak inhibitory effect against the Gram- negative bacterium E.coli)whereas they revealed no effect, or very weak against p.aerogenosa.

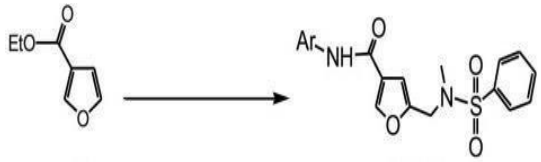


FIG:10 Anti-bacterial activity of furan derivative

Anti-oxidant activity:

Some novel pyridine and imidazole derivatives bearing a biologically active furan moiety was to synthesize and evaluate the antioxidant activity using ABTS method. The strongest antioxidant activity, comparable to ascorbic acid, was shown by compound.[11]

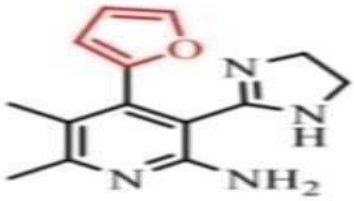


FIG:11 Anti-oxidant activity of furan derivative

Anti-Cancer activity:

Silylation of 5-hydroxyl group in mucobromic acid (MBA) bearing furan-2(5H)-one core leads to develop a set of novel compounds with increased cytotoxic potency against cancer cells. Interestingly, compound showed to be most active against colorectal cancer cell lines.[12]

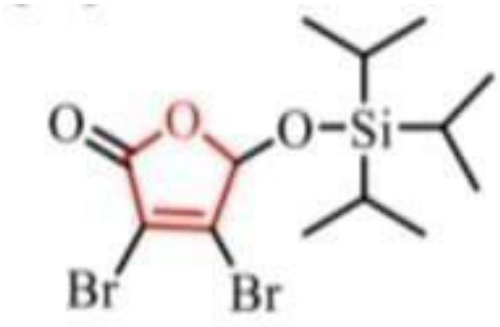


FIG:12 Anti-Cancer activity of furan derivative

Anti-ulcer activity:

Recently, significant gastrointestinal cytoprotective activity of dehydroleucodine xanthatin, and 3-benzyloxymethyl-5H-furan-2-one 27e is efficacious in

an animal modelof stomach ulcer prompted by mast cell stimulation, these finding suggest that lactones could be effective in treating peptic ulcer disease in humans and may become valuable tools for designing and developing novel therapeutic agents for digestive disorders associated with inappropriate mast cell activation.[13]

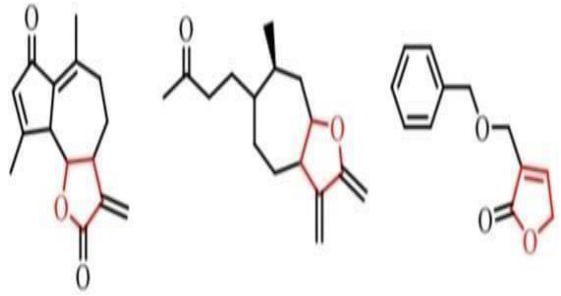


FIG:13 Anti-ulcer activity of furan derivatives

Anti-viral activity:

Galal et al. 2009 synthesized derivatives can serve as lead compound for further investigation and act as antiviral activity. Compound (11 H- Benzo[4,5] imidazole[1,2-a] [1,4] diazepin-4- yl) (6-hydroxy-4,7- dimethoxy- benzofuran-5-yl) methanone.

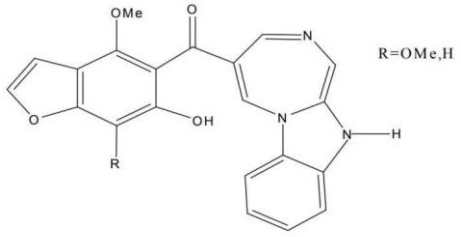


FIG:14 Anti-viral activity of furan derivative

Anti-glaucoma activity:

Three furan sulfonyl hydrazones derivatives were produced and estimated for their carbonic anhydrase inhibitory activity. Among them compound containing withdrawing group (NO2) has highest inhibitioneffect on hCA I isozyme than others.[14]

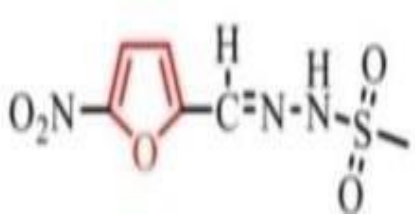


FIG:15 Anti-glaucoma activity of furan derivative

Muscle relaxant activity:

The general synthesis of dantrolene and its analogues with various substituents on its phenyl ring has been developed. Two different Ca^{2} release modes from the sarcoplasmic reticulum (SR) of mouse skeletal muscle fibers have been used to assess the effects of synthetic analogues: the rate of Ca^{2} induced Ca^{2} release (CICR) in saponin-treated skinned muscle fibers and the measurement of twitch contraction caused by physiological Ca^{2+} release (PCR) of intact skeletal muscle. Although the main compound dantrolene inhibits both twitch contraction and CICR, other structurally modified counterparts, such as only inhibit twitch contraction, while showed inhibitory effect on CICR.[15]

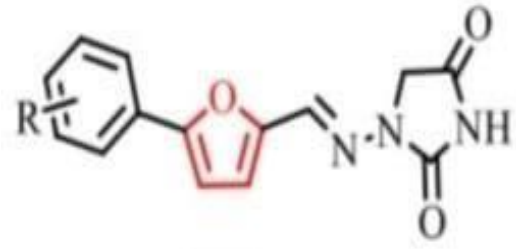
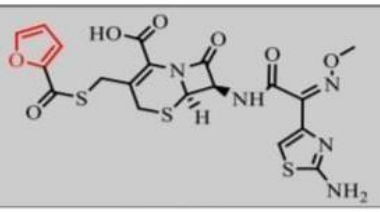
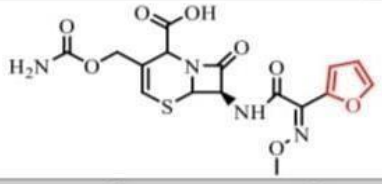
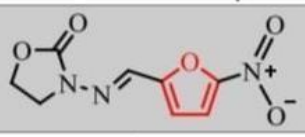
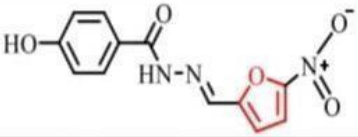
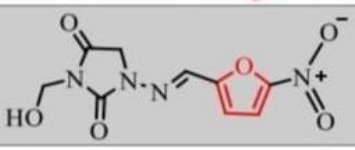
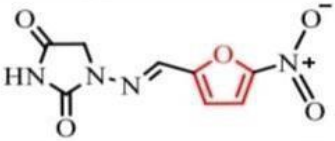
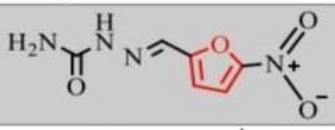
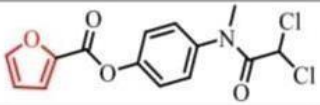
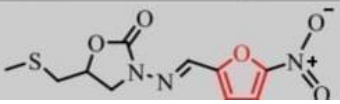
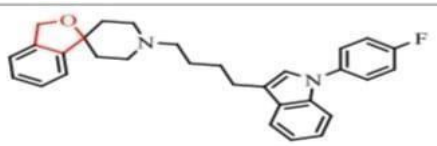
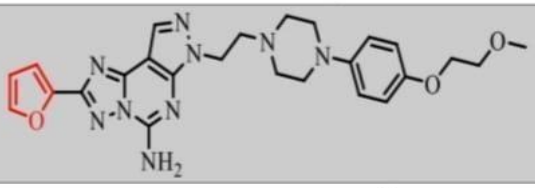
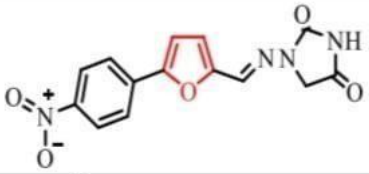
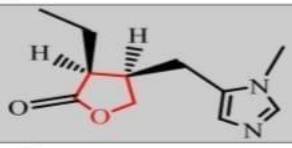
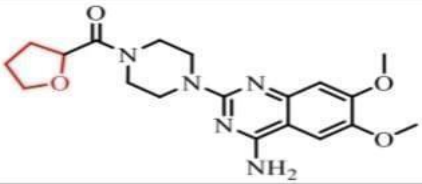
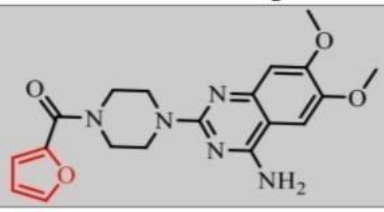
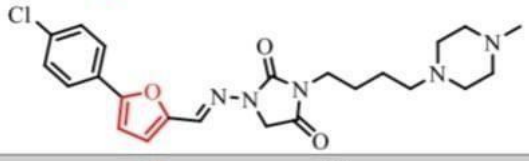
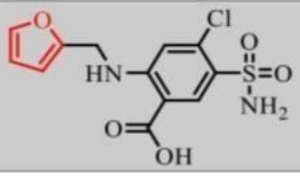
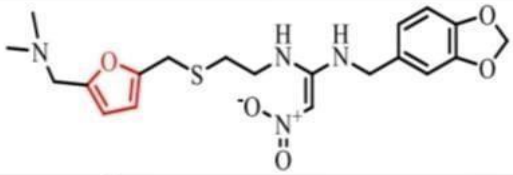
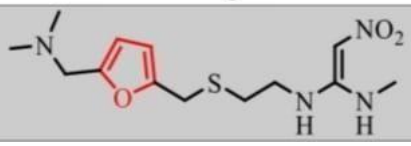
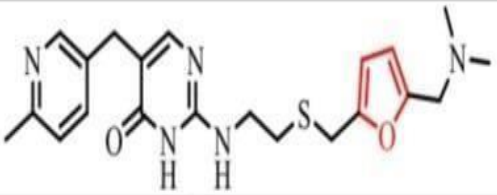
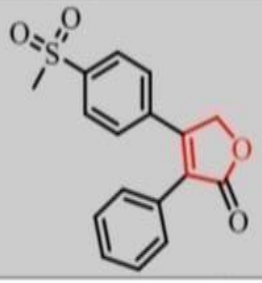
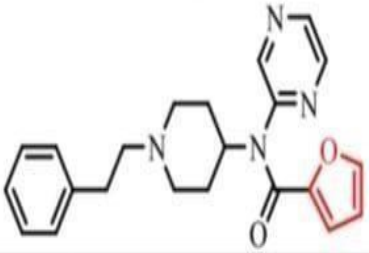
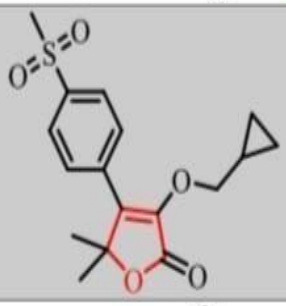
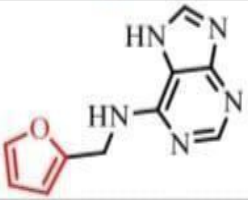
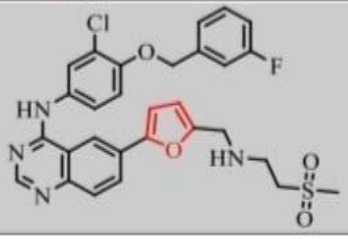


FIG:16 Muscle relaxant activity of furan derivative

Clinically approved drugs containing Furan ring

Sr.no	Name of the drug	Structure	Approved activity
1	Ceftiofur		Antibacterial activity
2	Cefuroxime		Antibacterial activity
3	Furazolidone		Antibacterial activity
4	Nifuroxazide		Antibacterial activity
5	Nifurtoinol		Antibacterial activity
6	Nitrofurantoin		Antibacterial activity
7	Nitrofurazone		Antibacterial activity
8	Diloxanide		Antiprotozoal activity
9	Nifuratel		Antiprotozoal and antifungal activity

10	Siramesine		Antidepressant activity
11	Preladenant		Anti-parkinsonian activity
12	Dantrolene		Muscle relaxant activity
13	Pilocarpine		Antiglaucoma activity
14	Terazosin		Antihypertensive activity
15	Prazosin		Antihypertensive activity
16	Azimilid		Antiarrhythmic activity
17	Furosemide		Diuretic activity
18	Niperotidine		Antiulcer activity
19	Ranitidine		Antiulcer activity

20	Lupitidine		Antiulcer activity
21	Rofecoxib		Analgesic and anti-inflammatory activity
22	Mirfentanil		Analgesic and anti-inflammatory activity
23	Firocoxib		Analgesic and anti-inflammatory activity
24	Kinetin		Anti-ageing activity
25	Lapatinib		Anti-cancer activity

SUMMARY REPORT:

In summary, I conclude that this comprehensive review on Furan and it's biological activity has unveiled the versatile nature of furan compounds, these molecules exhibit a wide range of biological activities, including anti-malarial, anti-bacterial, anti-cancer, anti-convulsant, anti- oxidant activities. The importance of furan derivatives plays a major role in drug devolpment and therapeutic interventions and it holds premises for the development of novel treatments and medicines, benefitting both scientific advancements and human health.

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