REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No.1 (2024)
http://www.veterinaria.org
Article Received: Revised: Published:

Synthesis Of Dibenzofuran-1,3-Thiazole Carboxamide Derivatives And Screened For Anti-Inflammatory Potential

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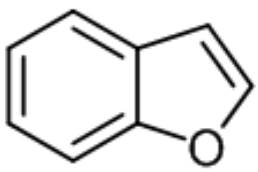
ABSTRACT
Objective: Synthesis of dibenzofuran-1,3-thiazole carboxamide derivatives and screened for anti-inflammatory potential
Material and methods: The goal of the current study was to synthesize a few dibenzofuran-1,3thiazolecarboxamide derivatives using four-step processes and several substituted benzylamines with the help of an appropriate catalyst. The following compounds were prepared: compound 1 (S-((4-chlorodibenzo[b,d]furan-1-yl)methyl) thiohydroxylamine), compound 2 (ethyl 2-(4 chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxylate), compound 3 (2-(4-chlorodibenzo[b,d]furan-1-yl)-5 methylthiazole-4-carboxylic acid), and compound 4 (N-benzyl-2-(4-chlorodibenzo[b,d] furan-1-yl)-5-methyl thiazole 4-carboxamide). Compounds TC-1 through TC-14 are the codes for Compound 4. A total of twelve compounds have been created in these four processes, and the protein denaturation assay has been used to assess each compound's potential for reducing inflammation.
Result and Discussion: The IR spectrum of the compounds has shown the characteristics peak (cm-1) of N-H at 3412; C=C-H at 3470; C=O at 1735; C=C at 1624–1446; C-N at 1015; p-substitution at 792; C-F at 1102; C-Cl at 855; C-Br at 1015; N-O at 1356; N=O at 1558. The 1HNMR spectra of Final compounds (TC-1 to TC-12) depicted the peak at 2.90 (3H, CH3); 4.64 - 4.65 (2H, CH2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 - 7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40 (1H, N-H). Compound TC-1, mass spectrum has shown peak at m/z = 450.85, which matches the chemical formula C24H16ClFN2O2S. The protein denaturation assay of synthesized compound stated that most active compound are TC-1, TC-2, TC-3, TC-4 and TC-5 and compounds TC-7 & TC-9 has shown the mild activity and compound TC-6, TC-8, TC-10, TC-11 and TC-12 has shown modest activity.
Conclusion: The substitution of fluoro, chloro, bromo, iodo, and nitro was one of the main groups that significantly increased the activity with para-substituent.

Keywords: *Thiazole, Anti-inflammatory, Protein Denaturation Assay*

INTRODUCTION:

One of the most intricate areas of chemistry is the study of heterocyclic compounds. Heterocyclic compounds are abundant in nature and are crucial for controlling various biological processes. Chemotherapeutic agents, medications, dyestuffs, and copolymers are among the many uses for heterocyclic compounds. Benzofuranes are a particularly intriguing class of heterocyclic compounds that contain oxygen and have a wide range of applications in synthetic and medicinal chemistry. Benzofuranes, which are found in coal tar and are isolated as picrate, have a significant role in medicine and insecticides. Another synthetic technique is the Palladium-protonated cyclization of O-substituted aryl aryl ether. Numerous artificial derivatives of benzofurans possess intriguing characteristics. These are also employed as step-ins in the manufacturing of fungicides, herbicides, and parasiticides.



Condensation of a benzene ring at the 2,3, or 3,4 position results in the formation of benzofuran, depending on the benzene ring's location. One is called iso-coumaran or iso-benzofuran, while the other is called coumaran (or) benzofuran.

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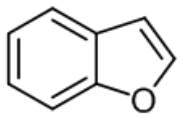
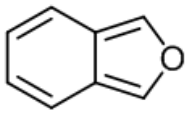


benzo (b) furan



benzo (c) furan

The benzofuran nucleus is found in coal tar and is extracted as picrate. It has significant value in medicines and pesticides. It is also synthesized by cyclizing O-substituted aryl aryl ether by palladium protonation. Numerous artificial benzofuran compounds possess intriguing characteristics. These are further employed as intermediaries in the manufacturing of fungicides, herbicides, and parasiticides. Numerous biological actions have been linked to benzofurans; in particular, dibenzofurans have been shown to have analgesic, antiviral, anti-inflammatory, cough-inhibiting, hypo-lipidemic, and herbicidal effects.
The creation of novel molecules that are effective and pharmaceutically active is the biggest benefit of heterocyclic chemistry. Chemical reactions occur at every stage of the synthesis process; also, the conditions and reagents must be chosen to produce pure molecules and high yields. Because of their unique properties, heterocyclic compounds may find use in the management of infectious disorders. An important advance in the history of contemporary medicine has been the discovery and development of an efficient anti-inflammatory drug. A review of the literature revealed that the creation of pharmacologically relevant compounds involved the use of thiazole and its derivatives. It was intended to create a few novel bioactive compounds with thiazole moiety in light of these findings.

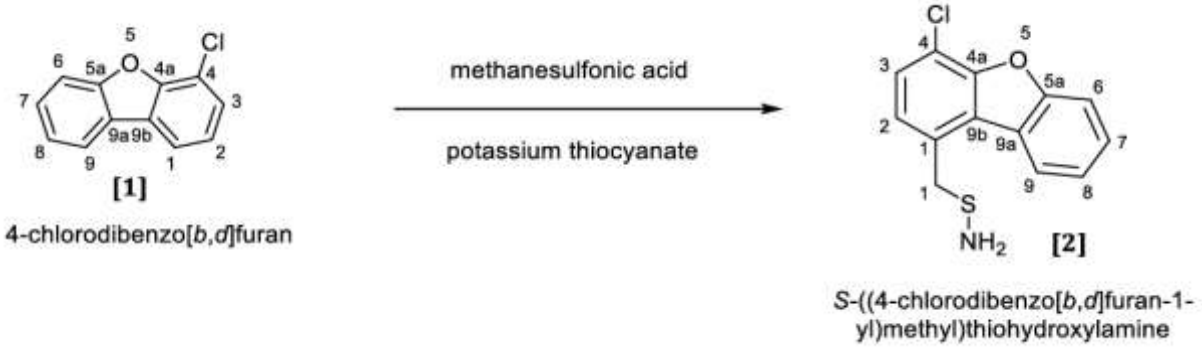
INFLAMMATION
Your body's white blood cells and the substances they produce, known as inflammation, serve as a defense against infections brought on by external invaders like bacteria and viruses.However, in certain illnesses, such as arthritis, your immune system—your body's defensive mechanism—induces inflammation even in the absence of outside invaders to repel. Your immune system damages ordinary tissues in certain autoimmune illnesses by acting as though they are abnormal or contaminated.

Inflammation Types:- Inflammation can be either short-lived (acute) or long-lasting (chronic). Acute inflammation goes away within hours or days.

MATERIALS AND METHOD:
Methanesulfonic acid, potassium thiocyanate, 4 chlorobenzo [b,d] furan, potassium carbonate, ethyl-3 bromo-2-oxocutanoate, potassium ethanol, dichloromethane, hydroxide, triethylamine and substituted benzyl amine were purchased from sigma Aldrich. All solvents used for the reactions were distilled before use.

Synthesis Scheme:-he synthesis of the final compound was achieved through four Schemes.
- **Scheme-I:** Synthesis of S-((4-chlorodibenzo[b,d]furan-1-yl)methyl) thiohydroxylamine
- **Scheme-II:** Synthesis of ethyl 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4 carboxylate
- **Scheme-III:** Synthesis of 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxylic acid
- **Scheme-IV:**Synthesis of N-benzyl-2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl thiazole-4 carboxamide

Scheme-I: Synthesis of S-((4-chlorodibenzo[b,d]furan-1-yl)methyl) thiohydroxyl amine



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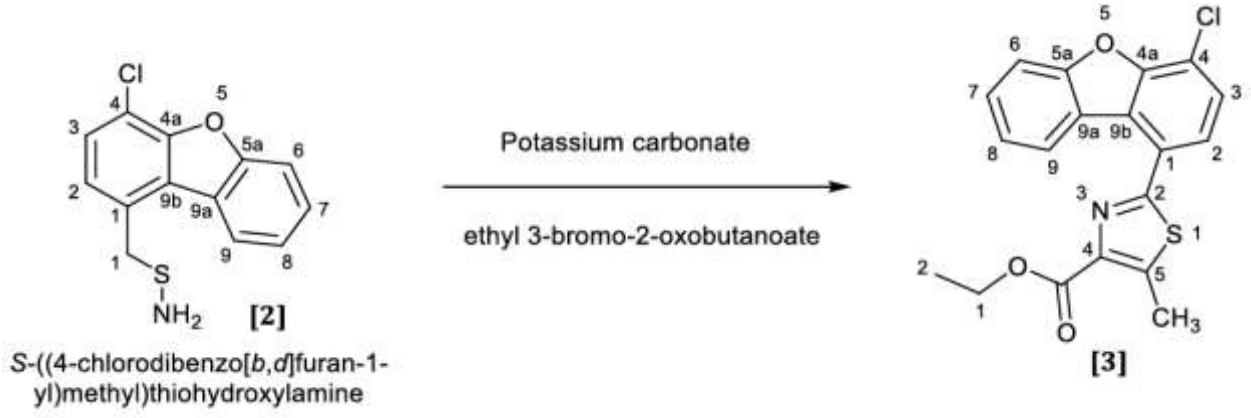
Procedure: 4-chlorodibenzo[b,d]furan (0.02M) Compound 1, was taken in round bottomed flask and dissolved in 20 ml of methane sulfonic acid. The mixture then stirred for 10 min. Then potassium thiocyanate (0.02M) was added slowly to above mixture and reaction was kept at 0–5°C in salt-ice and the reaction mixture was stirred at room temperature for 15min. The reaction mixture was poured into crushed ice, to obtained the solid product (Compound 2), was filtered and then triturated with n-hexane to get a pale brown colour solid. Yield-82%; Mass m/z: 263.74

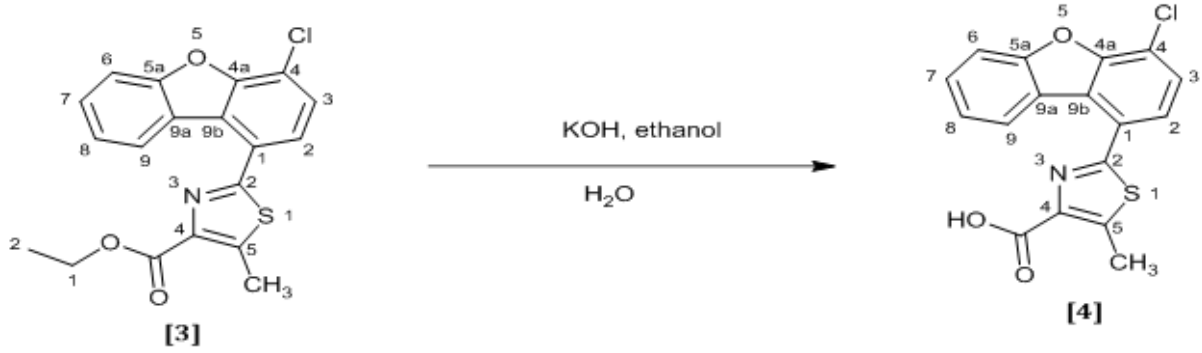
Scheme-II: Synthesis of ethyl 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxylate



S-((4-chlorodibenzo[*b*,*d*]furan-1-yl)methyl)thiohydroxylamine

Procedure: S-((4-chlorodibenzo[b,d]furan-1-yl)methyl) thio hydroxylamine (0.02M) Compound 2,was dissolved in 15ml ethanol and stirred for 15 min. Then potassium carbonate (0.02M) followed by ethyl 3-bromo-2-oxobutanoate (0.02M) was added at room temperature. The reaction mixture was refluxed at 80°C for 2 hrs. with occasional shaking, subsequently it was poured into 50 ml of cold water and the precipitate which obtained was filtered to get a peach colored solid[43] (Compound 3), yield –72.50%; Mass (m/z): 371.84.

Scheme-III: Synthesis of 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxylic acid



Procedure: The ethyl 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxylate(0.01M), (Compound 3)was dissolved in 15 ml of ethanol and potassium hydroxide (0.02M)wasadded followed by addition of 20 ml distilled water and stirred at room temperature for 2hrs. Subsequently the reaction mixture was poured into cold water, acidified with 1NHCl (pH3) and precipitated solid was filtered and triturated with ether followed by n-hexane to give off-white solid[44] (Compound 4); Yield:- 72% Mass (m/z): 343.78.

Scheme-IV: Synthesis of N-benzyl-2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxamide

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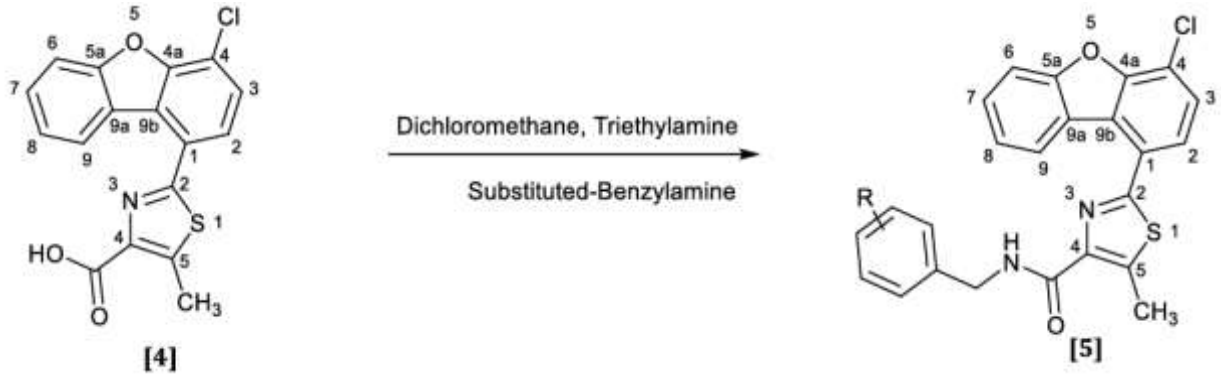


Procedure: In a 50ml round bottom flask 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4 carboxylic acid (0.02M), (Compound 4) was dissolved in 10 ml dichloromethane. 0.32g (0.002M) of TBTU and 0.15 ml (0.002M) of triethylamine were added to that solution, and it was agitated for five minutes in a nitrogen environment. Next, for three hours, substituting benzyl amine (0.02M) was added and mixed. below the ambient temperature. Ethyl acetate was used to extract the reaction mixture as the reaction was being monitored for completion using TLC. To obtain a solid product, the organic layer was removed and dried on anhydrous sodium sulphate after being cleaned with sodium bicarbonate solution, water, and brine solution. (Compound 5)

Table No. 1:- Quantity of chemicals taken

S. NO.	Name of Chemicals	Mol. Formula	Mol. Weight	Quant. (gm)
1	2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4 carboxylic acid	C17H10ClNO3S	343.78	6.87
2	N-chloro-1-(4-fluorophenyl)methanamine	C7H7ClFN	159.59	3.19
3	N-chloro-1-(4-Chlorophenyl)methanamine	C7H7Cl2N	176.04	3.52
4	N-chloro-1-(4-bromophenyl)methanamine	C7H7BrClN	220.49	4.40
5	N-chloro-1-(4-Iodophenyl)methanamine	C7H7ClIN	267.49	5.34
6	N-chloro-1-(4-nitrophenyl)methanamine	C7H7ClN2O2	186.60	3.72
7	N-chloro-1-(4-methylphenyl)methanamine	C8H10ClN	155.63	3.11
8	N-chloro-1-(4-methoxyphenyl)methanamine	C8H10ClNO	171.62	3.43
9	N-chloro-1-(4-ethylphenyl)methanamine	C9H12ClN	169.65	3.39
10	N-chloro-1-(4-ethoxyphenyl)methanamine	C9H12ClNO	185.65	3.71
11	N-chloro-1-(4-(trifluoromethyl)phenyl)methanamine	C8H7ClF3N	209.60	4.19
12	N-chloro-1-(4-propylphenyl)methanamine	C10H14ClN	183.68	3.67
13	N-chloro-1-(4-propyloxyphenyl)methanamine	C10H14ClNO	199.68	3.99

CHARACTERIZATION OF THE SYNTHESIZED COMPOUNDS

Table No. 2: Physicochemical properties and list of final synthesized compounds

S. No.	Code	Chemical Name	Mol. Weight	Chemical Formula	Percent Yield	Melting point
1	TC-1	2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-fluorobenzyl)-5-methylthiazole 4-carboxamide	450.91	C24H16ClFN2O2S	78	186-188˚C
2	TC-2	N-(4-chlorobenzyl)-2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole 4-carboxamide	467.36	C24H16Cl2N2O2S	82	166-178˚C
3	TC-3	N-(4-bromobenzyl)-2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole 4-carboxamide	511.82	C24H16BrClN2O2S	76	175-178˚C
4	TC-4	2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-iodobenzyl)-5-methylthiazole-4 carboxamide	558.82	C24H16ClIN2O2S	75	145-147˚C

5	TC-5	2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4-nitrobenzyl)thiazole 4-carboxamide	477.92	C24H16ClN3O4S	73	152-154˚C
6	TC-6	2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4 methylbenzyl)thiazole-4-carboxamide	446.95	C25H19ClN2O2S	68	116-118˚C
7	TC-7	2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-methoxybenzyl)-5 methylthiazole-4-carboxamide	462.95	C25H19ClN2O3S	62	115-118˚C
8	TC-8	2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-ethoxybenzyl)-5-methylthiazole 4-carboxamide	476.98	C26H21ClN2O3S	80	162-164˚C
9	TC-9	2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-ethylbenzyl)-5-methylthiazole 4-carboxamide	460.98	C26H21ClN2O2S	85	158-160˚C
10	TC-10	2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4 (trifluoromethyl) benzyl)thiazole-4-carboxamide	500.92	C25H16ClF3N2O2S	80	115-117˚C
11	TC-11	2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4-propylbenzyl) thiazole-4-carboxamide	475.00	C27H23ClN2O2S	75	175-177˚C
12	TC-12	2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4 propoxybenzyl)thiazole-4-carboxamide	491.00	C27H23ClN2O3S	78	145-147˚C

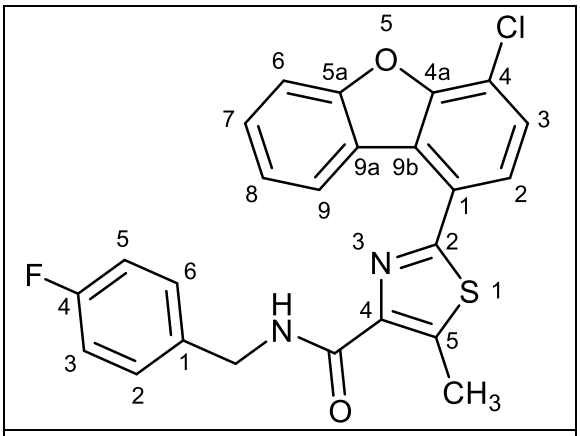
Characterization of the Synthesized compounds by IR, NMR, MASS and elementary analysis
All substances were analyzed by elemental analysis, mass spectroscopy, infrared spectroscopy, and IR.

IR spectra were recorded on Bruker alpha-II software.

NMR spectra were recorded on C13 Advance Brucher DRX 400 MHz spectrometer.

Mass spectra were recorded on JeolSx 102/DA-6000 mass spectrometer using fast moving bombardment (FAB) technique.

Compound Code: TC-1



TC-1

$C_{24}H_{16}ClFN_2O_2S$

IUPAC NAME: 2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-fluorobenzyl)-5 methylthiazole-4-carboxamide

Elemental Analysis:

Elements	C	N	O	S

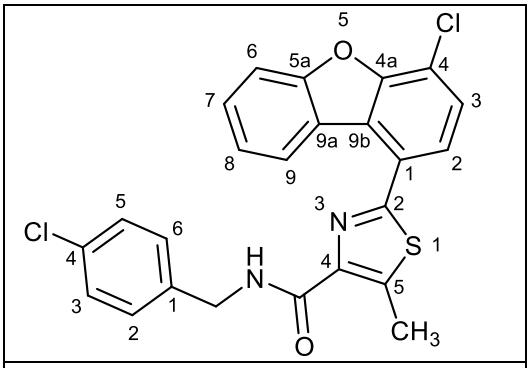
Calculated	63.93	6.21	7.10	7.11
Found	63.92	6.20	7.09	7.12

IR (cm^{-1}): 3412(N-H); 3470(C=C-H);1735 (C=O); 1624–1446 (C=C);1015(C-N); 792**(**p-substitution); 1102 (C-F)**;** 855(C-Cl)

1HNMR (ppm): 4.64 -4.65 (CH_2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 -7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H); 2.90 (3H, CH_3)

FAB Mass (m/z): 450.85

Compound Code: TC-2



TC-2

$C_{24}H_{16}Cl_2N_2O_2S$

IUPACname: N-(4-chlorobenzyl)-2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxamide

Elemental Analysis:

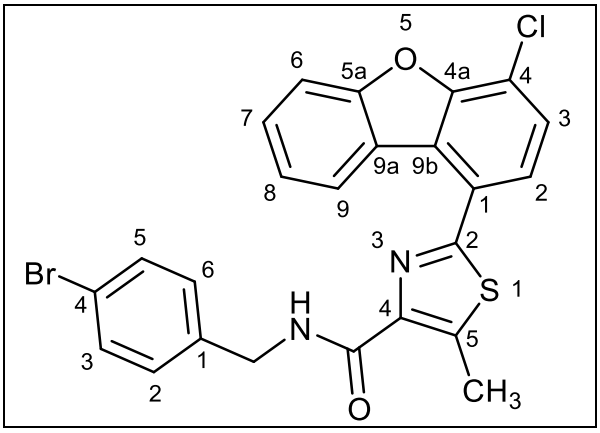
Elements	**C**	**N**	**O**	**S**
Calculated	61.68	5.99	6.85	6.86
Found	61.65	5.89	6.82	6.85

IR (cm^{-1}): 3412(N-H);3470(C=C-H); 1735 (C=O); 1624–1446 (C=C); 1015(C-N); 792 (Parasubstitution)**;** 852 (C-Cl)

1HNMR (ppm):2.90 (3H, CH_3); 4.64 -4.65 (2H, CH2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33–7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 - 7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H).

FAB Mass (m/z): 467.30

Compound Code: TC-3



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TC-3
$C_{24}H_{16}BrClN_2O_2S$

IUPACName: N-(4-bromobenzyl)-2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxamide

Elemental Analysis:

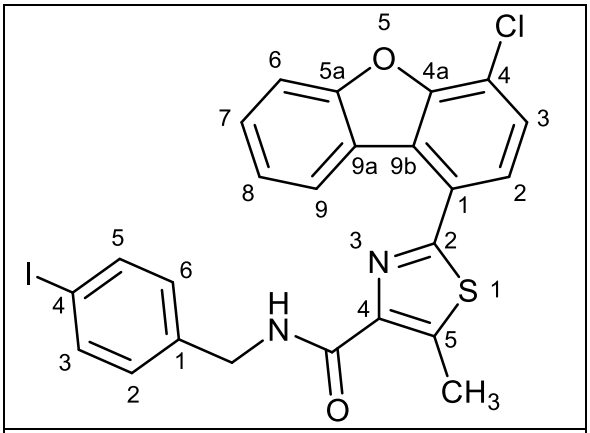
Elements	**C**	**N**	**O**	**S**
Calculated	56.32	5.47	6.25	6.26
Found	56.30	5.42	6.22	6.25

IR (cm^{-1}): 3412(N-H);3470 (C=C-H); 1735 (C=O); 1624–1446 (C=C); 1015(C-N); 792 (Para substitution); 850 (C-Cl); 1015(C-Br)

1HNMR (ppm): 2.90 (3H, CH3); 4.64 -4.65 (2H, CH2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 - 7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H).

FAB Mass (m/z): 511.80

Compound Code: TC-4



TC-4
$C_{24}H_{16}ClIN_2O_2S$

IUPAC NAME: 2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-iodobenzyl)-5-methylthiazole-4-carboxamide

Elemental Analysis:

Elements	**C**	**N**	**O**	**S**
Calculated	51.58	5.01	5.73	5.74
Found	51.54	4.99	5.72	5.70

IR (cm^{-1}): 3412(N-H);3470(C=C-H);1735 (C=O); 1624–1446 (C=C);1015(C-N); 792 (Parasubstitution)**;** 855 (C-Cl)

1HNMR (ppm): 2.90 (3H, CH_3); 4.56-4.58 (2H, CH_2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 - 7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H).

FAB Mass (m/z):558.80

CompoundCode: TC-5

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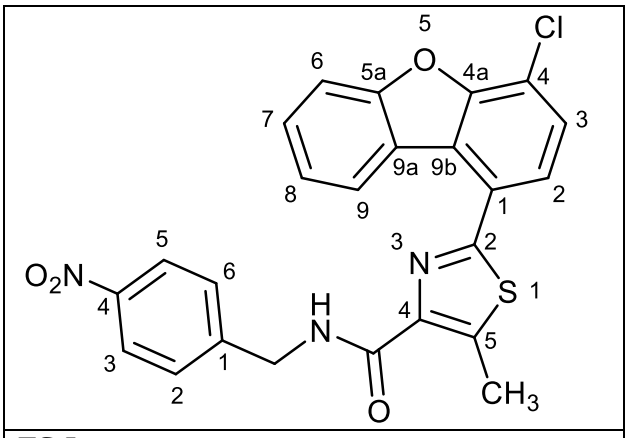


TC-5

$C_{24}H_{16}ClN_3O_4S$

IUPACNAME: 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4-nitrobenzyl)thiazole-4-carboxamide

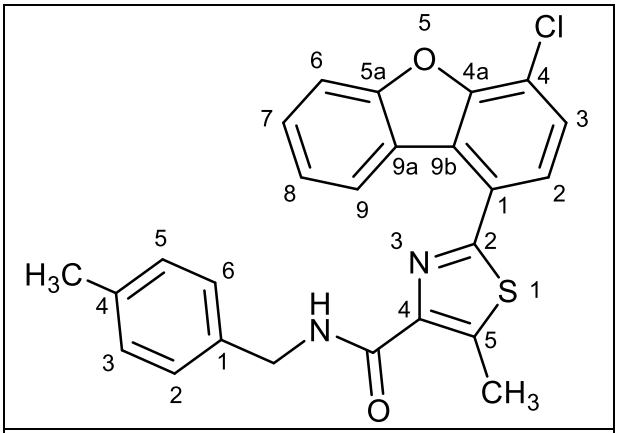
Elemental Analysis:

Elements	**C**	**N**	**O**	**S**
Calculated	60.32	8.79	13.39	6.71
Found	60.28	8.75	13.35	6.70

IR (cm^{-1}): 3412(N-H);3470(C=C-H);1735 (C=O); 1624–1446 (C=C); 1015(C-N); 792 (Parasubstitution)**;**852 (C-Cl); 1356 (N-O); 1558 (N=O)

1HNMR (ppm): 2.90 (3H, CH_3); 4.64 -4.65 (2H, CH_2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 - 7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H).
FAB Mass (m/z): 477.90

Compound Code: TC-6



TC-6

$C_{25}H_{19}ClN_2O_2S$

IUPAC NAME: 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(methylbenzyl)thiazole-4-carboxamide

Elemental Analysis:

Elements	**C**	**N**	**O**	**S**
Calculated	67.18	6.27	7.16	7.17
Found	67.15	6.20	7.15	7.12

IR (cm^{-1}): 3412 (N-H);3470(C=C-H);1735 (C=O); 1624–1446 (C=C); 1015(C-N); 792 (Parasubstitution); 850 (C-Cl)

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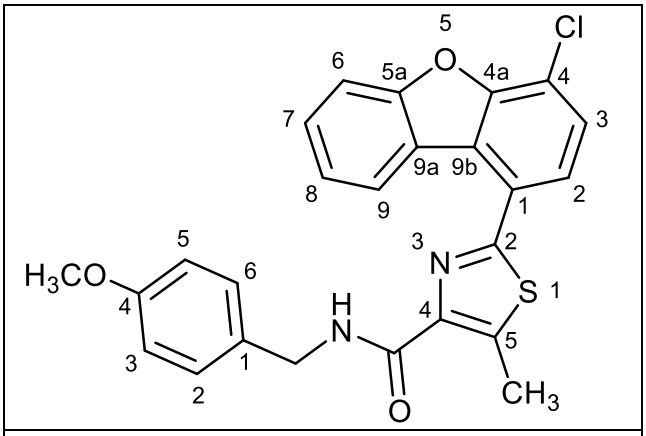
1HNMR (ppm): 2.90 (3H, CH_3); 4.56-4.58 (2H, CH_2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 - 7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H).

FAB Mass (m/z): 447.10

CompoundCode: **TC-7**



TC-7
$C_{25}H_{19}ClN_2O_3S$

IUPAC NAME: 2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-methoxybenzyl)-5-methylthiazole-4-carboxamide

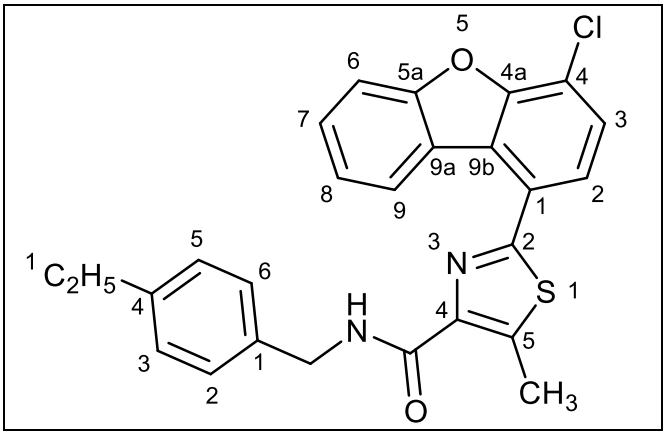
Elemental Analysis:

Elements	**C**	**N**	**O**	**S**
Calculated	64.86	6.05	10.37	6.93
Found	64.82	6.02	10.35	6.90

IR (cm^{-1}): 3412(N-H);3470(C=C-H);1735 (C=O); 1624–1446 (C=C); 1015(C-N); 792 (Parasubstitution)**;** 852 (C-Cl)
1HNMR (ppm): 2.90 (3H, CH_3); 4.11 (3H, OCH_3); 4.64-4.65 (2H, CH2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 - 7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H).

FAB Mass (m/z): 462.90

Compound Code: TC-8



TC-8
$C_{26}H_{21}ClN_2O_3S$

IUPAC NAME: 2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-ethoxybenzyl)-5-methylthiazole-4-carboxamide

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Elemental Analysis:

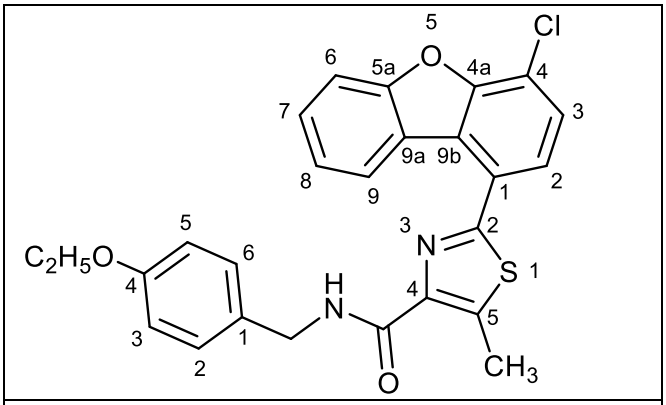
Elements	**C**	**N**	**O**	**S**
Calculated	65.47	5.87	10.06	6.72
Found	65.45	5.82	10.02	6.70

IR (cm^{-1}): 3412(N-H);3470 (C=C-H);1735 (C=O); 1624–1446 (C=C); 1015(C-N);792 (Parasubstitution)**;** 850 (C-Cl)

1HNMR (ppm): 2.90 (s, 3H, CH_3); 4.64 -4.65 (2H, CH_2); 7.05-7.10 (2H, Ar-H); 7.35 (Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 -7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H).

FAB Mass (m/z): 476.90

Compound Code: TC-9



TC-9

$C_{26}H_{21}ClN_2O_2S$

IUPAC NAME: 2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-ethylbenzyl)-5-methylthiazole-4-carboxamide

Elemental Analysis:

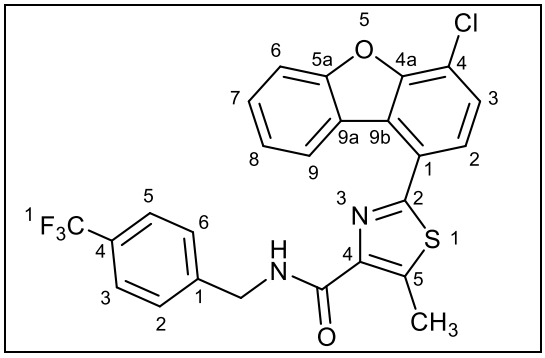
Elements	**C**	**N**	**O**	**S**
Calculated	67.74	6.08	6.94	6.95
Found	67.72	6.05	6.90	6.92

IR (cm^{-1}): 3412(N-H), 3470(C=C-H); 1735 (C=O); 1624–1446 (C=C); 1015(C-N);792 (Parasubstitution)**;** 852 (C-Cl)

1HNMR (ppm): 2.90 (3H, CH_3); 4.64 -4.65 (2H, CH2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33–7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 - 7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H).

FAB Mass (m/z): 460.90

Compound code: TC-10



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TC-10
$C_{25}H_{16}ClF_3N_2O_2S$

IUPAC NAME: 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4-(trifluoromethyl)benzyl)thiazole-4-carboxamide

Elemental Analysis:

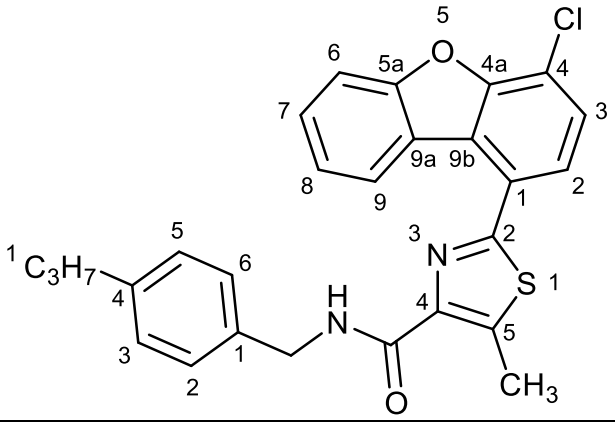
Elements	C	N	O	S
Calculated	59.94	5.59	6.39	6.40
Found	59.90	5.55	6.35	6.38

IR (cm^{-1}): 3412(N-H);3470(C=C-H);1735 (C=O); 1624–1446 (C=C); 1015(C-N);792 (Para substitution); 1160 (C-F); 850 (C-Cl)

1HNMR (ppm): 2.90 (3H, CH_3); 4.56-4.58 (2H, CH_2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33–7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.50-7.52 (1H, Ar-H); 7.62-7.63 (1H, Ar-H); 7.90-7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H).

FAB Mass (m/z): 500.90

Compound Code: TC-11



TC-11
$C_{27}H_{23}ClN_2O_2S$

IUPAC NAME: 2-(4-chlorodibenzo[b,d] furan-1-yl)-5-methyl-N-(4-propylbenzyl)thiazole-4-carboxamide

Elemental Analysis:

Elements	**C**	**N**	**O**	**S**
Calculated	68.27	5.90	6.74	6.75
Found	68.25	5.88	6.72	6.70

IR (cm^{-1}): 3412(N-H); 3470(C=C-H);1735 (C=O); 1624–1446 (C=C); 1015(C-N); 792 (Parasubstitution); 852(C-Cl)

1HNMR (ppm): 2.90 (3H, CH_3); 4.56-4.58 (2H, CH_2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 - 7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40(1H, N-H).

FAB Mass (m/z): 475.00

Compound Code: TC-12

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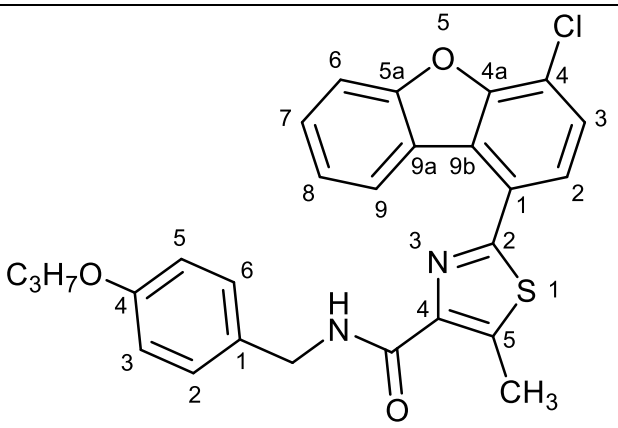

TC-12

$C_{27}H_{23}ClN_2O_3S$

IUPAC NAME: 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4-propoxybenzyl)thiazole-4-carboxamide

Elemental Analysis:

Elements	**C**	**N**	**O**	**S**
Calculated	66.05	5.71	9.78	6.53
Found	66.02	5.70	9.72	6.50

IR (cm^{-1}): 3412(N-H);3470(C=C-H);1735(C=O); 1624–1446 (C=C); 1015(C-N);792(Para substitution)**;** 850 (C-Cl)

1HNMR (ppm): 2.90 (3H, CH_3); 4.64 - 4.65 (2H, CH_2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.50-7.52 (1H, Ar-H); 7.62-7.63 (1H, Ar-H); 7.90 -7.92 (1H, Ar-H); 8.38-8.40(1H, N-H).

FAB Mass (m/z): 491.00

PHARMACOLOGICAL EVALUATION:

Inflammation is the body's response to injury, illness, or damage; symptoms include heat, swelling, redness, discomfort, and changed physiological processes. As a natural defensive reaction to tissue damage brought on by microbial, toxic, or physical stress, inflammation occurs. Chemical mediators released by wounded tissues and migratory cells cause it to occur. The goal of the current investigation was to assess if synthetic drugs may have an anti-inflammatory impact in vitro by preventing protein denaturation.

In vitro anti-inflammatory properties via denaturation of proteins

A solution of 0.2% of bovine serum albumin (BSA) was prepared in tris buffer saline and pH was adjusted to 6.8 using glacial acetic acid. The synthesized compounds (TC-1 to TC 12) of different concentration (25, 50, 100, 200, 300 and 400µg/ml) was prepared using ethanol as solvent. The 50µl of each test drug was transformed to test tubes using micropipette. 5 ml of 0.2% w/v of BSA solution was added to the test tubes. The control consists of 5 ml of 0.2% w/v of BSA solution and 5µl alcohol. The test tubes were heated at 72˚C for 5 min and then cooled for 10 min.

The absorbance of these solutions was determined using UV–visible (UV) spectrophotometer at 660 nm. % of Denaturation Inhibition was computed using the control, in which no medication was added. Diclofenac sodium was used as standard and treated similarly for determination of absorbance. The percentage inhibition of protein denaturation was calculated using the following formula.

Percentage inhibition of protein denaturation = $\frac{AC-AE}{AC} \times 100$

RESULT AND DISCUSSION

Chemistry

The target structures of the synthesized compounds were characterized by elemental, mass spectral, IR, and NMR examinations. Compound 2 was produced via the 4-chlorodibenzo[b,d]furan (0.02M) reaction. Compound 1 has a solid pale brown color, a yield of 82%, and a mass (m/z) of 263.74 with methane sulfonic acid.S-((4-chlorodibenzo[b,d]furan-1 yl)methyl) thiohydroxylamine (0.02M) was used to create compound 3.To get a peach-

colored solid (Compound 3), combine Compound 2 with potassium carbonate and ethyl 3-bromo-2-oxobutanoate (0.02M); yield: 72.50%; mass (m/z): 371.84.Ethyl 2-(4 chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxylate (0.01M), (Compound 3) and aqueous potassium hydroxide solution were reacted to create Compound 4, an off-white solid with a yield of 72% and a mass (m/z) of 343.78%. 2-(4 chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxylic acid (0.02M), compound 4, and substituted benzyl amine reacted to create the final chemical (Compound 5).

The compound TC-1 to TC-12 has characterized by the IR, 1HNMR, elemental and Mass spectral analysis. The IR spectrum of the compounds has shown the characteristics peak (cm-1) of N-H at 3412; C=C-H at 3470; C=O at 1735; C=C at 1624–1446; C-N at 1015; p-substitution at 792; C-F at 1102; C-Cl at 855; C-Br at 1015; N-O at 1356; N=O at 1558.The 1HNMR spectra of Final compounds (TC-1 to TC-12) depicted the peak at 2.90 (3H, CH3); 4.64 - 4.65 (2H, CH2); 7.05-7.10 (2H, Ar-H); 7.35 (1H, Ar-H); 7.33 – 7.39 (4H, Ar-H); 7.45 (1H, Ar-H); 7.48 - 7.50 (1H, Ar-H); 7.62 - 7.63 (1H, Ar-H); 7.90 - 7.92 (1H, Ar-H); 8.38 – 8.40 (1H, N-H).

CompoundTC-1, mass spectrum have shown peak at m/z = 450.85, which matches the chemical formula C24H16ClFN2O2S. All the other synthesized compound has also shown the molecular ion peak similar to their molecular formula and weight.

In-vitro anti-inflammatory activity

Protein denaturation

An examination of the synthetic compounds' capacity to denaturize proteins was conducted in order to assess their anti-inflammatory properties. It proved successful in preventing the denaturation of proteins caused by heat. A common anti-inflammatory drug with greatest percentage inhibition is diclofenac sodium. Table No. 3 showed how the synthetic chemicals (TC-1 to TC-12) affected protein denaturation.

Table 3: The percentage inhibition as protein denaturation of synthesized compounds (TC-1 to 12)

S. No.	Compounds	25	50	100	200	300	400
1	TC-1	21.47	30.77	41.03	53.00	57.58	82.38
2	TC-2	27.44	33.50	51.30	54.98	56.85	88.96
3	TC-3	16.06	21.89	36.08	41.83	42.61	77.03
4	TC-4	15.60	33.50	50.68	56.85	62.99	84.36
5	TC-5	24.76	43.86	57.71	66.30	69.37	89.06
6	TC-6	16.50	17.81	35.11	37.08	38.91	55.49
7	TC-7	3.02	10.75	32.26	39.57	53.91	65.30
8	TC-8	6.04	7.42	15.70	19.76	25.16	48.63
9	TC-9	8.72	18.24	32.07	36.11	48.59	65.77
10	TC-10	4.40	05.46	21.23	32.32	38.99	62.03
11	TC-11	2.40	04.02	11.50	28.54	32.35	58.30
12	TC-12	1.15	08.02	21.05	15.36	35.23	60.20
13	Diclofenac Sodium	14.20	40.32	53.77	62.49	67.22	84.94

(Values are Mean±S.E.M., where n=6) in each group, P< 0.05 *, P< 0.01 (significant) compared with control. Statistical analysis was done by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test.**

The result data of protein denaturation assay denotes that compound TC-1 has shown the 82.38% of inhibition, compound TC-2 has shown the 88.96% inhibition, compound TC-3 has shown the 77.03% inhibition compound TC-4 has shown the 84.36% of inhibition, TC 5 has shown 89.06% of inhibition. The compound TC-1, TC-2, TC-3, TC-4, and TC-5 has shown the better activity as percentage of inhibition compare to diclofenac sodium (84.94%).

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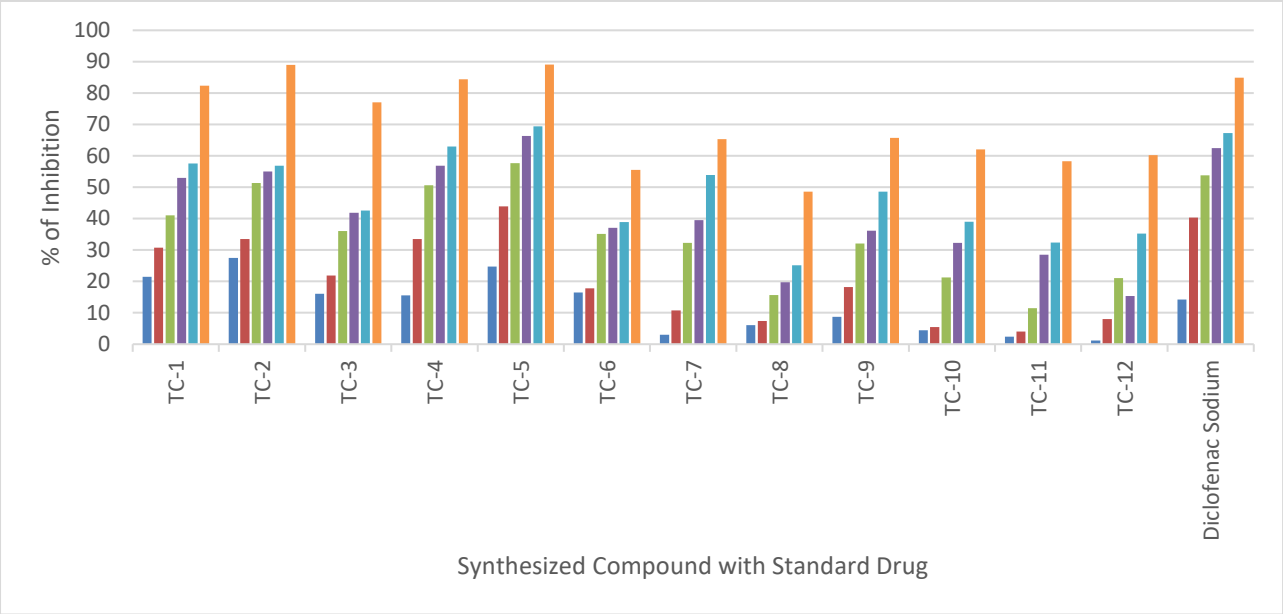

Graph 1:- Percentage of inhibition of synthesized compound (TC-1 to TC-12) as compared to diclofenac sodium

The data of protein denaturation assay result stated that compound TC-6, TC-7,TC 8,TC-9TC-10,TC-11and TC-12 has shown the mild activity as compared to the standard drug. The compound TC-6 has shown the 55.49% inhibition, compound TC-7 has shown the 65.30% inhibition, compound TC-8 has shown the 48.63% inhibition, compound TC-9 has shown the 65.77% inhibition, compound TC-10 has shown the 62.03% inhibition, compound TC-11 has shown the 58.30% inhibition and compound TC-12 has shown the 60.20% inhibition. The most active compound TC-1, TC-2, TC-3, TC-4 and TC-5, the compounds TC-7 & TC-9 has shown the mild activity and compound TC-6, TC-8, TC-10, TC-11 and TC-12 has shown modest activity.

CONCLUSION:

The synthesis of twelve substances is reported in the current article, "Synthesis of dibenzofuran-1,3-thiazole carboxamide derivatives and screened for anti-inflammatory potential." It is commonly known that the existence of compounds derived from dibenzofuran-1,3-thiazole carboxamide has produced pharmacologically and physiologically active drugs with a variety of heterocyclic structural types.

The compounds' structures were verified by the use of mass spectroscopy, FTIR, 1HNMR, and melting point measurements. TC-1, TC-2, TC-3, TC-4, and TC-5 in particular shown promising activity when compared to the reference medication diclofenac sodium. This investigation revealed that the halogenic derivative with para substitution is primarily responsible for the dibenzofuranthiazole carboxami dederivatives' anti-inflammatory effect. One of the main groups that significantly improved the activity with the para substituent was the fluro, chloro, bromo, iodo, and nitro substitution.

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