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SYNTHESIS, SPECTRAL CHARACTERIZATION OF DIBENZOFURAN-1,3-THIAZOLE CARBOXAMIDE DERIVATIVES AND EVALUATED FOR ANTI-INFLAMMATORY POTENTIAL

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Abstract:

Objective: *The objective of the paper is synthesis and characterization of dibenzofuran-1,3-thiazole carboxamide derivatives and screened for anti-inflammatory potential*

Material and methods: *The present work was aimed to synthesis some dibenzofuran-1,3 thiazole carboxamide derivatives by four step reactions with the substitution of various substituted benzylamine under suitable catalyst. The 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) were prepared. The Compound 4 coded as compound TC-1 to TC-14. In this four steps process total 12 compounds have been synthesized and evaluated for the anti-inflammatory potential by protein denaturation assay.*

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, 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). Compound TC-1, mass spectrum has shown peak at m/z = 450.85, which matches the chemical formula $C_{24}H_{16}ClFN_2O_2S$. 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 Cl, Br, I, NO_2 and F substitution enhance the activity when it attached to 4-position of the thiazole ring with addition of electronegative atom also enhance the anti-inflammatory potential of compounds.*

Keywords: *Anti-inflammatory, thiazole, protein denaturation assay, dibenzofuran*

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INTRODUCTION:

The Chemistry of heterocyclic compound is one of the most complex branches of Chemistry. Heterocyclic compounds are widely distributed in the nature and play an important role in regulating biological processes.[1] A large number of heterocyclic compounds are as chemotherapeutic agent, drugs, dyestuffs and copolymers. Among these benzofuran is very interesting class of oxygen containing heterocyclic compounds having wide range of application in medicinal of synthetic chemistry.[2] The benzofuran nucleus ae have considerable importance as pharmaceuticals, insecticides, it occurs in coal tar & are isolated as picrate. It also synthesis via palladium protonated cyclization of O-substituted aryl aryl ether.[3] Many synthetic benzofuran derivatives have interesting properties. These are further used as intermediates for the preparation of herbicides, fungicides & parasiticides.[4] Benzofuran possessing various biological activities, particularly the dibenzofurans are reported to have analgesics, antiviral, anti-inflammatory, cough inhibiting, hypolipidemic and herbicidal properties.[5-7] Some study reported that the synthesis of anticholestatic, benzofuranyl, N-alkyl carbamates and a new synthesis of novel dibenzofuran and two new xanthones from calophyllum panciflorum has been reported.[8]

The greatest reward of the heterocyclic chemistry is to develop new pharmaceutically active and efficient compounds. Each step of the synthesis involves a chemical reaction; more over the reagents and conditions need to be designed to give a good yield and pure compounds. Heterocyclic compounds, by virtue of their specific activity, could be employed in the treatment of infectious diseases.[9] The discovery and development of effective anti-inflammatory agent, has been significant break out in the history of modern medicine. Review of literature indicated that, thiazole and its derivatives found a significant place in the development of pharmacologically important molecules. Keeping in view of these observations, it was planned to synthesize some new bio-active compounds carrying thiazole moiety.[10]

There-fore novel and effective drugs are the immediate need of present days to treatment of infectious disease.[11] Based on the literature reports on the promising analgesic and anti-inflammatory activity exhibited by thiazole system,[12] it has been planned to design and synthesize new molecules with thiazole containing various pharmacophores. The object of the present work involves synthesis characterization and biological studies of new derivatives of dibenzofuran-1,3-thiazole carboxamide**.**

MATERIALS AND METHOD:

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

Chemistry:

The synthesis of the final compound was achieved through four Schemes

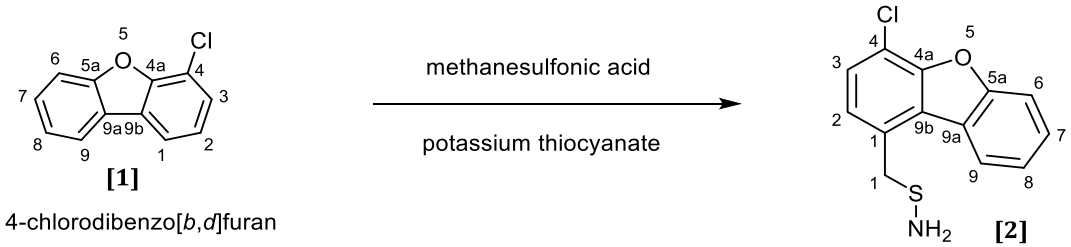
Scheme-I: Synthesis of S-((4-chlorodibenzo[b,d]furan-1-yl)methyl)thiohydroxylamine

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

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

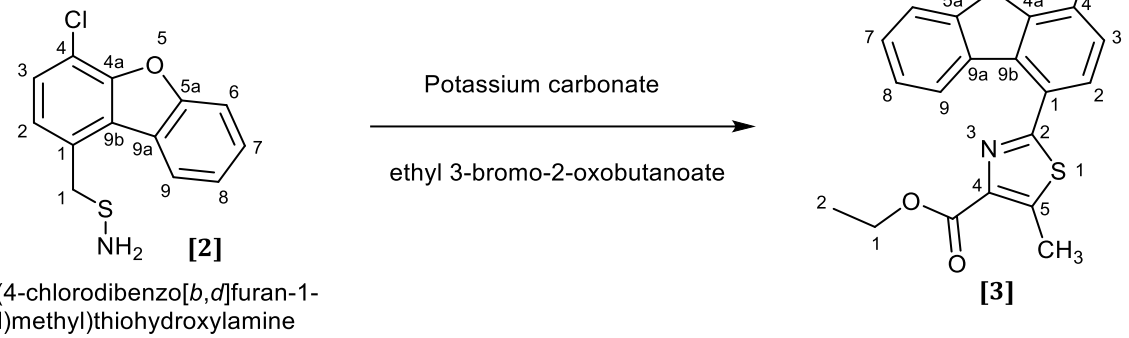


[1] 4-chlorodibenzo[*b*,*d*]furan

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

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 15 min. The reaction mixture was poured into crushed ice, to obtained the solid product (Compound 2),[13]was filtered and then triturated with n-hexane to get a pale brown color solid. Yield-82%; Mass m/z: 263.74

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



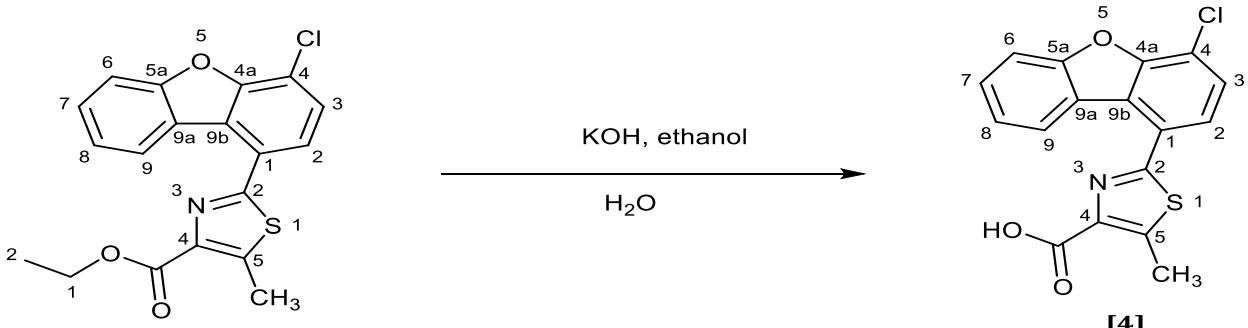
[2]

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

[3]

Procedure: S-((4-chlorodibenzo[b,d]furan-1-yl)methyl)thiohydroxylamine (0.02M) Compound 2, was dissolved in 15 ml 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 [14] (Compound 3), yield – 72.50%; Mass (m/z): 371.84.

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

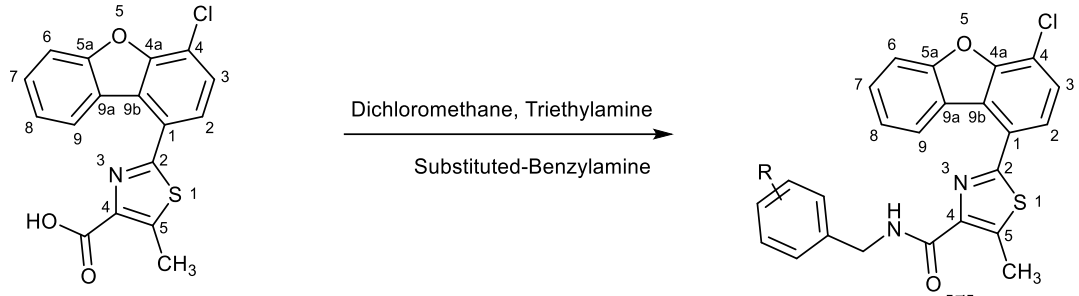


[3]

[4]

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) was added followed by addition of 20 ml distilled water and stirred at room temperature for 2 hrs. Subsequently the reaction mixture was poured into cold water, acidified with 1N HCl (pH 3) and precipitated solid was filtered and triturated with ether followed by n-hexane to give off-white solid[15] (Compound 4); Yield:- 72% Mass (m/z): 343.78

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



[4] **[5]**

Procedure: In a 50 ml 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. To that solution 0.32g (0.002M) TBTU and 0.15 ml (0.002M) Triethylamine was added and stirred for 5 min under nitrogen atmosphere. Then substituted benzyl amine (0.02M) was added and stirred for 3 hrs. under room temperature. The completion of the reaction was monitored by TLC and the reaction mixture was extracted with ethyl acetate. The organic layer was washed with sodium bicarbonate solution, water, brine solution, which was separated and dried over anhydrous sodium sulphate to get solid product (Compound 5).[16]

Pharmacological evaluation:

***In-vitro* anti-inflammatory activity though protein denaturation**

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) were 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.[17] 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.[18]

The absorbance of these solution was determined using UV–visible (UV) spectrophotometer at 660 nm. Percentage of Inhibition of denaturation was calculated from control where no drug was added. Diclofenac sodium was used as standard[19] and treated similarly for determination of absorbance. The percentage inhibition of protein denaturation was calculated using the following formula.

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

AC- absorbance of control; AE- absorbance of extract

RESULT AND DISCUSSION:

Chemistry:

IR, NMR, mass spectral, and elemental studies were used to characterize the target structures of the synthesized compounds. Compound 2, was synthesized by the reaction of 4-chlorodibenzo[b,d]furan (0.02M) Compound 1 with methane sulfonic acid with pale brown color solid having yield-82% and Mass (m/z)- 263.74. Compound 3, was synthesized by the reaction of S-((4-chlorodibenzo[b,d]furan-1-yl)methyl)thiohydroxylamine (0.02M) Compound 2 with potassium carbonate followed by ethyl 3-bromo-2-oxobutanoate (0.02M) to get a peach colored solid (Compound 3), yield – 72.50%; Mass (m/z): 371.84. Compound 4 was synthesized by the reaction of ethyl 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxylate (0.01M), (Compound 3) with aqueous potassium hydroxide solution to get off-white solid (Compound 4); Yield:- 72% and Mass (m/z): 343.78. The final compound (Compound 5) was synthesized by the reaction of 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxylic acid (0.02M), (Compound 4) and substituted benzyl amine get solid product (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, 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). Compound TC-1, mass spectrum have shown peak at m/z = 450.85, which matches the chemical formula $C_{24}H_{16}ClFN_2O_2S$. All the other synthesized compound has also shown the molecular ion peak similar to their molecular formula and weight.

TC-1: 2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-fluorobenzyl)-5-methylthiazole-4-carboxamide
Chemical Formula: $C_{24}H_{16}ClFN_2O_2S$; Molecular Weight: 450.91; 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 (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); 2.90 (3H, CH3); FAB Mass (m/z): 450.85

TC-2: N-(4-chlorobenzyl)-2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxamide
Chemical Formula: $C_{24}H_{16}Cl_2N_2O_2S$; Molecular Weight: 467.36; IR (cm^{-1}): 3412 (N-H); 3470 (C=C-H); 1735 (C=O); 1624–1446 (C=C); 1015 (C-N); 792 (Para substitution); 852 (C-Cl); 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): 467.30

TC-3: N-(4-bromobenzyl)-2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methylthiazole-4-carboxamide
Chemical formula: $C_{24}H_{16}BrClN_2O_2S$; Molecular Weight: 511.82; 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.

TC-4: 2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-iodobenzyl)-5-methylthiazole-4-carboxamide
Chemical formula: $C_{24}H_{16}ClIN_2O_2S$;
Molecular weight: 558.82; IR (cm^{-1}): 3412 (N-H); 3470 (C=C-H); 1735 (C=O); 1624–1446 (C=C); 1015 (C-N); 792 (Para substitution); 855 (C-Cl) 1HNMR (ppm): 2.90 (3H, CH3); 4.56-4.58 (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): 558.80.

TC-5: 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4-nitrobenzyl)thiazole-4-carboxamide
Chemical Formula: $C_{24}H_{16}ClN_3O_4S$; Molecular Weight: 477.92; IR (cm^{-1}): 3412 (N-H); 3470 (C=C-H); 1735 (C=O); 1624–1446 (C=C); 1015 (C-N); 792 (Para substitution); 852 (C-Cl); 1356 (N-O); 1558 (N=O); 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): 477.90.

TC-6: 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4-methylbenzyl)thiazole-4-carboxamide
Chemical Formula: $C_{25}H_{19}ClN_2O_2S$; molecular weight: 446.95; 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, CH3); 4.56-4.58 (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): 447.10

TC-7: 2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-methoxybenzyl)-5-methylthiazole-4-carboxamide
Chemical formula: $C_{25}H_{19}ClN_2O_3S$; Molecular weight: 462.95; IR (cm-1):3412 (N-H); 3470 (C=C-H); 1735 (C=O); 1624–1446 (C=C); 1015 (C-N); 792 (Para substitution); 852 (C-Cl); 1HNMR (ppm): 2.90 (3H, CH3); 4.11 (3H, OCH3); 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

TC-8: 2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-ethoxybenzyl)-5-methylthiazole-4-carboxamide
Chemical formula: $C_{26}H_{21}ClN_2O_3S$; molecular weight: 476.98; 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 (s, 3H, CH3); 4.64 - 4.65 (2H, CH2); 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

TC-9: 2-(4-chlorodibenzo[b,d]furan-1-yl)-N-(4-ethylbenzyl)-5-methylthiazole-4-carboxamide
Chemical formula: $C_{26}H_{21}ClN_2O_2S$; molecular weight: 460.98; IR (cm^{-1}): 3412 (N-H), 3470 (C=C-H); 1735 (C=O); 1624–1446 (C=C); 1015 (C-N); 792

(Para substitution); 852 (C-Cl); 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): 460.90

TC-10: 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4-(trifluoromethyl)benzyl) thiazole -4-carboxamide

Chemical formula: $C_{25}H_{16}ClF_3N_2O_2S$; molecular weight: 500.92; 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, CH3); 4.56-4.58 (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); 7.50-7.52 (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

TC-11: 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4-propylbenzyl) thiazole-4-carboxamide

Chemical formula: $C_{27}H_{23}ClN_2O_2S$; Molecular weight: 475.00; IR (cm-1): 3412 (N-H); 3470 (C=C-H); 1735 (C=O); 1624–1446 (C=C); 1015 (C-N); 792 (Para substitution); 852 (C-Cl); 1HNMR (ppm): 2.90 (3H, CH3); 4.56-4.58 (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): 475.00

TC-12: 2-(4-chlorodibenzo[b,d]furan-1-yl)-5-methyl-N-(4-propoxybenzyl)thiazole-4-carboxamide

Chemical Formula: $C_{27}H_{23}ClN_2O_3S$; Molecular weight: 491.00; 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, 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); 7.50-7.52 (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

***In-vitro* anti-inflammatory activity:**

Protein denaturation:

The anti-inflammatory activity of the synthesized compound (TC-1 to TC-12) were determined by the protein denaturation assay. It was effective in inhibiting heat induced protein denaturation. Diclofenac sodium a standard anti-inflammatory agent possesses maximum percentage of inhibition. The protein denaturation effect of synthesized compounds (TC-1 to TC-12) was represented in Table 1.

Table 1: 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%).

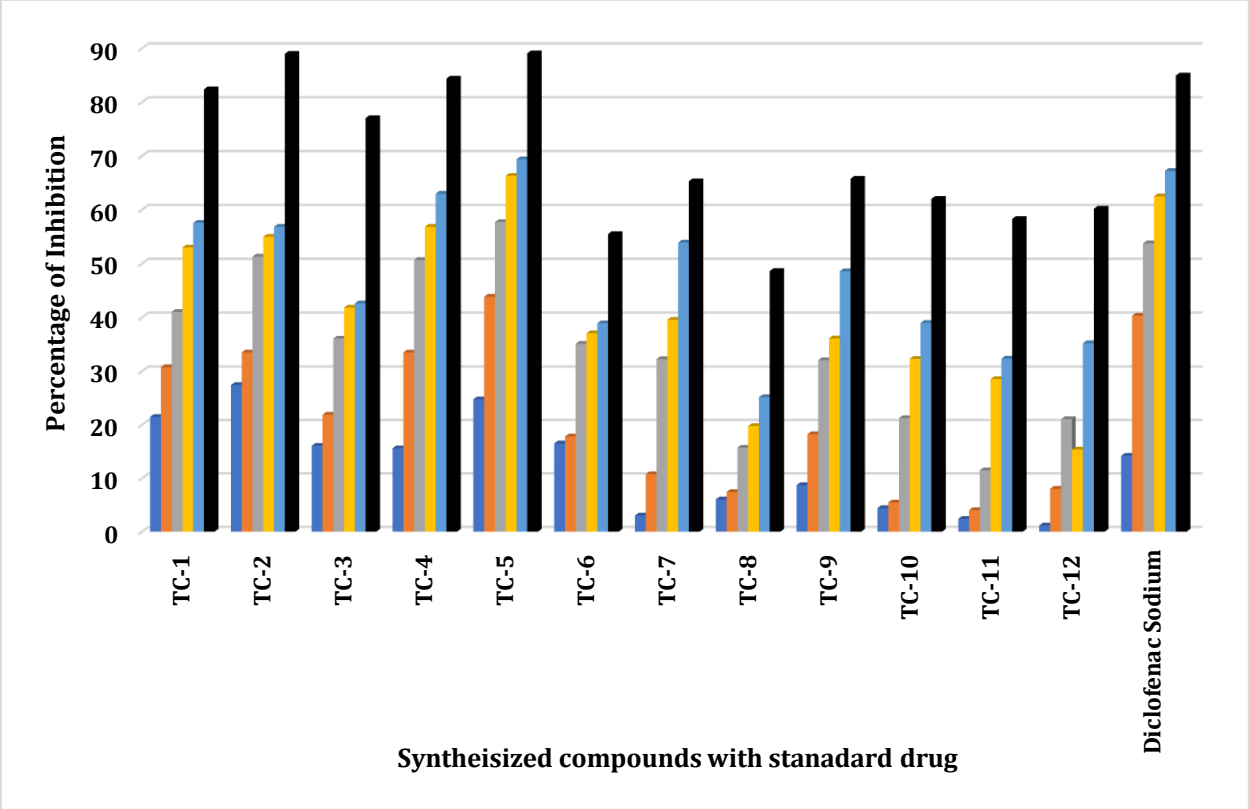


Figure 1: Percentage of inhibition of synthesized compound (TC-1 to TC-12) as compared to diclofenac sodium

The data of protein denaturation assay result stated that compound TC-6, TC-7, TC-8, TC-9 TC-10, TC-11 and 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. Percentage of inhibition of synthesized compound (TC-1 to TC-12) as compared to diclofenac sodium was shown in Figure 1. 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.

SUMMARY AND CONCLUSION:

In present work twelve compounds has been synthesized and It is well established that the presence of dibenzofuran-1,3-thiazole carboxamide derivatives as molecules has resulted in pharmacologically and biologically active agents these are having a varied type of heterocyclic structures. All the structures of the compounds were confirmed by FTIR, 1HNMR and Mass spectroscopy. Among these particularly compounds TC-1, TC-2, TC-3, TC-4 and TC-5 showed promising activity when compared to standard drug diclofenac sodium. This experiment suggested that the anti-inflammatory activity of dibenzofuranthiazole carboxamide derivatives mainly due to the halogenic derivative with para substitution. The fluro, chloro, bromo, iodo and nitro substitution was one of the key groups to enhance greatly the activity with para substituent.

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Conflicts of Interest:
The author declares no conflicts of interest.

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