WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

In-Silico and Synthesis of Furan Sulphanilamide Derivatives as a Potential Anti-Hypertensive Agents.

Pramod. N[1], Chethan. R[1], Gobinda Manna[1], Khushi. M. S[1], Akshatha Hiregoudra[1].

[1]Department of Pharmaceutical Chemistry, Shridevi Institute of Pharmaceutical Sciences,
Sira Road, Tumakuru, Karnataka, India-572106.
Email id: pramodnayanapalli@gmail.com

ABSTRACT:

In pursuit of effective treatments for hypertension, we synthesized 4-[(furan-2-yl methylene) amino] benzaldehyde Derivatives by the reaction between furfural and sulphanilamide followed by characterization using IR, NMR and Mass spectral Techniques. The sulphanilamide derivatives series Denoted by CGKA 1-CGKA6. All the analogues shown good interaction by inhibiting ACE than the standard Captopril. All the derivatives were screened for in-vitro Antihypertensive activity in comparison with the standard drug captopril, the results revealed that the some furan-sulphanilamide derivatives shown potent antihypertensive activity when compared to standard were some compounds shown mild to moderate antihypertensive activity.

Key words: Furan, Sulphanilamide, Docking, Schiff Bases, In-silico studies, Anti-hypertension.

Introduction:

SULPHANILAMIDE.

Para-aminobenzenesulfonamide is the parent chemical of sulfonamides. In the combination SO2NH2, the nitrogen atom is given the number 1, and the NH_2 group is given the number 4. Since the nitrogen atom in $–RSO_2NH_2$ is numbered 1, the $–NH_2$ group is numbered 4. The kind of N1 (sulfonamide N) substitution that determines solubility, efficiency, and pharmacokinetic properties varies between members. For antibacterial action, a loosened amino group at the p-position (N4) is required [1].

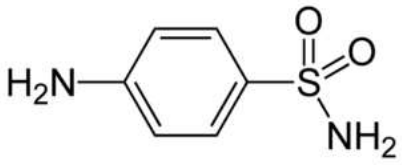


Fig1

In typical temperature and pressure conditions, sulfanilamide is a potent chemical. It is incompatible with potent oxidizing agents and extremely light-sensitive. Sulfanilamide is more soluble in acetone (~200 mg/cm3) and ethanol (~27 mg/cm3) than in water. Because of the strong electron-attractive action of the SO_2 substituent and resonance stabilization of the resultant compound, sulfanilamide is a weak acid (pKa=10.4). Anion Ionization of sulfanilamide is provided in fig2 [2].

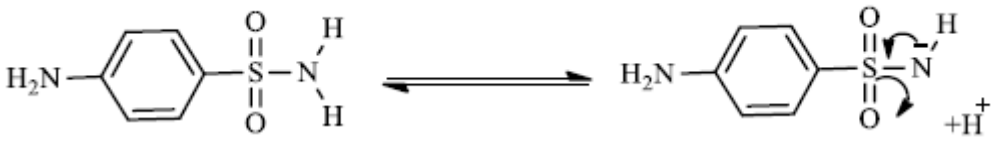


Fig2

Numerous biological activities, including antimicrobial, antihypertensive, anti-HIV, translation initiation inhibitors, anticancer, cyclooxygenase-2 inhibitors, anticonvulsants, ant migraine agents, carbonic anhydrase inhibitors, hypoglycaemic protease inhibitors, antidiabetic agents, and herbicides, have been demonstrated by derivatives of sulfanilamide. Sulpha medication has demonstrated efficaciousness against breast cancer cells. [3]

FURAN-2-CARBALDEHYDE.

FUR ($C_5H_4O_2$, furan-2-carbaldehyde, 2-furaldehyde) is a heteroaromatic compound characterized by a furan ring containing an aldehyde functional group. FUR is primarily used directly as a solvent that is selective. The furan ring's polarity and aromatic nature provide FUR strong solvent selectivity for aromatics and unsaturated molecules in general. Additionally, FUR is somewhat soluble in both highly polar and non-polar substances because to its intermediate polarity. [4]

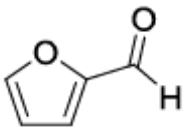


Fig3

Furfural is a heterocyclic aldehyde with oxygen as the heteroatom replacing one of the carbon atoms of the five membered ring. It has a density of 1160 kg/m3 and boils at 161.7°C. [5]

Materials and Methods:

All the chemicals were purchased by Loba Chemie PVT.LTD.Mumbai, Maharashtra 400005. Melting Point was determined using digital melting point

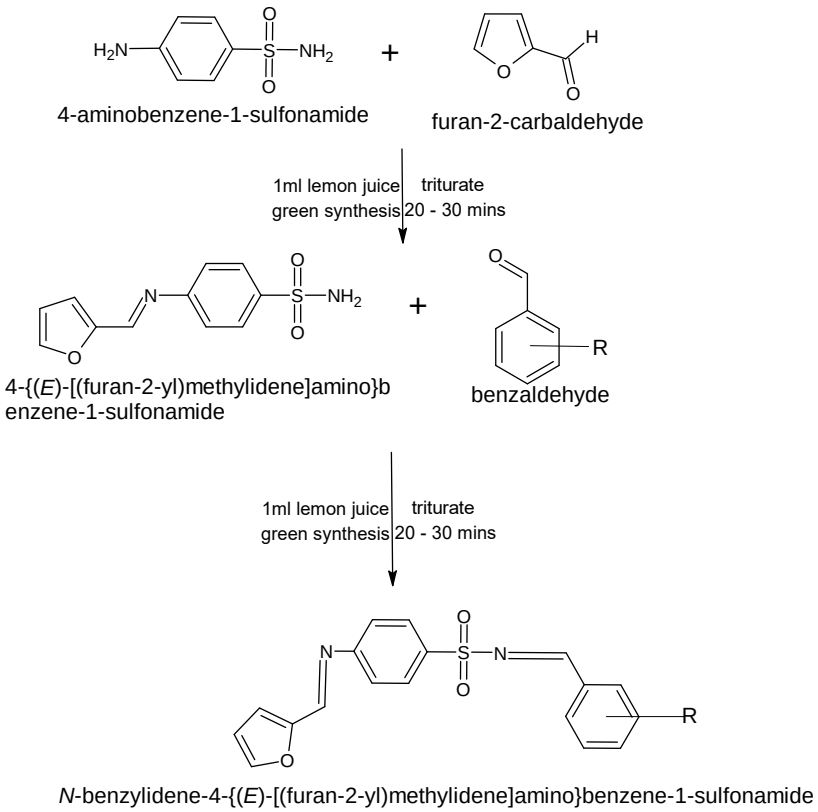
Methods:

Molecular docking Studies:

Molecular docking has emerged as a powerful method for lead optimization and discovery. Over the previous three decades, numerous docking programs based on various search algorithms and scoring functions have been created. A computer software called molecular docking is used to find potential interactions between the target active site and the ligand. Molecular docking experiments were performed on the synthesized compounds to estimate their likely binding mechanisms and interactions with target proteins. Auto dock is the best version of the many docking methods, Chemspider, Chemsketch, Pass online, Discovery studio. [6-7]

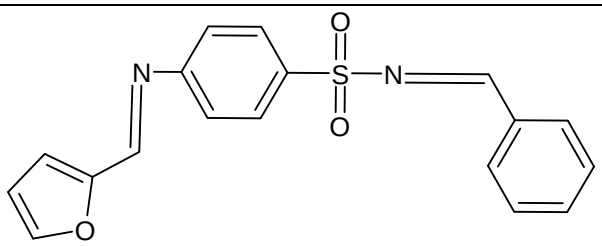
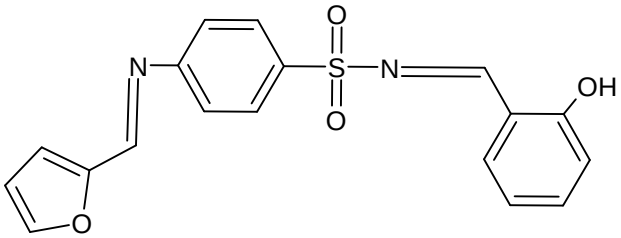
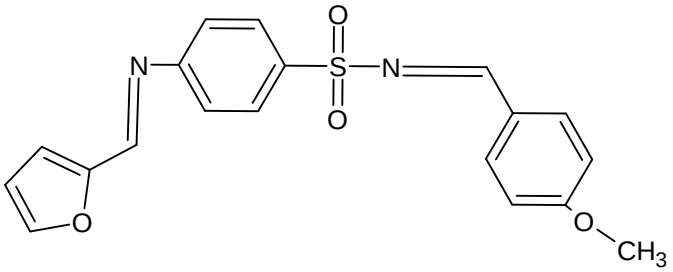
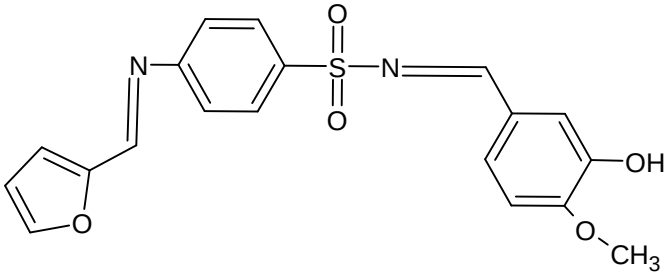
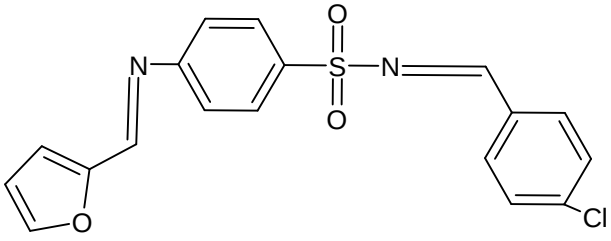
EXPERIMENTAL WORK

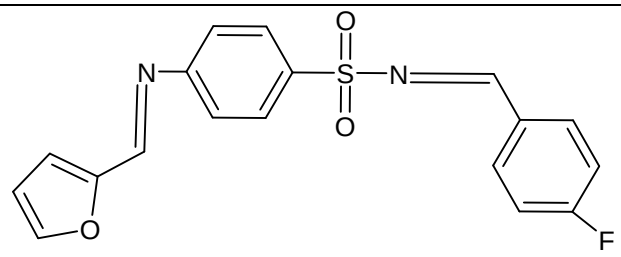
SCHEME



THE 'R' SUBSTITUION:-

SLNO.	C0MPOUND NAME	COMPOUND CODE	R
1	BENZALDEHYDE	CGKA-1	-H
2	SALICYALDEHYDE	CGKA-2	2-OH
3	ANISALDEHYDE	CGKA-3	4-OCH_3
4	VANILINE	CGKA-4	4-OCH_3 3- OH
5	P-CHLORO BENZALDEHYDE	CGKA-5	4-Cl
6	P-FLURO BENZALDEHYDE	CGKA-6	4- F

SL NO	COMPOUND CODE	STRUCTURE
1	CGKA-1	
2	CGKA-2	
3	CGKA-3	
4	CGKA-4	
5	CGKA-5	

6	**CGKA-6**	

METHOD:

General Schiff base synthesis process

Mixture of sulphanilamide (0.02 mol), furfuraldehyde (0.02 mol), lemon juice 1ml and add 25ml 0f water was taken into mortar and pulverized with pestle for 25 minute. Filter the contents after the completion of reaction confirmed by thin layer chromatography. The resultant solid was dried after being filtered apart. Pure products were produced when the solid was recrystallized from Ethanol. [8]

PROCEDURE:

STEP 1: 4-(furan-2-ylmethylene) amino) benzene sulfonamide synthesis.

Transfer to a mortar and pestle after precisely weighing 0.02 moles (1.722g) of sulfanilamide and 0.02 moles (0.960g) of furfuraldehyde. Add 1 ml of lemon juice into the mortar and add about 10 ml of water. After that, triturate this mixture for 20 to 30 minutes. The reaction was monitored by TLC using chloroform for 9:1 ratio and observed under UV light. After filtering, this mixture was thoroughly cleaned with water and allowed to dry.

STEP 2: REACTING WITH ALDEHYDE DERIVATIVES:

The synthesized product is weighed for 0.02 moles (5g) and then mixed with 0.02 moles of substituted aldehyde derivatives, such as anisaldehyde, benzaldehyde, etc., and put into a mortar and pestle. Add 1 ml of lemon juice to the mortar and add about 10 ml of water. Triturate the mixture for 25–30 minutes. The reaction was monitored by TLC using chloroform for 9:1 ratio and observed under UV light. After filtering, this mixture was thoroughly cleaned with water and allowed to dry. Then the dried product derivatives was recrystallized by using ethanol. And allowed to dry.

Biological Activity: IN-VITRO SCREENING

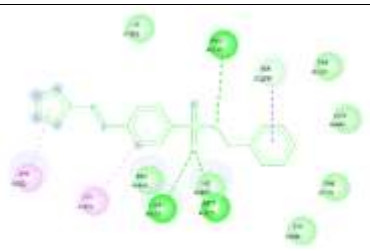
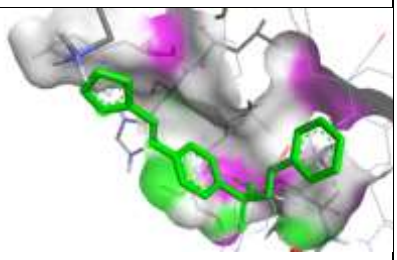
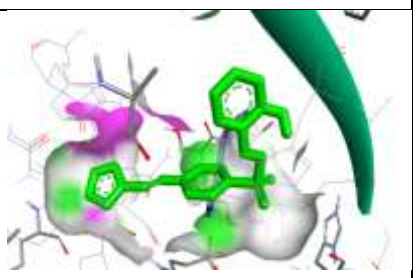
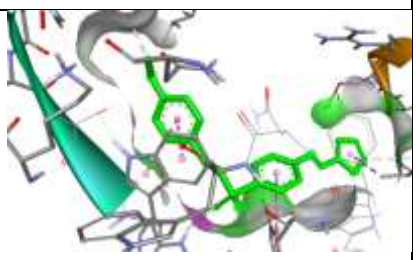
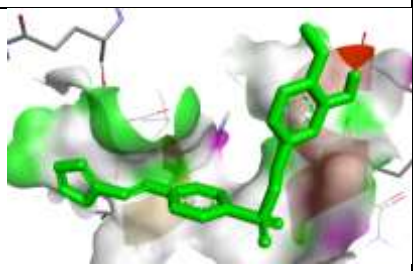
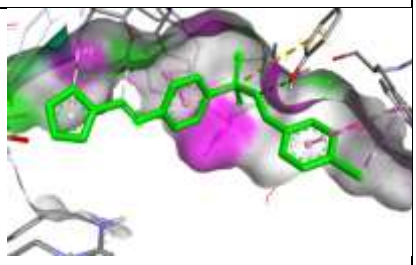
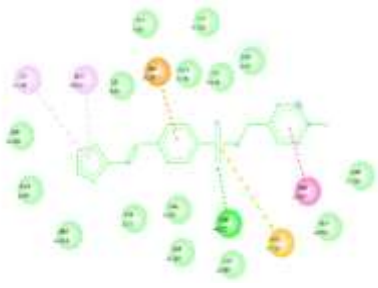
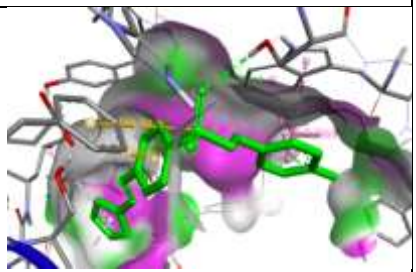
All the targeted compound derivatives on angiotensin-converting enzyme (ACE) were assessed using a six distinct concentrations for each compound.IR, Mass spectroscopy, HNMR and IC50 of synthesized compound was calculated from Activity - [synthesized derivatives] graphs for each compound. The inhibition types and KI values. [9-10]

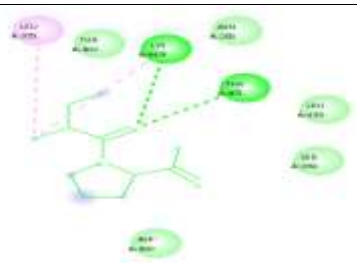
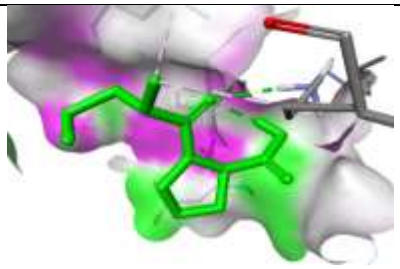
RESULT AND DISCUSSION:

MELTING POINT AND RF VALUE

SI no	COMPOUND CODE	MELTING POINT	RF VALUE
1	CGKA-1	167	0.848
2	CGKA-2	175	0.885
3	CGKA-3	147	0.84
4	CGKA-4	109	0.846
5	CGKA-5	155	0.857
6	CGKA-6	132	0.923

DOCKING STUDIES:

COMPOUND CODE	**BINDIING/ AFFINITY ENERGY**	**2D IMAGE**	**3D IMAGE**
CGKA-1	**-6.92**		
CGKA-2	**-5.81**		
CGKA-3	**-6.1**		
CGKA-4	**-5.72**		
CGKA-5	-7.49		
CGKA-6	-6.35		

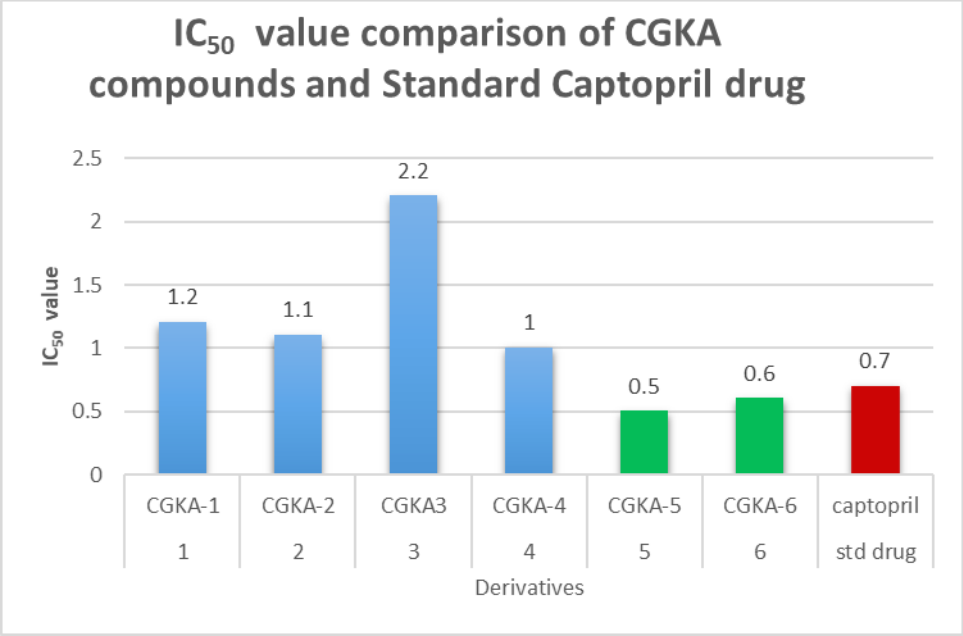
STANDARD DRUG: CAPTOPRIL	-3.34		

In Vitro Antihypertensive Activity of Furan Sulfanilamide Derivatives: ACE Inhibition Assay

Sl.no	Compound code	IC_{50} value
1	**CGKA-1**	**1.2 µM**
2	**CGKA-2**	**1.1 µM**
3	**CGKA-3**	**2.2 µM**
4	**CGKA-4**	**1.0 µM**
5	**CGKA-5**	**0.5 µM**
6	**CGKA-6**	**0.6 µM**
7	**Captopril (standard drug)**	**0.7 µM**

Objective: To assess the ACE inhibitory activity of furan sulfanilamide derivatives and compare it with the standard ACE inhibitor **Captopril**.

GRAPHICAL REPRESENTATION:



DISCUSSION

Six compounds were designed by using computational tools. The designed compounds were docked using Autodock 4.2 version for anti-hypertension activity. From the above results it was revealed that all the derivatives shown less Binding or Affinity energy and good interaction against pdb_00001o8a. When compared to the standard the order of anti-hypertension activity

[CGKA-5>CGKA-1>CGKA-6>CGKA-3>CGKA-2>CGKA-4>Standard Captopril Drug].

Six derivatives were synthesized and characterized by using IR, H^1NMR and Mass spectroscopy. The results are confirmed its structure. All the six derivatives are screened for Anti-Hypertension activity using ACE In-Vitro method of screening. The results revealed that IC_{50} value of compound derivative CGKA-5 and CGKA-6 shows more potent inhibition to ACE and other all the derivatives are close to the standard captopril drug. The in-silico and screening of anti-hypertension were moderately co-relative with each other

Reference:

1. **Sulphonamides Unveiled: A Comprehensive Review of Mechanisms, Applications, and Therapeutic Insights**

Shriyanshi Singh Rana*, Amrita Singh1

2. **Sulfonamides: Synthesis and The Recent Applications in Medicinal Chemistry**

Mohamed S. A. El-Gabya*, Yousry A. Ammarb, Mohamed I.H. El-Qalieia*, Ahmed M. Alia ,

Modather F. Husseina, c, Faraghally A. Faraghallya.

3. **Sulphanilamide: A Privileged Scaffold with Diverse Pharmacological Actions** Gagandeep a, Hardeep Kaura, Monika Gupta*,a and Suman Lataa

4. **Furfural: A renewable and versatile platform molecule for the synthesis of chemicals and fuels**

R. Mariscal,*a* P. Maireles-Torres,b M. Ojeda,*a* I. Sadaba*a* and M. LopezGranados*a*,*

5. **Furfural: A Versatile Derivative of Furan for the Synthesis of Various Useful Chemicals**

Kazeem Adelani Alabi, Rasheed Adewale Adigun,Ibrahim Olasegun Abdulsalami and Mariam Dasola Adeoye.

6. **Synthesis of some Schiff base Derivatives using One pot Grinding Method and Its Biological activities**

Anusuya.V1, Muruganantham.N1*, Anitha.P2 and Mahesh.S3.

7. **Comparison of conventional and green approaches to the synthesis of aromatic Schiff bases**

Beata Kołodziej

8. **Design and synthesis of novel 4-aminophenazone Schiff bases by grinding technique as prospective anti-inflammatory agents**

Rashmi Arora, Rishi Sharma, Abhishek Tageza, Ajmer Singh Grewal, Balraj Saini, Sandeep Arora, Rajwinder Kaur*

9. **Synthesis, Characterization and IN-SILICO Studies of Novel (E)-4-(((3-(substituted phenyl)-1-phenyl-1H-pyrazol-5-yl) methylene) amino) benzene sulfonamide as Diuretic agents**

VISWASKUMAR PANCHAL1*, ZAKIRHUSEN GADHAWALA2, ARUN MALAVIYA3 and SHREEKANT PRAJAPATI4

10. **Synthesis and characterization of Schiff base derivatives and its effect on urinary parameters of Wistar rats: A comparative analysis with different classes of diuretics.**

panelJonathan R.U. Adão [a], Priscila de Souza [a], Thaise Boeing [a], Luísa N.B. Mariano [a], Ana M.F. Brandt [a], Johann V. Hemmer [a], Heitor A.G. Bazani [a], Sergio F. de Andrade [b], Rogério Corrêa [a], Luiz C. Klein-Júnior [a], Rivaldo Niero [a]