

**INSILICO DESIGN, SYNTHESIS AND SCREENING OF NOVEL 1, 3, 4-  
OXADIAZOLE DERIVATIVES FOR Analgesic, Anti-Inflammatory And  
Antimicrobial Activity**

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**ABSTRACT**

1,3,4-oxadiazoles are biologically important group of compounds having activities like analgesic, anti-inflammatory, bactericidal, antifungal, anticonvulsant, psychotropic, plant growth regulating and mono amino oxidase inhibition. In the review of the above fact, we report here with the preparation and biological activities of new series of compounds bearing 1, 3, 4-oxadiazole moiety. Isoniazid is a well known and well acknowledged antimycobacterial agent. In view of the important biological properties of oxadiazole, it was planned to suitably incorporate the oxadiazole ring system into isoniazid moiety to explore the possibilities of some altered biological action and hence the following oxadiazole derivatives were synthesized and screened for their analgesic, anti-inflammatory and antimicrobial activities. The synthesized compounds are characterized by MP, TLC, IR, NMR, MASS, etc and analgesic, anti-inflammatory, and antimicrobial activity were carried out. Almost all the synthesized compound possess good activity as compared to the standard.

**KEY WORDS:** Analgesic; Anti-Inflammatory; Antimicrobial Activity

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**INTRODUCTION**

**In-Silico Studies For Lead Identification**

Structure-Based Drug Design is based on a firm understanding of molecular recognition between active site groups and interacting molecules and is a strategy that has become an integral part of modern drug discovery. For the past ten years, combinatorial chemistry and diversity-based high-throughput screening were the approaches of choice for lead identification while computational methods were employed predominantly in

lead optimization activities. Due to the recent volume and pace at which the 3-D structures of protein targets and their co-crystals have been made available, coupled with advances in computation tools, Structure-Based Drug Design has become a tool for lead generation as well as for optimization. Computational approaches to lead identification and design show many advantages over diversity-based, high-throughput screening, including reduced reagent storage and handling of large libraries, lowering of false positives often

associated with HTS, and the ability to find low-molecular-weight leads even when HTS fails.<sup>24</sup>

Target and lead discovery constitute the main components of today's early pharmaceutical research. The aim of target discovery is the identification and validation of suitable drug targets for therapeutic intervention, whereas lead discovery identifies novel chemical molecules that act on those targets. *In silico* models of biopharmaceutical, pharmacokinetic, and physiological properties related to the absorption, distribution, metabolism, excretion and toxicity (ADMET) have become a valuable tool for reducing the number of experiments that need to be conducted in order to find a drug candidate with less chance of failure during development. Using this software, the medicinal chemist can quickly evaluate the biological effect of structural modifications, and design a selection of analogs with enhanced physicochemical properties.

### **Descriptors of *in-silico* molecular analysis**

*In-silico* approach attempts to identify and quantify the physico-chemical properties of a drug and to see whether any of these properties has an effect on drugs biological activity. The physicochemical parameters of the proposed molecule are carried out using different softwares. Using ACD Labs, ChemsSketch 10.0,<sup>25</sup> we can have different parameters like molar volume molar refractivity, parachor, index or refraction, polarizability, surface tension etc. cLogP value of proposed molecules can be carried out by using Episute Knowitt software.<sup>26</sup> In the present study limited parameters are considered and studied. The parameters like cLogP,

molar volume, surface tension molar refractive index etc were determined. The important molecular descriptors could be determined by using the software Dragon. Drug likeness and violation of the "Lipinski rule of 5" were carried out using Molinspiration software. The various scores obtained by different substituents were studied and evaluated and most suitable compounds were used for synthesis. Synthesized compounds were ascertained for their purity and characterized by using spectral analysis. Prototype molecules from the synthesized compounds were screened for safety and other pharmacological activities.

### **Synthesis of Oxadiazole Analogues**

#### **a) Conventional method**

In the conventional method, the derivatives are prepared by two steps. In the first step, isoniazid is treated with suitable aromatic aldehydes in ethanol to yield corresponding hydrazones. The resulting hydrazones are treated with chloramine-T in presence of ethanol to give 2-aryl-5-pyridyl-1,3,4-oxadiazoles.

#### **b) Microwave (MORE) Synthesis**

Microwave-enhanced synthesis represents a fundamental step forward in the capabilities of synthetic chemistry. It allows organic chemists to work faster, generating higher yields with increased product purity, and to scale experiments up reliably from milligrams to much larger quantities without the need to alter reaction parameters. It offers much more precise control over conditions of temperature and pressure than any previous technology. Ultimately, by eliminating much of the time and effort from the process of performing chemical

reactions, it allows chemists to focus on what is most important—the development of new compounds, or refined methods for generating known products. In a solvent-less reaction all the microwave energy is directly absorbed by the reactant molecules. Under these conditions, the non thermal microwave effect, if any, will be operative at high efficiency.

## PLAN OF WORK

This work aim at the development of newer Isoniazid based oxadiazole ring system .1,3,4-oxadiazole derivatives show a broad spectrum of biological activities, which include analgesic and anti-inflammatory, antimicrobial, anticonvulsant, antifungal, anticancer, antimycobacterial etc. The research envisages in a meaningful exploration of this lead molecule for novel analgesic, anti-inflammatory and antimicrobial activities with minimum toxicity and high potency.

Isoniazid is a well known and well acknowledged antimycobacterial agent. In view of the important biological properties of oxadiazoles, it was planned to suitably incorporate the oxadiazole ring system in to the isoniazid moiety to explore the possibilities of some altered biological actions and hence some newer oxadiazole derivatives were synthesized and screened for their analgesic, anti-inflammatory and antimicrobial activity.

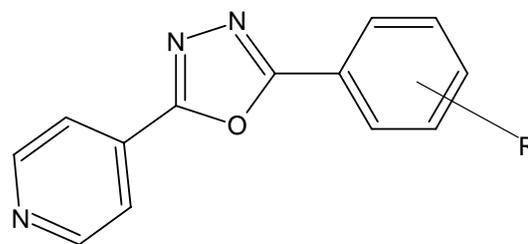
The lead compound was structurally modified by incorporating various substitutions at the second and fifth position of the heterocyclic ring system. From the literature review it is clear that 2,5 disubstituted 1,3,4-oxadiazole and the thiol derivatives of oxadiazole possess

remarkable analgesic, anti-inflammatory and antimicrobial activity.

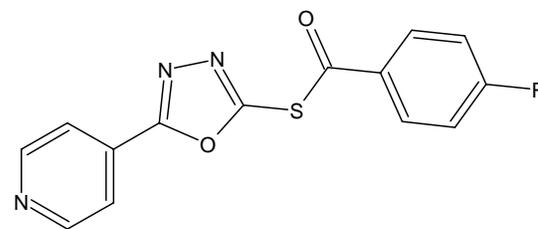
Most of the potent NSAIDs having a ketone group possess good analgesic and anti-inflammatory activities. This leads to design and synthesize some novel agents bearing keto group. The reviews of literature confirm that the thiol derivatives of oxadiazole containing a keto group in its structure show good analgesic activity.

The proposed structures of the lead molecule of novel 2,5 disubstituted 1,3,4-oxadiazole is shown below.

1.



2.



## MATERIALS

### Chemicals

All chemicals and reagents used were of analytical/synthetic grade.

Isonicotinic acid hydrazide (Lupin Ltd), Ethanol (Bengal Chemicals), Chloramine-T (CDH Ltd), Chloramine-T (CDH Ltd),

Carbon disulphide (CDH Ltd), Carbon disulphide, Potassium hydroxide (NICE), Para hydroxy benzaldehyde (CDH Ltd)

**Animals (CPCSEA approval reference no.): 58/IAEC/MCT/07; Dated 9/2007**

Albino mice

Albino rats (male)

### Software used

ALOGPS, Episuite, Molinspiration and Chems sketch

### Purification

#### a) Melting point

Melting points of the compounds were found out in an open capillary tube method by electrically heated melting point apparatus were uncorrected.

#### b) Thin layer chromatography

TLC techniques were adopted to check the reaction and purity of the compound.

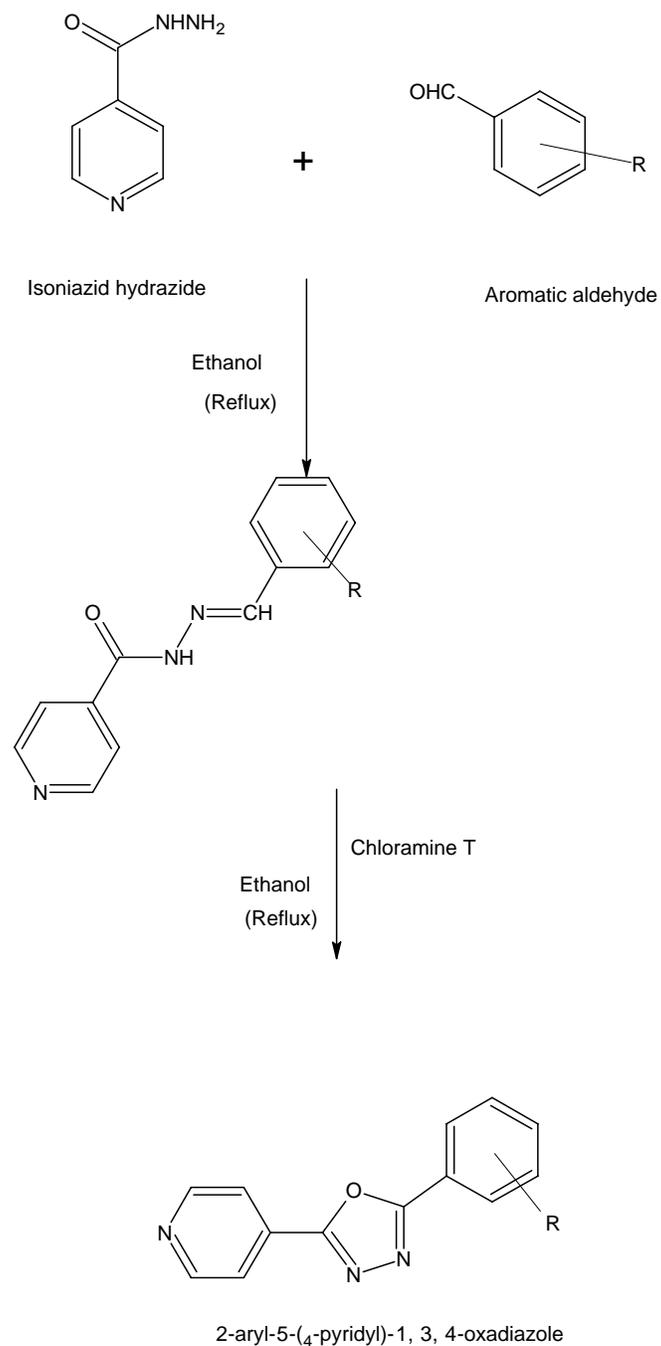
Stationary phase: Silica gelG

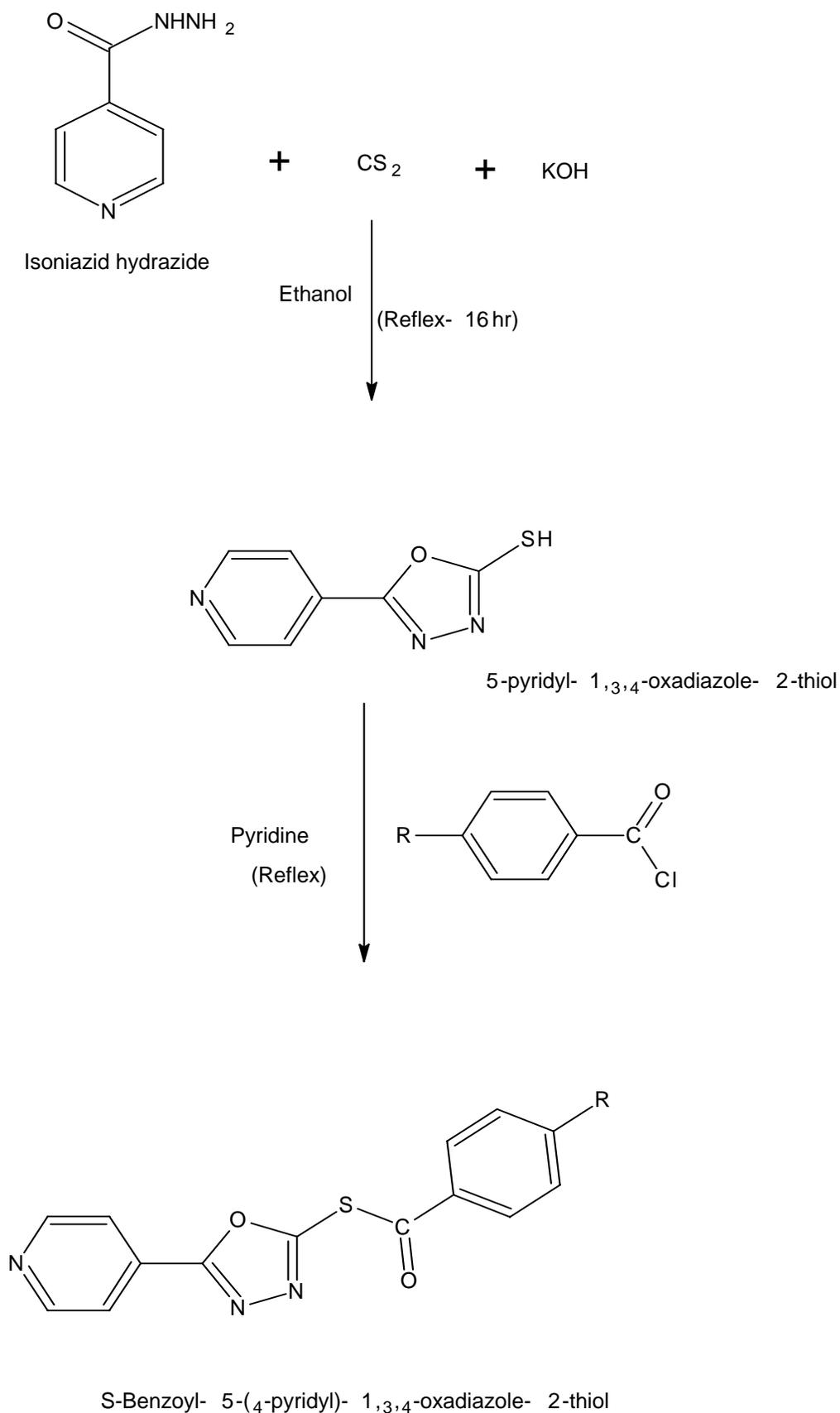
Mobile phase: Different solvent combinations used, are shown in the respective procedures.

Location of spots: Iodine chamber

### SYNTHESIS AND CHEMICAL MODIFICATION

### SCHEME OF WORK





## SYNTHETIC PROCEDURE

### General procedure

#### STEP-1

##### **Synthesis of hydrazones from isoniazid and aromatic aldehyde.**

Isoniazid (0.01 mole, 1.37g) was dissolved in ethanol and to it added an equimolar quantity of selected aromatic aldehyde (0.01 mole,). The solution was refluxed for 4 hours. After completion of the reaction, solvent was removed by evaporation on a water bath. The residue was crystallized from ethanol to give corresponding hydrazones.(1)<sup>96</sup>

#### STEP-2

##### **Synthesis of 2-aryl-5-(4-pyridyl)-1, 3, 4-oxadiazole from 1**

Compound 1 (0.01 mole,) (Hydrazone) was dissolved in ethanol and chloramine-T(0.05 mole) was added to it. The solution was refluxed for 4 hours; sodium chloride which separated out during the course of the reaction was filtered off. Excess ethanol was completely removed from the filtrate by boiling on a water bath, leaving behind a solid mass which was recrystallized from ethanol to give compound 2(oxadiazole).

### Procedure-2

#### STEP-1

##### **Synthesis of 5-pyridyl-1,3,4-oxadiazole-2-thiol from Isoniazid hydrazide by treatment with carbon disulphide and potassium hydroxide.**

Isoniazid (0.01mole, 1.37g) was dissolved in ethanol (50ml) and equimolar quantities of carbon disulphide (3ml) and potassium hydroxide (0.01mole) were

added to this solution. The content was refluxed for 16 hours. The reaction mixture was concentrated, dissolved in water and acidified with HCl. The precipitate was filtered and recrystallized from ethanol.<sup>97</sup>

#### Step-2

##### **Synthesis of S-Benzoyl-5-(4-pyridyl)-1,3,4-oxadiazole-2-thiol**

Compound 1(0.01mole) was dissolved in pyridine (10ml) and equimolar quantity of benzoyl chloride was added to the solution. The reaction mixture was refluxed for 3 hours. The contents were then poured into crushed ice and a solid mass which separated out was filtered and recrystallized from petroleum ether to give TLC pure compound 2.<sup>98</sup>

### **Microwave assisted synthesis of compound 1(Hydrazone)**

#### STEP-1

A mixture of (0.01 mole, 1.37g) Isoniazid, (0.01 mole) aromatic aldehyde and DMF (5 drops) was subjected to microwave irradiation at 300w internally at 30 second intervals for 3 minutes. The reaction mixture was cooled and treated with ice cold water. The resulting solid product was filtered, washed with water and recrystallized from ethanol.<sup>99</sup>

### **Microwave assisted synthesis of compound 2(oxadiazole)**

#### STEP-2

To a solution of compound 1a (0.01 mole) in ethanol (15 ml), chloramine-T (0.01 mole) was added. The reaction mixture was exposed to microwave irradiation at 300W internally at 30 second intervals for 4 minutes. The reaction mixture was

cooled and digested with cold water. The solid thus obtained was filtered, washed with water and recrystallized from methanol to give the product 2.<sup>99</sup>

The purity of the synthesized molecules was ascertained routinely by TLC, and melting points were noted with an open capillary tube method and are uncorrected.

IR spectrum of each analogue showed characteristic peaks for the functional group present in it. The conversion of hydrazide to hydrazone (schiff's base, imine) can be confirmed by the presence of two characteristic peaks.

- (1) An intense peak in the region of  $1630-1575\text{cm}^{-1}$  which is due to C=N stretching in the case of imines.
- (2) NH stretching in imines results in a characteristic peak in the region of  $3500-3300\text{cm}^{-1}$ .

### <sup>1</sup>H NMR spectral analysis

Proton NMR (300 MHz) spectra were recorded in CDCl<sub>3</sub>. Chemical shifts are recorded in parts per million downfield with reference to internal standard Tetra Methyl Silane (TMS) on Burker Avance DPX 300. The total number of proton obtained from NMR spectra was in accordance with that of respective analogues.

NMR spectra of compounds 2c is shown. Cyclisation of hydrazone to oxadiazole could be confirmed by NMR spectrum. Absence of a singlet at 3-5 ppm, which is due to the N-H proton, indicates the conversion of hydrazone, containing N-H, to the oxadiazole.

NMR spectrum revealed the following peaks

- A singlet is obtained at 2.40225 ppm, which indicates the presence of hydroxylic proton (O-H). Normal chemical shift value for the O-H proton is 1-5.5 ppm.
- Two signals are obtained in the region between 7.2-7.7 ppm. These signals indicate the aromatic protons.

Compound	<sup>1</sup> H NMR(CDCl <sub>3</sub> ) δ ppm
2c	<sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm: 2.40(1H, O-H), 7.23-7.78(Ar-H, 8H)

## PHARMACOLOGICAL SCREENING

### Acute toxicity study

A prototype molecule was randomly selected for the study of safety dose range of the analogues. In this study it was found that up to 1600 mg/Kg dose, the compound is safe i.e. there was no mortality or gross behavioral change in animals used.

### Analgesic activity of the selected compounds

Acetic acid induced writhing syndrome method using in albino mice was used for screening peripheral analgesic activity. Five molecules were selected and evaluated for the activity at a dose of about 500mg/Kg. The standard drug aspirin was used at a dose of 40 mg /Kg body weight. The results observed for analgesic activity by acetic acid induced writhing syndrome in albino mice is given in table.

Analgesic activity of the compound 2a, 2c and 2l (750 mg/Kg) exhibit significant

analgesic activity in acetic acid induced writhing method. This indicate that the test compound act peripherally similar to aspirin which as employed in a dose of 40 mg/Kg. The test compound was acting orally shows that better absorption and not degradable in GIT.

### **Antiinflammatory activity of the selected compounds**

Carageenan induced rat paw edema was a valuable test used in predicting the activity of antiinflammatory agents that act by inhibiting the mediators of acute inflammation. Randomly selected molecule, about five in number from the set of synthesized compounds, were evaluated for the activity at a dose of about 500mg/kg body weight. The results observed for antiinflammatory activity by Carrageenan induced rat paw edema is given in table

Test compounds when administered orally produce significant antiinflammatory activity in carageenan induced rat paw edema model at 500mg/kg body weight comparable with that of indomethacin 10mg/kg body weight. The analysis of result shows that the compound 2a ,2c and 2l shows maximum activity .Study of the biological activity shows the title compound are having significant NSAID action similar to that of indomethacin. The rest of the biological screening is supported by the inference we got from study of molecular properties.

### **Antibacterial Activity**

Studies on the antibacterial activity of synthesized compounds 2a & 2c have been carried out against Staphylococcus aureus (G+) and

Escherichia coli (G-). Activity of the newly synthesized compounds in the present investigation was assessed by the cup-plate method. The results of the antibacterial studies are shown in table .The tested compounds showed good activity against the bacteria E. coli, and moderate activity against S. aureus.

### **Antifungal Activity**

The antifungal activity studies of the newly synthesized oxadiazole derivatives (2a and 2c) have been carried out against the fungi Candida albicans by the cup-plate method. The results of the antifungal studies are shown in table. The tested compounds showed good activity against the fungal strain.

## **SUMMARY AND CONCLUSION**

This research work was focused on the rational approach in design and development of 1,3,4 oxadiazole derivatives as novel analgesic, antiinflammatory and antimicrobial drugs.

1,3,4 oxadiazole are biologically an important lead molecule having activities like analgesic, antiinflammatory, bactericidal, antifungal anticonvulsant, psychotropic, plant growth regulating and mono amino oxidase inhibiting activities. Thus it is worthing to explore this lead molecule to develop an ideal NSAID and anti bacterial agent.

The present research work involved the preliminary *in silico* screening of various novel 1,3,4 oxadiazole analogues for quantifying their drug likeness using molinspiration software. The candidates which obeyed Lipinski rule of five were taken for wet lab synthesis. Twelve

different analogues were synthesized by both conventional and microwave methods and comparative study for yield and reaction time was also carried out. Purity of the compounds thus synthesized was ascertained by consistency in melting point and Rf value and characterized by UV, IR 1HNMR and Mass spectral studies.

Among the twelve newly synthesized 1,3,4 oxadiazole analogues only five were screened for analgesic and Anti-inflammatory activity and the compounds 2a,2c and 2l were showed good analgesic and Anti-inflammatory activity. The novel analogues were also screened for antibacterial and antifungal activities. Acute toxicity studies showed that the analogues were safe with low toxicity. So these derivatives may be future leads for

analgesic and anti-inflammatory drug discovery.

#### ACKNOWLEDGEMENT

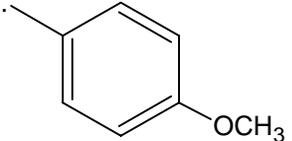
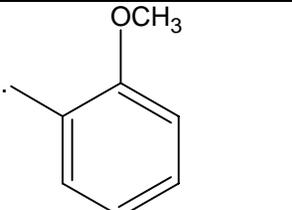
It gives me great pleasure to express my deep sense of gratitude and immense respect to my esteemed guide, **Sri. P.N.Presannakumaran**, Assistant Professor of Pharmaceutical chemistry, College of Pharmaceutical Sciences, Medical College, Thiruvananthapuram, for his zealous guidance, never diminishing encouragement, I am deeply grateful to **Dr Luxmi Varma** of organic section and **Mr.Jineesh** of **Regional Research Laboratory**, Thiruvananthapuram for their active and generous contribution in carrying out NMR and MASS spectral analysis of compounds synthesized.

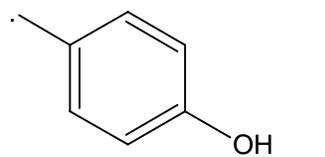
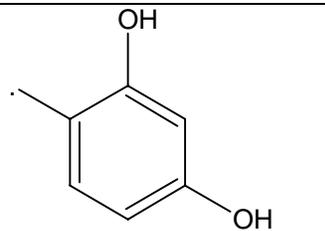
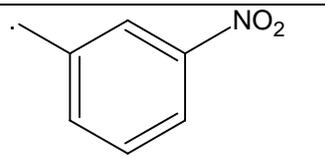
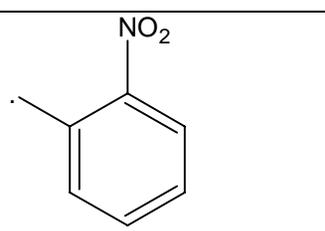
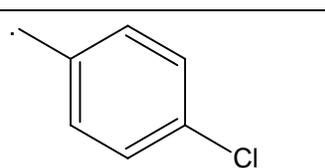
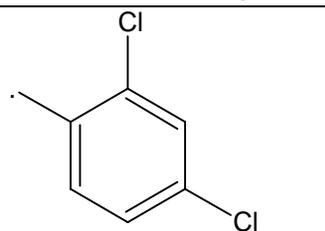
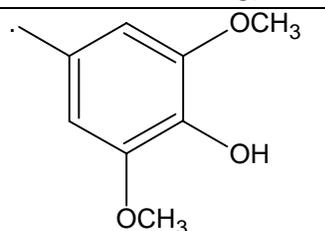
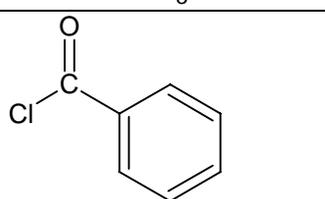
**Table-1** Physicochemical properties of the proposed analogues

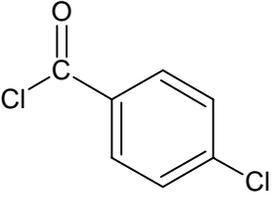
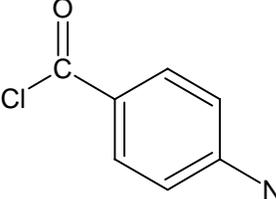
Compound	Molar refractivity cm <sup>3</sup>	Molar volume cm <sup>3</sup>	Parachor cm <sup>3</sup>	Polarizability cm <sup>3</sup>	clogP
2a	68.68 ± 0.3	206.4 ± 3.0	547.0 ± 4.0	27.23 ± 0.5 10 <sup>-24</sup>	2.494
2b	68.68 ± 0.3	206.4 ± 3.0	547.0 ± 4.0	27.23 ± 0.5 10 <sup>-24</sup>	2.446
2c	63.89 ± 0.3	180.8 ± 3.0	505.4 ± 4.0	25.32 ± 0.5 10 <sup>-24</sup>	1.958
2d	65.77 ± 0.3	179.3 ± 3.0	520.4 ± 4.0	26.07 ± 0.5 10 <sup>-24</sup>	1.667
2e	68.55 ± 0.3	194.3 ± 3.0	545.8 ± 4.0	27.17 ± 0.5 10 <sup>-24</sup>	2.372
2f	68.55 ± 0.3	194.3 ± 3.0	545.8 ± 4.0	27.17 ± 0.5 10 <sup>-24</sup>	2.348
2g	66.90 ± 0.3	194.4 ± 3.0	526.2 ± 4.0	26.52 ± 0.5 10 <sup>-24</sup>	3.115
2h	71.80 ± 0.3	206.3 ± 3.0	562.1 ± 4.0	28.46 ± 0.5 10 <sup>-24</sup>	3.721
2i	77.24 ± 0.3	228.9 ± 3.0	618.7 ± 4.0	30.62 ± 0.5 10 <sup>-24</sup>	1.792
2j	74.80 ± 0.4	198.2 ± 5.0	589.0 ± 6.0	29.65 ± 0.5 10 <sup>-24</sup>	2.712
2k	79.63 ± 0.4	209.1 ± 5.0	626.1 ± 6.0	31.56 ± 0.5 10 <sup>-24</sup>	3.39
2l	80.83 ± 0.4	209.5 ± 5.0	646.0 ± 6.0	32.04 ± 0.5 10 <sup>-24</sup>	2.671

**Statistical Analysis:** Data originated by using Chemskech Software

**Table-2** Physicochemical data of newly synthesized compounds

Compound	Substituent	Molecular formula	Molecular weight	mp <sup>0</sup> C	R <sub>f</sub>
2a		C <sub>14</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub>	253.261	163	0.57
2b		C <sub>14</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub>	253.261	165	0.74

2c		$C_{13}H_9N_3O_2$	239.234	159	0.61
2d		$C_{13}H_9N_3O_3$	255.233	160	0.53
2e		$C_{13}H_8N_4O_3$	268.232	160	0.57
2f		$C_{13}H_8N_4O_3$	268.232	168	0.55
2g		$C_{13}H_8ClN_3O$	257.68	163	0.63
2h		$C_{13}H_7Cl_2N_3O$	292.125	163	0.67
2i		$C_{15}H_{13}N_3O_4$	299.286	164	0.52
2j		$C_{14}H_9N_3O_2S$	283.312	110	0.61

<b>2k</b>		$C_{14}H_8ClN_3O_2$ S	317.757	114	0.60
<b>2l</b>		$C_{14}H_8N_4O_4S$	328.309	118	0.52

**Table-3** Characteristic IR peaks of the synthesized compounds

Compound	IR (KBr v $cm^{-1}$ )
<b>2a</b>	3240.79(Methyl C-H stretching),1597.739(C-H bend, alkyl),1326.79(C-N stretching(ring)),1151.29 (Phenolic C-Ostretch),1085.73 (Symmetric C-O-C ring stretch),670.14 (aromatic bend)
<b>2b</b>	3340.79(N-H stretching),1597.739(C-H bend, alkyl),1326.79(C-N stretching(ring)),1151.29(Phenolic C-Ostretch),1085.73(Symmetric C-O-C ring stretch),670.14(aromatic bend)
<b>2c</b>	3322.39(O-H (Phenolic )stretching),1573.63(C=C (aromatic) stretching),1495.53(O-H bending),1325.82(C-N(stretching(ring))),1172.51(asymmetric C-O-C ring stretch)670.14(C-H aromatic bend)
<b>2d</b>	3322.39(O-H (Phenolic )stretching),1573.63(C=C (aromatic) stretching),1495.53(O-H bending),1325.82(C-N(stretching(ring))),1172.51(asymmetric C-O-C ring stretch)670.14(C-H aromatic bend)
<b>2e</b>	3434.6(Aromatic C-H stretch),1529.27 (asymmetric(ArNO <sub>2</sub> )(N=O)stretch),1411.64(C-N stretching (ring)),1299.79 (symmetric(ArNO <sub>2</sub> )(N=O)stretch),1155.15(asymmetric C-O-C ring stretch)814.77(C-N stretch(ArNO <sub>2</sub> ))
<b>2f</b>	3434.60(Aromatic C-H stretch),1303.64 (symmetric(ArNO <sub>2</sub> )(N=O) stretch),1159.01 (asymmetric C-O-C ring stretch)
<b>2g</b>	3019,(C-H str), 1590.02,(C=N imine stretching)1260(C-O str),820(C-H aromatic bending),614.21(C-Cl stretching)
<b>2h</b>	3019,(C-H str), 1590.02,(C=N imine stretching),1260(C-O str),820(C-H aromatic bending),614.21(C-Cl stretching)
<b>2i</b>	3359.39 (O-H stretching), 3261.04 (Methyl C-H stretch), 1495.53 (O-H bending), 1389.46 (Alkyl C-H bend), 1159.01 (Phenolic C-O stretch), 1097.3 (Symmetric C-O-C (ring) stretch).669.17(C-H bend)
<b>2j</b>	2920.2(C-H stretching), 716(C-S str) 1692(C=O str),1610(C=N)1060(C-O str of the ring).1350.89(C-N(stretching(ring))).

<b>2k</b>	3006.1(C-H stretching), 1692(C=O str), 1590.02,(C=N imine stretching),),716(C-S str).
<b>2l</b>	2920.2(C-H stretching),716(C-S str) 1692(C=O str),1610(C=N)1060(C-O str of the ring).1350.89(C-N(stretching(ring)))

**Table-4** Analgesic activity (Acetic acid induced writhing method)

Sl.No	Name of group	Treatment	NO. of writhing in 20 min(Mean + SEM)	Percentage reduction of writhing
1	Vehicle control(1%CMC)	20mg/kg	39.2 ± 0.04	-
2	Aspirin	40mg/kg	16.4 ± 0.08	58.16
3	2a	500mg/kg	13.6 ± 0.74	65.30
4	2c	500mg/kg	12.8 ± 0.48	67.34
5	2e	500mg/kg	19.9 ± 0.74	49.23
6	2g	500mg/kg	19.4 ± 0.87	50.51
7	2l	500mg/kg	16.2 ± 0.73	58.86

**Table-5** Antiinflammatory activity (Carageenan induced rat paw edema method)

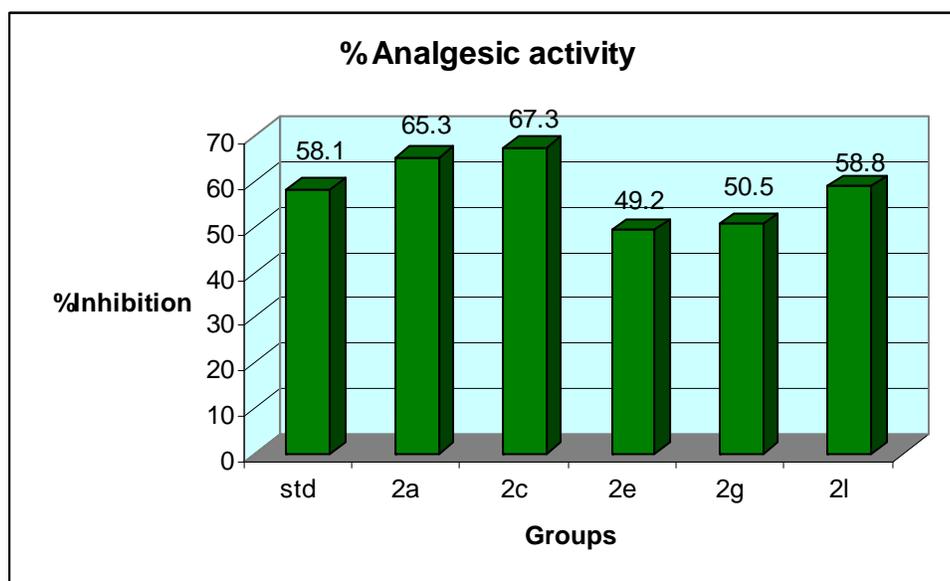
Sl.No	Treatment	Dose(per Kg)	Mean difference in paw thickness=SEM	Percentage inhibition of edema
1	Vehicle control(1%CMC)	20mg/kg	2.23 ± 0.09	-
2	Indomethacin	10mg/kg	0.72 ± 0.08	67.71
3	2a	500mg/kg	0.70 ± 0.03	68.60
4	2c	500mg/kg	0.69 ± 0.04	69.05
5	2e	500mg/kg	0.96 ± 0.03	56.95
6	2g	500mg/kg	0.89 ± 0.02	60.08
7	2l	500mg/kg	0.86 ± 0.04	61.43

**Table-6** Zone of inhibition: Antibacterial activity

Compound	Diameter of zone of inhibition (mm) at 750µg conc:	
	Staphylococcus aureus	Escherichia coli
2a	7	25
2c	9	28
Gentamicin (std)	20	22
Solvent control (DMF)	-	-

**Table -7** Zone of inhibition: Antifungal activity

Compound	Diameter of zone of inhibition (mm) at 750µg conc:
	<i>Candida albicans</i> .
2a	19
2c	18
Fluconazole (std)	22
Solvent control (DMF)	-

**Fig-1**

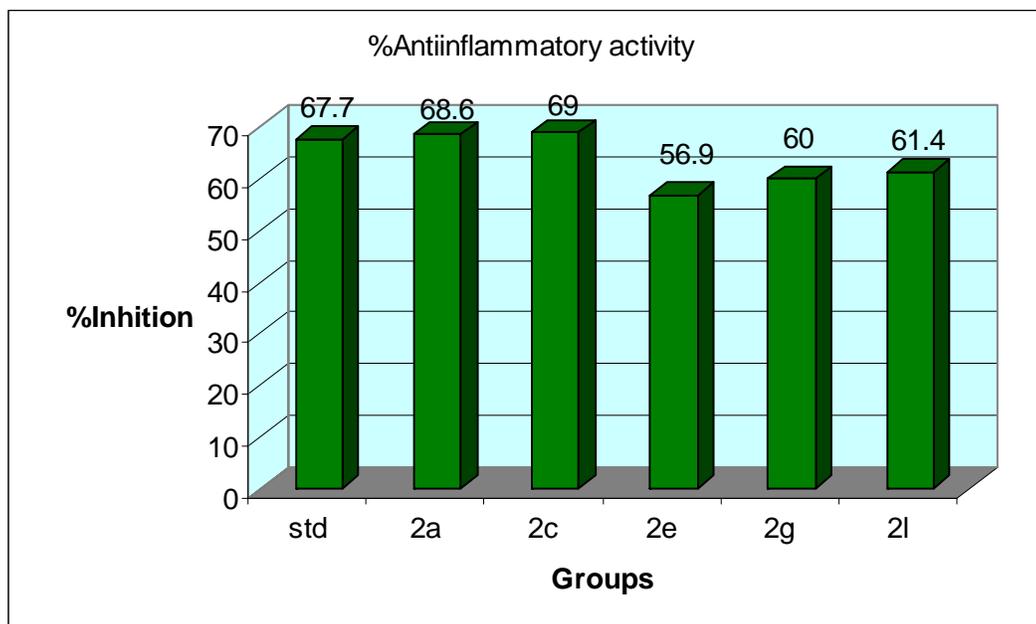


Fig-2