SYNTHESIS AND EVALUATION OF NEWER BENZOTHIAZOLE DERIVATIVES FOR DEVELOPING THE NEW ANALGESIC AND ANTI-INFLAMMATORY AGENTS

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Abstract

This investigation is divided into two parts: synthesis and biological evaluation. The aim was to synthesize benzothiazole 1, 3, 4-oxadiazole derivatives based on their potential anti-inflammatory and analgesic activities. Two series of compounds were prepared: 2-(5-substituted-1, 3, 4-oxadiazole-2-yl)-1, 3-benzothiazole and N-(2, 3-dimethylphenyl)-2-(5-substituted-1, 3, 4-oxadiazole-2-yl) benzenamine. The synthesized compounds were characterized using advanced analytical techniques such as FTIR spectroscopy, hydrogen-1 NMR, and mass spectroscopy. The biological evaluation of the synthesized compounds was performed using Carrageenan-induced acute paw edema in rats and Eddy's hot plate method to assess their anti-inflammatory and analgesic activities, respectively. Screening at the initial level was conducted for each compound, followed by further evaluation using *in-vivo* models. Compound Vt8 from Scheme 1 exhibited equipotent anti-inflammatory efficacy compared to the standard drug Diclofenac sodium. Compound Vt-9 to Vt-14 showed moderate anti-inflammatory efficacy. In analgesic screening, compound Vt11 displayed equipotent activity compared to the standard drug pentazocine. Several other compounds from both series showed excellent or moderate analgesic efficacy. The study concluded that the presence of specific substitutions in the 1, 3, 4-oxadiazole ring led to enhanced anti-inflammatory and analgesic activities. The findings supported the need for further derivatization of the synthesized compounds to explore structure-activity relationships. The research aligns with previous studies on synthetic patterns of 1, 3, 4-oxadiazole analogues and their anti-inflammatory and analgesic properties. The results suggest that more 1, 3, 4-oxadiazole analogues can be synthesized by substituting other positions of benzothiazole/1, 3, 4-oxadiazole to develop potent biological agents. The highly potent compounds identified in this study warrant further investigation for their analgesic and anti-inflammatory potential. Future research should focus on elucidating the molecular mechanisms of 1, 3, 4-oxadiazole analogues and conducting clinical studies to develop new analgesic and anti-inflammatory drugs with reduced side effects.

Keywords: Analgesic, Anti-inflammatory activities, benzothiazole 1, 3, 4-oxadiazole, FTIR spectroscopy, hydrogen-1 NMR, and mass spectroscopy.

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1. Introduction

Anti-inflammatory Efficacy:
Dangerous chemicals or microbiological agents and physical trauma may cause tissue injury resulting in a protective reaction known as inflammation. Acute and chronic inflammation are the two primary divisions of inflammation. An increased in migration of WBCs, capillary infiltration and vascular permeability causes acute inflammation. Angiogenesis (new cells production), fibrosis, neutrophils, monocytes and macrophages were interconnected with chronic inflammation. 1% of the total population of developing countries suffers from a chronic disease named rheumatoid arthritis. In this, the general changes are reddishness, functioning defect, enlargement of cells. Acute inflammation and arthritis form the nitric oxide used as an intermediary of inflammation with a small life span. In the biosynthesis of nitric acid, the enzyme nitric oxide synthase (NOS) play an essential role, and the path of biosynthesis is oxidation through the L-arginine. In this, the terminal N-atom has participated. Nitric Oxide Synthase (NOS) enzyme was present in three isoforms in which two are calcium/calmodulin-dependent, and the third is independent. Both acute and chronic models increase the rate of NOS efficacy, causes increased and paw swelling and developed adjuvant arthritis. Generally, $NSAID_s$ are used. So that in orthopaedic problems, these drugs are used, such as osteoarthritis, fleshy tissue injuries. Acute inflammation consists of three primary and interrelating components: vascular dilatation, endothelial activation, and neutrophil activation.

- Magnification of tissues of blood from relaxed, smooth muscles is called **vascular** dilatation.
- If the plasma proteins enter the tissues, the endothelial permeability, called endothelial activation, is enhanced.
- The appearance of the sticking molecules formed neutrophils to the stuck endothelium layer. This increased mobility formed neutrophil activation.

Mechanism of Inflammation:
Inflammation is a process that involves many pathways, including the production of PG, IL, or another chemical toxin, adhesive protein receptor, and PAFs. All can perform as chemotactic members. Initiation of inflammation founded from membrane strain, from activating hydrolysis and breakage of the phospholipids cell membrane through phospholipase A and then this transfer into arachidonic acid in the presence of COX and LOX (lipooxygenase) enzymes. All the by products of these reactions are LTC4, LTB4 inleukotrienes and prostaglandins in PGE2, PGH2. IL-1, TNF-a and IL-1, TNF types cytokines played a role in inflammatory process development, and these are considered mediators of some biological reactions, called endotoxin. Sometimes inflammation is produced from many cytokines and $GF_{s,}$ including IL-8 and other granulocytes, which formed protein formation with translation. When prostaglandin secretion is elevated in blood cells and increased cell permeability, causing a release of nitric acid, vasodilatation occurs, and chemotoxin is released. Some of the leukotrienes are responsible for the inflammation in which LTB4 is responsible for prior inflammation mentioned as a chemotactic agent. Thus, the increased concentration of leukotrienes causes the neutrophils to adhere, resulting in dilatation of the cell.

Analgesic:
Those type of drugs which act to relieve pain is called pain killer or analgesic. The painkillers used should be

appropriate for tissue damage or surgical trauma if occurred, should take for those situations like postoperative or post-traumatic pain, and should be based on a measurable assessment of their doses of both the ADR reactions effects of pain the effectiveness of the painkiller. The term analgesic is used for those medicines used for pain alleviates and not form any attentiveness. There are different classes of painkillers, which are differed by their chemical structures and mechanism of action. International Association studied defined pain in the form "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". The principles that are used to define pain according to its severity such as soft, modest, harsh. According to duration, these are divided into acute/chronic. Also, based on type is divided into nociceptive, inflammatory, and neuropathic. From the survey, plenty of research enforcing the appreciation of the neurobiology of pain. From this, tenderness of tissues (peripheral nerve wound) would be considered. These conditions formed innocuous stimuli detected as painful (alloying); this is a higher hyperalgesia response (painful stimuli).

Analgesics mechanism of action:

Three main components define the mechanism of analgesia in which; There are three types of pain inhibitory neurons in the spinal cord: those in the spinal cord dorsal horns, those in the midbrain (periaqueductal grey matter), and those in the medulla (nucleus raphe Magnus).

Synthetic Drugs for Analgesic Efficacy:

Various analgesic agents exist in markets, such as COX-2 inhibitors, paracetamol, Ibuprofen, some NSAIDs, etc.

Analgesics Agents Originated from Natural Sources:

Numerous plants found in the natural environment have analgesic properties. Some of them are opioid analgesics; these are extracted from the opium plant mainly the juice obtained from Papaver Somniferous. The mechanism of opioid agents binds with opioid receptors and has shown potent analgesic efficacy in the central nervous system. In this way, these agents relieve the pain, either mild or chronic.

Pain & Pain Management:

Pain is one of the most typical symptoms of numerous diseases. Pain is an extensive protective mechanism threatening the body that something is wrong, and hence one can take measures to diagnose the difficulty. Pain is a very effective procedure of the body's immune mechanisms & it is fast threatening to communicate the order of motor neurons of the CNS to minor physical injury. Its cause can classify pain into somatic, visceral, cutaneous, and neuropathic pains, among others. Pain can be of two types:

Acute Pain:

Acute pain is the body's signal that surrounding soft tissue or illness is causes injury. Aching pain is an example of its sharp and fast pain. The duration of this type of pain is extremely brief, or the cause of acute pain with readily identified reasons.

Chronic Pain:

Chronic pain consists of a longer duration than pain typically occurred upon a specific injury. Chronic pain gradually runs and is stable or intermittent and is usually challenging to treat in comparison to acute pain.

2. MATERIALS AND METHODS:

Chemicals, Reagents, and Solvents:

SD Fine Chemicals, Mumbai, sourced the chemicals used in the synthetic work (o-aminothiophenol, Phosphorous

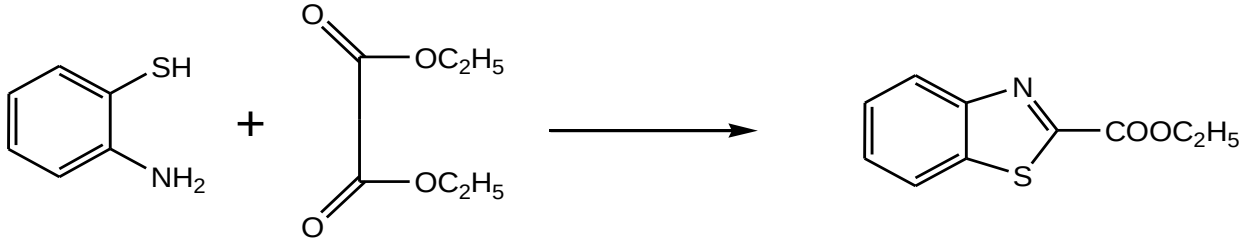
oxychloride, Hydrazine hydrate), Spectrochem, Mumbai (Absolute ethanol), CDH New Delhi (Conc. Hydrochloric acid), SAS Chemicals Co, Mumbai (P-toluic acid, 1-napthelene acetic acid, Gallic acid). Rolex Laboratory, Mumbai (Salicylic acid, p-Anisic acid, Thio salicylic acid, Mefenamic acid). The i*n-vivo* biological efficacy was carried out at the Pharmacology lab of Vivek College of Technical Education, Bijnor.

Methods:

All chemicals were weighed constantly a single pan analytical balance of Donna Pvt. Ltd. All the reagents were of L.R/ A.R. category and were purified and dried before operating in many reactions. The transition temperature of freshly synthesized compounds using open capillary tubes was measured. Fourier transforms infrared (FTIR) spectra have engaged in diffuse reflectance to identify functional groups of newly-synthesized substances using KBr powder utilizing JASCO spectrophotometer V460. Hydrogen-1 NMR spectra are predicted in Deuterated chloroform ($CDCl_3$) and d^6DMSO at δppm on Bruker Ultraspec spectrometer, 400 MHz spectrophotometers. Tetramethyl saline (TMS) was an internal standard for digesting the chemical transformation of various protons on a small scale. Mass spectra (LCMS) using the LCMS-2010-A data summary were also recorded on Shimadzu. Thin-coated glass plates are used to evaluate the responsiveness and purity of synthesized derivatives using thin-layer chromatographies (TLC) utilizing silica-gel G-coated glass plates: hexane (0.5:1.5). The spots were visualized in U.V chamber or display to iodine vapours. The reactions were accomplishing successive reported methods. TLC (Thin layer chromatography) was carried out at unlike time intervals to monitor the reaction. The reaction blend was designed to produce the required/anticipated solid product after recognizing its creation. It was purified/ recrystallized/ crystallized with appropriate solvent for removing any impurities present. It was accomplished that no minor product(s) were obtained during the experiments.

Experimental Work:

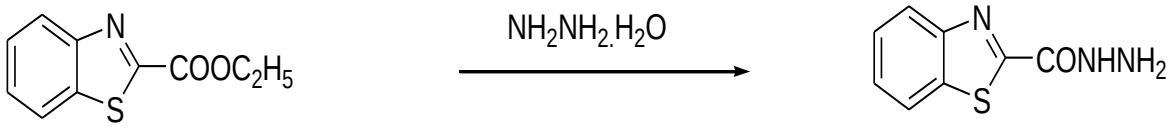
Synthesis of ethyl benzol [d] thiazole-2-carboxylate Rajeev. B et al (2009)



o-Amino thiophenol Diethyl oxalate ethyl benzo[*d*]thiazole-2-carboxylate

Synthesis of benzo[*d*]thiazole-2-carbohydrazide:

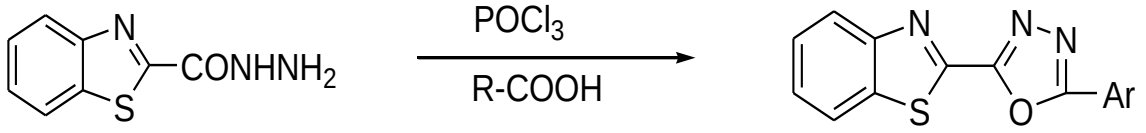
In a 100 ml round-bottomed flask, ethyl-2-benzothiazole carboxylate (0.01mol) was dissolved in 60 mL ethanol, added regularly with stirring, and allowed to dissolve in the ethanol. The Hydrazine monohydrate (0.02 mol) (99 %) was then poured in a regular mode with stirring. After refluxing for eight hours at room temperature, the chemical was collected. Approximately 80% of the solid was obtained after filtering, washing with water, and drying, then recrystallizing with ethanol, with a melting point of 176-178 ^{0}C.



ethyl benzo[*d*]thiazole-2-carboxylate

benzo[*d*]thiazole-2-carbohydrazide

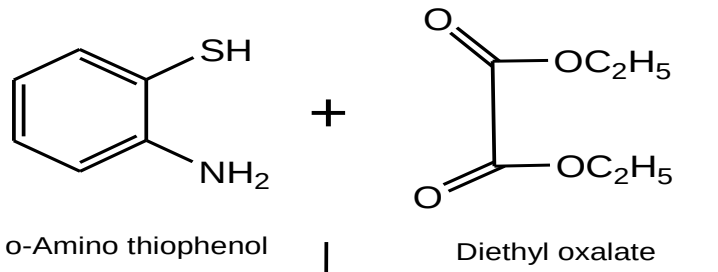
Preparation of 2-(5-substituted-1, 3, 4-oxadiazole-2-yl)-1,3-Benzothiazole from substituted benzo[*d*]thiazole-2-carbohydrazide



benzo[*d*]thiazole-2-carbohydrazide

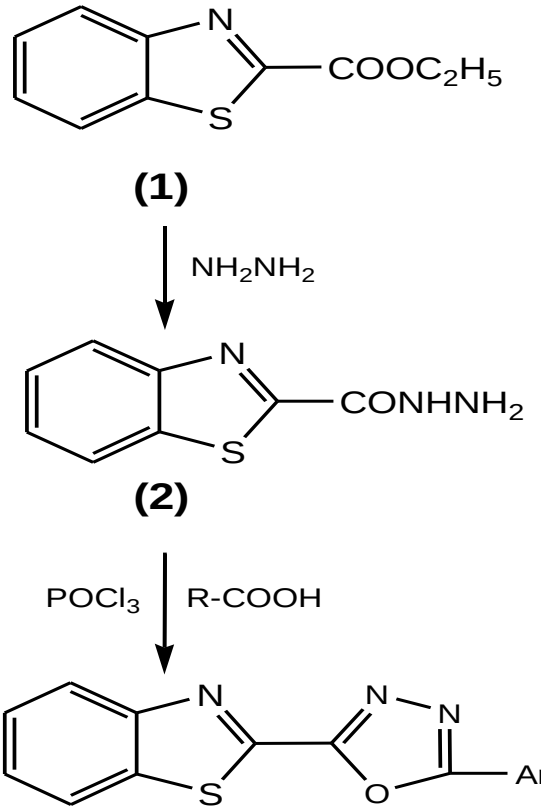
2-(5-methyl-1,3,4-oxadiazol-2-yl)benzo[*d*]thiazole

Where Ar = CH_3, NH_2, OH, NO_2, OCH_3

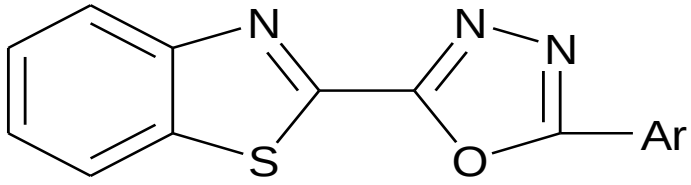


o-Amino thiophenol

Diethyl oxalate

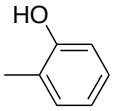


SCHEME 1: General Synthetic Procedure for Title compounds (Vt_1-Vt_{14})



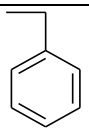
(Vt$_1$-Vt$_{14}$)

Table.1: Physical data of compound Vt$_1$- 2-(5-(benzo [*d*]thiazole-2-yl)-1, 3, 4-oxadiazole-2-yl)phenol

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow fluffy solid	63	$C_{15}H_9N_3O_2S$	0.71	242-244	

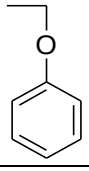
Spectral data:
IR (ν, cm^{-1}): 3100 (OH); 3010 (CH, Ar);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 6.12-7.81 (m, 8H, Ar-H), 9.27(s, 1H, OH)
MS: [M/]$^+$at*m/z* 295

Table.2: Physical data of compound Vt$_2$- 2-(5-benzyl-1, 3, 4-oxadiazole-2-yl) benzo [*d*] thiazole

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow fluffy solid	80	$C_{16}H_{11}N_3OS$	0.68	210-212	

Spectral data:
IR (ν, cm^{-1}): 3061 (CH, Ar); 2873 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.34 (s, 2H, CH_2), 6.04-6.71 (m, 9H, Ar-H)
MS: [M/]$^+$at*m/z* 293

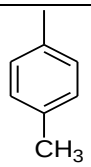
Table.3: Physical data of compound Vt$_3$- 2-(5-(phenoxy methyl)-1, 3, 4-oxadiazole-2-yl) benzo [*d*] thiazole

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Pale yellow fluffy solid	84	$C_{16}H_{11}N_3O_2S$	0.72	168-170	

Spectral data:
IR (ν, cm^{-1}): 3083 (CH, Ar); 2863 (CH, Ali);
^{1}H NMR (δ , ppm/ DMSO-d$_6$): 1.54 (s, 2H, CH_2), 6.08-7.14 (m, 9H, Ar-H)
MS: [M/]$^+$at*m/z* 309

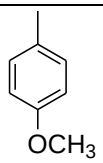
Table.4: Physical data of compound Vt$_4$- 2-(5-*p*-tolyl-1, 3, 4-oxadiazole-2-yl) benzo [*d*]thiazole

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**

Pale yellow fluffy solid	78	$C_{16}H_{11}N_3OS$	0.64	145-147	

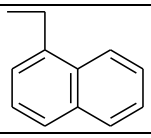
Spectral data:
IR (ν, cm^{-1}): 3087 (CH, Ar); 2863 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.27 (s, 3H, CH_3), 6.18-6.82 (m, 8H, Ar-H)
MS: $[M/]^+$ at*m/z* 293

Table.5: Physical data of compound Vt$_5$- 2-(5-(4-methoxyphenyl)-1, 3, 4-oxadiazole-2-yl) benzo [*d*] thiazole

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow fluffy solid	80	$C_{16}H_{11}N_3O_2S$	0.79	135-137	

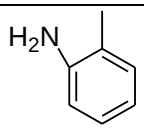
Spectral data:
IR (ν, cm^{-1}): 3053 (CH, Ar); 2871 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.62 (s, 3H, OCH_3), 6.06-6.82 (m, 8H, Ar-H)

Table.6: Physical data of compound Vt$_6$- 4-(5-(benzo [*d*] thiazole-2-yl)-1, 3, 4-oxadiazole-2-yl) benzene-1, 2-diamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Creamy crystalline solid	51	$C_{20}H_{13}N_3OS$	0.66	106-108	

Spectral data:
IR (ν, cm^{-1}): 3052 (CH, Ar); 2872 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.84 (s, 2H, CH_2), 6.13-7.78 (m, 11H, Ar-H)

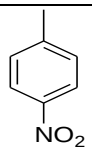
Table.7: Physical data of compound Vt$_7$- 2-(5-(benzo [*b*]thiophen-2-yl)-1, 3, 4-oxadiazol-2-yl) benzenamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Orange fluffy solid	69	$C_{15}H_{10}N_4OS$	0.69	160-162	

Spectral data:
IR (ν, cm^{-1}): 3310 (NH_2); 3310 (CH, Ar);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 6.12-7.23 (m, 8H, Ar-H), 3.93 (s, 2H, -NH_2)
MS: $[M/]^+$ at*m/z* 294

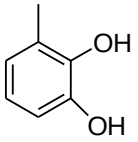
Table.8: Physical data of compound Vt$_8$- 2-(benzo[*b*]thiophen-2-yl)-5-(4-nitrophenyl)-1, 3, 4-oxadiazole

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**

Pale yellow fluffy solid	65	$C_{15}H_8N_4O_3S$	0.72	240-242	

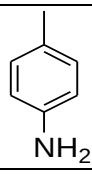
Spectral data:
IR (ν, cm^{-1}): 1315 (NO_2); 3025 (CH, Ar);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 6.23-8.11 (m, 8H, Ar-H)

Table.9: Physical data of compound Vt$_9$- 4-(5-(benzo [b]thiophen-2-yl)-1, 3, 4-oxadiazole-2-yl) benzene-1, 2-diol

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow fluffy solid	74	$C_{15}H_9N_3O_3S$	0.63	170-174	

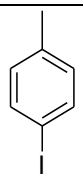
Spectral data:
IR (ν, cm^{-1}): 3210 (OH); 3020 (CH, Ar);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 6.93-7.46 (m, 7H, Ar-H), 9.28(s, 2H, OH)

Table.10: Physical data of compound Vt$_{10}$- 4-(5-(benzo [b]thiophen-2-yl)-1, 3, 4-oxadiazole-2-yl) benzenamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow fluffy solid	71	$C_{15}H_{10}N_4OS$	0.68	210-212	

Spectral data:
IR (ν, cm^{-1}): 3410 (NH_2); 3055 (CH, Ar);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 6.31-7.58 (m, Ar-8H, Ar-H), 3.94(s, 1H, NH_2)
MS: [M/]$^+$at*m/z* 294

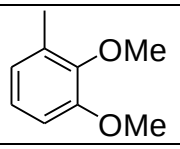
Table 4.11: Physical data of compound Vt$_{11}$- 2-(5-(4-iodophenyl)-1, 3, 4-oxadiazole-2-yl)benzo [*d*] thiazole

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Dark yellow fluffy solid	70	$C_{15}H_8N_3OS$	0.62	180-182	

Spectral data:
IR (ν, cm^{-1}): 1325 (I); 3045 (CH, Ar);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 6.11-7.64 (m, Ar-8H, Ar-H)

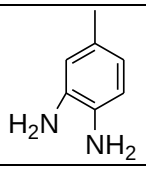
Table.12: Physical data of compound Vt$_{12}$- 2-(5-(4-iodophenyl)-1, 3, 4-oxadiazole-2-yl) benzo[*d*] thiazole

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**

Pale yellow fluffy solid	67	$C_{17}H_{13}N_3O_3S$	0.77	178-180	

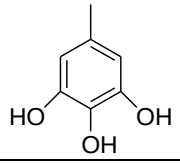
Spectral data:
IR (ν, cm^{-1}): 3110 (CH, Ar); 2850 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.28-2.08 (m, 6H, CH_3), 6.24-7.35 (m, 7H, Ar-H)

Table.13: Physical data of compound Vt$_{13}$- 4-(5-(benzo [*d*]thiazole-2-yl)-1, 3, 4-oxadiazole-2-yl) benzene-1, 2-diamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Creamy fluffy solid	72	$C_{15}H_{11}N_5OS$	0.61	100-104	

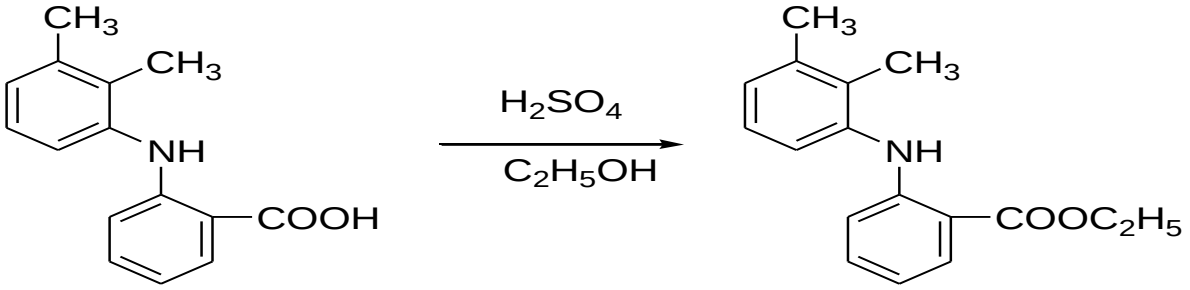
Spectral data:
IR (ν, cm^{-1}): 3490 (NH_2); 3130 (CH, Ar);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 3.84-4.26 (m, 4H, NH_2), 6.81-7.94 (m, 7H, Ar-H)

Table 4.14: Physical data of compound Vt$_{14}$- 5-(5-(benzo [*d*]thiazole-2-yl)-1, 3, 4-oxadiazole-2-yl) benzene-1, 2, 3-triol

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Orange fluffy solid	78	$C_{15}H_9N_3O_4S$	0.75	195-197	

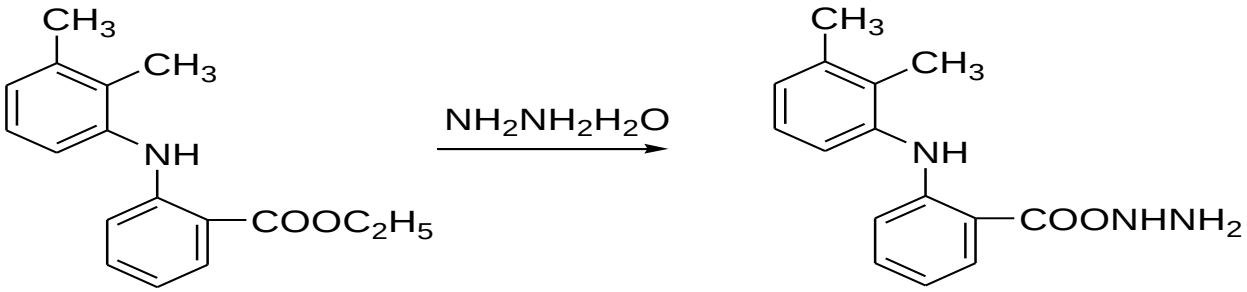
Spectral data:
IR (ν, cm^{-1}): 3213 (OH); 3073 (CH, Ar);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 8.06 (s, 3H, 3×OH), 6.06-6.73 (m, 6H, Ar-H)
MS: [M/]$^+$at*m/z*327

Synthesis of ethyl 2-(2, 3-dimethylphenylamino) benzoate from 2-(2, 3-dimethylphenyl) amino benzoic acid. Somani and Bhanushali (2011):



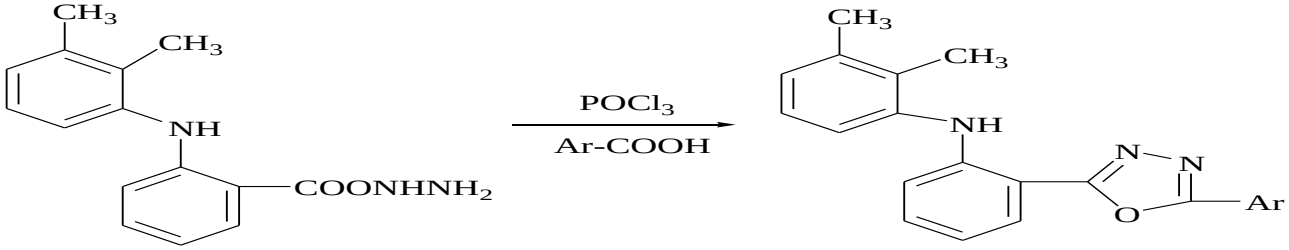
2-(2, 3-dimethylphenylamino) benzoic acid ethyl 2-(2,3-dimethylphenylamino)benzoate

Synthesis of {2-[(2, 3-dimethylphenyl)amino]phenyl}(hydrazinyloxy) methanone from ethyl 2-(2, 3-dimethylphenylamino)benzoate



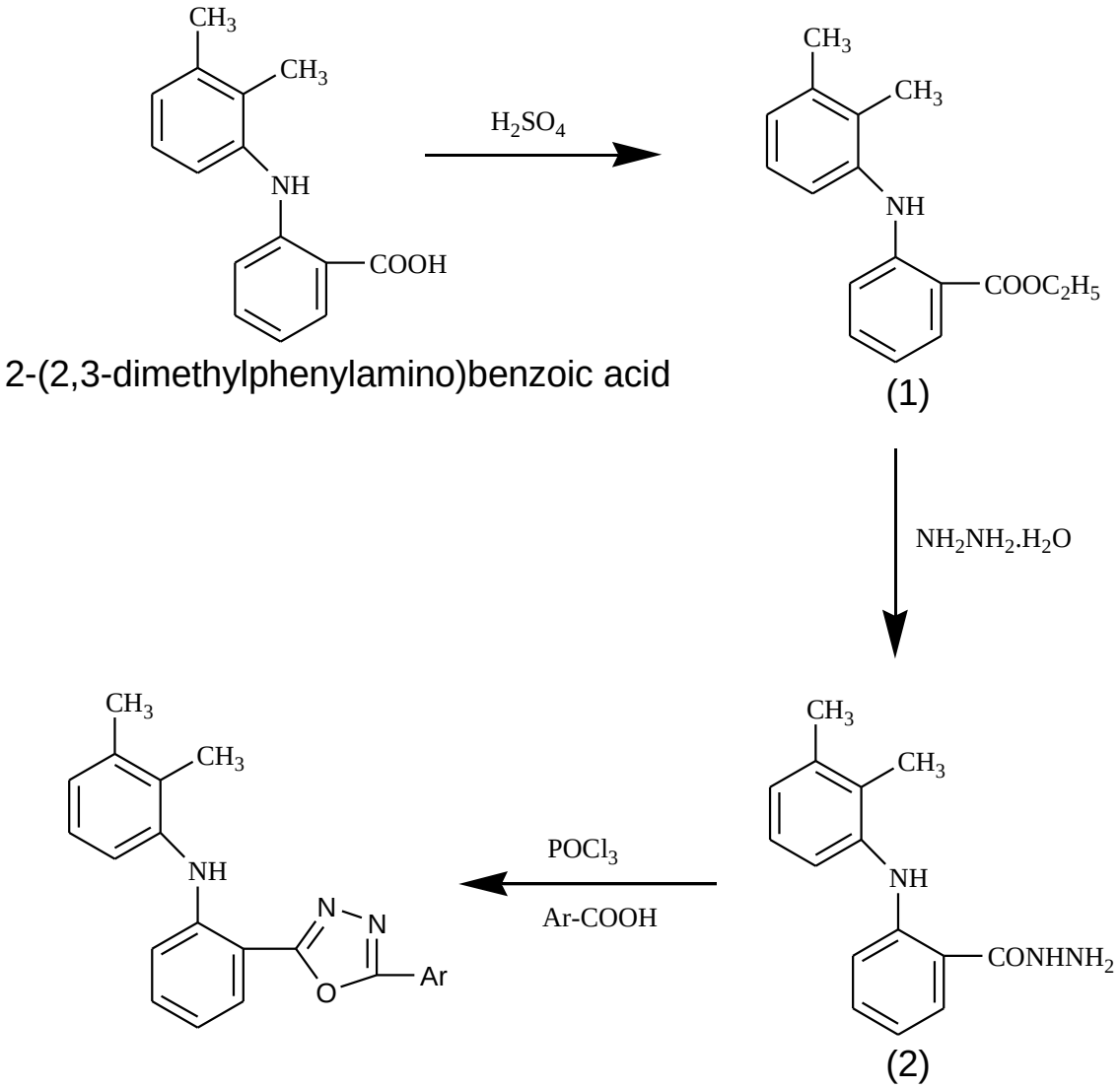
Ethyl 2-(2, 3-dimethylphenylamino) benzoate {2-[(2, 3-dimethylphenyl) amino] phenyl}(hydrazinyloxy) methanone

Synthesis of 5-(2-(2, 3-dimethylphenylamino) phenyl)-2-(aryl)-1, 3, 4-oxadiazole from {2-[(2, 3-dimethylphenyl) amino]phenyl}(hydrazinyloxy) methanone:

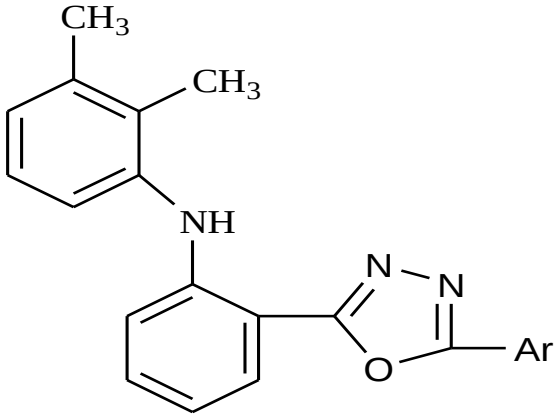


Where,

Ar=CH_3, NH_2, OH, NO_2, OCH_3 5-(2-(2, 3-dimethylphenylamino) phenyl)-2-(aryl)-1, 3, 4-oxadiazole



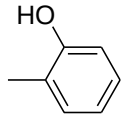
SCHEME I1: Protocol for the synthesis of title compounds (VT_1-VT_{16})



(VT_1-VT_{16})

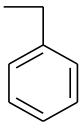
Table 4.15: Physical data of compound VT_1- 2-(5-{2-[(2, 3-dimethylphenyl)amino] phenyl}-1, 3, 4-oxadiazol-2-yl)phenol

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**

Yellow fluffy solid	63	$C_{22}H_{19}N_3O_2$	0.68	242-244	

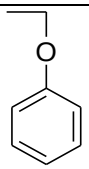
Spectral data:
IR (ν, cm^{-1}): 3119 (NH); 3070 (CH, Ar); 2933 (CH, Ali), 3268 (OH);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.14-1.72 (m, 6H, 2×CH_3), 6.37-7.84 (m, 11H, Ar-H), 9.34 (s, 1H, OH), 9.98 (s, 1H, NH)
MS: [M/]$^+$ at*m/z* 357

Table.16 Physical data of compound VT_2- 2-(5-benzyl-1, 3, 4-oxadiazole-2-yl)-*N*-(2, 3-dimethylphenyl) benzenamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow fluffy solid	54	$C_{23}H_{21}N_3O$	0.70	155-157	

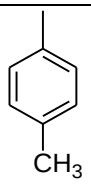
Spectral data:
IR (ν, cm^{-1}): 3316 (NH); 3070 (CH, Ar); 2861 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.22-1.64 (m, 6H, 2×CH_3), 6.34-7.19 (m, 12H, Ar-H), 2.12 (s, 2H, CH_2), 8.04 (s, 1H, NH)
MS: [M/]$^+$at*m/z* 355.

Table.17: Physical data of compound VT_3- N-(2, 3-dimethylphenyl)-2-(5-(phenoxy methyl)-1, 3, 4-oxadiazole-2-yl) benzenamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Pale yellow fluffy solid	57	$C_{23}H_{21}N_3O_2$	0.76	164-166	

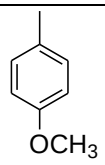
Spectral data:
IR (ν, cm^{-1}): 3324 (NH); 3056 (CH, Ar); 2916 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.14-1.72 (m, 6H, 2×CH_3), 6.14-7.28 (m, 12H, Ar-H), 2.14 (s, 2H, CH_2), 8.14 (s, 1H, NH)
MS: [M/]$^+$at*m/z* 371

Table.18: Physical data of compound VT_4- 2, 3-dimethyl-*N*-{2-[5-(4-methylphenyl)-1, 3, 4-oxadiazol-2-yl] phenyl} aniline

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Pale yellow fluffy solid	78	$C_{23}H_{21}N_3O$	0.69	145-147	

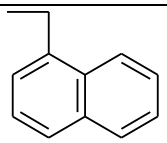
Spectral data:
IR (ν, cm^{-1}):3136 (NH); 3112 (CH, Ar); 2896 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$):1.18-1.90 (m, 9H, 3×CH_3), 6.18-7.89 (m, 11H, Ar-H), 9.96 (s, 1H, NH)

Table.19: Physical data of compound VT_5- *N*-(2, 3-dimethylphenyl)-2-(5-(4-methoxyphenyl)-1, 3, 4-oxadiazole-2-yl) benzenamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow fluffy solid	70	$C_{23}H_{21}N_3O_2$	0.72	135-137	

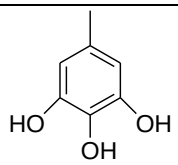
Spectral data:
IR (ν, cm^{-1}): 3338 (NH); 3064 (CH, Ar); 2863 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.28-1.92 (m, 9H, 3×CH_3), 6.06-6.89 (m, 11H, Ar-H), 8.26 (s, 1H, NH)

Table.20: Physical data of compound VT_6- *N*-(2, 3-dimethylphenyl)-2-(5-(naphthalene-1-ylmethyl)-1, 3, 4-oxadiazole-2-yl) benzenamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Creamy crystalline solid	66	$C_{27}H_{23}N_3O$	0.74	180-182	

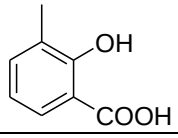
Spectral data:
IR (ν, cm^{-1}): 3326 (NH); 3063 (CH, Ar); 2861 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.37-1.82 (m, 6H, 2×CH_3), 6.12-7.68 (m, 16H, Ar-H), 8.52 (s, 1H, NH).

Table.21: Physical data of compound VT_7- 5-(5-(2-(2, 3-dimethylphenylamino) phenyl)-1, 3, 4-oxadiazole-2-yl) benzene-1, 2, 3-triol

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Orange fluffy solid	42	$C_{22}H_{19}N_3O_4$	0.76	190-192	

Spectral data:
IR (ν, cm^{-1}): 3346 (NH); 3074 (CH, Ar); 2863 (CH, Ali); 3329 (OH);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.31-1.78 (m, 6H, 2×CH_3), 6.12-7.32 (m, 9H, Ar-H), 8.86 (s, 3H, 3×OH), 8.21 (s, 1H, NH)

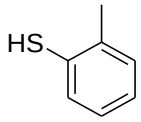
Table.22: Physical data of compound VT_8- 3-(5-(2-(2, 3-dimethylaminophenyl)-1, 3, 4-oxadiazole-2-yl)-2) hydroxyl benzoic acid

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow fluffy solid	46	$C_{23}H_{19}N_3O_4$	0.79	188-190	

Spectral data:
IR (ν, cm^{-1}): 3363 (NH); 3073 (CH, Ar); 2864 (CH, Ali); 3321 (OH);

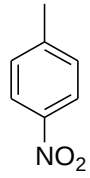
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.08-1.72 (m, 6H, 2×CH_3), 6.09-6.92 (m, 10H, Ar-H), 9.24 (s, 2H, OH), 8.09 (s, 1H, NH)

Table.23: Physical data of compound VT_9- 2-(5-(2-(2, 3-dimethylphenylamino) phenyl)-1, 3, 4-oxadiazole-2-yl) benzenethiol

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow fluffy solid	80	$C_{22}H_{19}N_3OS$	0.67	225-227	

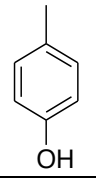
Spectral data:
IR (ν, cm^{-1}): 3368 (NH); 3057 (CH, Ar); 2869 (CH, Ali); 1324 (SH);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.28-2.11 (m, 6H, 2×CH_3), 6.14-7.32 (m, 11H, Ar-H), 9.04 (s, 1H, SH), 8.22 (s, 1H, NH)

Table.24: Physical data of compound VT_{10}- N-(2, 3-dimethylphenyl)-2-(5-(4-nitrophenyl)-1, 3, 4-oxadiazole-2-yl) benzenamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Pale yellow fluffy solid	63	$C_{22}H_{18}N_4O_3$	0.64	156-158	

Spectral data:
IR (ν, cm^{-1}): 3328 (NH); 3119 (CH, Ar); 2918 (CH, Ali); 1321 (NO_2);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.12-2.18 (m, 6H, 2×CH_3), 6.14-7.39 (m, 11H, Ar-H), 8.29 (s, 1H, NH)
MS: [M/]$^+$at*m/z* 386

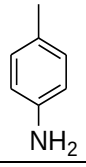
Table.25 Physical data of compound VT_{11}- 4-(5-(2-(2, 3-dimethylphenylamino)phenyl)-1, 3, 4-oxadiazole-2-yl) phenol

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Grey crystalline solid	51	$C_{22}H_{19}N_3O_2$	0.73	136-138	

Spectral data:
IR (ν, cm^{-1}): 3319 (NH); 3074 (CH, Ar); 2928 (CH, Ali), 3158 (OH);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.04-1.62 (m, 6H, 2×CH_3), 6.28-7.91 (m, 11H, Ar-H), 9.14 (s, 1H, OH), 8.04 (s, 1H, NH)
MS: [M/]$^+$ at*m/z* 357

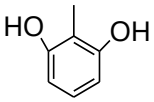
Table 4.26 Physical data of compound VT_{12}- 2-(5-(4-aminophenyl)-1, 3, 4-oxadiazole-2-yl)-N-(2, 3-dimethylphenyl) benzenamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**

Pale yellow fluffy solid	68	$C_{22}H_{20}N_4O$	0.63	140-142	

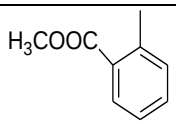
Spectral data:
IR (ν, cm^{-1}): 3416 (NH); 3129 (CH, Ar); 2928 (CH, Ali); 3230 (NH_2);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.31-1.72 (m, 6H, 2×CH_3), 6.04-7.12 (m, 11H, Ar-H), 4.34 (s, 2H, NH_2), 8.14 (s, 1H, NH)
MS: [M/]$^+$a*t m/z* 356.

Table 4.27Physical data of compound VT_{13}- 2-(5-(2-(2, 3-dimethylphenylamino) phenyl)-1, 3, 4-oxadiazole-2-yl)benzene-1,3-diol

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Pale Yellow fluffy solid	76	$C_{22}H_{19}N_3O_3$	0.69	165-167	

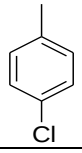
Spectral data:
IR (ν, cm^{-1}): 3383 (NH); 3136 (CH, Ar); 2864 (CH, Ali); 3227 (OH);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.19-2.04 (m, 6H, 2×CH_3), 6.30-7.22 (m, 10H, Ar-H), 8.76 (s, 2H, 2×OH), 8.12 (s, 1H, NH)

Table.28: Physical data of compound VT_{14}- methyl 2-(5-(2-(2, 3-dimethylphenylamino) phenyl)-1, 3, 4-oxadiazole-2-yl)benzoate

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow fluffy solid	78	$C_{24}H_{21}N_3O_3$	0.76	185-187	

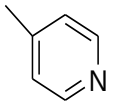
Spectral data:
IR (ν, cm^{-1}): 3373 (NH); 3086 (CH, Ar); 2834 (CH, Ali);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.12-2.04 (m, 9H, 3×CH_3), 6.11-7.08 (m, 11H, Ar-H), 8.10 (s, 1H, NH)

Table.29: Physical data of compound VT_{15}- 2-(5-(4-chlorophenyl)-1, 3, 4-oxadiazole-2-yl)-*N*-(2, 3-dimethylphenyl)benzenamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Dark yellow solid	80	$C_{22}H_{18}ClN_3O$	0.69	144-146	

Spectral data:
IR (ν, cm^{-1}): 3332 (NH); 3136 (CH, Ar); 2873 (CH, Ali); 624 (Cl);
^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.49-1.64 (m, 6H, 2×CH_3), 6.21-6.94 (m, 11H, Ar-H), 8.23 (s, 1H, NH)
MS: [M/]$^+$a*t m/z* 375

Table.30: Physical data of compound VT_{16}- N-(2, 3-dimethylphenyl)-2-(5-(pyridine-4-yl)-1, 3, 4-oxadiazole-2-yl) benzenamine

Physical characteristics	**Yield %**	**Molecular formula**	**Rf value**	**M.P. (^{0}C)**	**Ar**
Yellow amorphous solid	62	$C_{21}H_{18}N_4O$	0.79	115-117	

Spectral data:

IR (ν, cm^{-1}): 3258 (NH); 3072 (CH, Ar); 2856 (CH, Ali);

^{1}H NMR (δ, ppm/ DMSO-d$_6$): 1.04-1.83 (m, 6H, 2×CH_3), 6.23-7.74 (m, 11H, Ar-H), 9.37 (s, 1H, NH)

Biological Evaluations:

General:

It is now well established that only clinical trials performed before drug approval are insufficient for a complete modern pharmacological evaluation of drugs and treatments. The need for both pharmacovigilance and pharmacoepidemiology is underlined in order to evaluate drugs under natural conditions.

An examination of the pharmacological activity of synthesized compounds involves testing their analgesic and anti-inflammatory effects in different animal models in order to evaluate potency and effectiveness. Anti-inflammatory drugs may act as interrupting among any distinct mechanism, along with immunological mechanism serving as antibody origination and antigen-antibody complexation activation of complement, cellular actions like phagocytosis, obstruction with the development and discharge of the inflammatory chemical mediators.

The suitable test for rats is carrageenan-induced acute paw edema. Based on this method, the inflammatory reaction is easily originated in rats in paw edema due to irritants that produce acute paw edema. The acute paw edema indicates the percentage of anti-inflammatory efficacy in terms of paw volume of standard and test compounds.

It has been demonstrated that the 1, 3, 4-oxadiazole ring exhibits anti-inflammatory properties when combined with benzothiazole and oxadiazole moiety [Singh etal (2013); Nargund et al (1994); Raman**].**

The anti-inflammatory effect of the synthesized chemicals was evaluated and confirmed to be effective. To determine their effectiveness in reducing edema caused by carrageenan in humans, all synthesized compounds were tested. Analgesic efficacy is performed i*n-vivo* to evaluate pain stimulation by measuring licking or jumping as response latency in terms of the reaction of mice to a painful stimulus. There are three well-known methods to perform the efficacy.

(1) Morphine induced hot plate method.

(2) Morphine induced tail-flick method.

(3) Carrageenan-induced acute paw edema in rats.

The International Association considers pain as "unpleasant sensory and emotional experiences connected with or characterized in terms of actual or potential tissue harm." Symbolic pain may be elaborated in various ways, depending on their indication, such as diminishing or rising mode and their inflammatory effects. According to an extensive literature survey, oxadiazole moiety 1, 3, 4 oxadiazole rings offers analgesic efficacy Dewangan et al (2016); Kumar et al (2015); Biju et al (2012).

In-vivo, analgesics were further screened in order that some powerful analgesic medicines were offered to the society by leading compounds that have shown low anti-inflammatory action in conventional drug testing.

Calculation Method of Acute Toxicity (LD_{50}):
The acute toxicity of the synthesized compounds is calculated by male or female albino mice (male or female). The mass of the mice should be 20-30 gm and placed these mice in standard conditions. For experimental animals should be fasted before one night of the experiment as mentioned above, and the planned dose according to OECD guideline No. 420 process of CPCSEA was approved to examine its toxicity.

Anti-inflammatory Efficacy:
The term inflammation refers to the inflammatory response that occurs in the body after an injury is caused by chemical toxins, physical trauma, or micro-organisms Thangam C and Dhananjayan R (2003).
Inflammation is bringing by releasing the chemical mediators from migrating cells and damaged tissue. Chemical mediators alter inflammatory actions and activate amines like serotonin, lipids, for example, prostaglandins and limited peptides and histamine Kinins Cotran RSet al (2001)**.**
The acute inflammatory reaction has three primary objectives.
1. The concerned field is engaged through acute inflammatory exudates. The discharges carry cells, proteins, and fluid to the damaged area so that it can mediate local protection.
2. Some time bacteria played the role of infective agent present in damaged areas and may be migrated from exudates components.
3. The tissue that has been damaged may be affected and liquefied somewhat, and the debris may be removed.

Mechanism and working of inflammation:
Inflammation contributors mostly in host defences versus infectious representatives and injury, but it again furnished the pathophysiology for their different types of chronic diseases. Different conditions of chronic and acute inflammation that helps in controlling diseases of different organs are the inborn immune system, inflammatory mediators orchestrate, and communication of cells present in the adaptive immune system. The organized set of different systems helps in controlling of disease of different organs. These systems are the inborn immune system, inflammatory mediators orchestrate, and adaptive immune system. An organized set of frequent effectors mechanism of inflammation furnish about oxidative stress, injury in tissue, remodeling of the extracellular matrix, angiogenesis of different targeted tissues. Atherosclerosis provides an example for different chronic disease that deals with inflammatory processes. The formation of blood leukocytes explains the starting of this type of disease. Its beginning consists of different inflammatory moderators that are infected by cells of inborn as well as adaptive immunity. The issues concerning inflammation are counting plaque disruption, atheroma, and thrombosis. Inflammatory should have the ability to provide advancement of narrative strategies that diagnose the disease, control therapy, and the way by which it can be treated that help with aging, for example, atherosclerosis Libby P (2007).

Procedure:
In the case of antiphlogistics action, carrageen-induced acute paw edema is assessed in rats for synthesized compounds **Vt_1-Vt_{14}**and **Vt_1-Vt_{16}**. Then the active compound production is evaluated with the Eddy hot plate method. The induced paw edema in rats utilized in carrageenan is as follows Winter CA et al (1968).

Animals:
The anti-inflammatory efficacy is only taken in healthy Wistar albino rats that weigh between 125-200 gm. The animals were parted into four group's particularly having four animals. Hindustan Lever Ltd, in Mumbai, reported that the animals were fed a traditional pellet diet and had access to water. Prior to experimentation, all animals fasted.

Drugs Carrageenan suspension:

The test compounds, the normal control, and standard diclofenac, were injected into the rats thirty minutes before injecting at 0.1 ml 1% with 1% of carrageenan suspension in ordinary saline. Carrageenan suspensions are administrated at the left hind paw in the region of the sub-planar and right hind paw served in the act of reference. The mercury displacement method is used to study about edema volume of the inserted paws. The average edema volume was determined by comparing the paw volume of the diagnosed animals **Roy A et al (1980)**.

A formula was used to the determined percentage reduction in edema volume.

$$\text{Percentage reduction} = \frac{V_O - Vt}{Vo} \times 100$$

Where,

Vo = Paw volume of control found in time't'.

Vt = Paw volume of drug-treated found in time't.'

With this information, we calculated the volume of AVERAGE edema, standard error, and % reduction. Table.31 shows the decrease in paw edema volume.

Table.31: Percentage inhibition shows by the synthesized compounds against Carrageenan induced rat paw edema. (Scheme 1)

Group	Treatment	Dose mg/kg	Paw edema volume							
			After 1st hr		After 2nd hr		After 3rd hr		After 4th hr	
			Average/ ±SEM	% ROV	AVERAGE/±SEM	% ROV	AVERAGE/±SEM	% ROV	AVERAGE/±SEM	% ROV
1	Cont.	1.5 ml	0.70±0.025	-	0.76±0.006	-	0.61±0.026	-	0.84±0.015	-
	Std.	50	0.25±0.018	64.28	0.20±0.009	73.60	0.15±0.009	74.09	0.15±0.014	82.14
3	Vt_1	200	0.31±0.012	55.71	0.29±0.012	61.84	0.23±0.009	62.29	0.25±0.023	69.28
4	Vt_2	200	0.32±0.018	51.12	0.31±0.012	55.71	0.31±0.016	55.71	0.29±0.012	61.84
5	Vt_3	200	0.33±0.009	52.42	0.32±0.018	51.12	0.28±0.023	61.70	0.25±0.023	64.28
6	Vt_4	200	0.31±0.016	55.71	0.28±0.023	61.70	0.25±0.023	64.28	0.23±0.009	66.80
7	Vt_5	200	0.30±0.020	56.00	0.29±0.012	61.84	0.20±0.010	76.19	0.20±0.010	76.19
8	Vt_6	200	0.32±0.018	51.12	0.28±0.023	61.70	0.23±0.009	66.80	0.18±0.014	79.08
9	Vt_7	200	0.25±0.023	64.28	0.21±0.009	72.36	0.15±0.010	75.40	0.20±0.010	76.19
10	Vt_8	200	0.30±0.014	57.14	0.25±0.015	67.10	0.17±0.009	71.31	0.15±0.010	81.91

11	Vt_9	200	0.30±0.020	56.00	0.25±0.023	66.05	0.20±0.012	67.20	0.16±0.014	80.23
12	Vt_{10}	200	0.33±0.009	52.42	0.28±0.018	62.76	0.22±0.009	63.11	0.17±0.014	79.16
13	Vt_{11}	200	0.30±0.023	56.00	0.25±0.022	66.05	0.20±0.007	67.20	0.16±0.007	80.23
14	Vt_{12}	200	0.31±0.016	55.71	0.28±0.011	62.72	0.21±0.009	66.22	0.23±0.009	70.50
15	Vt_{13}	200	0.30±0.020	57.14	0.25±0.018	67.10	0.16±0.020	73.32	0.15±0.009	81.54
16	Vt_{14}	200	0.25±0.022	66.05	0.16±0.007	80.23	0.15±0.009	74.09	0.15±0.009	81.54

Animals used: Albino rat, Route of administration: P.O, standard used- Diclofenac Sodium, ROV- Reduction in paw edema volume. Each value defines the average ±SEM (n = 4), *p <0.05, **p < 0.01, ***p < 0.001 (compare to standard). Data was screened by ANNOVA's bonferron's multiple tests.

Evaluation of Analgesia efficacy:

Dominant derivatives that conceded modest anti-inflammatory efficacy with differentiation of standard drugs were more analyzed for *in-vivo* analgesic efficacy applying Eddy's hot plate method Kulkarni (1999).

Procedure:

The method was represented by and has been altered by several investigators. A total of six groups of more sex of albino mice that comprise four animals of 20-25gm of weight have the demerit for food and water of about 18 hours before the experiment. Timers were used to monitor when the animals started jumping or licking after being put on the hot plate. Standard or test chemical was administered orally/subcutaneously at 0, 20, 40, 60, 80, 100 and 120 minutes. Pentazocine was used as a reference medication.

Table.32 Analgesic efficacy of newly synthesized compounds by hot plate method (Scheme 1)

Treatment	No. of animals	Avg mass of animals (grams)	Avg. Dose (mg)	Basal reaction time (sec.) after						
				0 min	20 min	40 min	1 hour	1hr 20 min	1hr40min	2 hrs
Control (gum acacia)	4	22	-	3.9±0.367	4.12±0.473	4.12±0.553	4.22±0.503	4.27±0.324	3.88±0.372	5.20±0.647
Standard (Pentazocin (20mg/kg)	4	23.6	0.236	6.53±0.889	12.87±1.332	12.91±1.320	13.87±0.279	13.65±0.851	11.83±1.042	12.33±0.918

Compound (Vt_1)	4	25	2.5	4.093±0.239	4.26±0.130	12.976±0.645	12.243±0.850	11.136±1.145	10.116±1.520	9.146±0.938
Compound (Vt_2)	4	25.5	2.55	3.836±0.212	6.066±0.468	7.31±0.519	11.943±0.450	12.136±1.145	11.190±0.980	11.346±0.938
Compound (Vt_3)	4	24	2.4	5.003±0.308	4.996±0.230	10.106±0.745	11.113±0.870	11.636±0.988	12.001±1.010	9.146±0.978
Compound (Vt_4)	4	24	2.4	4.676±0.648	9.470±0.950	13.073±1.219	13.101±1.012	13.636±1.010	10.001±1.540	10.146±0.923
Compound (Vt_5)	4	25.7	2.57	4.093±0.239	4.26±0.130	12.976±0.645	10.59±0.628	12.76±0.774	14.04±0.450	13.42±0.912
Compound (Vt_6)	4	26	2.6	4.116±0.748	12.47±1.600	11.903±1.498	13.23±0.202	12.44±1.176	10.986±0.516	11.663±0.757
Compound (Vt_7)	4	24.33	2.433	3.36±0.521	4.2±0.351	10.16±1.837	9.53±1.080	12.273±1.093	11.326±1.374	11.18±1.955
Compound (Vt_8)	4	22.33	2.233	3.433±0.212	13.373±0.521	13.07±1.219	11.866±1.611	14.493±0.320	13.24±1.111	10.39±0.610
Compound (Vt_9)	4	26	2.6	4.116±0.748	12.47±1.600	11.90±1.498	13.23±0.202	12.446±1.176	10.986±0.516	11.663±0.757
Compound (Vt_{10})	4	20.66	2.066	5.156±0.99	7.106±0.431	12.20±0.866	14.55±0.284	12.991±0.938	14.793±0.130	13.2±1.138

Compound (Vt_{11})	4	23.33	2.33	3.836±0.202	6.066±0.368	7.3±0.719	10.59±0.628	12.76±0.774	14.04±0.450	13.42±0.912
Compound (Vt_{12})	4	24.33	2.43 3	4.977±0.540	5.497±0.417	10.99±1.075	13.063 ±0.897	13.607 ±0.881	13.693 ±0.826	12.093 ±1.143
Compound (Vt_{13})	4	24.33	2.43 3	3.36±0.521	4.2±0.351	10.1±1.837	9.53±1.080	12.273 ±1.093	11.326 ±1.374	11.18±1.955
Compound (Vt_{14})	4	25.70	2.57 0	5.73±0.800	11.87±0.891	12.51±1.320	13.00±0.779	13.65±0.881	13.693 ±0.928	12.33±1.201

Dose: 20, 25mg/kg as analgesic efficacy. AVERAGE ± SEM, (n=4)

Table.33: Percentage inhibition shows by the synthesized compounds against Carrageenan induced rat paw edema. (Scheme 2)

Group	Treatment	Dose mg/kg	Paw edema volume							
			After 1st hr		After 2nd hr		After 3rd hr		After 4th hr	
			AVERAGE/± SEM	% ROV	AVERAGE/ ±SEM	% ROV	AVERAGE/± SEM	% ROV	AVERAGE/ ±SEM	% ROV
1	Cont.	1.5 ml	0.72	-	0.78	-	0.81	-	0.76	-
2	Std.	50	0.18±0.645	68.2	0.18±0.651	76.92	0.17±0.635	79.8	0.15±0.590	80.26
3	VT1	200	0.24±0.664	77.69	0.25±0.639	71.65	0.19±0.651	80.76	0.16±0.652	75.78
4	VT2	200	0.38±0.650	71.47	0.39±0.662	69.88	0.27±0.709	80.6	0.20±0.653	75.73
5	VT3	200	0.34±0.639	71.52	0.39±0.779	77.5	0.32±0.942	80.7	0.29±0.656	75.61
6	VT4	200	0.27±0.653	71.62	0.29±0.698	75.6	0.31±0.709	80.6	0.19±0.651	75.75
7	VT5	200	0.28±0.645	71.0	0.24±0.655	72.21	0.24±0.654	71.23	0.30±0.658	75.6

8	VT 6	200	0.35±0.674	51.38	0.35±0.660	55.12	0.32±0.866	60.49	0.29±0.634	61.84
9	VT 7	200	0.36±0.766	50.32	0.24±0.655	72.21	0.18±0.582	81.43	0.16±0.707	78.94
10	VT 8	200	0.29±0.586	70.65	0.24±0.553	72.21	0.16±0.538	83.43	0.16±0.712	78.94
11	VT 9	200	0.50±0.630	30.55	0.45±0.678	40.78	0.22±0.639	72.82	0.15±0.569	80.26
12	VT 10	200	0.34±0.615	52.67	0.25±0.713	71.76	0.23±0.813	71.65	0.23±0.629	69.73
13	VT 11	200	0.26±0.656	63.88	0.36±0.588	54.43	0.21±0.511	74.05	0.18±0.689	77.77
14	VT 12	200	0.38±0.555	47.22	0.28±0.610	60.56	0.24±0.627	70.66	0.18±0.689	77.77
15	VT 13	200	0.27±0.685	62.97	0.24±0.563	72.21	0.34±0.660	58.88	0.17±0.743	78.12
16	VT 14	200	0.46±0.563	35.21	0.40±0.594	44.44	0.40±0.751	51.01	0.28±0.614	62.65
17	VT 15	200	0.35±0.608	51.54	0.35±0.654	55.76	0.24±0.617	70.66	0.19±0.611	76.56
18	VT 16	200	0.38±0.551	47.22	0.25±0.713	71.76	0.29±0.516	64.12	0.14±0.604	81.57

Animals: Albino rat, Route: P.O, standard- Diclofenac Sodium, ROV- Reduction in paw edema volume. Each value shows the AVERAGE ±SEM (n = 4), *p < 0.05, **p < 0.01, ***p < 0.001 (compare to standard). Data was analyzed by ANNOVA's bonferron's multiple tests.

Table.34 Analgesic efficacy of newly synthesized compounds by hot plate method.(Scheme 2)

Treatment	No. of animals	Avg mass of animals (grams)	Avg. Dose (mg)	Basal reaction time (sec.) after						
				0 min	20 min	40 min	60 min	80 min	100 min	120 min
Control (gum acacia)	4	22	-	3.9±0.367	4.12±0.473	2.12±0.553	3.22±0.503	4.27±0.324	3.88±0.372	2.20 ±0.647

Standard (Pentazocine) (10 g/kg)	4	22.6	0.226	6.53± 0.889	12.87± 1.332	12.91± 1.320	13.87± 0.279	13.65± 0.851	11.83 ±1.042	12.33 ±0.918
Compound (VT_1)	4	25	2.5	5.46± 0.413	4.911± 1.173	4.4±1.153	3.90±1.017	5.50±0.913	3.0±1.187	2.98±1.086
Compound (VT_2)	4	24.5	2.45	2.26± 0.989	2.95±1.108	2.80±0.981	3.85±1.101	2.98±1.306	4.5±1.405	4.85±0.907
Compound (VT_3)	4	24	2.4	3.26± 1.119	3.45±0.909	2.45±1.111	3.15±1.105	3.0±0.906	4.1±0.905	3.85±1.107
Compound (VT_4)	4	24.2	2.42	3.34± 1.129	4.95±1.549	2.80±1.431	2.85±0.910	3.20±0.786	4.55± 0.995	4.18±1.007
Compound (VT_5)	4	23.7	2.37	4.21± 1.679	2.9±1.239	2.84±1.781	3.04±1.760	2.05±0.987	3.75±1.445	3.3±1.217
Compound (VT_6)	4	26	2.6	5.25± 0.777	4.9±1.219	3.95±1.203	6.5±1.834	6.14±0.867	5.90±0.765	3.3±0.554
Compound (VT_7)	4	22.33	2.233	7.53± 0.819	7.67±1.132	2.91±1.290	4.87±0.979	5.65±0.899	3.83 ±1.242	4.33±0.998
Compound (VT_8)	4	21.33	2.133	6.55± 0.989	7.81±1.001	4.91±1.327	5.87±0.288	5.65±1.811	6.83±0.942	4.10±0.977
Compound (VT_9)	4	26	2.6	5.63± 1.129	9.12±1.630	6.921± 1.770	5.89±1.243	6.64±0.899	5.80±0.988	4.90±0.810
Compound (VT_{10})	4	20.58	2.058	8.10± 0.909	8.82±1.245	7.98±1.333	6.10±0.679	5.70±0.854	4.95±1.142	4.10±0.898
Compound (VT_{11})	4	24.33	2.433	6.10± 0.770	6.95±0.767	7.10±0.955	5.95±0.882	6.45±1.045	8.05±0.980	5.35±1.118
Compound (VT_{12})	4	25.33	2.533	6.53± 0.889	12.87± 1.332	12.91± 1.320	13.87± 0.279	13.65 ±0.851	11.83± 1.042	12.33± 0.918
Compound (VT_{13})	4	21.33	2.133	9.45± 0.556	7.85±0.555	5.75±1.450	6.85±0.979	4.75 ±0.899	5.75±0.992	5.30±0.956
Compound (VT_{14})	4	21.20	2.120	5.54± 0.799	8.83±1.134	7.95±1.320	6.90±1.501	5.77 ±0.995	5.70±0.799	4.98±0.878
Compo		20.	2.0	7.05±	6.67±1.	5.97±1.	07.15±	4.70	3.94±1.	2.56±1.

und (VT_{15})	4	66	66	1.121	012	445	0.856	±0.894	567	301
Compound (VT_{16})	4	23.12	2.312	6.35± 0.819	12.05± 0.535	9.80±1.001	5.65±1.211	9.55 ±0.878	6.95±1.664	7.10±0.968

Statistical Analysis:

Results of synthetic compounds are presented as AVERAGE ± S.E.M. Estimation and determination of total variation present in a group of data from ANOVA (linear analysis of deviation), which pursue through Dunnet's posthoc test. $P< 0.05$was believed to be significant. Graphpad Instar Trial software was used to conduct descriptive analysis using Fisher analysis of variance and regression models. Data of groups are accessible as AVERAGE values ± standard error, which was analyzed and plotted using Microsoft Excel software.

3. RESULTS AND DISCUSSION:

Chemistry:

Spectral analysis of2-(5-substituted-1, 3, 4-oxadiazole-2-yl)-1, 3-benzothiazole derivatives:

The treatment-related to 2-aminobenzae-1- thiol with diethyl oxalate in the existence of conc. H_2SO_4 like a strong dehydrating agent yielded ethyl 2-amino-benzothiazole-6-carboxylate. Ethyl 2-amino-benzothiazole-6-carboxylate dissolves in ethanol as a solvent that reacts with hydrazine hydrate yield 1, 3-benzothiazolr -2 carboxyhydrazide. Phosphoryl chloride and aromatic acid get mixed with 1,3 -benzothiazole -2- carboxyhydrazide that forms the title compound;2-(5-substituted 1, 3, 4-oxadiazole -2-yl)-1, 3-benzothiazole **(Vt_1-Vt_{14})**. It was noticeable that ketonic groups (C=O) present is morecompatible with the fusion of primary amine group ($-NH_2$) of hydrazide, and the reaction is followed by elimination of water molecule, ($-NH_2$) because it acts as a typical amide due to the closer to nitrogen atom present in the benzothiazole ring.IR, ^{1}H-NMR and mass spectroscopy perfectly performed the concluded derivates. Infrared, mass spectroscopy and NMR were used to validate this structural elucidation. The IR spectra of the concluding compounds were verified to range between 3375 and 3200cm^{-1} for N-H stretching, 3000-3200 cm^{-1} for Azanide, 3075-2850 cm^{-1} for C-H aliphatic and aromatic, 3200-3325 cm^{-1} for -OH, and 1300-1400 cm^{-1} for nitrogen dioxide (NO_2). A-C aliphatic and aromatic proton signals started around 2.36-3.68, 8.06-6.30, ppm in ^{1}HNMR spectra. Mass spectra are dependent on the presence of suitable molecular ion peaks.

Spectral analysis of N-(2, 3-dimethylphenyl)-2-(5-substituted-1, 3, 4-oxadiazole-2-l) benzenamine derivatives:

5-(2,3-dimethylanilino)phenyl) We developed and synthesised aryl-1, 3, 4-oxadiazole. The process produces 5-(2,3-dimethylphenylamino)phenyl. -1, 3, 4-oxadiazole In the presence of H_2SO_4 as a powerful dehydration agent, 2-(2, 3-dimethylphenyl)aminobenzoic acid carboxylate **(1)**. 5-(2-(2,3-dimethylanilino)phenyl) When 2-(aryl)-1, 3, 4-oxadiazole and hydrazine hydrate were mixed together, 5-(2-(2, 3-dimethylphenylamino)phenyl) was formed as a result of the reaction -1, 3, 4-oxadiazole -2-carbohydrazide **(2).** Suitable aromatic acid and phosphoryl chloride reacts with 5-(2-(2,3-dimethylphenylamino)phenyl)-1, 3, 4-oxadiazole-2-carbohydrazide to furnished the title compounds; 5-(2-(2,3-dimethylanilino)phenyl)-2-(aryl)-1, 3, 4-oxadiazole **(VT_1-VT_{16}).** The keto group of compounds **(1)** and **(2)** reacted with the primary amine to eliminate water molecules. All final compounds (**VT_1-VT_{16})** were pure and stable. IR, ^{1}H-NMR and the explanation of structure is verified by mass spectroscopy, NMR and IR. IR spectral peaks for the different concluded

compounds are confirmed for various purposes like 3375–3200cm^{-1} used for stretching of N-H, NH_2 at 3000-3200 cm^{-1}, C-H aliphatic and aromatic at 3075-2850 cm-^{1},3200-3325 of -OH and 1300-1400 cm-^{1} at NO_2. When analysing ^{1}H NMR spectra, it was discovered that signals from the proton spectrum for C-H aliphatic, aromatic, and N-H were recognized in the range of 3.55 to 2.25 ppm, 7.91 6.04 and 10.41 to 9.12ppm, and N-H protons may be replaceable with heavy water.

Biology:

The acute paw edema indicates the percentage of anti-inflammatory efficacy in terms of paw volume of standard and test compounds.

Anti-inflammatory efficacy of 2-(5-substituted-1, 3, 4-oxadiazole-2-yl)-1, 3-benzothiazole derivatives. (Vt$_1$-Vt$_{14}$):

All latest synthesized 2-(2, 5- dihydro-1, 3, 4-oxadiazole 2-yl) benzo[d] thiazole derivatives incorporated with chemotherapeutic pharmacophore were examined with anti-inflammatory activities making use of the *in-vivo* model. The activities of anti-inflammatory of a synthesized compound show that all the compounds are sufficiently active in inhibiting the inflammation. The acute paw edema shows that the percentage of the efficacy of anti-inflammatory in relation with paw volume of every derivative was undetermined when compared with diclofenac sodium, referred to as standard drug. The derivatives being evaluated are made from 0.2 ml of 5 % gum acacia to prepare the standard solution. Compounds containing OH, NO_2, NH_2, and I are more active when compared with diclofenac solution. The compounds that show fewer efficacies with oxadiazole ring at position 2 are MeO and EtO. The finding of the anti-inflammatory evaluation presented that maximum compounds that show the same efficacy against the new edema volume. The synthesized compounds **(Vt$_1$-Vt$_{14}$)** of this series found those compounds **Vt$_5$** to **Vt$_{14}$** exerted better anti-inflammatory efficacy against paw edema volume in comparison to standard drug Diclofenac Sodium. While compound **Vt$_1$** to**Vt$_4$**, were capable of showing moderate anti-inflammatory efficacy against the paw edema volume. The efficacy was found to increase with the presence of electron-withdrawing substituent at all substituted places.

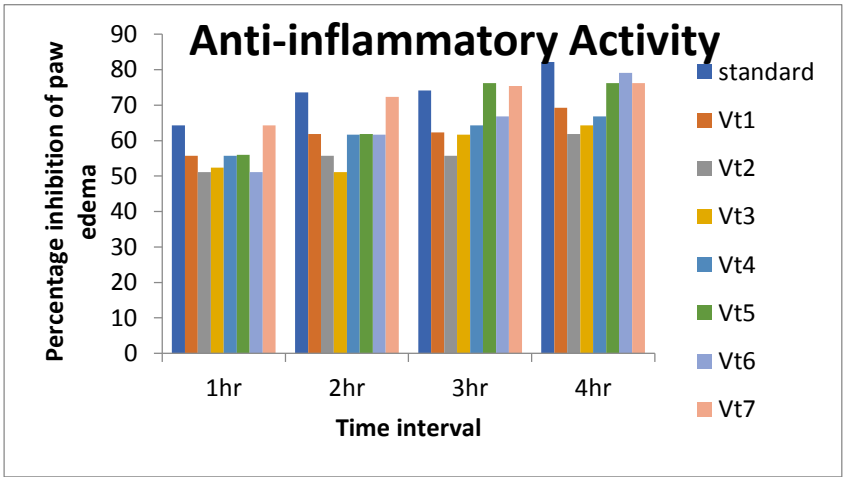


Fig.1: A comparative study of Anti-inflammatory efficacy of Compounds Vt$_1$-Vt$_7$

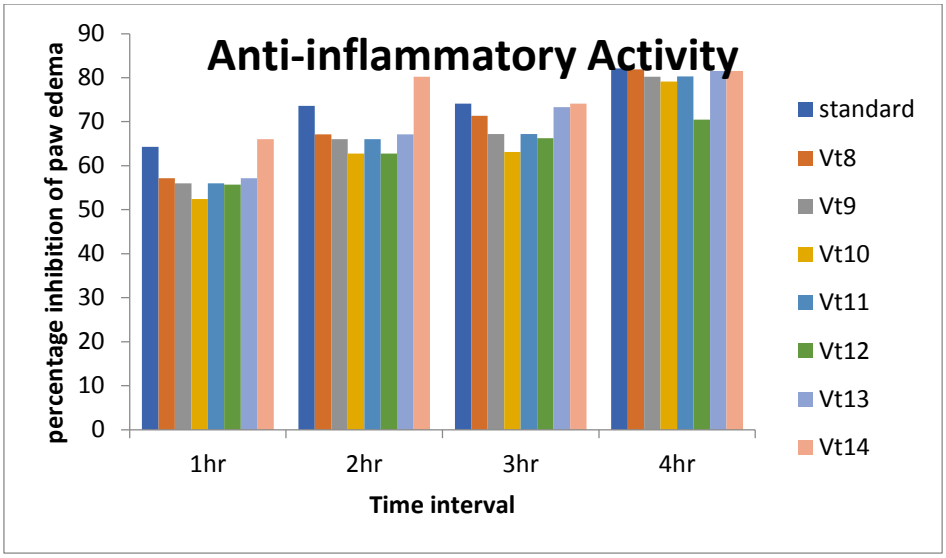


Fig.2: A comparative study of Anti-inflammatory efficacy of Compounds Vt_8-Vt_{14}

Anti-inflammatory efficacy of N-(2,3-dimethylphenyl)-2-(5-substituted-1, 3, 4-oxadiazole-2-yl)benzenamine derivatives. (VT_1-VT_{16}):

In **scheme 2,** all newly synthesized 5-(2-(2, 3-dimethylanilino) phenyl)-2-(aryl)-1, 3, 4-oxadiazole derivatives **(VT_1-VT_{16}).** The anti-inflammatory effect of the rats has recently been demonstrated to suppress inflammation through carrageenan-induced acute paw edema. Compounds were administered via oral route with the standard drug diclofenac sodium in a 20 mg kg^{-1} suspension, and the efficacy profile was analysed. At 0, 30, 60, 90 and 120 minutes after oral administration of the medication, paw edema was evaluated. By comparing the AVERAGE value of treated and control groups and by examining the difference using ANOVA, the difference was determined. In **scheme 2**, compounds containing (Cl, OH, NH_2 and SH) groups were also effective than diclofenac sodium, whereas compounds including (CH_3O and C_2H_5O) groups exhibited lesser efficacy at 2nd position oxadiazole ring. The findings of the anti-inflammatory evaluation presented that most of the compounds have similar efficacy against the paw edema volume. Among all the synthesized compounds **(VT_1- VT_{16})** of this series, it was found that those compounds **VT_1**to **VT_5, VT_7, VT_8, VT_9, VT_{11}, VT_{12}, VT_{13}, VT_{15}** and **VT_{16}** exerted better anti-inflammatory efficacy against paw edema volume in comparison to standard drug diclofenac sodium. While compound **VT_6, VT_{10}** and **VT_{14}** showed moderate anti-inflammatory efficacy against the paw edema volume. The efficacy was found to increase with the presence of electron-withdrawing substituent at all substituted places.

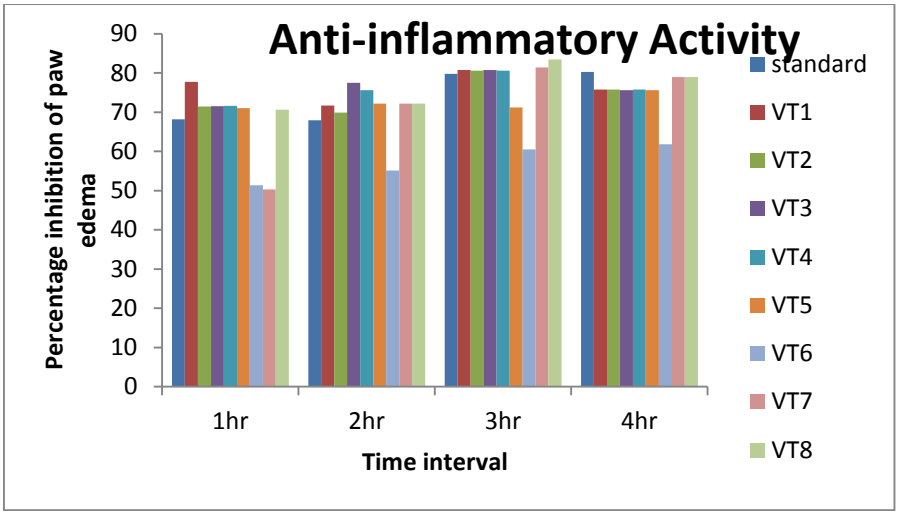


Fig.3: A comparative study of Anti-inflammatory efficacy of Compounds VT_1-VT_8

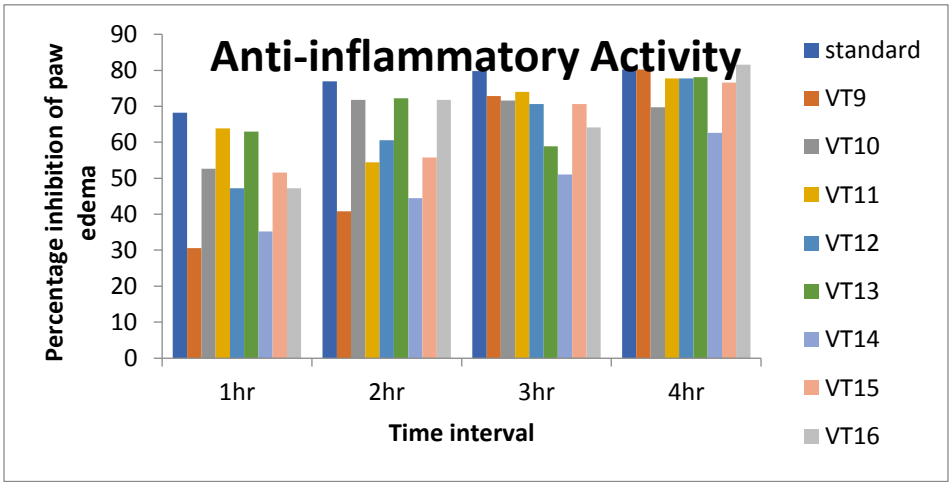


Fig.4: A comparative study of Anti-inflammatory efficacy of Compounds VT_9-VT_{16}

Analgesic efficacy:

In the acetic acid-induced writhing study, all newly-manufactured compounds were again estimated with analgesic effectiveness of 20 mg kg^{-1}. The abdominal constrictions of the mouse were also quantified as a writhing response. The chemicals analgesic efficacy correlated well with their anti-inflammatory action. Additionally, the compounds that have a higher anti-inflammatory efficacy (>60%) have been evaluated for their analgesic efficacy. Table 4.4.5 and Table 4.4.7 show the rate of protection of mice by administering the drugs. In **Scheme 1** among the dominant compounds,2-(5-(4-methoxyphenyl)-1, 3, 4-oxadiazole-2-yl)benzo[*d*]thiazole **Vt_5** was establishing to be the most active derivative with presenting the jumping response;a stopwatch records this. Compounds containing chlorophenyl, hydroxyl phenyl, iodophenyl, nitrophenyl groups, and the oxadiazole ring are on the fifth position exhibited strong analgesic efficacy compared to normal 20 mg kg^{-1} i.p. dosage, standard drug pentazocine. Compounds **Vt2, Vt6, Vt7, Vt10, Vt11, Vt12,** and **Vt14** show considerable analgesic efficacy. While compounds **Vt_1, Vt_3, Vt_4** and **Vt_8** were capable of showing moderate analgesic efficacy against the standard drug. In **Scheme 2,** among the dominant compounds, **VT_2, VT_7, VT_9, VT_{12}, VT_{13}, VT_{14},** and **VT_{16}** was establishing to be the most potent derivatives with presenting the jumping response; a stopwatch records this. There was a greater analgesic effect from compounds that contained electron-withdrawing groups at

position 5 of the 1, 3, 4-oxadiazole ring if compared with the standard drug pentazocine, 20 mg kg^{-1} intravenously.

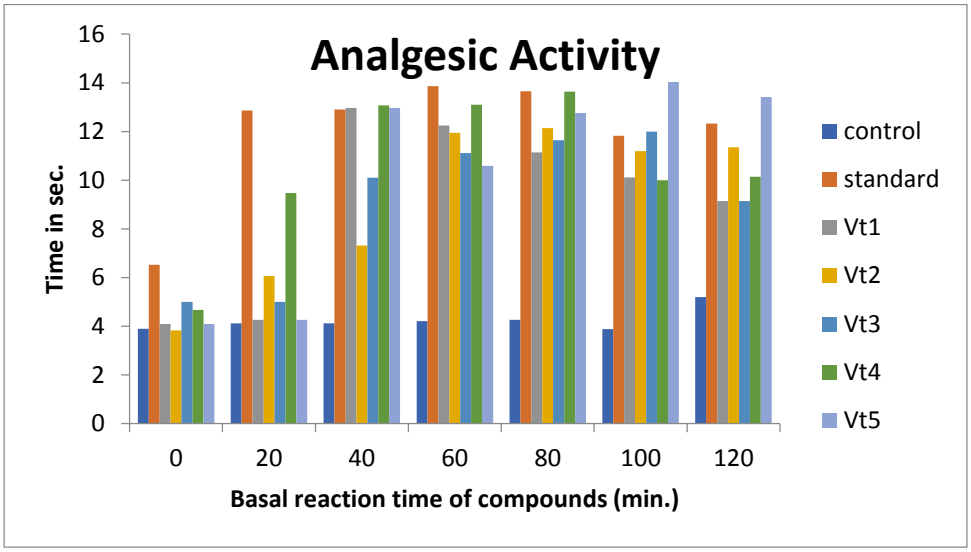


Fig.5: A comparative study of the Analgesic Efficacy of Compounds Vt_1-Vt_5 (Scheme 1)

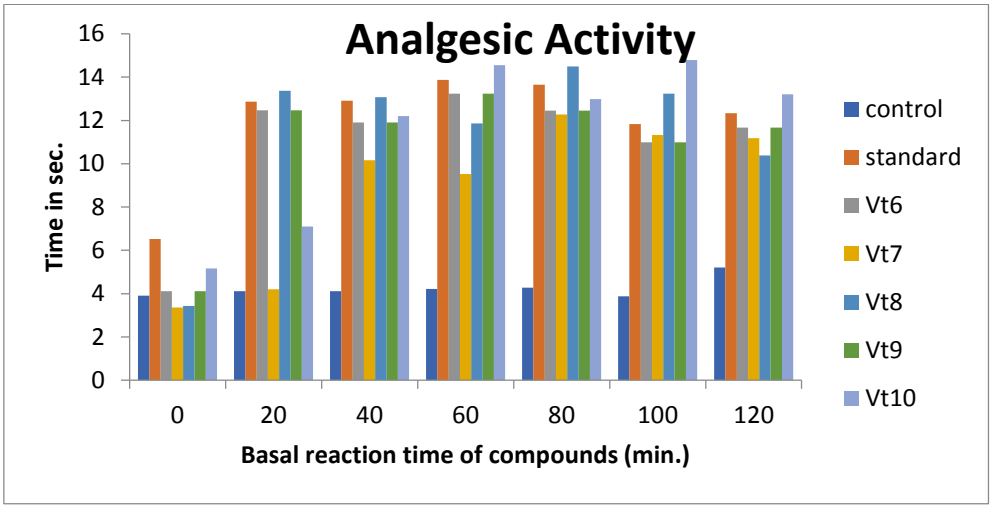


Fig.6: A comparative study of the Analgesic Efficacy of Compounds Vt_6-Vt_{10} (Scheme 1)

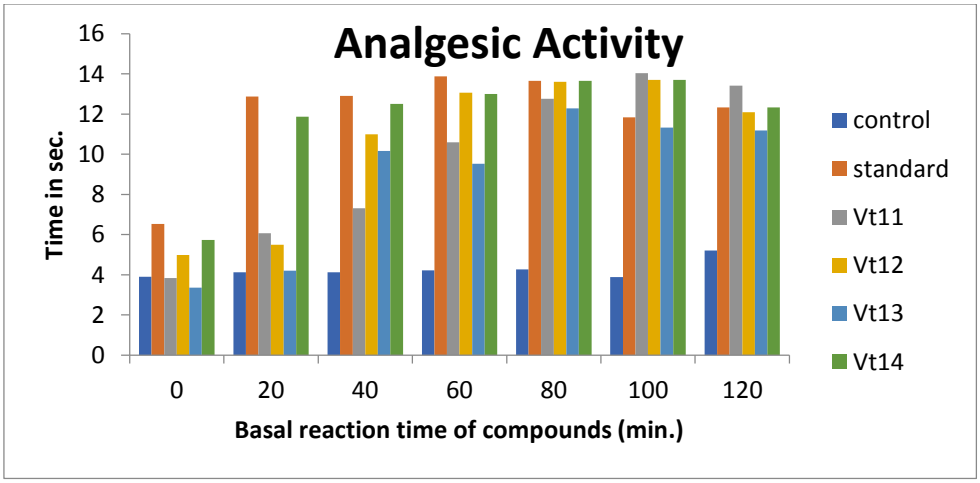


Fig.7: A comparative study of the Analgesic Efficacy of Compounds Vt_{11}-Vt_{14} (Scheme 1)

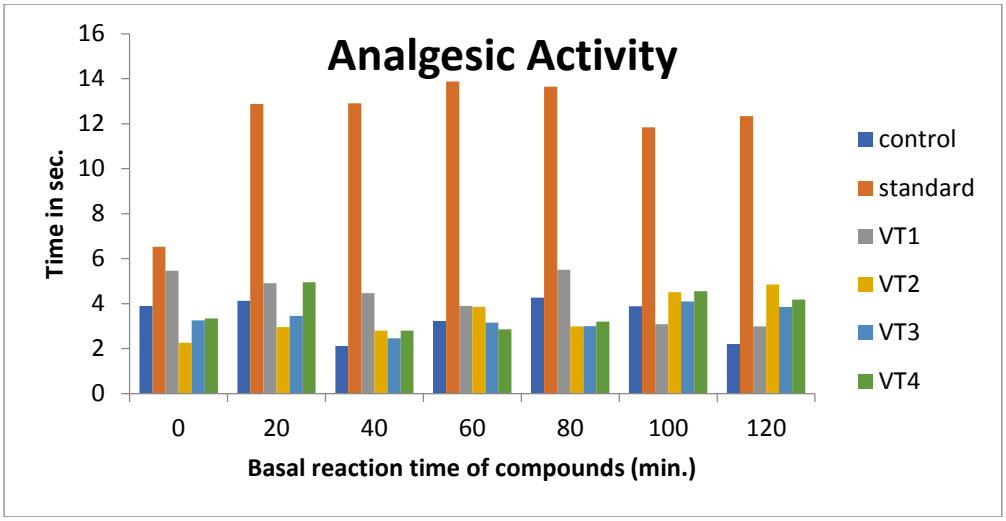


Fig.8: A comparative study of the Analgesic Efficacy of Compounds VT_1-VT_4 (Scheme)

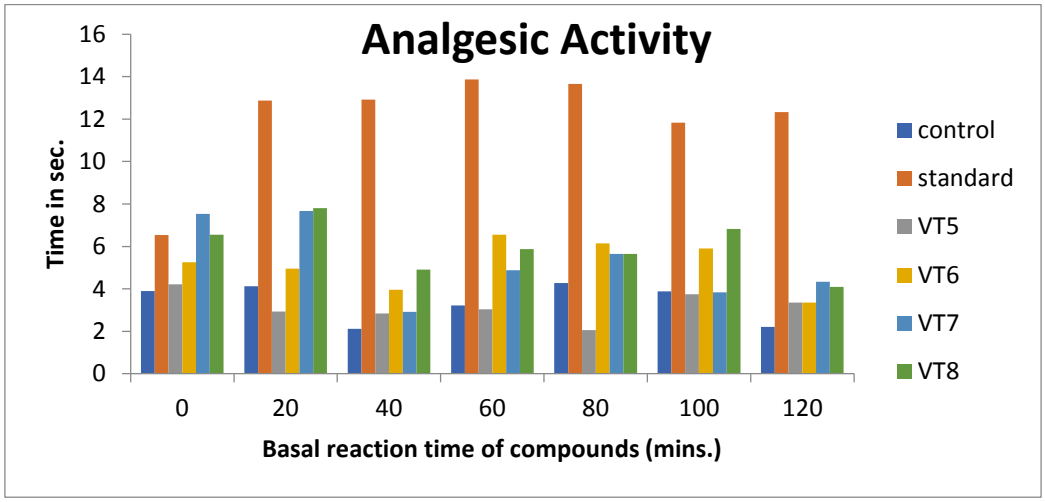


Fig.9: A comparative study of the Analgesic Efficacy of Compounds VT_5-VT_8 (Scheme 2)

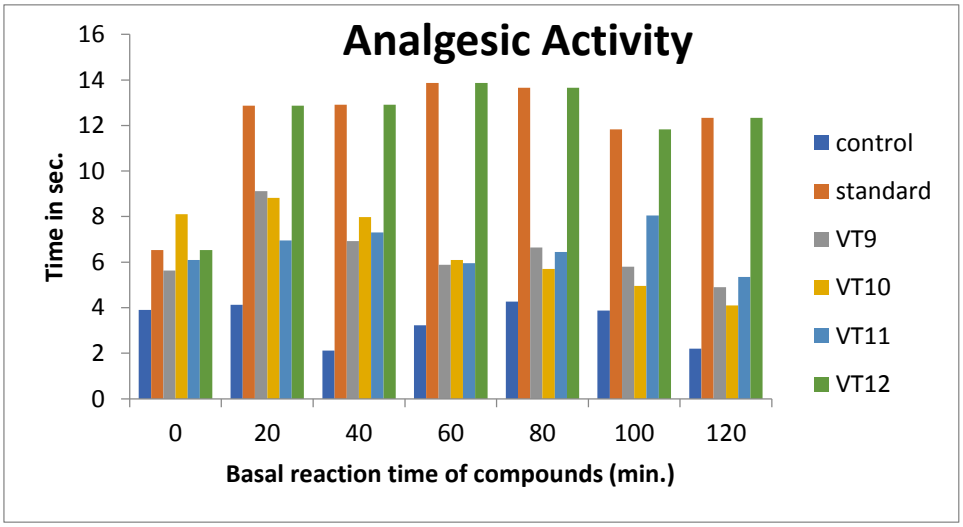


Fig.10: A comparative study of the Analgesic Efficacy of Compounds VT_9-VT_{12} (Scheme 2)

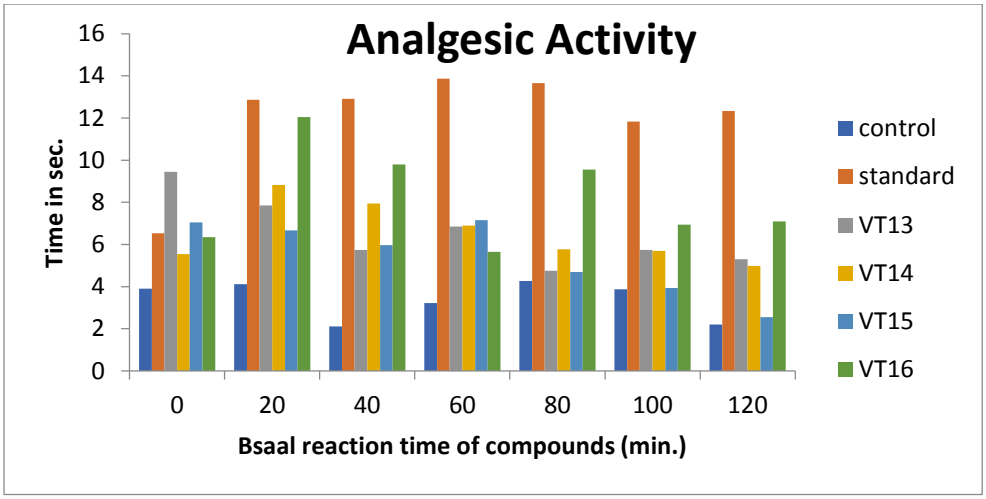


Fig.11: A comparative study of the Analgesic Efficacy of Compounds VT_{13}-VT_{16} (Scheme 2)

STRUCTURE EFFICACY RELATIONSHIP (SAR):

The biological effectiveness of analgesic and anti-inflammatory action based on the synthesised derivatives of benzothiazole derivatives 2-(5-substituted —1, 3, 4- oxadiazole — 2-yl)-1, 3 and 5-(2-(2,3-dimethylene-phenyl) -2-(aryl) -1, 3, 4- derivatives of oxadiazole have been produced following generalization.

All the synthesized compounds **(Vt_1-Vt_{14}, VT_1-VT_{16})** in both Schemes, bearing electron-withdrawing groups (-Cl, -OH, and -NO_2) at 2nd position of substitutions over the ring were marked excellent anti-inflammatory efficacy against the paw edema volume.

The analgesic efficacy of substituted compounds with an electronegative group (-Cl) on the benzothiazole moiety at the 2nd position and on the oxadiazole moiety at the 2nd position (-Cl, -OH, and -NO_2) was strong. Replacement of substituted phenyl group with benzoyl group at 2nd position of oxadiazole nucleus resulted in decreased efficacy. The efficacy is also decreased whenever the replacement at the 2nd position of oxadiazole nucleus of phenyl group by a group of bulk, for example, naphthoyl. In oxadiazole, the reaction of electrophilic substitution is not practical. The reason is that the density of electron found in the carbon atoms are low that keeps on withdrawing its effects present in pyridine type of nitrogen when any type of electron group is attached with it.

In the procedure, the substituted compounds with a much higher electron-donating group such as CH_3, NH_2, OCH_2 and OCH_3 are found at the 2nd position of the oxadiazole nucleus that causes an increase in the efficacy of anti-inflammatory that is against the paw edema volume. Compounds that include the oxadiazole ring electron withdrawal group (-NO_2) were more powerful as compared to the compounds with only an additional electron withdrawal group such as -Cl, Br Groups and compounds in the electropositive group such as -NH_2 could not produce substantially.

Replacement of substituted phenyl group with benzoyl group at 2nd position of oxadiazole nucleus resulted in decreased efficacy. The efficacy is also decreased when replacement is done at the 2nd position of the group name phenyl of oxadiazole nucleus by a bulky group like naphthoyl. The increased hydrophobic nature due to the methyl group and electron-donating nature of the methoxy group substituted at phenyl moiety in the structure may be accountable for the higher efficacy.

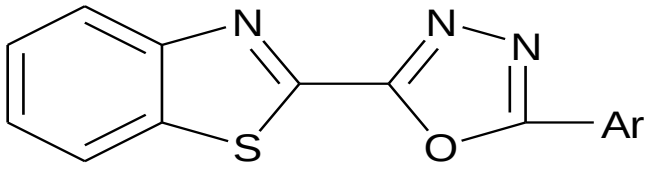
Conclusion:

The current investigation has been separated into two parts i.e. synthesis and biological evaluation. Based upon broad literature survey on biologically active heterocyclics first it was planned to synthesize, benzothiazole 1, 3, 4-oxadiazole derivatives, in relation to biological activities such as anti-inflammatory and analgesic activities. Thus it was planned to develop

some modern benzothiazole/1, 3, 4-oxadiazole derivatives containing above specified nucleus. In the initial phase of the present study two individual series with distinct moieties were prepared:

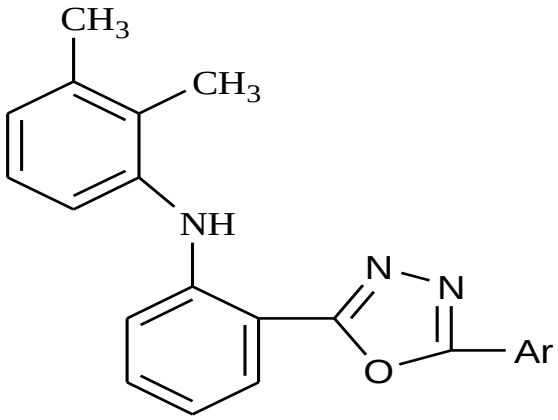
- 2-(5-substituted-1, 3, 4-oxadiazole-2-yl)-1,3-benzothiazole
- N-(2,3-dimethylphenyl)-2-(5-substituted-1, 3, 4-oxadiazole-2-yl)benzenamine

The synthetic practice involved for the conversion of the compounds in Scheme1 and Scheme 2 was found to be successful synthetic route. The mentioned synthesized derivatives were found in fine quality crystals and yield.



(Vt_1-Vt_{14})

Where Ar = CH_3, NH_2, OH, NO_2, OCH_3, I



(VT_1-VT_{16})

Where Ar = CH_3, NH_2, OH, NO_2, OCH_3, I

The most advanced analytical techniques were used to determine the structures of the newly synthesized title compounds, including FTIR spectroscopy, hydrogen-1 NMR and mass spectroscopy. Spectral characterization of the established compound confirmed the origination of the desired derivative.

In the second part the evaluation of the synthesized innovative compounds containing two series of anti-inflammatory and analgesic activity were conducted by using carrageenan-induced acute paw oedema in rats and Eddy's hot plate method. Screening at the beginning level was carried out for every compound which was again checked for analgesic activity using *in-vivo* model.

Among the 1, 3, 4- oxadiazole derivatives **(Vt_1-Vt_{14}), Scheme 1,** It was noticeable that compound **Vt_8** was found to be equipotent in anti-inflammatory efficacy in comparison to standard drug Diclofenac sodium. While compound **Vt_9**to **Vt_{14}** were capable to display moderate anti-inflammatory efficacy against the percentage of paw volume. In analgesic screening, compound **Vt_{11}** was found to be equipotent in comparison to standard drug pentazocine. **Vt_2**, **Vt_5**, **Vt_6**, **Vt_7**, **Vt_9, Vt_{10}, Vt_{12}, Vt_{13}** and **Vt_{14}** were also used to possess excellent efficacy, and compounds **Vt_1, Vt_3**, **Vt_4**, and **Vt_8** showed moderate analgesic efficacy, which is comparable with the standard. While among the oxadiazole derivatives **(VT_1-VT_{16}), Scheme 2**, compounds **VT_9** and **VT_{16}** were marked to be the most active derivative versus

carrageenan-induced oedema in rats. The conclusions of anti-inflammatory screening are in the variety of 61.84 to 81.57%, although standard drug diclofenac sodium displayed an efficacy of 80.26% next 4 hr. It can be concluded that the existence of 5-benzyl and 4-nitrophenyl or substitution at the 5th location of the 1, 3, 4-oxadiazole ring causes notable enhancement in anti-inflammatory action. In analgesic screening, compounds **VT_{12}** and **VT_{16}** were found to be equipotent to the standard drug pentazocine. Moderate analgesic activity was demonstrated by the compounds **VT_2, VT_4, VT_7,** to **VT_{14}**. In **Scheme 1** among the potent compounds **Vt_8** was found to be the most active derivative presenting the percentage of paw volume is 81.91%, while compound **Vt_9, Vt_{10}, Vt_{12}, Vt_{13}** and **Vt_{14}** showed moderate anti-inflammatory activity. In **Scheme 2** compound **Vt_9** and **Vt_{16}** were considered as the most active derivative with percentage of paw volume of 80.26 and 81.57 and compounds **VT_1**to **VT_4, VT_7**to **VT_{13}** and **VT_{15}** were found to be moderate active against diclofenac sodium.

All available reports motivated us to synthesize newer benzothiazole and 1, 3, 4- oxadiazole derivatives such as anti-inflammatory and analgesic activities. Our current research work provides that additional derivatization of the prepared compounds could retain potent anti-inflammatory and analgesic activity and thus develop newer approaches of structure activity relationship (SAR). The step in health science research is to maintain superior physical health for human beings. An extensive literature review recommends that the outcome of the present study corresponds with the findings of other reported investigations in accordance with a synthetic pattern of 1, 3, 4-oxadiazole analogues and research on their anti-inflammatory and analgesic properties. An analysis of results of present studies indicates that more 1, 3, 4-oxadiazole analogues may be prepared by substituting in other positions of benzothiazole /1, 3, 4- oxadiazole to develop potent biological agents. The highly potent compounds prepared in this work may be studied further to establish the potential of analgesic and anti-inflammatory activity. Further research is required to elucidate the molecular mechanisms of 1, 3, 4- oxadiazole analogues for various biological activities by *in-vivo* models. It may be evaluated through clinical studies for the development of the new analgesic and anti-inflammatory drugs with fewer side effects.

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