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Research Article

**ANALGESIC AND ANTI INFLAMMATORY ACTIVITY OF
NEW SUBSTITUTED THIAZOLIDIN-4-ONE
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Gulbarga - 585102**Abstract:**

4-thiazolidinones are among the most extensively investigated class of organic compounds. Thiazolidin-4-one has been considered as magic moiety, which is a core structure in various synthetic pharmaceuticals displaying a broad spectrum of biological activities. They are widely used as anti-inflammatory, anticonvulsant, analgesic, antimicrobial, anti-HIV, CNS depressant, carcinostatic, antihypertensive and cytotoxic. In view of the wide spectrum activities of condensed 4-thiazolidinones, it was thought worthwhile to undertake the synthesis of heterocyclic systems in which 4-thiazolidinone nucleus is linked to another biologically active moiety. Semicarbazide/Thiosemicarbazide was reacted with benzoyl chloride to obtain N-hydrazinocarbonyl benzene-1-carboxamide/N-hydrazinocarbothioyl benzene-1-carboxamide respectively. These were then condensed with various aldehydes to yield the intermediate Schiff bases. Thiazolidin-4-ones were prepared by the reaction of Schiff bases with mercaptoacetic acid in dry benzene by refluxing for 16-18 hours.

The purity of the compounds synthesized was established by TLC. The synthesized derivatives were characterized by FT-IR, ¹H NMR and Mass spectral analysis.

All the derivatives synthesized were screened for their analgesic and anti-inflammatory potency. The compounds 3A3, 3A5, 3B2, 3B6 have shown equipotent analgesic activity when compared to standard Ibuprofen. The compounds 3A2, 3A5, 3B2, and 3B3 have been evaluated for their anti-inflammatory properties at a dose of 50 mg/kg using carrageenan induced rat paw edema method. All the tested compounds exhibited significant anti-inflammatory activity in acute inflammatory models in rats. Compounds 3A2, 3A5, 3B2, and 3B3 exhibited significant reduction in edema volume when compared to standard Ibuprofen.

Keywords: Schiff bases, Thiazolidin-4-one, Analgesic, Anti-inflammatory.

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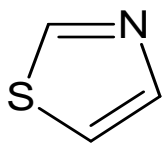
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INTRODUCTION:

The history of 4- thiazolidinone can be traced back to the early work on thiazoles. (1)



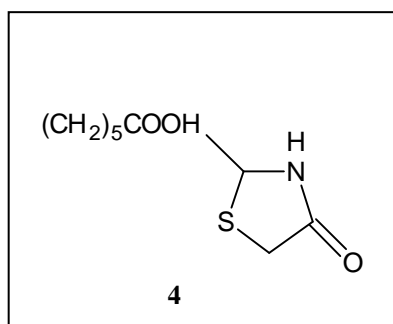
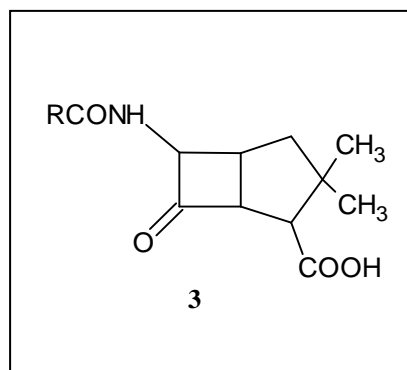
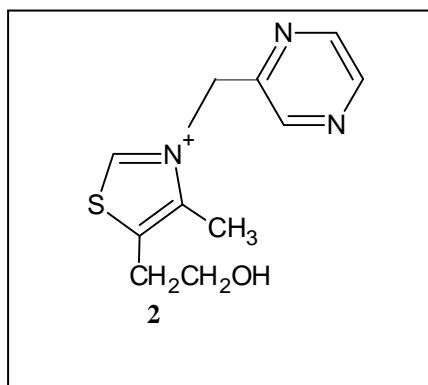
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Compound containing a simple thiazole nucleuses were first reported by Hantzsch[1] in a series of paper beginning from 1887. After this pioneering work, knowledge of the thiazole system developed shortly. Many thiazole derivatives were found to have biological and commercial interest. Green[2] in 1888 described a yellow

primuline base and dihydro-thio-*p*-toluidine. These were obtained by fusion of *p*-toluidine with sulfur. These compounds were recognized as benzothiazole derivatives. Subsequently many related compound were prepared.

In 1935, Williams et al [3] demonstrated the existence of a simple thiazole moiety in the structure of Vitamin B1 (2). It was combined with 4-thiazolidinone with a view to increase the antibacterial activity [4].

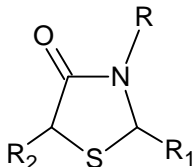
The historical importance of thiazole derivatives was further emphasized during the period 1941-45, when work on the structure of penicillins (3) showed the thiazolidine ring in it. The occurrence of thiazole derivative in nature was reported in 1952 when actithiazic acid (4), an antibiotic was found to be a 4-thiazolidinone derivative[5,6].



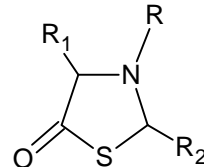
Thiazolidinones[7,8] are derivatives of thiazolidine, which belongs to an important group of heterocyclic compounds. Thiazolidinones with a carbonyl group at position 2,4 or 5 have been subject of extensive study in recent years [9-14].



2 - thiazolidinone



4 - thiazolidinone



5 - thiazolidinone

In recent years, 4-thiazolidinones and 2,4-thiazolidinediones have been among the most extensively investigated classes of organic compounds.

Thiazolidine derivatives are reported to show a variety of biological activities.

The presence of a thiazolidine ring in penicillin and related derivatives was the first recognition of its occurrence in nature [15]. Thiazolidine-4-one represents a prevalent scaffold in drug discovery [16]. Thiazolidine-4-ones have many interesting activity profiles, namely COX-1 inhibitors [17], inhibitors of the bacterial enzyme MurB, which was a precursor acting during the biosynthesis of peptidoglycan [18], non-nucleoside inhibitors of HIV-RT [19] and anti-histaminic agents [20]. Thiazolidinones has been considered as magic moiety (wonder nucleus), which is a core structure in various synthetic pharmaceuticals displaying a broad spectrum biological activities [21-23].

Condensed 4-thiazolidinones have received interest and attention from a large number of organic chemists, pharmacologists and biologists world over, on account of significant therapeutic and other properties associated with thiazolidinone nucleus. Applications of 4-thiazolidinones are manifold and versatile.

They are widely used as anticonvulsant [24], antimicrobial [25], anti-inflammatory [26], antihypertensive [27], hypnotic [28], antidiabetic [29], antifungal [30], antibacterial [31], antitumor [32], anti-HIV [33], antiviral [34], anticancer [35], cardiostonic [36], antitubercular [37], etc.

Condensed 4-thiazolidinones have also found applications in the synthesis of cyanine and merocyanine dyes and it has been reported that the introduction of arylidene moieties at different positions of the thiazolidinone ring enhanced biological activity [38-40]. Some authors examined the ability of this ligand structure to form complexes with some radionuclides for potential use in nuclear medicine [41].

OBJECTIVES

The search for an ideal chemotherapeutic agent has begun long ago. Molecular modification of a promising lead compound is still a major line of approach for the discovery of new drug. Molecular modification involves substituting, eliminating, or adding new moieties

to a parent lead compound, thereby making gradual changes in the structure of the compound resulting in gradual changes in the physico-chemical properties of the parent compound and thus biological activity of the compound. It is clear from the literature review that a number of substituted thiazolidinones derivatives are known to possess antitubercular, analgesic, anti-microbial, anti-HIV, anticonvulsant, antifungal activities. It has been reported that thiazolidinones also possess analgesic, anti-inflammatory and antimicrobial activities.

Thiazolidinones are of great interest due to their exceptional biological activity. The treatment of pain continues to be the subject of considerable pharmaceutical and clinical research in recent years. A systematic investigation of this class of heterocycle revealed that thiazolidinones containing pharmacologically active agents play an important role in medicinal chemistry. Chemotherapeutic analgesic and anti-inflammatory drugs are prescribed simultaneously in normal practice.

By considering the above factors, in the present investigation it was planned to undertake the research work as follows:

1. To synthesize some of the thiazolidin-4-one derivatives and to characterize the new compounds by analytical spectral methods viz. Infrared (IR), Mass spectra and Nuclear Magnetic Resonance (NMR).
2. To assess the acute toxicity of the derivatives synthesized following (OECD Guidelines - 420).
3. To screen few of the derivatives for their analgesic activities using Eddy's hot plate method.
4. To screen few of the derivatives for their anti-inflammatory activities using Carrageenan induced rat paw edema method.

METHODOLOGY:

The importance of thiazolidin-4-one moiety has been discussed in the previous chapter. Among the many methods available for the synthesis of thiazolidinone derivatives, in the present chapter a convenient and versatile methodology has been adopted for the synthesis of thiazolidin-4-one derivatives. In the present case semicarbazide/Thiosemicarbazide was reacted with benzoyl chloride to obtain N-

hydrazinocarbonylbenzene-1-carboxamide/*N*-hydrazinocarbothioylbenzene-1-carboxamide respectively. These were then condensed with various aldehydes to yield the intermediate Schiff bases. Thiazolidin-4-ones were prepared by the reaction of Schiff bases with mercaptoacetic acid in dry benzene by refluxing for 16-18 hrs.

All the reactions were carried out under prescribed laboratory conditions and were monitored by TLC technique using Precoated TLC plates. The products were purified by recrystallization. Melting points were determined by capillary method and were uncorrected.

¹H NMR spectra of the final compounds were recorded on Bruker Avance II 300 NMR spectrometer (300 MHz). All spectra were obtained in a mixture of DMSO. Further evidence about the structure was obtained by recording the mass spectrum of few typical compounds, along with their IR spectra and ¹H NMR.

Material and Methods

a) The entire chemicals used were procured from Qualingens, Himedia and Loba-chemicals. Purity of starting materials used for reaction was confirmed by checking their melting point or boiling point and by thin layer chromatography.

b) Melting points were determined in open capillary tube using precision melting point apparatus and uncorrected.

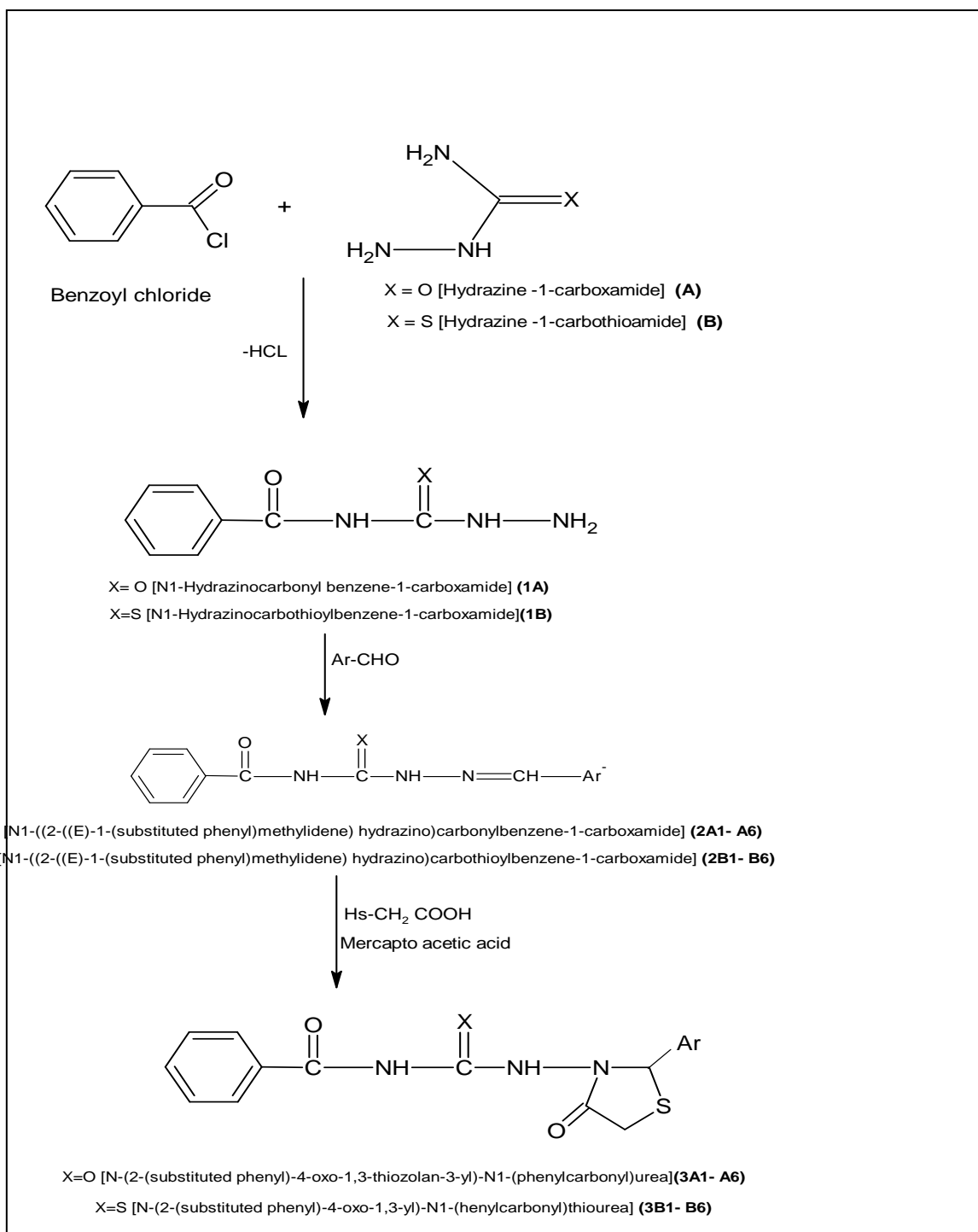
c) The FT-IR spectra of the synthesized compounds has been obtained from **NGSM Institute of Medical Sciences Deralakatte, Mangalore**. The IR spectra were carried out by SHIMADZU PERKIN EKMER 8201 PC IR SPECTROMETER using a thin film on potassium bromide pellets.

d) The ¹H NMR spectra of the selected compounds has been obtained from **Indian Institute of Chemical Technology Hyderabad**. The PMR spectra were recorded on **BRUKER AVANCE II 300 NMR SPECTROMETER** in a mixture of DMSO. Chemical shift values are reported as values in ppm relative to TMS (d=0) as internal standard.

e) The Mass spectrum of the selected synthesized compounds has been performed in **Indian Institute of Chemical Technology Hyderabad**. The FAB mass spectra were recorded on **JEOL SX-102/DA-6000 Mass Spectrometer** using Argon/Xenon (6Kv, 10Ma) as the FAB gas.

f) Purity of compounds was checked on "Silica Gel G" coated on laboratory micro slides prepared by dipping method or precoated plates, eluent was the mixture of different polar and non-polar solvents in varying proportions and detection was done either by observing in UV (ultra-violet) light or exposure to iodine vapours as required. The absence of TLC spots for starting materials and appearance of new TLC spot at different R_f value ensured the completion of reaction.

**EXPERIMENTAL:
SCHEME**



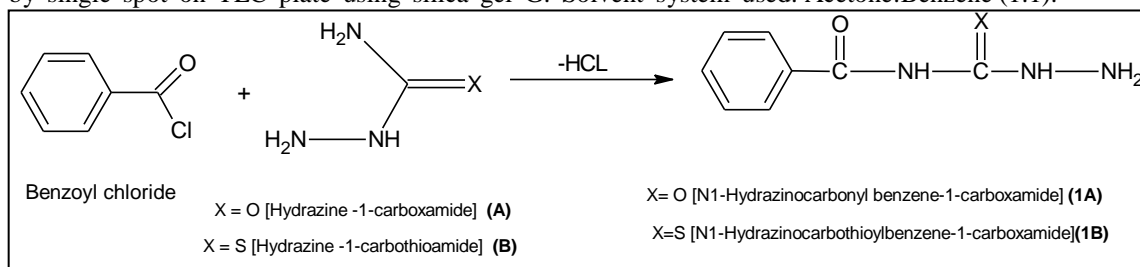
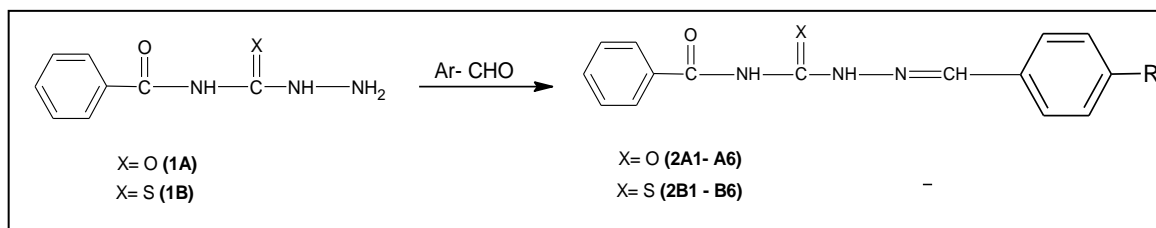
$\text{X} = \text{O}$	$\text{X} = \text{S}$	Ar
3A1	3B1	-H
3A2	3B2	4-NO ₂
3A3	3B3	4-OCH ₃
3A4	3B4	4-F
3A5	3B5	4-Cl
3A6	3B6	4-Br

SYNTHETIC STUDIES:

In the present dissertation by the condensation of semicarbazide or thiosemicarbazide with benzoyl chloride, substituted thiazolidine-4-ones derivatives synthesized. The synthesis consists of three steps, which are as follows:

Preparation of *N*-hydrazinocarbonylbenzene-1-carboxamide/*N*-hydrazinocarbothiyl benzene-1-carboxamide (1A and 1B):

The mixture of Semicarbazide (0.1 mol) and Thiosemicarbazide (0.1mol) in benzoyl chloride (0.1 mol) in 75 ml of dry alcohol was refluxed for 3-4 hours. The excess of alcohol was removed by distillation and the contents of the flask were poured onto crushed ice. The product separated was filtered, washed with water dried overnight and recrystallized from aqueous ethanol. The purity of all the compounds was established by single spot on TLC plate using silica gel G. Solvent system used: Acetone: Benzene (1:1).

**Preparation of *N*¹-((2-((*E*)-1-(Substituted Phenyl) methylidene)hydrazino) carbonyl benzene-1-carboxamide (2A1-2A6) / *N*¹-((2-((*E*)-1-(Substituted Phenyl) methylidene) hydrazino)carbothiyl benzene-1-carboxamide (2B1-2B6):**

To a mixture of *N*-hydrazinocarbonylbenzene-1-carboxamide/-hydrazino carbothiylbenzene-1-carboxamide (0.1mol) and aromatic aldehyde (0.1 mol) in dry ethanol (25 ml), 2-3 drops of Conc H₂SO₄ was added and was refluxed for 3-4 hours. The contents are poured onto crushed.

The solid, *N*¹-((2-((*E*)-1-(Substituted Phenyl) methylidene) hydrazino) carbonylbenzene-1-carboxamide/*N*¹-((2-((*E*)-1-(Substituted Phenyl) methylidene) hydrazino) carbothiylbenzene-1-carboxamide formed was filtered, dried and recrystallized from ethanol to obtain the compound in pure form. The purity of all the compounds was established by single spot on TLC plate using silica gel G. Solvent system used: Acetone: Benzene (1:1).

Preparation of *N*-(2-(substituted phenyl)-4-oxo-1,3-thiazolan-3-yl)-*N*¹-(phenylcarbonyl) urea (3A1-3A6)/*N*-(2-(substituted phenyl)-4-oxo-1,3-thiazolan-3-yl)-*N*¹-(phenylcarbonyl) thiourea (3B1-3B6):

To a mixture Schiff bases (0.1mol)(2A1-2A6&2B1-2B6) obtained as above mercapto acetic acid (0.1) in dry benzene(75ml) was added slowly to the above flask Dean stark apparatus was set to remove the water continuously which was formed during the course of reaction, then the reaction mixture was refluxed for 15-16 hrs and the excess of benzene was distilled off to get solid thiazolidin-4-ones derivatives. The solid product was filtered, dried and recrystallised from absolute alcohol. The purity of all the compounds was established by single spot on TLC plate using silica gel G.

Solvent system used: Acetone: Benzene (1:1).

BIOLOGICAL ACTIVITY:**ANALGESIC ACTIVITY:**

Analgesia is an ill-defined, unpleasant sensation, usually evoked by an external or internal noxious stimulus. Analgesic is a drug that selectively relieves pain by acting in the CNS or on peripheral pain mechanisms, without significantly altering consciousness.

Analgesics are divided into two groups, viz (a) Opioid/Narcotic /morphine like analgesics. (b) Non-opioid /Aspirin like /Antipyretic or anti-inflammatory analgesics. After the discovery of morphine as an analgesic, lot of research work has been carried out to increase the discovery of morphine as an analgesic to increase the efficacy of morphine and reduce toxic effects. Many non-steroidal anti-inflammatory drugs, (E.g. Diclofenac sodium, ketorolac, nimesulide, aspirin, ibuprofen etc) used as analgesics along with anti-inflammatory activity.

Animals:

All the experiments were carried out with male albino rats aged seven to eight weeks (180-250 g), obtained from the Central Animal House, Luqman College of pharmacy Gulbarga, Karnataka, India and were approved by the (IAEC). Annexure No.25/1/99-AWD. The animals were housed in polypropylene cages and provided with water and standard pellet diet (Karnataka Agro Food Corporation Limited, Bangalore, India).

Toxicity Study:

The acute toxicity study was carried out in adult female albino rats by "up and down" method (OECD guidelines-420). Swiss albino mice of either sex weighing 18-25 g were used for the study.

The thiazolidin-4-one derivatives are orally administered at a dose of 50, 100, 500, 1000, 3000 mg/kg of the body weight. After administration were observed continuously for the first three hours for any toxic manifestation. Thereafter, observations were made at regular intervals for 24 hrs.

Further the animals were under investigation up to a period of one week. This study showed that the synthesized compounds at a dose of 50 mg/kg of the body weight showed the reaction in experimental animals. No mortality was reported even after 72 hours. This indicates that the synthesized thiazolidine-4-one compounds are safe at a dose of 50 mg/kg of the body weight.

Method of testing

Eddy's Hot Plate Method[44]: In hot plate method, a group of 6 mice of either sex with an initial weight 20 to 25g are used for each dose. The hot plate, which is commercially available, consists of an electrically heated surface. The temperature is controlled between 55 to 56°C. This can be a copper plate or a heated glass surface.

The animals are placed on the hot plate and the time until either licking or jumping occurs is recorded by a stopwatch. The latency is recorded before and after 30, 60, 90 min following oral administration of the standard or the test compound.

Animals were randomly divided into six groups, each containing 6 animals as follows:

1. Group I: Served as control (Distilled water) p.o.
2. Group II: Standard group received ibuprofen (20mg/kg. p.o)
3. Group III and VI: The animal of group 3 and 6 were administered with the gum acacia suspension of thiazolidin-4-one derivatives in a dose of (50mg/kg.p.o) half an hour prior to study. Percentage protection against heat stimulus was taken as an index of analgesia.

Where:

It was calculated as:
$$\frac{I_t - I_o}{I_o} \times 100$$

I_t - Mean paw licking or jumping time of test or standard group

I_o - Mean paw licking or jumping time of control group.

ANTI-INFLAMMATORY ACTIVITY:

Inflammation is one of the common clinical conditions caused by a variety of noxious stimuli like chemicals, physical agents, microbes, local injury etc. Inflammation [45] is defined as the local response of living mammalian tissue to injury due to any agent, it is a body defence reaction in order to eliminate or limit the spread of injurious agent [46]. Tissue injury caused by introduction of a foreign antigen, trauma or local exposure to certain chemicals triggers the complex process of inflammation [47]. It consists of fluid stasis as well as accumulation of several cellular and non-cellular elements of the immune response.

There are several factors involved in the inflammatory reactions such as release of histamine, bradykinin and prostaglandins. Inflammation is not one event, but a series of events occurring in an orderly sequence, through not necessarily dependent on each other for their development.

Inflammation can be explained by three phenomena:

1. Dilation and increased permeability to Portion of the small blood vessels.
2. Emigration of leucocytes from venules and capillaries into the site of application.
3. Subsequent development of the cellular exudates in the injured tissues.

Inflammation is commonly divided into three phases:

1. Acute
2. Sub-acute
3. Chronic

Acute inflammation is the initial response to tissue injury; it is mediated by the releases of autocooids and usually precedes the developments of immune response. It is characterized by a sudden onset and

has short cause (a few minutes to several hours). Sub-acute inflammation is said to last for one to six weeks (or more) and is usually seen in the tubular structures like an appendix or fallopian tube. It is characterized by both vascular exulative changes of acute inflammation and proliferative changes of chronic inflammation.

Chronic inflammation persists for months or years and is characterized by proliferation of connective tissue and blood vessels.

In view of the above facts, it seemed desirable to evaluate the anti-inflammatory activity of some selected Thiazolidin-4-one compounds synthesized in the presents research programme.

Carrageenan induced rat paw edema[44]:

Among the many methods used for screening of anti-inflammatory drugs, one of the most commonly employed techniques is based upon the ability of such agents to inhibit the edema produced in the hind paw of the rat after injection of a phlogistic agent. (Carrageenan, egg albumin, histamine, etc) Rats were divided into six groups each consisting of six animals. They were fasted overnight and supplied with water *ad libitum* prior to the day of experiment.

1. Group I : Served as control (Distilled water) p.o.
2. Group II : Standard group received ibuprofen(20mg/kg.body weight. p.o)
3. Group III and VI: The animal of group 3 and 6 were administered with the gum acacia Suspension of thiazolidinone derivatives in a dose of (50mg/kg.p.o) half an hour prior to study.

Thirty minutes after the administration of test compound administration, 0.1 ml. of 0.6% carrageenan in distilled water was injected into the sub-plantar region of right hind paws of all groups. A mark was put on the leg at the

malleolus to facilitate uniform dipping at subsequent readings.

The paw edema volume was measured using plethysmometer at zero hr. (immediately after injecting carrageenan).

The same procedure was repeated at 1., 2, 3 and 4 hours. The difference between 1 hours and subsequent hours reading was taken as actual edema volume. The percentage inhibition of paw edema in the various treated groups was calculated by using the formula.

Percentage inhibition = $(1 - V_t/V_c) \times 100$

Where, V_t = is the edema volume in the drug treated group.

V_c = is the edema volume in the control group

RESULTS:

Biological activities

In view of the wide spectrum activities of the condensed 4-thiazolidinone nucleus, the synthesis of heterocyclic systems was undertaken in which 4-thiazolidinone nucleus is linked to another biologically active moiety.

The compounds screened for analgesic and anti-inflammatory activities following Eddy's hot plate method and Carrageenan induced paw edema method respectively at the concentration of 50mg/kg body weight. Ibuprofen, analgesic and anti-inflammatory drug was used as standard drug in both the studies. The results are compiled in **Table-1** and **Table-2** and graphically depicted in **Fig.1** and **Fig.2** respectively.

Analgesic activity:

The result of analgesic activity showed that all the compounds screened were found to possess significant analgesic activity and shown increase in reaction time upto 3hrs, afterwards the decreased in reaction time was observed as with standard drug also. Among the compounds evaluated for analgesic activity the compound **3A5** was found to be more potent as analgesic.

Table-1: Data showing analgesic activity of substituted thiazolidin-4-ones derivatives

Group	Dose (mg/kg)	% increase in reaction time (in sec.)				
		30 min.	1 hour	2 hour	3 hour	4 hour
-						
Control	Tween80,1%	3.433±0.166	3.567±0.272	3.400±0.288	3.400±0.300	3.33±0.409
Standard (Ibuprofen)	20	4.367±0.328	5.067±0.491	6.267±0.375**	8.600±0.264***	7.700±0.208***
3A3	50	3.533±0.166*	4.367±0.290**	5.400±0.360**	6.733±0.318**	6.667±0.233***
3A5	50	4.167±0.218**	5.233±0.352**	6.033±0.145***	7.733±0.578***	7.133±0.664**
3B2	50	3.623±0.166*	3.867±0.290*	4.400±0.360**	5.933±0.318***	5.879±0.263**
3B6	50	3.722±0.166*	3.916±0.221*	5.400±0.341**	6.933±0.353**	6.167±0.291**

Results are expressed in mean ± SEM (n=6) significance levels * P<0.05, **P < 0.01 and *** P < 0.001 as compared with the respective control.

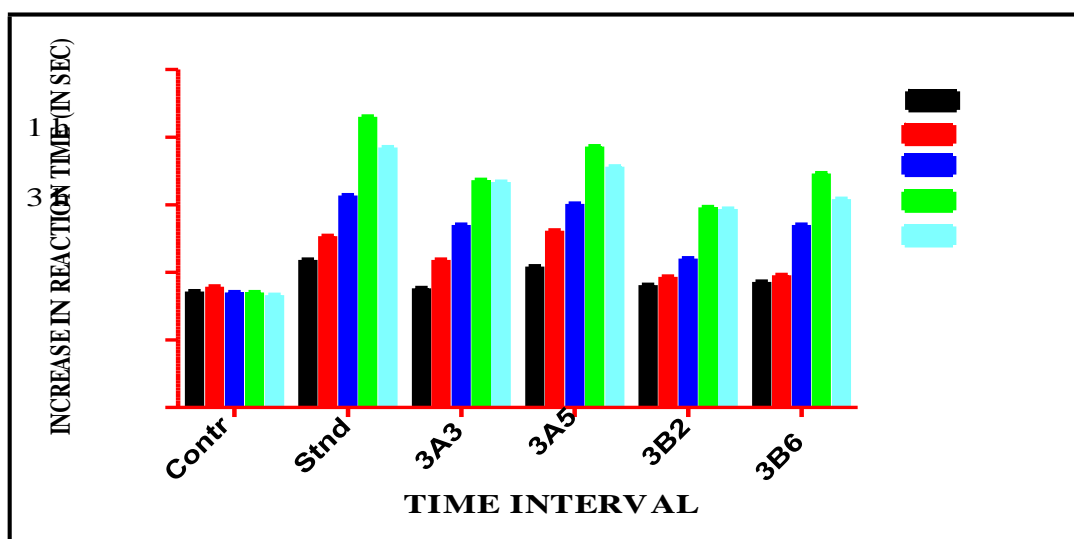


Fig. 1: Data showing analgesic activity of substituted thiazolidin-4-ones derivatives

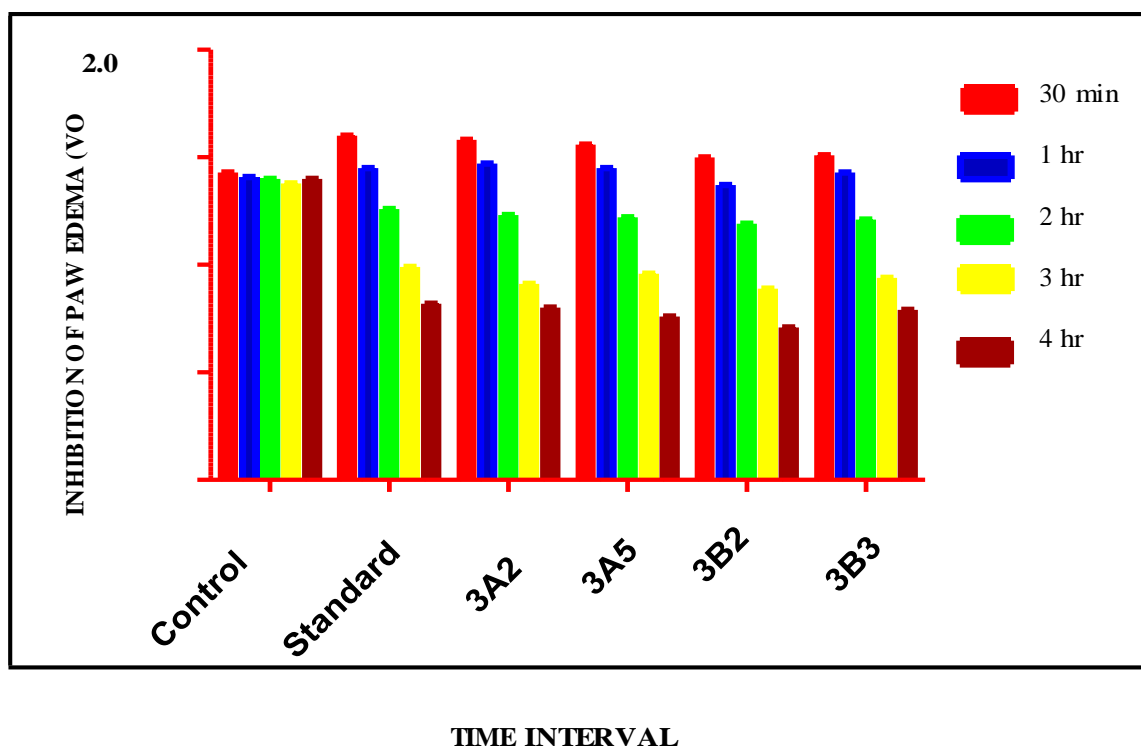
Anti-inflammatory:

The derivatives of the thiazolidine-4-ones evaluated for their anti-inflammatory activity have shown good anti-inflammatory activity and the results obtained at the end of 3rd and 4th hour were comparable to that of standard drug Ibuprofen. The onset of action by all the

compounds were found to be slow when compared to standard where as activity reducing the paw oedema volume was significantly increasing upto 4hrs that was comparable to the activity of standard drug Ibuprofen.

Table-2: Anti-inflammatory activity of Thiazolidin-4-one derivatives by Carrageenan induced paw edema method

Group	Dose (mg/kg)	Percentage reduction paw edema volume				
		30 min.	1 hour	2 hour	3 hour	4 hour
-	1 ml (1%)					
Control	Tween 80, 1%	1.43 ± 0.037	1.41 ± 0.066	1.40 ± 0.64	1.38 ± 0.037	1.40 ± 0.03
Standard (Ibuprofen)	50	1.60 ± 0.05	1.45 ± 0.0298	1.26 ± 0.04**	0.99 ± 0.033***	0.82 ± 0.014***
3A2	50	1.58 ± 0.042	1.47 ± 0.048**	1.23 ± 0.02*	0.91 ± 0.012**	0.80 ± 0.04**
3A5	50	1.56 ± 0.060	1.45 ± 0.037*	1.22 ± 0.014***	0.96 ± 0.018***	0.71 ± 0.030***
3B2	50	1.50 ± 0.043	1.37 ± 0.048*	1.19 ± 0.002***	0.89 ± 0.018***	0.76 ± 0.04***
3B3	50	1.51 ± 0.021	1.43 ± 0.034*	1.21 ± 0.006**	0.94 ± 0.044**	0.79 ± 0.015**



1 Fig. 2: Data showing Anti-inflammatory activity of substituted Thiazolidin-4- ones derivatives

DISCUSSION:

The analgesic activity studies following Eddy's hot plate method revealed that, the compounds evaluated **3A3**, **3A5**, **3B2** and **3B6** have found to possess significant analgesic activity. Particularly the compound **3A5** was found to be more potent than the other screened compounds and showed almost equipotent analgesic activity as that of standard drug Ibuprofen. The pattern of action of all the compounds along with the standard drug Ibuprofen, was similar throughout the study and all the compounds showed peak action at the end of 3 hours.

The compounds **3A2**, **3A5**, **3B2** and **3B3** were found to possess anti-inflammatory activity carried out by carrageenan induced rat paw edema method. Even though the onset of action was slow during first and second hours, later the activity of the compounds was of greater significance and comparable with that of standard drug ibuprofen.

SUMMARY:

The object of the present work is to synthesize certain new derivatives of thiazolidin-4-one which has been considered as magic moiety and is a core structure in various synthetic pharmaceuticals displaying wide spectrum of biological activities.

The target molecules were successfully synthesized in which thiazolidin-4-one nucleus is linked to other biologically active moieties. The purity of the compounds synthesized was established by using TLC technique and the structures were established by their FT-IR, ¹H NMR and MASS spectrum.

All the derivatives synthesized were screened for their analgesic and anti-inflammatory activities.

The compounds evaluated for analgesic activity have been found to possess significant activity. One of the compounds showed almost equipotent analgesic activity as that of standard drug. The anti-inflammatory activity screening of few of the compounds also suggests that these possessed significant anti-inflammatory activity that is comparable with the standard drug. All these above results only showed that the thiazolidin-4-one moiety can be rich source for further exploitation. The thiazolidin-4-one moiety needs more attention and if it is suitably exploited by molecular modification can still give better lead compounds

CONCLUSION:

The compounds evaluated for analgesic activity have been shown to possess significant analgesic activity. The pattern of the action throughout the study was similar to that of standard ibuprofen and **3A5** has been found to possess

almost equipotent activity to that of standard ibuprofen.

The thiazolidin-4-one derivatives evaluated for anti-inflammatory activity shown slow onset of action and at the end of 3rd and 4th hour the activity was significant and comparable to that of standard ibuprofen.

From the above results one can establish that the synthesized substituted thiazolidinones can be rich source of exploitation. Therefore, in the search of new generation of active compounds, it may worth while to explore the possibility in this area by making or introducing different functional group as substitution of primary amine moieties which may result in better pharmacological agents with higher potency.

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