SUMMARY

Recent epidemiological studies have revealed that roughly more than 800 million people of the world are suffering from different types of arthritis leading to the loss of several million working man-days.

For the alleviation of inflammation both acute and chronic as well as for the treatment of inflammatory diseases, many drugs like Indomethacin, Sulindac, Ibuprofen, Naproxen, Piroxicam, Nabumetone etc. are in use. The corticosteroids have high anti-inflammatory activity and provide significant relief in many types of inflammation. But they have major disadvantage of equally harmful side-effects. Narcotic analgesics which are highly effective in relieving pain, lack the property to suppress inflammation. Thus the only drugs that are commonly used in inflammatory disorders are non-steroidal anti-inflammatory agents (NSAIDs) which have comparatively less side effects. These agents are a heterogenous group of compounds which have a carboxy group in their structure and are therefore acidic in nature. The important acidic non-steroidal compounds are Aspirin, Indomethacin, Mefenamic Acid, Flufenaminc Acid, Naproxen, Sulindac, Tolmetin, Ibuprofen, Naproxen etc. Most of these acidic compounds are organic acids and non-selectively inhibit the COX-1 and COX-2 enzymes. Due to their modest selectivity of inhibition of COX-1, they exhibit these drugs possessed serious inherent side-effects like gastric haemorrhage, perforation, bone marrow depression and particularly gastric ulcer. On the contrary the recently developed non-steroidal, non acidic or weakly acidic anti-inflammatory agents like nabumetone are preferentially COX-2 isoform inhibitor. Since COX-2 is not normally present in tissues but is induced at the site of inflammation, the COX-2 inhibitors selectively inhibit the inflammation and are devoid of producing gastric ulceration which is due to suppression of COX-1, therefore they posses substantially lower incidence of gastric ulcer.
In spite of considerable progress in the field of anti-inflammatory drug, there is no single drug available which can be termed as ideal. Since currently available drugs show variable response in different individuals and possess serious side effects like gastric haemorrhage, perforation, bone marrow depression and gastric ulcer. The search for the better drug for the treatment of inflammation is the need of the day.

Thus, overwhelming bulk of development of novel drug encompasses molecular modification of the currently known agents. The work delineated in the present study is based on the approach. In the present work, the following types of compounds have been synthesized and evaluated for their anti-inflammatory activity. The work delineated in the present study is based on this approach. Number of indoles, phenothiazines, naphthalenes, quinazolinones, anthranilic acid, thiazoles, formazenes, azetidinones, pyrazoles, thiadiazoles, oxadiazoles, thiazolidinones etc. have been synthesized and evaluated for the anti-inflammatory and analgesic activities which are summarized as follows:

**SCHEME-I**

3-Chloroacetyl-2-(4-chlorophenyl) indole; 3-(2'-aminothiazol-4'-yl)-2-(4-chlorophenyl) indole; 3-(2'-aminooxazol-4'-yl)-2-(4-chlorophenyl) indole; N-(substituted benzylidene)-4-(2-(4-chlorophenyl)-1H-indol-3-yl)thiazol-2-amine; N-(substituted benzylidene)-4-(2-(4-chlorophenyl)-1H-indol-3-yl)oxazole-2-amine; N-((substituted phenyl)((E)-(substituted phenyl)diazenyl)methylene-4-(2-4-chlorophenyl)-1H-indole-3-yl) thiazol-2-amine; N-((substituted phenyl)((E)-(substituted phenyl)diazenyl)methylene-4-(2-4-chlorophenyl)-1H-indole-3-yl)-4,5-dihydrooxazol-2-amine (4a'-4h').

Indole moiety is an essential component of different pharmacological and physiological active endogenous as well as exogenous substances. Compounds having indole as the parent moiety are associated with different medicinal chemistry like antiinflammatory, anticonvulsant, hypnotic, antidepressant,
antiparkinsonian, and cardiovascular etc. The discovery of Indomethacin, Sulindac, indole derivatives, as potent anti-inflammatory agents, has led to the exploration of indole nucleus. Moreover, large number of indole derivatives having substitution at 1, 2 and 3 positions by different heterocyclic moieties increases the anti-inflammatory potential of indole derivatives. In the light of these observations, scientists have synthesized several indole derivatives which possess potent anti-inflammatory activity.

The synthetic route of compounds is shown in scheme-1. Reaction of 2-(4-chlorophenyl indole and chloroacetyl chloride yielded the starting compound (1) i.e. 3-chloroacetyl-2-(4-chlorophenyl) indole. This compound on reaction with thiourea and urea yielded the compounds 2 and 2' respectively. These compounds on refluxing with different 2-substituted-3-indolealdehydes in presence of glacial acetic acid resulting into the next compounds i.e. N-(substituted benzylidene)-4-(2-(4-chlorophenyl)-1H-indol-3-yl)thiazol-2-amine (3a-3d) and N-(substituted benzylidene)-4-(2-(4-chlorophenyl)-1H-indol-3-yl)-oxazole-2-amine (3a'-3d'). By diazotising these compounds (3a-3d & 3a'-3d') with substituted anilines yielded the next compounds N-((substituted phenyl)((E)-(substituted phenyl) diazenyl)methylene-4-(2-4-chlorophenyl)-1H-indole-3-yl) thiazol-2-amine (4a-4h) and N-((substituted phenyl)((E)-(substituted phenyl) diazenyl)methylene-4-(2-4-chloro-phenyl)-1H-indole-3-yl)oxazol-2-amine (4a'-4h'). The structure of all the newly synthesized compounds was confirmed on the basis of spectral (IR, ¹H NMR and mass and analytical data) Compounds 3a-3d have shown the antiinflammatory activity from 19.7-53.3 %. When the compound was substituted with 4-chloro group at the second position of thiazol moiety (3b) it showed better anti-inflammatory activity (53.3%) than reference drug (38.8%) at the dose of 50 mg/kg p.o. Due to the potentiality, this compound and reference drug were tested at the three graded doses (25, 50 and 100 mg/kg p.o.). Compound 3b have shown better activity at 25 and 50 mg/kg. p.o. (36.4, 53.3% respectively) than reference drug (15.2, 38.8% respectively).
While the same compound possess almost equal degree of anti-inflammatory activity (68.2%) at the dose of 100 mg/kg p.o. as compared to standard drug (65.4%). Compound 3a, which was substituted by 2-chloro also showed good activity (31.8%) but it is less active than standard drug. When the compound was substituted by 2-bromo group at 2-position of indole moiety (3c) it was found to be less active (25.8%) than 3a and 3b. While compound 3d, having phenyl group at the second position exhibited lesser degree of antiinflammatory activity (19.7%) than 3a-3c.

The compounds 4a to 4g, which were formed by the substitution of hydrogen of azomethine group of 3a-3d with 4-methoxy phenyl azo (4a, 4c, 4e and 4g) and 4-chlorophenyl azo (4b, 4d, 4f and 4h) groups respectively, have shown mild degree of anti-inflammatory activity (9.6-23.1%). Compound 4h, which was substituted by 4-chloro phenyl azo group have shown good anti-inflammatory activity (23.1%) among these eight compounds, while the compound 4b, which was also substituted by 4-chlorophenyl azo group and having unsubstituted indole exhibited mild degree of activity (9.6%). The other compounds of this step have shown the activity ranging between 11.5%-19.2%.

Indolidene oxazolyl indoles (3a'-3c') exhibited lesser degree of inhibition of oedema (17.3-22.7%) as compared to indolidene thiazolyl indoles (3a-3c). On the contrary compound 3d' which was substituted by 4-bromophenyl indole possesses greater activity (25.3%) than thiazolyl indole (3d, 17.5%) which was also substituted by same moiety but was less active than phenyl butazone.

However, oxazolyl diazenyles (4a'-4h') were formed by diazotisation of indolidene oxazolyl indoles with 4-methoxy phenyl azo (4a', 4c', 4e', 4g') and 4-chlorophenyl azo groups (4b', 4d', 4f', 4h') respectively. The activity of these compounds range between 16.2-27.9%. It is interesting that 4-chlorophenyl azo substituted compounds (4d', 4f' and 4h') were found to be more active than 4-methoxy azo substituted compounds (4c', 4e' and 4g') but 4a', substituted with
4-methoxy phenyl azo group was found to be more active (20.6%) than 4b' (16.2%), which was substituted by 4-chlorophenyl azo group.

All these compounds generally more active than thiazolyl formazanes (9.6-23.1%).

SCHEME-II

2-Chloro-10-chloroacetyl phenothiazine (1); 2-chloro-10- (2-aminothiazol-4-yl)-phenothiazine (2); 2-chloro-10- (2-aminooxazol-4-yl)-phenothiazine (2'); 2-Chloro-10- [2-(substituted benzylidene)-aminothiazol-4-yl]-phenothiazines (3a-3g); 2-chloro-10-[2-(substituted benzyldene)-aminooxazol-4-yl]-phenothiazines (3a'-3g'); 2-chloro-10-[2-[3'-chloro-2'-oxo-4'-(substituted phenyl)-1'-azetidinyl]-thiazol-4-yl]-phenothiazines (4a-4g); 2-chloro-10-[2-[3'-chloro-2'-oxo-4'-(substituted phenyl)-1'-azetidinyl]-oxazol-4-yl]-phenothiazines (4a'-4g').

Phenothiazines possess a wide spectrum of pharmacological activities like anti-inflammatory, anti-psychotic, anti-parkinsonian, anti-convulsant activities etc. Furthermore, the introduction of different aryl, alkyl or heterocyclic moieties at 10-or 2-position of phenothiazine nucleus markedly enhances the anti-inflammatory properties. Various scientist have synthesized several 2- or 10-substituted derivatives of phenothiazine and reported the promising anti-inflammatory activity.

Compound 1 i.e. 2-chloro-10-chloroacetyl phenothiazine was prepared by the reaction of 2-chloro phenothiazine with chloroacetyl chloride in dry benzene chloroform. Compound 1 when reacted with urea and thiourea yielded compounds 2 i.e. 2-chloro-10-(2-aminothiazol-4-yl) phenothiazine and 2' i.e. 2-chloro-10-(2-aminooxazol-4-yl) phenothiazine respectively. These compounds 2 and 2' on reacting with substituted aldehydes gave 2-chloro-10-[2-substituted phenyl methylene amino thiazol-4-yl]phenothiazines 3a-3g and corresponding oxazoles 3a'-3g' respectively. The next compounds (azetidinones) i.e. 2-chloro-10-[2-[3'-chloro-2'-oxo-4'-(substituted-phenyl)1'-azetidinyl] thiazol-4-yl]
phenothiazines 4a-4g and their oxazoles 4a'-4g' were prepared from the compounds 3a-3g and 3a'-3g' respectively on treatment with chloroacetyl chloride in the presence of tri ethylamine. The structures of these compounds were elucidated by elemental (C,N,H) analysis, IR, ¹H-NMR and mass spectroscopic data.

The antiinflammatory activity of the compounds (3a-3g), i.e. 2-chloro-10-[2-(substituted benzylidene)-aminothiazol-4-yl]-phenothiazines varying from 10.82 to 27.03%. It is clear that when the compound was substituted with 2, 6-dichlorophenyl (compound 3a, 27.03%) showed more potent anti-inflammatory activity than the compound which was substituted with 2, 6-dibromophenyl (compound 3b, 16.22%) and with 2, 6-diiodophenyl group (compound 3c, 13.52%). The compounds 3d and 3e, substituted by 2-chloro and 2-bromophenyl groups respectively were less active (24.33%, 21.63%) than compound 3a but more active than 3b. However the compound 3f, which was substituted by 2-iodophenyl group was found to be less active (10.82%) than its disubstituted compound (3c). And compound 3g which was substituted by N,N-dimethyl aminophenyl exhibited promising anti-inflammatory activity (18.92%).

It is interestingly enough, the anti-inflammatory activity of 2-chloro-10- [2-{3'-chloro-2'-oxo-4'- (substitutedphenyl) 1'-azetidinyl} thiazol-4-yl] phenothiazines (4a-4g) is more (ranging between 12.59 to 29.55%) than that of their parent compounds (3a-3g). Moreover, corresponding oxazoles, i.e. 2-chloro-10-[2-(substitutedbenzylidene) aminooxazol-4-yl] phenothiazines (3a'-3g') showed a decrease in activity (9.24-25.21%) as compared to their corresponding thiazoles (3a-3g).

The cyclised compounds (4a'-4g'), i.e. 2-chloro-10-[2-{3'-chloro-2'-oxo-4'-(substitutedphenyl) 1'-azetidinyl} oxazol-4-yl] phenothiazines, very clearly showed an increase in anti-inflammatory activity (14.69-48.56%) at a dose of 50 mg/kg. p.o. The compound which was substituted by 2, 6-dichlorophenyl
group (4a') was more active (48.56%) than the reference drug phenylbutazone (38.8%) at 50 mg/kg p.o. Considering the potentiality of compound 4a', it was tested at three graded doses, i.e. 25, 50 and 100 mg/kg p.o. This compound showed better activity (35.93%, 48.56%, 71.42%) at all the three tested doses (25, 50 and 100 mg/kg p.o. respectively) as compared to reference drug phenylbutazone (15.2%, 38.8%, 65.4%).

SCHEME-III

7-Methoxy-β-(chloroacetyl)amino naphthalene (1); 7-methoxy-β-(2-aminothiazol-4-yl)amino naphthalene (2); 7-methoxy-β-[2-(2-substituted-indole)-aminothiazol-4-yl]-amino naphthalenes (3a-3d); 7-methoxy-β-[2-(1'di/mono substituted phenyl-3'-2-substituted indole formazan -4'-yl)-thiazol-4-yl]-amino naphthalenes (4a-4l); 7-methoxy-β-[2-(3'-chboro-2'-oxo-4'-2-substitutedindole-1'-azetidinyl)-thiazol-4-yl]-aminonaphthalenes (5a-5d).

Naproxen and Nabumetone, substituted naphthalene derivatives, are one of the most widely used NSAIDs other than Aspirin, and have been found to possess potent anti-inflammatory activity. Heterocyclic/aliphatic functionalized systematic variations at α- or β-position of naphthalene nucleus markedly modulate the anti-inflammatory activity. Some of the naphthalene derivatives exhibiting various biological activities especially anti-inflammatory.

The chemical synthesis initiates with the reaction of chloroacetyl chloride to 7-methoxy-β-aminonaphthalene to yield 7-methoxy-β-(chloroacetyl)amino naphthalene (1). This compound in ethanol was refluxed with thiourea to form 7-methoxy-β-(2-amino-thiazol-4-yl)amino naphthalene (2), on reaction with various 2-substituted 3-indole aldehydes compound 2 converted into compounds (3a-3d) 7-methoxy-β-[2-(2-substituted-indole)-aminothiazol-4-yl]-amino naphthalenes. Further on diazotisation of above compounds converted into corresponding formazans (4a-4l) 7-methoxy-β-[2-(1'di/mono substituted phenyl-3'-2-substituted indole formazan -4'-yl)-thiazol-4-yl]-amino
naphthalenes, while azetidinyl (5a-5d) 7-methoxy-β-[2-(3′-chloro-2′-oxo-4′-2-substitutedindole-1′-azetidinyl)-thiazol-4-yl]-aminonaphthalenes of compounds (3a-3d) have been formed by the reaction of triethyl amine and chloroacetyl chloride.

The compounds 3a-3d have shown varying degree of anti-inflammatory activity, i.e. varying from 18.75-35.41%. It has been observed that the compound 3c, in which azomethine (N=CH) group having indole moiety with ethyl group at second position, showed the low degree (18.75%) of anti-inflammatory activity. However, the compound 3d which has indole moiety with phenyl group at second position showed the higher degree (35.41%) of activity as compared to 3c.

Moreover, conversion of these compounds (3a-3d) into formazanes (4a-4l), generally shown the low degree of anti-inflammatory activity (15.27-34.72%) than 3a-3d.

The azetidinones (5a-5d), which are formed by the cyclisation of compounds 3a-3d, exhibited better activity (20.68-60.34%) than the compounds 3a-3d. The compound 5d showed better anti-inflammatory activity (60.34%) than that of standard drug phenyl butazone (38.8%) at the dose of 50mg/kg p.o. Considering its potentiality, this compound and standard drug were tested at the three graded doses, i.e. 25, 50 and 100 mg/kg p.o. This compound (5d) showed better activity (44.82, 60.34, 75.87%) at all the three doses 25, 50 and 100 mg/kg p.o. as compared to reference drug, phenyl butazone (15.2, 38.8, 65.4%).

**SCHEME-IV**

2-Ethyl-6-bromo-benzoazin-4-one (1); 3-anilino-2-ethyl-6-bromo-quinazolin-4-one (2); 3-(N-chloroacetyl)-anilino-2-ethyl-6-bromo-quinazolin-4-one (3); 4-phenyl-6-dihydro-2-ethyl-10-bromo-[1′,2′,4′]-triazino-quinazolin-5-one (4); 5-Chloro-4-phenyl-2-ethyl-10-bromo-[1′,2′,4′]-triazino-quinazoline (5); 5-Hydrazino-4-phenyl-2-ethyl-10-
bromo-[1',2',4']-triazino-quinazoline (6); 5-substituted-arylidene-hydrazino-4-phenyl-2-ethyl-10-bromo-[1',2',4']-triazino-quinazolines (7a-7g); 5-(3'-methyl-2''-oxo-5'''-substituted arylidene-4'''-thiazolidinyl)-amino-4-phenyl-2-ethyl-10-bromo-[1',2',4']-triazino-quinazoliens (8a-8g).

Quinazolinones are the versatile nitrogen heterocyclic compounds displaying a wide-variety of biological and pharmacological activities like anti-inflammatory, anticonvulsant, hypnotic, sedative, tranquilizers, antidepressant and anti-parkinsonian in animals as well as in human system. The chemistry and pharmacology of quinazolinones have been of great interest to medicinal chemists. Recently several scientists have elucidated that quinazolinone system possess the various variable sites like position 2 and 3, which can be suitably modified by the introduction of different heterocyclic moieties to yield the potent anti-inflammatory agents. Various derivatives of quinazolinone have been synthesized and evaluated for anti-inflammatory activity.

Compound (1) was prepared by the reaction of 5-bromoanthranilic acid with propionic anhydride, which converted into quinazolinone derivative (2) on reaction with phenyl hydrazine. Compound (2) in DMF, and chloroacetyl chloride after refluxing converted into 3-(N-chloroacetyl)-anilino-2-ethyl-6-bromo-quinazolin-4-one (3). This compound converted into triazino quinazolinone (4) on reacting with ammonium acetate. The next compound (5) was prepared by heating the previous compound with POCl₃. Compound 5 in acetone on refluxing with hydrazine hydrate synthesized compound 5-Hydrazino-4-phenyl-2-ethyl-10-bromo-[1',2',4']-triazino-quinazoline (6).

This compound reacted with various substituted benzaldehydes in presence of glacial acetic acid to yielded 5-substituted-arylidene-hydrazino-4-phenyl-2-ethyl-10-bromo-[1',2',4']-triazino-quinazolines (7a-7g) and these were converted into thiazolidiniles (8a-8g) 5-(3''-methyl-2''-oxo-5'''-substituted arylidene-4'''-thiazolidinyl)-amino-4-phenyl-2-ethyl-10-bromo-[1',2',4']-triazino-quinazoliens on reacting with thiolactic acid.
The anti-inflammatory activities of synthesized compounds have been depicted in tables-2 and 3. Compounds 7a-7g have shown anti-inflammatory activity from 9.52 to 33.33% out of these seven compounds, compound 7a and 7d, which were substituted by dichloro and monochloro phenyl respectively have shown good anti-inflammatory activity (30.95 and 23.81%). But the compound which was substituted by 4-methoxy phenyl (7g) have shown better anti-inflammatory activity (33.33%) than out of these seven compounds. While the other four compounds (7b, 7c, 7e and 7f) were found to be less active (19.04, 14.28, 11.90, 9.52% respectively) than other three compounds. But all these were also found to be less active than reference drug phenyl butazone.

Compounds 8a-8g, which were respectively formed by the reaction of thiolactic acid with compounds 7a-7g in presence of 1, 4-dioxane. These compounds have shown mild degree of anti-inflammatory activity (16.07-57.14%). Out of these seven compounds, the compound which was substituted by 4-methoxyphenyl (8g), has shown anti-inflammatory activity (57.14%) more than reference drug phenyl butazone (38.8%) at the dose of 50mg/kg. p.o. Due to the potential activity this compound was also tested at the three graded doses (25, 50 and 100 mg/kg p.o.) Compound 8g have shown better activity at 25 and 50 mg/kg p.o. (41.07 and 57.14% respectively) than reference drugs (15.2, 38.8% respectively) but shown almost same degree of anti-inflammatory activity (71.42%) as phenyl butazone (65.4%) at the dose of 100 mg/kg p.o. The other compounds have shown less activity than reference drug. While compound 8a which was substituted by 2, 6-dichlorophenyl has shown almost same degree (37.5%) of anti-inflammatory activity as phenyl butazone (38.8%).

**SCHEME-V**

5-Bromoanthranilic acid (1); 5-bromo-N- ethylacetoanthranilic acid (2); 5-bromo-N-(semicarbazido-carbonyl-methyl) anthranilic acid (3); 5-bromo-N-(2'-amino-1',3',4'-oxadiazol-5'-yl-methyl)-anthranilic acid (4); 5-bromo-
N-(2'-aminoacetyl-1',3',4'-oxadiazol-5'-yl-methyl)-anthranilic acid (5); 5-bromo-N-[2'-amino-(2-substituted indolidene)-acetyl-1',3',4'-oxadiazol-5'-yl-methyl]-anthranilic acids (6a-6d); 5-bromo-N-[2'-amino-{1''-acetyl-5''-(2-substituted indolyl)-2''-pyrazolin-3''-yl}-1',3',4'-oxadiazol-5'-yl-methyl]-anthranilic acids (7a-7d); N-ethylacetoanthranilic acid (1'); N-(thiosemicarbazido-carbonyl-methyl)-anthranilic acid (2); N-(2'-amino-1',3',4'-thiadiazol-5'-yl-methyl)-anthranilic acid (3'); N-(2'-aminoacetyl-1',3',4'-thiadiazol-5'-yl-methyl)-anthranilic acid (4'); N-[2'-amino-(2-substituted-indolidene)-acetyl-1',3',4'-thiadiazol-5'-yl-methyl]-anthranilic acids (5a'-5d'); N-[2'-amino-{1''-acetyl-5''-(2-substituted indolyl)-2''-pyrazolin-3''-yl}-1',3',4'-thiadiazol-5'-yl-methyl]-anthranilic acids (6a'-6d').

The fenamates are a family of non-steroidal anti-inflammatory drugs (NSAIDs), which are derivatives of N-phenylanthranilic acid. This family includes mefenamic, meclofenamic and flufenamic acid etc., which are useful agents for clinical treatment of inflammatory disorders. The fenamates have anti-inflammatory, analgesic and anti-pyretic properties. Considerable amount of work has been done on structural variation of this sub-class of NSAIDs. It has been observed that the best know NSAIDs are acidic in nature. Furthermore, substitution pattern at N-position of anthranilic acid plays a pivotal role in delineating the anti-inflammatory activity of these agents. Structural variations, as given by various scientists, which prove that anthranilic acid derivatives have potent anti inflammatory activity.

5-Bromoanthranilic acid (1) was synthesized by the reaction of bromine in acetic acid and anthranilic acid, which was converted into compound (2) on reacting with ethylchloroacetate and anhydrous K₂CO₃ in acetone while the corresponding compound (1') N-ethylacetoanthranilic acid was prepared by the reaction of anthranilic acid with ethylchloroacetate and anhydrous K₂CO₃.
The next compound 5-bromo-N-(semicarbazo-carbonyl-methyl)-anthranilic acid (3) and corresponding compound (2') synthesized by the reaction of compound 2 and (1') with semicarbazide hydrochloride. Cyclisation of these compounds into oxazoles (4&3') took place on reacting with sulphuric acid. These compounds on reacting with acetyl chloride converted into compound (5) 5-bromo-N-(2'-aminoacetyl-1',3',4',-oxadiazol-5'-yl-methyl)-anthranilic acid and (4') N-(2'-aminoacetyl-1', 3', 4'-thiadiazol -5-yl-methyl)-anthranilic acid respectively, which yielded compounds 5-bromo-N-[2'-amino-(2-substituted indolidene)-acetyl-1',3',4'-oxadiazol-5'-yl-methyl]-anthranilic acids (6a-6d) and N-[2'-amino-(2-substituted-indoline)-acetyl-1',3',4'-thiadiazol-5'-yl-methyl]-anthranilic acids (5a'-5d') by the reaction of various 2-substituted 3-indolealdehydes. The pyrazolines of next step 5-bromo-N-[2'-amino-{1"-acetyl-5"-(2-substitutedindolyl)-2"-pyrazolin-3"-yl]}-1',3',4'-oxadiazol-5'-yl-methyl]-anthranilic acids (7a-7d) and N-[2'-amino-{1"-acetyl-5"-(2-substituted indolyl)-2"-pyrazolin-3"-yl]}-1',3',4'-thiadiazol-5'-yl-methyl]-anthranilic acids (6a'-6d') were synthesized by the reaction of hydrazine hydrate with previous compounds.

Compounds 6a-6d have shown the varying range (17.77-28.88%) of anti-inflammatory activity. Out of these the compound which was substituted by 2-methylindole (6b) was found to possess good activity (28.88%). However the corresponding thiadiazole anthranilic acids (5a'-5d') have shown less activity (13.23-25.03%) than oxadiazole anthranilic acids.

Compounds 7a-7d, which were respectively formed by the reaction of hydrazine hydrate with compounds 6a-6d in presence of glacial acetic acid have shown better activity (21.15-32.69%) as compared to their parent compounds (6a-6d). Out of 7a-7d the compound 7c which was substituted by 2-ethylindole possess prominent anti-inflammatory activity (32.69%). Whereas, corresponding thiadiazoles (6a'-6d') have shown better range of anti-inflammatory activity (21.62-51.35%). Out of these the compound which was substituted by phenylindole (6d') showed less activity (21.62%). Compound 6a'
which was substituted by indole possess better activity (32.43%) than the compound which have methylindole moiety (6b') (24.32%). The compound 6c' which was substituted by ethylindole was found to be most potent inflammation inhibitor and possess 51.35% activity at the dose of 50 mg/kg p.o. On considering the potentiality it was tested at all the three graded doses (25, 50 and 100 mg/kg p.o.) and was found to more active than reference drug phenyl butazone at the dose of 25 and 50 mg/kg p.o. (6c' = 37.83, 51.35% and phenyl butazone = 15.2, 38.8%), but found to having almost same activity (67.56%) at the dose of 100 mg/kg p.o. as reference drug (65.4%).