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# Effect of methotrexate and pioglitazone in treatment of rheumatoid arthritis: Experimental study done on albino rat

**[1] Dr. AN Mishra, [2] Dr. Gajendra Kumar**
[1] MD (Pharmacology), Prof and HOD Pharmacology, MGM Medical College, Jamshedpur, Jharkhand, India
[2] MD (Pharmacology), Assoc. Prof Pharmacology, MGM Medical College, Jamshedpur, Jharkhand, India

**Abstract**
**Introduction:** Rheumatoid arthritis is a chronic inflamatory disorder which involves the immobilicity of the joint clinical course of the disease is very wide ranging from mild to server disease with extra articular manifestation NSAIDS, disease modifying and rheumatic drugs (DMARD) like methotrexate, sulfasalazine, Hydroxychloroquire are used for treatment. When used as a single drug therapy the efficacy and potenty of these drugs are low therefore multidrug therapy is used more than morodrug therapy. Methortrexate is the primary drug of Rleamatoid arthritis. Suggested mechanism includes (I) inhibition of T- cell proliferation by affecting purine and pyrimidine metabolism (II) inhibits aceumulation of monocytes at the site of inflammation in the joints. Pioglitazone is oral antidiafetic drugs. They induce apoptosis in the mecrophage and T-cymptocytes which are lmportant in perpituatiing rhenrnatoid arthritis. Prerent study was done to find out the effent of methotrexate and pioglitanone combination thesapy in the treatment of rheumatoid arthritis in albino rat models.
**Methods:** Arthritis was induced in twenty (20) albino rats by giving single dose of subcutaneous injeetion into five groups. Each group contain four rats two control groups one group treated with methotrexate only, one group with pioglitazone only, one with combined methotrexate anp pioglitazone. Treatment was given from day 10 to day 21 of the induction of diseace. Parameters used for the assessment were paw edema & Rediological assessment of joint. P value of 0.05 was considered significant. Paw diameter on day zero paw diameter of both hind limbs of each rat was measured. These measurements were repeated on day 3, 6, 9, 12, 15, 18 and 21 after enjection of CFA. Pas diameter in group II to V on day I increases upto 0.71 ± 0.013, 0.72 ± 0.013, 0.73 ± 0.014, 0.7 ± 0.014 as compared to group I (0.62 ± 0.022). However after treatment paw diameter on day 21 decreared from the value of day 9 in group III to V (0.68±0.012, 0.66±0.2, 0.63±0.011) but in group II value increases upto 0.78±0.019 value in the group I was constant.
**Conclusion:** Significant improvement was observed in the group treated with methotrexate and combination of methotrexate and pioglitazone as compared to piogitazone mono drug therapy which shous no significant improment. We concluded that methotrexate and pioglitanove combination offer better control in rheumatoid arthritis as compared to mono therapy with methopexate or pioglitazone.

**Keywords:** methotrexate, pioglitazone, rheumatoid arthritis, albino rat

## Introduction

Rheumatoid arthritis is a chronic inflamatory disorder which involves the immobilicity of the joint clinical course of the disease is very wide ranging from mild to server disease with extra articular manifestation currently the management of rheumatoid artaritis encludes NSAIDS, disease modifying and rheumatic drags (DMARD) like methotrexate, sulfasalazine, Hydroxychloroquine. When used as a single drug therapy the efficacy and potenty of these drugs are low therefore multidrug therapy is used more then morodmy thrapy.
Methortrexate is the primary drug of Rleamatoid arthritis. Suggested mechanism includes (I) inhibition of T- cell proliferation by affecting purine and pyrimidine metabolism (II) inhibits aceumulation of monocytes at the site of inflammation in the joints.
Pioglitazone is oral antidiafetic drugs. They induce apoptosis in the mecrophage and T-cymptocytes which are lmportant in perpituatiing rheumatoid arthritis.
As these two drugs produces anti inflamatony effect by two different mechanism. Combination therapy of these drugs can be used in treatrent of rleumation arthritis,
Prerent study was dove to find out the effent of methotrexate and pioglitanone combination thesapy in the treatment of rheumatoid arthritis in albivs rat models.

## Material and Methods

Arthritis was induced in twenty (20) albino rats by giving single dose of subcutaneous injeetion into five groups. Each group contain four rats two control groups one group treated with methotrexate only, one group with pioglitazone only, one with combined methotrexate anp pioglitwone.
0.5% solution of carboxymethyl allulose in double didtil water was used as vehicle. Methortrexate 2.5mg and pioglitazone 15mg were dissolved in the vechicle for oral administration through gastric lavage.
Frands adjurvant used for induction of Arthritis contain paraffin oil mannide monoleate heat killed mycobacteria 0,1ml (0.1%w/v) of this solution was injected in the tail of

each rat except one of the control group. It taves on average lo days to produce disease. Special care was given and normal pillet diet was given to rats. Animals were allowed 2 weeks before experiment to acclimatize with laboratory condition.
They were new divided into following groups :-

1. Group (I): Rats in this group were treated with carboxy methyl cellulose Na(0.5%W/V) solution per oral.
2. Group (II): No trcatment was given to this group after induction of arthritis.
3. Group (III): This group receive pioglitazone only 1.35mg/kg/d dissolved in 0.5%w/v solution of carboxy cellublose – Na solution.
4. Group (IV): This group receive nethotrexate at the dose of 0.225mg /kg/d dissolved in 0.5% carboxy methylcelluse-Na solution.
5. Group (V): This group receive combination of methoperate and piogtitrove. In above mention dose in 0.5% w/v solution of carboxy methy cellulose Na solution.

Treatment was given from day 10 to day 21 of the induction of diseace. Parameters used for the assessment were paw edema, (60 day weight and blood glucose level) & Rediological assessment of joint [biochemical and hematological estimations and was analysed by using SPSS version 17] P value of, 0.05 was considered significant

**Result**

1. Paw diameter on day zero paw diameter of both hind limbs of each rat was measured. These measurements were repeated on day 3,6,9,12,15,18 and 21 after enjection of CFA. Pas diameter in group II to V on day I increases upto 0.71 ± 0.013, 0.72 ± 0.013, 0.73 ± 0.014, 0.7 ± 0.014 as compared to group I (0.62 ± 0.022). However after treatment paw diameter on day 21 decreared from the value of day 9 in group III to V (0.68±0.012, 0.66±0.2, 0.63±0.011) but in group II value increases upto 0.78±0.019 value in the group I was constant.

**Radiological Analysis**

Inflammation at joint was seen in arthritic rats as compared to normal. Normal control (group I) shows normal joint Arthritic control (group II) shous reduction of joint space and destruction of joint. Similar features were seen in group III piogliatazone treated group but to a lesser extent. Where as in group IV & V treated with methotrexate and combination of piogletazone and methotrexate these changes were normalized.

Radiological images of (a) hind paw of normal rat (b) hind paw of arthritis rat (c) X-ray of hind paw of normal rat (d) X-ray of hind paw of arthritis rat (e) X-ray of hind paw of pioglitazone-treated rat (f) X-ray of hind paw of methotrexate-treated**.** (g)) X-ray of hind paw of pioglitazone and methotrexate-treated**.**

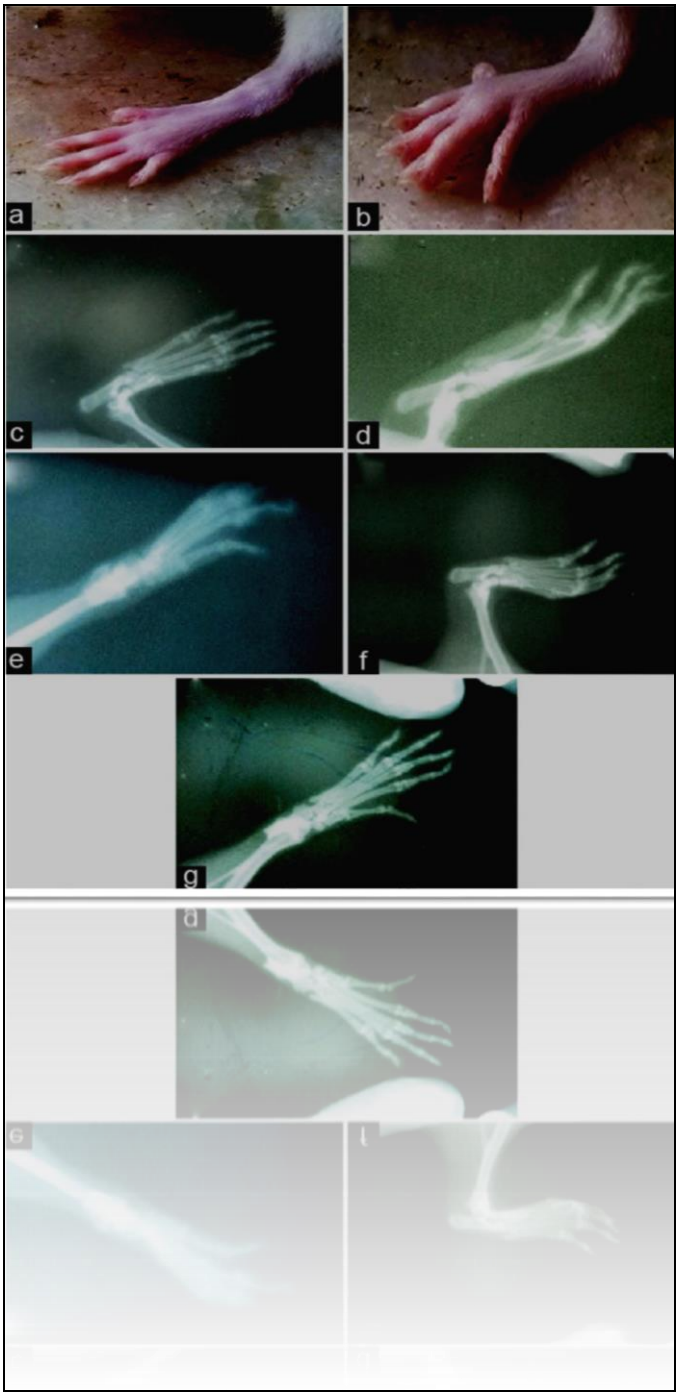


**Fig 1**

**Discussion and Conclusion**

Paw edema serves as a simple marker for evaluation of therapectic efficacy of drug therapy significant emprovement was observed in the group treated with methotrexate and combination of methotrexate and pioglitazone as compared to piogitazone mono drug therapy which shous no significant imprroment.

We concluded that methotrexate and pioglitanove comfination affer better control in rheumatoid arthritis as compased to mono therapy with methopexate or pioglitezone. However farther study is recommended to ascertain the dose range of pioglitazone in clinical settings.

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