SUMMARY & CONCLUSION
SUMMARY AND CONCLUSION

This study was conducted jointly in the Department of Pharmacology, LLRM Medical College, Meerut and also at Department of Biochemistry of Muzaffarnagar Medical College, Muzaffarnagar after approval from Intuitional animal ethical committee.

Experiment 1.

Forty albino rabbits of either sex were used and were divided into 4 groups with 10 animals in each group. They were treated with drug for one month per kg body wt. as the prescribed format

Group I - Control, Normal Saline

Group II - INH (2.5mg) or RIF (5mg) or PYZ (12.5mg) or ETH (7.5mg) or Allopurinol (0.75mg)

Group III - INH (5mg) or RIF (10mg) or PYZ (25mg) or ETH (15mg) or Allopurinol (1.5mg)

Group IV - INH (10mg) or RIF (20mg) or PYZ (50mg) or ETH (30mg) or Allopurinol (3mg)

Experiment 2.

Fifty albino rabbits of either sex were used and were divided into 5 groups with 10 animals in each group. They were treated with drug for three months per kg body wt. as the prescribed format

Group I - Control, Normal Saline

Group II - INH (5mg)

Group III - RIF (20mg)

Group IV - PYZ (25mg)
Group V    -    Allopurinol (3mg)

**Experiment 3.**

Seventy albino rabbits of either sex were used and were divided into 7 groups with 10 animals in each group. They were treated with drug for three months per kg body wt. as the prescribed format.

Group I    -    Control, Normal Saline
Group II   -    INH (5mg) + RIF (20mg)
Group III  -    INH (5mg) + RIF (20mg) + PYZ (25 mg)
Group IV   -    INH (5mg) + RIF (20mg) + PYZ (25 mg) + Vitamin E
Group V    -    INH (5mg) + RIF (20mg) + PYZ (25 mg) + Vitamin C
Group VI   -    Allopurinol (3mg) + Vitamin E
Group VII  -    Allopurinol (3mg) + Vitamin C

Blood samples were drawn before drug administration on day 1 in each group and then after completion of drug administration i.e. after 7 days.

Serum was separated from the blood sample by centrifugation at 2500 rpm and stored at refrigerated temperature till analysis (2-4 weeks). Serum was assayed for the levels of all biochemical parameters.

**Biomarkers used for study:**

**For measuring Hepatotoxicity:**

1. Serum alanine aminotransferase (ALT)
2. Alkaline phosphatase (ALP) &
3. Serum bilirubin (Total)
For measuring Renal Toxicity:

4. Blood Urea
5. Serum Uric Acid &
6. Serum Creatinine

Other parameters:

7. ESR
8. ASO Titre
9. Ra Factor
Results:

Experiment 1.

Liver Function Test

1. *Serum Alanine Transaminase* - S.ALT level was significantly increase with INH 5mg/kg body wt, RIF 20mg/kg body wt while PYZ 25mg/kg body wt, Allopurinol 0.75mg/kg body wt and ETHM of any dose (7.5, 15, 30mg/kg body wt) was not found to be any significant change on end of the experiment.

2. *Serum Alkaline Phosphatase* - S.ALP level was significantly increase with INH 5mg/kg body wt, RIF 20mg/kg body wt while PYZ 25mg/kg body wt, Allopurinol 0.75mg/kg body wt and ETHM of any dose (7.5, 15, 30mg/kg body wt) was not showing any significant change on end of the experiment.

3. *Serum Bilirubin* - S. Bil. Level was found significantly increase with INH 5mg/kg body wt, RIF 20mg/kg body wt while PYZ 25mg/kg body wt, Allopurinol 0.75mg/kg body wt and ETHM of any dose (7.5, 15, 30mg/kg body wt) was not showing any significant change on end of the experiment.

Kidney Function Test

4. *Blood Urea* - B. Urea level was found significantly increase with RIF 20mg/kg body wt, PYZ 25mg/kg body wt while INH 5mg/kg body wt and ETHM of any dose (7.5, 15, 30mg/kg body wt) was not found to be significant on end of the experiment.
5. **Serum Uric Acid**- S. Uric Acid level was showing significant increase with Rif 20mg/kg body wt, Pyrazinamide 25mg/kg body wt while INH 5mg/kg body wt and ETHM of any dose (7.5, 15, 30mg/kg body wt) was not found to be significant on end of the experiment.

6. **Serum Creatinine**- S. Creatinine level was showing significant increase with Rif 20mg/kg body wt, Pyrazinamide 25mg/kg body wt while INH 5mg/kg body wt and ETHM of any dose (7.5, 15, 30mg/kg body wt) was not found to be significant on end of the experiment.

**Conclusion:** Therefore the significant data is taken into consideration with 5mg/kg body wt. of Isoniazid, 20mg/kg body wt. of Rifampicin, 25mg/kg body wt. of Pyrazinamide and 3mg/kg body wt. of Allopurinol.

**Experiment 2:**

**Liver Function Test**

1. **Serum Alanine Transminase**- S.ALT level was significantly increase with INH 5mg/kg body wt and Rif 20mg/kg body wt when treated for 90 days alone. However Pyrazinamide 25mg/kg body wt and Allopurinol 3mg/kg body wt did not show any significant change.

2. **Serum Alkaline Phosphatase**- S.ALP level was significantly increase with INH 5mg/kg body wt and Rif 20mg/kg body wt when treated for 90 days alone. However Pyrazinamide 25mg/kg body wt and Allopurinol 3mg/kg body wt did not show any significant change.
3. **Serum Bilirubin** - S. Bil. Level was found significantly increase with INH 5mg/kg body wt and RIF 20mg/kg body wt when treated for 90 days alone. However PYZ 25mg/kg body wt and Allopurinol 3mg/kg body wt did not show any significant change.

**Kidney Function Test**

4. **Blood Urea** - B. Urea level showed slight significant increase with RIF 20mg/kg body wt. However PYZ 25mg/kg body wt and Allopurinol 3mg/kg body wt shows highly significant increase, while INH 5mg/kg body wt and was not found to be significant on end of the experiment.

5. **Serum Uric Acid** - S. Uric Acid level showed slight significant increase with RIF 20mg/kg body wt. However PYZ 25mg/kg body wt and Allopurinol 3mg/kg body wt shows very highly significant increase, while INH 5mg/kg body wt and was not found to be significant on end of the experiment.

6. **Serum Creatinine** - S. Creatinine level showed slight significant increase with RIF 20mg/kg body wt. However PYZ 25mg/kg body wt and Allopurinol 3mg/kg body wt shows very highly significant increase, while INH 5mg/kg body wt and was not found to be significant on end of the experiment.

**ESR** - ESR was found to be highly significant increase in all drug doses of INH 5mg/kg body wt, RIF 20mg/kg body wt, PYZ 25mg/kg body wt and Allopurinol 3mg/kg body wt.

**ASO Titre and Ra Factor** - In all drug doses the ASO Titre and Ra factor was found to be negative.
**Conclusion:** Therefore the significant data taken into consideration is showing 5mg/kg body wt. of Isoniazid is causing hepatotoxicity but no effect on kidney, 20mg/kg body wt. of Rifampicin causing hepatotoxicity and renal toxicity, 25mg/kg body wt. of Pyrazinamide and 3mg/kg body wt. of Allopurinol is affecting only kidney function. Negative ASO Titre and Ra Factor reflects the absence of any chronic secondary infection or decrease in immunity.

**Experiment 3:**

**Liver Function Test**

1. **Serum Alanine Transaminase** - S.ALT level was significantly increased with INH 5mg/kg body wt and RIF 20mg/kg body wt when used in combination. And inclusion of PYZ 25mg/kg body wt in this combination shows very highly significant increase, treatment with Vitamin C also shows no improvement in the S.ALT levels, However with Vitamin E it shows a highly significant decrease in the S.ALT levels and Allopurinol 3mg/kg body wt with Vitamin C did not show any significant change but with Vitamin E S.ALT level significantly decreases.

2. **Serum Alkaline Phosphatase** - S.ALP level was significantly increased with INH 5mg/kg body wt and RIF 20mg/kg body wt when used in combination. And inclusion of PYZ 25mg/kg body wt in this combination shows very highly significant increase, treatment with Vitamin C also shows no improvement in the S.ALP levels, However with Vitamin E it shows a significant decrease in the S.ALP levels and Allopurinol 3mg/kg body wt with Vitamin C did not
show any significant change but with Vitamin E S.ALP level significantly decreases.

3. **Serum Bilirubin**- S.Bil. Level shows highly significant increase with INH 5mg/kg body wt and RIF 20mg/kg body wt when used in combination. And inclusion of PYZ 25mg/kg body wt in this combination shows very highly significant increase, treatment with Vitamin C also shows no improvement in the S.Bil. levels, However with Vitamin E it shows a significant decrease in the S.Bil. levels and Allopurinol 3mg/kg body wt with Vitamin C did not show any significant change but with Vitamin E S.Bil. level significantly decreases.

**Kidney Function Test**

4. **Blood Urea**- B.Urea Level shows highly significant increase with INH 5mg/kg body wt and RIF 20mg/kg body wt when used in combination. And inclusion of PYZ 25mg/kg body wt in this combination shows very highly significant increase treatment with Vitamin C also shows no improvement in the B.Urea levels, However with Vitamin E it shows a significant decrease in the B.Urea levels and Allopurinol 3mg/kg body wt with Vitamin C did not show any significant change but with Vitamin E S.Bil. level significantly decreases.

5. **Serum Uric Acid**- S. Uric acid Level shows highly significant increase with INH 5mg/kg body wt and RIF 20mg/kg body wt when used in combination. And inclusion of PYZ 25mg/kg body wt in this combination shows very highly significant increase treatment
with Vitamin C also shows no improvement in the S. Uric acid levels, However with Vitamin E it shows a significant decrease in the S. Uric acid levels and Allopurinol 3mg/kg body wt with Vitamin C did not show any significant change but with Vitamin E S. Uric acid level significantly decreases.

6. **Serum Creatinine**- S. Creatinine Level shows highly significant increase with INH 5mg/kg body wt and RIF 20mg/kg body wt when used in combination. And inclusion of PYZ 25mg/kg body wt in this combination shows very highly significant increase treatment with Vitamin C also shows no improvement in the S. Creatinine levels, However with Vitamin E it shows a significant decrease in the S. Creatinine levels and Allopurinol 3mg/kg body wt with Vitamin C did not show any significant change but with Vitamin E S. Creatinine level significantly decreases.

**ESR**- ESR was found to be highly significant increase in all drug doses of INH 5mg/kg body wt + RIF 20mg/kg body wt + PYZ 25mg/kg body wt + Vitamin C + Vitamin E and Allopurinol 3mg/kg body wt. + Vitamin C + Vitamin E.

**ASO Titre and Ra Factor**- In all drug doses the ASO Titre and Ra factor was found to be negative.

**Conclusion:** Therefore it is concluded that when Vitamin E is given in combination with antitubercular drug the risk of hepatotoxicity is reduced, however it is not reduced by Vitamin C therapy. Like that allopurinol also reduces its toxic effect on kidney when given along
with Vitamin E. This statement was not found to be true with Vitamin C. Negative ASO Titre and Ra Factor is suggesting that there is no chronic infection.