OBSERVATIONS AND RESULTS
RESULTS AND OBSERVATIONS

In the present study the effects of concurrent administration as well as repeated pre-treatment with anti-inflammatory and beta-adrenergic blocking agents on tolbutamide induced hypoglycemic response and serum tolbutamide concentration and its plasma half-life were studied. Among the anti-inflammatory agents acetophenylcyclohex (aspirin), the most well studied nonsteroidal anti-inflammatory drug; trimazol and talnafen comparatively recent and newly introduced anti-inflammatory drugs were selected for interaction study. Similarly propamolol the oldest, potent and most clinically used beta-adrenergic blocking agent, and some new and selective beta-blocking agents like metoprolol, atenolol and acebutolol were chosen amongst a vast number of beta-blockers.

Tolbutamide and anti-inflammatory agents selected for interaction study were administered orally as a suspension in 2.5% gum acacia, since they are not soluble in water. But the beta-blockers, although soluble in water were administered orally prepared in 2.5% gum acacia to maintain homogeneity of the vehicle. In central experiments 2.5% gum acacia was used to see the effect of only vehicle on blood sugar. The drugs were administered at 6 AM and
Table 5: Effect of thiaminoids (on 25 dose) on blood sugar level in normal and diabetic rabbits.

<table>
<thead>
<tr>
<th>Type of Rabbit</th>
<th>Blood Sugar Change in % Hours ± S.E.</th>
<th>0 hour</th>
<th>2 hour</th>
<th>3 hour</th>
<th>7 hour</th>
<th>9 hour</th>
<th>11 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 mg/day</td>
<td></td>
<td>100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 mg/day</td>
<td></td>
<td>100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 mg/day</td>
<td></td>
<td>100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diabetic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 mg/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 mg/day</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 mg/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* * * indicate P values > 0.05, > 0.01, > 0.00 respectively.
Fig. 2: Shows effect of graded doses of tolbutamide on blood sugar level in normal and diabetic rabbits. Peak hypoglycaemic response is observed at 5 hours in normal and at 3 hours in diabetic rabbits (alloxan, 155 mg/kg I.V.). **, *** indicate P values < 0.01 and < 0.001 respectively.
blood sugar and serum tolbutamide concentration were measured from 8 A.M. to 7 P.M. In chronic treatment groups the drugs were administered daily at 1 P.M. for 7 consecutive days. The time of drug administration and measurement of blood sugar and serum tolbutamide level was kept constant to avoid variations due to circadian effect.

**EFFECT OF TOLBUTAMIDE ON BLOOD SUGAR OF RABBITS**

Following oral administration of 2.5 gm aceta tide the blood sugar level over 11 hours of study was not significantly affected. Tolbutamide produced a dose dependent hypoglycemia. The hypoglycemic response reached a peak level after five hours and complete recovery was observed after 9 hours. For subsequent interaction studies tolbutamide was used at a dose of 50 mg/kg. In diabetic rabbits also tolbutamide produced hypoglycemia but the peak response was observed at 2 hours comparatively earlier than that of normal rabbits. However, the blood sugar level returned to control value within 9 hours, almost similar to normal rabbits (Table 5, Fig. 2).

**EFFECT OF ACTI-LIPID MOTEX BIDAS ON BLOOD SUGAR OF NORMAL RABBITS**

Actilip at a dose of 40 mg/kg produced a marked hypoglycemia with a peak effect at 6 hours and the effect persisted beyond 9 hours.
### Table 6: Effect of Anti-Inflammatory Agents and Adrenergic Beta-Blockers (Single Dose) on Blood Glucose Levels in Normal Rats

<table>
<thead>
<tr>
<th>Drug (mg/kg)</th>
<th>0 hour</th>
<th>1 hour</th>
<th>2 hour</th>
<th>3 hour</th>
<th>5 hour</th>
<th>7 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Acetaminophen (25)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Naproxen (2)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Naproxen (5)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Naproxen (10)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Naproxen (15)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Naproxen (30)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

* * * indicates p values ≤ 0.05, ≤ 0.01, and ≤ 0.001 respectively.

Note: 0, 1, 2, 3, 5, 9, and 11 hours indicate 0 AM, 1 AM, 2 AM, 3 AM, 5 AM, and 7 AM of the day of experiment. Drugs are administered at 8 AM.
TABLE 7b

EFFECT OF INJECTED TREATMENT (4x3 days) OF ANTI-INFLAMMATORY AGENTS AND HETERODERMA BLOCKERS ON BLOOD SUGAR OF NORMAL RATS.

<table>
<thead>
<tr>
<th>INJECTION (every 3 days)</th>
<th>Blood sugar (mmol/L)</th>
<th>Blood sugar change (%) on 3rd day</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2% glycerol (5 ml)</td>
<td>100</td>
<td>98.0 ± 1.45</td>
<td></td>
</tr>
<tr>
<td>Aspirin (40)</td>
<td>100</td>
<td>98.0 ± 1.45</td>
<td></td>
</tr>
<tr>
<td>Tannic acid (100)</td>
<td>100</td>
<td>98.0 ± 1.45</td>
<td></td>
</tr>
<tr>
<td>Salicylic acid (20)</td>
<td>100</td>
<td>98.0 ± 1.45</td>
<td></td>
</tr>
<tr>
<td>Symptom (4)</td>
<td>100</td>
<td>98.0 ± 1.45</td>
<td></td>
</tr>
<tr>
<td>Nootropil (40)</td>
<td>100</td>
<td>98.0 ± 1.45</td>
<td></td>
</tr>
<tr>
<td>Metoprolol (40)</td>
<td>100</td>
<td>98.0 ± 1.45</td>
<td></td>
</tr>
<tr>
<td>Metoprolol (30)</td>
<td>100</td>
<td>98.0 ± 1.45</td>
<td></td>
</tr>
</tbody>
</table>

* a = indicates / 3 whereas / 0.05 and / 0.01 respectively

Notes: Aspirin 50, 5, 0, 2, 0 and 2 hours indicates 0 AN: 0 AN: 0 AN: 1 PRA: 0 PRA: 0 PRA: 0 and 2 PRA: respectively on 3rd day, bases are administered daily at 9:00.

For 7 consecutive days.
EFFECT OF ANTI-INFLAMMATORY AGENTS ON BLOOD SUGAR LEVEL IN NORMAL RABBITS.

- GUM ACACIA
- TROMARIL
- ASPIRIN
- TOLMETIN

![Graph showing effect of anti-inflammatory agents on blood sugar level in normal rabbits.](image)

**Fig. 3**: Shows effect of aspirin (40 mg/kg), tromaril (150 mg/kg) and tolmetin (20 mg/kg) on blood sugar level in normal rabbits after single dose administration. Aspirin and tolmetin show significant hypoglycaemic response. *, **, *** indicate P values ≤ 0.05, ≤ 0.01 and ≤ 0.001 respectively.
EFFECT OF BETA-BLOCKERS ON BLOOD SUGAR IN NORMAL RABBITS

![Graph showing the effect of different beta-blockers on blood sugar levels in normal rabbits.]

**Fig. 4:** Shows effect of propranolol (8 mg/kg), metoprolol (10 mg/kg), atenolol (6 mg/kg) and acebutolol (30 mg/kg) on blood sugar level in normal rabbits after single dose administration. Propranolol and atenolol show significant hypoglycaemia. ●, ○ indicate P values ≤ 0.05 and ≤ 0.01 respectively.
Fig. 5: Shows effect of anti-inflammatory agents on blood sugar level in normal rabbits after daily oral treatment for 7 days. Blood sugar level is recorded from 8 A.M. to 7 P.M. on the 8th day without drug administration. The hypoglycaemic response of aspirin and tolmetin persists up to 7 P.M. •, •• indicate P values $\leq 0.01$ and $\leq 0.001$ respectively.
Fig. 6: Shows effect of beta-blockers on blood sugar level in normal rabbits after daily oral treatment for 7 consecutive days. Blood sugar level was recorded on 8th day from 8 A.M. to 7 P.M. without drug administration. Beta-blockers do not show any persistent hypoglycaemia on 8th day.
Tolbutamide at a dose of 20 mg/kg also exhibited a significant hypoglycemic response with a peak effect at 3 hours and complete recovery was attained at 11 hours. However, tolbutamide at a dose of 100 mg/kg did not show any effect on blood sugar level (Table 6, Fig. 3).

Aspirin and tolbutamide were administered daily orally for 7 days. On the 8th day, without the drug administration, hypoglycemic effect persisted significantly up to 3 hours. But tolbutamide did not show any such effect (Table 7, Fig. 6).

**EFFECT OF β-ADRENERGIC BLOCKERS ON BLOOD SUGAR OF NORMAL RABBITS**

Propranolol (5 mg/kg) and atenolol (5 mg/kg) produced a slight but significant lowering of blood sugar level with a peak hypoglycemia at 3 hours and the effect almost reversed after 11 hours. However, the other two beta-blockers metoprolol (10 mg/kg) and acebutolol (30 mg/kg) did not influence the blood sugar concentration to any extent (Table 6, Fig. 4). Beta-blockers after daily treatment for 7 days did not show any effect on blood sugar on the 8th day (Table 7, Fig. 6).

**EFFECT OF SIMULTANEOUS ADMINISTRATION OF ANTI-INFLAMMATORY AGENTS ON HYPETREMIA INDUCED HYPERGLYCEMIA**

(a) Single dose effect

Simultaneous administration of aspirin (40 mg/kg) and tolbutamide (5 mg/kg) increased the hypoglycemia (mean of tolbutamide alone), the potentiation of hypoglycemia by tolbutamide was however, significant at 3, 6, and 12.
<table>
<thead>
<tr>
<th>Drug</th>
<th>0 hour (± S.E.)</th>
<th>3 hour (± S.E.)</th>
<th>9 hour (± S.E.)</th>
<th>7 hour (± S.E.)</th>
<th>9 hour (± S.E.)</th>
<th>11 hour (± S.E.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salicylurate</td>
<td>100</td>
<td>92.87</td>
<td>92.33</td>
<td>93.65</td>
<td>90.83</td>
<td>102.92</td>
</tr>
<tr>
<td>Salicylurate</td>
<td>100</td>
<td>79.91*</td>
<td>20.35*</td>
<td>74.77*</td>
<td>71.55</td>
<td>100.87</td>
</tr>
<tr>
<td>Aspirin</td>
<td>100</td>
<td>70.94</td>
<td>70.03</td>
<td>70.07</td>
<td>70.67</td>
<td>103.32</td>
</tr>
<tr>
<td>Salicylurate</td>
<td>100</td>
<td>70.94</td>
<td>70.03</td>
<td>70.07</td>
<td>70.67</td>
<td>103.32</td>
</tr>
<tr>
<td>Salicylurate</td>
<td>100</td>
<td>70.94</td>
<td>70.03</td>
<td>70.07</td>
<td>70.67</td>
<td>103.32</td>
</tr>
</tbody>
</table>

* * indicates P values ≤ 0.05 and ≤ 0.01 respectively.
# Table 9.1

**Effect of Enforced Administration of Anti-Inflammatory Agents on Glucose Intolerance in Normal Rats.**

<table>
<thead>
<tr>
<th>Drug (mg/kg, PO)</th>
<th>0 hour</th>
<th>3 hour</th>
<th>5 hour</th>
<th>7 hour</th>
<th>9 hour</th>
<th>11 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (30)</td>
<td>100</td>
<td>80.85</td>
<td>64.88</td>
<td>47.68</td>
<td>30.36</td>
<td>102.31</td>
</tr>
<tr>
<td>Aspirin (30)</td>
<td>100</td>
<td>73.67</td>
<td>69.61</td>
<td>59.89</td>
<td>59.00</td>
<td>102.92</td>
</tr>
<tr>
<td>Naproxen (30)</td>
<td>100</td>
<td>77.69</td>
<td>70.67</td>
<td>72.08</td>
<td>101.36</td>
<td>96.5</td>
</tr>
<tr>
<td>Indomethacin (30)</td>
<td>100</td>
<td>79.5</td>
<td>73.43</td>
<td>28.57</td>
<td>± 1.46</td>
<td>± 2.66</td>
</tr>
<tr>
<td>Indomethacin (50)</td>
<td>100</td>
<td>78.56</td>
<td>61.65</td>
<td>67.32</td>
<td>100.71</td>
<td>100.11</td>
</tr>
</tbody>
</table>

* a = Statistically significant at P < 0.05 and P < 0.01 respectively.
EFFECT OF CONCURRENT ADMINISTRATION OF ANTI-INFLAMMATORY AGENTS (SINGLE DOSE) ON TOLBUTAMIDE HYPOGLYCAEMIA IN NORMAL RABBITS.

- TOLBUTAMIDE (TOL.)
- TOL. + TOLMETIN
- TOL. + ASPIRIN
- TOL. + TROMARIL

Fig. 7: Shows effect of anti-inflammatory drugs on tolbutamide (50 mg/kg) induced hypoglycaemia in normal rabbits. Tolmetin and aspirin show potentiation. ●, ○, ○ indicate P values < 0.05 and < 0.01 respectively.
EFFECT OF REPEATED ADMINISTRATION (7 DAYS) OF ANTI-INFLAMMATORY AGENTS ON TOLBUTAMIDE (T) HYPOGLYCAEMIA IN NORMAL RABBITS.

Fig. : 8 - Shows effect of repeated administration (7 days) of anti-inflammatory drugs on Tolbutamide (T) induced hypoglycaemia in normal rabbits. Aspirin and Tolmetin produce significant potentiation. • • • indicate P values ≤ 0.05 and ≤ 0.01 respectively.
hours of administration hypoglycemia produced by the combination of terazosin (20 mg/kg) and tolbutamide (60 mg/kg) was almost equal to the hypoglycemia produced by tolbutamide (60 mg/kg) alone. Telmetin potentiated the hypoglycemic response of tolbutamide. The potentiation was significantly observed up to 7 hours only (Table 3, Fig. 7).

(b) Effect of Repeat administration

Pre-treatment with atorvastatin (40 mg/kg) for 7 days increased significantly the hypoglycemic response of tolbutamide than that of untreated rabbits. Significant change was seen at 3, 5 and 7 hours. Quantitatively similar potentiation of hypoglycemia was noted with telmetin (20 mg/kg/day for 7 days). However, it was only significant at 5 and 6 hours. But treatment with terazosin for 7 days did not affect tolbutamide-hypoglycemic response significantly (Table 3, Fig. 8).

Results on Increase in the Blood Glucose Levels in Tolbutamide-Induced Hypoglycemia

(a) Similar dose effects

Pregnanatal (5 mg/kg) and atorvastatin (6 mg/kg) slightly increased the hypoglycemic effect of tolbutamide when administered concomitantly. In addition, they also prevented the hypoglycemic response on blood sugar level.
Fig. 9: Shows effect of concurrent administration of beta-blockers on Tolbutamide (50 mg/kg) induced hypoglycaemia in normal rabbits. Propranolol and atenolol show potentiation. *, ** indicate P values ≤ 0.05 and ≤ 0.01 respectively.
EFFECT OF REPEATED ADMINISTRATION (7 DAYS) OF BETA-BLOCKERS ON TOLBUTAMIDE HYPOGLYCAEMIA IN NORMAL RABBITS.

![Graph showing blood sugar change in response to different treatments.](image)

**Fig. 10:** Shows effect of repeated administration (7 days) of beta-blockers on tolbutamide-induced hypoglycaemia in normal rabbits. Propranolol and atenolol show potentiation. *, ** indicate P values $\leq 0.05$ and $\leq 0.01$ respectively.
did not return to normal level even upto 11 hours. But metoprolol (10 mg/kg) and acebutolol (30 mg/kg) neither increased the hypoglycemic nor prolonged the hypoglycemic effect of tolbutamide (50 mg/kg) (Table 10, Fig. 9).

(b) EFFECT OF REPEATED ADMINISTRATION

Propenolol (5 mg/kg/day) after repeated treatment for 7 days further increased the hypoglycemic effect of tolbutamide. The duration of hypoglycemia was also found to be increased. In tolbutamide group blood sugar level was 120.62 ± 3.61 mg/dl at 11 hours whereas with propenolol the blood sugar level was on 80.96 ± 1.48 mg/dl. Similarly, surprisingly, had no effect upto 6 hours, but potentiated the hypoglycemia from 7 to 9 hours.

Other cardioselective beta-blocking agents metoprolol (10 mg/kg/day) and acebutolol (30 mg/kg/day) had no significant effect on tolbutamide hypoglycemia (Table 11, Fig. 10).

EFFECT OF CONCURRENT ADMINISTRATION OF ANTI-HYPERTENSIVE AGENTS ON POLYUrine-LEvElRED HYPERTENSIA IN ALGINATE LEARNER BLADDER BARRIERS

Again in the dose of 40 mg/kg potentiated the hypoglycemic response of tolbutamide significantly after 3, 6 and 7 hours of drug administration in diabetic
EFFECT OF CONCURRENT ADMINISTRATION OF ANTI-INFLAMMATORY AGENTS (SINGLE DOSE) ON TOLBUTAMIDE-HYPOGLYCAEMIA IN DIABETIC RABBITS.

- TOLBUTAMIDE (TOL.)
- TOL. + TOLMETIN
- TOL. + ASPIRIN
- TOL. + TROMARIL

**Fig. 11:** Shows effect of concurrent administration of anti-inflammatory agents on tolbutamide hypoglycaemia in diabetic rabbits. Aspirin and tolmetin show potentiation. • indicates P value < 0.05.
EFFECT OF CONCURRENT ADMINISTRATION OF BETA-BLOCKERS (SINGLE DOSE) ON TOLBUTAMIDE-HYPOGLYCAEMIA IN DIABETIC RABBITS

- TOLBUTAMIDE (TOL.)
- TOL. + ATENOLOL
- TOL. + PROPRANOLOL
- TOL. + ACEBUTOLOL
- TOL. + METOPROLOL

**Fig. 12**: Shows effect of concurrent administration of beta-blockers on tolbutamide hypoglycaemia in diabetic rabbits, propranolol, atenolol and metoprolol show potentiation. ⋅ ⋅⋅ indicate P value \( \leq 0.05 \) and \( \leq 0.01 \) respectively.
Antimicrobial activity of telbutamide in diabetic rabbits: Telbutamide (30 mg/kg) also enhanced the hypoglycemic response of telbutamide in diabetic rabbits. Enhancement of hypoglycemia was significant only at 3 and 6 hours. Tramadol in the dose of 150 mg/kg did not significantly influence the telbutamide induced hypoglycemia (Table 12, Fig. 11).

**EFFECT OF CONCURRENT ADMINISTRATION OF NITRIC-OXYGEN BLOCKERS ON POLYHYPERGLYCEMIA IN ALLERGIC INDIABETIC RABBITS**

In diabetic rabbits, propylsalol (3 mg/kg), acetosalol (30 mg/kg), acetosalol (6 mg/kg) as well as acetosalol (30 mg/kg) potentiated telbutamide (30 mg/kg) induced hypoglycemia. But the potentiation was delayed in nature. Significant potentiation was observed at 7 hours with all the drugs. However, the potentiation remained significant up to 9 hours with propylsalol only (Table 12, Fig. 11).

**EFFECT OF CONCURRENT ADMINISTRATION OF ANTI-INFLAMMATORY AGENTS ON POLYHYPERGLYCEMIA INDUCED IN ALLERGIc INDIABETIC RABBITS**

(a) Single dose effect:

With concurrent administration of anti-inflammatory agents, the serum telbutamide concentration after constant
EFFECT OF CONCURRENT ADMINISTRATION OF ANTI-INFLAMMATORY AGENTS ON SERUM TOLBUTAMIDE (T) CONCENTRATION.

Fig. 13: Shows effect of concurrent administration of anti-inflammatory agents on serum tolbutamide concentration in normal rabbits. Aspirin and tolmetin significantly reduced serum tolbutamide concentration. • and ** indicate P value ≤ 0.05 and ≤ 0.01 respectively.
EFFECT OF REPEATED ADMINISTRATION OF ANTI-INFLAMMATORY AGENTS ON SERUM TOLBUTAMIDE (T) CONCENTRATION IN NORMAL RABBITS.

Fig. 14: Shows effect of repeated administration (7 days) of anti-inflammatory agents on serum tolbutamide concentration in normal rabbits. Aspirin tolmetin or tromaril do not show any significant change in serum tolbutamide.
and tolunitin remained at low level compared to that of only tolbutamide, without any marked change after tolmetin. In the control group tolbutamide reached a peak concentration (270.66 ± 5.64 ug/ml) at 5 hours. With anti-inflammatory drugs the peak time of serum tolbutamide level, although, remained same at 5 hours but serum concentrations were 345.67 ± 5.44 ug/ml with aspirin, 382.63 ± 6.12 ug/ml with tolmetin and 367.61 ± 6.3 ug/ml with tolmetin.

These anti-inflammatory agents also did not markedly change the biological half-life of tolbutamide (Table 10, Fig. 13).

(b) Effect of repeated treatment

The effect of prior treatment with anti-inflammatory agents for 7 days on serum tolbutamide level and biological t½ was almost similar to single dose pretreatment. The serum tolbutamide concentration remained at low level without significant change in t½ after aspirin and tolmetin. However, the effect with tolmetin is statistically significant. Trenmetil had no effect at all (Table 10, Fig. 14)

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EFFECT OF CONCURRENT ADMINISTRATION OF BETA-BLOCKERS ON SERUM TOLBUTAMIDE LEVEL IN NORMAL RABBITS.

Fig. 15: Shows effect of concurrent administration of beta-blockers on serum tolbutilamide level in normal rabbits. Propranolol, metoprolol, atenolol and acebutolol do not show any significant change.
EFFECT OF REPEATED ADMINISTRATION OF BETA-BLOCKERS ON SERUM TOLBUTAMIDE CONCENTRATION IN NORMAL RABBITS.

- TOLBUTAMIDE (T)
- T + METOPROLOL
- T + PROPRANOLOL
- T + ATENOLOL
- T + ACEBUTOLOL

Fig. 16: Shows effect of repeated administration of beta-blockers (7 days) on serum tolbutamide concentrations. Propranolol, metoprolol, atenolol or acebutolol do not show any effect.
Fig. 17: Shows the effect of concurrent administration of anti-inflammatory drugs on serum tolbutamide level in diabetic rabbits. Aspirin, tromaril or tolmetin do not show any significant change in serum tolbutamide concentration.
EFFECT OF CONCURRENT ADMINISTRATION OF BETA-BLOCKERS ON SERUM TOLBUTAMIDE LEVEL IN ALLOXAN DIABETIC RABBITS.

- TOLBUTAMIDE (T)
- T + METOPROLOL
- T + PROPRANOLOL
- T + ATENOLOL
- T + ACEBUTOLOL

Fig. 18: Shows the effect of concurrent administration of beta-blockers on serum tolbutamide level in alloxan-induced diabetic rabbits. No significant change occurred after the administration of propranolol, metoprolol, atenolol, & acebutolol.