SUMMARY I

Sub-acute toxicity study of Cefepime+Amikacin combination on swiss albino mice.

Swiss albino mice (n=48) were divided two groups as per the sex of mice. These two groups were further subdivided into four groups, Group I- Control, Group II(125mg/kg Cefepime-Amikacin i.v.), Group III (250mg/kg Cefepime-Amikacin i.v.) and Group IV (500mg/kg Cefepime-Amikacin i.v.). Control group animals were treated with vehicle only. Animals were treated for 14 days and sacrificed on 15^{th} day. Biochemical and hematological parameters were studied along with histological examination. No significant change in hematological parameters (hemoglobin, total leuckocyte count, total RBC count, platelets and retics) was observed in treated mice of either sex as compared to respective control groups. Similarly no significant change in plasma glucose levels, alkaline phospahatase (ALP) and Alanine amino transferase (ALT)activity, albumin, creatinine, calcium and phosphorus levels were observed. Histological examination of liver, kidney, correlated well with biochemical observation as no alterations were observed in morphology. The results clearly suggests non toxic nature of fixed dose combination of Cefepime and Amikacin in mice.

FLOW CHART OF SUB ACUTE TOXICITY STUDY OF CEFEPIME-AMIKACIN FDC STUDIES IN MICE

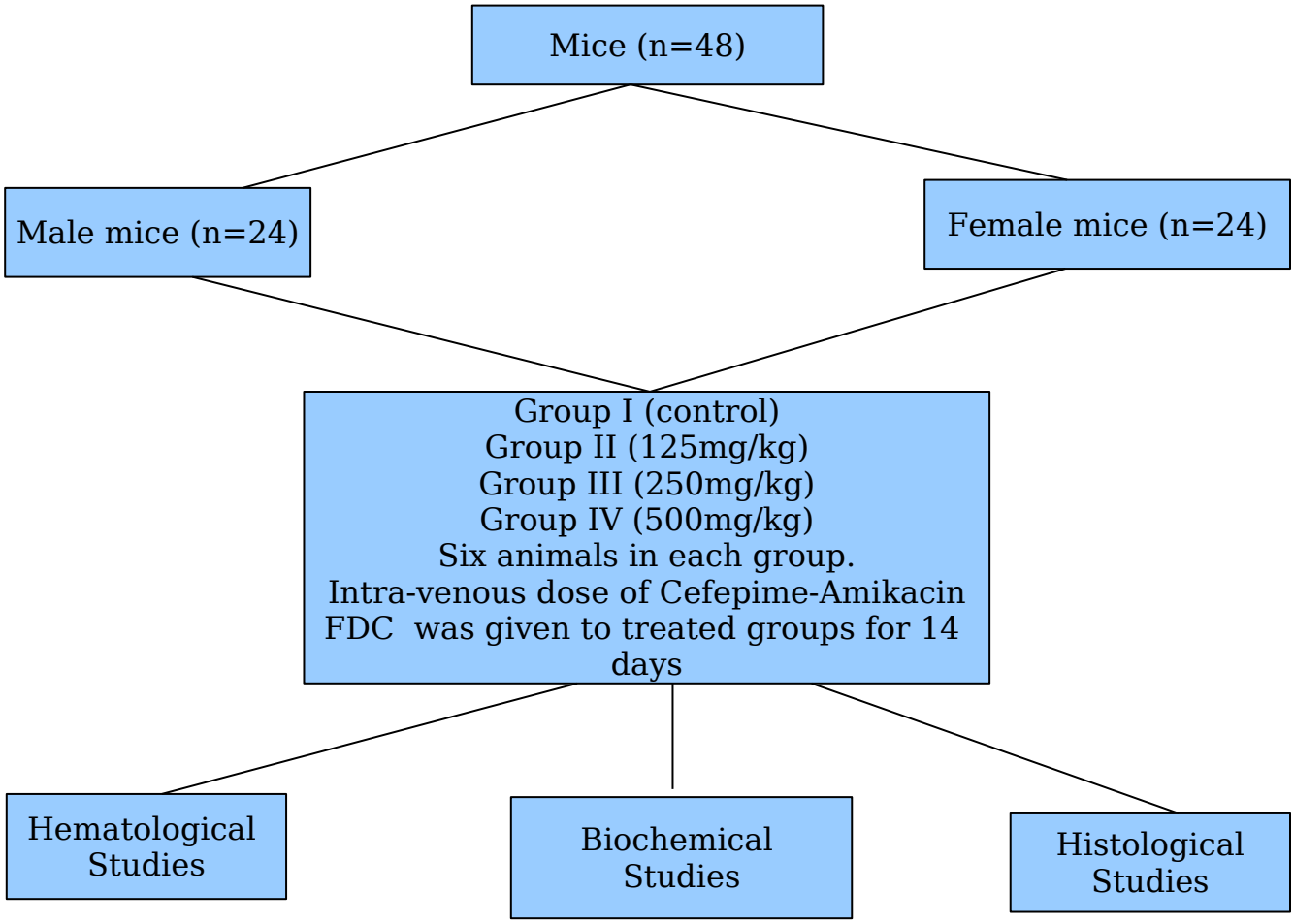

Fig. 1) Effect of sub acute dose of Cefepime-Amikacin FDC on hemogram in male mice.

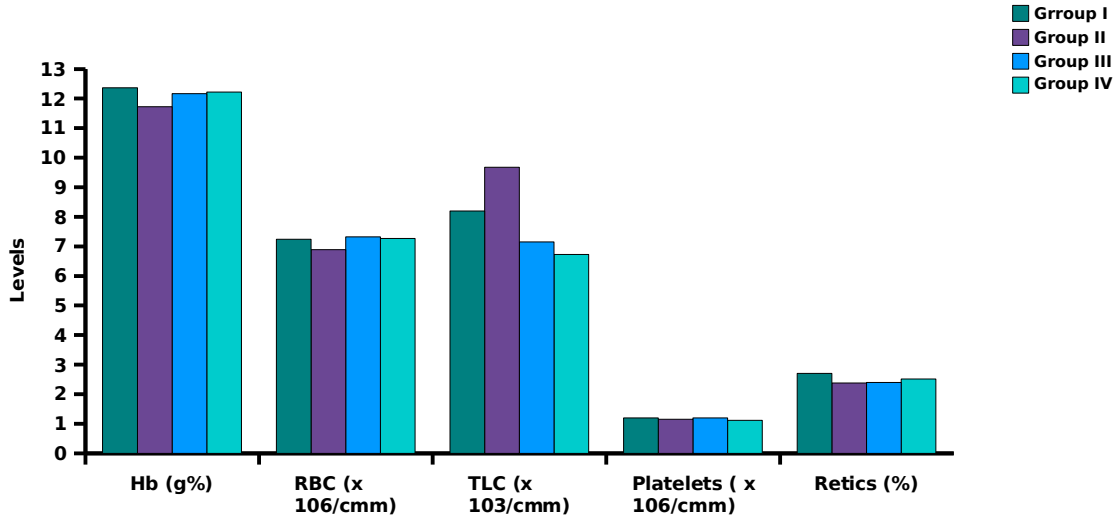

Fig. 2) Effect of sub acute dose of Cefepime-Amikacin FDC on hemogram in female mice.

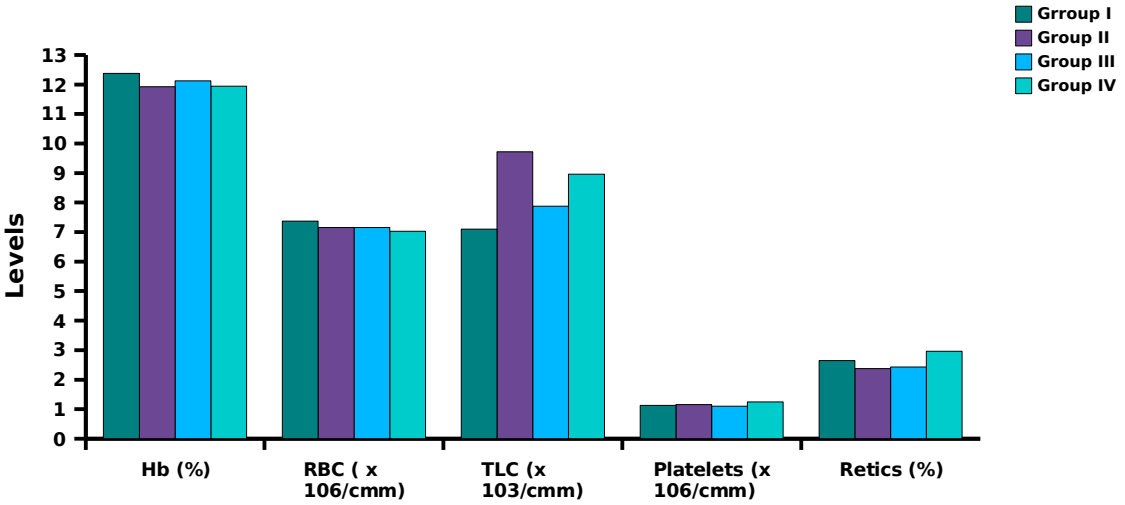

Table 1) Effect of sub acute dose of Cefepime-Amikacin FDC on biochemical parameters in male mice.

	Group I	Group II	Group III	Group IV
Total Protein (g%)	5.85 ± 0.63	6.08 ± 0.39	6.22 ±0.34	7.38 ± 0.35
Glucose (mg/dl)	107.38 ± 16.11	117.57 ± 13.16	84.69 ±15.92	142.33 ± 28.39
ALP (IU/l)	131.50 ± 13.46	135.87± 27.95	134.33 ±11.64	164.17 ± 34.95
ALT (IU/l)	78.45 ± 13.21	74.0 ± 25.37	65.83 ± 37.81	138.61± 51.61
Albumin (g%)	2.48 ± 0.25	2.53 ± 0.08	2.63 ± 0.10	2.93 ± 0.08
Creatinine (mg/dl)	1.31 ± 0.32	1.22 ± 0.26	1.23 ± 0.30	1.20 ± 0.285
Calcium(mg/dl)	11.00 ± 0.59	10.68 ± 0.66	10.78 ± 0.31	9.20 ± 4.70
Phosphorus (mg/dl)	8.73 ± 0.72	7.49 ± 0.85	7.82 ± 1.20	9.20 ±1.85

Table 2) Effect of sub acute dose of Cefepime-Amikacin FDC on biochemical parameters in female mice.

	Group I	Group II	Group III	Group IV
Total Protein (g%)	6.07 ± 0.35	6.10 ± 0.62	6.80 ± 0.35	6.92 ± 0.94
Glucose (mg/dl)	139.32 ± 36.95	133.23 ± 22.84	125.25 ± 32.82	143.60 ± 22.46
ALP (IU/l)	113.17 ± 22.89	128.72 ± 26.82	102.88 ± 48.0	206.80 ± 60.58
ALT (IU/l)	96.25 ± 62.37	61.08 ± 13.15	69.78 ± 47.66	66.75 ± 24.85
Albumin (g%)	2.60 ± 0.09	2.72 ± 0.19	2.85 ± 0.30	3.24 ± 0.76
Creatinine (mg/dl)	1.40 ± 0.67	1.42 ± 0.33	1.30 ± 0.14	1.30 ± 0.14
Calcium(mg/dl)	12.48 ± 3.74	10.43 ± 0.21	8.42 ± 2.83	9.00 ± 3.10
Phosphorus (mg/dl)	8.19 ± 0.99	8.43 ± 1.21	7.80 ± 1.78	10.42 ± 2.48

SUMMARY II

Subacute intravenous toxicity study of Cefepime+Amikacin on SD rats

Rats (n=48) were divided two groups as per the sex of mice. These two groups were further subdivided into four groups, Group I- Control, Group II(125mg/kg Cefepime-Amikacin i.v.), Group III (250mg/kg Cefepime-Amikacin i.v.) and Group IV (500mg/kg Cefepime-Amikacin i.v.). Control group animals were treated with vehicle only. Animals were treated for 14 days and sacrificed on 15th day. Biochemical and hematological parameters were studied along with histological examination. No significant changes in hematological parameters (hemoglobin, total leuckocyte count, total RBC count, platelets and retics) were observed in treated female rats as compared to respective control groups. Lowering of Hb and RBC was observed in male rats but was not dose related. No significant change in retics and platelet counts was observed in male rats.

Similarly no significant changes in plasma glucose levels, alkaline phospahatase (ALP) and alanine amino transferase (ALT) activity, albumin, creatinine, calcium and phosphorus levels were observed as compared to respective control group animals. Histological examiniation of liver, kidney, correlated well with biochemical observation as no alterations were observed in morphology. The results clearly suggests non toxic nature of fixed dose combination of Cefepime and Amikacin in rats.

FLOW CHART OF SUB ACUTE TOXICITY STUDY OF CEFEPIME-AMIKACIN FDC STUDIES IN RATS

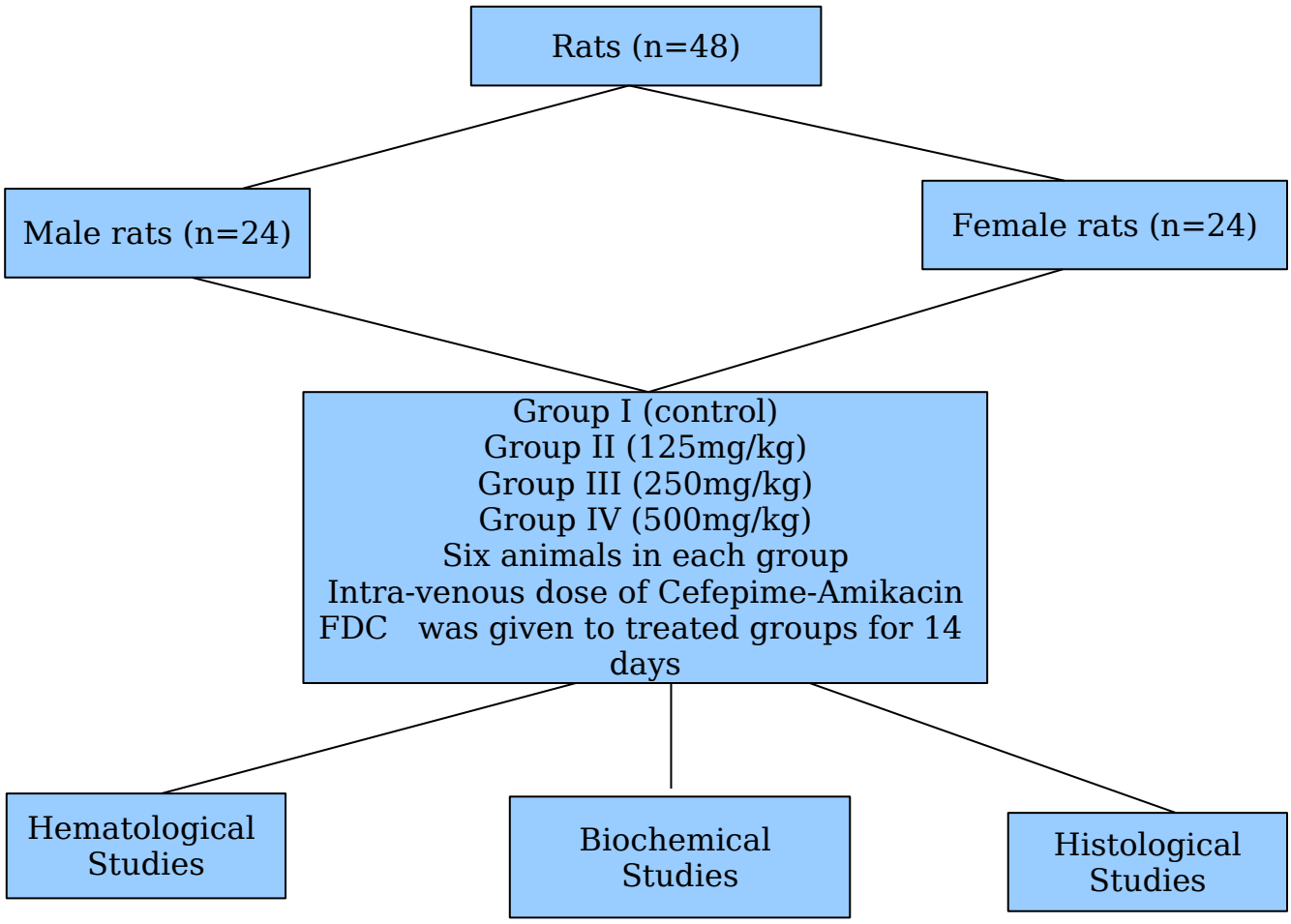

Fig 3) Effect of sub acute dose of Cefepime-Amikacin FDC on hematological parameters in male rats.

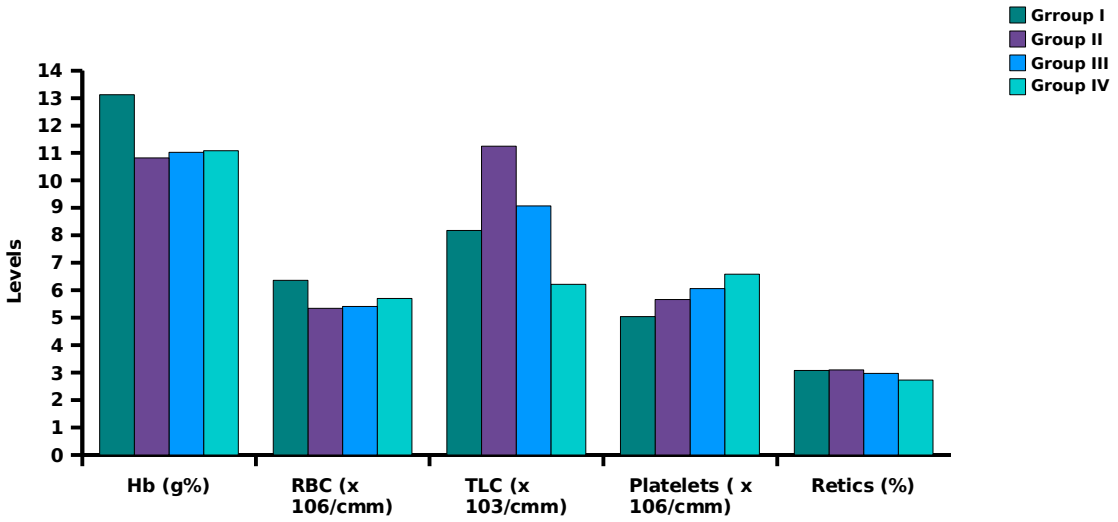

Fig 4) Effect of sub acute dose of Cefepime-Amikacin FDC on hematological parameters in female rats.

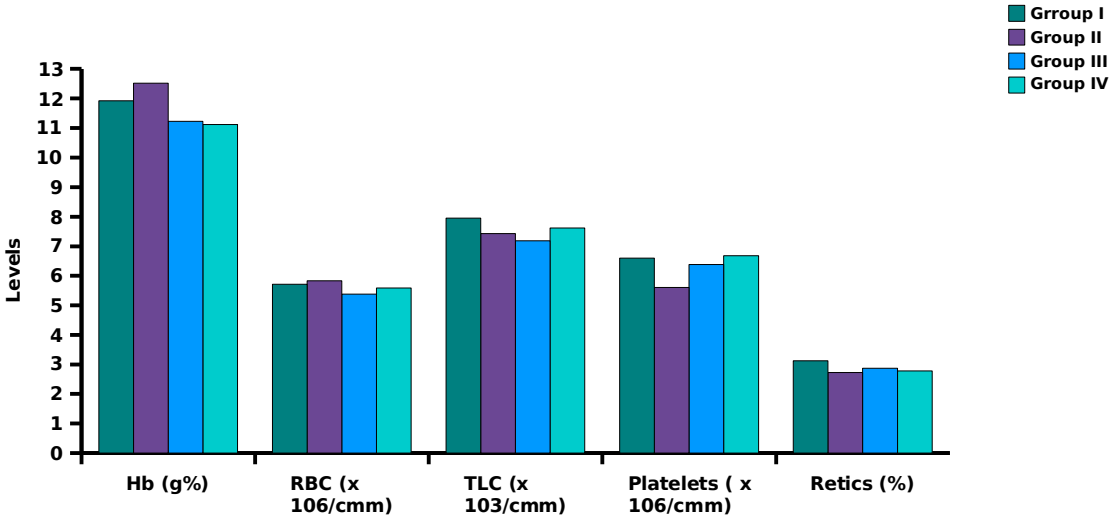

Table 5) Effect of sub acute dose of Cefepime-Amikacin FDC on biochemical parameters in male rats.

	Group I	Group II	Group III	Group IV
Total Protein (g%)	7.28 ± 0.47	7.12 ± 0.41	7.62 ± 0.30	7.10 ± 0.32
Glucose (mg/dl)	74.33 ±1 6.10	90.25 ± 11.87	75.58 ± 6.08	79.68 ± 13.30
ALP (IU/l)	235.00 ± 53.11	244.50 ± 37.03	261.33 ± 43.55	207.83 ± 59.00
ALT (IU/l)	62.43 ± 14.53	54.40 ± 16.08	61.33 ± 19.38	58.30 ± 7.60
Albumin (g%)	3.05 ± 0.16	3.08 ± 0.12	3.22 ± 0.18	3.20 ± 0.13
Creatinine (mg/dl)	0.98 ± 0.18	1.03 ± 0.05	0.98 ± 0.03	1.05 ± 0.05
Calcium(mg/dl)	11.55 ± 1.35	10.68 ± 0.41	9.90 ± 0.55	9.43 ± 0.88
Phosphorus (mg/dl)	11.18 ± 1.25	10.67 ± 0.69	11.53 ±1.59	9.40 ± 0.73

Table 6) Effect of sub acute dose of Cefepime-Amikacin FDC on biochemical parameters in female rats.

	Group I	Group II	Group III	Group IV
Total Protein (g%)	7.53 ± 0.22	7.90 ± 0.33	7.43 ± 0.45	7.30 ± 0.33
Glucose (mg/dl)	82.60 ± 7.54	85.67 ± 9.58	81.17±14.33	86.03 ± 10.08
ALP (IU/l)	156.78 ± 52.97	172.17 ± 39.81	208.50 ± 52.41	183.00 ± 54.38
ALT (IU/l)	48.45 ± 4.87	45.98 ± 6.02	55.33 ± 9.13	54.57 ± 7.45
Albumin (g%)	3.30 ± 0.13	3.37 ± 0.14	3.35 ± 0.14	3.32 ± 0.19
Creatinine (mg/dl)	1.64 ± 0.55	1.07 ± 0.12	1.15 ± 0.19	1.08 ± 0.04
Calcium(mg/dl)	11.13 ± 0.12	11.22 ± 0.75	10.38 ± 0.55	9.67 ± 0.30
Phosphorus (mg/dl)	8.75 ± 0.58	8.65 ± 0.72	10.30 ± 0.81	8.83 ± 0.88