SUMMARY AND CONCLUSIONS
The present study was carried out to investigate the effect of magnesium deficiency on calcium and oxalate metabolism and its relation to urolithiasis in rats. The important aspects of these investigations are summarized as below:

1. Magnesium deficiency was induced in male weanling rats by feeding a magnesium-deficient diet for a period of thirty days, which led to a significant \(p<0.001\) decrease in the body weight of the deficient rats as compared to the pair-fed controls, thereby suggesting that magnesium is indispensable for growth. Magnesium deficiency was biochemically ascertained by a significant \(p<0.001\) hypomagnesemia, hypomagnesuria and hypercalcemia usually observed in magnesium deficiency.

2. Magnesium deficiency led to a significant \(p<0.001\) decrease in the erythrocyte transketolase activity with a significant \(p<0.001\) increase in the percentage stimulation index for TPP in magnesium-deficient group, thereby showing that magnesium deficiency alters the thiamine metabolism.

3. The urinary excretion of lithogenic and inhibitory substances revealed a significant \(p<0.001\) hypocalciuria, hyperoxaluria, hypocitraturia, hyperphosphaturia \(p<0.01\) with no change in the excretion of uric acid and creatinine in magnesium-
deficient rats as compared to the pair-fed controls, suggesting the enhanced risk of stone formation in magnesium deficiency.

4. Magnesium deficiency caused a significant ($p<0.001$) increase in the activity of hepatic GAO. A significant ($p<0.01$) increase in the activity of hepatic GAD with a significant ($p<0.01$) decrease in the activity of ALT was observed in magnesium deficient group. However, LDH activity in liver and kidney remained unaltered. Cellulose acetate electrophoresis of kidney LDH revealed a significant ($p<0.01$) increase in the percentage distribution of LDH-I isoenzyme with a compensatory significant ($p<0.01$) decrease in the percentage distribution of LDH-V isoenzyme.

5. Magnesium deficiency significantly blocked the conversion of $^{14}$C-glyoxylate into $^{14}$C-CO$_2$ via glyoxylate oxidation cycle in both liver and kidney mitochondrial preparations by 26 percent and 17 percent respectively in magnesium deficient animals. The TPP dependent enzyme $\alpha$-ketoglutarate: glyoxylate carboligase activity was almost three times more in kidney mitochondria than in liver mitochondria. The enzyme activity was also decreased by 35 percent and 27 percent in the liver and kidney mitochondria respectively as compared to the pair-fed control.
rats, leading to increased glyoxylate pool, which is converted into oxalate. Thus magnesium deficiency in rats causes enhanced synthesis of oxalate in the liver as well as kidneys of deficient animals.

6. Intestinal absorption of calcium across BBM of both the control and magnesium-deficient groups revealed a simple passive diffusion process for calcium in the concentration range 0.1 to 1.0mM. However, the rate of uptake of calcium was significantly (p<0.01) higher in magnesium-deficient rats as compared to the pair-fed controls, suggesting that magnesium deficiency leads to hyperabsorption of calcium in the deficient animals.

7. Intestinal uptake of $^{14}$C-oxalate in both control and magnesium-deficient rats revealed a positive linear relationship between the uptake rate and the extravesicular oxalate concentration (0.1 to 1.0mM), thereby suggesting that oxalate is transported across the microvillus membrane by a simple passive-diffusion process. However, the rate of uptake of oxalate was significantly (p<0.001) higher in magnesium-deficient rats as compared to the pair-fed controls. Thus magnesium deficiency also leads to enhanced oxalate absorption in magnesium deficient rats.
8. Uptake of calcium by kidney cortical BBMV revealed a saturable kinetics (in the concentration range 0.1 to 1.0mM) in both the groups. However, the rate of calcium uptake was significantly (p<0.001) higher in magnesium-deficient group as compared to the pair-fed control group. Double reciprocal plot of the uptake data also suggested enhanced uptake of calcium (decrease in Km) through increased affinity towards its carrier in the magnesium-deficient group.

9. Renal uptake of oxalate by kidney cortical BBMV revealed a biphasic transport mechanism for oxalate in both the groups. A saturable hyperbolic relationship between oxalate uptake and extravesicular concentration (0.1 to 0.8mM) and a simple passive diffusion (0.8 to 1.0mM) was revealed in both the groups. However, the rate of uptake of oxalate was significantly (p<0.01) higher in deficient group as compared to the pair-fed controls. Double reciprocal plot of saturable component demonstrated the enhanced uptake rate due to increased turnover of transport carriers in deficient rat kidney cortical BBM.

10. Lipid composition of the intestinal BBMV revealed no change in the total lipid content of the membrane in magnesium-deficient group. However, a significant (p<0.01) decrease in the cholesterol content with a
significant increase in triglycerides (p<0.01) and total fatty acids (p<0.001) was observed in BBMV from magnesium-deficient rats. However, total phospholipid and glycolipid content remained unaltered.

11. Similar changes in the kidney cortical BBMV were observed in magnesium-deficient BBMV as compared to the BBMV from pair-fed control rats. The changes in the lipid composition of intestinal and renal cortical BBMV suggested increased membrane fluidity of the BBM.

12. A significant (p<0.001) enhanced transmembrane oxalate flux was observed in magnesium-deficient erythrocytes as compared to that from pair-fed control group, suggesting that defective membrane function may be the primary lesion underlying the cellular disturbances that occur in magnesium deficiency.

Deficiency of magnesium leads to enhanced risk of stone formation by not only altering the endogenous synthesis but also the intestinal absorption and retention of oxalate in magnesium-deficient rats. On the other hand, alterations in calcium metabolism i.e. hyperabsorption and enhanced renal uptake, contributing to hypercalcemia can be
attributed to PTH, suggesting a state of hyperparathyroidism. The above observations clearly indicate that maintenance of normal magnesium status is essential to avoid the risk of stone formation.