INTRODUCTION
Urolithiasis is documented as one of the oldest diseases afflicting mankind. Even today, it is considered to be a major cause of morbidity in individuals with considerable socioeconomic costs for health care and productivity in the community (Goldsmith, 1986; Maher, 1986). Although the treatment of urinary stones has been considerably improved with the introduction of a new non-surgical techniques, i.e. extracorporeal shock wave lithotripsy, (ESWL) the prevention of stone formation still needs to be developed, as ESWL neither cures nor prevents the disease (Goldsmith, 1986; Maher, 1986). The main reason for this is the obscurity of the biochemical mechanisms underlying calcium oxalate nephrolithiasis. Several epidemiological studies show that the incidence of urolithiasis is more predominant in males than females (Abdel-Halim et al., 1989; Bytyci and Mesaric, 1989). Majority of the stones analyzed consist of calcium and oxalate as their major constituents (Thind et al., 1989; Borghi et al., 1990), thus making calcium and oxalate metabolism a focal point to the medical scientists for the last few decades.

Oxalic acid is the end product of metabolism in the animal system and needs to be eliminated via renal clearance. Majority of the urinary oxalate is either derived endogenously or by absorption of preformed dietary oxalate (Hodgkinson, 1977). Jejunum in the small intestine is the
major site of oxalate absorption (Madorsky and Finlayson, 1977). Hyperoxaluria (Baggio et al., 1983; Lindsjo et al., 1987; Yendt and Cohanim, 1989; Trinchieri et al., 1991) rather than hypercalciuria (Sidhu et al., 1987; Jacob and Gray, 1989; Trinchieri et al., 1991) in stone formers has been suggested as an important causative factor of calcium oxalate nephrolithiasis (Robertson and Peacock, 1980; Robertson et al., 1981).

Several epidemiological, clinical and experimental studies have related the incidence of calcium oxalate nephrolithiasis to dietary factors, such as, excesses in animal protein and/or salt consumption (Goldfarb, 1988; Kok et al., 1990). Deficiency of various dietary components, particularly vitamins is of great importance in the genesis of oxalate stones. Experimental hyperoxaluria and urolithiasis has been produced by diets deficient in Vitamin B₁ and B₆ (Sidhu 1985; Ravichandran and Selvam, 1990a) and also in Vitamin A (Sharma et al., 1990). Marginal deficiency of Vitamin B₆ has been reported in stone formers (Murthy et al., 1982a). Similarly, a higher incidence of stone formation has been reported in thiamine-deficient population (Valyasevi et al., 1967).

Magnesium is of paramount importance in urolithiasis. Magnesium has been shown to bind oxalate in the gastrointestinal tract (Barilla et al., 1978; Berg et al., 1986). It also increases the solubility of calcium oxalate
(Berg et al., 1986) and inhibits the precipitation of calcium oxalate (Desmars and Tawashi, 1973) and calcium phosphate (Bisaz et al., 1978). Magnesium has also been shown to decrease both the growth and nucleation rates of calcium oxalate crystals (Li et al., 1985; Kohri et al., 1988). Studies have demonstrated the depressive effect of magnesium on endogenous oxalic acid formation (Thomas et al., 1973; Brundig et al., 1981). Hypomagnesuria is a common finding in stone formers (Vagelli et al., 1987; Wangoo et al., 1989). A subclinical magnesium deficiency has been reported amongst general population from affluent countries, as the dietary intake of magnesium from the prepared meals is far below the recommended dietary allowance (Marier, 1982; Abdulla, 1988).

Hammersten (1929) reported that magnesium deficiency causes experimental production of urolithiasis. Subsequently, several experimental and clinical studies have shown a positive relationship between dietary and urinary magnesium and stone formation. Nephrocalcinosis has been demonstrated by many investigators studying laboratory rats on magnesium deficient diet (MacIntyre and Davidsson 1958; Bunce et al., 1974; Al-modhefer, 1986).

It has been established that magnesium deficiency causes hypocalcemia in a number of species including man (Estep et al., 1969; Muldowney et al., 1970). The rat is the only experimental animal model that consistently develops hypercalcemia in response to magnesium depletion (McIntyre
Magnesium deficiency in rats has also been shown to result in significant hypomagnesemia, hypophosphatemia, hypomagnesuria and hyperphosphaturia (Whang and Welt, 1963; Tongyai et al., 1989; Okuno et al., 1990). These changes in calcium metabolism suggest a state of hyperparathyroidism, which has been diagnosed in 2-17% of patients with nephrolithiasis (Jaegar et al., 1986; Broadus, 1989; Galic et al., 1989). Deficiency of magnesium accelerates renal tubular calcium oxalate deposition in rats on hyperoxaluric protocol involving chronic ethylene glycol administration (Rushton and Spector, 1982; Ebisuno et al., 1987). Magnesium deficiency in rats induces imbalance of thiamine content in liver and kidneys (EL-Hindi and Amer, 1989). Aggravation of thiamine deficiency by magnesium depletion has been reported (Dyckner et al., 1985). Thiamine plays an important role in the mitochondrial oxidation of glyoxylate via glyoxylate oxidation Cycle (Dekker and Gupta, 1979) and TPP dependent enzyme α-ketoglutarate: glyoxylate carboligase enzyme (O'Fallon and Brosemer, 1977). Thus deficiency of magnesium may lead to increased glyoxylate pool in the animal system.

Defective membrane function has been implicated to be the primary lesion underlying the cellular disturbances that occur in magnesium deficiency. Increased gastrointestinal absorption of calcium has been reported in patients of
hyperparathyroidism (Kaplan et al., 1976, 1977). Increased calcium absorption may also lead to increase in oxalate absorption. Hyperabsorption of both calcium and oxalate has been reported in stones-formers (Lindjo et al., 1989). To understand the transport mechanism, methods have been developed in plasma membrane vesicles isolated from intestinal and renal cells (Kessler et al., 1978; Malathi et al., 1979).

Several studies show a relation between magnesium deficiency and lipid metabolism. In experimental magnesium deficiency, hypertriglyceridemia, hypercholesterolemia with an increase of free cholesterol and decrease of esterified cholesterol has been reported (Rayssiguier, 1981, Jaya and Kurup, 1987). Increased plasma levels of thio-barbituric acid reacting substances used as a measure of lipid peroxidation has also been reported (Mahfouz and Kummerow, 1989). The effect of magnesium deficiency on the function of the erythrocyte membrane has also been reported. Increased fluidity of erythrocyte ghosts has been related to the decreased amounts of cholesterol and sphingomyelin (Heaton et al., 1989; Tongyai et al., 1989). Although several reports confirm the effect of magnesium and its deficiency on calcium oxalate nephrolithiasis, the detailed biochemical mechanisms underlying magnesium deficiency has not been worked out. Therefore, the present study was carried out to clearly elucidate the effect of magnesium
deficiency on endogenous synthesis of oxalate, intestinal absorption and renal handling of calcium and oxalate, lipid composition of brush border membrane and oxalate handling by erythrocytes in magnesium-deficient rats with the following aims and objectives.

1) To produce dietary magnesium deficiency in male weanling rats and to biochemically assess the magnesium status of these animals.

2) To study the enzymes of oxalate biosynthesis viz. GAO, GAD and LDH in liver and kidney of magnesium-deficient rats.

3) To study the oxidative degradation of glyoxylate to CO₂ by the liver and kidney mitochondria via the glyoxylate oxidation cycle and the enzyme α-keto glutarate: glyoxylate carboligase in magnesium-deficient rats.

4) To investigate the effect of magnesium deficiency on intestinal absorption and renal handling of calcium and oxalate.

5) To study the effect of magnesium deficiency on the lipid composition of intestinal and kidney brush border membrane.

6) To investigate transmembrane oxalate flux in red blood cells of magnesium-deficient rats.