INTRODUCTION
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Multiple medication has become common feature in most prescriptions in modern medical practice. Concurrent use of one drug may alter the intensity of pharmacological effect(s) of another drug. Concurrent use of multiple drugs sometimes produces beneficial interactions and is often essential to obtain a desired therapeutic objective. But on most occasions such medication produces harmful side effects. The frequency of significant beneficial or adverse drug interactions is unknown. Survey that include data obtained in vitro, in animals and in case reports tends to predict a frequency of interaction that is higher than that actually occurs. While such reports have contributed to skepticism about the overall importance of drug interactions (Kush - Vessar and Green Blatt, 1977), the physician must be alert for their occurrence.

When a diabetic individual remains untreated or not adequately treated cardiovascular, neurological renal and retinal complications arise in the future clinical course (Foster, 1980).
Due to reduced body resistance diabetic patients are always prone to various microbial infections (Foster, 1980).

In the medical management of diabetes mellitus a physician always faces multiprong problems particularly in the treatment of associated complications. Prescription of multiple medications along with insulin and/or oral antidiabetic agents is a clinical problem to physicians due to drug interacting potentialities.

Beta-adrenoceptor blockers and nonsteroidal anti-inflammatory analgesics are very commonly prescribed for the treatment of associated hypertension,clusive coronary diseases and pain arising from diabetic ulcers and other inflammatory diseases. A thorough knowledge of drug interactions particularly of various common groups of drugs with antidiabetic agents is necessary to prevent any possible side effects arising from use of their concomitant administration. Anti-inflammatory agents and beta-blocking drugs are known to produce drug interactions with sulphonamides (Hasten, 1975). Despite of large number of reports the mechanism of interactions still remains unexplored. In course of time due to discovery of newer drugs and replacement of older drugs the clinicians have to alert for their interaction. At present many
agents have been recently introduced in clinical therapy. Studies on these drugs with antidiabetics are very much limited.

In the present study tolbutamide was selected among the sulphonylureas because of its low toxicity, higher safety and high clinical efficacy besides it can be estimated by standard procedure in the blood. For interaction studies with tolbutamide, aspirin, talnetin and trandil among the anti-inflammationary drugs and propranolol, stenodil, metoprolol and acetaminol among the beta-adrenoeceptor blockers have been selected for this study.

For interaction study with tolbutamide blood sugar estimation has been used as the major parameter but to make the study more conclusive the serum tolbutamide measurements have been also made.

The present study was undertaken with the following aims in view:

1. To confirm the hypoglycemic effect of tolbutamide in normal and experimentally induced (alloxan) diabetic rabbits and to select a suitable dose of tolbutamide for further interaction studies.

2. To study the effect of anti-inflammationary agents after single and repeated treatment on tolbutamide
induced hypoglycemia, corresponding serum tolbutamide concentrations and tolbutamide biological half-life in normal and diabetic rabbits.

(2) To study the effect of beta-blocking agents after single or repeated treatment in normal and diabetic animals on tolbutamide-hypoglycemia and corresponding serum tolbutamide concentration and its half-life.