### Abstract or synopsis of the proposal (200 words or less):

In diabetes mellitus the increased availability of glucose in insulin-insensitive tissues such as lens, nerve, and retina leads to the increased formation of sorbitol through the polyol pathway. In this pathway, glucose converts to sorbitol and then fructose through the enzymatic activity of aldose reductase and sorbitol dehydrogenase. The polyol pathway is involved in diabetic cataract. Since aldose reductase is localized primarily in lens epithelial cells, osmotic insults induced by the accumulation of sugar alcohols occur first in these cells. It is possible to prevent cataract via inhibition of the activity of aldose reductase. It is shown that apoptosis in epithelial cells can be prevented by an aldose reductase inhibitor, suggesting that this apoptosis is linked to the accumulation of sugar alcohols.

### Hypothesis or scientific justification of the proposal

Aldose reductase (ALR or AKR1B1; EC: 1.1.1.21) belongs to the aldo–keto reductase (AKR) superfamily. It is the first and rate-limiting enzyme in the polyol pathway and reduces glucose to sorbitol utilizing NADPH as a cofactor. Sorbitol is then metabolized to fructose by sorbitol dehydrogenase. Accumulation of sorbitol leads to osmotic swelling, changes in membrane permeability and also oxidative stress.

Several studies have revealed that hyperglycaemia has an important role in the pathogenesis of diabetic complications by enhancing aldose reductase related polyol pathway and increase in advanced glycation end products formation. Camel displayed high blood glucose concentration (9.7 ± 2.8 mM) as compared to other mammals.
In the case of the lens, the accumulation of the polyols could result in opacification of the lens nucleus and finally of the entire lens. The fact that aldose reductase inhibitors can block or delay the appearance of sugar cataracts emphasized the role of aldose reductase as a major contributory factor in the formation of diabetic cataracts. Unfortunately, no relationship between the structure of all inhibitors tested and the aldose reductase has so far emerged. This raises the question of the selectivity of these inhibitors. For instance, flavonoids are known to inhibit other enzymic systems such as aldehyde reductase or ATPase and are capable of binding to collagen. So the question remains as to whether aldose reductase initiates the primary event leading to sugar cataracts. The use of specific and potent inhibitors should give a clear-cut answer.

### Specific objectives

| Methodology & Major Techniques to be used | The purpose of the present study is to:  
1. Isolate and purify aldolase reductase from camel lens using different chromatographic methods  
2. Monitoring the initial rate of reactions using standard conditions  
3. Thermal and pH stability.  
4. Determination of kinetic constants and inhibition kinetics of the two flavonoids, naringin and quercetin |
| Availability of Samples | YES |
| If the answer is no, kindly justify |  |
| Availability of Chemicals | YES |
| If the answer is no, kindly justify |  |
| Availability of Instruments | YES |
| Availability of Ethical Approval (if needed) | YES |
national business coalition on health activities related to diabetes, may 2007, summary of activities related to diabetes, NBCH.


