1. INTRODUCTION

Nonenzymatic glycation of protein by reducing sugars is a complicated pathway of various modifications that lead to formation of advanced glycation end products (AGEs). Stable Amadori products are formed by organic reactions with the Schiff base which will further undergo a series of reactions through dicarbonyl intermediates to form AGEs. It is also assumed to be formed by sequential glycation and oxidation reactions called glycoxidation. The accumulation of the reaction products of protein glycation in living organisms leads to structural and functional modifications of tissue proteins (Takeuchi et al. 2004).

The role of advanced glycated end-product proved to be significantly responsible in diabetic microvascular complications of retinopathy, neuropathy and nephropathy as well as their role in the accelerated hyperlipidemia (Singh et al. 2001). There is evidence that glycosylation leads to biochemical modification of Immunoglobulin, and other macromolecules and is cause for pathogenesis of diabetic complications (Mendez 2003).

Elevated glucose level is etiologic agent for the pathogenesis of diabetic complications by increasing protein glycation and formation of advanced glycation end products (AGEs). Even in the absence of Diabetes Mellitus the formation of AGEs progressively increases with normal aging. However, they are formed at more paced levels in diabetes. AGEs are not only markers but also important causative factors for the pathogenesis of diabetes, hyperlipidemia, ketoacidosis, cataract, diabetic nephropathy, and neuropathy. Thus, the design and discovery of inhibitors of AGEs formation is proved to be a boon for the prevention of diabetic or other pathogenic complications (Brwonlee M et al. 1998). Aminoguanidine, a hydrazine-like small molecule, is the first AGEs inhibitor explored in clinical trials. However, the drug was not used commercially due to its side effects in phase III clinical trials in
patients associated with diabetes, although related to some extent to the confiscation of pyridoxal, resulting in vitamin B6 deficiency (Brownlee 1995).

Process of treatment of purified human IgG with glucose induced its glycation is time and pH dependent. (Kenedy et al. 1994) proved that the level of glycated IgG, IgM, and IgA increased in diabetic patients.

In 1912, Louis Camille Maillard explained the browning of proteins in food and called it as Maillard reaction. This is also known as non-enzymatic glycation of proteins, or a process which links chronic hyperglycemia to a series of physiopathological alterations considered important in the development of chronic complications of different diseases like diabetes and hyperlipidemia (Takeuchi et al. 2004). The further rearrangement of these glycated proteins give rise to a stable amadori product that degrades into a variety of compounds which, more reactive than the sugars from which they are derived (Wautier J.L. and A.M. Schmidt 2004). These propagators again form yellow-brown, often fluorescent (some are non fluorescent), irreversible compounds, usually called Advanced Glycation End-Products (AGEs) or Maillard products. Candidate active AGE compounds include N-(carboxymethyl)-Lysine (CML) pyrraline, pentosidine and their crosslinks (Kaysen G. 2001).

Medicinal plants have been used for decades to treat diseases in subcontinent. The vast use of herbal remedies and health care preparations, described in ancient holy texts gave evidence for the occurrence of natural products with medicinal properties. In fact, wild plants produce a multi range of bioactive molecules, making them enriched source of various types of medicines (Kala et al. 2006). Higher plants, as sources of medicinal compounds, have continued to play a significant role in the maintenance of human health since ancient times (Farombi 2003). Over 50% of all modern clinical drugs are of natural product origin (Stuffness and Douros 1982) and natural products play an important role in drug designing programs in the pharmaceutical industry (Baker et. al. 1995).

It is known that medicinal plants have little or no side effects. Metformin is the only ethical drug approved for the treatment of non insulin dependent diabetes
mellitus (NIDDM) patients (Beisswenger P.J et al. 1999), which is derived from a medicinal plant *Galega officinalis* and historically used for treatment of diabetes. (Oubre, A.Y et al. 1970) There are many anti-diabetic plants, which might provide useful sources for the development of drugs, in the treatment of diabetes mellitus. The literature on medicinal plants with hypoglycemic activity is vast, as many of these plants were used for many centuries and sometimes as regular constituents of the diet. Synthetic inhibitors and inhibitors from plant extracts have their own importance and now are studied extensively.

There are reports of some natural substances isolated from plants with AGE-inhibitory effects. One such compound is curcumin isolated from *Curcuma longa* (Turmeric), commonly known as Haldi. Ginger (*Zingiber officinale* Rosc.) is another spice useful for diabetic therapy. (Broadhurst CL et al. 2000) When type 2 diabetic rats were fed with ginger, they show hypoglycemic activity, thus improving their diabetic condition (Kar A.et al. 2003). Now it is the need of time to develop some new compounds either from plants or synthetically to control diabetes and other age accelerating diseases. As plants have fewer side effects so these should be preferred to study.

In this study Salep (*Eulophia campestris*) & Whitton root (*Eulophia nuda*) extract were used to study its effect on glycation and Maillard products. The major object of this study was to investigate the effect of salep and whitton root as inhibitor of AGE or Maillard reaction under *in vitro* conditions and measure its activity against AGE production or inhibition.