Introduction

Diabetes mellitus (DM) is characterized as a disorder of metabolism leading to high blood glucose, either due to absolute or relative deficiency of insulin in the body. DM is divided into two types: type I DM – when the pancreas do not produce any insulin and type II DM – when there is relative deficiency of insulin in the body and can be managed by oral hypoglycemic agents. Chronic hyperglycemic state has been known to produce various secondary diabetic complications; Nephropathy, Retinopathy and Neuropathy. Further, diabetes induced vascular complications can also be divided into two types: Macrovascular - cardiovascular complications and Microvascular - Retinopathy and nephropathy.

WHO and the international diabetes federation have predicted that the number of adult-onset diabetics worldwide would more than double by 2030 from the present level of 171 million to 366 million (Wild S et al., 2004). This increase would be approximately 42% in developed countries and approximately 150% in developing countries. Recent epidemiological studies have pointed to the growing epidemic of diabetes in India (Ramachandran et al., 2001; Mohan et al., 2001, 2003, 2006; Simmons et al., 1989). Indeed, according to the recent Diabetes Atlas produced by the International Diabetes Federation (IDF), India is home to the largest number of people with diabetes in the world, 40.9 million diabetic subjects in 2007, and these numbers are predicted to increase to 69.9 million by 2025 (Sicree et al., 2006; Mohan et al., 2008). In India, diabetic retinopathy (DR) was the 17th cause of blindness 20 years ago; today it has taken 6th position. DR is the common diabetes associated retinal complication and leading cause of vision loss all over the world. After 15-20 years of DM almost all the patients with type I DM have retinopathy of some degree. In case of type II DM patients, 20-30% patients suffer from DR after a decade (Fong et al., 2004).

DR is a disorder of microvasculature of the retina caused by various abnormal metabolic pathways as triggered by uncontrolled hyperglycemia. Hyperglycemia is the key abnormality in diabetes mellitus that promotes oxidative stress (Wolff et al., 1987, Baynes 1991, Jennings et al., 1992) and it results in increased oxidative stress,
and elevated oxidative stress plays an important role in the pathogenesis of diabetic retinopathy (Baynes, 1991). Further, Oxidative stress leads to the production of reactive oxygen species which is considered as a strong stimulus for the release of cytokines (IL-1β, TNF-α); they can damage endothelial cells, increase release of vascular permeability factor (VEGF), and finally leads to retinal neovascularisation (Kowluru and Odenbach, 2004; Chang and LoCicero, 2004; Wilkinson-Berka, 2004; Ailleo and Wong, 2000). Capillary BM thickening is the most widely reported lesion of diabetic microangiopathy, being observed consistently in human diabetes and experimental diabetes in several different animal models (Stitt, et al., 1994).

Pharmacotherapy of DR is still incomplete as there is no standard drug which can completely stop its progression or treat the existing damages done in the retina. Corticosteroids and anti-VEGF agents have shown some beneficial results with regard to prevention of neovascularisation and vascular leakage, but remained limited in use due to their short-duration effects and serious side effects (like cataract and elevation of Intra Ocular Pressure). More importantly none of these agents have been able to substitute the durability and effectiveness of panretinal photocoagulation in preventing vision loss in the late stages of DR. Therefore, pharmacotherapy of DR is still an adjunct to panretinal photocoagulation and which is the only option to restore vision during severe damages.

Bioflavonoids are polyphenolic compounds, which are widely found in fruits and vegetables. To date about 8000 bioflavonoids have been identified and belongs to various classes: flavones, flavanols, flavanones, flavanols, anthocyanins and isoflavones. Flavanoids have gained importance in therapeutics because of their beneficial biological effects in humans. Bioflavonoids have been found to possess strong anti-oxidant, anti-inflammatory, anti-angiogenic and anti-apoptotic properties. Bioflavanoids have played very important role in reducing ocular inflammation, strengthening of retinal microvasculature, improving ocular blood flow and neuroprotection. Many of these compounds have already being used for the prevention/treatment of age related macular degeneration as antioxidants and are successfully being marketed by leading pharmaceutical companies.
Therefore, the present is aimed to screen bioflavanoids and some natural plant based products for the prevention of neurovascular degenerations in DR, where no standard drug therapy is available which can completely stop the progression of this devastating disease.