INTRODUCTION

Diabetes mellitus is a metabolic disorder which arises as a result of multiple genetic, environmental and different lifestyle factors. This disease is characterized by hyperglycemia due to impaired insulin secretion or increased insulin resistance to the cells. According to the information from WHO, the highest increase in diabetes prevalence are among low and middle income countries, predominantly within the 40-59 years age group, although the increased risk is seen for onset at younger age itself. Therefore there is a need for the developments of more effective, preventive and therapeutic approaches that challenges and increases life span with improved quality of life. Its occurrence is mainly due to primarily rooted genetic level and modern life style related factors like obesity, physical inactivity, aging, nutrition and stress [1,2].

The hyperglycemic condition of a diabetic patient is untreatable but the blood glucose level can be controlled by daily dose of antidiabetic drugs. Numerous US-FDA (United States Food and Drug Administration) antidiabetic drugs are chemically synthesized and utilized in the treatment protocol. Mainly the aforementioned groups of synthetic drugs tend to control blood glucose level in diabetic patient. Nevertheless, in recent time much of explorations are made and focused in peculiar towards naturally formulated antidiabetic composition due to their less toxicity and negligible side effect to the body. Various formulations are available in the market for diabetes, but none of them is a promising tool to cure diabetes [3]. This is predominantly because of malevolent side effects and diminution in response to prolonged usage.

In recent years, scientists spotted and evaluated antidiabetic potential of traditionally used medicinal plants in various animal models. Therefore herbal drugs are gradually gaining popularity in the treatment of diabetes and its related complications associated with oxidative stress. The major trait of herbal medicine seems to be their supposed efficacy, low incidence of serious adverse effects and economic [4]. Natural products and their derivatives have been a successful source of bioactive molecules in medicine before the advancement of other modern therapeutics in the post-genomic era.
Most studied natural products are flavonoids that they were predominantly used for various purposes and as part of daily food consumption. These are polyphenolic compounds expected to deliver various benefits like antidiabetic, anti-inflammatory, anticancer, antioxidant and antiviral activities. Substantial reports on the flavonoids prove that they are capable to interact with more than one target. Further, recent reports effectively exhibit flavonoids as promising antidiabetic agent. For instance various flavonoid isolates like quercetin are under investigation in type 2 diabetes mellitus. Hypoglycemic and antidiabetic activities of such flavonoids are studied in diabetes induced animal models for blood glucose level and serum lipid profile [5].

More than 8000 species of plants are bound to present flavonoids and they are omnipresent in fruits, vegetables, wine, tea, and cocoa. The biologically active flavonoids are food-borne polyphenolic compounds which tend to increase the capillary permeability. Later the attention has been focused on metabolically active phytochemicals possessing potential benefits such as flavonoids [6]. The concept has been widely accepted in recent time as polyphenols protecting the body against the various chronic diseases including diabetes and oxidative stress related complications.

The implications of such antidiabetic potential flavonoids are numerous in approaching the disease with alternative natural substance. Antidiabetic effect of extracts of various plant species put us under realization of specific activity to which it is intended. Nevertheless, their utilization very limited because of its poor solubility, bioavailability and degradation by enzymes. Secondly extensive first pass metabolism before reaching the systemic circulation is a major lapse in reaching systemic adequacy of flavonoids. Different methods are there to improve the solubility of flavonoids and to overcome the aforementioned hindrances. One such approach is selection of nanocarrier for the delivery of such substances. As it is the most promising appeal is to use biodegradable polymeric system to encapsulate the biomolecule for better activity. Various efforts has been put forth for the effective preparation of nanoparticles containing bioflavonoids, and it has provided us the valuable input for the feasibility of using the less utilized antidiabetic and antioxidant potential natural substances [7].
Novel drug delivery technologies have gained the importance to achieve modified delivery of herbal drugs thereby increasing the therapeutic value as well as reducing toxicity. There are numerous novel herbal formulations available like polymeric nanoparticles, nanocapsules, liposomes, phytosomes, nanoemulsion, microsphere, transferosomes and ethosomes has been reported using bioactive and plant extracts. Of which fabrication of herbal constituents as nanoparticulates is extremely popular, basically nanoparticles are particulates dispersions or solid particles with a size in the range of 10-1000nm. The primordial objective of nanoparticulate concept is to control the particle size, surface properties and release of pharmacologically active agents to achieve site specific action and so on. The issues related to solubility of poorly soluble drugs are effectively turns holistic by incorporation of various novel technologies of aforementioned. Antioxidant biomolecules are used as therapeutic agents in many diseases like cancer, diabetes, cardiovascular disease, autoimmune disease and neurodegenerative disorder. Consequently, stable and viable alternative is in handy for delivery of such plant bioconstituents with utmost safe.

Nanoparticles have received a tremendous attention for acting as a carrier and delivery vehicle for most of the candidates. The submicron size of nanoparticles offers a number of distinct merits as compared to microparticles precluding higher intracellular uptake and uptake of nanoparticles by intestinal epithelia. The nanoparticle surface and size is an important aspect for its activity both physiologically and pharmacologically. The behavior of nanoparticles in a system is determined by the polymeric substances which are intended into it. Provided with the ample scope of available polymers, tailoring and fabrication of nanoparticles are done with ease. The polymeric composition of nanoconstituents have a positive control and great influence on absorption, biodistribution pattern and elimination by altering the polymer, associated drug and adjutants like surfactants.

The incorporation of novel method of polymeric nanoparticulate carriers for the flavonoids is recently been in existence. Generally, polymeric nanoparticles render potential drug carrier, optimal size, surface charge and hydrophilic-hydrophobic balance, biocompatibility and tailored drug release patter. Thus produced nanoparticulate carriers
for biomolecules certainly deliver the drug at specific site, as usually a particle size of 100 nm or less have increased cellular intake for maximum activity \[11\]. Loading of more than one flavonoid or related substances is a viable option for increased activity of the component. Contemporarily evidences are robust relating to the combined loading of components into the nanocarriers. Current interests are mainly shown to distinguish, compare and differentiate the nano-loaded components against the pure compound of the same substance in various animal models. Substantial achievement in gaining the attention of researchers towards the loading of plant biomolecules into the polymeric chain network is increasingly addressed in recent while \[12\]. So with no ambiguity solid and potential substantiation are there to do a much in this field of overcoming in bringing out, a treatment schedule for the chronic disease, with specialized novel technology like nanotechnology inculcation and positive interference.

In spite of regarding the above fact, the present study aims to prepare a novel dual bioflavonoid isolate loaded nanoparticles by various techniques using factorial design to optimize the preparation. Further study we moved into evaluating and comparing the in-vitro as well as in-vivo antidiabetic and antioxidant activity of the components with the single loaded nanoparticles as compared to pure isolate and dual loading.