INTRODUCTION
1. INTRODUCTION

In recent years, the pharmacological effects of traditional medicine, which is an important natural resource, is receiving serious attention worldwide [1]. There is a great demand for natural medicine. Complementary and alternative medicines (CAMs) are used in more than 80% of the world’s population. It includes several major categories such as alternative medical systems, biologically based therapies, manipulative therapies, mind-body therapies, and energy therapies [2]. Folk herbal medicine is the most used remedy to cure common and widespread diseases because they contain components of therapeutic value [3]. The increasing use of plant extracts in the food, cosmetic and pharmaceutical industries suggest that, in order to find active components, a systematic study of medicinal plants is very important [4-5].

Oxidative stress plays an important role in the pathogenesis of various degenerative diseases such as coronary artery disease, diabetes, stroke, alcoholic liver cirrhosis and cancer. Free radicals induction and oxidative stress are initiated by reactive oxygen species (ROS), such as superoxide anion (O2 -), perhydroxy radical (HOO-) and hydroxyl radical (HO-) which are produced in the body, primarily as a result of aerobic metabolism [6-7]. Antioxidants are essential substances which possess the ability to protect the body from damage caused by free radical induced oxidative stress [8]. Synthetic antioxidants are being restricted due to their side effect. Therefore, attention has been directed toward the development and isolation of natural antioxidants in foods or medicines to replace synthetic antioxidants [6].

*Ziziphus jujuba Mill.* are species of the genus *Ziziphus Tourn. ex L.* *Ziziphus* belongs to the family Rhamnaceae. It is indigenous and naturalized throughout many Asian and African countries. Some common names of this plant are Annab, ber, black date, Chinese date, Chinese jujuba, common jujuba, jujuba, jujuba date, jujuba plum, onnab, red date and unnab [9]. *Ziziphus* is probably best known in the system of ancient Chinese medicine for its key role. *Ziziphus* is sour and balanced in nature; being neither too warming nor cooling effects [9-10]. According to studies, *Ziziphus jujuba* provides other actions related to anti-complement [11], hypolipidemic effects [12-13], anti-inflammatory [14], antioxidant [15], antimicrobial [16-17], antidiabetic [12], immunological activity [18], hepatoprotective [19], cardiovascular effect [20]
and gastrointestinal effects [21]. Various pharmacological studies support its traditional uses and also exploit its new benefits for human health.

Chemical constituents such as triterpenes, saponins, related triterpene compounds [22], Zizipin Jujubosides A1 and C and acetyljujuboside B, protojujubogenin type triterpene bisdesmosides, protojujubosides A, B, and B1, some fatty acids like lauric acid, myristic acid, palmitic acid, palmitoleic acid, stearic acid, oleic acid, linoleic acid, arachidic acid and docosanoic acid [23], vitamin A, B2 and C, sugars, mucilage, calcium, phosphorus and iron are reported to be present in Ziziphus jujuba Mill. [24].

Dyslipidemia, especially, atherogenic dyslipidemia, has been strongly linked to the pathophysiology of cardiovascular disease (CVD) [25-26]. Cardiovascular disease is now a principal cause of death. By 2020, it will become the leading cause of death and disability worldwide [27]. The disease has been estimated to affect 10% of adults older than 35 years of age in Indian cities and to have caused 1.5 million deaths in India in 2000 [28]. Asian Indians are predisposed to metabolic syndrome and insulin resistance, which is often characterized by low HDL cholesterol levels and hypertriglyceridemia [29-30]. Particularly with regard to Indians, the mortality due to CVD [31] and risk of metabolic syndrome and insulin resistance [29-30] has increased while decreasing among western countries [31]. The prevalence of small-dense LDL (pattern B) and TG/HDL ratio > 3 is significantly increased among Asian Indians compared to whites in the United States. In the US, the prevalence of coronary artery disease (CAD) in Asian Indians is 4-fold higher than Whites (10% versus 2.5 %) [32]. The burden of CAD in Asian Indians is much higher than that reflected by the prevalence data [33]. In developing countries, the prevalence of the metabolic syndrome varies from 13% in China to 30% in Iran [34]. Cardiovascular diseases are one of the major causes of mortality in Iran [35], and the prevalence of these disorders continues to rise [36]. A study in Iran-Tehran reported an estimated prevalence of >30% in adults [37], which is significantly higher than the prevalence in most developed countries [38]. Compared with non diabetic individuals, type 2 diabetics have a two to four fold higher risk of CVD, and dyslipidemia is a main contributor to the increased risk in this population [39]. India is facing a major burden
from the rising prevalence of CVD, type 2 diabetes and early sub clinical stage of glucose intolerance [40-42]. The greatest number (50.8 millions) of people worldwide with diabetes was reported in India in 2010 and there will be predicted to increase to 87 million by 2030 [43].

The Chennai Urban Population Study, a population-based study in Chennai, in South India, reported a prevalence of coronary artery disease (CAD) of 11% which is 10 times more than what it was in 1970 [44]. The authors report clustering of risk factors for CAD such as hyperglycemia, central body obesity, dyslipidemia and hypertension tends to occur, and interaction of these risk factors could explain the enhanced CAD risk in Indians [45]. Studies conducted in Mysore region also report similar trend among diabetic subjects [46]. A study demonstrates presence of definite metabolic abnormalities among pre and post menopausal employed women in Mysore city. A higher prevalence of metabolic syndrome was seen among post menopausal group and irrespective of menopausal status; the mean values for TC, LDL and FBS were higher than the desirable cutoffs for Asian Indians. Also, a high majority were in pre-diabetic state in pre menopausal women [47].

Most recently, guidelines for management of dyslipidemia highlighted the aggressive lipid-lowering strategy in subjects with documented CVD or previous myocardial infarction (MI). Statins are the first-line therapy for reducing low-density lipoprotein (LDL) levels in patients at high risk for atherosclerotic cardiovascular disease (ASCVD) [48]. These agents are being used in millions of high-risk people worldwide.

In many countries, most practitioners formulate and dispense their own recipes. However, this requires proper documentation and research. Furthermore, unexpected effects of many popular herbal products are described in the literature. Thus, the researcher's role in ensuring protection of the consumer continues to grow. It is the responsibility of all medical professionals to apply the best evidence available when caring for patients. However, the application of statins might be restricted by the adverse effect on the liver function and creatine kinase, especially in patients with old age, multiple co-morbid diseases, high-dose statins, or a combination lipid-lowering therapy [49]. Thus, there is an attempt to promote the rational, safe and
appropriate use of herbal medicines and mainstreaming of traditionally used herbal remedies.

Different parts of *Ziziphus jujuba* such as peel, pulp and seed are commonly used as food, food additives and flavorings as a supplement for promoting health [50-51]. Therefore, the interest in the evaluation of activity of different tissue types of *Ziziphus jujuba* may explain some of the hypolipidemic effects [12, 52] and empirical uses in folk medicine. However, hypolipidemic activity and mechanism of action remain to be elucidated [12].

Very limited data is available on clinical studies in human subjects. One clinical trial has reported concerning the hypolipidemic effects of *Ziziphus jujuba* fruit in the human [13].

With the above background, the present study was conducted to investigate the prevalence of metabolic syndrome and cardiovascular risk in type 2 diabetics with dyslipidemia residing in Mysore city and to validate the lipid lowering effect of *Ziziphus jujuba Mill.* supplementation in dyslipidemic subjects.

**The objectives of the present investigation were,**

1. To study the nutrient composition, antinutrients, antioxidant components and analyze antioxidant capacity of *Ziziphus jujuba Mill.*
2. To assess the nutritional and biochemical status of selected hyperlipidemic subjects with reference to atherogenic risk.
3. To evaluate the effect of *Ziziphus jujuba Mill.* supplementation on blood lipid profile.