7. Discussion

Effective blood glucose and hypertension control is the key for preventing or reversing diabetic hypertensive complications. In present study, we used unilaterally nephrectomised rats followed by DOCA administration for 4 weeks superimposed on type 2 diabetes (Jadhav & Upasani, 2011). This model of mineralocorticoid-induced, volume-expanded experimental hypertension resulted in an increase in blood pressure in diabetic as well as nondiabetic rats from 4 weeks onwards. Administration of TSE (120 and 240 mg/kg/day, p.o. for 4 weeks) in unilaterally nephrectomised diabetic and non-diabetic hypertensive rats significantly (p<0.05) reduced the BP as compared to diabetic hypertensive group. It has been established that the mineralocorticoid induced hypertension is associated with increased oxidative stress, which is dependent upon NADPH oxidase. The causal factor implicated in stress mechanism is either increased production, or decreased scavenging, of oxidants such as superoxide anion can give rise to hypertension by superoxide interacting with NO, forming peroxynitrite, and thereby decreasing NO availability for smooth muscle relaxation (Seto et al., 2006).

STZ could induce NO formation and which further leads to mitochondrial membrane potential changes and hence the release of cytochrome C, which triggers apoptosis (Hirst & Robson, 2010). TSE treatment to diabetic rats had shown a decrease in serum NO level. These findings can be correlated with number of polyphenolic phytochemicals, such as resveratrol, quercetin (Kawada et al., 1998), and catechins (Pannala et al., 1997) which have been reported to inhibit the reactive nitrogen species effect. Chan et al., (1997) found that epigallocatechin gallate could inhibit inducible nitric oxide synthase (iNOS) activity and its mRNA expression in LPS-activated macrophage. Pumthong (1999) reported that Tamarind seed coat was composed of polyphenols including tannins, anthocyanidin, and oligomeric anthocyanidins. In addition, Tamarind fruit extract improved SOD, glutathione peroxidase activity in obese rats besides reduction in lipid and body weight (Khairunnuur et al., 2010). In present study, the amelioration of antioxidant enzymes in TSE treated diabetic rats signify that the results are in accordance with earlier findings of *T. indica*.

The importance of the sympathetic nervous system in DOCA-NaCl hypertension is well illustrated by studies in which central catecholamine depletion reversed hypertension (Lamprecht et al., 1977). Therefore, the proposed mechanism of antihypertensive activity for *T. indica* may be through decrease in catecholamine release or partly 5 hydroxytryptamine (5HT) antagonistic property, or may be combination of these two above mentioned mechanisms as it is well known fact that endothelin-1(Matsumura et al., 2000), atrial
natriuretic peptides (Ogawa et al., 1999), vasopressin (Bereck et al., 1982), and 5HT (Dawson et al., 1988) are involved in the pathogenesis of DOCA salt hypertension.

Nevertheless, the possibility that endothelial derived vasoconstrictor or vasodilator factors might contribute to or modulate the tone cannot be excluded. NO is synthesized by vascular endothelium and is important for the regulation of vasodilator tone and the control of blood pressure (Calver et al., 1993). According to the results obtained in present study, serum NO concentration in hypertensive group (Group II) was lower than normotensive control. However, there were no significant alterations in serum NO concentration in treatment groups compared to hypertensive control. Therefore, we conclude that the majority of the antihypertensive effect of *T. indica* in DOCA-salt hypertensive rats may be due to sympathoinhibition rather than a direct action on vascular smooth muscle. Whereas, STZ diabetic rats superimposed with DOCA resulted in increased level of serum NO. The TSE treatment resulted in significant decrease in NO which supports the antioxidant nature of herb.

Lipids are very susceptible to attack by free radicals, and oxidized LDL species appear to contribute to the atherosclerosis pathobiology within the artery wall. In recent years, several compounds from vegetables and fruits i.e., food especially rich in natural antioxidants like polyphenols, have been used to prevent oxidized LDL (oxLDL) formation. An inverse relationship between oxLDL formation and polyphenol/flavonoid contents has been reported (Aviram & Fuhrman, 1998). Tamarind fruit extract in hypercholesteremic hamster reported to present excellent antilipidemic and antioxidant activity (Martinello et al., 2006) which can be corroborated with the present findings (Table 1). Hypertriglyceridemia, and even more threatening hypercholesterolemia, are found frequently in untreated hypertensives (Sankar et al., 2005). In the present study, increased MBP in non-treated DOCA-salt hypertensive rats were accompanied with significant increase of fasting serum cholesterol and LDL levels, and a significant decrease in serum HDL level when compared to the corresponding normotensive non-treated group. These findings can be explained by increased activity of the sympathetic nervous system in DOCA-salt hypertension. Evidence supporting this conclusion includes the presence of increased circulating catecholamines levels in DOCA-salt hypertensive rats (Luo et al., 2003). Catecholamines induce lipolysis leading to rise of free fatty acids (FFA). The resultant burden acetyl CoA molecules exceed the oxidative capacity of the cycle and leads to hypercholesterolemia. Moreover, these FFA could be re-esterified in liver with glycerol forming TG with a significant rise in TG level (Tosukhowong et al., 2002). Recently, it was
reported that oxidative stress can affect lipids causing remarkable decrease in lipoprotein lipase enzyme with severe increase in TG and decrease in HDL levels (Kaysen et al., 2004). The decrease in serum HDL may be explained by the known inverse correlation of HDL-cholesterol with adiposity and TG levels and a positive correlation with lipoprotein lipase activity (Sankar et al., 2005).

8. Conclusion

In conclusion, oxidative stress in conjunction with sodium reabsorption plays an important role in the development of combine diabetic hypertension and TSE efficacious in glucose and lipid homeostasis showed antihypertensive activity may be through anti-atherosclerotic activity and sympathoinhibition in conjunction to antioxidant action.