

## ABBREVIATIONS

AER	:	Albumin excretion rate
AGE	:	Advanced glycation end products
Ang II	:	Angiotensin II
ARB	:	Angiotensin receptor antagonist
ARI	:	Aldose reductase inhibitors
AT1	:	Angiotensin II type 1 receptor
BSA	:	Bovine serum albumin
Bw	:	Body weight
CrCl	:	Creatinine clearance
CTGF	:	Connective tissue growth factor
DM	:	Diabetes mellitus
DN	:	Diabetic nephropathy
ECM	:	Extracellular matrix
ESRD	:	End stage renal disease
FBG	:	Fasting blood glucose
GBM	:	Glomerular basement membrane
GDM	:	Gestational diabetes mellitus
GFR	:	Glomerular filtration rate
GLUT	:	Glucose Transporter
GPx	:	Glutathione peroxidase
GR	:	Glutathione Reductase
GSH	:	Reduced glutathione
GSSG	:	Oxidized glutathione
HbA1C	:	Hemoglobin A1C
HDL	:	High-density lipoprotein
HFD	:	High fat diet
HMG-CoA	:	Hydroxy methyl glutaryl CoA
HOMA-IR	:	Homeostasis model assessment-insulin resistance
HPLC	:	High performance liquid chromatography
IGF	:	Insulin-like growth factor
IL-1	:	Interleukin-1
iNOS	:	Inducible NO synthase
LDL	:	Low-density lipoprotein
LPO	:	Lipid peroxidation
MCP-1	:	Monocyte chemoattractant protein-1
MDA	:	Malondialdehyde
NO	:	Nitric oxide
PAS	:	Periodic acid-Schiff
PKC	:	Protein kinase C
PMS	:	Post-mitochondrial supernatant
PO	:	Palm oil
PPAR	:	Peroxisome proliferator-activated receptor
RBO	:	Rice bran oil
RIPA	:	Radio Immuno Precipitation Assay

ROS	:	Reactive oxygen species
SOD	:	Superoxide dismutase
STZ	:	Streptozotocin
T3	:	Tocotrienol
TBA	:	Thiobarbituric acid
TBARS	:	Thiobarbituric acid reactive substances
TC	:	Total cholesterol
TCA	:	Trichloroacetic acid
TG	:	Triglycerides
TGF- $\beta$	:	Transforming growth factor- $\beta$
TNF- $\alpha$	:	Tumor necrosis factor- $\alpha$
TOC	:	Tocopherol
TRF	:	Tocotrienol rich fraction
VEGF	:	Vascular endothelial growth factor
VLDL	:	Very low-density lipoprotein
WHO	:	World Health Organization
$\alpha$ -TTP	:	$\alpha$ -Tocopherol transfer protein

## CONTENTS

	Page no.
<b>CHAPTER 1. INTRODUCTION &amp; OBJECTIVES</b>	<b>1-3</b>
<b>CHAPTER 2. REVIEW OF LITERATURE</b>	
1. Diabetes mellitus	4-6
2. Global epidemiology of DM	6-7
3. Socio-economic burden of DM in India	8-9
4. Diabetic complications	9-10
5. Diabetic nephropathy-a major diabetic complication	
5.1. Prevalence of diabetic nephropathy	10
5.2. Signs and symptoms of diabetic nephropathy	11
5.3. Pathophysiology of diabetic nephropathy	12-26
5.4. Recent advances in pharmacotherapy for diabetic Nephropathy	26-30
6. Vitamin-E family	31
7. Biological sources of Vitamin-E(T3 and TOC)	31-32
8. Tocotrienol rich fraction	
8.1. Tocotrienol rich fraction from palm oil (TRF-PO)	33
8.2. Tocotrienol rich fraction from rice bran oil (TRF-RBO)	33
9. Absorption and distribution of T3 and TOC in various tissues	34
10. Biological activities of T3 and TOC	
10.1. Hypolipidemic and cardioprotective activity	35-37
10.2. Antioxidant activity	37-38
10.3. Neuroprotective activity	38-39
10.4. Anticancer activity	39-40
10.5. Effects on bone metabolism	40-41
10.6. Immunomodulatory activity	41
10.7. Gastroprotective activity	41
10.8. Antidiabetic activity	42
11. Varying biological effectiveness: T3 are more potent than TOC	
11.1. In vitro studies	43-44
11.2. In vivo studies	44-45
12. Potential of TRF to act as nephroprotective agent	45
<b>CHAPTER 3. MATERIALS AND METHODS</b>	<b>46-55</b>
<b>CHAPTER 4. TYPE 1 DIABETES</b>	
1. Objectives	56
2. Induction of type 1 diabetes and experimental design	56-57
3. Results	
3.1. Establishment of a non genetic rat model of type 1 diabetes	57-58
3.2. Dose dependent study of hypoglycemic and nephroprotective effects of PO-TRF and RBO-TRF	59-70

3.3. Comparative study of hypoglycemic and nephroprotective activities of PO-TRF and RBO-TRF at similar doses	71-76
3.4. Assessment of dyslipidemia	77-82
3.5. Assessment of Oxidative stress in the kidney	83-88
3.6. Western blot analysis of protein expression of TGF- $\beta$ , fibronectin and collagen type IV in the kidney	89-92
3.7. Histopathological analysis of Kidney	93-94

## **CHAPTER 5. TYPE 2 DIABETES**

1. Objectives	95
2. Induction of type 2 diabetes and experimental design	95-96
3. Results	
3.1. Establishment of a non genetic rat model of type 2 diabetes	96-97
3.2. Hypoglycemic and nephroprotective activities of PO-TRF and RBO-TRF	98-105
3.3. Estimation of serum lipid profile	106
3.4. Assessment of Oxidative stress in the kidney	107
3.5. Western blot analysis of protein expression of TGF- $\beta$ , fibronectin and collagen type IV in the kidney	108-111
3.6. Histopathological analysis of Kidney	112-113

## **CHAPTER 6. DISCUSSION**

114-124

## **CHAPTER 7. SUMMARY & CONCLUSIONS**

125-128

## **REFERENCES**

129-164