7. Summary

7.1. To investigate the anti-diabetic potential of TMP, using HFD-STZ-induced T2D rat model, and to examine the role of PI3K/Akt pathway in the anti-diabetic mechanism of TMP (Objective I).

The antidiabetic activity of TMP on the high-fat diet and streptozotocin-induced type-2 diabetes in rats and its plausible mechanism via PI3K/Akt/GLUT-4 signalling pathway were first time explored in this experiment. Our results demonstrated that the TMP has dose-dependent hypoglycemic activity as determined through various biochemical parameters. Also, TMP (200 mg/kg) could up-regulate the expression of the crucial PI3K/Akt signal pathway proteins such as p-PI3K-p85, p-Akt and GLUT-4 and it was also confirmed through gene expression analysis of corresponding genes, indicating that TMP could produce compelling stimulation of this insulin signalling pathway. In conjunction, TMP also reduced the level of pro-inflammatory cytokines such as IL-6 and CRP through insulin sensitisation and glycemic control that lead to the inhibition of inflammation-induced potentiation of insulin resistance. Therefore, it can be stated that TMP produces antidiabetic activity in T2D through PI3K/Akt/GLUT-4 signalling and suppression of inflammation-induced facilitation of insulin resistance. To demonstrate, the prominent clinical applications of TMP further clinical experiments are recommended.

7.2. To explore the protective effect of TMP on DN, using STZ-NCT-induced T2D rat model, and to identify the role of Akt signalling pathway and oxidative stress in providing good therapeutic resolution for DN treatment (Objective II).

In summary, TMP protects against the development of nephropathy in streptozotocin and nicotinamide induced type-2 diabetic rats. This effect occurs together with correction of diabetes-induced metabolic alterations, suppression of hyperglycemia-induced oxidative stress with preservation of antioxidant activity and probably results from an anti-apoptotic action of TMP through the activation of Akt signalling pathway. Our results suggest that TMP should be considered as a valuable candidate in the search for new therapeutic tools aimed at controlling DN.