The prevalence of diabetes mellitus (DM) is rapidly increasing in modern societies and currently affects 5-7% of the population worldwide. DM frequently coincides with depression and has been associated with higher risk of dementia and cognitive decline. However, the underlying mechanism remain poorly defined. The kynurenine pathway, the main metabolic route of tryptophan degradation, produced several neuroactive molecules (such as the excitotoxin antagonist kynurenic acid (KYNAC) and the excitotoxin quinolinic acid (QA)). Alterations in the kynurenine pathway have been described in a number of neurological disorders; a feature of special importance is the elevation of neurotoxic metabolites, which may promote glutamate-mediated excitotoxic neuronal damage. The delicate balance between the neurotoxic and neuroprotective compounds participating in the kynurenine pathway has been suggested to play an important role in the regulation of glutamatergic neurotransmission and in inflammatory processes. Recently it was shown that streptozotocin-induced experimental diabetes mellitus type 1 increases hippocampal content of KYNAC (Chmiel-Perzynska et al. 2014). The increased KYNAC level may stem from the activation of endogenous neuroprotection, however, it may also have negative impact on cognition. Furthermore, increased synthesis of KYNAC in the course of DM could be associated with an enhanced ketone body formation. In cortical slices and glial cultures beta-hydorybutyrate, augments KYNAC production by stimulating KATs activity in the protein kinase-A
dependent way. The other important metabolite of kynurenine is QA. QA is the precursor of NAD which transports hydrogen from the Szent-Györgyi-Krebs cycle. Pantethine, is the stable disulfide form pantetheine, is the major precursor of Coenzyme A (CoA), which plays a central role in the metabolism of lipids and carbohydrates. Transporting the acetyl group CoA markedly influences the Szent-Györgyi-Krebs cycle. Pantethine has beneficial effects in vascular disease, it able to decrease the hyperlipidaemia, moderate the platelet function and prevent the lipid-peroxidation. It was found that orally active multi-functional antioxidants including pantethine delay cataract formation in streptozotocin (Type1) diabetic and gamma-irradiated rats. Pantethine should be considered for the treatment of lipid abnormalities also in patients at risk such as those with diabetes mellitus.