ABSTRACT

The current work intends to screen the leaves of *Cinnamomum zeylanicum*, *Cinnamomum camphora*, *Cinnamomum tamala*, *Anethum graveolens*, *Triticum aestivum* and *Coriandrum sativum* for the antidiabetic and antioxidant effects in animals with experimental type 2 diabetes. The leaves of the plant materials were subjected to sequential solvent extraction (aqueous extraction and extraction using n-hexane, acetone, ethyl acetate and methanol). Preliminary phytochemical analysis were conducted in all the extracts and it was observed that the methanolic extracts of *Cinnamomum zeylanicum*, *Cinnamomum camphora*, *Cinnamomum tamala*, *Anethum graveolens*, *Triticum aestivum* and *Coriandrum sativum* showed the presence of flavonoids in abundance. These crude extracts were also tested for *in-vitro* alpha amylase, alpha glucosidase and DPPH to determine the antidiabetic and antioxidant activities respectively. The results showed that the crude methanolic extracts from the leaves of *Cinnamomum tamala*, *Anethum graveolens*, *Triticum aestivum* and *Coriandrum sativum* showed the maximum activity in the *in-vitro* assays.

The methanolic extracts from the leaves of *Cinnamomum tamala*, *Anethum graveolens*, *Triticum aestivum* and *Coriandrum sativum* were further subjected to bioassay (*alpha* amylase assay and DPPH assay) guided fractionation using column chromatography and thin layer chromatography for the isolation of specific flavonoids. Repeated column chromatography and thin layer chromatography yielded pure compounds which were concentrated and used for in-vivo studies in streptozotocin induced diabetic rats (male albino rats of Wistar strain). The purified compounds were also subjected to HPLC and NMR analysis to characterise the isolated flavonoids. Seven compounds were characterised namely 2, 5, dihydroxy-6, 7-dimethoxy flavone and 3, 7, 3′, 5′-tetramethoxy-4-hydroxy flavone from *Anethum graveolens*, Quercetin-3-O-α-L-rhamnopyranoside from *Triticum aestivum*, Quercetin and Quercetin-3-O-α-L-arabinopyranoside from *Coriandrum sativum*, Kaempferol-
3,7-O-\(\alpha\)-L-dirhamnoside and Kaempferol-3-O-\(\beta\)-D-glucopyranosyl-(\(\beta\)\(\rightarrow\)4)-\(\alpha\)-L-rhamnopyranosyl--7-O-\(\alpha\)-L-rhamnopyranoside from \textit{Cinnamomum tamala}.

\textit{In-vivo} studies indicated that the compounds isolated from \textit{Anethum graveolens} and \textit{Triticum aestivum} had combined effect on the transcription factor Nrf2 and antioxidant enzymes regulated by this factor namely Glutathione peroxidase (GPx) and Glutathione-S-transferase (GST) and other antioxidant enzymes such as superoxide dismutase and catalase. The flavonoid compounds from \textit{Anethum graveolens} and \textit{Triticum aestivum} also normalised the glucose levels, insulin receptor levels, creatinine, urea, glycated haemoglobin, liver glycogen, triglycerides, phospholipids, total cholesterol, plasma insulin levels, carbohydrate metabolising enzymes glucokinase, glucose-6-phosphate dehydrogenase, glucose-6-phosphatase, Alanine amino transferase, Aspartate amino transferase and leptin in diabetic rats. Thus, this categorically proves that the compounds 2, 5, dihydroxy-6, 7-dimethoxy flavone and 3, 7, 3', 5'-tetramethoxy-4-hydroxy flavone from \textit{Anethum graveolens}, Quercetin-3-O-\(\alpha\)-L-rhamnopyranoside from \textit{Triticum aestivum} have antidiabetic and antioxidant properties apart from having protective action on DNA against reactive oxygen species. Compounds isolated from \textit{Cinnamomum tamala} showed considerable antihyperglycemic effect and modulatory effect on insulin receptor but not as effective as \textit{Anethum graveolens} and \textit{Triticum aestivum}. Quercetin and Quercetin-3-O-\(\alpha\)-L-arabinopyranoside isolated from \textit{Coriandrum sativum} did not show significant effect on the diabetic status in rats.

The present work assesses the unexploited pharmaceutical prospective of flavonoids isolated from \textit{Anethum graveolens} and \textit{Triticum aestivum} in successfully controlling type 2 diabetes and associated oxidative damage. A thoughtful approach is required in this regard as further investigations are needed to assess the long term efficacy and toxicity. Molecular docking
studies will provide insights into the mechanism of action of these compounds on various molecular targets implicated in type 2 diabetes like Nrf2, Enzymes and DNA.