ABSTRACT

The Diabetes Mellitus is rapidly growing metabolic disorder with multiple side complications and modern life style is playing an important role in initiation and propagation of this disease. High caloric dietary intake, lack of physical exercise and obesity are major contributing factor in initiation and progression of metabolic disorder through oxidative stress oriented mechanism. Many synthetic drugs are available to patients for reduction in high blood glucose levels. But these compounds have well reported and commonly observed health deteriorating effects. Plants are rich source of natural antioxidants which work in synergistically to scavenge reactive species in living system and inhibit activity of dietary enzymes. Therefore, plants are the best alternate of synthetic drugs to treat and manage diabetes with no or negligible side effects. The current work was performed to evaluate the antidiabetic potential of *Conocarpus lancifolius* and *Conocarpus erectus* leaves. The leaves of *Conocarpus lancifolius* and *Conocarpus erectus* were quenched in liquid nitrogen and extracted with solvents system composed of ethanol and water. The extracts were prepared by using water, 20% ethanol, 40% ethanol, 60% ethanol, 80% ethanol and pure ethanol through ultrasonication for 30 min. The extracts were freeze dried at -68°C for 24 Hours to make them moisture free. The ultrasonicated and freeze dried extracts were subjected to determine total phenolic and flavonoid contents. The antioxidant activities were determined by DPPH radical scavenging assay, total antioxidant power assay and beta carotene linoleic acid assay. The iron chelating activity was also done for all extracts. The *in vitro* antidiabetic potential of extracts was assessed by measuring their ability to inhibit the activity of α-glucosidase and α-amylase. The findings indicated that 60% ethanolic extracts of both plants emerged as most potent fraction. The 60% ethanolic extracts of both plants exhibited high phenolic and flavonoid contents, however the phenolic and flavonoid contents in 60% ethanolic extract of *Conocarpus lancifolius* (349.39 ± 2.13 mg GAE/PE and 116.95 mg RE/PE, respectively) were comparatively higher than the *Conocarpus erectus* for which the values were 117.00 ± 2.05 mg GAE/PE and 70.10 mg RE/PE, respectively. The findings regarding antioxidant activities, iron chelating potential, α-glucosidase and α-amylase inhibitory properties were very promising for both plants but relatively better in case of *Conocarpus lancifolius*. The IC-50 values to inhibit the activity of α-glucosidase by 60% ethanolic extract of *Conocarpus lancifolius* and *Conocarpus erectus* was 38.64 ± 0.93 µg/mL 42.50 ± 1.01 µg/mL,

respectively. A similar trend was observed for the α-amylase inhibition by the extracts of both plants. Peaks in region 6-9 ppm of ^{1}H-NMR spectrum of most potent extract predicted the presence of polyphenols which were later profiled by UHPLC-QTOF-MS/MS. The UHPLC-QTOF-MS/MS analysis of 60% ethanolic extract of *C. lancifolius* revealed the presence of many high value phytochemicals including gallic acid, galloyl HHDP-glucoside isomers, corilagin, terflavin B, ellagic acid and its derivatives, ellagi tannin, kaempferol-3-O-rutinoside, caffeic acid derivative and isorhamnetin. The phyto-constituents in 60% ethanolic leaf extract of *C. erectus* were mainly ellagic acid, 3-O-methyl ellagic acid, 5,2′-dihydroxy-6,7,8-trimethyl flavone, ferujol, kaempferol glucoside and its derivative. The docking studies provided a deep insight regarding the modes of interaction adopted by the identified compounds with the active site residues of α-glucosidase and α-amylase to inhibit their action. The significant *in vitro* activities and phytochemical profiling urged to check the antidiabetic potential of 60% ethanolic plant extracts in albino mice. The mice were injected with a single dose of Alloxan (150 mg/kg body weight) to induce the diabetes. The mice having blood glucose level >200 mg/dL were characterized as diabetic. The mice treated with extract dose of 450 mg/kg body weight exhibited substantial reduction in blood glucose levels and were quite comparable to metformin. However, the 60% ethanolic extract of *C. lancifolius* was more promising than *C. erectus* and this difference was might be due to compositional variations and nature of phyto-ingredients. The proximate analysis indicated that both plants have high nutritive value. The mineral composition analysis depicted the presence of some vital nutrients like Mn, Zn, Ca, Mg and K in reasonable amounts. The extracts also showed negligible toxicity and acceptable thermal stability. The functionalities observed during current study for the leaf extracts of *C. lancifolius* and *C. erectus* may bolster the functional food development with hyperglycemic attributes. Both plants can serve as indigenous and natural low-cost source to contribute in low-cost naturopathy to reduce the socio-economic burden in lieu of metabolic disorder.