ABSTRACT

Oxidative stress is a major cause of metabolic health disorders including obesity and diabetes. The existing synthetic drugs and antioxidants are proved to cause serious side effects. Medicinally important plants can serve the purpose of controlling and manage both obesity and diabetes with no or nominal side impacts. Moreover, plants based phytotherapeutics are also cost effective. *Fagonia indica* (*F. indica*) and *Heliotropium strigosum* (*H. strigosum*) are being used to treat obesity and diabetes in local or folk medicinal system of Pakistan. But no sound scientific evidence exists in this regard. In the current work, optimum solvent was selected for extraction using methanol, ethanol, ethyl acetate, chloroform and n-hexane. The *F. indica* and *H. strigosum* plants were collected from their natural habitat and immediately quenched in liquid nitrogen to preserve the metabolites. The whole plant material was ground and sieved to get fine powder. The powdery plant material was subjected to freeze drying at -68°C for 48 hours to remove the water. The freeze-dried plant material was dissolved in pure ethanol, methanol, chloroform, ethyl acetate and n-hexane in 1:10 proportion by weight. The material was allowed to stay for 24 hours in the dark. The mixtures were also shaken for 24 hours followed by ultrasonication and filtration. The filtrates obtained were carried to rotary evaporation under vacuum for removal of extra solvents. The extracts obtained after rotary evaporation were evaluated for the yield percentages. The total phenolic contents and total flavonoid contents were determined for all extracts. The antioxidant activities of extracts were determined using DPPH and FRAP assays. The *in-vitro* antidiabetic potential of extracts was evaluated using α-glucosidase and α-amylase inhibition assays. The *in-vitro* antiobesity attributes were determined using porcine pancreatic lipase inhibition assay. The iron chelating potential was also evaluated for the extracts. The methanolic extracts of both plants yielded highest extract yield, phenolic and flavonoid contents. The methanolic extract of *F. indica* exhibited highest DPPH scavenging % 90.15±0.35 and FRAP 244.65±3.95 % based antioxidant potential as compared to *H. strigosum* and the values were statistically significant among all extracts. The values of α-glucosidase (78.36±1.18, 68.33±1.11), α-amylase inhibition (68.56±1.15, 62.86±1.23) and pancreatic lipase inhibition (80.50±1.15, 71.57±1.13) were also significantly higher for the methanolic extracts of both plants. The methanolic extracts were observed as most potent extract and therefore subjected to hemolytic toxicity assay and thermal stability. The methanolic extracts exhibited negligible toxicity and reasonable thermal stability. On the basis of performed assays, the methanolic extracts of both plants were used to assess the improvement in oxidative stability

of sunflower oil at elevated temperatures using Schaal's oven test. The rancidity indicators including free fatty acid value (FFA), peroxide value (PV), ρ-anisidine value, conjugated dienes and trienes and iodine value (IV) were examined. Both plant extracts substantially improved the oxidative stability of treated sunflower oil in comparison to BHA used as standard antioxidant. The kinetic parameters of sunflower oil enriched with plant extracts were also computed in comparison to the blank oil samples. The kinetic parameters including activation energies, rate constants, shelf-life prediction and Q_{10} were noted by Arrhenius plots. The kinetic study evidently supported the role of plant extracts to delay the oxidation reaction, hence improving the shelf life of sunflower oil. The sunflower oil stabilized with *F. indica* extract exhibited highest shelf-life of 109 weeks with energy of activation value of 102 kj/mol being much higher than the blank sunflower oil, sample treated under same conditions. However, the performed analytical work elaborated that the medicinal and therapeutic potential of *F. indica* was more pronounced as compared to *H. strigosum*. The UHPLC-Q-TOF-MS/MS analysis of *F. indica* and *H. strigosum* extracts revealed the presence of some high valued metabolites including corilagin, kaempferol, isorhamnetin, ellagic acid, gallic acid, apigenin and caffeic acid derivatives. The presence of these phenolic and flavonoid compounds was most probably responsible for the antioxidant, antidiabetic and antiobesity functionality of *F. indica* and *H. strigosum*. The findings also supported the ethnopharmacological use of these plants especially in context of Pakistan. The results of toxicity assay and thermal stability revealed that both the plants can be utilized to develop evidence based naturopathic approach to treat diabetes mellitus and obesity at cheaper cost to reduce the socio-economic burden in lieu of cost to benefit ratio. Further, added that both plants can be a rich source of natural antioxidant system to stabilize the edible oil for longer shelf life and oxidative stability rather using toxic and costly synthetic antioxidants. It can also be concluded that *F. indica* and *H. strigosum*, both have the potential to develop functional foods fortified with these plants for healthier lifestyle and disease management by exploiting indigenous natural resources.