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COMPARATIVE *IN VITRO* ANTIDIABETIC ACTIVITY OF TWO AMIDES FROM BLACK PEPPER SEEDS (*PIPER NIGRUM* L.) AGAINST POSTPRANDIAL GLUCOSE REGULATORY ENZYMES

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Postprandial high blood sugar could be a risk factor for diabetes mellitus, and this condition is one of the critical points in diabetic treatments. Medication of postprandial hyperglycemia could be attained by mainly inhibiting key regulatory enzymes such as α-amylase and α-glucosidase, which are involved in carbohydrate digestion. Herbal plants are an excellent source to treat this disease and improve the ease of health. *Piper nigrum* L. (black pepper) is a well-known herbal plant belonging to the Family Piperaceae, and it contains a higher number of bioactive compounds. The present study reports the anti-postprandial hyperglycemic activity of an amide (pipnoohine) isolated from the hexane extract of *P. nigrum* seeds and compares it with that of isolated piperine (an antidiabetic compound from *P. nigrum* plant) and commercially available acarbose (a standard antidiabetic drug). The piperine and pipnoohine have been previously isolated from the genus Piper (*P. nigrum*, *Piper longum*, *Piper chaba*). However, the comparison of *in vitro* anti-postprandial hyperglycemic activity of these two compounds is untapped up to date. The two compounds were isolated from hexane extract of *P. nigrum* seeds using chromatographic techniques (vacuum liquid chromatography and flash column chromatography), and they were identified as piperine and pipnoohine, using ^{1}H and ^{13}C NMR, liquid chromatography-mass spectrometry (LC-MS), UV, IR spectroscopy and melting point data. The *in vitro* anti-postprandial hyperglycemic activity of the isolated compounds was determined in terms of the 50% inhibitory potential of α-amylase and α-glucosidase enzymes. Both piperine and pipnoohine inhibited 50% of α-amylase enzyme activity at 37.04±0.94 and 62.22±2.06 mg l^{-1} concentrations, respectively. In the α-glucosidase assay, the piperine and pipnoohine inhibited 50% of the enzyme activity at 51.12±0.09 and 82.42±2.25 mg l^{-1} concentrations, respectively. The pipnoohine showed no significant difference between the above activities with the piperine ($p>0.05$). The acarbose inhibited 50% of the α-amylase and α-glucosidase enzymes at concentrations of 5.72±0.33 and 17.72±0.48 mg l^{-1}, and the activities, however, showed significant differences with the inhibition activities of piperine and pipnoohine ($p<0.05$). This is the first report of α-amylase and α-glucosidase inhibitory activities of pipnoohine and the comparison of *in vitro* anti-postprandial hyperglycemic activity of piperine and pipnoohine. Results concluded that pipnoohine exerted considerable α-amylase as well as α-glucosidase inhibitory activities that indicate that it also can be considered a drug lead for the treatment of diabetes mellitus.

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Keywords: Diabetes mellitus, Enzyme inhibition assays, Piperine, *Piper nigrum*, Pipnoohine