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UNRAVELLING THE BIOCHEMISTRY AND METABOLIC PROFILES OF ACACIA HONEY IN AMELIORATING STRESS-DEPRESSION BEHAVIOUR IN VIVO

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ABSTRACT

Malaysian Acacia honey has been widely explored for its chemical characteristics but has received little attention in illness models. Our early investigation revealed that Acacia honey (AH) might have the capacity to alleviate stress-induced depression in rats. However, the mechanism remains unknown. Recent research on stress disorders has established a relationship between the gut and mental health via the gut-brain axis. Therefore, this study was conducted to elucidate the activity of AH in alleviating stress-depression disorder through the gut-brain axis by using the chronic unpredictable mild stress (CUMS) model to induce stress (S) in rats. AH undergoes a physicochemical and rheological test before being subjected to the in vivo study. Forty-two (42) male Sprague-Dawley rats were divided into seven groups [(1) normal control (NC), (2) Acacia honey (AH), (3) amitriptyline (AMT), (4) S, (5) S+AH, (6) S+AMT (positive control), and (7) S+AH+AMT] were subjected to physical, sucrose preference and open field tests before being sacrificed to obtain serum, blood, and organs (kidney, liver, ileum, caecum and hypothalamus). Serum, blood and histopathological analysis were performed, followed by protein expression (ELISA, Western blot, and immunofluorescence), as well as metabolomics. Data were analysed using the unpaired T-test or one-way/two-way ANOVA. The physicochemical and rheological tests confirm the originality of the AH used in this study. Current findings have shown that AH reduced the effect of CUMS-induced stress depression in rats by the increase in bodyweight [S+AH (31.34 % ± 1.88) versus the S group (28.60 % ± 1.86), $p < 0.05$] and the sucrose preference ratio [S+AH (83.67 % ± 1.20) versus the S group (44.33 % ± 12.17), $p < 0.05$] while protecting against abnormal histopathological changes in the liver and kidney, as well as the behavioural activities of stress rats. AH supplementation has been shown to activate the NPY1 receptor (Neuropeptide Y1 receptor) to inhibit CORT (corticosterone) and PYY (peptide YY), which inhibit satiety and neuronal injury during stress in the hypothalamus, respectively. Subsequently, AH was shown to reduce the level of AChE (acetylcholine esterase), cortisol, and C-FOS in the serum of stressed rats. Apart from that, AH was shown to increase the NPY and AChE levels in the ileum by an unknown receptor to improve appetite and decrease gut motility by inhibiting ACh (acetylcholine). AH demonstrated that caecum activates the GLP1 (Glucagon-like peptide 1) receptor, leading to an increase of pro-BDNF. The protection of AH is shown to inhibit the PKC that triggers C-FOS. AH was found to not be involved in regulating COX-1 and COX-2 expression during stress in all organs. The involvement in metabolic pathways such as tryptophan, arachidonic acid, taurine, and hypotaurine, a carbon pool through folate, pentose, and glucuronate interconversions, lysine degradation, tyrosine, and primary bile acid biosynthesis was revealed by data from the serum metabolomes of stressed rats. The results demonstrated the activation of NPY1, unknown, and GLP1 receptors during stress by AH by regulating various proteins, hormones, and neurotransmitters in the hypothalamus, ileum, and caecum, respectively. Furthermore, this study provides an insight into the AH mechanism in reducing stress-depression disorder.

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