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NMDA AND TRPV1 RECEPTORS: POTENTIAL THERAPEUTIC TARGETS OF *PASPANGUWA* HERBAL FORMULA

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Despite the broad use of cough (antitussive and expectorant) medicine, there is little evidence for its clinical use. Dextromethorphan is a widely used antitussive that is considered effective by the U.S. Food and Drug Administration. N-methyl D-aspartate (NMDA) receptors are the therapeutic target of dextromethorphan. The transient receptor potential vanilloid 1 (TRPV1) receptor stimulates the cough reflex and has recently been identified as a potential drug target for treating cough. We hypothesize that the mechanism of the anti-cough effects of *paspanguwa*, an ayurvedic herbal drink, is due to inhibiting NMDA and TRPV1 receptors. This study aimed to identify natural products in the formula that bind favourably to the active sites of the receptors. Twenty-three natural products from *paspanguwa* were examined. The cryo-EM structures of NMDA receptor (PDB 7eu7) and TRPV1 receptor (PDB 3J5P) were used as receptor coordinates. AutoDock Vina was used for molecular docking at four active sites: glycine-binding site, glutamate-binding site and the ion-channel of NMDA, and the active site of TRPV1 receptor. Diosgenin, solasodine and tomatidenol showed the highest binding affinity to both the glutamate-binding site and glycine-binding site; the affinity well above that of references indicates the possibility of these natural products acting as NMDA antagonists and non-competitive antagonists. Diosgenin, tomatidenol, and oleanolic acid showed the highest affinity to the NMDA channel; an affinity higher than that of references indicates the ability to act as better channel blockers. At the active site of TRPV1, solasodine, diosgenin, and tomatidenol showed binding affinity on par with the references, indicating that they might act as TRPV1 antagonists. Findings from the study show that natural products from *paspanguwa* bind to active sites of NMDA and TRPV1 receptors. The reported anti-cough properties of the formula may, at least in part, be due to inhibiting NMDA and TRPV1 receptors.

Keywords: Anti-cough, Molecular docking, Natural products