Thonningianin A

Thonningianins A (1) and B (2), have been isolated from the African medicinal herb Thonningia sanguinea and their structures elucidated by interpretation of spectroscopic data. Both 1 and 2 showed strong free radical scavenging activity against 1,1-diphenyl-2-picrylhydrazyl (DPPH) as shown by ESR analysis [1)].

Results indicate that the antioxidant properties of Th A involve radical scavenging, anti-superoxide formation and metal chelation [2)].

Four ellagitannin flavonoids, including pinocembrin-7-O-[4″,6″-hexahydroxydiphenoyl]-glucoside (PHG), pinocembrin-7-O-[3″-O-galloyl-4″,6″-hexahydroxydiphenoyl]-glucoside (PGHG), thonningianin A (TA), and thonningianin B (TB), were identified to be autophagy enhancers in PCP.

Among these, TA exhibited the strongest autophagy induction effect, and the mechanistic study demonstrated that TA activated autophagy via the AMPK/ULK1 and Raf/MEK/ERK signaling pathways. In addition, TA effectively promoted the autophagic degradation of NLRP3 inflammasome in Aβ(1-42)-induced microglial cells and ameliorated neuronal damage via autophagy induction. In vivo, TA activated autophagy and improved behavioral symptoms in C. elegans. Furthermore, TA might penetrate the blood-brain barrier and could improve cognitive function and ameliorate the Aβ pathology and the NLRP3 inflammasome-mediated neuroinflammation via the AMPK/ULK1 and Raf/MEK/ERK signaling pathways in APP/PS1 mice.

Zhou et al. identified thonningianin A as a potent microglial autophagy enhancer in enthorum chinense Pursh (PCP) that promotes the autophagic degradation of the NLRP3 inflammasome to alleviate the pathology of Alzheimer's disease via the AMPK/ULK1 and Raf/MEK/ERK signaling pathways, which provides novel insights for TA in Alzheimer's disease treatment [3)].

1)
Ohtani II, Gotoh N, Tanaka J, Higa T, Gyamfi MA, Aniya Y. Thonningianins A and B, new antioxidants from the African medicinal herb Thonningia sanguinea. J Nat Prod. 2000 May;63(5):676-9. doi: 10.1021/np990396w. PMID: 10843586.
2)
Gyamfi MA, Aniya Y. Antioxidant properties of Thonningianin A, isolated from the African medicinal herb, Thonningia sanguinea. Biochem Pharmacol. 2002 May 1;63(9):1725-37. doi: 10.1016/s0006-2952(02)00915-2. PMID: 12007576.
3)
Zhou XG, Qiu WQ, Yu L, Pan R, Teng JF, Sang ZP, Law BY, Zhao Y, Zhang L, Yan L, Tang Y, Sun XL, Wong VKW, Yu CL, Wu JM, Qin DL, Wu AG. Targeting microglial autophagic degradation of the NLRP3 inflammasome for identification of thonningianin A in Alzheimer's disease. Inflamm Regen. 2022 Aug 3;42(1):25. doi: 10.1186/s41232-022-00209-7. PMID: 35918778.