Abstract

Autoinflammatory diseases exhibit chronic and severe inflammation without infection. Both genetics and abnormalities in metabolism are the main cause. Gout is a representative condition which cause by precipitation of monosodium urate in tissues as the concentration of blood uric acid is higher than normal. The common main causes of these diseases are hyperproduction of inflammatory cytokines, mainly interleukin 1 β) IL-1β) and IL-18 via inflmmasom activation. Inflammasome is a multisubunit protein complex of at least 3 proteins including zymogen of caspase-1 (pro-caspas-1). Upon exposure to stimuli such as uric acid crystals, inflammsome is formed, leading to autocatalytic cleavage of pro-caspase-1. Caspase-1 is a cysteine protease responsible for cleavage of pro-IL-1β. This cleavage results in secretion of IL-1β. Therefore, compounds with the ability to suppress activity of inflammasome have potentials to be therapeutic drugs for autoinflammatory diseases. This study aimed to screen for compounds with such activity of inflammasome suppression in human monocytic cell line. The samples used in this study are crude or partially purified extracts from flowers, leaves, branch and fruits of the cannonball tree (*Couroupita guianensis*) and roots of *Tiliacora triandra* (Colebr.) Diels. The total numbers of samples screened were 73 and the purification and activity screening were done in parallel by following the secretion of IL-1β. Cellular toxicity was screened through MTT assay. The inhibitory concentration 80 or higher were used for the assay of IL-1β secretion by ELISA. The results showed that 19 samples of crude extracts and partially purified compounds from branch, flower and leaves of cannon ball trees suppressed IL-1β secretion. In particular, sample No. AS-TP 1007 and AS-TP 2027 from branches and flowers showed strong inhibitory activity. To study the mechanism of action, quantitative realtime RT-PCR were conducted and 4 out of 9 samples decreased the transcription level of *IL-1β*, suggesting that they may act upstream of inflammasome, including ASTP-1007. To monitor inflammasome activation, the activity of caspase 1 was monitored using reporter assay. The results showed that most samples did not decrease the activity of caspase 1, but only AS-TP2027 from flowers suppressed caspase 1 acitivity. Therefore, partially purified ASTP-2017 is promising to contain pure compound(s) that can suppress inflammasome activation. Two samples purified from AS-TP 2027, i.e. AS-TP 2038 and AS-TP 2039 also showed strong inhibitory activity. The purification and mode of action of these compounds needs further investigation.