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Development of an immuno-suppressive agent, Cyn-1324 for treating with asthma

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Cyn-1324 (C18H25NO5; MW: 335 g/mol; patents: ROC/I481600; USA/9,126,968; China/in pending) is a derivative of Cynarin (Cyn) which was found by using chip-based innovative screening method. A simple protocol for synthesis of Cyn-1324 has been established and satisfied with the regulation of chemical-manufacture-control (CMC). Molecular-based computer simulation of the association between Cyn-1324 and CD28 shows that the minimum energy is about - 8.59 kcal/mol which is the smallest energy minimization as compared with that of the association between CD28 and CD80. This implies that Cyn-1324 can exclude CD80 to bind with CD28. The cross validation for identifying the blocking effect of Cyn-1324 on CD28 was done on: (1) Protein-protein level: CD28-Cyn-1324-CD80; (2) Cell-protein level: T-cell (including CD28)-Cyn-1324-CD80; (3) Cell-cell level: T-cell (including CD28)-Cyn-1324-Bcell (including CD80). Their binding forces are measured by atomic force microscopy (AFM) showing the blocking effect of 30.5%, 41.25 and 19.0% for protein-protein, cell-protein and cell-cell levels, respectively. Toxicity test of animal model using Cyn-1324 (5 repeated doses, 50 mg/kg per time) verified that there has no toxicity on organs (spleen, liver and kidney) of BALB/c mice. The disease-model (asthma) test, via intra-peritoneal injection, further shows that Cyn-1324 could suppress airway hyper-responsiveness and eosinophil infiltration of the lung in OVA-sensitized mice. Further experiments will be done in detail about the possible treatment of Cyn-1324 on asthma disease.

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