The discovery of new inhibitors of adenosine deaminase

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Adenosine deaminase (ADA) is an enzyme involved in purine metabolism, playing significant role in immune system development and maintenance. The enzyme activity changes in various pathologies, for instance, it increases upon different cancers, autoimmune diseases, chronic hepatitis and liver cirrhosis. The increased level of ADA activity has been recognized as a suitable, low-charge ADA-test in differential diagnosis of some diseases (tuberculosis, rheumatoid arthritis, etc.). The increasing of enzyme activity upon inflammation diminished the concentration of its substrate, adenosine, well-known as anti-inflammatory agent. This ubiquitous enzyme also can deaminase adenosine analogs widely used in chemotherapy, immunotherapy and in treatment of several other pathologies. Therefore, the discovery of new compounds with ability to inhibit or activate ADA is required in modern biochemistry and pharmacology.

We studied the influence of more than 100 new synthesized derivatives of piperazine, pyridine, imidazole, etc. on ADA activity purified from bovine lung. Some of studied compounds possessed the ability to inhibit ADA about 40%. The compound D011 182 demonstrated the higher effect with IC_{50} value equal 19.95 μg/ml. Besides the radical scavenging capacity of novel synthesized compounds D011 180, D011 181, D011 182 were estimated with ABTS assay and IC_{50} values of these compounds were determined 38.6±0.66 mg/ml; 42.6±0.499 mg/ml; 47.9±1.53mg/ml respectively. The low activity was obtained for these compounds with DPPH radical scavenging method. The studied compound D011 182 exhibits both antioxidant and ADA inhibiting properties.

Consequently, in the base of our studies we can recommend chemists to synthesize derivatives that could potentially demonstrate enhanced ADA inhibition and antioxidant capabilities for further promising application in medicine.