A lesson from catechins: Development of probe molecules and lead compounds for drug discovery

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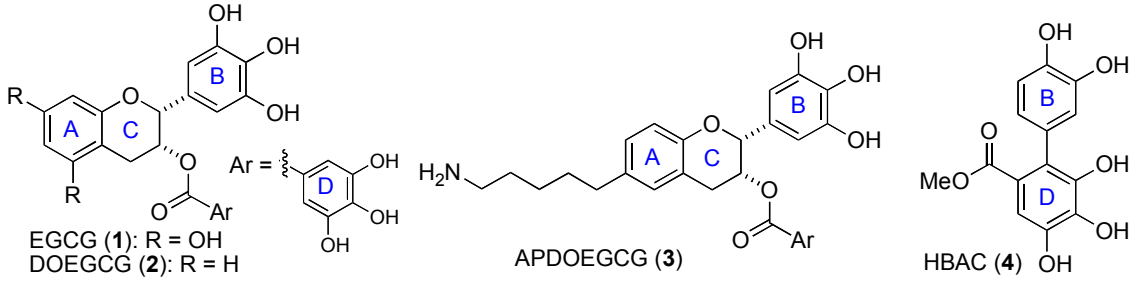
(–)-Epigallocatechin gallate (EGCG) (**1**) is a major constituent of green tea extract, which has various bioactivities such as cancer prevention and antiviral or antimicrobial activity. Since these unique bioactivities are expected to be candidates for drug development, the detailed structure-activity relationship (SAR) study has been a significant work. However, investigations of such bioactivities have been limited to natural products and/or their derivatives. Thus, developing an efficient and flexible synthetic method has strongly been desired. During the course of our synthetic investigation on the gallocatechins, we have found that synthetic 5,7-dideoxy-epigallocatechin gallate (DO-EGCG) (**2**) possesses more potent anti-influenza activities than natural EGCG (**1**). Inspired by this finding, we have launched an investigation into the synthesis of aminopentyl 5,7-dideoxy-gallocatechin gallate (APDOEGCG: **3**) and hydroxybiarylcarboxylic acid derivatives (HBAC: **4**). The amino group of **3** would be enable for readily incorporation of probe units (biotin, fluoresent and radioactive compounds) and immobilization with gel and/or carrier protein (BSA). The biaryl derivative **4** was also designed from our hypothesis that A ring unit would be unnecessary for the activity based on the result of **2**. Surprisingly, the synthetic **4** exhibited 10^3 times more potent anti-influenza effect than EGCG (**1**).



References

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