The molecular basis of anti-influenza virus activity on catechins

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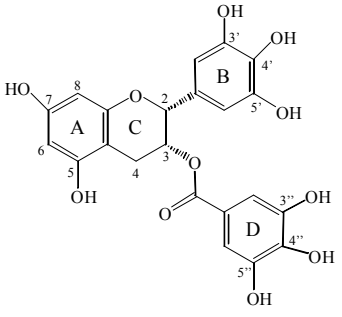
Epigallocatechin gallate (EGCG), which is one of green tea polyphenolic catechins, have been known to inhibit influenza virus replication, however the structural and biological machinery remains unknown. We designed seven novel derivatives of dideoxy-epigallocatechin gallate (1) and examined for their abilities to inhibit influenza virus replication in vitro. The analogs modified by deoxyl substituents at 5-,7-positions on the A-ring exhibited potent anti-influenza virus activity compared to that of EGCG, indicating that the phenolic hydroxyl groups on the A-ring are not crucial for anti-influenza virus activity. While, the phenolic hydroxyl groups at 5'-position on the B-ring played a critical role on anti-influenza virus activity. 2,3-trans stereogenic isomers on the C-ring of the derivatives, in which modified by deoxyl substituents at 5'-position or 3'-,5'-positions on the B-ring, exhibited strong anti-influenza virus activity in comparison with that of 2,3-cis stereogenic isomers on the C-ring. Additionally, phenolic hydroxyl group at 4''–position substitution on the D-ring affected the antiviral activity.

Catechin derivatives with pentylamine substitution at the 6-hydroxyl group on the A-ring were synthesized and their abilities to inhibit influenza virus replication were evaluated in vitro. The derivatives showed about 10-fold increase in anti-influenza virus activity compared to that of EGCG. We are planning to clarify the binding site of catechins to influenza virus. Our findings would provide useful information for development of anti-influenza virus compounds based on EGCG.

(1) Furuta, T. et al. Bioorg. Med. Chem. Lett. 17, 3095-3098 (2007)



Structure of EGCG