Synthetic studies of prodrugs using the dissociation mechanism of sialic acid by NA (IX): Comparison of Drug Release of Two Types of Prodrugs

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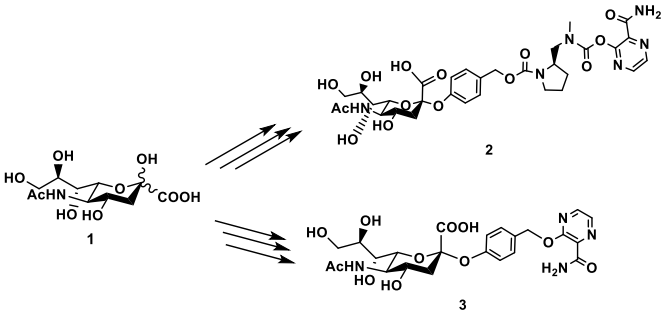
Two types of prodrugs with different linkers were synthesized using T-1105 as an analog of the anti-influenza drug favipiravir and a sialic acid, which will be hydrolyzed by the neuraminidase of an influenza virus spike protein and.



Scheme 1 Synthesis of two prodrugs.

The sialic acid derivatives **2** and **3** were treated in the presence of Welsh neuraminidase under room temperature conditions in PBS buffer at pH=6.5 and the changes over time were followed using HPLC as shown in Fig. 1 &2.

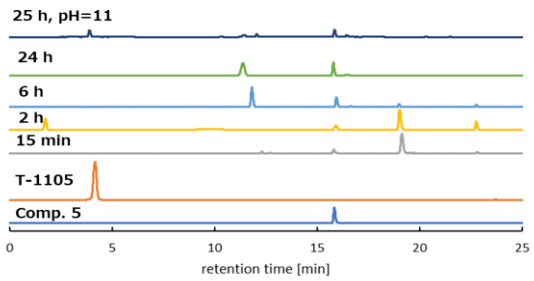


Fig. 1 Enzymatic reaction of compound 2.

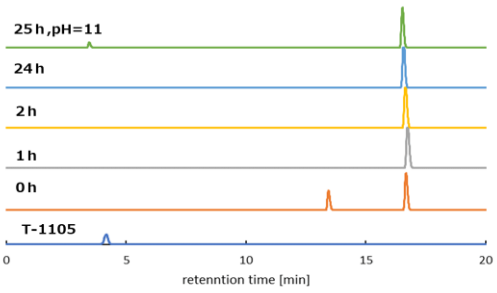


Fig. 2 Enzymatic reaction of compound 3.

The results showed that the release of T-1105 could not be confirmed even after 24 hours under neutral conditions, but when the solution was subjected to basic conditions, the disintegration of the linker was accelerated and the release of T-1105 was confirmed.

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