

## **Role of sialidase in the skin and transdermal delivery technology of sialidase**

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Sialidase is a hydrolase that cleaves a sialic acid residue from sialoglycoconjugate. We have previously developed a fluorescent probe (BTP-Neu5Ac) that allows highly sensitive visualization of the enzymatic activity of sialidase on tissue. Staining of the rat skin using BTP-Neu5Ac revealed intense sialidase activity in the lower layers of the dermis. However, the role of sialidase in the skin is not well understood. In the present study, we investigated the role of sialidase in the skin and developed the transdermal delivery technology of sialidase. We first examined changes in sialidase activity with aging and found that sialidase activity increased with growth and decreased with aging. Next, to investigate the role of sialidase, we delivered the sialidase to the dermis and studied its effect on elastin which gives skin elasticity. The barrier function of the skin is high and cannot allow substances with a molecular weight of 500 or more to pass through. Therefore, we used choline and geranate (CAGE), one of the ionic liquids, to deliver sialidase transdermally. CAGE can provide the sialidase subcutaneously while maintaining the enzymatic activity. The elastin level in the dermis was increased by applying sialidase from *Arthrobacter ureafaciens* with CAGE on the skin for five days in rats and senescence-accelerated mice prone 1 and 8. Sialidase activity in the dermis was considered to be mainly due to Neu2 based on the expression level of sialidase isozyme mRNA. Transdermal administration of Neu2 with CAGE also increased the level of elastin in the dermis. Therefore, Neu2 would be involved in elastic fiber assembly. The reduction of elastin in the skin causes various skin diseases as well as wrinkles and sagging with aging. Thus, transdermal administration of sialidase is expected to be helpful for the improvement of wrinkles and skin disorders due to the loss of elastic fibers.