S15-3 Development of a novel transdermal patch of bisphosphonates for the treatment of osteoporosis

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Bisphosphonates are widely used for the treatment and prevention of postmenopausal osteoporosis. Alendronate is a primary amino bisphosphonate and one of the most commonly used members of this group. However, the oral bioavailability of alendronate is 1-2%. In addition, oral administration of alendronate has been associated with mucosal damage, including gastritis, gastric ulcer, and erosive esophagitis. To prevent these adverse drug events, patients should sit up or walk for more than 30 min after taking alendronate. Considering most patients with osteoporosis are elderly people, many patients have difficulties with following the oral administration. Therefore, improvement of compliance and QOL of patients is highly desirable. To this end, we developed a novel transdermal patch of alendronate for the treatment of osteoporosis.

The maximum permeation fluxes from alendronate patch in the rat and human skin were 20.3 and 0.6 $\mu g/cm^2/h$, respectively, indicating that alendronate patch showed sufficient skin permeation for the treatment of osteoporosis. The bioavailability of alendronate after administration of alendronate patch in rats was approximately 25%. Furthermore, the plasma calcium level, which is an indicator of pharmacological effects of alendronate, was effectively decreased after administration of alendronate patch in hypercalcemia rats. Alendronate patch also effectively suppressed the decrease of bone mineral density in osteoporosis rats. However, alendronate patch induced skin damage after its administration. Coadministration of various antioxidants with alendronate completely suppressed the alendronate-induced skin damage, while maintaining sufficient skin permeation of alendronate.

These findings indicate that our transdermal delivery system of alendronate is a promising approach to improve compliance and QOL of patients for the treatment of postmenopausal osteoporosis.