In vitro and in vivo evaluation of anaphylactoid reaction induced by the main components of Houttuynia cordata injection via Mrgprb2 knockout mouse model

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Abstract
Anaphylactoid reactions caused by the *Houttuynia cordata* injection (HCI) have been reported. The mast cell surface receptor MRGPRX2 is recognized as one of the core genes triggering anaphylactoid reactions, and in our previous studies, *Mrgprb2*- (the murine orthologue of human *MRGPRX2* gene) knockout mice have been successfully generated. The roles of 2-Undecanone and tween 80, two main components of HCI, in the HCI-induced anaphylactoid reactions were studied with this model. In the experiment, C48/80 (positive drug) group and three other groups, HCI, 2-Undecanone and Tween 80, were tested to explore their roles in *Mrgprb2*-knockout and wildtype mice. The anaphylactoid reaction caused by those treatments was evaluated by three indices: the release of β-hexosaminidase and histamine by mast cells, and the Evans blue staining of the hind paw. After drug treatment ,three evaluated indices in WT mice increased with higher drug concentrations in the following order: C48/80 > Tween 80 > HCI > 2-Undecanone , where 2-Undecanone is almost comparable to the control .In all treated groups of *Mrgprb2*-KO mice, the release of β-hexosaminidase in abdominal mast cells and histamine in serum decreased significantly compared with WT mice .And except for positive drug and Tween 80 high dose group, there was no obvious Evans blue extravasation and swelling in the paws of KO mice after drug injection .In conclusion, 2-Undecanone has no obvious effects on anaphylactoid reactions, while Tween 80 can induce mast cell activation through Mrgprb2 receptor and cause anaphylactoid reaction in mice.

Key words： *Houttuynia cordata* injection， anaphylactoid reactions， *Mrgprb2*-knockout mice, 2-Undecanone